"EFFECT OF PHARMACEUTICAL CARE ON ENHANCEMENT OF SAFETY, MEDICATION ADHERENCE AND QUALITY OF LIFE IN PATIENT WITH BIPOLAR DISORDER: A PROSPECTIVE STUDY IN TERTIARY CARE HOSPITAL"

Thesis submitted to

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For the award of the degree of

Doctor of Philosophy

In the Faculty of

Pharmacy

by

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Affectionately Dedicated

To my

Beloved Grand Parent,

Entire Family

&

Almighty

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Ashish Singh Parihar

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LIST OF ABBREVIATIONS

S.No.	Abbreviation	Full Form of Abbreviation
1.	ADR	Adverse Drug Reaction
2.	AE's	Adverse Event
3.	ADNS	Antidepressants Native Inpatients
4.	ADTS	Antidepressant-Treated Inpatients
5.	BPAD	Bipolar Affective Disorder
6.	BL	Baseline
7.	CM	Crisis Management
8.	CI	Confidence Interval
9.	DALY	Disability-Adjusted Life Of The Year
10.	DDI	Drug-Drug Interaction
11.	DRPs	Drug-Related Problems
12.	DSM	Diagnostic And Statistical Manual
13.	DM	Diabetes Mellitus
14.	ECT	Electroconvulsive Therapy
15.	FFT	Family-Focused Treatment
16.	GBD	Global Burden Of Disease
17.	HAMD	Hamilton Depression Rating Scale
18.	HRQOL	Health Related Quality Of Life
19.	ICF	Informed Consent Form
20.	IPD	In Patient Department
21.	LAR	Legally Authorized Representative
22.	MA	Medication Adherence
23.	MMAS-8	Morisky-8 Medication Adherence Questionnaire
24.	NCMH	National Center For Mental Health
25.	OPD	Out-Patient Department
26.	PCNE	Pharmaceutical Care Network Europe
27.	PIS	Participant Information Sheet
28.	PvPi	Pharmacovigilance Programme Of India
29.	QOL	Quality of Life
30.	RCT	Randomized Control Trials

31.	SD	Slandered Deviation
32.	SFPC	French Society Of Clinical Pharmacy
33.	WHO	World Health Organization
34.	YMRS	Young Mania Rating Scale

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ABSTRACT

BACKGROUND

BPAD is a lifelong intricate and heterogeneous mood disorder which is also known as grievous mental illness due to repeated occurrence of an overcast of mood with lesser energy (depression), euphoric mood with elevated energy and activity (manic & hypo-manic), cyclothymic, dysthymic and mixed episodic interval of longer and shorter duration with 0.3-1.2% prevalence. The BPAD impairs the QOL & MA of patients by changes in mood; personal suffering; troubled family support and irregular socio-economic functioning as well as BPAD have a long-term therapy hence the patients are most vulnerable to DRPs. This study was an initiative to adapt the Pharmacist-led collaborative care to improve the management of BPAD.

OBJECTIVES

Primary objectives:

- To compare the two groups with the effect of Pharmaceutical care on compliance towards medication and health status (HRQOL) of the patients with Bipolar disorder at different time point.
- To assess and resolve the susceptible drug-related problems (DRPs) of the patients.

Secondary Objectives:

- To assess the extent of bipolar disorders (depression and mania) by using different scales (like the Hamilton Depression rating scale and Young mania rating scale)

MATERIAL AND METHOD

The current work was a prospective, open level, randomized interventional study, which was conducted at the psychiatry unit of tertiary care hospital. The sample size of study has been measured through hypothesis proportion formula. The patients of either sex aged between 18 to 65 years with BPAD has been enrolled in the study whereas, patients with the epileptic disorder, mental retardation, presence of any cognitive impairment with ECT and who were chronic alcoholic and drug abuse were excluded out from the study. The selected patients randomly allocated into control group with usual therapy and in interventional group with pharmaceutical care for the duration of 12 month with four follow-up. The study related data

like QOL, MA, DRP and mood outcome have been collected and analyzed during the study period.

RESULT

Total 304 patients were screened for the study, of them 286 patients were met with the selection criteria. The selected patients were randomly allocated into control group (n=143) and interventional group (n=143). During the study period 19 patients were met with withdrawal criteria and final analysis has been done on 266 patients. At baseline level there were no significant difference have been observed in demographic data, MA (p=0.524), QOL (p=0.395) and mood outcome (mania p=0.9086) (depression p=0.2363) in both groups. Whereas till the final follow-up, there were statistically and clinical significant improvement have been seen in MA, QOL and mood outcome (p<0.0001***) of interventional group patients. In the study positive correlation has been observed in between the medication adherence and quality of life in interventional group (r_s= +0.181, p=0.03*) instead of control group (r_s= +0.013, p=0.83) Among the both groups the most common DRPs were drug DDI followed by ADR (χ^2=0.9360, p=0.626) for the same 65 pharmacist intervention has been proposed at prescriber level of them 66.1% interventions has been accepted by psychiatrist due to good acceptance rate of intervention ~63.0% DRPs has been resolved.

CONCLUSION

The mental health system in current scenario among Indian masses to be neglected segment of the society. This study helps to cut through the stigma associated in the Indian society wherein the pharmacist should represent themselves as a part of an inter-disciplinary solution that resolves the gaps by helping to diligently adhere to the medication-related services. This enhances pharmacotherapy outcomes which facilitate the rapid retrieval with mental illness. Here, we felt the need for specialty pharmacist to provide long-term medication management for patients with chronic mental illness. The collaborative care approach towards mental health can be an executable choice to address the unmet needs in bi-polar disorder patients.

INTRODUCTION

1.1 BACKGROUND

Bipolar Affective Disorder (BPAD) is a complex and heterogeneous mood disorder which is also known as sever chronic mental illness defined by the occurrence of depressive, manic, hypomanic and mixed episode divided by interval of longer and shorter duration.[1] As per WHO, mental health gap action program, data for the Indian population, show a prevalence of 200 cases per 1,0**0**,000 people for BPAD and schizophrenia. BPAD has a sixth rank in leading causes of disability adjusted life of the year (DALY's).[2]

BPAD has been documented as the highest rank of suicidal behaviors compared to other psychiatric disorders. Approx. 61% BPAD patients experience suicidal ideation.[3] In that 25%-56% patients attempt suicide and 10%-19% of patients commit it.[4] In India, the suicide rate for male is 12.2 per 1,00,000 population and for females is 9.1 per 1,00,000 population.[5] As per the report of NMHP the prevalence of BD rural and urban area 34/1000 and 37/1000, respectively.[5]

Looking the seriousness of above mentioned statistics, we have found similar problem at our psychiatry setting. Hence, it is evident that, role of clinical pharmacist is well documented and it can play an important role to the contribution and management of this problem by working with psychiatrist and multidisciplinary team, The clinical pharmacist can contribute by providing the information to patient about proper use of medication, assessing and improving therapeutic adherence, following effectiveness and safety of pharmacotherapy and pharmaceutical care for improving the quality of life.[4] The Pharmaceutical care is based on the relationship between patient and pharmacist who accept responsibility of the patient. According to the definition of Hepler and Strand, the Pharmaceutical care is "the responsible provision of medicine therapy for the purpose of defining outcome that improves patient's quality of life".[6,7]

The concept of pharmaceutical care is an indispensable elements of patient centered health-care and requires a change of traditional professional attitude, it implies on actively participate patient in making decision regard to pharmacotherapy, to improve medication adherence to achieve goal of desire therapeutic outcome, medication education and disease management for patients, interdisciplinary cooperation of health-care providers, assessment of drug related

problem (DRPs), direct benefit to patients, development of care plan as well as continuous follow-up are the important steps of pharmaceutical care.[6-8]

1.1.1 Pharmaceutical care

The traditional role of the pharmacist in health-care is to manufacture, dispense and sell the medication which was no longer adequate for the pharmacy profession.[9] The concept of pharmaceutical care is a pharmacist-led combine collaborative approach, which was introduced in the 1980s. According to Hepler and Strad, Pharmaceutical care is the accountable provision of pharmacological approach in order to attain a definite result for the patient.[6,7]
Pharmaceutical care is an interdisciplinary component of patient-centric health care instead of traditional professional attitude as well as this is an option that seeks to enhance the use of drugs and the rational use of medicines[8,10], that is based on the relationship between patients and pharmacist. This concept mainly focuses on-

1) Pharmacotherapy of patients.
2) Interdisciplinary cooperation with other health care professionals.
3) Improve the patients complains toward medication.
4) Assessing the drug-related problems (DRP's)
5) Develop a proper care plan.
6) Follow-up of the health condition of the patient.

These all are very important steps of pharmaceutical care in achieving a better outcome and good QOL of the patients.[7,8]

We have gone through various Cochrane review and meta-analysis but we obtained few studies related to psychiatry, especially with Bipolar Affective Disorder (BPAD) patient. For same purpose current study aimed to assessed and compare the effect of pharmaceutical care on medication compliance, their health status through QOL assessment as well as identify and resolve the Drug Related Problems (DRP's) of the patient with BPAD.

1.1.2 Bipolar Affective Disorder (BPAD)

Bipolar Affective Disorder (BPAD) is an intricate and heterogeneous mood disorder which is also known as grievous mental illness due to repeated occurrence of an overcast of mood with lesser energy (depression), euphoric mood with elevated energy and activity (manic & hypomanic), cyclothymic, dysthymic and mixed episodic interval of longer and shorter duration.[1] Bipolar disorder is one of the two main types of mood disorder (the other being unipolar depression)[11] and is distinguished by discrete episodes of abnormal expansive, elevated, or

irritable mood (mania or hypomania) associated with separate distinct episodes of anhedonia or depressed mood.[12] It has been categorized into 2 major forms.[13]

Bipolar I: at least 1 episode of mania has occurred.

Bipolar II: hypomanic episodes but no manic episodes have occurred.

Bipolar disorder generally appears to affect men and women equally.[12] Although bipolar II disorder may be more common in women. Gender appears to be a factor in the number and type of manic/hypomanic and major depressive episodes. Men may be more likely to experience a manic episode as their first episode, while in women, it is more likely to be major depression. The number of manic episodes equals or exceeds the number of major depressive ones in males. Whereas Depressive or mixed episodes and rapid cycling are more likely to occur in women.[12]

Bipolar disorder is a chronic and episodic illness with a variable course that currently cannot be cured, although treatment may be able to modify and control symptoms. According to the Diagnostic and Statistical Manual of Mental Disorders IV, Text Revision (DSM-IV-TR) criteria, individuals with bipolar I disorder must experience at least 1 episode of mania and Some patients have already experienced a depressive episode prior to the manic episode. However in BPAD I, most individuals will have subsequent episodes that are either manic or depressive. Hypomanic and mixed episodes may occur as well.[14]

Bipolar II disorder differs in that individuals meeting these criteria have a history of major depressive episodes and hypomanic episodes only (milder than manic).[15] When an individual previously diagnosed with bipolar II disorder develops a manic or mixed episode, the diagnosis is changed to bipolar I disorder.[14] The severity of mania can vary significantly, and mild episodes without significant functional impairment, psychotic symptoms, or symptoms of being dangerous to oneself or to others are referred to as hypomania. The Hypomanic episodes can occur in individuals with a history only of depression. The combination of major depressive episodes and hypomanic episodes has been labeled as bipolar II disorder in order to differentiate it from bipolar I disorder. There is some controversy as to whether bipolar II disorder is actually a milder version of the disorder, as much of the morbidity and mortality is due to the presence of depressive episodes and the attendant risk for suicidal behavior. These types of episodes occur in both bipolar I and II disorders.[13]

The pathophysiology of BPAD has not been determined, and no objective biological markers that correspond definitively with the disease state have been discovered yet. For assessment of BPAD, Potential changes in the function of neurotransmitters, such as norepinephrine, do-

pamine, and serotonin, has been studied for several decades. Some reports indicate that lower than normal concentrations of choline, a direct precursor of acetylcholine, have been observed in the red blood cells of patients with bipolar disorder who experience predominantly manic episodes. Whereas, Concentrations of homovanillic acid, a metabolite of dopamine, are reduced in the cerebrospinal fluid of patients with depression.[11]

A hypothesis that has been studied since the 1970s is that electrolyte fluxes in individuals with bipolar disorder may be caused by a deficit of the membrane sodium potassium-ATPase. As per the hypothesis the Concentrations of erythrocyte ATPase may be reduced in patients with bipolar disorder, when compared with healthy controls.[11]

BPAD affect more than 46 million global populations with the lifetime prevalence of 0.3 to 1.2%. In all country, women are more likely for BPAD than a man with a lifetime prevalence of 0.65% and 0.55% respectively.[2]

GBD 2017 & WHO-led mental health gap action program data on Indian population reveals that the prevalence of BPAD is 0.56% (~200 cases per 1, 00,000 people). This is the leading causes of disability-adjusted life of the year (DALY's).[16]

Among all the mental conditions BPAD has been documented as the highest rank of suicidal behaviors. One report states that ~61% of patients of BPAD experience suicidal ideation at least one time in their life.[3]Among them, 25%-56% of patients attempt suicide and 10%-19% of patients successfully commit it.[4]

In India, the suicide rate for a male is 12.2 per 1, 00,000 population and for females is 9.1 per 1, 00,000 population.[10] As per the report of NCMH the prevalence of BPAD rural and urban area 34/1000 and 37/1000, respectively.[17]

1.1.3 Medication Adherence (MA):

Maintain the adherence toward medication is a challenging job in case of BPAD patients who shows very low adherence (35%) for prescribing medication in compare to schizophrenia and (50-60%) and other psychiatry disorder.[18,19] As per the senses report of National Mental health survey of India 2015–2016 medication non-adherence of medication is the one of paramount cause for symptom acceleration.[20] Few studies suggested that the rate of non-adherence among patients with BPAD is approx. 30-65%.[21] Commonly non-compliance correlated with recurrence of symptoms, high risk of suicidal ideation as well as commitment and hospital admission.[22]

Hence improving the MA of patients with BPAD is a must for improving the QOL. According to Celio J and Sabate E., MA is the extent to which a patient behavior toward consuming medication; sticking to a diet and adopting lifestyle modification as well as preconditions of a health care professional like Clinician, Pharmacist, Nurses etc.[23,24]

Clinical pharmacist-led pharmaceutical care to BPAD patient is one of the ways to improve MA as well as the QOL. In the current study, we aimed to improve patient adherence through pharmacist intervention and patient counselling. Adherence of patients towards medication has been assessed by MMAS-8.

1.1.4 Quality Of Life (QOL):

Good QOL is a looming issue in the health care sector, globally; hence this is the first priority of each health priority for each health care professional. It is not only a better state of health, although it is an outstanding amount of physical; mental; environmental; socio-economic health and spiritual well-being.[25,26] It is an important broad metric life aspect to the health status of individuals.[27]

World Health Organization states, QOL is an external perception of their role in life in the context of the culture and value system in which they reside and relate to their objective, expectations, norms and issues.[28]

The BPAD impairs the QOL of patients by changes in mood; private suffering; troubled family support and irregular socio-economic functioning.[29] By the help of the current study, we assessed the impact of clinical pharmacist leads a collaborative approach to the different dimensions of QOL of BPAD patients via WHO-BREF QOL.

1.1.5 Drug Related Problems (DRP's):

The drug is an active chemical entity existing in the dosage forms; used for the diagnosis and prevention of disease circumstances.[30]Advancement in pharmaco-therapy leading to the discovery of fresh solutions to drug therapy for clinical issues, while at the same moment exploring the clinical applications of the drugs and their Drug Related Problems (DRP).[31]

As per PCNE and SFPC classification, A DRP is an event pharmacological therapy that possibly interfere the patient attaining an ideal outcome of medical care. This is the main public health concern because of its effect on morbidity, mortality and the burden on the patient's pocket.[32-35]

Several types of research have revealed an incidence of DRPs of roughly 1.7% to 25.1%, of which only 5% of studies were reported hospital admission.[36] According to the study from Pharmacy Today, the DRPs are increasing healthcare expenditure costs around $177.4 billion. They estimated that 40 per cent of the price and 120,000 fatalities from DRPs could be prevented through clinical pharmacist efforts to ensure adequate pharmacological therapy.[37]

Nearly all psychiatric diseases or disorders have a temporary cure and long-term pharmacological therapy. Due to their psychiatric illness and long-term therapy, the population of psychiatric patients is most vulnerable to DRP.[38] DRP is a challenge for healthcare practitioners because of its health-related burden on patients, particularly the psychiatric population such as patients with BPAD. As a patient with BPAD may experience different stages of mania and depression, there are more chances of a drug-related problem in this situation.[39] Therefore, clinical pharmacist can play a significant role in contributing and managing such an issue by offering the information about the correct use of medication, evaluating and improving compliance, evaluating, reporting and resolving the DRP's.

1.2 LITERATURE REVIEW

Pharmaceutical care based a randomized study has been initiated by Sadik A et al. to evaluated the effect of pharmacist intervention on QOL and MA on 104 patients over the 12 months of duration. At a baseline level, there were no significant differences among both group but during follow-up, the follow-up improvement ($P<0.05$) has been observed in all domains of QOL. Even the good adherence noted in interventional group patients (n=75) instead of control group (n=29) ($P>0.05$, df=1) patients. The study's outcome suggests that pharmacist-led pharmaceutical care may lead humanistic as well as clinical outcome.[40]

A meta-analysis was performed by Berk M et al. to assess the effect of a psychopharmacological collaborative approach on BPAD patients. The author has gone through Various Medline, Ovid and Science direct search from 1975 to 2004. As per the literature, review author concluded that collaborative treatment alliance in the real world setting can lead the integration in a psychiatry care setting.[41]

A Narrative review by Valera M R et al. enlightens the new part of the pharmacist in psychiatry multidisciplinary team, medication review, improving the adherence of antipsychotic and barrier and facilitator to the enforcement of pharmacy services in mental health. Total 166 scientific journals were assessed related to the role of the pharmacist and Pharmaceutical care. The review scientific journals demonstrated that the pharmacist has a wide variety of abilities in managing medicines, providing information on medicines to prescribe counseling, patient about medication and facilitating adherence to medication policies in mental health care delivery.[42]

Aaltone SE et al. conducted a health survey with international students of 6 different countries to assess the barrier for the counselling of the patients with psychiatric illness. As per the collected data of India, the primary cause of counselling barrier was pharmacist related factor followed by patient-related factor, social and culture related factor instead of another country survey.[43]

Pakpour AH et al. assessed the impact of the intervention on MA, QOL and mood outcome among the BPAD patients for 6 months of duration. As per the data, there were no statistical differences ($p=0.26$) in MA among the control group (6.17 ± 2.90) and experimental group

(6.03±2.56). After the intervention, There has been a substantial improvement (p<0.001) in MA has been seen in the experimental group (9.53±3.84). Similarly, the improvement (p=0.02) have been seen in QOL, from baseline (39.14±11.34) to end follow-up (43.56±12.37). Improvement (p<0.001) in the scale of mania from baseline (15.03±2.76) to follow-up (10.4±2.01) and in the scale of depression from baseline (22.21±5.71) to follow-up (17.13±7.55) has been observed in the experimental group. The author concluded that a proper intervention of collaborative approach can improve MA, health status and mood outcome.[18]

A study by Mishra A et al. States, pharmacist intervention on BPAD patient improves MA as well as the QOL. In their study assessed statistically significant improvement (p<0.001) in MA from baseline (5.44±0.55) to follow-up (7.31±0.66) as well as in the QOL from baseline (36.72±12.37) to follow-up (57.29±20.11).[44]

Miklowitz DJ et. al., performed a RCT in which 101 BPAD patients were allocated to two groups with family-focused treatment (FFT) and less intensive crisis management (CM) with pharmacotherapy respectively. FFT consisted of 21 psycho-education sessions whereas CM consisted of only 2 sessions. Data of the study have been taken during 3 to 6 months of intervention for 2 years.

Characteristics	FFT (n=31)	CM (n=70)	*P*-Value
relapses	(11/31,35%)	(38/70,54%)	
Depression	(73.5 ±28. 8)	(53.2 ±39. 6)	*P*=0. 003
Adherence	2.77±0.43	2.56 ±0.48	*P=0*.04

The author concluded that FFT psycho-education, as well as medication-related education, have shown a greater reduction in the symptom of depression and improvement of medication adherence.[45]

Lizer MH et. al., observed the effect of the pharmacist-assisted psychiatric clinic on the improvement of health outcome and compliance of medication of BPAD patients. In this prospective single centred study, 27 participants were enrolled. Of them, 20 participants completed the study, 10 (50%) were non-adherent at baseline and 9 (45%) were non-adherent at 6 months (*P*=1. 00). At study completion, the WHO QOL Questionnaires showed statistically significant changes in the physical and psychological domain (*P*<0.001) there were clinically

improvement has been seen. Because of small sample size, there was a low significant improvement in study outcome, Author said.[46]

Murata A et. al., has assessed the implementation of pharmacist assist MA on antidepressant-treated patients. Total of 151 patients was enrolled in the study. Among them, 71 patients were antidepressant-treated inpatients (ADTS) and 80 antidepressants native inpatients (ADNS). At a baseline level, they didn't find any statistical difference but during follow-up, significant improvement has been observed *(P*<0.01) in pharmacist assist group

Characteristics	ADTS (n=71)	ADNS (n=70)	*P*-Value
DAI-10 score	6(4-8)	2(0-6)	*P*<0.01

The author state that, the melancholic depression and antidepressant side effect are risk factors for antidepressant non-adherence in routine treatment of depression and BPAD, at same place pharmacist adherence and instruction can ameliorate antidepressant nonadherence.[47]

A systemic review has been carried out by Bell S et. al., the primary objective of that review was to assess the impact of pharmacist-delivered community-based service to optimize the use of mental illness medication. Total 22 randomized controlled trial based scientific literature has been reviewed. These three studies shown that, pharmacist counseling and surveillance of treatments can enhance compliance of medicine. four trails mentioned that the pharmacist conducted a medication review may reduce the number of prescription inappropriateness. The result of the systemic review concluded that pharmacist can contribute to optimizing the use of medication for mentally ill patients (schizophrenia and BPAD) in the community setting.[48]

The project by Hira I et. al., on male patients has examined the effectiveness of pharmacotherapy, psychotherapy and factor affecting non-compliance of the patients. Total of 100 patients was enrolled in the study. From where patients were on psychotherapy 5%, pharmacotherapy 35% and 60% on both psychotherapy and pharmacotherapy. After the pharmacist intervention, patient compliance and MA were improved (68%) in patients. The study result was supported that, pharmacist intervention along with pharmacotherapy and psychotherapy are helpful in the diagnosis of BPAD patients.[49]

Stephenson J.J. et. al., has assessed the physician perception of MA versus pharmacy claims on antipsychotic MA in patients with schizophrenia and BD. Total 214 (48 with schizophrenia and 166 patients with BD) patients were enrolled in the study, most doctors (60%) have no special training for adherence. The significance of compliance was recorded by 68% and approximately 76% of their patients adhered. 16 out of 17 (94%) patients with low-to-moderate (70%) adherence in the schizophrenia group. 62 of 92 (67%) patients with low to moderate adherence in the BPAD group.

Claim based	Physician reported adherence (n=214)					Schizo/BD diagnosis code (n=214)									
	low	mod	high	Kappa coefficient	*P*-Value	low		mode		high		Kappa coefficient		*P*-Value	
						BD	Sch	BD	Sch	BD	Sch	BD	Sch	BD	Sch
Low	5	12	32	0.0572	0.1908	4	0	12	0	24	7	0.0478	0.0088	0.3522	0.9089
Moderate	2	13	50			2	0	12	1	38	9				
High	0	19	81			0	0	17	2	52	25				

As per outcome, the author found that the discrepancy between physician perceptions of patient adherence and claim-based adherence was measured by pharmacy claims analysis.[22]

In a systemic review Batista TA et. al., the author assessed the efficacy of psycho-education in bipolar patients. Out of 320 articles, 23 were selected. Of which only 23 articles were selected. 10 articles were excluded because of the duplication of the database. A total of 13 publications reviewed. 6 RCT found decrease relapse in clinical course. 6 of 13 found to increase the time of recurrence. In 4 studies no of days of hospitalization decrease. 2 studies were found hypomanic and manic symptoms. MA was found in 5 studies. The author concluded that psycho-education also appears to be the key intervention to improve drug adherence and long-term results in multiple medical circumstances.[50]

In a study, Behredar MJ et. al, assessed the efficacy of the psychoeducation program for MA and global functioning of BD patients. Total of 45 patients with BD-I was enrolled in the 3 groups. 1) Psycho-education plus pharmacotherapy, 2) Pharmacotherapy, 3) Placebo and pharmacotherapy. There was no baseline, significant in Age, Disease onset and Education in groups. The results of the study were found as follows;

Variable	Group	Baseline	1st assessment	2nd assessment	*P*-Value

Medication adherence	Psyco-edu.	6.27±0.88	8.33±0.65	7.92±1.38	[F(2,31)=55.09, P=0.0001]
	Control	6.53±0.64	5.08±0.79	4.33±0.49	
	Placebo	6.47±0.52	4.91±0.54	4.36±0.67	
Global functioning	Psyco-edu.	56.6±3.58	64.83±1.9	64.17±2.12	[F(2,31)=90.93, P=0.0001]
	Control	56.27±3.17	55.25±3.91	54.17±5.08	
	Placebo	56.67±4.5	56.27±3.6	56.0±4.36	

The author concluded that psycho-education plus pharmacotherapy is effective in improving MA and global functioning of BD.[51]

In the study Mert DG et. al., carried out to evaluate factors resulting in non-adherence to BD, schizophrenia, depression and other mental disorders. Patients were classified according to their diagnosis. During follow up, the data of MA were as follows.

Medication nonadherence	BD n=68	Schizo n=59	Depression n=39	Other n=37	Total
Present	45 (45.5%)	24 (24.2%)	12 (12.1%)	18 (18.2%)	99 (100%)
Absent	23 (22.1%)	35 (33.7%)	27 (26.0%)	19 (18.3%)	104 (100%)

The author concluded that, in the case of BPAD patients, there were more non-adherences in comparison to other groups. The proper management through MA can be beneficial for the early diagnosis of disease.[52]

A cross-sectional study has been performed by Ibrahim A.W. et. al., Total of 358 patients was enrolled. The study consists of 181 patients with schizophrenia and 177 patients with BPAD. In the survey, they assessed the medication-related problem for non-adherence. The overall prevalence of non-adherence has been found at 54.2%. The level of adherence and medication-related factor for non-adherence were as follows;

Variables **Level of adherence (N=358)**	**Schizophrenia (%)**	**Bipolar Disorder (%)**	**Total (%)**
Low	104 (57.5)	52 (29.4)	156 (47.6)
Medium	9 (5.0)	29 (16.4)	38 (10.6)
High	68 (27.5)	96 (54.2)	164 (45.8)

As per the result, the author recommended that the use of guidelines to promote monotherapy-based rational pharmacotherapy, consider reduced routine dosage prescriptions, and integrate monitoring of AE's and early evolution in clinical practice.[21]

Trijntje FFYG et. al., performed collaborative care based randomized control trial in BPAD affected the patient population. Total of 138 patients was enrolled and randomized. Patient outcome viz; MA, the severity of the symptom and depressive symptom have been assessed in 6^{th} and 12^{th} month of duration. As per the obtained result of the study, collaborative approach has clinically significant improvement during the follow-up. For depressive symptom, the clinically significant value was found, both at 6 months (Z=2. 6, P= 0.01) and 12 months (Z=3. 1, P= 0.002). However there was no difference has been found in manic symptom as well as in MA.[53]

A systemic review have been carried out by Conn VS *et. al.,* Author reviewed approx. 13 database, 19 research register and 57 research journals which are concerned with MA and patient compliance. 176 comparative study along with 23,318 subjects have been assessed by the author. Of which, statistically significant improvement has been found in MA (d=0.127), QOL (d= 0.127) and patient-centred positive outcomes were observed after MA Intervention.[54]

Ho SC *et. al*[2] reviewed 11 articles to assess the clinical and economic impact of Non-adherence in psychiatry population. As per the result of the study, patients who were with Non-adherence were more likely to experience an increased risk of relapse, further complications, reoccurrence of the disease condition, decrease response and remission rate, which directly or indirectly leads to economic burden on the patients. A proper pharmaceutical care Intervention helps this group of population to re-adhere with their medication plan.[55]

Nieznaska A et. al., carried out a review on BD patients. The review contained 24 major publications from the year 2009-2014, including 17 related to the assessment of QOL and 7 studies on the social functioning of BD. It's concluded that reduction in the symptom of depressive phase can help BD patients to improve QOL and improve the patients social functioning.[56]

In the review, Crowe M et. al. assessed the effectiveness of interventions to enhance adherence to medication in BPAD, in which, 11 scientific articles were assessed. 5 of 11 studies demonstrated improvement in MA and all studies demonstrated improvement in clinical outcome. The reviewer concluded that the rate of MA in BPAD is not significantly different. Further study requires to look more closely at this relationship with specific emphasis on how the medication is prescribed and what alternatives are accessible to patients.[57]

Zohra G. et. al., Assessed the QOL of the patient with a mood disorder by providing psycho-education. Total 32 patients were admitted in the study, who were randomly allocated into control group and study group. Psycho-education has been served in the study group. For recording the patients' QOL, WHO BREF-QOL questionnaires have been applied. The result of the study was found as follows;

S. No.	**Time group**	**Before intervention**		**After intervention**		***P*-Value**
	Study group	Mean	SD	Mean	SD	
1	Physical health	63.3	18.4	66.8	14.8	0.1
2	Mental health	53	22	59	17	0.04
3	Social relationship	51.9	23.1	57.1	18.1	0.04
4	Environmental health	50.4	15.6	54.7	13.3	0.1
5	QOL (mean)	54.4	15.9	59.1	12.9	0.04
	Control group					
1	Physical health	61.8	9.1	60.3	8.2	0.4
2	Mental health	49.9	12.2	49	10.6	0.3
3	Social relationship	51	12.1	47.4	9	0.1
4	Environmental health	47.9	9.1	46.9	8.6	0.4
5	QOL (mean)	53.1	9.3	51.6	7.6	0.09

As per the obtained finding, the author concluded that group psycho-education program promotes the QOL. It's suggested to conduct a study with a large number of sample size and long duration of follow-up, to investigate the effect of group psycho-education program not only for the health status of the patients with a mood disorder but also the patients' medication-related problems.[58]

Keila Maria Mendes Cereser et. al., has initiated a pilot study on the execution of pharmaceutical care on BPAD patients. Total 28 patients was allocated in the study. Dadar method of pharmacotherapy has been applied to study participant. Only 2% of patients were identified DRPs, being all of them resolved along with the study. 32.14% of patients were observed with low adherence to therapy and 55.56 percent of these patients have excellent compliance after follow-up of the pharmaceutical care intervention. The study concluded that pharmaceutical care of BPAD patients can help to minimize symptoms and it can enhance the adherence with a high number of sample size and long duration of study.[9]

Valenstein M et. al., conducted a RCT, using a pharmacy-based intervention on schizophrenia and BPAD patients, who were on the long duration of antipsychotic. Total 118 patients were allocated in two groups, usual care (n=60) and pharmacy-based intervention (n=58).

Characteristics	UC (n=60)	MPRs (n=58)	*P*-Value
MPRs (baseline)	0.55	0.54	*P*=0.767
MPRs (after 12 months)	0.64	0.91	*P*<0.0001

The author was concluded that pharmacy-based intervention increased antipsychotic adherence on the patient BPAD and schizophrenia.[59]

Abunahlah N et al. conducted a cross-sectional study to identify the DRP's and its causes. The survey has been done on 100 patients and the DRP's assessed through PCNE classification. The author assessed 163 DRP's among the patients with the rate of 1.61±1.17. the author says that the most common causes of were Dose / Drug selection followed by medication process. The pharmacist-based early intervention of DRP may minimize the AE's.[60]

Celine A et al assessed the DRP's on 108 patients with stroke, over the period of one year. During the study, the author observed a total of 80 DRP's among the patients. Of them, most common DRP was DDI's (25%), followed by ADR (15%) and drug without indication. The author proposed intervention on DRP's among them the acceptance rate was 97.9% by the clinician. Hence early detection of DRP's can gives good therapeutic outcome.[61]

Francesco Colom et. al., has carried out a randomized control trial on D patients, to know the efficacy of psycho-education. 120 patients with BPAD I and II were assigned in the study, selected patients were allocated into two groups with 21 sessions of psycho-education. There was no baseline statistical difference in between both of the groups.

Characteristics	Treatment phase				Follow-up phase			
	Control	interventional	X^2	*P*	Control	interventional	X^2	*P*
Recurrence	36(60)	23(38.3	5.63	0.01	55(91)	40(66.7)	11.36	<.001
Mania or hy-pomania	20(33.3	12(21.1)	2.21	.13	45(75)	28(49.1)	8.34	.003
Mixed episode	13(21.7)	7(12.5	1.70	.19	11(19.6)	11(19.6)	8.45	.003
Depression	19(31.7)	8(13.6)	5.56	.01	24(40.7)	24(40.7)	11.61	<.001

As per result author reported that effective intervention prevent s the recurrence of BD and it also helps to reduce the symptoms of mania and depression.[62]

Weiss RD et al. have conducted a randomized control trial on integrated group therapy versus group counselling by the help of health professionals. Total 62 patients were enrolled in the study and followed till 32 weeks, to assess the impact of both therapy in mood outcome at baseline Level the score of HAM-D was ($Z=4.23$, $p<0.001$) and YMRS were ($Z=4.41$, $p<0.001$) among the group. After the 32 weeks of follow-up, the author assessed positive mood outcome in the drug counselling group instead of an integrated therapy group.[63]

1.3 JUSTIFICATION

BPAD is a lifelong chronic disorder with 0.3-1.2% prevalence. Mean out of 1, 00,000 people 200 sufferings with this condition. As the nature of this disorder is lifelong due to this the chances of symptomatic severity are very high as well as the rate of suicidal attempt is also very high up to 10-19% in comparison to other conditions. [04, 16]

Few surveys and the original study suggested various reasons which are responsible for symptomatic severity of BPAD. Among them complains towards medication, Lack of knowledge about medication as well as their illness, drug-related complications and lack of familial as well as socio-economical support.[20, 22]

Such barriers can be eliminated through psycho-education as well as medication-related education led-collaborative approach.[8] We have found very few collaborative approaches led study in this direction. Hence Pharmacist led-Pharmaceutical care is a collaborative approach towards this direction to improve the health outcome of the patients.

Hence, looking into the gravity of the problem and similar findings in literature; this study was taken-up to address the issues, of in principle address the issues related to the medication adherence; reduce the drug related problems and increase the compliance towards the mediation adherence, where in this enhance the better quality of life.

1.4 RESEARCH HYPOTHESIS

Null Hypothesis (H0): There is no statistically significant difference in medication adherence and health status outcome among Control group and Interventional group.

Alternative Hypothesis: There is a statistically significant difference in medication adherence and health status outcome among Control group and Interventional group.

1.5 OBJECTIVES

Primary objectives:

- To compare the two groups with the effect of pharmaceutical care on compliance towards medication and health status (HRQOL) of the patients with BPAD at different time point.
- To assess and resolve the susceptible drug-related problems (DRPs) of the patients.

Secondary Objectives:

- To assess the extent of BPADs (depression and mania) by using different scales (like the Hamilton Depression rating scale and Young mania rating scale)

2.0 MATERIALS AND METHODS

2.1 Study site and setting:

The research was performed at the Psychiatric Department, KLE'S Dr Prabhakar Kore Charitable Hospital and Medical Research Centre, Nehru Nagar, Belagavi,

2.2 Study Design:

The current study was a Prospective, Randomized Interventional study.

2.2.1 Sampling technique and sample size estimation:

$$N = \frac{2(Z\alpha+Z\beta)2\ pq}{(P0-P1)2}$$

$$N = \frac{2\ (1.96 + 1.28)2\ \times\ 45\ \times\ 55}{(35 - 60)2}$$

$$N = 129.9 \approx 130$$

With 10% of attrition "n" = 143 patients in each group

Total sample size = 286 patients

Where, P_0=35%,

P_1=60%

p=45%,

q=55%,

Z_α = 1.96,

Z_β=1. 28

For 95% CI. The sample size has been increased by 10% as attrition.

2.3 Patient selection criteria of the study: As per the study criteria patients those who matched with study criteria were included in the study. The study criteria were as follows;

2.2.1 Inclusion criteria:

1. Patients diagnosed with BPAD and who have been discharged from the Department of Psychiatry (IPD/OPD patients).
2. Patients of either sex aged between 18 to 65 years.
3. Patient or patient's representatives (LAR) willing to provide written informed consent.

2.2.2 Exclusion criteria: The following patients were excluded during screening;

1. Patients with the epileptic disorder, mental retardation, presence of any cognitive impairment.
2. Patients who are chronic alcoholic and drug abuse.
3. Patient with electroconvulsive therapy (ECT).

2.4 Study enrollment procedures

2.4.1 Screening Process

Researcher on his daily round in the psychiatry OPD/IPD, screened all the patients according to patient selection criteria, patients and members of their families were informed regarding the proposed study details. Patients and their family members were informed about procedure in proposed work and withdrawal criteria from the study at any moment. Furthermore, patients may at any moment leave the study. Patient data on the reason for withdrawal were registered and archived for statistical assessment before completion of the research.

2.4.2 Eligibility Assessment

After thorough screening, the eligible patients were checked against the inclusion and exclusion criteria. The patients qualifying as per the norms were considered as an eligible patients for further enrollment process.

2.4.3 Informed Consent Process

2.4.3.1 Participant information sheet (PIS): PIS in the local language (Kannada and Marathi) was provided to all the eligible patients prior to randomization. PIS document provided following detail of

- Statement mentioning that it is research.
- Purpose and methods of the research in simple language.
- Expected duration of the participation and frequency of contact with estimated number of participants to be enrolled.
- Types of data collection and method.
- Benefits to the participant.
- Any foreseeable risks.
- Extent to which confidentiality of records could be maintained

- Freedom of the individual to participate and/or withdraw from research at any time without penalty or loss of benefits to which the participant would otherwise be entitled
- The identity of the research team and contact persons with addresses and phone numbers

2.4.3.2 Informed consent form: The interested participants were explained about the consent details, a brief introduction about the study and its purpose, the procedures involved in the study such as screening, randomization, interventions, benefits, confidentiality terms, the rights of the participant and researcher contact information. Patient understanding for the PIS- Informed Consent form (ICF) was cross verified. Concerns or queries regarding the study have been addressed. Participant's right of withdrawing from the study at any time with or without stating reasons were assured with no unintended consequences affecting their future care in such a case.

Upon agreeing to participate after going through the informed consent documents (ICD), two copies of the ICF were signed by the patient and the researcher on the same date. The participants who were unable to read and write the ICD were asked to provide their thumbprint impression in the presents of LAR, plus the signature of an impartial witness & LAR was taken. The participants were provided with a copy of a signed PIS & ICF was filed in the patient study file and stored at the participating site. The researcher has been ensured the proper collection and storage of the participant consent forms.

2.4.4 Randomization

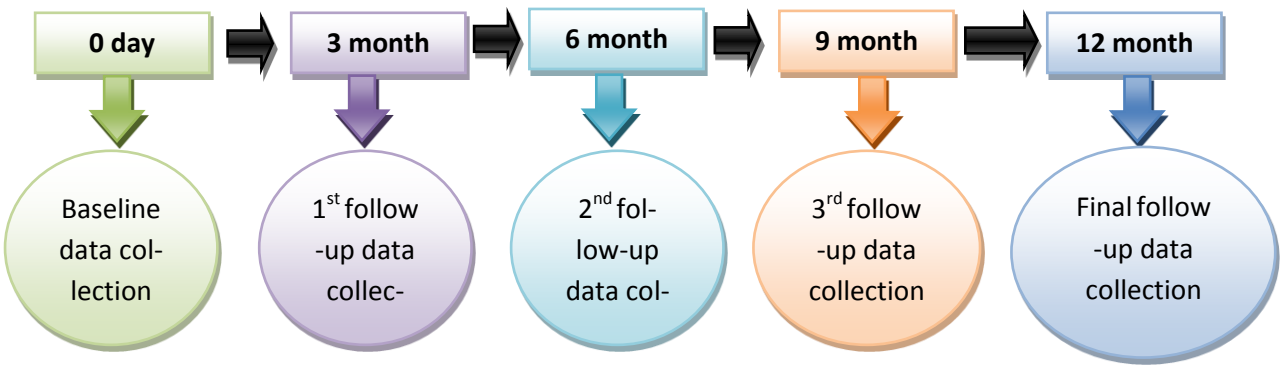
Screened patients were allocated to the intervention or control group by method of computer-generated randomization list by simple randomization method with the help of Microsoft Excel Sheet, intended by a third individual.

2.4.5 Study Groups

After randomization and allocation of the participants, the intervention group patients has been served pharmaceutical care along with the standard care delivered by a clinical pharmacist at the study sites and those allocated to the control group received standard care. The detail of the intervention has been mentioned below in control arm and interventional arm.

2.4.5.1 Control arm

Patients who met the requirements for inclusion criteria and agreed to sign the ICF, were considered in this group as per inclusion and exclusion criteria. Standard care was given to the control group. Randomization took place at week zero (baseline) and patients met again every three months (3, 6, 9, and 12 months) with the clinical pharmacist. At the baseline level patients' data related to background information, demographic data, history related to their illness and variables linked to the research such as efficacy, safety, adherence, QOL, DRPs were collected. Here patients received standard care which has provided by the psychiatrist. The same standard care has been served to them at each appointment during the study and study related data has been collected from them. In the end of the study data has been segregated and analyzed through the help of statistical software.



2.4.5.2 Intervention Arm

After the randomization, the patients those were enrolled in the interventional group were served with pharmaceutical care as well as the standard care by psychiatrist and nurses. The pharmaceutical care influenced collaborative care team include psychiatrists, psychiatry nurses, psychologist and clinical pharmacist to provide better care to the patients. In same instance, verbal and written information of the medication and education about mental health and BPAD have been provided to the patients and their families. The PIL focused on the goals and enhancement of MA to achieve treatment goals. The clinical pharmacist followed the patients at 3, 6, 9, and 12 months during the study.

Most of patients have been enrolled and followed from the psychiatry OPD rather than IPD among the both group. During the study period at the day 0 (Baseline), the study related data like demographic data, background information and other variable related data have been collected from the patients. After collecting the data, patients were served with pharmaceutical care as well as standard care. In pharmaceutical care intervention, the clinical pharmacist ed-

ucate the patients and their family members about the medications, its use and medication related aspect like indication, contraindication, side effect and importance of medication adherence for their illness and health related quality of life. The standard care have been served by psychiatrist and nurses, where patients have been diagnosed for their illness. The PIL and information broachers have also been served to the patients for reinforce the education of the patients.

After the day 0, the further data of the study have been collected during the study period at the month of 3, 6, 9 and 12. The interval of each follow-up was 3 month. During the follow-up the questionnaire related to medication adherence (MMAS-8), quality of life (WHO BREF-QOL), mania (YMRS), depression (HAMD) and DRP (PCNE) were inserted to the patients and asked to mark the answers. The knowledge level of the patients towards the medication have been assessed at each appointment during the study period. The knowledge of patients and their family members have been reinforced at every appointment or follow-up. At each appointment, the clinical pharmacist assessed parameters of efficacy and safety, QOL, MA, DRPs and extent of disorder symptom of each subject.

2.4.6 Study completion

One follow-up before the study completion, patients and their family members were notified of the completion of the research. For ethical reason, all patients were followed by a routine appointment with the psychiatrist.

2.5 Study outcome

The primary outcomes of the study to be assessed were:

1. Medication adherence to treatment through Morisky 8-Item Medication Adherence Questionnaire.
2. Quality of life through the WHOQOL- BREF Health Status Questionnaire.
3. Drug related problems (DRPs) in the effectiveness and safety of drug treatment.

The secondary outcomes of the study measured are:

1. Evaluation of mania through the Young Mania Rating Scale.
2. Depression symptom through Hamilton Rating Scale.

Control and intervention groups were compared in terms of the proportion of changes from baseline to follow-up. The baseline and follow-up data helped to assess the primary and secondary outcomes.

2.6 Data collection:

Eligible subjects with BPAD had been assigned in the study. All patients have been followed through telephonic calls during study follow-up. Monitoring and evaluation of the variables of the thesis work were carried out at baseline to completion of the follow-up. The proposed study work aims to collect data from the following questionnaires and scales.

2.6.1 Morisky-8 medication adherence questionnaire (MMAS-8):

MMAS-8 is 8 item questionnaires to assess the MA of the patients. The response choice of item 1 to 7 is on "Yes and No" and the 8th item is on a Likert scale. Where the scoring of item 1 to 7 is "Yes=1" "No=0" and for 8th item scoring "A=0" "B-E=1". The total range of the score is 0 to 8. Score more than 2 indicate low adherence, 1 or 2 medium adherences and 0 indicates high adherence.[64] Scale enclosed in Annexure no 11.

2.6.2 WHOQOL- BREF Health Status Questionnaire:

It is a self-reported questionnaire, filled by patients with BPAD.[65,66] WHOQOL-BREF contain 26 item from which, two item represent overall QOL and health status of the patients and rest of 24 item contain four domain, including physical health domain with 7 item (Domain 1), Psychological health domain with 6 item (Domain 2), Social relationship with 3 item (Domain 3) and Environmental health domain with 8 item (Domain 4).[67] Each of the domains is being rated by 5 points Likert scale and scored from 1 to 5 in response scale. According to WHOQOL guideline, a raw score of each domain was transformed 4 to 20 score. All Domains' score was scaled in the ascending direction. The mean score in each domain was obtained by computing the mean of transformed scores converted to a 0–100 scale for each domain. A mean score of <40 in each domain denote poor, 41–60 indicates moderate and >60 indicates good QOL.[28, 65, 68] Questionnaire enclosed in Annexure no 12.

2.6.3 PCNE Classification:

DRP's has been monitored, identified, assessed, and analyzed daily as per the PCNE classification of the drug-related problem's Version 5.01. This classification is used to assess the nature, prevalence; the incidence of DRP's and also acts as an indicator of pharmaceutical care

outcome. As per this classification, DRP's are classified into six major categories.[34] PCNE Classification enclosed in Annexure no 06.

Adverse Reaction (P1): The Patients those who are suffering or are going to suffer from an adverse drug event such as an ADR or toxicity. This problem might occur due to prescription error. The ADRs may also immerge at fixed dosages of the appropriate drug. It consists of three major problems; P1.1 Side effect suffered (Non-allergic), P1.2 Side effect suffered (Allergic), and P1.3 Toxic effect suffered. Document enclosed in Annexure no 07.

Drug Choice Problem (P2): Under this domain patients those are getting or are going to get a wrong drug for their disease condition are included. This may occur due to a prescribing error. It's covered six major problems; P2.1 Inappropriate drug (not most appropriate for indication), P2.2 Inappropriate drug form (not most appropriate for indication), P2.3 Inappropriate duplication of therapeutic group or active ingredient, P2.4 Contra-indication for drug (include Pregnancy/breastfeeding), P2.5 No clear indication for drug use and P2.6 No drug prescribed but clear indication.

Dosing Problem (P3): Patient may get a low or high dose of a drug which is does not meet with their therapy requirements. It can be due to prescribing error or drug use error. This is classified in four categories; P3.1 Drug dose too low or dosage regime not frequent enough, P3.2 Drug dose too high or dosage regime too frequent, P3.3 Duration of treatment too short and P3.4 Duration of treatment too long.

Drug Use Problem (P4): Under this domain, willingly or unwillingly patient uses to take a wrong drug or no drug. Such a problem may occur because of drug use or administration errors and filling error in the pharmacy. It consists; P4.1 Drug not taken/administered at all and P4.2 Wrong drug took/administered.

Interactions (P5): Under this domain, mild, moderate, and major drug-drug or drug-food interaction covered. This may occur because of prescribing or drug use error. Under this P5.1 Potential interaction and P5.2 Manifested interaction are involved.

Others (P6): Problems like P6.1 Patient dissatisfied with therapy despite taking the drug(s) correctly, P6.2 Insufficient awareness of health and diseases (possibly leading to future prob-

lems), P6.3 Unclear complaints, further, clarification necessary and P6.4 Therapy failure (reason unknown) falls under this domain.[34]

2.6.4 Naranjo adverse drug reaction probability scale:

The Naranjo ADR probability scale comprises of 10 answers to questions as "Yes", "No" and "Don't know". The scoring of each question is different for "Yes and No" it maybe -1, +1 or +2 but for "don't know" it's 0 as assigned to each answer. The cut-off on scale ≥9 than ADR is definite, 5 to 8 Probable ADR, 1 to 4 possible and ≤0 is doubtful.[69] Scale enclosed in Annexure no 09.

2.6.5 Hartwig's severity assessment scale

Hartwig SC et al., categorize the severity of ADR in 7 Level. According to this classification Level 1 and 2 falls under the mild category, Level 3 and 4 under moderate and Level 5, 6 and 7 falls under the severe category.[70] Scale enclosed in Annexure no 10.

2.6.6 The Young Mania Rating Scale (YMRS)

YMRS is one of the most frequent scales for assessing the severity of mania in a patient with BPAD. It consists of 11 items of which there are 4 items (irritability, speech, thought and aggressive behavior) that are graded 0 to 8 scale. While the remaining 7 items (elevated mood, increased motor activity, sexual interest, sleep, language, appearance, insight) scored 0 to 4 which has low weight compared to above mentioned 4 items. The severity of symptom depends upon scoring of YMRS according to this cut-off are up to 13 Normal, 14 to 21 potential case of mania, 22-25 probable case of mania and >25 is mania.[71,72] Scale enclosed in Annexure no 13.

2.6.7 The Hamilton Depression Rating Scale(HAM-D)

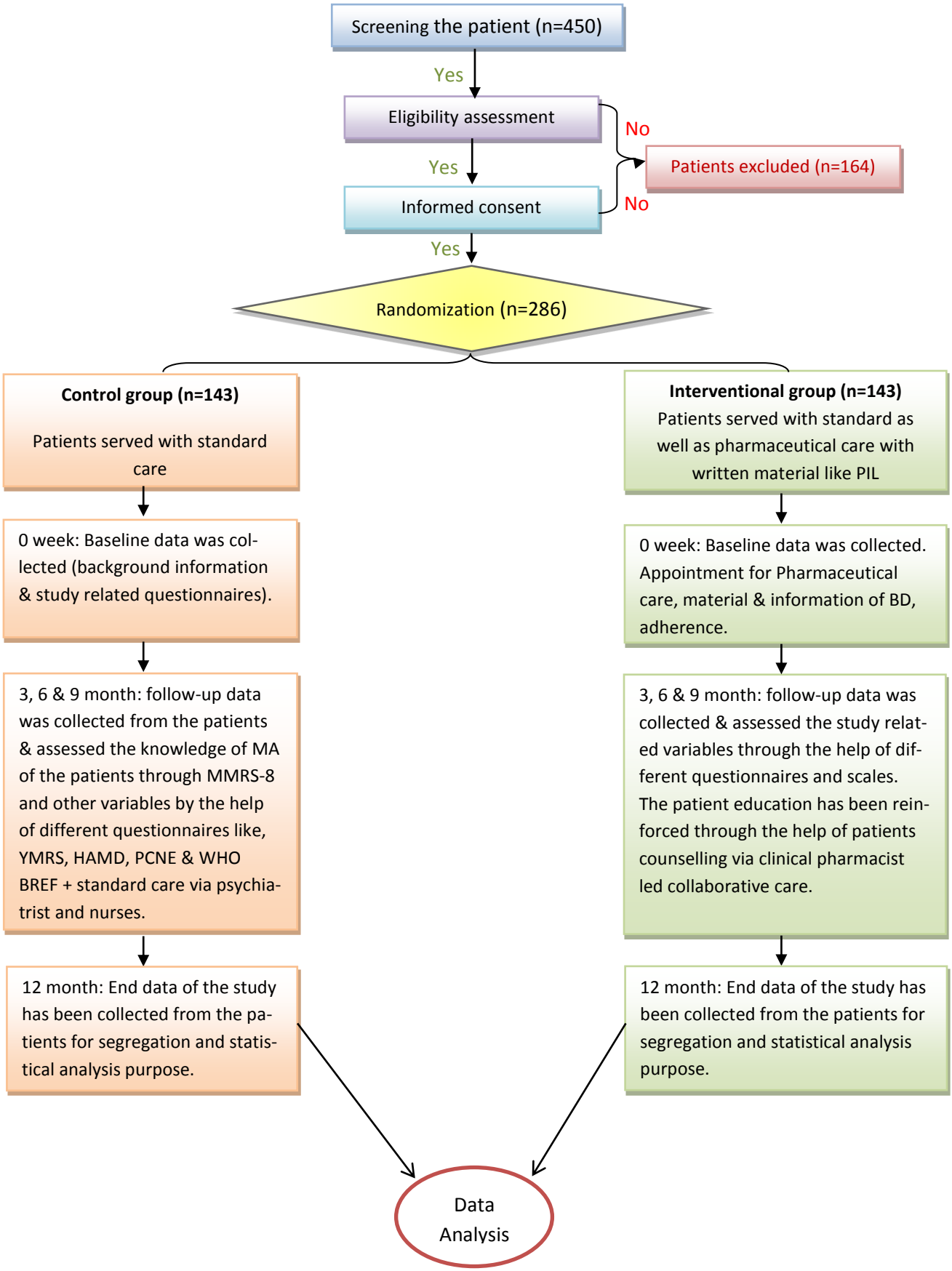
HAM-D is the most widely used scale for the assessment of depression. this is a 21 item scale of which item no 4, 5, 6 (Insomnia) 12, 13, 14 (Somatic symptom of GI, General Somatic Symptom, General Symptom) and item No. 17 (Insight) scored 0-2. Rest of question scored 0-4. The cut-offs of HAM-D is <7 normal, 8-13 mild depression, 14-18 moderate depression, 19-22 severe depression and >23 is Very severe depression.[73,74] Scale enclosed in Annexure no 14.

Medication history data, pharmacist interviews, DRPs, present health status, action plans were also recorded. Concerning the results, in addition to the data provided by patients and family members and medical history documents were observed.

2.7 Study materials:

1. Patient information sheet (PIS) & Informed Consent Form (ICF). (Annexure-I)
2. Patient data collection form. (Annexure-II)
3. Patient counselling form. (Annexure-III)
4. Pharmacist intervention form. (Annexure-IV)
5. Patient information leaflet (PIL). (Annexure-V)
6. PCNE Classification. (Annexure-VI)
7. ADR Documentation form. (Annexure-VII)
8. Adverse drug reaction notification form & alert card. (Annexure-VIII)
9. Naranjo adverse drug reaction probability scale. (Annexure-IX)
10. Hartwig's ADR severity assessment scale. (Annexure-X)
11. Morisky 8-Item Medication Adherence Questionnaire. (Annexure-XI)
12. WHOQOL- BREF Health Status Questionnaire. (Annexure-XII)
13. Young Mania Rating Scale. (Annexure-XIII)
14. Hamilton Depression Rating Scale. (Annexure-XIV)

Flow chart No 01: Schematic diagram of study detail plan.



3.0 DATA ANALYSIS PLAN

3.0 Statistical Analysis:

The Patients' sample size has been assessed through hypothesis proportion formula in the order to get the proper study outcomes. In total sample size, 15% attrition rate has been applied. At 95% confidence interval, probability was considered $P<0.05$ for statistical significance. The data of the current study was entered and analyzed on IBM SPSS Statistics Version-20 (IBM Corporation, United State).

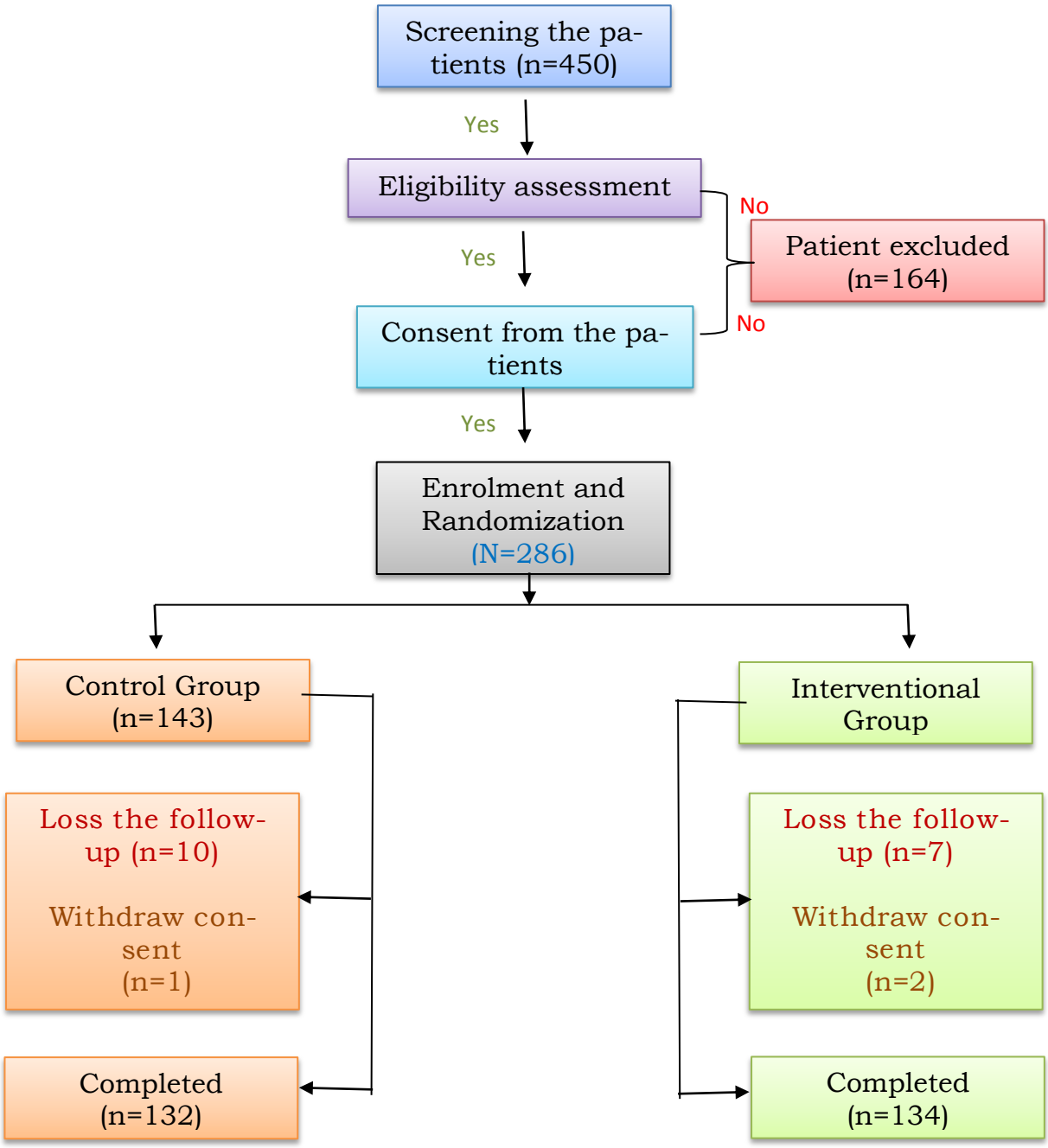
The demographic and clinical variables of the groups compared with the chi-square test with the mean, stander deviation, percentage, and degree of freedom and probability value. Before analyzing the health status (QOL), MA and mood outcome we applied Kolmogorov Simonov test for the analysis of normal distribution among the Variables.

Variables those who not followed the normal distribution, among them non-parametric test were applied; for comparison into the groups Mann-Whitney U test and for comparison within the group Wilcoxon matched pairs test were applied. Whereas, that variable followed the normal distribution were treated with the parametric test; for comparison between the group Independent student "t" test and within the group Dependent "t" test was applied for the analysis of study result. The Spearman Coefficient Correlation Test has been applied to assess the correlation in between the two ordinal variables.

4.0 RESULTS:

Total of 450 patients with Bipolar Affective Disorder (BPAD) were screened for the current work. Study participants those were enrolled after screening and provide their willingness to sign informed consent were randomized into two distinct groups. (Flowchart 1)

Flowchart No 02: Flowchart showing the distribution of patients, the usual care based control group and the pharmaceutical care based intervention group.



Total of 286 patients were enrolled in the study. At each group, 143 patients were enrolled of which control group was served with as usual care and the interventional group was served with pharmaceutical care. In the control group, 11 patients withdraw from study whereas in Interventional group 9 patients left the study. Finally, complete data analysis has been done on 266 patients.

4.1 Demographic Data:

4.1.1 Age Distribution

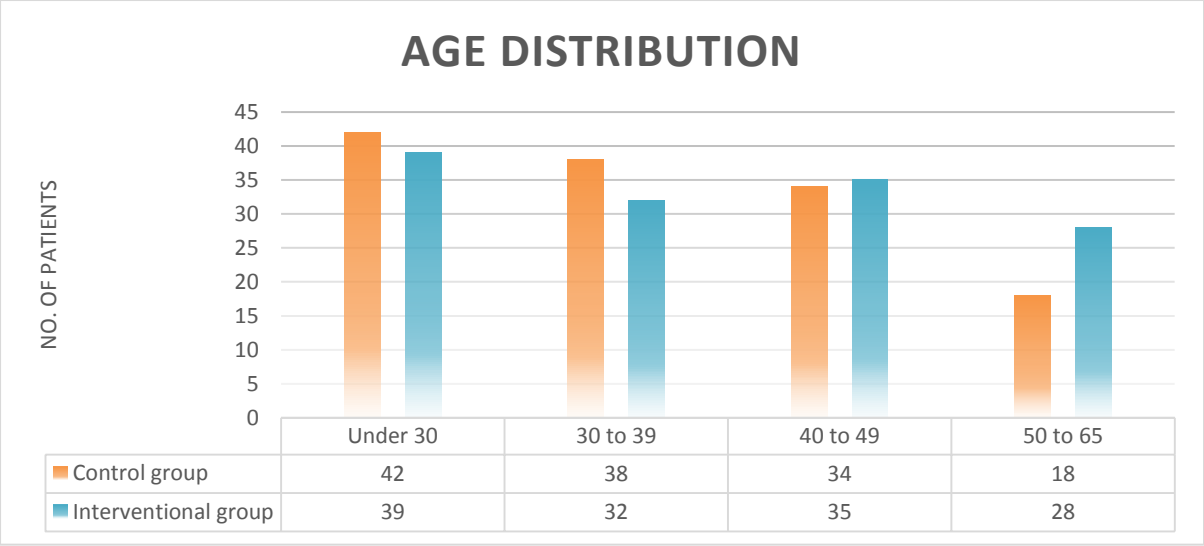
- The demographics related to age distribution suggest that the prevalence of BPAD is higher in the age group l8 to 30 year (30.4%) followed by 30 to 39 year in both control and Interventional group. As per the applied statistical test we didn't found any difference among the both group.

Table 1: Age Distribution at Different Age Group.

Age in a different category	Control group	%	Interven-tional group	%	Total	Chi-square	p-Value
Under 30	42	31.82	39	29.10	81	2.7990	0.4240
30 to 39	38	28.79	32	23.88	70		
40 to 49	34	25.76	35	26.12	69		
50 to 65	18	13.64	28	20.90	46		

p<0.05*, p<0.01**, p<0.0001***

Figure 1: Age Distribution at Different Age Group.



4.1.2 The onset age of the first BPAD:

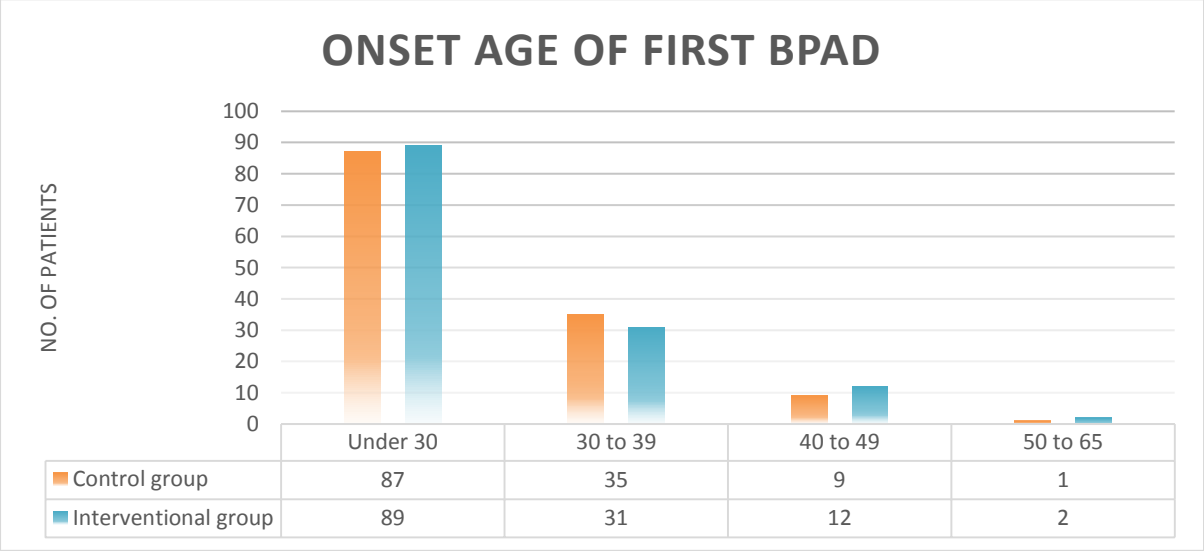
- The onset of the age of first BPAD was similar to the age distribution results stating the higher preponderance in 18 to 30 year to the age group for both control and interventional group. In current study 66.16% patients reported first onset age of BPAD was less than 30 year instead of other age group.

Table 2: Onset Age of First BPAD.

The onset age of first BPAD	Control group	%	Interven-tional group	%	Total	Chi-square	p-Value
Under 30	87	65.91	89	66.42	176	1.0120	0.7980
30 to 39	35	26.52	31	23.13	66		
40 to 49	9	6.82	12	8.96	21		
50 to 65	1	0.76	2	1.49	3		

p<0.05*, p<0.01**, p<0.0001***

Figure 2: Onset Age of First BPAD.



4.1.3 Gender Distribution:

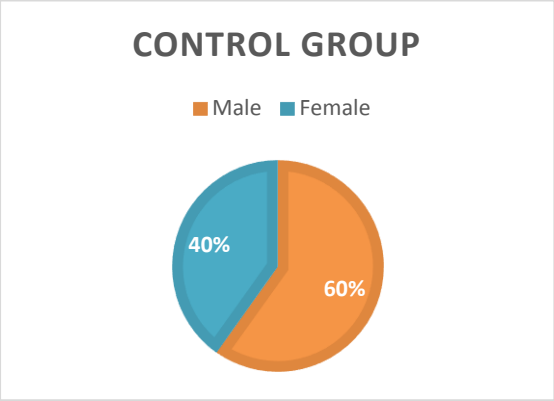
- The male predominance was prominent compared to female in control as well as an inter-ventional group. The other study shows that females are more susceptible to BPAD rather than male.

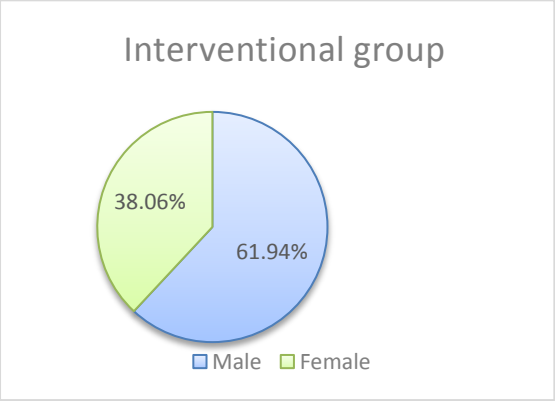
Table 3: Gender Distribution

Gender in a different category	Control group	%	Interven-tional group	%	Total	Chi-square	p-Value
Male	79	59.85	83	61.94	162	2.7990	0.4240
Female	53	40.15	51	38.06	104		

p<0.05*, p<0.01**, p<0.0001***

Figure 3: Gender Distribution in Control Group and Interventional Group





4.1.4 Marital status:

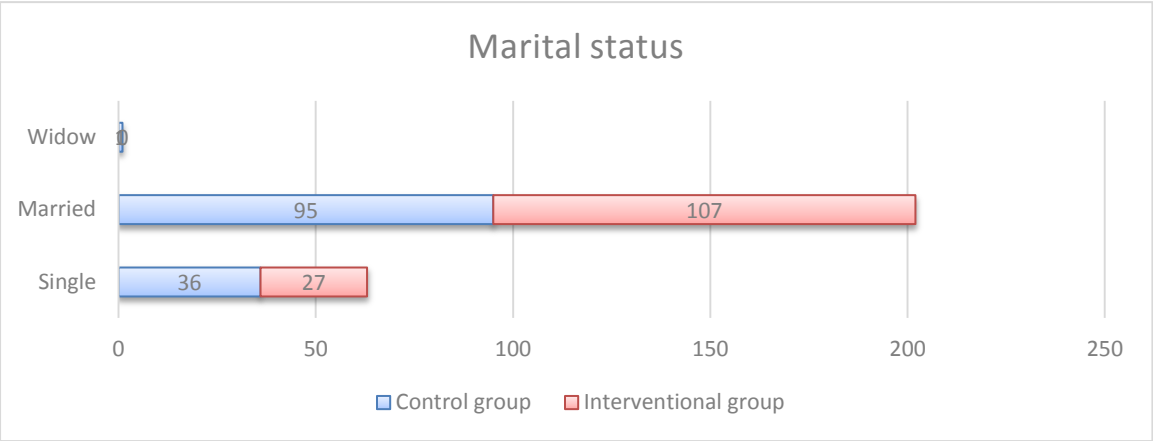
- The interpersonal relation of being married (75.9%) has increased risk of BPAD followed by singles and widow respectively. the statistical value suggested the equal distribution of the patients in both groups.

Table 4: Marital Status

Marital sta-tus	Control group	%	Interven-tional group	%	Total	Chi-square	p-Value
Single	36	27.27	27	20.15	63	2.9840	0.2250
Married	95	71.97	107	79.85	202		
Widow	1	0.76	0	0.00	1		

p<0.05*, p<0.01**, p<0.0001***

Figure 4: Marital Status



4.1.5 Socioeconomic Status:

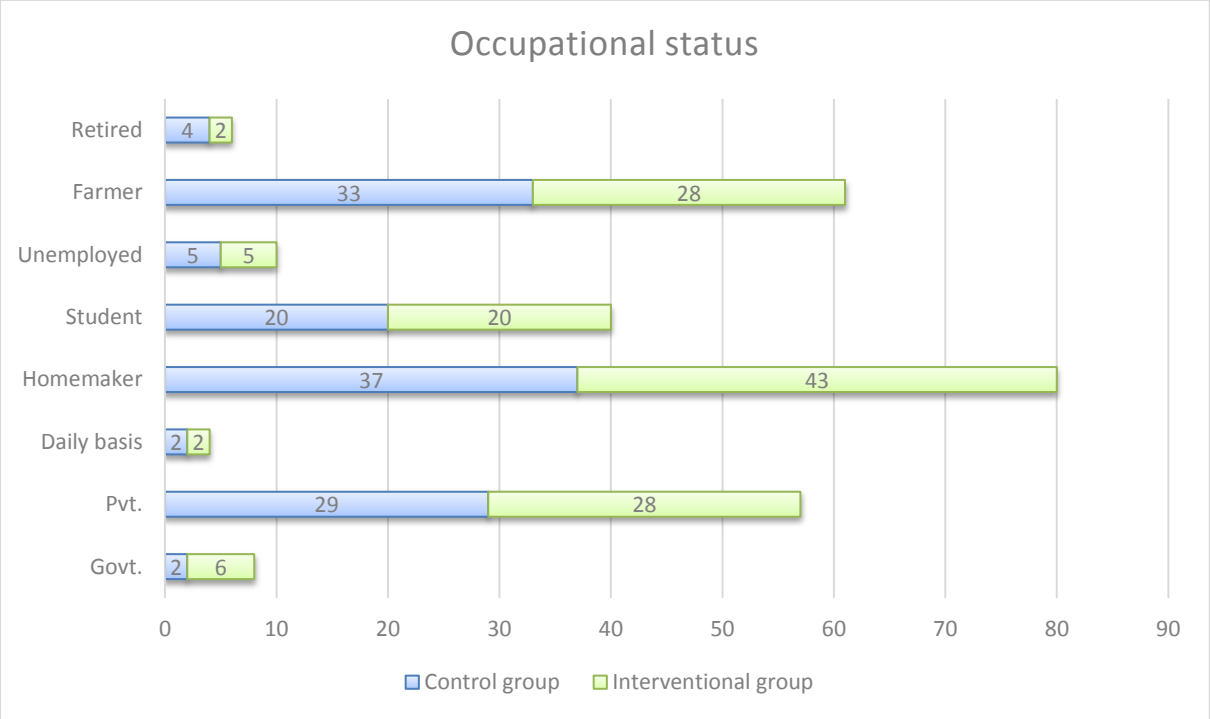
- As per the collected data, socioeconomic status reflects majorly bipolar condition primarily found in homemakers (30.0%) followed by farmer (22.9%) and 21.4% work on private sector. The participants, those who worked on government sector and retired patients reported less instead to others.

Table 5: Occupational Status of Patients.

Occupation	Control group	%	Interventional group	%	Total	Chi-square	p-Value
Govt.	2	1.52	6	4.48	8	3.5290	0.8320
Pvt.	29	21.97	28	20.90	57		
Daily basis	2	1.52	2	1.49	4		
Homemaker	37	28.03	43	32.09	80		
Student	20	15.15	20	14.93	40		
Unemployed	5	3.79	5	3.73	10		
Farmer	33	25.00	28	20.90	61		
Retired	4	3.03	2	1.49	6		

$p<0.05$*, $p<0.01$**, $p<0.0001$***

Figure 5: Occupational Status



4.1.6 Family History:

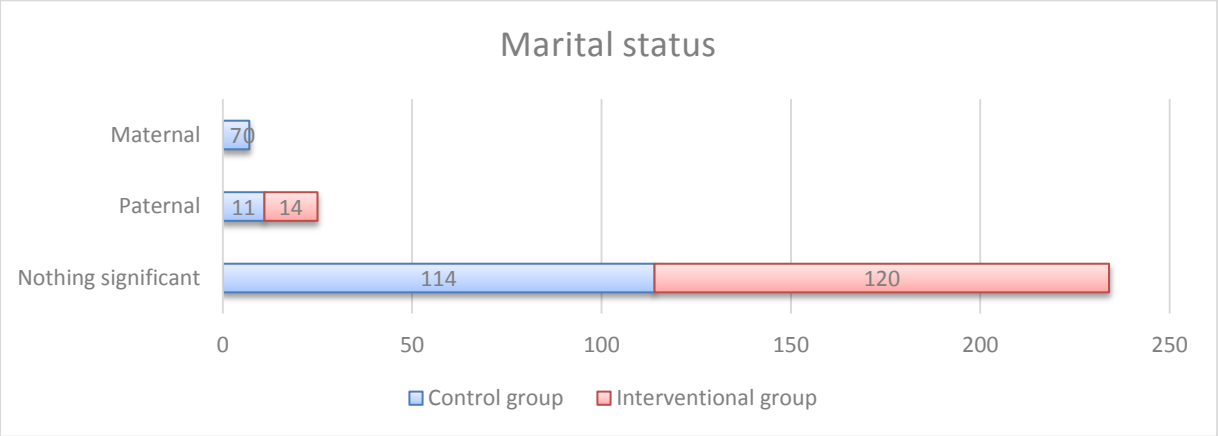
- Ideological factor is the one of the important consideration in case of BPAD because genetics and family history is the one of main cause of psychiatry illness, as per the collected data paternal family history denoted higher percentage (9.39%) in compare to maternal family history, but majority (87.9%) of patients population didn't reported any significant family history in both control and interventional group.

Table 6: Family History

Family history	Control group	%	Interventional group	%	Total	Chi-square	p-Value
Nothing significant	114	86.36	120	89.55	234	7.4990	0.024*
Paternal	11	8.33	14	10.45	25		
Maternal	7	5.30	0	0.00	7		

p<0.05*, p<0.01**, p<0.0001***

Figure 6: Family History



4.1.7 Childhood Adversity:

- The adversity in childhood was substantially absent followed by neglected attention from the family in the control and interventional group of the study.

Table 7: Childhood Adversity

Childhood Adversity	Control group	%	Interven-tional group	%	Total	Chi-square	p-Value
Neglect	9	6.82	12	8.96	21	3.4140	0.3320
Physical health	0	0.00	1	0.75	1		
Loss of par-ents	2	1.52	0	0.00	2		
Absent	121	91.67	121	90.30	242		

p<0.05*, p<0.01**, p<0.0001***

4.1.8 Smoking Habit:

- The majority of patients among both groups were non-smoker instead of smoker patients.

Table 8: Smoking Habit

Smoking habit	Control group	%	Interven-tional group	%	Total	Chi-square	p-Value
Yes	33	25.00	37	27.61	70	0.2340	0.6290
No	99	75.00	97	72.39	196		

p<0.05*, p<0.01**, p<0.0001***

4.1.9 Alcoholic

- The majority of patients among both groups were non-alcoholic instead of alcoholic patients.

Table 9: Alcoholism

Alcoholic	Control group	%	Interventional group	%	Total	Chi-square	p-Value
Yes	25	18.94	22	16.42	47	0.2910	0.5900
No	107	81.06	112	83.58	219		

p<0.05*, p<0.01**, p<0.0001***

4.1.10 Other Co-morbid Conditions:

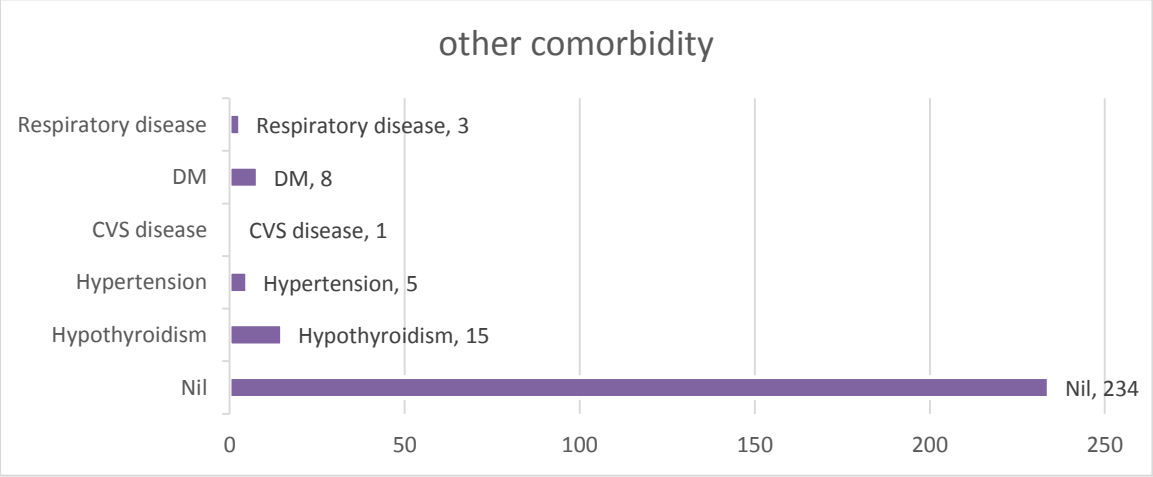
- The most common co-morbid condition was hypothyroidism followed by hypertension and DM.

Table 10: Other Co-morbid Condition of Patients.

Other Co-morbid Conditions	Control group	%	Interventional group	%	Total	Chi-square	p-Value
Nil	122	92.42	112	83.58	234	11.313	0.046*
Hypothyroidism	7	5.30	8	5.97	15		
Hypertension	0	0.00	5	3.73	5		
CFS disease	1	0.76	0	0.00	1		
DM	1	0.76	7	5.22	8		
Respiratory disease	1	0.76	2	1.49	3		

p<0.05*, p<0.01**, p<0.0001***

Figure 7: Other Co-morbid Conditions.



4.1.11 Medications:

The pharmacologic treatment may vary in BPAD, it is depending upon the condition of individuals (eg: acute mania, depression, maintenance and rapid cycle) and consist of monotherapy and combine therapy with Lithium, anticonvulsants, antipsychotic and antidepressants.

- In current study the most prescribed -medication for the patients was Lithium carbonate (77.4%). It is the potent mood stabilizer which is effecting in prevents the relapse of mania and depression from 40 to 61%. It is not a pharmaceutical per se but an alkali metal and monovalent cation that binds minimally to protein and does not undergo biotransformation. Lithium has a narrow therapeutic index, necessitating the need for close monitoring of serum levels in patients using the agent.
- Following the lithium, the antipsychotics were the second most consumed medication by the patients. Among them, the prescription of Olanzapine was 31.9%. it belongs from the Thienobenzodiazepine class. The exact mechanism of action by which olanzapine exerts its antipsychotic effect is unknown. However this effect may be mediated through combination of dopamine and serotonin 5-HT antagonism.
- The next highly prescribed antipsychotic was Quetiapine Fumrate 20.6% , which belong from the class of Dibenzothiazapine. The mechanism of action of this drug is still unknown, although it's believed that, the efficacy mood stabilization property is due to combine antagonism of dopamine and 5-HT receptor.
- Trifluoperazine HCl 13.9% was thirdly most prescribed antipsychotics, which is a phenothiazine neuroleptic. The exact mechanism of action of neuroleptics is unknown; however, it is known that these drugs block postsynaptic dopamine receptors in the hypothalamus, basal ganglia, limbic system, brainstem, and medulla. Phenothiazines bind avidly to both D1 and D2 receptors, whereas butyrophenones block mainly D2 receptors
- The next most prescribed antipsychotic was Risperidone 6.7% belongs from Benzisoxazole class. The mechanism by which Risperidone exerts its antipsychotic effect is unknown. Risperidone is a selective monoaminergic antagonist with a strong affinity for serotonin Type 2 (5-HT2) receptors and a slightly weaker affinity for dopamine Type 2 (D2) receptors. The antipsychotic activity of Risperidone may be mediated through antagonism at a combination of these receptor sites, particularly through blockade of cortical serotonin receptors and limbic dopamine systems.

- Under the antipsychotic the prescription of Haloperidol was 5.2%. Haloperidol is a butyrophenone antipsychotic whose mechanism of action is not clearly established
- Aripiprazole prescribed for 3.0% patients. it is an atypical antipsychotic agent that may exert its effects through partial agonist activity at dopamine D2 and serotonin 5-HT2(1A) receptors and antagonism of serotonin 5-HT2(2A) receptors
- Chlorpromazine HCl was the most leat prescribed antipsychotic for the 1.8% patients. is a dimethylamine derivative of phenothiazine which the exact mechanism of action is unknown. It is a psychotropic agent that produces sedative and antiemetic activities in the CNS, as well on other organ systems. It has weak anticholinergic and strong antiadrenergic activity and also possesses slight ganglionic, antihistaminic, and antiserotonin activity
- Antipsychotic medications are the most potent medication in the first line pharmacological treatment of the maniac and mixed episode. Basically it's preferred with the Lithium or Anticonvulsants.
- In the study the most common anticonvulsant used were Valproate Sodium 15.4% and Divalproex Sodium 10.5%. These both agents belong from the class of valproic acid. Which are used primarily to treat acute mania and for the maintenance prophylaxis. Anticonvulsive decrease the brain excitation and enhance inhibition by blocking low voltage sodium ion channel that than lower the level of glutamate and other excitatory amino acid.
- Lorazepam Intensol consumption was 23.3% in both group. This medication use as a antianxiety as well as anticonvulsive agent. Lorazepam Intensol bind to the GABA receptor and facilitate the action of GABA.
- Sertraline HCl was the most least (1.5%) consumed medication by the patients. This is used as an antidepressant agent comes under the class of Selective Serotonin Reuptake inhibitor (SSRI) which inhibits the CNS neuronal uptake of serotonin. Basically its use for major depressive disorder or panic attack.

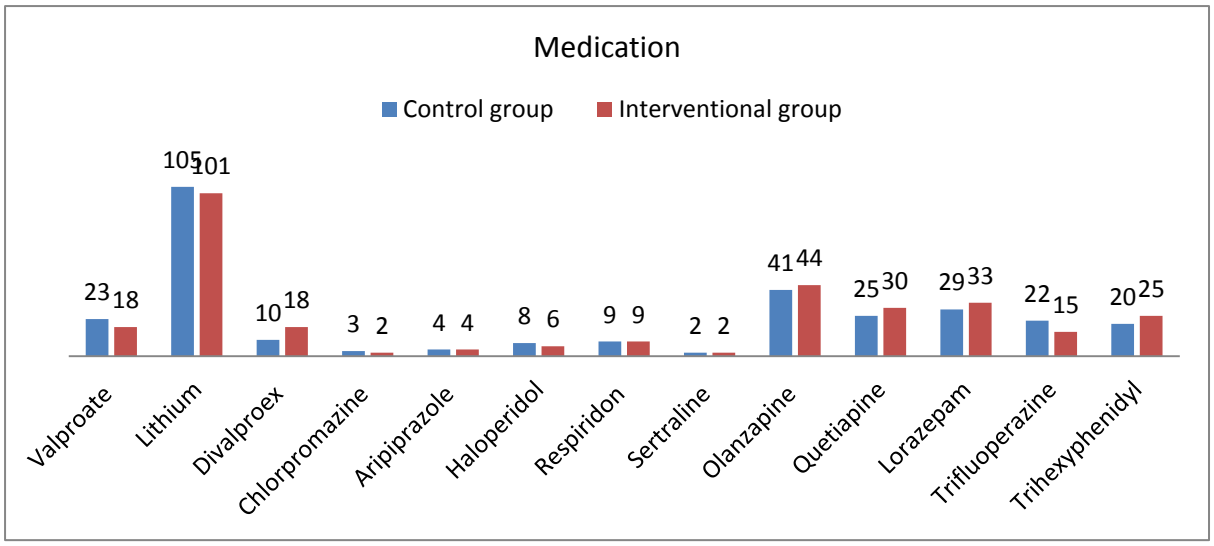
Table 11: Total Consumption of Medication.

Medications		**Con-trol group**	**%**	**Interven-tional group**	**%**	**To-tal**	**Chi-squar e**	**p-Value**
Valproate Sodium	Yes	23	17.42%	18	13.43%	41	0.8130	0.3670
	No	109	82.5%	116	86.57%	225		
Lithium Carbonate	Yes	105	79.55%	101	75.37%	206	0.6630	0.4160
	No	27	20.45%	33	24.63%	60		
Divalproex Sodium	Yes	10	7.58%	18	13.43%	28	2.4220	0.1200
	No	122	92.42%	116	86.57%	238		
Chlorprom-azine HCl	Yes	3	2.27%	2	1.49%	5	0.2190	0.6390
	No	129	97.73%	132	98.51%	261		
Aripiprazole	Yes	4	3.03%	4	2.99%	8	0.0000	0.9830
	No	128	96.97%	130	97.01%	258		
Haloperidol	Yes	8	6.06%	6	4.48%	14	0.3340	0.5630
	No	124	93.94%	128	95.52%	252		
Risperidone	Yes	9	6.82%	9	6.72%	18	0.0010	0.9740
	No	123	93.18%	125	93.28%	248		
Sertraline HCl	Yes	2	1.52%	2	1.49%	4	0.0000	0.9880
	No	130	98.48%	132	98.51%	262		
Olanzapine	Yes	41	31.06%	44	32.84%	85	0.0960	0.7560
	No	91	68.94%	90	67.16%	181		
Quetiapine Fumrate	Yes	25	18.94%	30	22.39%	55	0.4820	0.4870
	No	107	81.06%	104	77.61%	211		
Lorazepam Intensol	Yes	29	21.97%	33	24.63%	62	0.2630	0.6080
	No	103	78.03%	101	75.37%	204		
Trifluopera-	Yes	22	16.67%	15	11.19%	37	1.6630	0.1970

zine HCl	No	110	83.33%	119	88.81%	229		
Trihex-yphenidyl HCl	Yes	20	15.15%	25	18.66%	45	0.5810	0.4460
	No	112	84.85%	109	8.34%	221		

p<0.05*, p<0.01**, p<0.0001***

Figure 8: Total Consumption of Medication.



4.2 Medication Adherence:

- As per the obtained result from the study data, at the baseline level we didn't find any significant difference (U=8546.50, Z=-0.4742, *p*=0.635) in both groups the mean range in control group was 4.26±2.85 whereas the mean range in interventional group was 4.35±2.79. However, during the follow-up we assessed statistically significant improvement (p<0.0001) in the adherence of interventional group. At the final follow-up the mean adherence in control group was 4.25±1.78 whereas the mean adherence in interventional group was 1.95±1.29, which elaborate that, majority of patients from the interventional group shows mean increment in medication adherence from baseline to final follow-up (-2.40±1.84, *p*<0.001). As in our study "0= High Adherence, "1-2=Moderate Adherence" and >3 was low adherences, as per MMAS-8.

Table 12: Comparison of Control and Interventional Groups with Total Scores of Medication Adherence at Different Time Points by Mann-Whitney U Test.

Times	Control group			Interventional group			U-Value	Z-Value	*p*-Value
	Mean	SD	Mean rank	Mean	SD	Mean rank			
Baseline	4.26	2.85	131.25	4.35	2.79	135.72	8546.50	-0.4742	0.6353
Follow-up 1	4.08	2.53	156.95	2.77	1.69	110.40	5748.00	-4.9351	0.0001*
Follow-up 2	3.95	2.13	165.07	2.28	1.45	102.40	4676.50	-6.6431	0.0001*
Follow-up 3	4.22	1.93	173.14	2.19	1.37	94.45	3611.50	-8.3407	0.0001*
Follow-up 4	4.25	1.78	178.88	1.95	1.29	88.80	2854.00	-9.5482	0.0001*
BL to F1	-0.18	1.05	167.00	-1.58	1.54	100.50	4421.50	-7.0496	0.0001*
BL to F2	-0.30	2.01	165.84	-2.07	1.71	101.64	4575.00	-6.8049	0.0001*
BL to F3	-0.04	2.41	166.91	-2.16	1.76	100.59	4434.50	-7.0289	0.0001*
BL to F4	-0.01	2.69	168.13	-2.40	1.84	99.38	4272.50	-7.2871	0.0001*

p<0.05*, p<0.01**, p<0.0001***

Figure 09: Comparison of Control and Interventional Groups with Total Scores of Medication Adherence at Different Time Points.

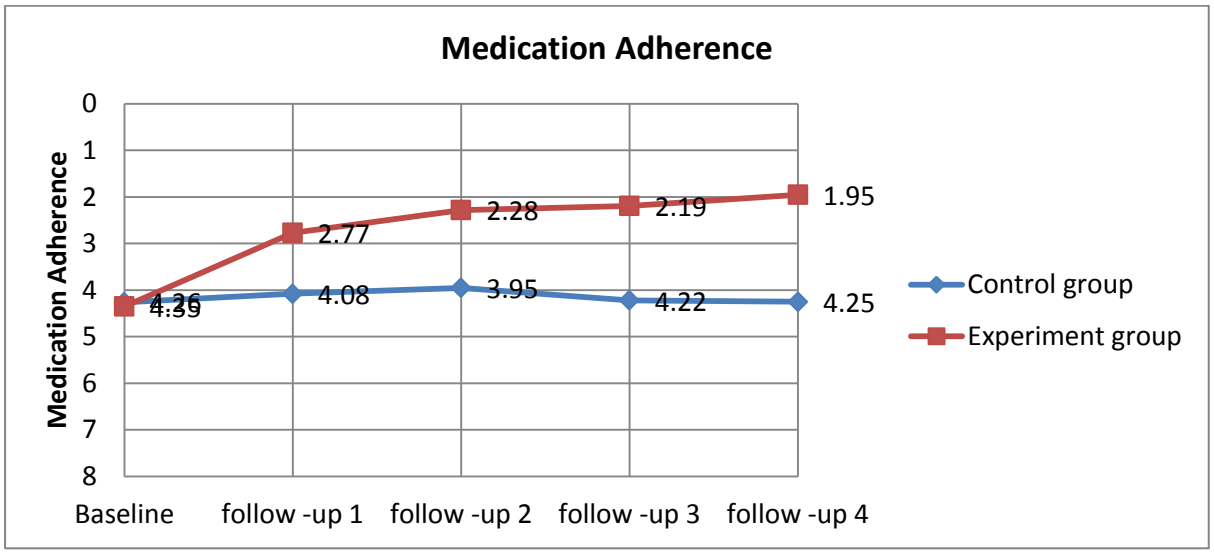


Table 13: **Comparison of Different Time Points with Total Follow-up Scores in Control and Interventional Groups by Wilcoxon Matched Pairs Test.**

Groups	Changes from	% of change	T-Value	Z-Value	P-Value
Control	BL to Follow-up 1	4.27	276.50	1.7944	0.0728
	BL to Follow-up 2	7.12	1195.00	1.8815	0.0599
	BL to Follow-up 3	0.89	2167.00	0.5883	0.5563
	BL to Follow-up 4	0.18	2734.50	0.3183	0.7502
Experiment	BL to Follow-up 1	36.36	24.50	7.7027	0.0001*
	BL to Follow-up 2	47.51	8.00	8.3884	0.0001*
	BL to Follow-up 3	49.74	7.00	8.4371	0.0001*
	BL to Follow-up 4	55.23	0.00	8.7249	0.0001*

$p<0.05$*, $p<0.01$**, $p<0.0001$***

- The percentage changes has been found clinically & statistically significant ($p<0.001$) in interventional group instead of control group which indicates that, clinical pharmacist intervention is effective for increasing the medication adherence of the patient. The percentage changes was quite higher at each follow-up in interventional group (Table no. 13)

Table 14: **Comparison of Control and Interventional Groups with the Status of Adherence at Different Time Points.**

Time points	Adherence	Control group	%	Interventional group	%	Total	Chi-square	p-Value
Baseline	High	22	16.67	14	10.45	36	3.0970	0.2130
	Medium	26	19.70	35	26.12	61		
	Low	84	63.64	85	63.43	169		
Follow-up 1	High	16	12.12	14	10.45	30	2.5610	0.2780
	Medium	29	21.97	41	30.60	70		
	Low	87	65.91	79	58.96	166		
Follow-up 2	High	13	9.85	21	15.67	34	19.8840	0.0001*
	Medium	18	13.64	45	33.58	63		
	Low	101	76.52	68	50.75	169		
Follow-up 3	High	7	5.30	21	15.67	28	32.1430	0.0001*
	Medium	18	13.64	49	36.57	67		
	Low	107	81.06	64	47.76	171		
Follow-up 4	High	4	3.03	25	18.66	29	49.3290	0.0001*
	Medium	21	15.91	56	41.79	77		
	Low	107	81.06	53	39.55	160		
	Total	132	100.00	134	100.00	266		

$p<0.05$*, $p<0.01$**, $p<0.0001$***

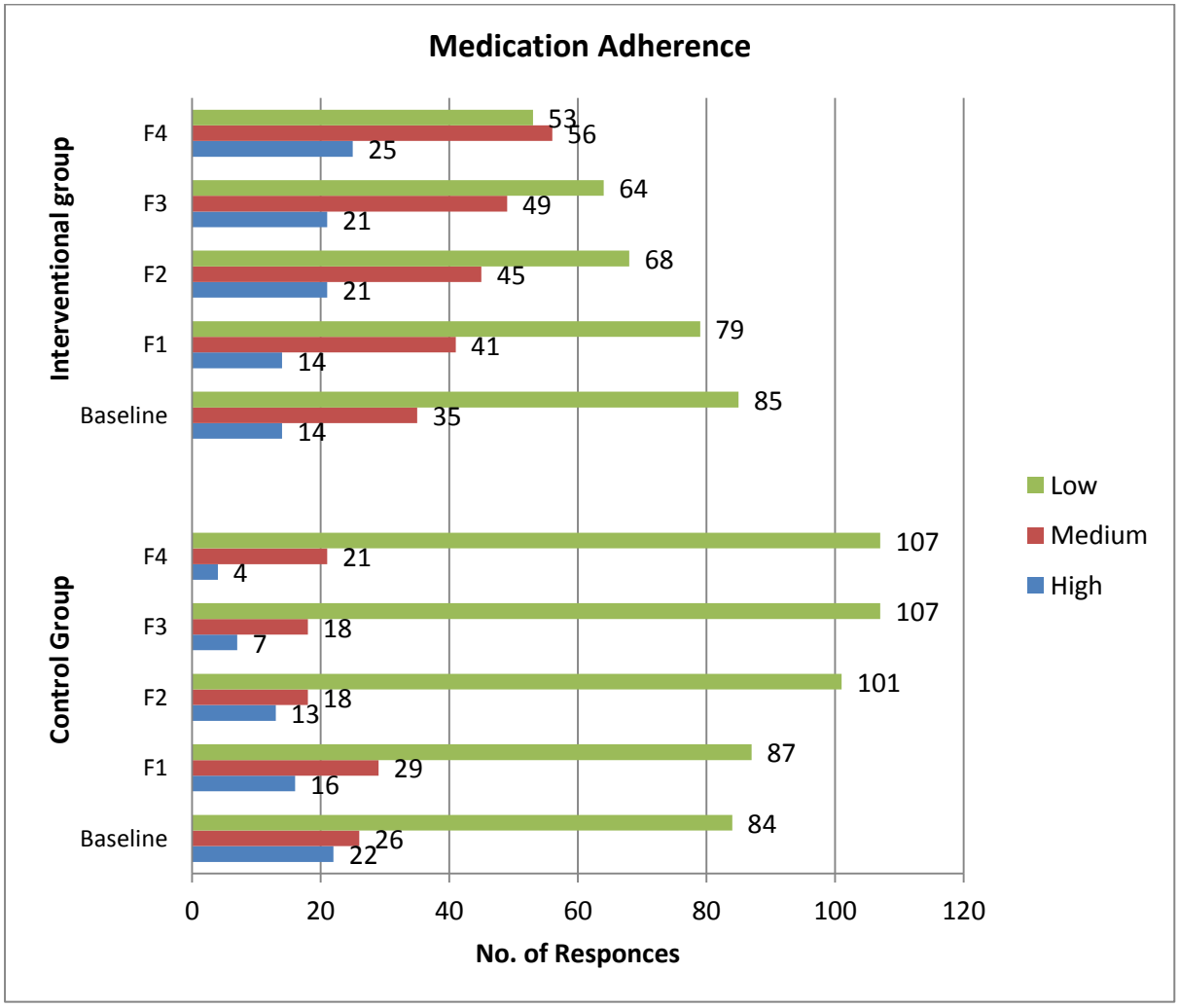
- As per the comparative matrix of high, medium and low adherence it was found that, at baseline level majority of patients from both control group and interventional group showed low adherence 63.64% and 63.43% reactively, whereas 16.67% patient from control group and 10.45% patients from the interventional group showed high adherence, which didn't show any significant difference ($p=0.213$) in both groups. At the final follow-up, in control group 81.06 % patients showed low adherence whereas, in interventional group only 39.55 % patients showed low adherence. The percentage increment of high adherence has been observed in interventional group from baseline (10.45%) to final follow-up (18.66%). which is shows that, 8.21% patients moved to high adherence and 15.67% patients moved to medium adherence from baseline to final follow-up in interventional group.

Table 15: **Comparison of Different Time Points with the Status of Adherence in Control and Interventional Groups by Wilcoxon Matched Pairs Test.**

Groups	Changes from	% of change	T-Value	Z-Value	P-Value
Control	BL to Follow-up 1	-2.76	6.00	2.4006	0.0164*
	BL to Follow-up 2	-7.98	0.00	4.1069	0.0001*
	BL to Follow-up 3	-11.66	37.50	4.4451	0.0001*
	BL to Follow-up 4	-12.58	119.00	4.3880	0.0001*
Experiment	BL to Follow-up 1	1.77	4.50	1.8904	0.0587
	BL to Follow-up 2	7.08	13.50	4.1145	0.0001*
	BL to Follow-up 3	8.26	15.50	4.4633	0.0001*
	BL to Follow-up 4	12.68	0.00	5.6454	0.0001*

p<0.05*, p<0.01**, p<0.0001***

Figure 10: Comparison of Control and Interventional Groups with the Status of Adherence at Different Time Points.



Q1. Do you sometimes forget to take your medicine?

- The medication adherence related to question 1 said, at baseline level there were no difference in both of group (p=0.524) whereas the high clinical as well as statistical significance (p<0.001***) from follow-up 1 to follow-up 4 in the Interventional group.

Table 16: Comparison of ***Do You Sometimes Forget To Take Your Medicine?*** In Both Group.

Items	Option	Control group	%	Interventional group	%	Total	Chi-square	p-Value
Baseline	Yes	78	59.09	74	55.22	152	0.4060	0.5240
	No	54	40.91	60	44.78	114		
Follow-up 1	Yes	75	56.82	50	37.31	125	10.156	0.0010*
	No	57	43.18	84	62.69	141		
Follow-up 2	Yes	67	50.76	40	29.85	107	12.088	0.0010*
	No	65	49.24	94	70.15	159		
Follow-up 3	Yes	68	51.52	40	29.85	108	12.941	0.0001*
	No	64	48.48	94	70.15	158		
Follow-up 4	Yes	67	50.76	34	25.37	101	18.192	0.0001*
	No	65	49.24	100	74.63	165		

p<0.05*, p<0.01**, p<0.0001***

Figure 11: Comparison of ***Do You Sometimes Forget To Take Your Medicine****?* In Both Group.

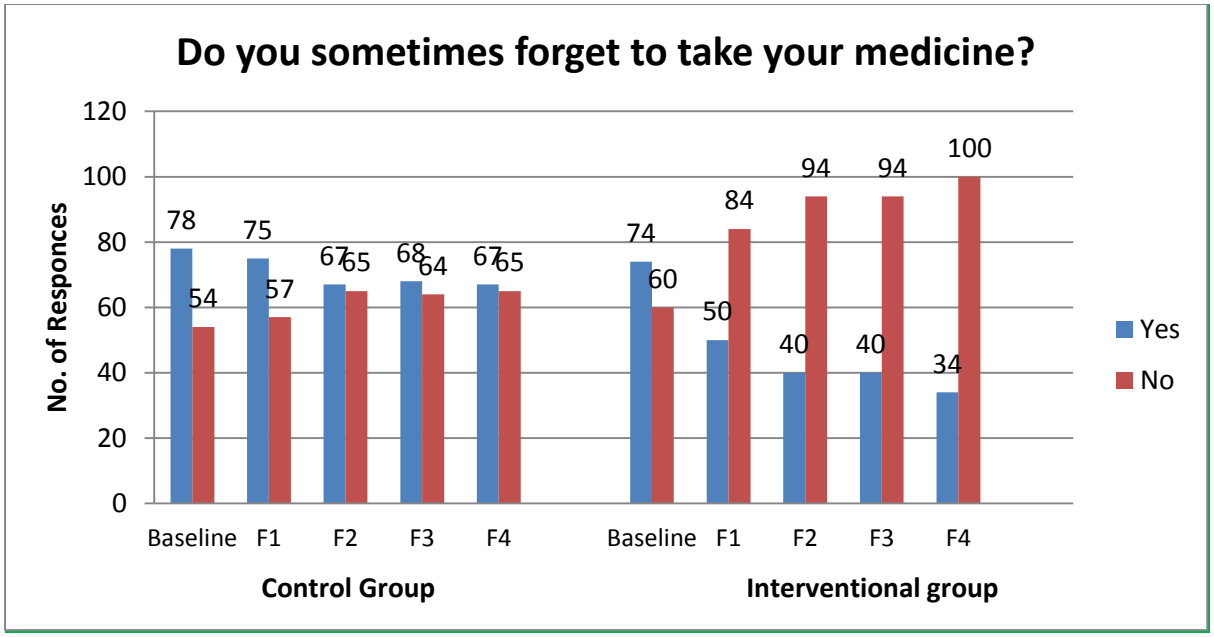


Table 17: Comparison of Different Time Points with **Do you sometimes forget to take your medicine?** In Control and Interventional Groups by Wilcoxon Matched Pairs Test

Groups	Changes from	T-Value	Z-Value	P-Value
Control	BL to Follow-up 1	8.00	1.0142	0.3105
	BL to Follow-up 2	27.00	2.3432	0.0191*
	BL to Follow-up 3	87.50	1.7857	0.0742
	BL to Follow-up 4	135.00	1.7839	0.0744
Experiment	BL to Follow-up 1	66.00	3.7024	0.0002*
	BL to Follow-up 2	86.00	4.5701	0.0001*
	BL to Follow-up 3	86.00	4.5701	0.0001*
	BL to Follow-up 4	98.00	5.0257	0.0001*

$p<0.05$*, $p<0.01$**, $p<0.0001$***

- The significant percentage improvement ($P<0.001$) has been seen in the interventional group at different time points. The same changes we observed at control group at comparison of baseline to second follow-up ($p<0.01$*).

Q2. Thinking over last the past 2 week, were there any days when you didn't take your medication?

- The question two, interprets adherence was statistically significant in follow-up 2 ($p<0.03$*) whereas, from follow-up 3 to follow-up 4 highly statistical and clinical significance ($p<0.001$) was observed in interventional group. But during second follow-up we didn't find any significant difference in both of group ($p=0.17$). The Interventional group portrays significant improvement in the results.

Table 18: Comparison of ***Thinking Over Last The Past 2 Week, Were There Any Days When You Didn't Take Your Medication?*** In Both Group.

Items	Option	Control group	%	Interventional group	%	Total	Chi-square	p-Value
Baseline	Yes	60	45.45	74	55.22	134	2.5390	0.1110
	No	72	54.55	60	44.78	132		
Follow-up 1	Yes	57	43.18	47	35.07	104	1.8350	0.1750
	No	75	56.82	87	64.93	162		
Follow-up 2	Yes	54	40.91	38	28.36	92	4.6300	0.0310*
	No	78	59.09	96	71.64	174		

Follow-up 3	Yes	62	46.97	35	26.12	97	12.4770	0.0001*
	No	70	53.03	99	73.88	169		
Follow-up 4	Yes	61	46.21	28	20.90	89	19.1430	0.0001*
	No	71	53.79	106	79.10	177		

p<0.05*, p<0.01**, p<0.0001***

Figure 12: Comparison of ***Thinking over last the past 2 week, were there any days when you didn't take your medication?*** In both group.

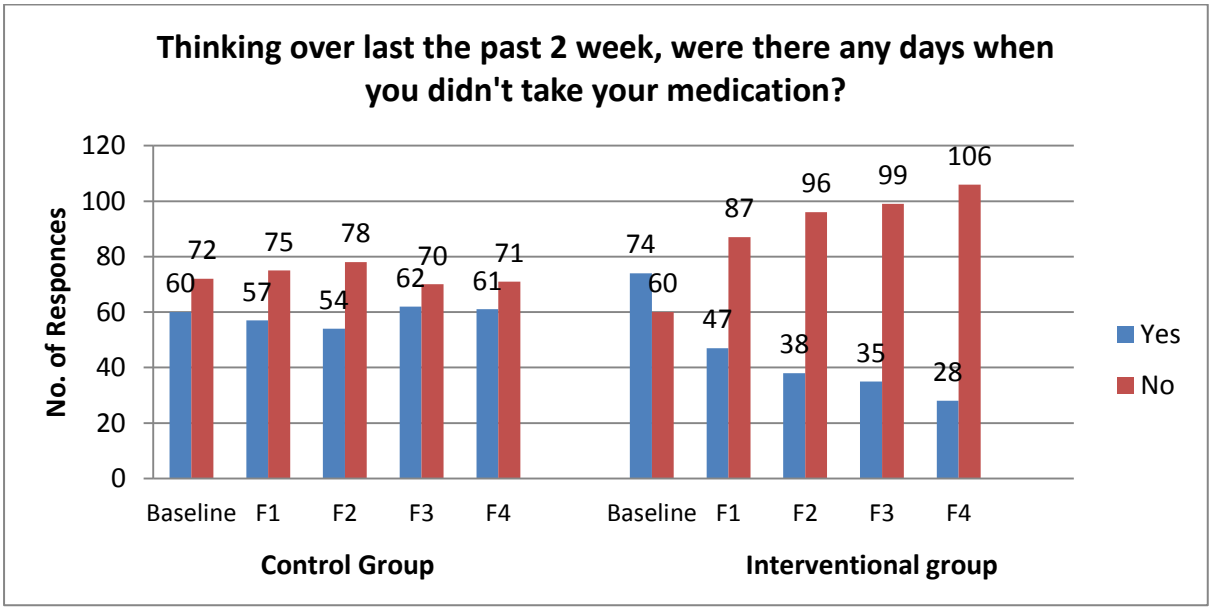


Table 19: Comparison of different time points with ***Thinking over last the past 2 week, were there any days when you didn't take your medication?*** In Control and Interventional Groups by Wilcoxon Matched Pairs Test

Groups	Changes from	T-Value	Z-Value	P-Value
Control	BL to Follow-up 1	3.00	1.2136	0.2249
	BL to Follow-up 2	92.00	1.1201	0.2627
	BL to Follow-up 3	188.50	0.3302	0.7413
	BL to Follow-up 4	342.00	0.1433	0.8860
Experiment	BL to Follow-up 1	15.00	4.3787	0.0001*
	BL to Follow-up 2	19.50	5.0903	0.0001*
	BL to Follow-up 3	21.00	5.3064	0.0001*
	BL to Follow-up 4	0.00	5.9052	0.0001*

p<0.05*, p<0.01**, p<0.0001***

Q3. Have you ever cut back or stooped your medication without telling your doctor because you felt worse?

- The obtained result said, at baseline level there were no significant difference observed (p=0.054). Whereas, during the follow-up at different time points we observed clinically & statistically improvement (p<0.001) in interventional group.

Table 20: Comparison of ***Have You Ever Cut Back Or Stooped Your Medication Without Telling Your Doctor Because You Felt Worse?*** In Both Group.

Items	Option	Control group	%	Interventional group	%	Total	Chi-square	p-Value
Baseline	Yes	68	51.52	64	47.76	132	0.3750	0.5400
	No	64	48.48	70	52.24	134		
Follow-up 1	Yes	61	46.21	35	26.12	96	11.6390	0.0010*
	No	71	53.79	99	73.88	170		
Follow-up 2	Yes	63	47.73	31	23.13	94	17.6010	0.0001*
	No	69	52.27	103	76.87	172		
Follow-up 3	Yes	68	51.52	27	20.15	95	28.4940	0.0001*
	No	64	48.48	107	79.85	171		
Follow-up 4	Yes	69	52.27	21	15.67	90	39.7920	0.0001*
	No	63	47.73	113	84.33	176		

p<0.05*, p<0.01**, p<0.0001***

Figure 13 Comparison of ***Have You Ever Cut Back or Stooped Your Medication Without Telling Your Doctor Because You Felt Worse?*** In Both Groups.

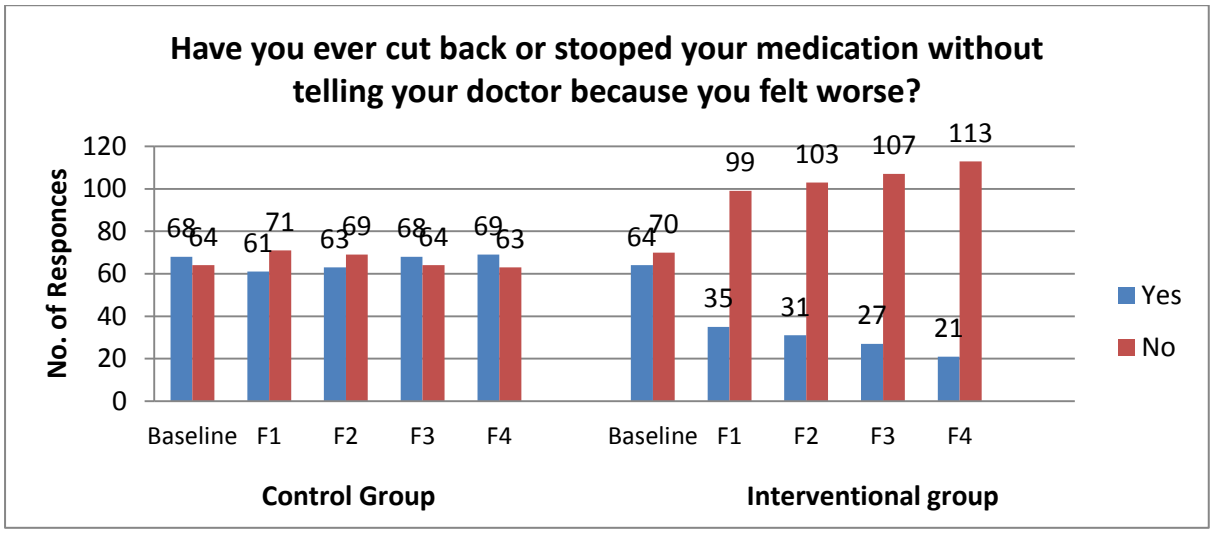


Table 21: Comparison of Different Time Points With ***Have You Ever Cut Back or Stooped Your Medication Without Telling Your Doctor Because You Felt Worse****?* In Control and Interventional Groups by Wilcoxon Matched Pairs Test

Groups	Changes from	T-Value	Z-Value	P-Value
Control	BL to Follow-up 1	5.00	2.0732	0.0382*
	BL to Follow-up 2	154.00	0.8409	0.4004
	BL to Follow-up 3	410.00	0.0001*	1.0000
	BL to Follow-up 4	552.00	0.1270	0.8990
Experiment	BL to Follow-up 1	34.00	4.4044	0.0001*
	BL to Follow-up 2	38.00	4.7296	0.0001*
	BL to Follow-up 3	42.00	5.0343	0.0001*
	BL to Follow-up 4	23.00	5.5817	0.0001*

$p<0.05$*, $p<0.01$**, $p<0.0001$***

- In control group, at baseline to follow-up 1 we observed little significance changes ($p=0.038$), whereas in interventional group we observed clinically & statistically improvement ($p<0.001$).

Q4. When you travel or leave home, do you sometime forget to bring along your medication?

- At baseline level there were no significant difference observed ($p=0.4500$). Whereas, during the first follow-up we observed significant improvement ($p=0.003$*) and from the second follow-up to last follow-up we found high clinically & statistically improvement ($p<0.001$) in interventional group.

Table 22: Comparison of ***When You Travel or Leave Home, Do You Sometimes Forget to Bring Along Your Medication?*** In Both Group.

Items	Option	Control group	%	Interventional group	%	Total	Chi-square	p-Value
Baseline	Yes	77	58.33	72	53.73	149	0.5720	0.4500
	No	55	41.67	62	46.27	117		
Follow-up 1	Yes	70	53.03	47	35.07	117	8.7010	0.0030*
	No	62	46.97	87	64.93	149		
Follow-up 2	Yes	67	50.76	36	26.87	103	15.9970	0.0001*
	No	65	49.24	98	73.13	163		

Follow-up 3	Yes	69	52.27	33	24.63	102	21.4970	0.0001*
	No	63	47.73	101	75.37	164		
Follow-up 4	Yes	68	51.52	32	23.88	100	21.6450	0.0001*
	No	64	48.48	102	76.12	166		

p<0.05*, p<0.01**, p<0.0001***

Figure 14: Comparison Of ***When You Travel Or Leave Home, Do You Sometimes Forget To Bring Along Your Medication?*** In Both Group.

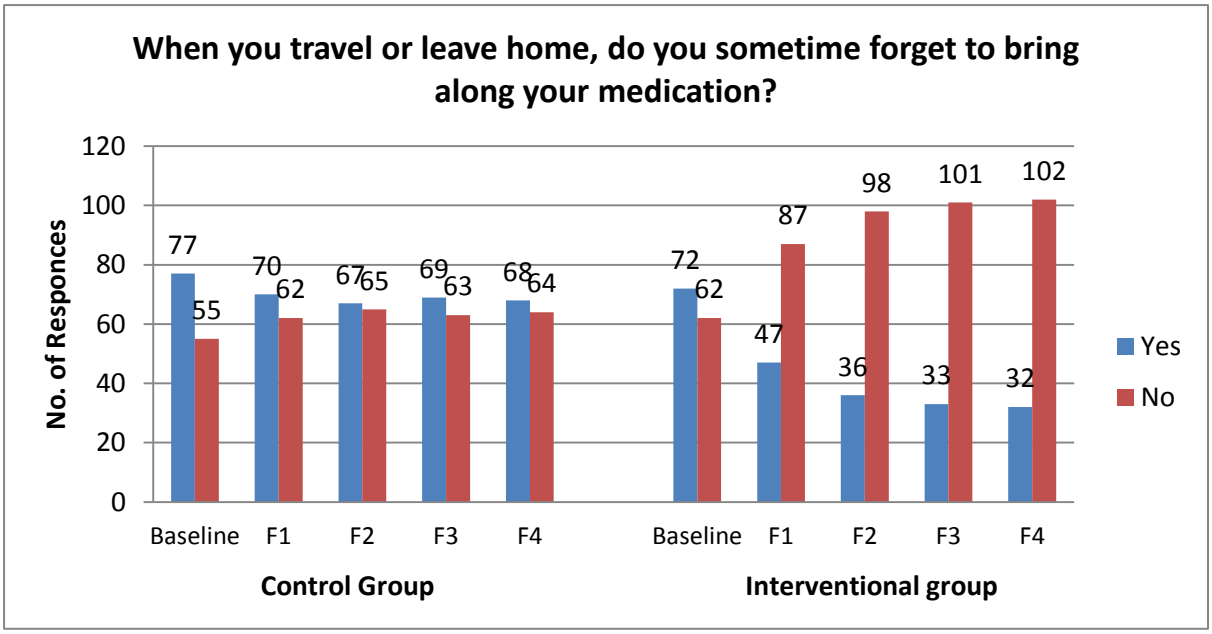


Table 23: Comparison Of **Different Time Points With When You Travel Or Leave Home, Do You Sometimes Forget To Bring Along Your Medication?** In Control and Interventional Groups by Wilcoxon Matched Pairs Test

Groups	Changes from	T-Value	Z-Value	P-Value
Control	BL to Follow-up 1	5.00	2.0732	0.0382
	BL to Follow-up 2	181.50	1.5427	0.1229
	BL to Follow-up 3	292.50	1.1312	0.2580
	BL to Follow-up 4	336.00	1.2246	0.2207
Experiment	BL to Follow-up 1	14.00	4.2044	0.0001*
	BL to Follow-up 2	0.00	5.2316	0.0001*
	BL to Follow-up 3	0.00	5.4424	0.0001*
	BL to Follow-up 4	0.00	5.5109	0.0001*

p<0.05*, p<0.01**, p<0.0001***

Q5. Did you take all your medicines yesterday?

- In current study, at baseline level there were no significant difference observed (p=0.1750). Whereas, during the first follow-up we observed significant improvement (p=0.013*) and from the second follow-up to last follow-up we found high clinically & statistically improvement (p<0.001) in interventional group.

Table 24: Comparison Of ***Did You Take All Your Medicines Yesterday?*** In Both Group

Items	Option	Control group	%	Interven-tional group	%	Total	Chi-square	p-Value
Baseline	Yes	57	43.18	69	51.49	126	1.8420	0.1750
	No	75	56.82	65	48.51	140		
Follow-up 1	Yes	60	45.45	41	30.60	101	6.2320	0.0130*
	No	72	54.55	93	69.40	165		
Follow-up 2	Yes	58	43.94	30	22.39	88	13.9510	0.0001*
	No	74	56.06	104	77.61	178		
Follow-up 3	Yes	60	45.45	27	20.15	87	19.3470	0.0001*
	No	72	54.55	107	79.85	179		
Follow-up 4	Yes	59	44.70	21	15.67	80	26.6390	0.0001*
	No	73	55.30	113	84.33	186		

p<0.05*, p<0.01**, p<0.0001***

Figure 15: Comparison Of ***Did You Take All Your Medicines Yesterday?*** In Both Group

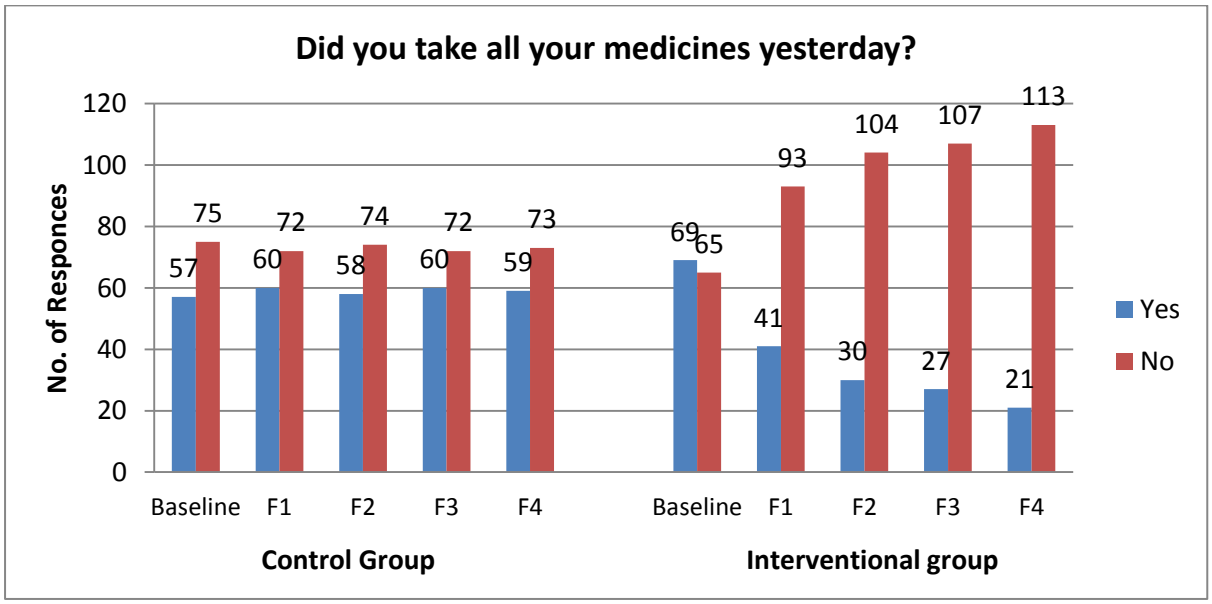


Table 25: Comparison of Different Time Points with **Did You Take All Your Medicines Yesterday?** In Control and Interventional Groups by Wilcoxon Matched Pairs Test.

Groups	Changes from	T-Value	Z-Value	P-Value
Control	BL to Follow-up 1	24.00	0.8002	0.4236
	BL to Follow-up 2	272.00	0.1519	0.8793
	BL to Follow-up 3	360.00	0.4186	0.6755
	BL to Follow-up 4	472.50	0.2626	0.7929
Experiment	BL to Follow-up 1	15.50	4.4633	0.0001*
	BL to Follow-up 2	0.00	5.4424	0.0001*
	BL to Follow-up 3	0.00	5.6454	0.0001*
	BL to Follow-up 4	0.00	6.0308	0.0001*

p<0.05*, p<0.01**, p<0.0001***

Q6. When you feel like your symptoms are under control, do you sometimes stop taking your medicine?

- On the assessment of question six of MMAS-8, at baseline level there were no significant difference observed (p=0.6300). Whereas, during the first follow-up we observed significant improvement (p=0.0070*) and from the second follow-up to last follow-up we found high clinically & statistically improvement (p<0.001) in interventional group.

Table 26: Comparison Of ***When You Feel Like Your Symptoms Are Under Control, Do You Sometimes Stop Taking Your Medicine?*** In Both Group

Items	Option	Control group	%	Interven-tional group	%	Total	Chi-square	p-Value
Baseline	Yes	70	53.03	75	55.97	145	0.2320	0.6300
	No	62	46.97	59	44.03	121		
Follow-up 1	Yes	68	51.52	47	35.07	115	7.3230	0.0070*
	No	64	48.48	87	64.93	151		
Follow-up 2	Yes	66	50.00	37	27.61	103	14.0470	0.0001*
	No	66	50.00	97	72.39	163		
Follow-up 3	Yes	75	56.82	37	27.61	112	23.2690	0.0001*
	No	57	43.18	97	72.39	154		
Follow-up 4	Yes	70	53.03	35	26.12	105	20.1560	0.0001*
	No	62	46.97	99	73.88	161		

p<0.05*, p<0.01**, p<0.0001***

Figure 16: Comparison Of ***When You Feel Like Your Symptoms Are Under Control, Do You Sometimes Stop Taking Your Medicine?*** In Both Group

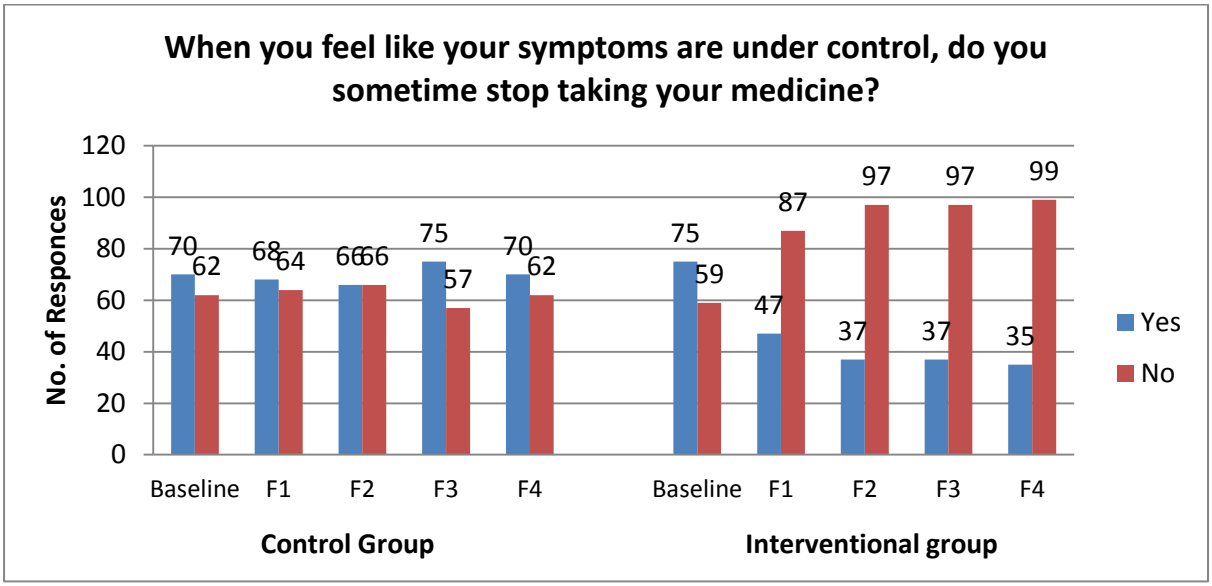


Table 27: Comparison Of Different Time Points With **When You Feel Like Your Symptoms Are Under Control, Do You Sometimes Stop Taking Your Medicine?** In Control and Interventional Groups by Wilcoxon Matched Pairs Test

Groups	Changes from	T-Value	Z-Value	P-Value
Control	BL to Follow-up 1	22.00	0.5606	0.5751
	BL to Follow-up 2	84.00	0.7840	0.4331
	BL to Follow-up 3	208.00	0.7839	0.4331
	BL to Follow-up 4	264.00	0.0001*	1.0000
Experiment	BL to Follow-up 1	0.00	4.6226	0.0001*
	BL to Follow-up 2	0.00	5.3731	0.0001*
	BL to Follow-up 3	0.00	5.3731	0.0001*
	BL to Follow-up 4	0.00	5.5109	0.0001*

$p<0.05$*, $p<0.01$**, $p<0.0001$***

Q7. Taking medication is an inconvenience for some people. Do you ever feel hassled about sticking to your treatment plan?

- Question 7 presented no statistical significance at baseline level (p=0.797). During the follow-up 1 (p=0.005) and follow-up 2 (p=0.002) found clinical and statistical significance. Follow-up 3 and follow-up 4 noted highly clinical and statistical significance ($p<0.0001$). The experimental showed improved results compared to the control group.

Table 28: Comparison Of ***Taking Medication Is An Inconvenience For Some People. Do You Ever Feel Hassled About Sticking To Your Treatment Plan?*** In Both Group

Items	Option	Control group	%	Interven-tional group	%	Total	Chi-square	p-Value
Baseline	Yes	73	55.30	72	53.73	145	0.0660	0.7970
	No	59	44.70	62	46.27	121		
Follow-up 1	Yes	67	50.76	45	33.58	112	8.0470	0.0050*
	No	65	49.24	89	66.42	154		
Follow-up 2	Yes	62	46.97	38	28.36	100	9.8180	0.0020*
	No	70	53.03	96	71.64	166		
Follow-up 3	Yes	65	49.24	37	27.61	102	13.1600	0.0001*
	No	67	50.76	97	72.39	164		
Follow-up 4	Yes	64	48.48	35	26.12	99	14.2350	0.0001*
	No	68	51.52	99	73.88	167		

p<0.05*, p<0.01**, p<0.0001***

Figure 17: Comparison Of ***Taking Medication Is An Inconvenience For Some People. Do You Ever Feel Hassled About Sticking To Your Treatment Plan?*** In Both Group

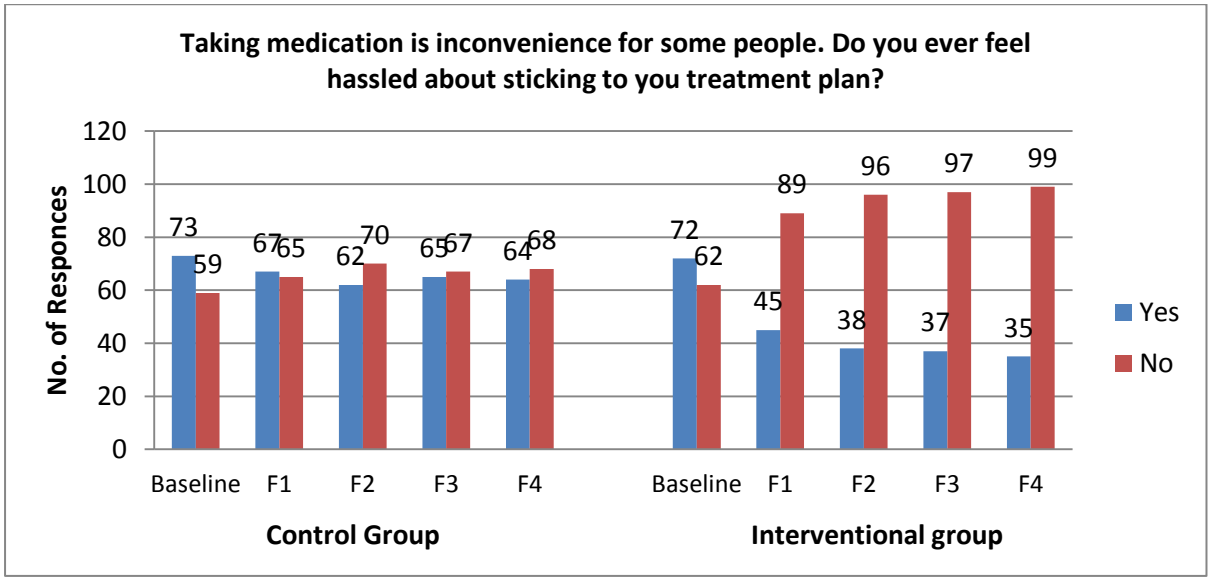


Table 29: Comparison Of Different Time Points With **Taking Medication Is An Inconvenience For Some People. Do You Ever Feel Hassled About Sticking To Your Treatment Plan**? In Control and Interventional Groups by Wilcoxon Matched Pairs Test

Groups	Changes from	T-Value	Z-Value	P-Value
Control	BL to Follow-up 1	19.50	1.5297	0.1261
	BL to Follow-up 2	40.00	2.2133	0.0269

	BL to Follow-up 3	100.00	1.4286	0.1531
	BL to Follow-up 4	150.00	1.4596	0.1444
Experiment	BL to Follow-up 1	32.00	4.2329	0.0001*
	BL to Follow-up 2	39.00	4.8075	0.0001*
	BL to Follow-up 3	40.00	4.8842	0.0001*
	BL to Follow-up 4	42.00	5.0343	0.0001*

$p<0.05$*, $p<0.01$**, $p<0.0001$***

Q8. How often do you have difficulty remembering to take all your medicine?

- As per the data of question 8 of MMAS-8, at baseline level (p=0.6650) to follow-up 1(p=0.261) and follow-up 2 (p=0.072) we didn't found significant difference. Whereas, during the third follow-up we observed significant improvement (p=0.012*) and at the last follow-up we found high clinically & statistically improvement (p<0.001) in interventional group.

Table 30: Comparison Of ***How Often Do You Have Difficulty Remembering To Take All Your Medicine?*** In Both of Group.

Items	**Option**	**Control group**	**%**	**Interventional group**	**%**	**Total**	**Chi-square**	**p-Value**
Baseline	Never/rarely	58	43.94	52	38.81	110	2.3850	0.6650
	Once in a while	23	17.42	32	23.88	55		
	Sometimes	16	12.12	17	12.69	33		
	Usually	20	15.15	16	11.94	36		
	All the time	15	11.36	17	12.69	32		
Follow-up 1	Never/rarely	52	39.39	69	51.49	121	5.2670	0.2610
	Once in a while	26	19.70	20	14.93	46		
	Sometimes	20	15.15	15	11.19	35		
	Usually	17	12.88	11	8.21	28		
	All the time	17	12.88	19	14.18	36		
Follow-up 2	Never/rarely	47	35.61	70	52.24	117	8.5880	0.0720
	Once in a while	27	20.45	19	14.18	46		
	Sometimes	21	15.91	15	11.19	36		
	Usually	18	13.64	11	8.21	29		
	All the time	19	14.39	19	14.18	38		
Follow-up 3	Never/rarely	42	31.82	70	52.24	112	12.8520	0.0120*

	Once in a while	27	20.45	19	14.18	46		
	Sometimes	22	16.67	15	11.19	37		
	Usually	21	15.91	11	8.21	32		
	All the time	20	15.15	19	14.18	39		
Follow-up 4	Never/rarely	34	25.76	72	53.73	106	23.1520	0.0001*
	Once in a while	30	22.73	18	13.43	48		
	Sometimes	24	18.18	15	11.19	39		
	Usually	23	17.42	11	8.21	34		
	All the time	21	15.91	18	13.43	39		

p<0.05*, p<0.01**, p<0.0001***

Figure 18: Comparison of ***How Often Do You Have Difficulty Remembering To Take All Your Medicine?*** In Both of Group.

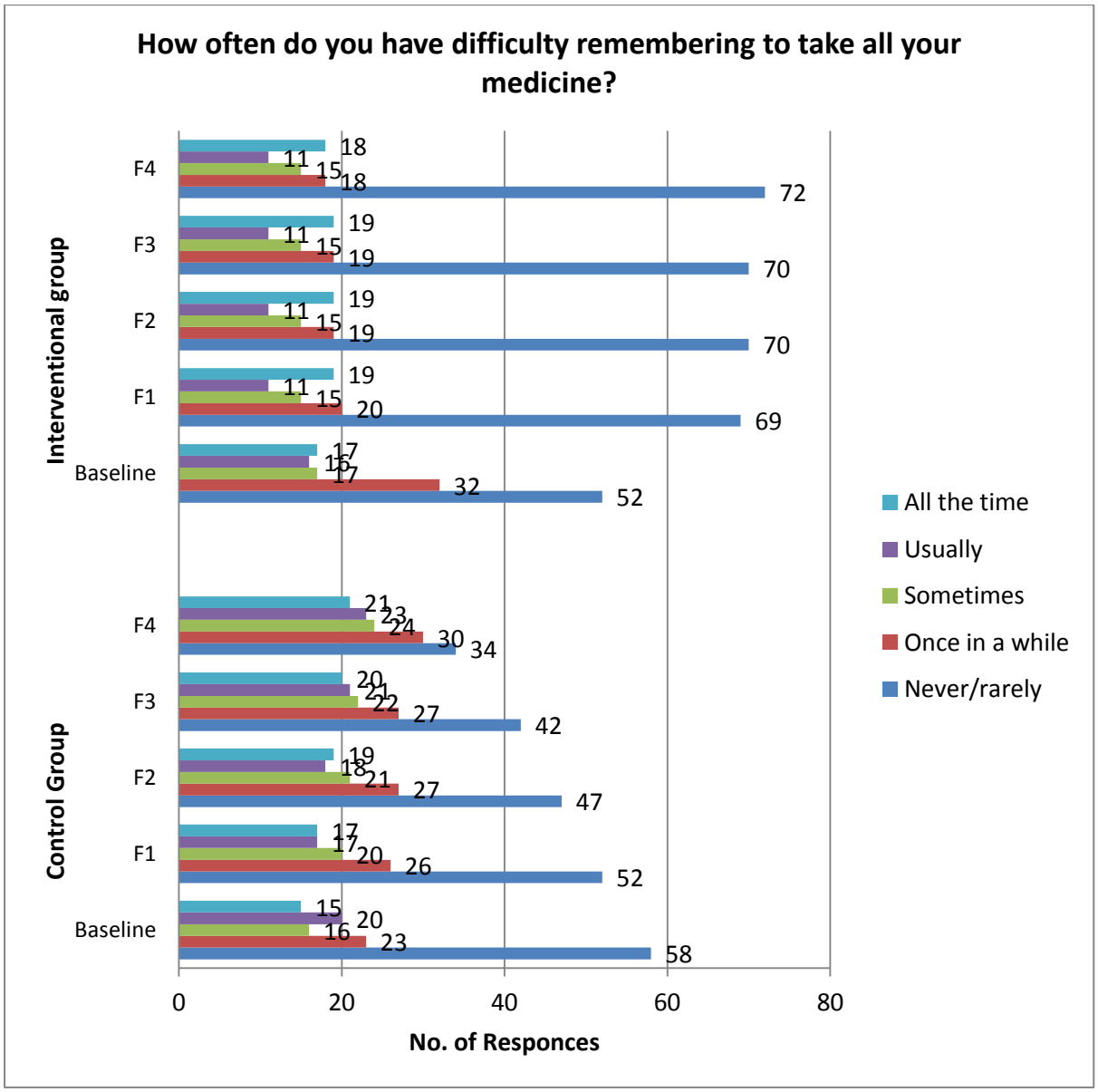


Table 31: Comparison Of Different Time Points With **How Often Do You Have Difficulty Remembering To Take All Your Medicine**? In Control and Interventional Groups by Wilcoxon Matched Pairs Test

Groups	Changes from	% of change	T-Value	Z-Value	P-Value
Control	BL to Follow-up 1	-3.26	75.50	0.7847	0.4326
	BL to Follow-up 2	-7.82	110.00	1.6636	0.0962
	BL to Follow-up 3	-12.70	123.00	2.4496	0.0143*
	BL to Follow-up 4	-18.24	130.00	3.3416	0.0008*
Experiment	BL to Follow-up 1	7.28	221.00	1.7596	0.0785
	BL to Follow-up 2	7.59	229.50	1.8405	0.0657
	BL to Follow-up 3	7.59	229.50	1.8405	0.0657
	BL to Follow-up 4	9.18	239.00	2.1072	0.0351*

$p<0.05$*, $p<0.01$**, $p<0.0001$***

4.3 Health-related quality of life (HR-QOL):

Table 32: **Normality of QOL With its Domain Scores in Two Groups At Different Time Points By Kolmogorov Smirnov Test.**

Variables	Time points	Control group		Interventional group	
		Z-Value	p-Value	Z-Value	p-Value
Physical health	Baseline	1.9190	0.0010*	2.0430	0.0001*
	Follow-up 1	2.4650	0.0001*	2.5390	0.0001*
	Follow-up 2	2.1430	0.0001*	2.4890	0.0001*
	Follow-up 3	2.0540	0.0001*	2.3790	0.0001*
	Follow-up 4	2.1530	0.0001*	2.5970	0.0001*
Psychological health	Baseline	2.4200	0.0001*	2.4730	0.0001*
	Follow-up 1	2.1580	0.0001*	2.3990	0.0001*
	Follow-up 2	2.2810	0.0001*	2.3700	0.0001*
	Follow-up 3	2.1560	0.0001*	2.7910	0.0001*
	Follow-up 4	2.6450	0.0001*	2.6130	0.0001*
Social relationship	Baseline	1.8840	0.0020*	2.5370	0.0001*
	Follow-up 1	2.4520	0.0001*	2.6440	0.0001*
	Follow-up 2	2.6370	0.0001*	2.2790	0.0001*
	Follow-up 3	2.3930	0.0001*	2.6050	0.0001*
	Follow-up 4	2.4290	0.0001*	2.4450	0.0001*
Environmental health	Baseline	2.1920	0.0001*	2.6000	0.0001*
	Follow-up 1	2.1190	0.0001*	2.3420	0.0001*
	Follow-up 2	2.3150	0.0001*	1.9780	0.0010*
	Follow-up 3	2.6740	0.0001*	2.1010	0.0001*
	Follow-up 4	2.3080	0.0001*	1.9460	0.0010*
Total QOL	Baseline	0.8930	0.4020	0.8370	0.4860
	Follow-up 1	0.9190	0.3670	0.9290	0.3530
	Follow-up 2	1.0370	0.2320	1.1030	0.1750
	Follow-up 3	1.1910	0.1170	1.0440	0.2260
	Follow-up 4	1.3720	0.0460	1.0590	0.2120

$p<0.05$*, $p<0.01$**, $p<0.0001$***

- Before applying the statistical test, we checked the normal distribution through Kolmogorov Smirnov Test. As per the obtained data the all domains of quality of life not followed the normal distribution at different time point. Whereas, total quality of life shows the normal distribution at different time point hence we applied the parametric test

Note: The domains of total QOL scores in two groups at different time points not follow a normal distribution, therefore the non-parametric tests were applied. But the total QOL scores followed a normal distribution. Therefore the parametric tests were applied

4.3.1 Total Quality of Life:

- The result of total quality of life, at baseline level we didn't find any significance difference between the group (p=0.395). the same result has been observed till the follow-up 1 and 2. During the 3rd and final follow-up we observed clinical as well as statistical significant difference in between the group (p=0.002**). However, we also observed the significant improvement in QOL in control group from baseline (49.29±4.01) to final follow-up (51.83±4.80). Paired difference in control group has been observed from baseline to final follow-up 2.54±4.51, p=0.001***. The same observation has been done with interventional group, here we found bit more clinically as well as statistically significance paired difference (4.12±5.52, p=0.001***) from baseline (49.72±0.37) to final follow-up (53.85±5.48).

Table 33: **Comparison of Control and Interventional Groups with Total QOL Scores at Different Time Points by Independent T-Test.**

Times	Control group			Interventional group			t-Value	p-Value
	Mean	SD	SE	Mean	SD	SE		
Baseline	49.29	4.01	0.34	49.72	4.35	0.37	-0.852	0.395
Follow-up 1	51.41	4.52	0.39	52.14	4.28	0.36	-1.332	0.184
Follow-up 2	51.24	4.92	0.42	52.37	4.97	0.42	-1.862	0.640
Follow-up 3	51.65	5.03	0.43	53.11	5.02	0.43	-2.375	0.018*
Follow-up 4	51.83	4.80	0.41	53.85	5.48	0.47	-3.192	0.002**

p<0.05*, p<0.01**, p<0.0001***

Figure 19: Comparison of Control and Interventional Groups with Total QOL Scores at Different Time Points

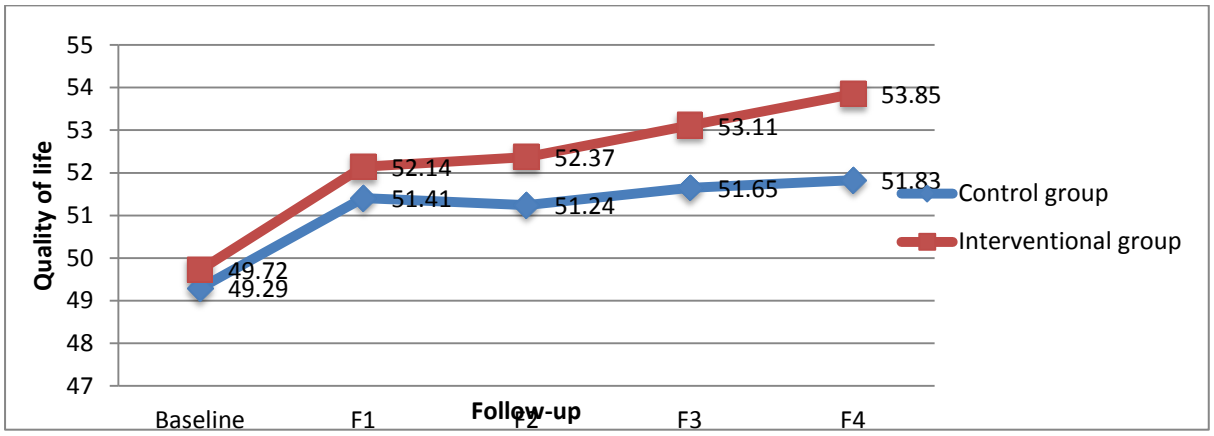


Table 34: Parried Difference Assessment in QOL from Baseline to Different Time Points in Control and Interventional Group by Paired T-Test.

Times	Control group					Interventional group				
	Mean	SD	SE	t-value	p-value	Mean	SD	SE	t-value	p-value
BL to F1	2.12	3.20	0.27	-7.60	0.001	2.40	3.56	0.30	-7.80	0.001
BL to F2	1.95	3.72	0.32	-6.01	0.001	2.64	4.36	0.37	-7.01	0.001
BL to F3	2.35	4.23	0.30	-6.39	0.001	3.38	4.86	0.42	-8.06	0.001
BL to F4	2.54	4.51	0.34	-6.47	0.001	4.12	5.52	0.47	-8.64	0.001

p<0.05*, p<0.01**, p<0.0001***

4.3.2 Physical Health Domain:

- As per the analysis of physical health domain, not much statistical significant difference in the baseline and different time point of follow-up. At the baseline the mean score in control group was 50.98±7.99 and in interventional group was 50.09±8.14 that was not significant statistically p=0.5704. At the end follow-up we have found clinically significant improvement in interventional group 56.90±6.83 instead of control group 55.07±6.47, p=0.065. At final follow-up, the mean improvement in quality of life in interventional group was 6.81±8.27. Whereas, in control group it was 5.11±8.79.

Table 35: **Comparison of Control and Interventional Groups with the Domain of Physical Health at Different Time Points by Mann-Whitney U Test**

Times	Control group			Interventional group			U-Value	Z-Value	p-Value
	Mean	SD	Mean rank	Mean	SD	Mean rank			
Baseline	50.98	7.99	136.20	50.09	8.14	130.84	8488.00	-0.567	0.5704
Follow-up 1	55.53	6.72	135.58	55.25	6.08	131.45	8569.00	-0.438	0.6611
Follow-up 2	55.46	6.46	136.05	55.16	6.26	130.99	8507.00	-0.537	0.5911
Follow-up 3	55.60	7.05	126.54	56.87	6.56	140.35	7925.50	-1.464	0.1432
Follow-up 4	55.09	6.47	128.21	56.90	6.83	138.71	8146.00	-1.112	0.0659
BL to F1	4.55	6.09	130.41	5.16	6.86	136.54	8436.50	-0.649	0.5160
BL to F2	4.48	7.76	131.12	6.07	8.27	135.84	8530.00	-0.500	0.6167
BL to F3	4.62	8.50	125.27	6.81	9.03	141.60	7758.00	-1.731	0.0834
BL to F4	5.11	8.79	127.14	6.81	9.18	139.77	8004.00	-1.339	0.1806

p<0.05*, p<0.01**, p<0.0001***

Figure 20: Comparison of Control and Interventional Groups with the Domain of Physical Health at Different Time Points

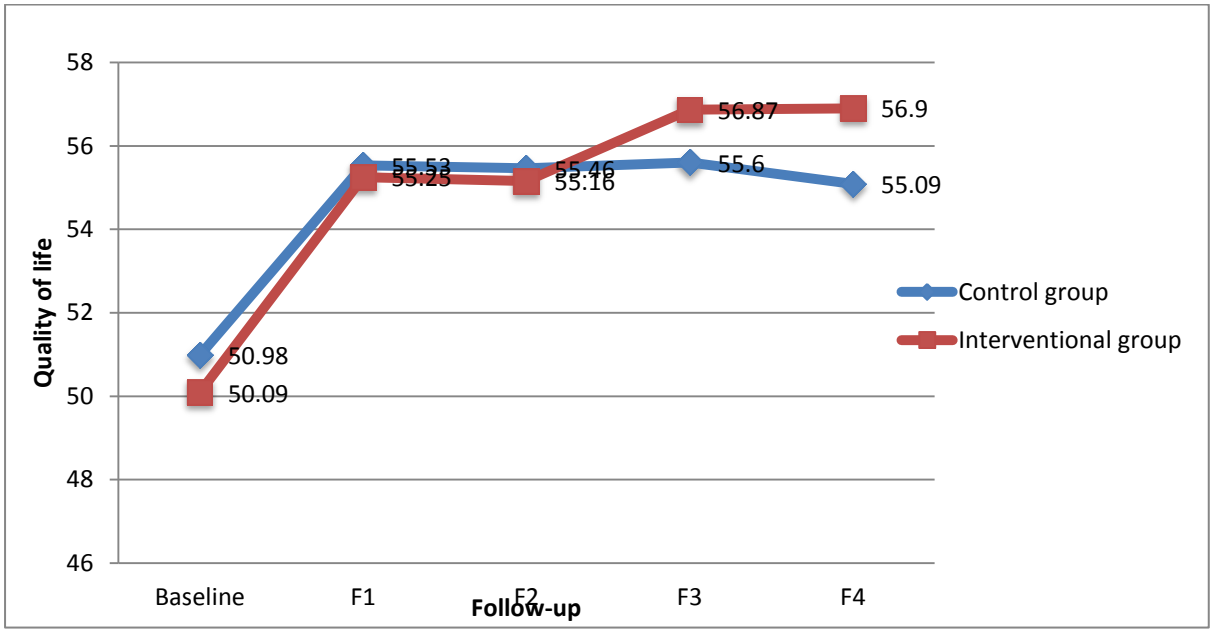


Table 36: **Comparison Of Different Time Points With The Domain Of Physical Health Scores In Control And Interventional Groups By Wilcoxon Matched-Pairs Test.**

- The comparison of different time points for physical health domains with Wilcoxon matched-pairs test presented highly statistically as well as clinical significance for both control and Interventional group ranging from baseline to follow-up 4. (p-Value <0.05). The percentage change in quality of life from baseline to final follow-up was quite significant (13.60%) in interventional group rather than control group (10.03%).

Groups	Changes from	% of change	T-Value	Z-Value	P-Value
Control	BL to Follow-up 1	-8.93	208.50	6.7026	0.0001*
	BL to Follow-up 2	-8.80	704.00	5.7639	0.0001*
	BL to Follow-up 3	-9.07	871.50	5.7725	0.0001*
	BL to Follow-up 4	-10.03	1014.50	5.9111	0.0001*
Experiment	BL to Follow-up 1	-10.29	308.00	7.0649	0.0001*
	BL to Follow-up 2	-10.12	799.50	6.1801	0.0001*
	BL to Follow-up 3	-13.54	606.50	6.9563	0.0001*
	BL to Follow-up 4	-13.60	773.50	7.0798	0.0001*

p<0.05*, p<0.01**, p<0.0001***

4.3.3 Psychological Health Domain:

- Data analysis of psychological health domain showed no statistical significant difference in the baseline and different time point of follow-up. At the baseline the mean score in control group was 49.63±7.06 and in interventional group was 50.02 ±6.80 that was not significant statistically p=0.549. At the end follow-up we have found clinically significant improvement in interventional group 52.00±5.78 instead of control group 50.78±6.01, p=0.099.

Table 37: Comparison of Control and Interventional Groups with Domain Psychological Health at Different Time Points by Mann-Whitney U Test

Times	Control group			Interventional group			U-Value	Z-Value	p-Value
	Mean	SD	Mean rank	Mean	SD	Mean rank			
Baseline	49.63	7.06	130.66	50.20	6.80	136.30	8468.50	-0.598	0.549
Follow-up 1	49.99	6.04	129.75	50.57	5.31	137.20	8348.50	-0.789	0.429
Follow-up 2	49.98	5.95	131.30	50.54	5.86	135.67	8553.00	-0.463	0.642
Follow-up 3	50.23	6.20	127.16	51.34	5.35	139.75	8007.00	-1.334	0.182
Follow-up 4	50.74	6.01	129.67	52.00	5.78	137.28	8338.00	-0.806	0.099
BL to F1	0.36	6.21	132.91	0.37	5.21	134.08	8766.50	-0.123	0.901
BL to F2	0.35	6.50	132.88	0.34	6.10	134.11	8762.00	-0.130	0.896
BL to F3	0.60	7.08	130.76	1.13	7.23	136.20	8482.00	-0.577	0.563
BL to F4	1.15	7.15	132.29	1.80	8.07	134.69	8684.50	-0.254	0.799

p<0.05*, p<0.01**, p<0.0001***

Figure 21: Comparison of Control and Interventional Groups with Domain Psychological Health at Different Time Points

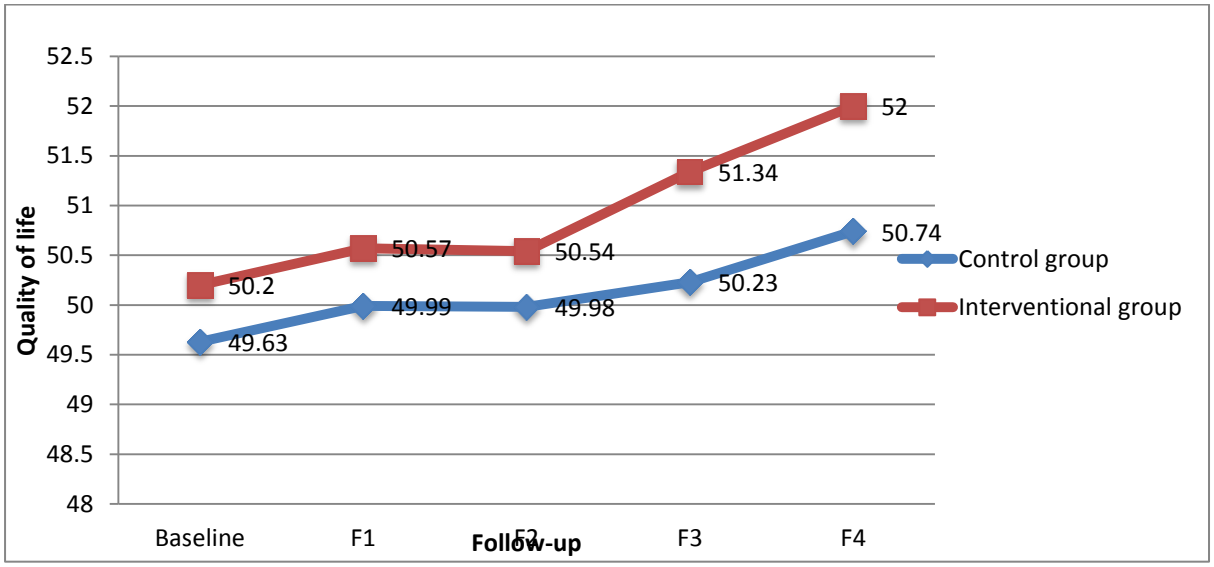


Table 38: Comparison of different time points with domain psychological health scores in control and Interventional groups by Wilcoxon matched pairs test

- The comparison of various time points with psychological health domain in control and Interventional group by Wilcoxon matched-pairs test resulted to have clinically significance Values from Baseline to Follow-up 3 respectively whereas the clinical, as well as statistical significance, observed for Baseline to Follow-up 4 with p-Value 0.0109, 0.0208 in control and Interventional group respectively.

Groups	Changes from	% of change	T-Value	Z-Value	P-Value
Control	BL to Follow-up 1	-0.73	1240.00	0.6075	0.5435
	BL to Follow-up 2	-0.70	1227.00	0.4882	0.6254
	BL to Follow-up 3	-1.21	1546.00	1.0659	0.2865
	BL to Follow-up 4	-3.04	1346.00	2.5464	0.0109*
Experiment	BL to Follow-up 1	-0.74	1369.00	0.8542	0.3930
	BL to Follow-up 2	-0.68	1491.00	0.7981	0.4248
	BL to Follow-up 3	-2.26	1326.00	1.7359	0.0826
	BL to Follow-up 4	-3.58	1582.00	2.3124	0.0208*

$p<0.05$*, $p<0.01$**, $p<0.0001$***

4.3.4 Social relationship Domain:

- As per the analysis of social relationship domain, not much statistical significant difference in the baseline and different time point of follow-up. At the baseline the mean score in control group was 49.02±7.89 and in interventional group was 48.90±7.89that was not significant statistically p=0.9873. At the end follow-up we have found clinically significant improvement in interventional group 53.98±6.03 instead of control group 52.18±6.07, p=0.0866. At final follow-up, the mean improvement in quality of life in interventional group was 5.08±8.52. Whereas, in control group it was 3.46±7.99.

Table 39: **Comparison of Control and Interventional Groups with Domain Social Relationship at Different Time Points by Mann-Whitney U Test**

Times	Control group			Interventional group			U-Value	Z-Value	p-Value
	Mean	SD	Mean rank	Mean	SD	Mean rank			
Baseline	49.02	7.89	133.58	48.90	7.89	133.43	8834.00	-0.015	0.9873
Follow-up 1	51.22	6.27	132.09	51.60	5.39	134.89	8658.00	-0.296	0.7669
Follow-up 2	51.35	6.23	127.27	52.22	6.27	139.64	8021.00	-1.311	0.1896
Follow-up 3	51.95	6.11	134.83	51.85	6.03	132.19	8668.00	-0.280	0.7791
Follow-up 4	52.18	6.07	127.22	53.98	6.48	139.68	8015.50	-1.320	0.0866
BL to F1	2.20	5.79	129.61	2.70	6.30	137.33	8330.50	-0.818	0.4131
BL to F2	2.33	7.02	128.09	3.32	6.99	138.83	8130.00	-1.138	0.2551
BL to F3	2.94	7.13	133.11	2.96	7.78	133.88	8792.50	-0.082	0.9346
BL to F4	3.46	7.99	127.83	5.08	8.52	139.08	8096.00	-1.192	0.1331

p<0.05*, p<0.01**, p<0.0001***

Figure 22: Comparison of Control and Interventional Groups with Domain Social Relationship at Different Time Points

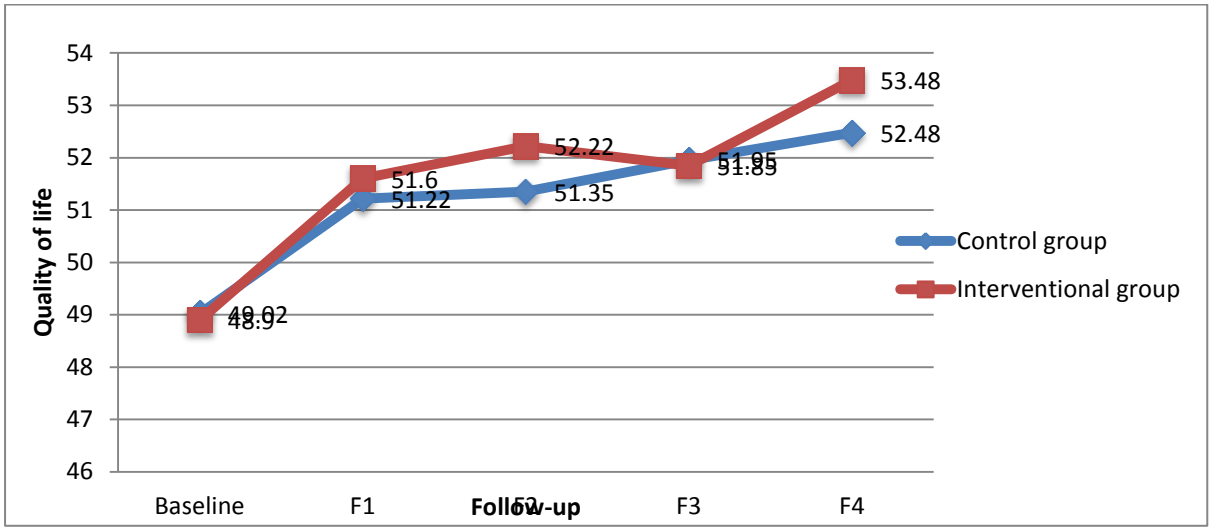


Table 40: **Comparison Of Different Time Points With Domain Social Relationship Scores In Control And Interventional Groups By Wilcoxon Matched-Pairs Test.**

- The comparison of different time frames with domain social relationship in Interventional group imparts the sense of clinical as well as statistically significant compared to control group among Baseline to Follow-up 4. The percentage change in quality of life from baseline to final follow-up was quite significant (9.37%) in interventional group rather than control group (7.06%).

Groups	Changes from	% of change	T-Value	Z-Value	P-Value
Control	BL to Follow-up 1	-4.50	389.00	4.1190	0.0001*
	BL to Follow-up 2	-4.76	838.00	3.7507	0.0002*
	BL to Follow-up 3	-6.00	935.00	4.2566	0.0001*
	BL to Follow-up 4	-7.06	1041.00	4.3853	0.0001*
Experiment	BL to Follow-up 1	-5.53	584.50	4.5483	0.0001*
	BL to Follow-up 2	-6.79	881.50	4.8966	0.0001*
	BL to Follow-up 3	-6.04	985.00	4.1629	0.0001*
	BL to Follow-up 4	-9.37	838.50	5.6237	0.0001*

$p<0.05$*, $p<0.01$**, $p<0.0001$***

4.3.5 Environmental Health Domain:

- As per the environmental health domain, we didn't find statistical significant difference in the baseline and different time point of follow-up1, 2 and 3. At the baseline the mean score in control group was 48.69±7.28 and in interventional group was 49.73±7.97 that was not significant statistically p=0. 2056. At the end follow-up we have found statistically & clinically significant improvement in interventional group 53.04±7.37 instead of control group 51.23±6.75, p=0.0284*. At final follow-up, the mean improvement in quality of life in interventional group was 3.31±5.57. Whereas, in control group it was 2.54±4.97.

Table 41: **Comparison of Control and Interventional Groups with Domain Environmental Health at Different Time Points by Mann-Whitney U Test**

Times	Control group			Interventional group			U-Value	Z-Value	p-Value
	Mean	SD	Mean rank	Mean	SD	Mean rank			
Baseline	48.69	7.28	127.48	49.73	7.97	139.43	8050.00	-1.265	0.2056
Follow-up 1	50.16	6.21	126.19	51.07	6.68	140.70	7879.50	-1.537	0.1242
Follow-up 2	49.95	6.02	124.30	51.49	7.07	142.56	7630.00	-1.935	0.0530
Follow-up 3	50.90	6.12	124.21	52.32	6.89	142.65	7618.00	-1.954	0.0507
Follow-up 4	51.23	6.75	123.08	53.04	7.37	143.76	7469.00	-2.191	0.0284*
BL to F1	1.47	4.24	136.77	1.34	4.01	130.28	8412.00	-0.688	0.4911
BL to F2	1.27	4.65	129.76	1.76	4.69	137.18	8350.50	-0.786	0.4315
BL to F3	2.21	5.03	131.91	2.59	4.98	135.07	8634.00	-0.334	0.7378
BL to F4	2.54	4.97	127.85	3.31	5.57	139.07	8098.00	-1.189	0.2344

p<0.05*, p<0.01**, p<0.0001***

Figure 23: Comparison of Control and Interventional Groups with Domain Environmental Health at Different Time Points

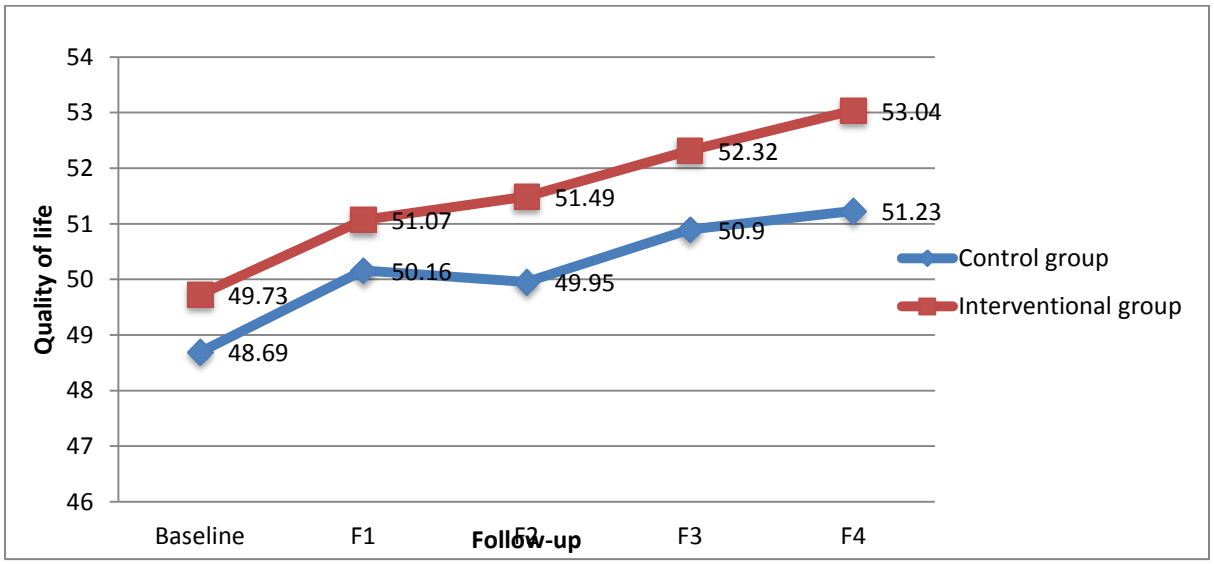


Table 42: **Comparison Of Different Time Points With Domain Environmental Health Scores In Control And Interventional Groups By Wilcoxon Matched-Pairs Test.**

- The highly clinical as well as statistical significance was observed from baseline to follow-up 3 and baseline to follow-up 4 in control group similarly baseline to follow-up 2, baseline to follow-up 3 and baseline to follow-up 4 in Interventional group respectively. (p-Value >0.05). The percentage change in quality of life from baseline to final follow-up was quite significant (5.21%) in interventional group rather than control group (6.66%).

Groups	Changes from	% of change	T-Value	Z-Value	P-Value
Control	BL to Follow-up 1	-3.02	234.00	3.6308	0.0003*
	BL to Follow-up 2	-2.60	346.50	2.9667	0.0030*
	BL to Follow-up 3	-4.54	558.00	4.5782	0.0001*
	BL to Follow-up 4	-5.21	553.50	5.0166	0.0001*
Experiment	BL to Follow-up 1	-2.70	117.00	3.3935	0.0007*
	BL to Follow-up 2	-3.54	198.00	4.2426	0.0001*
	BL to Follow-up 3	-5.21	269.50	5.3404	0.0001*
	BL to Follow-up 4	-6.66	430.00	5.9612	0.0001*

p<0.05*, p<0.01**, p<0.0001***

4.4 Drug-Related Problems (DRP's):

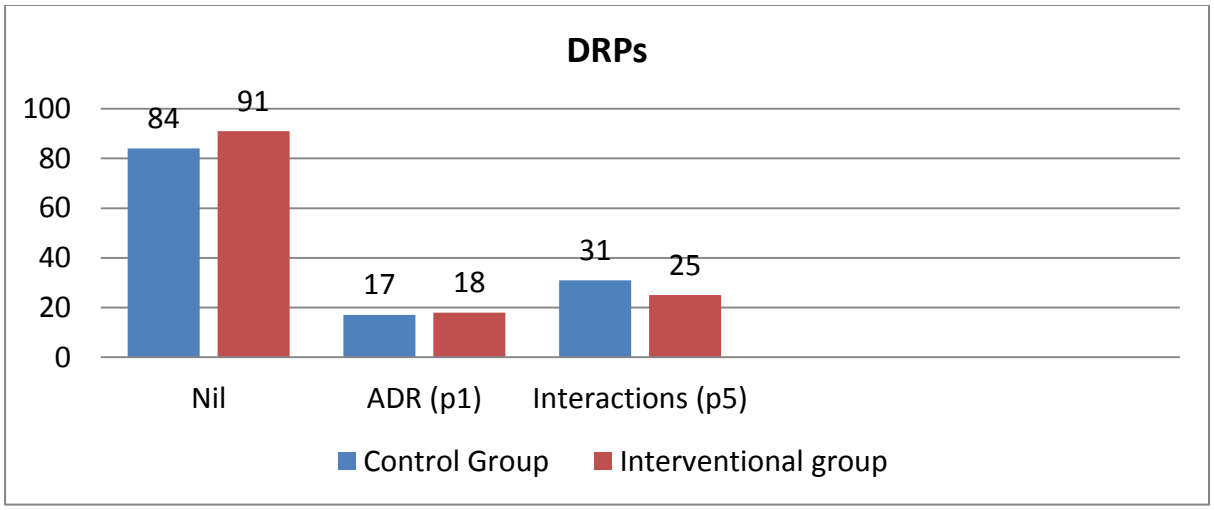
Table 43: Drug-Related Problems among the Group.

- The drug-related problems observed were nil (63.64%, 67.91%) followed by drug interactions (23.48%, 18.66%), ADR (12.88%, 13.43%) in control and intervention group respectively.

Drug-related problems	Control group	%	Interventional group	%	Total	Chi-square	p-Value
Nil	84	63.64	91	67.91	175	0.9360	0.6260
ADR (p1)	17	12.88	18	13.43	35		
Interactions (p5)	31	23.48	25	18.66	56		

p<0.05*, p<0.01**, p<0.0001***

Figure 24: Drug-related Problems among the group.



4.4.1 Adverse Drug Reaction (ADR):

- Total 35 ADRs were categorized into Side effect suffered (non-allergic) with 10.61 %, 12.69% and Toxic effects suffered from 2.27%, 0.75% in control and experimental groups respectively. There were no significant difference has been observed in the both control and interventional group

Table 44: Adverse Drug Reaction among Group

Variables		Control group	%	Interventional group	%	Total	Chi-square	p-Value
ADR	Side effect suffered (non-allergic)	14	10.61%	17	12.69%	31	1.2630	0.2610
	Toxic effects suffered	3	2.27%	1	0.75%	4		

p<0.05*, p<0.01**, p<0.0001***

Figure 25: Adverse drug reaction among the group

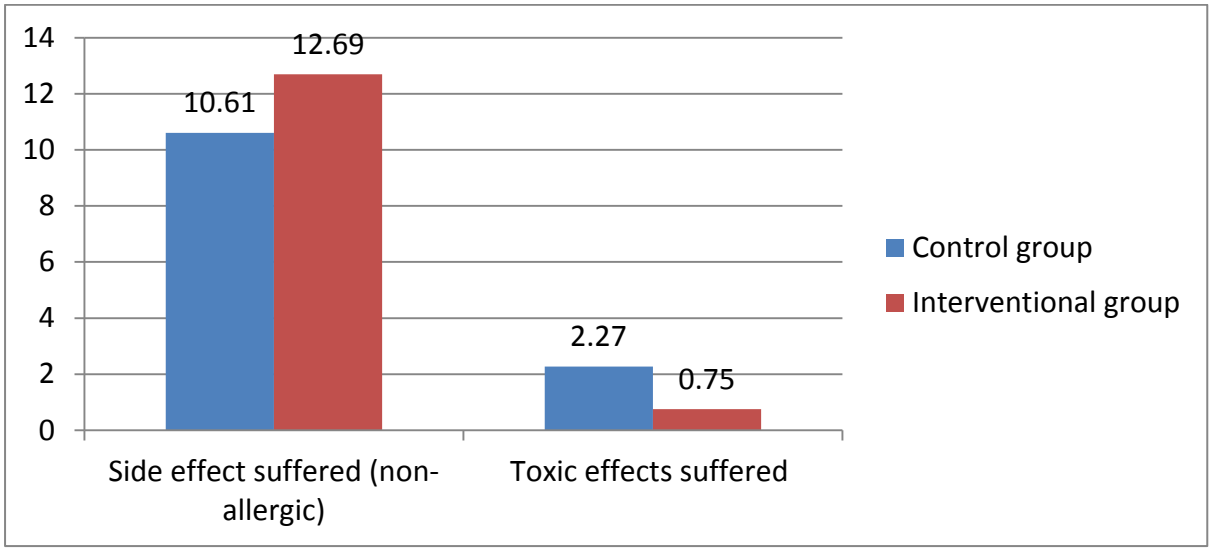


Table 45: Drug-Induced Adverse Drug Reaction among the Group.

- Among all the assessed ADRs, majority of ADR were Lithium-induced. Among them most of were hand tremor (5.30%, 4.48%) followed by hypothyroidism (0.76%, 3.73%) Muscle twitch (1.49%) and Dry mouth (0.75%), in control and interventional group re-spectively. Secondary drug-induced ADR was found as Olanzapine-induced weight gain (3.03%, 0.00%). Thirdly Valproate induced hand tremor and thrombocytopenia, fourthly Aripiprazole induced hyper salivation, and Trifluoperazine induced Bradykinesia and

lastly Risperidone induced weight gain has been found in control and interventional group. The results were clinically significant and statistically not significant.

ADR		**Control group**	**%**	**Inter-ventional group**	**%**	**Total**	**Chi-square**	**p-Value**
Lithium-induced	Hypothyroidism	1	0.76 %	5	3.73 %	6	4.4370	0.2180
	Hand tremor	7	5.30 %	6	4.48 %	13		
	Muscle twitch	0	0.00 %	2	1.49 %	2		
	Dry mouth	0	0.00 %	1	0.75 %	1		
Valproate induced	Hand tremor	0	0.00 %	2	1.49 %	2	3.0000	0.0830
	Thrombocyto-penia	1	0.76 %	0	0.00 %	1		
Trifluopera-zine induced	Bradykinesia	1	0.76 %	0	0.00 %	1		
Alprazolam induced	Impaired co-ordination	1	0.76 %	0	0.00 %	1		
Aripipra-zole-induced	Hyper salivation	0	0.00 %	1	0.75 %	1	2.0000	0.1570
	Tremor	1	0.76 %	0	0.00 %	1		
Olanzapine induced	Weight gain	4	3.03 %	0	0.00 %	4		
Risperidone induced ADR	Weight gain	0	0.00 %	1	0.75 %	1		
Trihex-yphenidyl induced	Constipation	1	0.76 %	0	0.00 %	1		

$p<0.05$*, $p<0.01$**, $p<0.0001$***

4.4.2 ADR Documentation:

The documentation of ADR's is the most important part for the proper reporting of ADR. The assessed ADR's has been reported to the regulatory authority through PvPi App.

- As per the assessed data, reported triggered induced whereas, 5.71% were not trigger associated.
- The proper management has been provided for the patient in same direction 31.4% medication dose has been altered , 40.0% patient has been served with specific treatment and rest of served with symptomatic treatment.
- The most of ADR's outcome (94.2%) was continuous because majority of them re-challenged (85.7%) by the psychiatrist and rest of were de-challenged. The main reason behind the re-challenge was the symptomatic treatment. As most of ADRs were occurred due to Lithium carbonate, which is the potent mood stabilizer medication in the treatment of BPAD.
- The probability of ADR has been assessed through Naranjo ADR assessment scale. As per the scoring of scale we found that, majority of ADR were probable (82.5%) followed by definite (14.2%). The affiliated severity has been assessed through hartwig's scale. As per the obtained data of severity, 51.4% ADRs falls in level 3 and rest of 40.0% matched the level 2.
- Almost ADRs were predictable of them 74.2% were preventable. All the patients those who were contracted with ADRs were properly counseled as well as served with the alert card of ADR so that they may take proper care for future therapy for their life long illness.

Table 46: Documentation of Adverse Drug Reaction among the Group.

ADR Documentation		**Control group**	**%**	**Interventional group**	**%**	**Total**	**Chi-square**	**p-Value**
Is there an ADR associated with the trigger	Yes	16	12.12	17	12.69	33	0.0020	0.9670
	No	1	0.76	1	0.75	2		
Management of ADR	Drug withdrawn	0	0.00	0	0.00	0	0.0620	0.8030
	Dose alter	5	3.79	6	4.48	11		
	No change	12	9.09	12	8.96	24		
Treatment given	Specific	9	6.82	5	3.73	14	2.8070	0.2460

	Symptomat-ic	5	3.79	6	4.48	11		
	Nil	3	2.27	7	5.22	10		
Outcome of ADR	Continuing	15	11.36	18	13.43	33	2.2460	0.1340
	Unknown	2	1.52	0	0.00	2		
De-challenge	Yes	4	3.03	1	0.75	5	2.3070	0.1290
	No	13	9.85	17	12.69	30		
Re-challenge	Yes	13	9.85	17	12.69	30	2.3070	0.1290
	No	4	3.03	1	0.75	5		
Causality as-sessment	Definite	5	3.79	0	0.00	5	6.8390	0.033*
	Probable	12	9.09	17	12.69	29		
	Possible	0	0.00	1	0.75	1		
	Unlikely	0	0.00	0	0.00	0		
Severity as-sessment	Level 1	2	1.52	0	0.00	2	3.4820	0.3230
	Level 2	6	4.55	8	5.97	14		
	Level 3	8	6.06	10	7.46	18		
	Level 4 (a)	0	0.00	0	0.00	0		
	Level 4 (b)	1	0.76	0	0.00	1		
Predictability	Predictable	17	12.88	18	13.43	35		
	Non-predictable	0	0.00	0	0.00	0		
Preventability	Definitely prevent able	14	10.61	12	8.96	26	1.1260	0.2890
	Probably prevent able	3	2.27	6	4.48	9		
	Not prevent able	0	0.00	0	0.00	0		
Predisposing factor	Age	0	0.00	0	0.00	0	-	-
	Gender	0	0.00	0	0.00	0		
	Genetics	0	0.00	0	0.00	0		
	Inter-current disease	17	12.88	18	13.43	35		
	Multiple drug therapy	0	0.00	0	0.00	0		
Patient inter-viewed	Yes	17	12.88	18	13.43	35	-	-
	No	0	0.00	0	0.00	0		
Alert card pro-vided	Yes	17	12.88	18	13.43	35	-	-
	No	0	0.00	0	0.00	0		

$p<0.05$*, $p<0.01$**, $p<0.0001$***

4.4.3 Drug-drug Interactions (DDI's):

- The drug interactions were classified into probable with (11.36%, 10.45%) and suspected with (12.12%, 8.21%) in control and experimental group respectively.

Table 57: Drug Interaction among Group

Drug-Drug Interactions		Control group	%	Intervential group	%	Total	Chi-square	p-Value
Drug-drug interaction	Probable	15	11.36	14	10.45	29	0.3210	.5710
	Suspected	16	12.12	11	8.21	27		

4.4.3.1 Type of Drug Interactions:

- The minor drug interactions suggest Sertraline and Lithium were leading (1.52%, 0.75%) in control and experimental group respectively. The chief significant drug interaction was Lorazepam and Olanzapine (3.03%, 5.97%) followed by Lorazepam and Trifluoperazine (3.78%, 2.24%) in control and experimental group respectively. Serious drug interactions ascertain was only Trifluoperazine and chlorpromazine (1.52%, 0.75%) in the control and experimental group respectively**.**

Table 48: Different Type of Drug Interaction among the Group

Drug-Drug Interactions		Adverse effect	Control group	%	Intervential group	%	Total	Chi-square	p-Value
Minor drug interaction	Haloperidol + chlorpromazine	Increase the chlorpromazine level	0	0.00	1	0.75	1	3.3330	0.3430
	Haloperidol + Aripiprazole	Increase the Aripiprazole level	0	0.00	1	0.75	1		
	Sertraline + lithium	Neurotoxicity	2	1.52	1	0.75	3		
	Sertraline + chlorpromazine	Increase the chlorpromazine level	1	0.76	0	0.00	1		
Significant drug interaction	Trihexyphenidyl+ Trifluoperazine	Decrease the effect of Trifluoperazine	2	1.52	1	0.75	3	9.1830	0.7590
	Lorazepam + Trifluoperazine	Increase Sedation	5	3.79	3	2.24	8		
	Lorazepam + haloperidol	Increase Sedation	2	1.52	1	0.75	3		

	Lorazepam + Quetiapine	Increase Sedation	1	0.76	2	1.49	3		
	Trihexyphenidyl +chlorpromazine	Decrease the chlorpromazine level	1	0.76	1	0.75	2		
	Lorazepam +olanzapine	Increase Sedation	4	3.03	8	5.97	12		
	Haloperidol +Quetiapine	Increase Sedation & anti-dopaminergic effect	1	0.76	0	0.00	1		
	Haloperidol + olanzapine	Increase Sedation, anti-dopaminergic effect & QT interval prolongation	0	0.00	1	0.75	1		
	Lithium + Trifluoperazine	Neurotoxicity	5	3.79	2	1.49	7		
	Quetiapine +Trihexyphenidyl	Neuroleptic malignancy & sedation	1	0.76	1	0.75	2		
	Sertraline +lithium	Increase serotonin effect	0	0.00	1	0.75	1		
	Aripiprazole +Quetiapine	Increase Sedation, anti-dopaminergic effect	1	0.76	0	0.00	1		
	Olanzapine +Trifluoperazine	Increase Sedation, anti-dopaminergic effect	1	0.76	0	0.00	1		
	Olanzapine +Quetiapine	Increase Sedation, anti-dopaminergic effect	2	1.52	1	0.75	3		
Serious drug interaction	Trifluoperazine +chlorpromazine	QT interval prolongation	2	1.52	1	0.75	3	-	-

$p<0.05$*, $p<0.01$**, $p<0.0001$***

4.4.4 Causes of DRPs

- As per the data of the current study we observed the drug/dose selection (29.55%, 27.61%) was the primary cause of DRPs whereas drug use process (7.58%, 3.73%) was another cause of DRP in control and Interventional group respectively.

Table 49: Causes of Drug-Related Problems among the Groups.

Level of DRP	Control group	%	Inter-ven-tional group	%	Total	Chi-square	p-Value
Drug/dose selection	39	29.55	37	27.61	76	3.5310	0.3170
Drug use process	10	7.58	5	3.73	15		

p<0.05*, p<0.01**, p<0.0001***

4.4.4.1 Drug/dose selection

- The primary cause of DRPs at drug/dose selection was due to pharmacokinetic problems of 21.21% in control group and 18.66% in the experimental group followed by manifest side effect, no other cause for 9.09% in control and 5.05% in the experimental group. The results suggested clinical significance for the interventional group.

Table 50: Causes of Drug-Related Problems at Drug/Dose Selection Level

Drug/dose selection	Control group	%	Inter-ven-tional group	%	Total	Chi-square	p-Value
Pharmacokinetic problems, incl. Ageing/deterioration in organ function and interactions	28	21.21	25	18.66	53	3.5310	0.3170
Synergistic/preventive drug required and not given	2	1.52	1	0.75	3		
New symptom or indication revealed/presented	2	1.52	6	4.48	8		

p<0.05*, p<0.01**, p<0.0001***

4.4.4.2 Drug use process:

- The cause of DRPs at drug use process was non-monitoring therapeutic drug Levels 1.52%, 1.49% in control and interventional group respectively presenting clinical significance.

Table 51: Causes of Drug-Related Problems at the Drug Use Process.

Drug Use Process	Control group	%	Inter-ven-tional group	%	Total	Chi-square	p-Value
Therapeutic drug Level not monitored	2	1.52	2	1.49	4	-	-

p<0.05*, p<0.01**, p<0.0001***

4.4.5 Pharmacist intervention:

The pharmacist intervention has been proposed at the prescribed Level, patient Level and drug Level. At prescriber Level total 65 intervention has been proposed of which the majority of 66.1% (n=43) intervention has been accepted by psychiatrist whereas 44.9% (n=22) interventions have not been accepted. The pharmacist intervention at the prescriber Level was statistically and clinically significant (p-Value 0.045) followed by the patient care Level (p-Value 0.0790). The drug Level was observed as clinically significant.

Table 52: Pharmacist Intervention at Different Level.

Pharmacist intervention		Control group	%	Inter-ven-tional group	%	Total	Chi-square	p-Value
At prescriber Level	Prescriber informed only	5	3.79	4	2.99	9	9.7410	0.045*
	Prescriber asked for information	2	1.52	7	5.22	9		
	Intervention proposed, approved by prescriber	23	17.42	20	14.93	43		
	The intervention proposed, not approved by the prescriber	11	8.33	11	8.21	22		
	Intervention proposed, outcome unknown	7	5.30	0	0.00	7		
At patient/care	Patient (medication) counseling	28	21.21	29	21.64	57		

Level	Written information provided only	4	3.03	8	5.97	12	6.7810	0.0790
	Patient referred to prescriber	12	9.09	4	2.99	16		
	Spoken to family member/caregiver	4	3.03	1	0.75	5		
At drug Level	Drug changed to	0	0.00	1	0.75	1	9.7250	0.1370
	Dosage changed to	5	3.79	9	6.72	14		
	Formulation changed to	3	2.27	0	0.00	3		
	Instructions for use changed to	6	4.55	5	3.73	11		
	Drug stopped	4	3.03	1	0.75	5		
	New drug started	9	6.82	13	9.70	22		
	No change	21	15.91	12	8.96	33		

p<0.05*, p<0.01**, p<0.0001***

4.4.6 The outcome of Intervention:

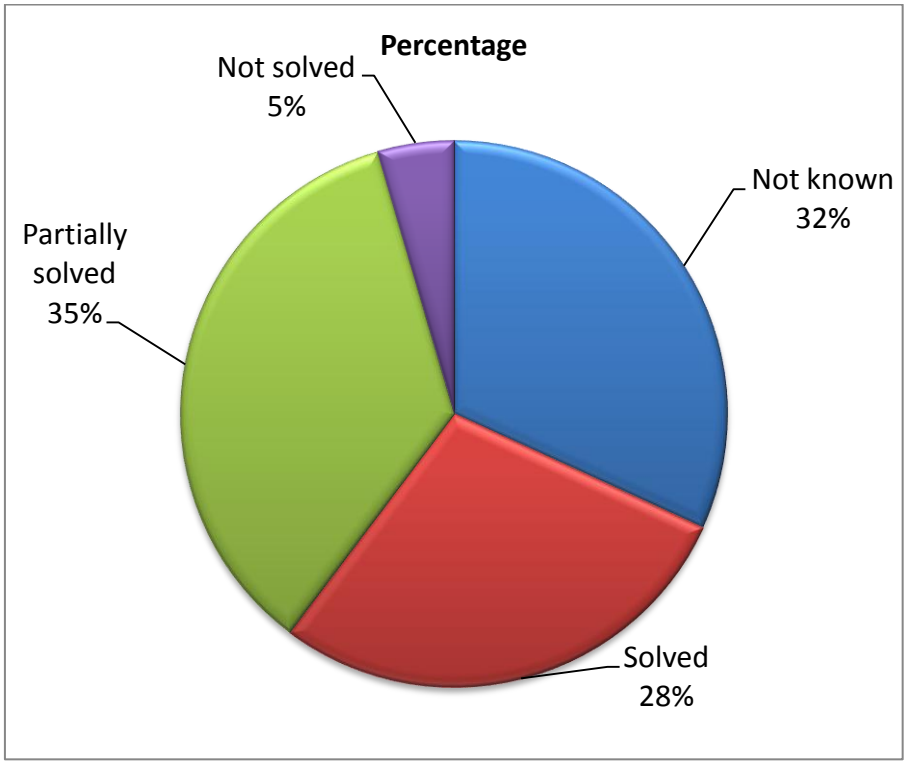
- The outcome of pharmacist intervention majorly suggested that the queries were partially solved followed by the not known and the solved. The result interprets the clinical significance but not the statistical.

Table 53: Outcome of Pharmacist Intervention.

Pharmacist intervention	**Control group**	**%**	**Interventional group**	**%**	**Total**	**Chi-square**	**p-Value**
Not known	16	12.12	12	8.96	28	5.4780	0.1400
Solved	10	7.58	15	11.19	25		
Partially solved	17	12.88	14	10.45	31		
Not solved	4	3.03	0	0.00	4		

p<0.05*, p<0.01**, p<0.0001***

Figure 26: Outcome of Pharmacist Intervention.



4.5 Mood Outcome:

Table 54: Normality Of YMRS And HAMD Scores In Two Groups At Different Time Points By Kolmogorov Smirnov Test.

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Variables	Time points	Control group		Interventional group	
		Z-Value	p-Value	Z-Value	p-Value
YMRS	Baseline	3.1810	0.0001*	2.9210	0.0001*
	Follow-up 1	2.7590	0.0001*	2.7250	0.0001*
	Follow-up 2	2.7740	0.0001*	2.9430	0.0001*
	Follow-up 3	3.1990	0.0001*	2.7240	0.0001*
	Follow-up 4	2.6230	0.0001*	2.9560	0.0001*
HAMD	Baseline	2.5330	0.0001*	2.2890	0.0001*
	Follow-up 1	1.5830	0.0130*	2.1230	0.0001*
	Follow-up 2	2.2790	0.0001*	2.4370	0.0001*
	Follow-up 3	2.2440	0.0001*	2.0950	0.0001*
	Follow-up 4	1.9540	0.0010*	2.1910	0.0001*

$p<0.05$*, $p<0.01$**, $p<0.0001$***

Note: The dimensions of YMRS and HAMD scores in two groups at different time points not follow a normal distribution, therefore the non-parametric tests were applied.

4.5.1 Young Mania Rating Scale (YMRS)

- In current study, the manic score has been assessed from the help of young mania rating scale. As per obtained result, at baseline level there were no statistical significant difference has been observed in between (p=0.9086) in control group (11.36±5.28) and interventional group (11.31±5.14). Whereas, during the study follow-up 1 (10.46±4.38, p=0.038), follow-up 2 (10.48±4.20, p=0.020) and follow-up 3 (10.11±3.91, p=0.011) slight clinical and statistical improvement in normal mood condition has been observed in interventional group. At the end follow-up we observed, high clinical as well as statistical improvement (p=0.0006) in interventional group (10.01±3.75) instead of control group (11.80±5.13). There were good percentage increment has been observed from baseline to final follow-up (-1.29±2.84) in interventional instead of control group (0.44±1.97). As per the scoring of YMRS, the lowest scoring represent good outcome of mood.

Table 55: **Comparison of Control and Interventional Groups with YMRS Scores at Different Time Points by Mann-Whitney U Test.**

Times	Control group			Interventional group			U-Value	Z-Value	p-Value
	Mean	SD	Mean rank	Mean	SD	Mean rank			
Baseline	11.36	5.28	132.95	11.31	5.14	134.04	8772.00	-0.114	0.9086
Follow-up 1	11.56	5.18	143.35	10.46	4.38	123.79	7543.50	-2.073	0.0382*
Follow-up 2	11.58	5.15	144.52	10.48	4.20	122.65	7389.50	-2.3185	0.0204*
Follow-up 3	11.48	5.37	145.57	10.11	3.91	121.61	7251.00	-2.5393	0.0111*
Follow-up 4	11.80	5.13	149.85	10.01	3.75	117.40	6686.00	-3.4399	0.0006*
BL to F1	0.20	1.84	158.06	-0.85	1.41	109.30	5601.50	-5.1686	0.0001*
BL to F2	0.22	1.86	153.29	-0.83	1.93	114.00	6231.50	-4.1644	0.0001*
BL to F3	0.13	3.74	154.68	-1.19	2.20	112.63	6048.00	-4.4569	0.0001*
BL to F4	0.44	1.97	161.86	-1.29	2.84	105.57	5101.00	-5.9664	0.0001*

p<0.05*, p<0.01**, p<0.0001***

Figure 27: Comparison of Control and Interventional Groups with YMRS Scores at Different Time Points.

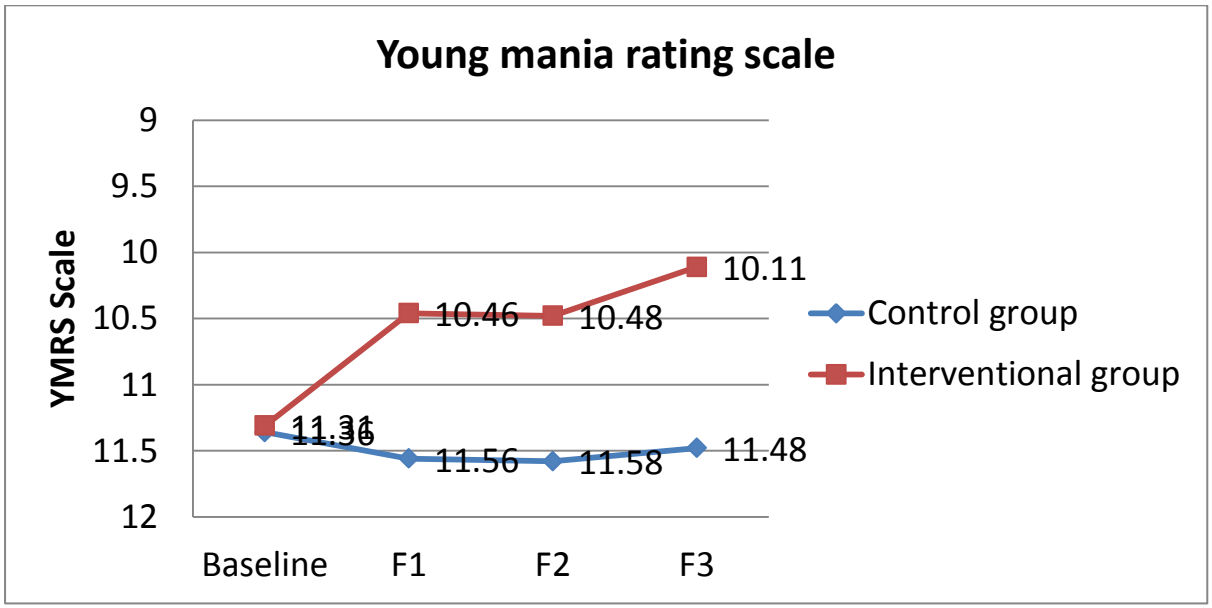


Table 56: **Comparison Of Different Time Points With YMRS Scores In Control And Interventional Groups By Wilcoxon Matched-Pairs Test.**

- Comparison of different time points with YMRS scores in control and Interventional groups by Wilcoxon matched-pairs test represented highly clinical and statistical significance in the Interventional group. As per the obtained result, in control group slight percentage difference (3.87%, p=0.0067) has been observed from baseline to final follow-up whereas in interventional group, clinical as well as statistically significant improvement in mood outcome (11.42%, p=0.0001) has been seen, that was quiet good in compare to control group.

Groups	Changes from	% of change	T-Value	Z-Value	P-Value
Control	BL to Follow-up 1	-1.80	317.50	1.2433	0.2138
	BL to Follow-up 2	-1.93	328.50	1.3218	0.1863
	BL to Follow-up 3	-1.13	221.50	0.5193	0.6035
	BL to Follow-up 4	-3.87	391.50	2.7093	0.0067*
Experiment	BL to Follow-up 1	7.52	25.50	6.0424	0.0001*
	BL to Follow-up 2	7.33	814.50	4.5471	0.0001*
	BL to Follow-up 3	10.56	426.00	5.8124	0.0001*
	BL to Follow-up 4	11.42	1029.50	5.1420	0.0001*

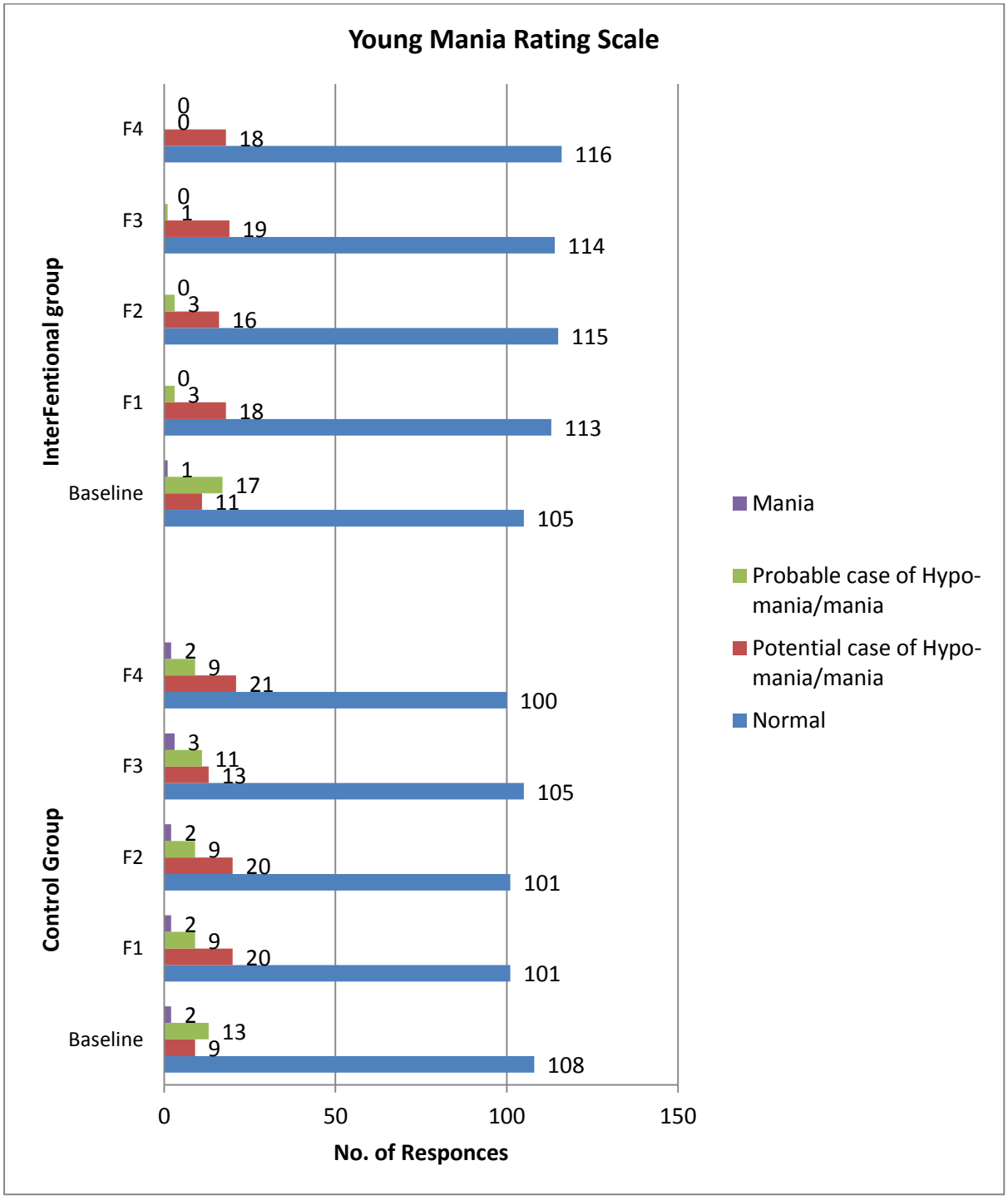
p<0.05*, p<0.01**, p<0.0001***

Table 57: **Comparison of Different Time Points with YMRS Scores in Control and Interventional Groups.**

- The YMRS scores were compared on different time points showed that, at baseline level maximum of patients (n=213) was in normal mood condition in control group (81.82%) and interventional group (78.36%). At final follow-up the patient shift in normal mood has been increased 8.51% in interventional group (86.87%) instead of control group (75.77%). In control group we observed negative improvement (-2.59%) in mood outcome.

Time	YMRS scores	Control group	%	Inter-ven-tional group	%	Total
Baseline	Normal	108	81.82	105	78.36	213
	Potential case of Hy-po-mania/mania	9	6.82	11	8.21	20
	Probable case of Hy-po-mania/mania	13	9.85	17	12.69	30
	Mania	2	1.52	1	0.75	3
Follow-up 1	Normal	101	76.52	113	84.33	214
	Potential case of Hy-po-mania/mania	20	15.15	18	13.43	38
	Probable case of Hy-po-mania/mania	9	6.82	3	2.24	12
	mania	2	1.52	0	0.00	2
Follow-up 2	Normal	101	76.52	115	85.82	216
	Potential case of Hy-po-mania/mania	20	15.15	16	11.94	36
	Probable case of Hy-po-mania/mania	9	6.82	3	2.24	12
	Mania	2	1.52	0	0.00	2
Follow-up 3	Normal	105	79.55	114	85.07	219
	Potential case of Hy-po-mania/mania	13	9.85	19	14.18	32
	Probable case of Hy-po-mania/mania	11	8.33	1	0.75	12
	Mania	3	2.27	0	0.00	3
Follow-up 4	Normal	100	75.76	116	86.57	216
	Potential case of Hy-po-mania/mania'	21	15.91	18	13.43	39
	Probable case of Hy-po-mania/mania	9	6.82	0	0.00	9
	Mania	2	1.52	0	0.00	2

Figure 28: Comparison of Different Time Points with YMRS Scores in Control and Interventional Groups



4.5.2 Hamilton Depression Rating Scale (HAMD):

- In current study, the depression score has been assessed from the help of Hamilton depression rating scale. As per obtained result, at baseline level there were no statistical significant difference has been observed in between (p=0.2363) in control group (9.27±4.56) and interventional group (9.90±4.62). During the study follow-up clinical significant improvement in normal mood condition has been observed in interventional group (8.39±3.55) instead of control group (9.41±4.40). There were good percentage increment has been observed from baseline to final follow-up (-1.51±1.81) in interventional instead of control group (0.14±1.46). As per the scoring of HAMD, the lowest scoring represent good outcome of mood.

Table 58: **Comparison of Control and Interventional Groups with HAMD Scores at Different Time Points by Mann-Whitney U Test**

Times	Control group			Interventional group			U-Value	Z-Value	p-Value
	Mean	SD	Mean rank	Mean	SD	Mean rank			
Baseline	9.27	4.56	127.87	9.90	4.62	139.04	8101.00	-1.1844	0.2363
Follow-up 1	9.27	4.20	139.28	8.68	3.96	127.80	8080.50	-1.2170	0.2236
Follow-up 2	9.17	4.00	142.22	8.16	3.35	124.91	7692.50	-1.8355	0.0664
Follow-up 3	9.30	4.31	140.67	8.47	3.69	126.44	7897.50	-1.5087	0.1314
Follow-up 4	9.41	4.40	141.58	8.39	3.55	125.54	7777.00	-1.7008	0.0890
BL to F1	0.01	1.61	163.78	-1.22	1.22	103.67	4847.00	-6.3713	0.0001*
BL to F2	-0.10	1.83	163.60	-1.74	1.99	103.85	4871.00	-6.3331	0.0001*
BL to F3	0.03	1.30	167.45	-1.43	2.69	100.06	4362.50	-7.1436	0.0001*
BL to F4	0.14	1.46	167.64	-1.51	1.81	99.87	4337.50	-7.1835	0.0001*

p<0.05*, p<0.01**, p<0.0001***

Figure 29: Comparison of Control and Interventional Groups with HAMD Scores at Different Time Points.

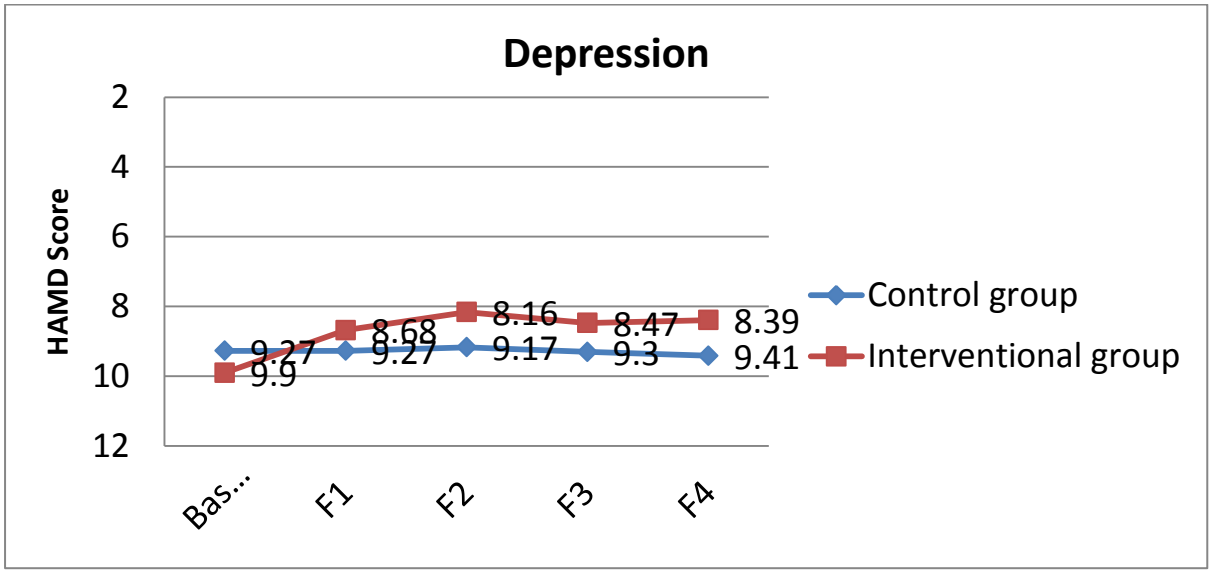


Table 59: **Comparison of Different Time Points with HAMD Scores in Control and Interventional Groups by Wilcoxon Matched Pairs Test**

- Comparison of different time points with HAMD scores in control and Interventional groups by Wilcoxon matched-pairs test represented highly clinical and statistical significance in the Interventional group. As per the obtained result, in control group no percentage significance difference (-1.55%, p=0.334) has been observed from baseline to final follow-up whereas in interventional group, high clinical as well as statistically significant improvement in mood outcome (15.30%, p=0.0001) has been observed.

Groups	Changes from	% of change	T-Value	Z-Value	P-Value
Control	BL to Follow-up 1	-0.08	2261.00	0.0705	0.9438
	BL to Follow-up 2	1.06	1405.50	0.6724	0.5013
	BL to Follow-up 3	-0.33	919.00	0.1903	0.8490
	BL to Follow-up 4	-1.55	1046.00	0.9656	0.3343
Experiment	BL to Follow-up 1	12.36	0.00	7.8181	0.0001*
	BL to Follow-up 2	17.56	756.00	7.7778	0.0001*
	BL to Follow-up 3	14.47	561.00	7.1690	0.0001*
	BL to Follow-up 4	15.30	525.50	7.6599	0.0001*

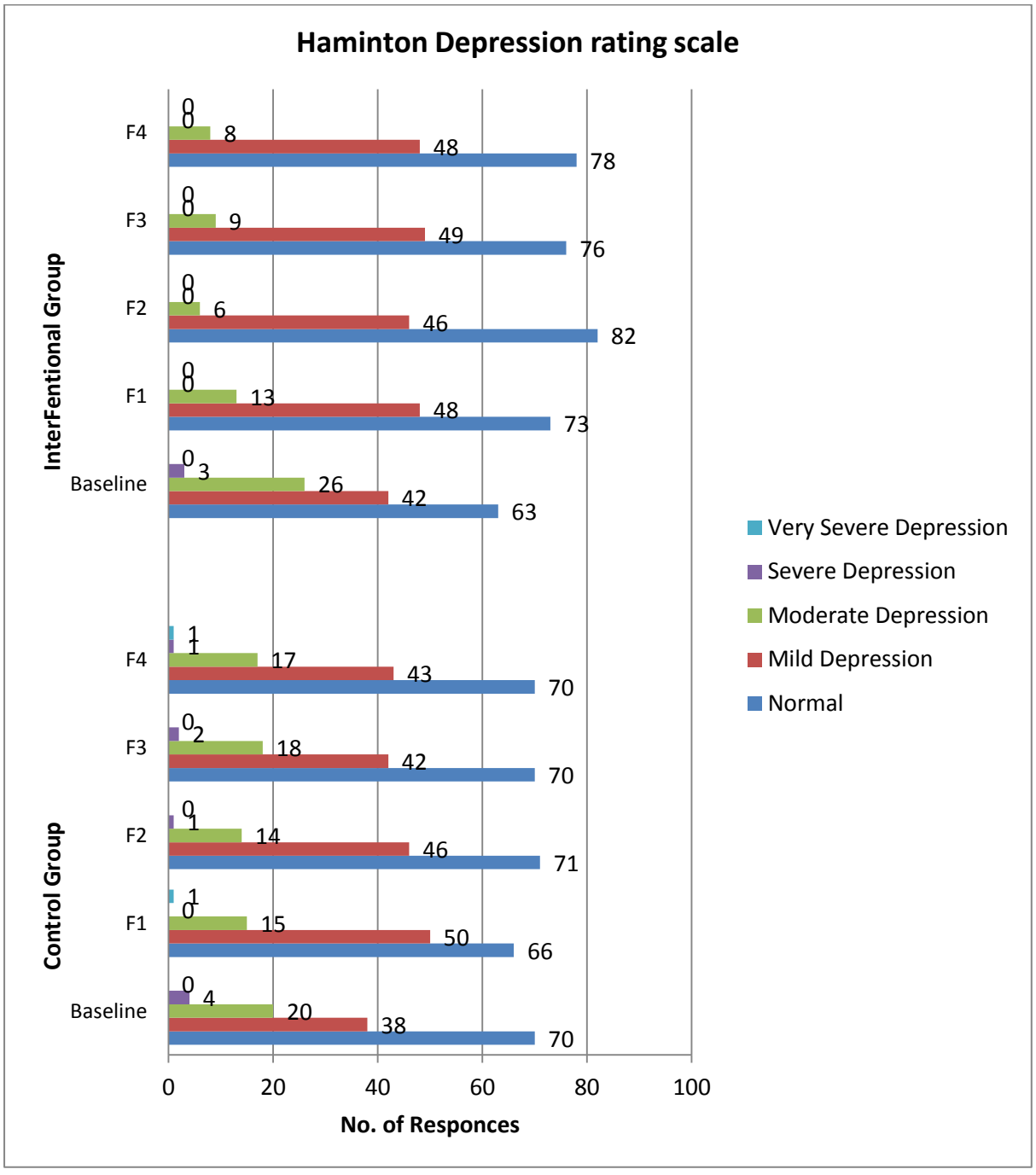
p<0.05*, p<0.01**, p<0.0001***

Table 60: **Comparison of Different Time Points with HAMD Scores in Control and Interventional Groups**

- The HAMD scores were compared on different time points showed that, at baseline level majority of patients (n=133) were in normal mood condition in control group (53.03%) and interventional group (47.01%). At final follow-up the patient shift in normal mood has been increased 11.20% in interventional group (58.21%) instead of control group (53.03%).

Time	HAMD scores	Control group	%	Intervention-al group	%	Total
Baseline	Normal	70	53.03	63	47.01	133
	Mild Depression	38	28.79	42	31.34	80
	Moderate Depression	20	15.15	26	19.40	46
	Severe Depression	4	3.03	3	2.24	7
	Very Severe Depression	0	0.00	0	0.00	0
Follow-up 1	Normal	66	50.00	73	54.48	139
	Mild Depression	50	37.88	48	35.82	98
	Moderate Depression	15	11.36	13	9.70	28
	Severe Depression	0	0.00	0	0.00	0
	Very Severe Depression	1	0.76	0	0.00	1
Follow-up 2	Normal	71	53.79	82	61.19	153
	Mild Depression	46	34.85	46	34.33	92
	Moderate Depression	14	10.61	6	4.48	20
	Severe Depression	1	0.76	0	0.00	1
	Very Severe Depression	0	0.00	0	0.00	0
Follow-up 3	Normal	70	53.03	76	56.72	146
	Mild Depression	42	31.82	49	36.57	91
	Moderate Depression	18	13.64	9	6.72	27
	Severe depression	2	1.52	0	0.00	2
	Very Severe Depression	0	0.00	0	0.00	0
Follow-up 4	Normal	70	53.03	78	58.21	148
	Mild Depression	43	32.58	48	35.82	91
	Moderate Depression	17	12.88	8	5.97	25
	Severe Depression	1	0.76	0	0.00	1
	Very Severe Depression	1	0.76	0	0.00	1

Figure 30: Comparison of Different Time Points with HAMD Scores in Control and Interventional Groups.



4.6 Correlation Analysis:

4.6.1 Correlation in Between Medication Adherence and Quality of Life

- In the correlation analysis of medication adherence and quality of life it is found that, in control group at baseline level there was negative correlation (r_s= -0.176,p =0.04) in between MA and QOL whereas in interventional group we found positive correlation but not statistically significant (r_s= +0.144, p=1.10). The same analysis has been performed on the final follow-up on control and interventional group. As per the obtained result in control group, we saw small positive correlation which was not statistically significant whereas in interventional group we assessed positive correlation coefficient as well as significant value (r_s= +0.181,p =0.03) in between MA and QOL. The obtained result strongly supports the coefficient in between the quality of life and medication adherence. Result state that, as the medication adherence will improve the quality of life of patients will also be improved.
- Here, we used ordinal variable to assess the correlation in between medication adherence and quality of life which illustrate that, as the medication adherence improve the quality of life of the patients would also be improve.

Table No. 61: Correlation Assessment in Between Medication Adherence (MMAS-8) and Quality of Life (WHO BREF QOL) at Different Point interval in Control group and Interventional Group by Spearman Coefficient Correlation Test.

Groups	Intervals	r_s	*P* Value
Control Group (n=132)	Baseline	-0.176	0.04*
	Final Follow-up	+0.013	0.88
Interventional group (n=134)	Baseline	+0.144	0.10
	Final Follow-up	+0.181	0.03*

P<0.05*, p<0.01**, p<0.0001***

4.6.2 Correlation in Between Medication Adherence and Mania

- Collected data of medication adherence and manic mood said that, the positive correlation is present in interventional group after the final intervention (r_s= +0.038,p =0.66) but not a strong correlation due to low statistical significance value, which state that, as MA increased normal mood condition. Whereas, in control group we found negative correlation (r_s= -0.42, p =0.63) which state that, non-adherence may lead the manic mood accretion.

Table No. 62: Correlation Assessment in Between Medication Adherence (MMAS-8) and Mania (YMRS) at Different Point interval in Control group and Interventional Group by Spearman Coefficient Correlation Test.

Groups	Intervals	r_s	*P* Value
Control Group (n=132)	Baseline	+0.078	0.37
	Final Follow-up	-0.42	0.63
Interventional group (n=134)	Baseline	+0.03	0.72
	Final Follow-up	+0.038	0.66

P<0.05*, p<0.01**, p<0.0001***

4.6.3 Correlation in Between Medication Adherence and Depression

- As per the obtain result of control group correlation coefficient in between depression and medication adherence (r_s= -0.19,p =0.02*), strongly support that non-adherence is clinically as well as statistically correlate the worst mood outcome with depressive patients as well as maniac patients, whereas positive correlation in interventional group (r_s= +0.047,p =0.59) partially support that, good adherence may lead the normal mood condition.

Table No. 63: Correlation Assessment in Between Medication Adherence (MMAS-8) and Depression (HAMD) at Different Point interval in Control group and Interventional Group by Spearman Coefficient Correlation Test.

Groups	Intervals	r_s	*P* Value
Control Group (n=132)	Baseline	-0.027	0.75
	Final Follow-up	-0.192	0.02*
Interventional group (n=134)	Baseline	+0.026	0.76
	Final Follow-up	+0.047	0.59

P<0.05*, p<0.01**, p<0.0001***

4.6.4 Correlation in Between Patients Age and Medication Adherence

- The correlation coefficient analysis has been applied in between age of the patients and medication adherence, to assess the correlation among these two variables in the study groups. As per the analysis, in control group we didn't observed any significant correlation in between age and medication adherence from the baseline to till final follow-up.

The same observation has been found at baseline level of interventional group. However, during the final follow-up of interventional group, we observed significant increment as well as correlation (1.97±1.26, $\mathbf{r_{s=}}$ -0.389, p= 0.023*) in medication adherence at the patients those age was more than 40 years instead of control group patients those age was more than 40 year correlation (4.50±1.76, $\mathbf{r_{s=}}$ +0.052, p= 0.749).

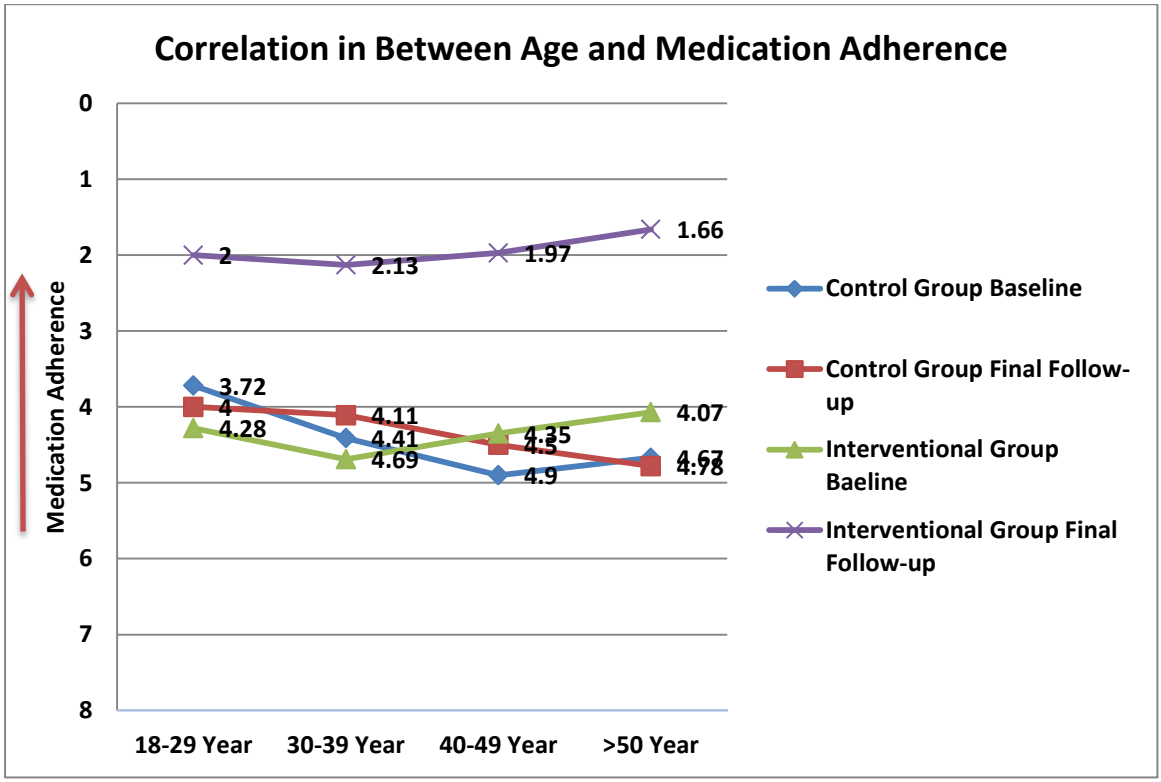
- Here, we found negative correlation value because of the descending value of medication adherence scale and ascending value of age. In our study we used MMAS-8 scale, as per the scoring of scale 0 value denoted high adherence, 1-2 medium adherence value more than 3 denoted low to poor adherence.

Table No. 64: Correlation Analysis In Between Age and Medication Adherence Through Spearmen Correlation Coefficient Test.

group	Time point	Age category (Year)	No. of patients	Mean±SD of MA	r_s	*P Value*
Control (n=132)	Baseline	18-29	43	3.72±3.05	+0.951	0.543
		30-39	37	4.41±2.69	-0.041	0.815
		40-49	40	4.90±2.71	+0.145	0.379
		>50	18	4.67±2.80	+0.436	0.070
	Final follow-up	18-29	43	4.00±1.87	+0.180	0.247
		30-39	37	4.11±1.83	-0.144	0.395
		40-49	40	4.50±1.76	+0.052	0.749
		>50	18	4.78±1.11	+0.650	0.796
Interventional (n=134)	Baseline	18-29	39	4.28±2.85	-0.015	0.928
		30-39	32	4.69±2.71	-0.004	0.981
		40-49	34	4.35±2.70	-0.364	0.340
		>50	29	4.07±2.98	+0.138	0.473
	Final follow-up	18-29	39	2.00±1.41	-0.067	0.687
		30-39	32	2.13±1.26	-0.095	0.606
		40-49	34	1.97±1.26	-0.389	0.023*
		>50	29	1.66±1.20	-0.017	0.931

P<0.05*, p<0.01**, p<0.0001***

Figure No. 31: Correlation Analysis In Between Age and Medication Adherence Through Spearmen Correlation Coefficient Test.



4.6.5 Correlation in Between Patients Age and Quality of Life

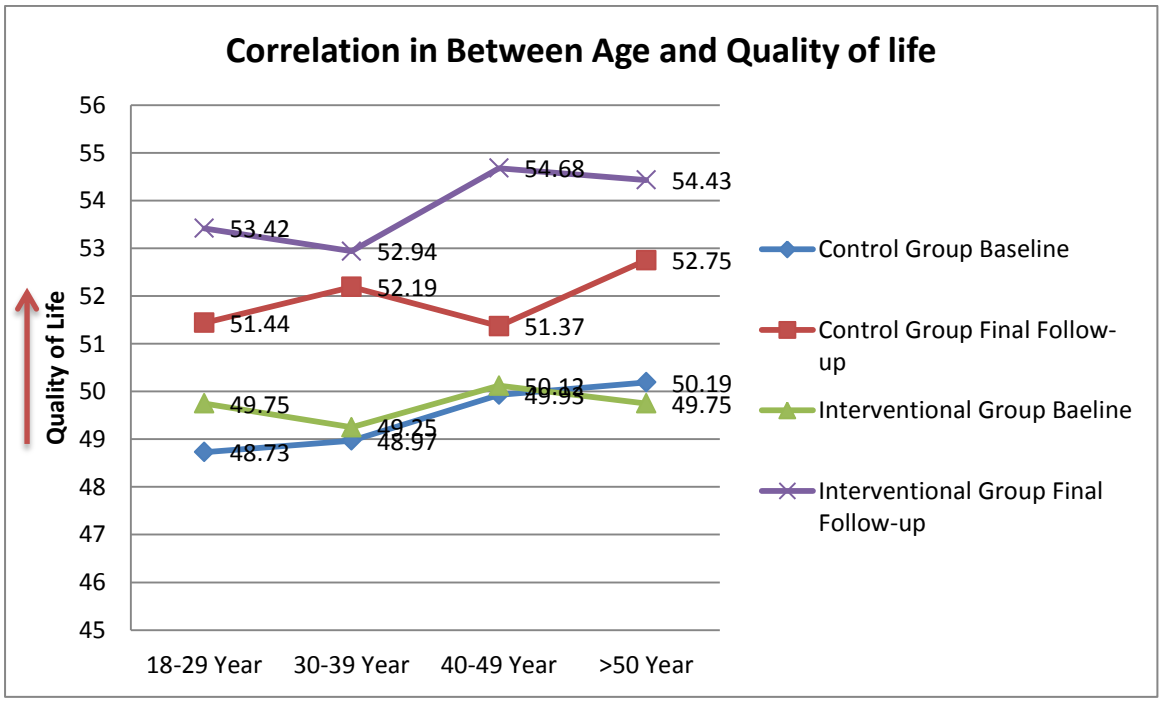
- The Pearson correlation rank analysis has been applied in between age of the patients and their health related quality of life, to assess the correlation among them. As per the analysis, in control group we didn't observed any significant correlation in between age group and quality of life from the baseline to till final follow-up. However, in interventional group during the final follow-up, we observed significant increment and strong positive correlation (52.94±5.54, $\rho =$ +0.066, p= 0.719) in quality of life at the patients those age was in between 30 to 65 years instead of control group patients (52.19±4.73, $\rho =$ -0.269, p= 0.107).
- Here we found the strong positive correlation in between increased age and quality of life because the value of both age and quality of life was in ascending order. Hence, it showed the positive correlation, which denoted that, as the age of patient improved till 50 year their quality of life also improved gradually.

Table No. 65: Correlation Analysis In Between Age and Quality Of Life Through Pearson Correlation Rank Test.

group	Time point	Age category (Year)	No. of patients	Mean±SD of QOL	ρ	*P Value*
Control (n=132)	Baseline	18-29	43	48.73±4.21	-0.121	0.401
		30-39	37	48.97±3.93	-0.275	0.099
		40-49	40	49.93±3.78	+0.118	0.470
		>50	18	50.19±4.16	+0.240	0.337
	Final follow-up	18-29	43	51.44±4.70	+0.076	0.628
		30-39	37	52.19±4.73	-0.269	0.107
		40-49	40	51.37±4.74	+0.040	0.806
		>50	18	52.75±5.23	-0.038	0.880
Interventional (n=134)	Baseline	18-29	39	49.75±4.39	-0.177	0.280
		30-39	32	49.25±4.14	-0.016	0.930
		40-49	34	50.12±5.06	-0.043	0.808
		>50	29	49.75±3.77	+0.127	0.513
	Final follow-up	18-29	39	53.42±5.23	-0.126	0.443
		30-39	32	52.94±5.54	+0.066	0.719
		40-49	34	54.68±5.90	+0.104	0.558
		>50	29	54.43±5.34	+0.049	0.799

P<0.05*, p<0.01**, p<0.0001***

Figure No. 32: Correlation Analysis In Between Age and Quality Of Life Through Pearson Correlation Rank Test.



5.0 DISCUSSION

BPAD is recurrence life-long disorder and usually require the long term therapy to maintain the patient's mood condition.[75] As per the network meta-analysis, maintain medication adherence is a critical job to control the symptom of BPAD. [76] It is estimated that the frequency of non-adherence of medication is approx. 10 -60%. [77] Non-adherence of medication increases the risk of relapse, hospital re-admission, poor QOL, drug-related problems and uncontrolled symptom of mania and depression.[78,79]

In the present study, we evaluated the different aspect of clinical pharmacist-led pharmaceutical care including MA, health-related QOL, drug-related problems and extent of patient's symptom through mood outcome.

In the current study, we took different measures to improve the MA, QOL, mood outcome and minimize the DRP's. For the same firstly, we prepared a collaborative team of well trained and qualified staff to improve the better therapeutic care of patients. Secondly, we screened patients to obtain a good and precise outcome through selective research criteria to target the real patient population as well as for the elimination of confounding bias. Thirdly, we prepared a suitable pharmaceutical care plan for patients were administered in the intervention group. Including medication-related education; psycho-education; evaluation and resolution of DRP and lifestyle-related education along with PIL in local language in Kannada, Marathi, Hindi and English. Fourthly, we randomized the patients through simple randomization method to eliminate the selection bias in the selection of patients. Finally, we were in touch with the patients during the study follow-up so that we could regulate the study's attrition rate.

5.1 Demographic Data:

As per the collected data of the study, patients' age distribution suggest the prevalence of BPAD higher under 30yrs (30.4%) in both Control and Interventional group. The finding of present study consent with that of an earlier report by Baldessarini R. J et. al. The present study acknowledges the finding of an earlier study that the onset of the age of first BPAD was similar to the age distribution results stating the higher preponderance under 30yrs to age group.[80]

In our study, the male predominance (60.8%) was prominent compared to female (40.2%) which is not correlated with the findings of earlier studies.[81] GBD 2017 state, that, the prevalence of BPAD is more in female 0.65% instead of male 0.55%. Even the interpersonal relation

of being married (75.18%) has an increased risk of BPAD. Few of studies correlated the same, as per Lieberman DZ et. al., married women are more sensitive for BPAD than a married man.[16, 82]

The family history of patients indicated the cause of BPAD was idiopathic significantly. As per the finding of present study family history is not significant with BPAD which is not correlated with earlier studies.[83, 84, 85] In most of the psychiatric problem childhood, adversity is one of the causes but in the current study, the adversity in childhood was substantially absent followed by neglected attention from the family in the control and interventional group of the study which is consent with that of an earlier report[84]

As per data of the result, there were very few patients with a smoking habit, but previous meta-analysis state that, the prevalence of tobacco smoking and alcohol misuse is high. The data of the current study does not consent with previous study data because in Indian scenario it's difficult to get female patients with such habits.[86] However, as per our study criteria we already exclude the patients those were chronic alcoholic and drug abusive, this might be the another reason to get less no of alcoholic patient.

5.2 Medication Adherence:

In current study, MA has been assessed by the help of the Morisky 8 MA questionnaire. The questions have been asked to the patients at each follow -up. Here we asked 8 questions to the patient and recorded the answers in "YES and NO" form at baseline label we didn't find any significant difference in between both of group (p=0.524). Whereas, significant improvement (2.40±1.84, p<0.0001*) have been observed in MA from follow-up 1 to follow-up 4 in the interventional group.

As per obtained result, the MA has been improved (p<0.0001*) from baseline to end the follow-up. Some previous study also acknowledges the current study data and pharmacist intervention for good medication (p<0.001*) adherence.[18, 44]

In a similar type of study Bahredar MJ et al., assessed the impact of medication-related education on MA. As per their data MA has been improved from 6.27(0.88) to 7.92(1.38) p=0.001 in the interventional group which also grants the findings of the current study which was improved MA from 4.35(2.79) to 1.95(1.29), p=0.0001 in interventional group.[51]

The results quoted above demonstrate that pharmaceutical care encourages the result of better adherence to medication. In the present study, we discovered that most patients and their relatives have lack of medication knowledge such as medication for what purpose; for what condition; when to take; with what to take; food constraint, etc. The current research has

focused on the whole point and educates the patients and their family members on medication and its use. We also administered education linked to lifestyle modification and their disease or disorder in addition to medication associated education.

Current research also found that most patients and their representative have forgotten administrative awareness of medication during follow-up after the first counseling. It might be due to length of study or mood swing, patient data leaflets were given for this account in order to strengthen the education so that we could accomplish the expected result towards medication.

5.3 Health-related quality of life (HR-QOL):

The patient's QOL have been measured through the WHO-BREF QOL, which is the 26 questioned health-related questionnaires with four different domains as physical health, psychological health, social relationship, environmental health. We have compared all these domains from baseline to the last follow-up. Interpreted data have clinically and statistically significance ($p=0.002$) in the Interventional group (53.86 ± 5.46) compared with the control group (51.83 ± 4.80).

The total QOL indicates the clinical significant enhancement into the groups from baseline to last follow-up. The QOL of the patients has been improved in term of less hospital readmission, normal mood condition, good adherence towards a treatment plan and healthy socio-economic life. A previous study by Pakpour AH et. al.[18] and Mishra A et. al,[44] gives similar insight to our study. These studies acknowledge the current study and pharmacist role was to enhance the patient QOL clinically as well as statistical significantly improved.

Similar studies evaluate the pharmacist intervention on psychiatry unit. As per author statement, statistically significant differences in physical health and psychological health ($p<0.001$) were observed. Similarly a pilot survey was performed to compare the impact of psycho-education on patient QOL. Statistically significant differences were noted in the QOL (mean) of both the research group ($p=0.04$) and the control group ($p=0.09$).[58] As per the evolution of the current data of research work, the QOL changed from baseline to last follow-up in the intervention group by 13.60%.

There have been many variables that can influence the QOL of the patient directly or indirectly, such as bad family support, social dilemma, economic situation, etc. The current enhancement in QOL was accomplished by adequate pharmacist interaction with the patients and their family member, as well as by offering counseling and the associated aids. Good ad-

herence to medication and resolved DRP's has been the most important factor in achieving better QOL. The patients' QOL has also been raised in the term of less hospital readmission, normal mood condition, less recurrence of symptom and good socio-economical life.

5.4 Drug-Related Problems (DRP's):

This study examined the pharmacist management of drug-related problems. We found a high occurrence of DRP's in both groups (34.2%). Among the DRP's drug-drug interaction (DDI) (21.05%) was more prevalent than adverse drug reaction (ADR) (13.15%). Approx. 34.2% of patients showed clinical or technical DRP's or both among the interventional and control group. In the current study, we have found quite low 32 DRP's per 100 patients compared to the previous study by Abunahlah N et. al.,[60] where they were found 163 DRPs per 100 patients. In 2018 Wali SC et. al.[87] found 45 DRPs per 100 patients whereas in few studies by Westerlund LT et. al[88], Hammerlein A et. al.[89], and Krahenbuhl JM et. al.[90] observed comparatively less 2.8, 0.93, 0.74 DRPs per 100 patients respectively. These figures illustrate the problem are hampered by different setting as well as the method of classification of DRPs. DDI was the most common DRP found in the current study followed by ADR. Some of the previous studies consent that DDI and ADR are the most frequent DRPs among the patients.[87, 90, 91]

5.4.1 Adverse Drug Reaction (ADR):

The ADRs were categorized into side effect suffered (non-allergic) with 10.61 %, 12.69% and Toxic effects suffered from 2.27%, 0.75% in Control and Interventional groups respectively. Among the ADR Lithium (**Lithosun SR 400 mg tablet, Sun Pharmaceutical Industries Ltd.**) induced adverse drug reactions were majorly, hand tremor (5.30%, 4.48%) followed by hypothyroidism (0.76%, 3.73%) in control and interventional group respectively. Muscle twitch (1.49%) and dry mouth (0.75%). Secondary drug-induced ADR was found as Olanzapine (**Oleanz 2.5 mg tab., Sun Pharmaceutical Industries Ltd.**) induced weight gain (3.03%,0.00%) in control and interventional group respectively. Thirdly, hand tremor and thrombocytopenia ADR induced by Sodium Valproate **(Torvate 500 mg tablet, Torrent Pharmaceuticals Ltd.,).** Rest of ADR like bradykinesia, impaired co-ordination, hypersalivation. constipation and weight gain has been observed which ware induced by Trifluoperazine, (**Benzyzine 10mg tablet, LA Pharmaceuticals**), Aripiprazole **(Arpizol 10mg tablet, Sun Pharmaceutical Industries Ltd.**) Alprazolam (**Alprax 0.25 mg tablet, Torrent Pharmaceuticals Ltd**.), Trihexyphenidyl (**Pacitane 2 mg tablet, Pfizer Ltd.)** and Risperidone

(**Sizodon 0.5 mg tablet, Sun Pharma Laboratories Ltd.)** respectively**.** A previous study in psychiatry setting by Shah A et. al.[92], Harichandran DF et. al.[38] and Gawali UP et. al.[93], consent the data of the current study. But in these all previous studies we didn't observe the trade name of the medication. Alert card for ADR was also given to the patient to generate knowledge about the ADR as well as instructions linked to ADR to prevent further complications in patient pharmacotherapy. The assessed ADR has been reported to the Pharmacovigilance commission of India through PvPi App.

5.4.2 ADR Documentation:

Among the ADRs 94.3% were associated with trigger factor, for the management of same the dose has been altered for 31.4% patients as well as specific treatment has been provided to the 40% of patients. A previous study in psychiatry by Khoda DA et. al., agreed on the ADR management data of the current study. Approx... 85.7% ADRs were re-challenged and outcome of 94.2% ADRs were continuous.

On the scale of causality assessment, we have observed 82.8% probable cases of ADR followed by definite and possible ADR. Some of the previous study in psychiatry as well as in Indian scenario by Shrivastav M et. al.[94], Mukherjee S et. al.[95] and Mishra S et al.[96] Consent the data of the current study.

The severity of ADR has been assessed by Hartwig's scale, as per the data of the current study, we observed 54.2% moderate ADR followed by mild, predictable and probable ADR. A previous study by Khoda D S et. al.[97], Shah A et. al.[92], and Gawali U P et. al.[93], assent the data of the current study.

5.4.3 Drug-drug Interactions (DDI's):

In the current study, the DDI's were classified into probable with (11.36%, 10.45%) and suspected with (12.12%, 8.21%) in Control and Interventional group respectively. The minor DDI suggests Sertraline and Lithium-induced risk of serotonin syndrome, which was leading (1.52%, 0.75%) in Control and Interventional group respectively. The chief significant DDI was Lorazepam and Olanzapine (3.03%, 5.97%) induced sedation and serious DDI ascertain was only Trifluoperazine and Chlorpromazine (1.52%,0.75%) induced QT interval prolongation in Control and Interventional group respectively. some of the previous studies in Indian scenario begs to differ the data due to patient population as well as disease and disorder condition.[61]

5.4.4 Causes of DRPs

As per the data of the current study we observed the drug/dose selection (29.55%, 27.61%) was the primary cause of DRPs whereas, drug use process (7.58%, 3.73%) was another cause of DRP in Control and Interventional group respectively. Drug and dose selection was the primary cause in previous studies by Ilickovic IM, et. al.[98], and Andrezza et. al.[99], which acknowledge the data of current study. Under the primary cause of DRPs at drug/dose selection was due to pharmacokinetic problems of 21.21% in Control group and 18.66% in Interventional group followed by manifest side effect, no other cause for 9.09% in Control and 5.05% in Interventional group. The results suggested clinical significance for the interventional group. The secondary cause of DRPs at drug use process was non-monitoring therapeutic drug Levels 1.52%, 1.49% in control and interventional group respectively presenting clinical significance. A pharmacist-led the previous study by Wolf C et. al.[100], consent with the current study.

5.4.5 Pharmacist intervention:

The pharmacist intervention has been proposed at the prescriber Level, patient Level and drug Level. At prescriber Level total 65 intervention has been proposed of which the majority of 66.1% (n=43) intervention has been accepted by psychiatrist whereas 44.9% (n=22) interventions have not been accepted. In a previous similar study, the acceptance rate of pharmacist intervention was 97% which correlated the data of the current study.[55]

At the patient level, the majority of patients were counselled. The maximum interventions have been proposed as a drug level of which there was no change in drug with 36.6% cases whereas, new drug start in 24.4% cases followed by 15.5% cases with drug change and so on. A similar study in psychiatry setting agreed on the intervention proposal as well as the acceptance rate of intervention by a psychiatrist.[98]

5.5 Mood Outcome:

In the current, study impact of a pharmacist, the intervention was assessed through symptomatic relief of BPAD. The extent of BPAD has been assessed through young mania rating scale (YMRS) for mania and Hamilton depression scale (HAMD) for depression. For assessment of better result, we applied normality distribution test on both of group, in which we have observed non-parametric distribution hence non-parametric tests were applied among the group.

As per the result of the current study, on a scale of mania at a baseline level, we didn't observe any significant difference among the group p=0.9086 whereas at follow-up there were clinically as well as statistically improvement (p=0.0006*) has been observed in interventional group patients with mania. The 8.21 positive percentage increment of normal mood has been seen in the interventional group (78.36% to 86.57%) instead of the control group (81.82% to 75.76%) from baseline to the last follow -up. Pakpour A H et al. also did a similar study which, observed mood improvement from baseline (15.32±2.76) to follow-up (10.40±2.01) p=0.02 which was consent with the data of the current study.[18]

Similarly on the scale of depression, at a baseline Level, we didn't observe any significant difference among the control group (9.27±4.56) and interventional group (9.90±4.62) p=0.2363. Whereas at follow-up there were clinically as well as statistically improvement (8.39±3.35) (p=0.001*) has been observed in interventional group patients with depression. The 11.11 positive percentage increment of normal mood has been seen in the interventional group (47.01% to 58.21%) instead of the control group from baseline to the last follow -up. A previous study observed improvement in mood outcome from baseline (22.21±5.71) to follow-up (17.13±7.55) p=0.001 which was consent with the data of the current study.[18] A similar study in 2007 by Wiess R D et. al., apprise that, group counselling of patient with BPAD is effective on maniac as well as a depressive symptom which acknowledge the data of our work.[63]

The study's ultimate result was the favorable result of mood. This was accomplished by improving compliance with medication, health status and less DRP. The collaborative strategy controlled the symptomatic relapse among patients with BPAD through which the current research achieved a better result in terms of restoring patients in normal social life. Here, we not only save the time of patients as well as money too.

5.6 Correlation Analysis

In this study correlation analysis has been applied, to assess the correlation in between medication adherence and quality of life. As per the obtained result in control group, we saw small positive correlation which was not statistically significant whereas in interventional group we assessed positive correlation coefficient as well as significant value (r_s= +0.181, p=0.03) in between MA and QOL. The smellier correlation analysis has been applied, to assess the correlation in between medication adherence and mania/depression. Obtained result of correlation in between MA & mania showed, positive correlation (r_s = +0.038, p=0.66) but not a

strong correlation due to low statistical significance value. The correlation coefficient in between depression and medication adherence (r_s = -0.19, p=0.02*), strongly support that non-adherence is clinically as well as statistically correlate the worst mood outcome with depressive patients as well as maniac patients, whereas positive correlation in interventional group (r_s = +0.047, p=0.59) partially support that, good adherence may lead the normal mood condition.

We also assessed the correlation of age with the medication adherence and quality of life. As per the obtained findings we observed that, as the age increased from vicenarian to quadragenarian; the patients' medication adherence (1.97±1.26, r_s= -0.389, p= 0.023*) as well as quality of life (52.94±5.54, ρ= +0.066, p= 0.719) increased in interventional group after the pharmaceutical care intervention instead control group. The parallel increment in quality of life and medication adherence has been seen in quadragenarian patients, which illustrated that, high medication adherence also leads the good quality of life of the patients. However, the vicenarian patients showed the least medication adherence as well as quality of life in both groups.

The above mention result of correlation analysis strongly support that, good medication adherence can increase the patients' quality of life and normal mood condition from the mania and depression. But we didn't find any of previous study related to correlation in between medication adherence and quality of life and mood outcome. Hence, we were not able to correlate the data of our study with previous study because this is the first study to evaluate the correlation in between medication adherence and QOL and mood outcome for the patients with bipolar disorder in India.

6.0 SUMMARY

The research aims for the pharmacist-led care in patients with BPAD, to improve the MA rate and mood outcome, with increased efficacy as well as safety of Pharmacotherapy in order to get therapeutic goals, and ultimately improving the QOL of the patients.

The preliminary objective of the research work was to compare the two groups with the effect of Pharmaceutical care on MA and HRQOL of the patients with BPAD at various time frames as well as to assess and resolve the susceptible DRPs of the patients. The secondary was to assess the extent of BPADs (depression and mania) by using different scales (like the HAMD & YMRS).

The study site was initiated at the department of Psychiatric, KLE's Dr P. K. Charitable Hospital, Nehru Nagar, Belagavi with the prospective, RCT study design. The patients were screened according to the selection criteria and further were randomized (control & experimental group) and recorded for the study. The interventional group was with the usual care as well as the pharmaceutical care whereas the control group with usual care only. Both the arms assessed variables like effectiveness, safety, adherence, QOL, DRPs.

The study outcome was ascertained with the Morisky 8-Item MA Questionnaire, WHOQOL-BREF Health Status Questionnaire, Drug-related problems (DRPs), Young Mania Rating Scale, Hamilton Rating Scale, Causes and Problems related to necessity, effectiveness, and security of the pharmacotherapy.

The total sample size estimation was calculated through hypothesis proportion formula with 15% attrition rate observed to be 286 patients with 95% of CI. Probability was considered $P<0.05$ for statistical significance. The data of the current study was entered and analyzed on IBM SPSS Statistics Version-20 (IBM Corporation, United State). The versatile parametric and non-parametric tests were applied for analysis contingent upon the normal distribution curve of the statistics.

The final data analysis was completed on 266 patients. The demographics presented male predominance higher towards the disorder compared to the female. Even the marital status of being married was at greater risk followed by singles. The socioeconomic status homemaker, farmer, private workers were affected by the disorder respectively. The other co-morbidities were significant with the p-value < 0.05. The MA was found to be highly significant $p < 0.05$

at different time points. At the point of correlation study has found positive as well as statistical significant correlation ($p<0.03$*) in between medication adherence and quality of life in interventional group. Normality of Health-related QOL (HR-QOL) with its domain scores in two groups at different time points by Kolmogorov Smirnov test presented as highly significant p-value < 0.05. The total QOL score at different time points by independent t-test interprets clinical significance but not statistical significance. Drug-induced Adverse Drug Reactions (ADR) showed clinical significance p-value > 0.05. The drug interactions and causes were clinically significant p-value > 0.05. The pharmacist intervention was highly significant at various prescriber, patient and drug levels respectively.

The study summarizes the mental health system in current scenario among Indian masses to be neglected segment of the society. This study helps to cut through the stigma associated in the Indian society wherein the pharmacist should represent themselves as a part of an interdisciplinary solution that resolves the gaps by helping to diligently adhere to the medication-related services. This enhances pharmacotherapy outcomes which facilitate the rapid retrieval with mental illness. Here, we felt the need for speciality pharmacist to provide long-term medication management for patients with chronic mental illness. The collaborative care approach towards mental health can be an executable choice to address the unmet needs in BPAD patients.

7.0 CONCLUSION

Conducted study result has given us the insight that, clinical pharmacist-led collaborative care with psychiatry professionals team (Psychiatrist, Nurses and psychologist) can enhance the patients' MA; health status (QOL) and mood outcome as well as its help to minimize the incidence of drug-related problems associated with patients' pharmacotherapy as well as pharmacist led collaborative care reduced the economic burden from the pocket of the patients in term of less symptom relapse and hospital re-admission. The result shows that clinical pharmacist intervention is very important in maximizing the beneficiary effect, minimizing the AE's and helping to lead the integration in the health care delivery system in the psychiatry department.

7.1 Limitations

Apart from these positive points, we have some limitation in the current study. The first limitation was patient-related recall bias which is also referred to as response bias or reporting bias. As the study patient population belonged to BPAD with the mood swing at different point of the interval were more susceptible to recall bias. In our study, we used self-administered questionnaires for the patients. During the study follow-up, we observed that most patients with manic phase reported high MA and QOL instead of depressive patients showed poor MA as well as the QOL. The second limitation was to control the patient attrition rate of the patient. The rate of voluntary withdrawal with without explanation was high among both groups. However, for the same, we used 10% attrition rate with a total sample size of the study. The third limitation was to control the mutual exposure of study participants. The mutual exposure can be a reason of knowledge transformation in between the group. This may deviate the study data.The fourth limitation was the socio-economic status of the patients. In the study, many patients belonged to a poor socio-economic background. For such patients, it was difficult to purchase prescribed branded medication and bear the load of hospital admission. Due to the same patient met with poor MA as well as poor QOL.

The last limitation was related to family member counselling. In many cases, at OPD patients used to come alone. In such a condition, we failed to counsel the LAR as well as sometimes patients.

7.2 Future Direction

In the current study, we missed to include certain points. Of them firstly, we didn't segregate the patients according to different phases of BPAD (BPAD-I and BPAD-II). Secondly, we have not done the pharmacoeconomical evolution in the study population. As the many patients were from poor economic background hence it was necessary to do pharmacoeconomic outcome so that patient can stick the therapeutic plan. Thirdly, about the reporting of DRP's. Among all DRP's we have reported only ADR at PvPi and fourthly, we have not checked the therapeutic level of the drugs like lithium. this was very important to assess the serum value of the medication for toxicity.

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Annexure I: PIS & ICF (English, Kannada & Marathi)

Patient Information Sheet

Effect of pharmaceutical care on enhancement of safety, medication adherence and quality of life in patient with Bipolar disorder: A prospective study in tertiary care hospital.

Introduction:-

You have invited to take part in a research study which compares the benefit of the pharmaceutical care along with the usual care versus pharmaceutical care of the patients with Bipolar disorder. Proposed study helps' patients with mental illness to return as quickly as possible to fulfill and to reduce the chances of further mental illness. We want to know whether pharmaceutical care of patients can provide better and effective quality of life for patients and improvement of mental health. We invited you to participate in a research study, that will help to answer this question.

Purpose of study:-

Pharmaceutical care is the responsible provision of medicine therapy for the purpose of definite outcome that improve patient quality of life, which is an interdisciplinary approachand indispensable element of patient centered health care and requires to change the traditional professional attitude, it implies on actively participate patients in making decision regard to pharmacotherapy, encouraging positive lifestyle changes, to improve medication adherence, medication education and disease management for patients.

Why have you been chosen to take part in the study:-

This study to see whether pharmaceutical care, reduce the chance of further consequence of mental illness and improve recovery of patients with Bipolar disorder. Since you had a recent incidence, you have been chosen to participate in this study.

What does it mean to participate?

Your participation is entirely voluntary; to help you make your decision, please read this information sheet. You are free to discuss the content of this document with a member of your family. You may take much time as you like to consider whether take or not to take part in the study. If you chose not to take part, your current and future care will not be affected. If you agree to take part you are free to withdraw from the study at any time without loss of benefits.

Once you understand what is involved in the study and you wish to participate, you will be requested to sign the consent form. If you have a question or query at any time during the research study you should feel free to ask us and obtain answers to your questions. You are not giving any of your legal rights by volunteering for this research study or by signing this consent form.

To participate in the study means that you have given your consent to be a part of this study for a duration of two years during which the following will be required from you.

During the study:-

You will be assessed for your mental health by using details from your medical records, if you found eligible, you will be assigned to one of the two groups. (1) Served with

pharmaceutical care and another one (2) served with usual care. Both groups are the beneficial for the patients.

The allocation to one or another group will be done by computerized sample randomization technique. Thus, each person will have 50:50 chances of being assigned to either of the two groups (like the flip of a coin).

If you assigned to the intervention group, you will receive an educational session on medication management, disease management and lifestyle modification during this session we will provide you patient information leaflets (PIL). The material will be free of cost for you.

Further contact after completion of baseline data collection:-

After the hospital visit or follow-up we will ask you some question about your health, daily activity and lifestyle. Subsequently, we will also collect your routine information from the hospital record and your follow-up in OP.

Benefits from the study:-

Pharmaceutical care is a patient oriented care, which is a beneficiary approach; provided by clinical pharmacist for improving patients' mental health and will be available to you free of charge. By participating in the study you may become more aware of your mental status and how you can look after it in the future by making positive lifestyle and other changes.

What are the risks in participating in the study:-

We do not expect that you will incur any risk by participating in the study. There is no invasive procedure involve in this study.

Who has reviewed the study?

This study has been reviewed by the institutional ethics committee, which has responsibility for scrutinizing proposal for medical research on human. The reviewing committee has raised no objection from the point of view of medical ethics.

Inquiries/Questions:-

If you have any question about research, develop a research related problem or note a change in your condition, you should contact to **Mr. Ashish Singh Parihar** Mob. No. +917022076752. Should you have any Question regarding your rights as a research participant, you may contact the Institutional Review Board.

"Thank you for taking to read this information sheet. If you wish to take part in this study, please sign and date the consent from giving to you, you will be given a copy of the information sheet and your signed consent form."

Participant initials……

Informed Consent Form

Effect of pharmaceutical care on enhancement of safety, medication adherence and quality of life in patient with Bipolar disorder: A prospective study in tertiary care hospital.

Researcher:- Ashish Singh Parihar

+91-8088244739, +91-7022076752

py.ashishsingh@gmail.com

Participant Name:-……Date:-…….

Date of Birth:-…… Age:-…….

Please read following before putting your signature before

1) I have read and understand the participant information sheet concerning this study and I understand what will be required of me and what will be happening to me if I take part on it.

2) My questions concerning this study have been answered by Mr. Ashish Singh Parihar.

3) I understand that at any time I mat withdrawn from this study without giving any reason and without affecting my normal care and management.

4) I understand that researcher and the authorities will not need my permission to look my health record, both for current study and further research that may be conducted in relation to it even if I stop taking part in the study.

5) I understand that my identity will not be revealed in any information related to another one.

6) I agree not to restrict the use of any of my information or results that arises from this study provided such a use is only for scientific purpose.

7) I have been given a copy of the information sheet and consent form to keep by signing this form I have not given up my legal rights.

8) I agree to take part in the study

Participant Name **Signature/ thumb impression**

Name of impartial witness **Signature/ thumb impression**

Name of researcher **Signature**

Name of psychiatrist **Signature**

ರೋಗಿಯ ಮಾಹಿತಿ ಪತ್ರ

ಸಾಮಾನ್ಯ ದರ್ಜೆಯ ಆಸ್ಪತ್ರೆಗಳಲ್ಲಿ ಬಾಯ ಪೋಲಾರ ರೋಗಿಗಳ ಔಷಧಿಗಳಿಗೆ ಬದ್ಧತೆ ಹಾಗು ರೋಗಿಯ ಜೀವನದ ಗುಣಮಟ್ಟ ಸುಧಾರಿಸುವ ಔಷಧಿಯ ಉಪಚಾರ ಹಾಗು ಭದ್ರತೆ ಹೆಚ್ಚಿಸುವ ಕುರಿತು ಭವಿಷ್ಯಕ್ಕೆ ಕುರಿತಂತೆ ಅಧ್ಯಯನ.

ಮುನ್ನುಡಿ:

ಸಾಮಾನ್ಯ ಉಪಚಾರಗಳ ಜೊತೆ ಔಷಧೋಪಚಾರಗಳ ಲಾಭ ಹಾಗು ಔಷಧೋಪಚಾರಗಳ ಕುರಿತು ತುಲನಾತ್ಮಕ ರೋಗಿಗಳ ಮೇಲೆ ಅಭ್ಯಾಸಕ್ಕೆ ಈ ಸಂಶೋಧನೆಯಲ್ಲಿ ಅಧ್ಯಯನಕ್ಕೆ ನಿಮ್ಮನ್ನು ಅಮಂತ್ರಿಸಲಾಗಿದೆ. ಸದರೀ ಅಧ್ಯಯನ ರೋಗಿಗಳ ಅನಾರೋಗ್ಯ ಉಲ್ಬಣದಂತೆ ಹಾಗು ಅವರ ಆರೋಗ್ಯದಲ್ಲಿ ಸುಧಾರಿಸುವಂತೆ ಮಾಡುವ ಪ್ರಯತ್ನದ ಅಧ್ಯಯನ ವಾಗಿದೆ. ರೋಗಿಗಳ ಜೀವನ ಮಟ್ಟ ಸುವ್ಯವಸ್ಥಿತ ಗೊಳಿಸಿವದರಲ್ಲಿ ಹಾಗು ಅವರ ಮಾನಸಿಕ ಆರೊಗ್ಯ ದಲ್ಲಿ ಸುಧಾರಿಸುವದರಲ್ಲಿ ಔಷಧೀ ಯೋಜನೆಯ ಪ್ರಯೋಜನೆ ಹೇಗಾಗುತ್ತದೆ ಎಂದು ತಿಳಿಯಲು ಸಹಾಯಕ ವಾಗುತ್ತದೆ. ಈ ಪ್ರಶ್ನೆಗಳಿಗೆ ಉತ್ತರ ಪಡೆಯಲು ನಾವು ಸದರೀ ಅಧ್ಯಯನವನ್ನು ಮಾಡುತ್ತಿದ್ದು ಅದರಲ್ಲಿ ಸಹಭಾಗಿಯಾಗಲು ತಮ್ಮನ್ನು ಅಮಂತ್ರಿಸಿದ್ದೇವೆ.

ಅಧ್ಯಯನದ ಉದ್ದೇಶ:

ಔಷಧೀಯ ಉಪಚಾರದಿಂದಾಗಿ ಔಷಧ ಶಾಸ್ತ್ರವು ರೋಗಿಯ ಆರೋಗ್ಯ ಮಟ್ಟವನ್ನು ಮೇಲಕ್ಕೆತ್ತುವದರಲ್ಲಿ ನಿಶ್ಚಿತವಾಗಿಯೂ ಸ್ಪಷ್ಟವಾಗಿಯೂ ಉಪಯೋಗಿಯಾಗಿದೆ. ಇದು ರೋಗಿ ಕೇಂದ್ರಿತ ಸಂಯುಕ್ತ ಉಪಚಾರ ಕ್ಕೆ ಅತ್ಯಾವಶ್ಯಕ ವಾಗಿದೆ. ಹಾಗು ಸಾಂಪ್ರದಾಯಿಕ ವ್ಯವಸಾಯಿಕ ದ್ರೀಷ್ಟಿಕೋನವನ್ನುಬದಲಾಯಿಸುವ ಅವಶ್ಯಕತೆ ಇದೆ. ಇದರಲ್ಲಿ ಔಷಧ ಶಾಸ್ತ್ರದ ಕಾರ್ಯದಲ್ಲಿ ರೋಗಿಯ ಸಕ್ರೀಯವಾಗಿ ಭಾಗವಹಿಸಿ ನಿರ್ಣಯ ತೆಗೆದುಕೊಳ್ಳುವದರಲ್ಲಿ ಸಹಾಯಕವಾಗುತ್ತದೆ. ಇದರಿಂದಾಗಿ ಸಕಾರಾತ್ಮಕ ಚಿಂತೆನೆ ಮಾಡಿ ಜೀವನಶೈಲಿಯಲ್ಲಿ ಸುಧಾರಣೆ ಔಷಧೋಪಚಾರಗಳ ಆಧಾರದಿಂದ ತರುವದಾಗಿದೆ ಹಾಗು ರೋಗಿಯ ಶಿಕ್ಷಣ ಹಾಗು ರೋಗ ವ್ಯವಸ್ಥಾಪನೆ ಕಾರ್ಯವನ್ನೂ ಮಾಡುವದಾಗಿದೆ.

ಈ ಅಧ್ಯಯನದಲ್ಲಿ ನಿಮ್ಮನ್ನೆಕೆ ಆಯ್ಕೆ ಮಾಡಲಾಗಿದೆ ?

ಬಾಯ ಪೋಲಾರ ದೋಷದಿಂದಾಗಿರುವ ಮಾನಸಿಕ ವಿಕಾರಗಳು ಪುನಃ ಉಲ್ಬಣ ಗೊಳ್ಳಬಾರದೆಂಬ ಉದ್ದೇಶದಿಂದ ಮಾಡಲಾದ ಔಷಧೋಪಚಾರಗಳ ಸೇವೆಯ ಕುರಿತು ಅಧ್ಯಯನ ಮಾಡುವ ಉದ್ದೇಶದಿಂದ ಈ ಸಂಶೋಧನೆ ಕೈಕೊಳ್ಳಲಾಗಿದೆ. ನಿಮಗೆ ಇತ್ತೀಚೆಗೆ ಇದ್ದು ಕುರಿತು ಅನುಭವ ಬಂದಿದ್ದರಿಂದ ನಿಮ್ಮನ್ನು ಆಯ್ಕೆ ಮಾಡಲಾಗದೆ.

ಇದರಲ್ಲಿ ಭಾಗವಹಿಸುವದೆಂದರೇನು ?

ನಿಮಗೆ ನಿರ್ಣಯ ತೆಗೆದುಕೊಳ್ಳಲು ಈ ಮಾಹಿತೀ ಪತ್ರಕದ ಓದು ಬಹಳ ಪ್ರಯೋಜನ ವಾಗುತ್ತದೆ. ನೀವು ಇದರಲ್ಲಿ ಸ್ವೇಚ್ಛೆಯಿಂದ ಇದರಲ್ಲಿ ಭಾಗವಹಿಸಿದ್ದೀರೀ ನಿಮ್ಮ ಮನೆಯವರ ಜೊತೆ ಈ ದಾಖಲಾತಿ ಯಲ್ಲಿನ ವಿಷಯಗಳ ಕುರಿತು ಮಕ್ತವಾಗಿ ವಿಚಾರವಿನಿಮಯ ಮಾಡಬಹುದಾಗಿದೆ. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸ ಬೇಕವೂ ಬೇಡವೂ ಇದರ ಕುರಿತು ನೀವೆ ನಿರ್ಣಯ ತೆಗೆದುಕೊಳ್ಳತಕ್ಕದ್ದು. ಇದಕ್ಕೆ ನಿಮಗೆ ಎಷ್ಟು ಬೇಕಾದಷ್ಟು ಸಮಯ ತೆ'ಗೆದುಕೊಳ್ಳ ನೀವು

ಭಾಗವಹಿಸದೆ ಇರುವ ನಿರ್ಣಯ ತೆಗೆದುಕೊಂಡರೂ ನಿಮ್ಮ ಸದ್ಯ ಹಾಗು ಮುಂದಿನ ಭವಿಷ್ಯ ದಲ್ಲಿ ಏನೂ ಪರಿಣಾಮವಾಗದೂ. ನೀವು ಭಾಗವಹಿಸುವ ನಿರ್ಣಯ ತೆಗೆದುಕೊಂಡ ನಂತರ ಕೂಡ ನಿಮಗೆ ಯಾವಾಗ ಬೇಕಾದಾಗ ಹೊರಗೆ ಹೊಗಬಹುದಾಗಿದೆ, ಇದರಿಂದ ನಿಮಗೆ ಯಾವುದೆ ಹಾನಿ ಯಾಗಲಾರದು.

ಒಮ್ಮೆ ನಿಮಗೆ ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸುವ ದೆಂದರೇನೂ ತಿಳಿದ ನಂತರ ನೀವೂ ಭಾಗವಹಿಸುವ ಇಚ್ಛೆಯನ್ನು ವ್ಯಕ್ತ ಪಡಿಸಿದರೆ ನೀವು ಒಂದು ಸಮ್ಮತೀ ಪತ್ರಕ್ಕೆ ಅಂಕಿತ ಹಾಕಬೇಕಾಗುವದು. ಸದರೀ ಅಧ್ಯಯನ ಕಾಲದಲ್ಲಿ ಅಧ್ಯಯನದ ಕುರಿತು ನಿಮಗೇನಾದರೂ ಶಂಕೆಗಳು ಬಂದರೇ ಅದರ ಕುರಿತು ನೀವು ಯಾವಾಗ ಬೇಕಾದಾಗ ಶಂಕೆ ಸಂಶಯ ನಿರಾಕರಿಸಬಹುದಾಗಿದೆ, ನೀವು ನಿಮ್ಮ ಸಂಶಯ ಗಳ ಕುರಿತು ಯಾವ ಬೇಕಾದ ಪ್ರಶ್ನೆಗಳನ್ನು ಕೇಳಿ ಉತ್ತರ ಪಡೆಯಲು ಪೂರ್ತಿ ಸ್ವತಂತ್ರರಿದ್ದೀರಿ. ಸದರೀ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸುವದರಿಂದ ನೀವು ಯಾವುದೇ ಕಾನೂನು ಬದ್ಧ ಹಕ್ಕುಗಳಿಂದ ವಂಚಿತ ರಾಗುವದಿಲ್ಲ. ಸದರೀ ಅಧ್ಯಯನದಲ್ಲಿ ನೀವು ಭಾಗವಹಿಸುವದೆಂದರೆ. ನೀವು ಎರಡು ವರ್ಷಗಳ ಅವಧಯ ಸಲುವಾಗಿ ಸದರೀ ಅಧ್ಯಯನದ ಭಾಗವಾಗಲು ಸಮ್ಮತಿಸಿರುತ್ತೀರೀ.

ಅಧ್ಯಯನದ ಕಾಲದಲ್ಲಿ:

ನಿಮ್ಮ ವೈದ್ಯಕೀಯ ದಾಖಲೆಗಳನ್ನು ಅಭ್ಯಸಿಸಿ ನಿಮ್ಮ ಮಾನಸಿಕ ಆರೋಗ್ಯವನ್ನು ನಿರ್ಣಯಿಸಿ ನೀವು ಪಾತ್ರರಾದರೆ ನಿಮ್ಮನ್ನು ಯಾವದಾದರೂ ಎರಡು ಗುಂಪುಗಳಲ್ಲಿ ಸೇರ್ಪಡೆ ಮಾಡಿ ಒಂದು ಗುಂಪಿನಲ್ಲಿ ಕೊಡಲಾಗುವದು (೧) ಒಂದರಲ್ಲಿ ಔಷಧೋಪಚಾರ ಸೇವೆ ಇದ್ದದ್ದು (೨) ಇನ್ನೊಂದರಲ್ಲಿ ಸಾಮಾನ್ಯ ಸೇವೆ ಪಡೆದದ್ದು. ಎರಡು ಗುಂಪುಗಳು ರೋಗಿಗೆ ಲಾಭದಾಯಕವಾಗಿವೆ.

ಒಂದು ಅಥವಾ ಇನ್ನೊಂದು ಗುಂಪುಗಳಲಿ ವಿಂಗಡಿಸುವ ಕಾರ್ಯವನ್ನು ಕಂಪ್ಯುಟರಿಜೆದ್ ಸ್ಯಾಂಪಲ ರ್ಯಾಂಡೊಮಾಯಜೆಶನ ತಂತ್ರದ ಮುಖಾಂತರ ಮಾಡಲಾಗುವದು. ಹೀಗೆ ಪ್ರತಿಯೊಬ್ಬರಿಗೆ ೫೦:೫೦ ಅವಧಿ ದೊರಕಿ ಯಾವದಾದರೊಂದು ಗುಂಪಿನಲ್ಲಿ ಕೊಡಲಾಗುವದು. (ರೊಪಾಯಿಯ ಚಿತ್ ಪಟ್ಟದಂತೆ)

ನಿಮಗೆ ಈ ಮಧ್ಯದ ಯಾವದಾದರೊಂದು ಗುಂಪು ಕೊಟ್ಟನಂತರ, ನಿಮಗೆ ಅಧ್ಯಯನದ ಅವಧಿಯಲ್ಲಿ ಔಷಧಿ ಉಪಾಯೋಜನೆ ವ್ಯವಸ್ಥಾಪನೆ ಕುರಿತು, ರೋಗ ವ್ಯವಸ್ಥಾಪನೆ ಹಾಗು ಜೀವನ ಪದ್ಧತಿ ದರ್ಜೆ ಸುಧಾರಣೆ ಕುರಿತು ನಿಮಗೆ ಶಿಕ್ಷಣ ಕೊಡಲಾಗುವದು. ಅಧ್ಯಯನದ ಕಾಲದಲ್ಲಿ ನಾವು ನಿಮಗೆ ರೋಗಿಗಳ ಮಾಹಿತಿ ಪತ್ರಕಗಳನ್ನು ಕೊಡುತ್ತೇವೆ. (ಪ್. ಆಯ್. ಎಲ್). ಎಲ್ಲ ಸರಕುಗಳನ್ನು ನಿಮಗೆ ಮುಫತ್ತಾಗಿ ಪೂರೈಸಲಾಗುವದು.

ಎಲ್ಲ ಮೂಲ ಪ್ರಾಥಮಿಕ ದಾಖಲಾತಿ ಮಾಹಿತಿ ಸಂಗ್ರಹಣೆಯ ನಂತರ ಮುಂದೆ ಮತ್ತೆ ಸಂಪರ್ಕ :–

ಆಸ್ಪತ್ರೆಯ ಭೇಟಿಯ ನಂತರ ಅಥವಾ ನೀವು ಫಾಲೊ ಅಪದಲ್ಲಿ ನಾವು ನಿಮಗೆ ನಿಮ್ಮ ಆರೋಗ್ಯ, ನಿಮ್ಮ ದಿನನಿತ್ಯದ ಕೆಲಸಗಳು ಹಾಗು ನಿಮ್ಮ ಜೀವನಶೈಲಿ ಕುರಿತು ಕೆಲವು ಪ್ರಶ್ನೆಗಳನ್ನು ಕೇಳುತ್ತೇವೆ. ನಂತರ ನಿಮ್ಮ ಕುರಿತು ನಾವು ಆಸ್ಪತ್ರೆಯ ದಾಖಲೆಗಳಂದ, ನಿಮ್ಮ ಹೊರ ರೋಗಿ ಭೇಟಿಯ ದಾಖಲಾತಿಗಳಂದ ಸಾಮಾನ್ಯ ಮಾಹಿತಿಯನ್ನು ಸಂಗ್ರಹಿಸುತ್ತೆವೆ.

ಸದರೀ ಅಧ್ಯಯನದಿಂದಾಗುವ ಲಾಭಗಳು:–

ಔಷಧಯೋಜನೆ ಸೇವೆ ಇದು ರೋಗಿ ಕೇಂದ್ರಿತ ವಾಗಿದೆ, ಇದು ಲಾಭದಾಯಕ ವಾಗಿದೆ. ಸದರೀ ಯೋಜನೆಯನ್ನು ರೋಗಿಗಳ ಮಾನಸಿಕ ಆರೋಗ್ಯ ಸುಧಾರಿಸಲು ಕ್ಲಿನಿಕಲ ಫಾರ್ಮಸಿಸ್ಟ ಇವರು ನಿಮಗೆ ಮುಫತ್ತಾಗಿ ಪೂರೈಸುತ್ತಾರೆ, ಸದರೀ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸುವದರಿಂದ ನಿಮಗೆ ನಿಮ್ಮ ಮಾನಸಿಕ ಸ್ಥಿತಿಯ ಕುರಿತು ನೀವು ಹೆಚ್ಚು ಜಾಗೃತರಾಗುತ್ತೀರಿ ಹಾಗು ನಿಮ್ಮ ಭವಿಷ್ಯದಲ್ಲಿ ಒಳ್ಳೆಯ ಜೀವನ ಶೈಲಿಯ ಹಾಗು ಇನ್ನಿತರ ಬದಲಾವಣೆಯನ್ನು ಕಾಣ ಬಲ್ಲರಿ.

ಸದರೀ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸುವದರಿಂದಾಗುವ ಹಾನಿಗಳು:–

ಇದರಲ್ಲಿ ಭಾಗವಹಿಸುವದರಿಂದ ನಿಮಗೇನಾದರೂ ಹಾನಿಗಳಾಗಬಹುದೆಂಬುದಿಲ್ಲ. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಶಾರೀರಿಕ ಘಾಯದ **(invasive provcedure)** ಯಾವುದೇ ಪದ್ಧತಿಗಳಿರುವದಿಲ್ಲ.

ಈ ಅಧ್ಯಯವನ್ನು ಯಾರು ವಿಮರ್ಶೆ ಮಾಡಿರುತ್ತಾರೆ.

ಯಾವ ಸಮೀತಿಗಳಿಗೆ ಮನುಷರ ಮೇಲೆ ವೈದ್ಯಕೀಯ ಸಂಶೋಧನ ಕುರಿತು ಪರೀಕ್ಷಣೆ ಮಾಡುವ ಜವಾಬ್ದಾರಿ ಇದೆಯೋ ಅಂತಹ ಸಂಸ್ಥಾಗತ ನೀತಿ ಶಾಸ್ತ್ರ ಸಮಿತಿಗಳು ವಿಮರ್ಷೆ ಮಾಡಿರುತ್ತವೆ. ವಿಮರ್ಷೆ ಮಾಡುವ ಸಮೀತಿಗಳು ವೈದ್ಯಕೀಯ ನೀತಿ ಶಾಸ್ತ್ರವ'ನ್ನು ಗುಣವಾಗಿ ಈ ಅಧ್ಯಯನದ ಕುರಿತಂತೆ ಯಾವದೆ ತಕಾರುಗಳನ್ನು ತೆಗೆದಿಲ್ಲ.

ಚೌಕಷೀ/ ಶಂಕೆಗಳು

ಸಂಶೋಧನೆಯ ಕುರಿತು ಏನಾದರೂ ಪ್ರಶ್ನೆಗಳಿದ್ದಾರೆ ಸಂಶೋಧನೆಯ ಕುರಿತು ಏನಾದರೂ ಸಮಸ್ಯ ಉದ್ಭವಿಸಿದರೆ ಅಥವಾ ನಿಮ್ಮ ಸ್ಥಿತಿಯಲ್ಲಿ ಬದಲಾವಣೆ ಕಂಡು ಬಂದಲ್ಲಿ ನೀವು ಶ್ರೀ ಅಶೀಶ ಸಿಂಗ ಪರಿಹಾರ ಇವರನ್ನು ಸಂಪರ್ಕಿಸಿ ಮೊಬಾಯಿಲ ನಂ. **+91 7022076752** ಸದರೀ ಸಂಶೋಧನೆಯಲ್ಲಿ ಪಾಲ್ಗೊಂಡಿದ್ದರಿಂದಾಗಿ ನಿಮ್ಮ ಅಧಿಖಾರಿಗಳು ಕುರಿತು ಎನಾದರೂ ಪ್ರಶ್ನೆಗಳಿದ್ದರೆ ನೀವು ಪರಿಶೀಲನಾ ಸಮೀತಿಗೆ ಸಂಪರ್ಕಿಸಬಹುದು

ಈ ಮಾಹಿತಿ ಪತ್ರಕವನ್ನು ಓದಲು ತಗೆದು ಕೊಂಡಿದ್ದಕ್ಕೆ ಧನ್ಯವಾದಗಳು ನೀವು ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗ ವಹಿಸಬೇಕೆನ್ನಿಸಿದಲ್ಲಿ ದಯಮಾಡಿ ನಿಮಗೆ ಕೊಟ್ಟ ಸಮ್ಮತೀ ಪತ್ರಕ್ಕೆ ಸಹೀ ಹಾಕಿ ನಿಮಗೆ ಮಾಹಿತೀ ಪತ್ರಾಕ ಹಾಗು ನೀವು ಸಹೀ ಹಾಕಿದ ಸಮ್ಮತೀ ಪತ್ರದ ಪ್ರತಿಯನ್ನು ನಿಮಗೆ ಕೊಡಲಾಗುವದು.

ಸಹಭಾಗಿ ಹೊಂದಿದವರ ಸಹೀ_____

ರೋಗಿ ಮಾಹಿತಿ ಒಪ್ಪಿಗ ಪತ್ರ

ಸಾಮಾನ್ಯ ದರ್ಜೆಯ ಆಸ್ಪತ್ರೆಗಳಲ್ಲಿ ಬಾಯ ಪೋಲಾರ ರೋಗಿಗಳ ಔಷಧಿಗಳಿಗೆ ಬದ್ಧತೆ ಹಾಗು ರೋಗಿಯ ಜೀವನದ ಗುಣಮಟ್ಟ ಸುಧಾರಿಸುವ ಔಷಧಿಯ ಉಪಚಾರ ಹಾಗು ಭದ್ರತೆ ಹೆಚ್ಚಿಸುವ ಕುರಿತು ಭವಿಷ್ಯಕ್ಕೆ ಕುರಿತಂತೆ ಅಧ್ಯಯನ.

ಸಂಶೋದಕರ ಹೆಸರು: ಆಶೀಶ ಸಿಂಘ ಪರಿಹಾರ

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ಸಹಭಾಗಿದಾರರ ಹೆಸರು_____ ದಿನಾಂಕ:_____

ಹುಟ್ಟಿದ ತಾರೀಖು _____ ವಯಸ್ಸು: _____

ನೀವು ಸಹಿ ಮಾಡುವ ಪೂರ್ವದಲ್ಲಿ ದಯಮಾಡಿ ಈ ಕೆಳಗಿನದನ್ನು ಓದಿ

೧) ನಾನು ಸಹಭಾಗಿತ್ವದ ಮಾಹಿತೀ ಪತ್ರವನ್ನು ಓದಿರುತ್ತೇನೆ ಹಾಗು ನನಗೆ ತಿಳಿದಿದೆ ಹಾಗು ನಾನು ಭಾಗವಹಿಸಿದರೆ ನನ್ನಿಂದ ಏನು ಅಪೇಕ್ಷೆ ಇದೆ ಹಾಗು ನನಗೆ ಏನಾಗುತ್ತದೆ ಎಂಬುದು ನನಗೆ ತಿಳಿದಿದೆ.

೨) ಸದರಿ ಅಭ್ಯಾಸದ ಕುರುತಾಗಿ ನನ್ನ ಪ್ರಶ್ನೆಗಳನ್ನು ಆಶೀಶ'ಸಿಂಗ ಉತ್ತರಿಸಿರುತ್ತಾರೆ.

೩) ಯಾವುದೇ ಕಾರಣ ಕೊಡದೆ ನನ್ನ ನಿಯಮಿತ ಸೇವೆ ಹಾಗು ವ್ಯವಸ್ಥಾಪನೆಗೆ ಅಡ್ಡಿ ಬರದಂತೆ ನಾನು ಯಾವಾಗ ಬೇಕೆಂದಾಗ ಸದರೀ ಅಭ್ಯಾಸದಿಂದ ಹೊರಗೆ ಬರುವೆನೆಂಬುದು ನನಗೆ ಗೊತ್ತು.

೪) ಪ್ರಸಕ್ತ ಅಧ್ಯಯನ ಅಥವಾ ಮುಂದೆ ಇದಕ್ಕೆ ಸಂಬಂಧಿಸಿದಂತೆ ಸಂಶೋಧನಕ್ಕಾಗಿ ನಾನು ಸದರೀ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಿದೆ ಇದ್ದರೂ ನನ್ನ ಆರೋಗ್ಯ ಧಾಖಲಾತಿಗಳನ್ನು ನೋಡಲು ಸಂಶೋಧಕರಿಗೆ ಹಾಗು ಅಧಿಕಾರಿಗಳಿಗೆ ನನ್ನ ಅನುಮತಿಯ ಅವಶ್ಯಕತೆ ಇಲ್ಲ ವೆಂಬುದು ನನಗೆ ಗೊತ್ತು

೫) ನನ್ನ ಹಾಗು ಬೇರೆಯವರ ಸಂಬಂಧಿತ ಮಾಹಿತಿಯ ಕುರಿತಾಗಿ ಇರುವಾಗ ನನ್ನ ಪರಿಚಯ ಬಹಿರಂಗ ಮಾಡಲಾರರು ಎಂಬುದು ನನಗೆ ಗೊತ್ತು

೬) ನನ್ನ ಮಾಹಿತಿಯ ಅಥವಾ ಈ ಸಂಶೋಧನೆದು ಪರಿಣಾರಾಮವಾಗಿ ಬರುವ ಮಾಹಿತಿ ಅದು ವೈಜ್ಞಾನಿಕ ಕಾರಣಕ್ಕಾಗಿ ಇದ್ದರೆ ಮಾತ್ರ ನಾನು ಯಾವದೇ ರೀತಿಯಿಂದ' ಅಡ್ಡಿಪಡಿಸಲಾರೆ.

೭) ಮಾಹಿತೀ ಪತ್ರಕ ಹಾಗು ಸಮ್ಮತಿ ನಮೂನೆಯನ್ನು ನನ್ನ ಸಹಿಗೆ ಕೂಡಲಾಗಿದೆ ಸಹೀಮಾಡುವದರಿಂದ ನಾನು ಯಾವುದೆ ನನ್ನ ನ್ಯಾಯಯುತವಾದ ಹಕ್ಕುಗಳನ್ನು ಬಿಟ್ಟು ಕೊಟ್ಟಿಲ್ಲ.

೮) ನಾನು ಸದರಿ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಿಸಲಿಚ್ಛಿಸುತ್ತೇನೆ.

ಸಹಭಾಗಿದಾರರ ಹೆಸರು: **ಸಹಿ/ಹೆಬ್ಬೆರಿಳಿನ ಮುದ್ರೆ**

ಸ್ವತಂತ್ರ ಸಾಕ್ಷಿದಾರರು: **ಸಹಿ/ಹೆಬ್ಬೆರಿಳಿನ ಮುದ್ರೆ**

ಸಂಶೋಧಕರ ಹೆಸರು: **ಸಹಿ**

ಮನೋವೈದ್ಯರ ಹೆಸರು: **ಸಹಿ**

रोगी माहिती प्रपत्र

सामान्य दर्जाच्या दवाखान्यामध्ये बाय पोलार रोग्यांशी, औषधांशी बांधिलकी व रोग्यांचा जीवनस्तर सुधारावयाचे औषधी उपचार व सुरक्षितता वाढविण्यासाठी भविष्यातील अध्ययन

प्रस्तावना

रोग्यांवर सामान्य उपचारांबरोबर औषधोपचारांचा फायदा व औषधोपचांराबद्दल तुलना अभ्यासासाठी या संशोधनामध्ये अध्ययनासाठी आपणाला आमंत्रित केले आहे. सदर अध्ययन रोग्यांचे आजार वाढू नयेत आणि त्यांच्या आरोग्यात सूधार करण्याच्या प्रयत्नासाठी हे अध्ययन आहे. रोग्यांचे जीवनस्तर सुव्यवस्थित करण्यात व त्यांचे मानसिक आरोग्य सुधारण्यात औषध योजनेचा उपयोग कसा होतो हे कळण्यास मदत होते. या प्रश्नांची उत्तरे मिळविण्यासाठी आम्ही सदर अध्ययन करीत असून त्यात सहभागी होण्यासाठी आपणाला आमंत्रित केले आहे.

अध्ययनाचा उद्देश

औषधीय उपचाराने औषधशास्त्र रोग्यांचे आरोग्यस्तर उंचवण्यात निश्चित व स्पष्टपणे उपयोगी आहे. हे रोगी केंद्रीत संयुक्त उपचारात अत्यावश्यक आहे व सांप्रदायिक दृष्टीकोन बदलण्याची आवश्यकता आहे. यामूळे सकारात्मक चिंतनाने जीवनशैली सूधारणे औषधोपचारांच्या **अध्ययन** करणे आहे. व रोग्यांना शिक्षण आणि आजार व्यवस्थापनाचे कार्य देखील करण्याचे आहे.

या अध्ययनासाठी आपली निवड का केली आहे. ?

बाय पोलार दोषामूळे मानसिक विकृती विकोपाला जाऊ नये या उद्देशाने केल्या जाणाऱ्या औषधोपचार सेवेबद्दल अध्ययन करण्याच्या उद्देशाने हे संशोधन हाती घेतले आहे. याबाबत तुम्हाला नुकतेच अनुभव आल्यामूळे तुमची निवड केली आहे. यात भाग घेणे म्हणजे काय.

अध्ययनात भाग घेणे म्हणजे काय ?

आपल सहभागितत्व पूर्णपणे स्वइच्छेचे आहे. आपणास निर्णय घेण्यासाठी या माहितीपत्रकाचे वाचन खूप उपयोगी होते. आपण यात स्वेच्छेने भाग घेतला आहे. आपल्या घरच्या लोकांशी या दाखल्यातील विषय मूक्तपणे विचार विनिमय करू शकता . या अध्ययनात भाग घ्यावा किंवा घेऊ नये हा निर्णय तुमच्यावर सोपवला आहे. यासाठी आपण कितीही वेळ घ्या. तुम्ही भाग न घेण्याचा निर्णय घेतलात तरी तुमच्या **वर्तमान** आणि **भविष्यातील** काळजी काहीही परीणाम होणार नाही. आपण भाग घेण्याचा निर्णय घेऊन देखील यातून केव्हाही बाहेर जाऊ शकता. त्यामूळे तुमचे काहीही नुकसान होणार नाही.

या अध्ययनात आपण भाग का घेणार आहोत हे कळल्यानंतर आपण भाग घेण्याची ईच्छा व्यक्त केल्यानंतर आपल्याला एका संमति पत्रावर सही करावी लागेल. सदर अध्ययन कालात अध्ययनाबाबत तुम्हाला शंका असल्यास त्या शंकाचे निराकारण

करून घेऊ शकता. तुमच्या संशयाबाबत तुम्ही कोणतेही प्रश्न विचारून उत्तरे प्राप्त करून घेण्यास तुम्ही पूर्ण स्वतंत्र आहात सदर अध्ययनात भाग घेतल्याने तुम्ही कोणत्याही कायदेशीर हक्कापासून वंचित होत नाही.

सदर अध्ययनात भाग घेणे म्हणजे तुम्ही दोन वर्षे अध्ययनासाठी कालावधी देण्याची संमति दिलेली आहे.

अध्ययनाच्या काळात

तुमचा वैद्यकीय दाखला आभ्यास करून तुमच्या मानसिक स्थितीचा निर्णय घेऊन तुम्ही पात्र असल्यास तुम्हाला कोणत्यातरी दोन गटांतील एका गटात तुम्हाला सामील केले जाईल (१) एकात औषधोपचारांची सेवा असेल व दुसऱ्यात (२)सामान्यसेवा असेल दोन्ही गट रोग्यांना फायदेशीर आहेत.

संगणकाव्दारे अनियमितपणे निवडलेल्या तंत्राव्दारे (Computerised Sample randomization technique) तुम्हाला कोणत्यातरी एका गटात सामिल केले. जाईल. अशा प्रकारे कोणत्यातरी गटात सामिल होण्याची तुम्हाला ५०:५० संधी मिळेल. (रूपयाच्या नाणेफेकीप्रमाणे)

यामधल्या तुमची कोणत्याही गटात निवड झाल्यानंतर तुमच्या अध्ययनाच्या कालात औषध उपाय योजना व्यवस्थेबद्दल, रोगव्यवस्थेबद्दल व जीवनशैली सुधारणेबद्दल तुम्हाला शिक्षण दिले जाईल. अध्ययनाच्या काळात तुम्हाला (रोग्यांचे माहिती पत्रक) दिले जाईल. Patient Information Leaflets (PIL) सदर सामूग्री आपल्याला मोफत दिलि. जाईल.

सर्व प्राथमिक माहिती गोळा झाल्यानंतर पुढे पून्हा संपर्क

दवखान्याच्या भेटी नंतर किंवा फॉलोअपमध्ये आम्ही तुम्हाला तुमच्या आरोग्याबद्दल तुमच्या रोजच्या कामाविषयी व तुमच्या जीवनशैलीबद्दल काही प्रश्न विचारू नंतर तुमच्याविषयीच्या दवाखान्याच्या दाखल्यातून व ओ. पी. डी. दाखल्यातून तुमची सामान्य माहिती संग्रहीत करू.

सदर अभ्यासातून होणारे फायदे:

औषध योजना सेवा ही रोगीकेंद्रीत आहे, ही फायदेशीर आहे. सदर योजना रोग्याच्या मानसिक आरोग्य सुधारणेसाठी क्लिनिकल फार्मासिस्ट आपणाला मोफत पुरवतात. सदर अध्ययनात भाग घेण्याने तुमच्या मानसिक स्थितीविषयी तुम्ही जास्त जागृत होता व तुमच्या भविष्यात चांगली जीवनशैली व इतर बदल पाहू शकता.

सदर अभ्यासात भाग घेण्याने होणारे नुकसान :

या अभ्यासात भाग घेण्याने तुमचे काहीही नुकसान होणार नाही. यामध्ये कोणतीही शारीरीक जखमेची (Invasive) पध्दत नाही.

सदर अध्ययनाचे कोणी समालोचन केलेत ?

ज्या समित्यांवर माणसांवर वैद्यकीय संशोधनाबद्दल काळजीपूर्वक छाननी करण्याची जबाबदारी आहे. अशा सदर अध्ययन संस्थागत नितीशास्त्र सामित्यासमालोचन करतात. परिक्षण करण्याऱ्या समित्यांनी वैद्यकीय नितिशास्त्रानुसार या अध्ययनाबाबत कोणतीहि तक्रार केली नाही.

चौकशी व शंका

संशोधनाबद्दल काहीतरी प्रश्न असल्यास संशोधनासंबंधित काही समस्या उदभवल्यास किंवा तुमच्या स्थितीत काही बदल पाहणीत आल्यास तुम्ही श्री अशिश सिंघ परिहार यांच्यांशी संपर्क साधा मोबाईल नंबर +९१७०२२०७६७५२,सदर संशोधनामध्ये भाग घेतल्याने तुमच्या अधिकाराबद्दल काही प्रश्न असल्यास परिक्षण करणाऱ्या समित्यांशी संपर्क साधू शकता.

"हि माहिती वाचण्यासाठी घेतल्याबद्दल धन्यवाद आपण अध्ययनामध्ये भाग घ्यावा असे वाटल्यास तुम्हाला दिलेल्या संमतिपत्रावर सही करा. तुम्हाला माहिती पत्रक व तुम्ही सही केलेल्या संमतिपत्राच्या प्रती दिल्या जातील."

सहभागीदाराची सही_____

माहितीपुर्ण संमती पत्रक

सामान्य दर्जाच्या दवाखान्यामध्ये बाय पोलार रोग्यांशी, औषधांशी बांधलकी व रोग्यांचा जीवनस्तर सुधारावयाचे औषधी उपचार व सुरक्षितता वाढविण्यासाठी भविष्यातील अध्ययन

संशोधक:– आशीष सिंह परिहार

+917022076752, +918088244739

py.ashishsingh@yahoo.com, py.ashishsingh@gmail.com

सहभागीदाराचे नांव : _____ तारिख : _____

जन्मतारिख : _____ वय :_____

आपण सही करण्यापूर्वी कृपया खाली वाचा.

१. मी अध्ययना संबंधीत सहभागीत्वाचे माहितिपत्रक वाचलेले आहे. व मला कळालेले आहे. व मी भाग घेण्याने माझ्याकडून काय अपेक्षा आहेत. आणि यात भाग घेण्याने मला काय होईल याची माहिती मला आहे.

२. सदर अभ्यासाबाबत माझ्या प्रश्नांना श्री अशिश सिंघ परिहारांनी उत्तर दिलेले आहे.

३. कोणतेही कारण न देता माझ्या नियमीत सेवा व व्यवस्थापनेत आड न येता मला सदर अभ्यासातून बाहेर पडता येते हे मला माहित आहे.

४) वर्तमान अध्ययनात किंवा भविष्यातील यांच्याशी संबंधित अध्ययनासाठी मी सदर अध्ययनात भाग न घेता देखील माझे आरोग्य दाखले पाहण्यास संशोधकांना व अधिकाऱ्यांना माझ्या संमतिची आवश्यकता नाही हे मला माहिती आहे.

५) दुसऱ्याशी संबंधित माहितीमध्ये माझी ओळख जाहीर होणार नाही हे मी जाणतो.

६) माझी माहिती किंवा या संशोधनाव्दारे उपलब्ध होणाऱ्या माहितिचा उपयोग केवळ वैज्ञानिक कारणासाठी असेल तर मी आडविणार नाही.

७) मला महिती पत्रक व संमति पत्रकाची प्रत माझ्या सहीसाठी दिली आहेत यात सही करण्याने मी कोणतेही कायदेशीर हक्क सोडले नाहीत.

८) मी अध्ययनात सहभागी होण्यास तयार आहे.

भाग घेणाऱ्याचे नांव सही /अंगठ्याची निशाणी

स्वतंत्र साक्षिदाराचे नांव सही /अंगठ्याची निशाणी

संशोधकाचे नांव सही

मानसशास्त्रज्ञाचे नांव सही

Annexure II: Data collection form

Baseline Data Collection Form

Effect of Pharmaceutical Care on Enhancement of Safety, Medication Adherence and Quality Of Life in Patient with Bipolar Disorder: A Prospective Study in Tertiary Care Hospital.

PATIENT PROFILE FORM

Name _____, Age_____ (Birth Date: / /)

Gender_____, Religion_____, IP/OP No._____, Date of enrolment: / /

Address_____

Contact No._____, _____ Email_____

(Yes=Y, No=N)

Single_____, Married_____, Divorced_____, Widowed_____ Living with partner_____

Profession_____

Employment Status: Govt._____, Pvt._____, Daily Basis_____, Homemaker_____

Student_____, Unemployed_____, Other_____

Family History of Psychiatric Illness: (Unipolar, Bipolar, Schizophrenia, alcoholic & drug abuse, suicide, others)

Paternal side	**Maternal side**
Grandfather_____ Grandmother_____	Grandfather_____ Grandmother_____
Father &his Siblings _____	Mother & her Siblings _____
Siblings_____ _____	_____ _____

Childhood Adversity (None, Mild, Moderate, Sever Experience)

Neglect_____ Age_____ to_____

Physical abuse_____ **Age_____ to_____**

Sexual abuse_____ Age _____ to _____

Loss of parents_____ Age_____ to _____

Age of onset of first: Depression_____, Mania_____, Mixed episode_____, Other_____

Precipitating factor: (*Yes/No)*

Depression_____ **Mania_____**
Latest Episode_____ _____

Characteristics of depression: (*Yes/No)*

Motor: Agitated_____, Retarded_____

Thoughts: Speeded_____, Blank_____, Ruminative_____, Slowed_____

Sleep: Insomnia_____, Hypersomnia_____

Mood: Irritable_____, Sad_____, Both_____, Guilt_____, Anger_____

Appetite: Decrease_____, Increase_____

Sucidal Ideation: Decrease_____, Increase_____

Hours of sleeping:

When Manic_____

When Normal_____

When depressed_____

Characteristics of early symptom of Mania: (*Yes/No)*

Insomnia_____, Anger_____, Religiosity_____, Rapid speech_____, Irritability_____
Explosiveness_____, Sexual indiscretions_____, Aggression_____, Lack of insight_____
Paranoid_____, Grandiosity_____, Eliveted mood_____, Hyperactivity_____
over familiarity_____ Increase Drug abuse_____Others (*if yes then mentioned*)_____

Predominant Illness Pattern:

Isolated episode M_____, D_____

Biphasic: mania than depression than well Vs. depression first than mania

Tricyclic_____

Seasonal (when illness is worst)_____

Continuous (cycling without a well interval)_____

Other _____

Fast episode frequency:	**Nonrapid**	**Rapid ≥4/yr.**	**Ultra rapid ≥4/month**	**Rhythmic ≤ 24 hrs.**	**Chaotic**
Ever	_____	_____	_____	_____	_____
Past Year	_____	_____	_____	_____	_____

Clinical Diagnostic of Patients:

Obesity: Mild_____, Moderate_____, Severe_____
Height_____, Weight_____, BMI_____
Waist circumference_____

(Yes/No)

DM_____, Hyperthyroidism_____, Hypothyroidism_____, Heart disease_____
Chronic Pain_____, Arthritis_____, Others_____

Parameters	Baseline	
	value	Date
Blood Pressure		
Fasting Sugar		
Cholesterol total		
HDL		
LDL		
Triglyceride		
TSH		
T3		
T4		
Scr.		
Liver transaminases,		
Alkaline phosphatase,		
Complete Blood count		
S Li		

Current Treatment Chart:

Current Drugs				
Generic Name	**Brand Name**	**Route**	**Dose**	**Frequency**

Susceptible DRPs:

DRPs	Comments

Clinical Pharmacist Intervention:-

Intervention	Comments

Followup Data Collection Form

Effect of pharmaceutical care on enhancement of safety, medication adherence and quality of life in patient with Bipolar disorder: A prospective study in tertiary care hospital.

Patient Name:________________________________ **Patient No.**______________				**OP /IP NO.** __________________
Date Of Visits:				
Status of Patients: date collected				
If Yes, assessment type: ☐ Home visit ☐ Clinical visit				
If No, reason: ☐ Patient withdrawn ☐ Patient died ☐ Other				

Characteristics of depression: ***(Yes/No)***

Motor: Agitated¬¬¬¬¬¬¬¬¬¬¬¬¬¬¬¬¬¬¬¬¬__________________, Retarded__________________

Thoughts: Speeded_________, Blank__________, Ruminative___________, Slowed____________

Sleep: Insomnia_________________, Hypersomnia________________

Mood: Irritable_________, Sad________, Both_________, Guilt_________, Anger___________

Appetite: Decrease_________________, Increase____________________

Hours of sleeping:

When Manic_____________________________

When Normal____________________________

When depressed__________________________

Characteristics of early symptom of Mania: *(Yes/No)*

Insomnia__________, Anger_________, Religiosity_________, Rapid speech_________, Irritability_________

Explosiveness_________, Sexual indiscretions_________, Aggression__________, Lack of insight__________

Paranoid_________, Grandiosity_________, Others (if yes then mentioned)_____________________________

Predominant Illness Pattern:

Isolated episode M_________________________, D_____________________________

Biphasic: mania than depression than well Vs. depression first than mania

Tricyclic____

Seasonal (when illness is worst)_____

Continuous (cycling without a well interval)_____

Other _____

Clinical Diagnostic of Patients:

Obesity: Mild_____, Moderate_____, Severe_____

Height_____, Weight_____, BMI_____

Waist circumference_____

Parameters	**I follow-up**		**II follow-up**		**III follow-up**		**Final follow-up**	
	value	**Date**	**value**	**Date**	**value**	**Date**	**value**	**Date**
Blood Pressure								
Fasting Sugar								
Cholesterol total								
HDL								
LDL								
Triglyceride								
TSH								
T3								
T4								
Scr.								
Liver transaminases								
Alkaline phosphatase								
Complete Blood count								

Current Treatment Chart:

Current Drugs				
Generic Name	**Brand Name**	**Route**	**Dose**	**Frequency**

Susceptible DRPs:

DRPs	**Comments**

Clinical Pharmacist Intervention:-

Intervention	**Comments**

Annexure III: Patient counselling form.

KLES UNIVERSITY COLLEGE OF PHARMACY

DEPARTMENT OF PHARMACY PRACTICE

Dr. PRABHAKAR KORE HOSPITAL & MEDICAL RESEARCH CENTER, BELGAUM

PATIENT COUNSELING FORM

Date:

Type of patient: ☐ In-patient: IP- No.: Unit: ☐ Out-patient: OP- No.:

Age: **Gender:** **Allergies:**

Current medical problem:

Current medication:

Weather patient specific background information collected? ☐ **Yes** ☐ **No**

Disease counseled:

Counseling step followed:

☐ Case sheet reviewed
☐ Self introduction done
☐ Actual counseling done
☐ Purpose of counseling told
☐ Initial drug related information obtained
☐ counseling point summarized
☐ Patient understanding gained towards therapy was ascertained.
☐ Patient was warned about taking other medicine including OTC's, Herbal drug etc.

Point covered during counseling session:

☐ Name and purpose of medicine
☐ Precaution to be taken
☐ Dosage regimen
☐ Storage recommendation
☐ Advice on missing dose
☐ Potential side effect
☐ Benefit of completing the case
☐ Life style modification
☐ Significant Interactions (Drug-Drug, Drug-Food, Drug–Disease)

Any major barriers involved: ☐ Yes ☐ No

If yes: Patient based
- ☐ Provider based
- ☐ System based

Quote specific barrier (if any)

If yes, whether barrier was rightly outcome? ☐ Yes ☐ No

Time taken for counseling:
- ☐ Less than 10 min.
- ☐ 10-20 min.
- ☐ More than 20 min.

counseling provided to:
- ☐ Patient
- ☐ Patient's representative

Whether counseling was conducted at appropriate place? ☐ Yes ☐ No

If patient representative, given reason:
- ☐ Patient is unconscious
- ☐ Language problem
- ☐ Hearing problem
- ☐ Pediatric patient
- ☐ Other (specify)

counseling aids used:
- ☐ Pictogram
- ☐ Dummy inhaler device
- ☐ Spacer
- ☐ None
- ☐ Other (specify)

counseling material provided:
- ☐ patient information leaflets
- ☐ Pamphlets
- ☐ Product information leaflets
- ☐ None
- ☐ Other (specify)

Understanding of the patient ascertained: ☐ Yes ☐ No

Name of counselling pharmacist: **Signature:**

Name of patient: **Signature:**

FOR THE USE OF PATENT COUNSLING ASSESMENT PANEL
PATIENT COUNSELLING QUALITY ASSURANCE FORM

1. Whether counseling Stage Was Followed?
   ☐ Yes ☐ No
2. Whether Consoling Point Was Covered During counseling Session?
   ☐ Yes ☐ No
3. Whether counseling Aids Were Provided?
   ☐ Yes ☐ No
4. Whether counseling Material Were Provided?
   ☐ Yes ☐ No
5. Whether The Barrier Was Rightly Overcome?
   ☐ Yes ☐ No
6. Was The Understanding Of The Patient Ascertained?
   ☐ Yes ☐ No
7. Was The Time Taken For Counseling Appropriate?
   ☐ Yes ☐ No
8. Was The Process Of Patient Counseling Appropriate?
   ☐ Yes ☐ No

GREAD: **A** (Excellent), **B** (Good), **C** (can improve), **D** (Should Improve)
NOTE: A= 7-8 points, B= 5-6 points, C= 3-4 points, D= <3

REMARKS:

Annexure-IV: Pharmacist intervention form.

KLES UNIVERSITY COLLEGE OF PHARMACY

DEPARTMENT OF PHARMACY PRACTICE

Dr. PRABHAKAR KORE HOSPITAL & MEDICAL RESEARCH CENTER, BELGAUM

PHARMACIST INTERVENTION

Date: **Unit:** **IP No.**

Patient details: **Age:** **Gender:**

Past medical History:

Diagnosis:

Date of diagnosis:

Drug (S) prescribed:

Date of prescription:

DRP Identified: ☐ Untreated indication
☐ Drug use without Indication
☐ Sub therapeutic Dose
☐ Overdose
☐ ADR
☐ Drug interaction
☐ Improper drug selection
☐ Alternative dosage form
☐ Other (specify)

Specific background information collected? ☐ **Yes** ☐ **No**

Reason for intervention:

Problem identified discussed with concerned HCP: ☐ **Yes** ☐ **No**

Suggestions made:

Suggestion made at appropriate time: ☐ **Yes** ☐ **No**

Accepted: ☐ **Yes** ☐ **No** **Changed:** ☐ **Yes** ☐ **No**

If No, given reason (S):

Significance of intervention: ☐ **Minor**
☐ **Moderate**

☐ **Major**

Reference consulted:

Follow up:

Name of Pharmacist: **Signature:**

Name of staff In-charge: **Signature:**

Minor: problem requiring small adjustment and optimization of therapy, which are not expected to significantly alert hospital stay, resource utilization or clinical outcome.

Moderate: problem requiring adjustment, which are expected to enhance effectiveness of the drug therapy producing minor reduction in patient morbidity and treatment cost.

Major: problem requiring intervention to prevent or address very serious drug related problem leading to prevention or minimizing the estimated effect and reducing hospital stay.

Annexure-V: Patient Information Leaflet (PIL) in English, Kannada & Marathi.

Escitalopram: available in white colour tablet form with 10-20 mg/day dose, used as an antidepressant agent. During taking this medication if you contacted with heart burn, loss if sexual ability, constipation, diarrhoea and dry mouth, than inform about this to your doctor.

Quetiapine: initial dose of quetiapine is 25 mg twice a day up to 800mg/day. This is basically used for the bipolar depression. The most common side effects are chills, cold sweat, confusion, dizziness, faintness, drowsiness etc.

Complementary treatments and food supplements

Medication is the cornerstone of treating bipolar, but there are many other aspects to keeping well including diet, physical exercise and complementary therapies. Avoiding the "Western" style diet. Eat a balance of protective, nutrient-dense foods. These foods include fresh fruits, vegetables, legumes, whole grains, lean meats, cold-water fish, eggs, low-fat dairy, soy products, and nuts and seeds.

For Further Information Please contact:

DEPARTMENT OF PHARACY PRACTICE
KLES Dr. Prabhakar Kore Hospital
& MRC, Nehru Nagar, Belagavi.
Tel: 2473777, ext. 1768

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DR. PRABHAKAR KORE HOSPITAL & Medical Research Centre

You have been diagnosed with Bipolar - how you can manage it

Bipolar, sometimes known As manic depression, is a serious mental-health illness which is characterized by extreme mood Swing extreme manic highs and depressive lows.

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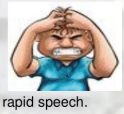
KLES Dr. Prabhakar Kore Hospital
& MRC, Nehru Nagar, Belagavi.
Tel: 2473777, ext. 1768

Report to Doctor if: You feel

- Expansiveness.
- Grandiosity.
- Overconfidence.
- Increase sexual preoccupation.
- Increased interest in religion.
- Inappropriate spending.
- Intolerance.
- Increase smoking, drinking.
- Increase use of phone.
- Reduce need of sleep.
- Irritability and much more rapid speech.



Can Bipolar be cured?

Still, there are no any clear answer for this ques. But certainly there is no cure for bipolar disorder.

Bipolar medications.

It's important that you take all of your pills, even if you feel better. It will helpful for maintaining your quality of life.

Side effects:

A few people will develop side effect which should report to the doctor. If a side effect is severe, your doctor may switch you to another drug or change your bipolar medication dose.

- Weight gain
- Drowsiness
- Excessive thirst
- Elevation of cholesterol level
- Weakness or fatigue
- Tremor
- Stomach pain
- Thyroid problem
- Nausea
- Vertigo
- Diarrhea
- Dizziness
- Dry mouth
- Sexual dysfunction
- Constipation
- Blurred vision43

Lithium: lithium available in white coloured. The starting dose of lithium is usually 250-2000 mg tablet take with food and a glass of water two to three times daily. 2L of water/day is advisable with normal balance diet. It is used as mood stabilizer, while taking this medicine, your thyroid should be checked in 3 mionths of duration.

Carbamazepine: it is available in both tablet and suspension form with the dose of 600-1500 mg/day. You have to take this medicine before the meals. This is use for controlling manic or mixed episodes. The common side effect are cerebellovestibular, occlimotur dysfunction, atrexia etc.

Valproate Sodium: it is available in swellowing tablet form with 500-2000mg/day of dose. valproate is an efficacious treatment for acute mania. When taking any medicine you should be aware that it might interfere with your ability to drive or operate machinery safely. It may cause mild gastrointestinal upset, weight gain fine tremor and sedation.

Olanzapine: this is an atypical antipsychotic agent. Available in tablet form with maximum dose upto 20mg/day. You have to take this with or without food, same time around a day. Take exactly as per direction of your physician; don't stop your medicine without your doctor permission.

ಎಸ್ಕಿಟಲೊಪ್ರಮ್: ಖಿನ್ನತೆ-ಸಿರೋಧಕವಾಗಿ ಉಪಯೋಗಿಸಲಾಗುತ್ತಿದ್ದು, ದಿನಕ್ಕೆ 10-20 ಮಿಗ್ರಾ ಡೋಸ್‌ನಲ್ಲಿ, ಬಿಳಿ ಬಣ್ಣದ ಮಾತ್ರೆಯ ರೂಪದಲ್ಲಿ ಲಭ್ಯವಿದೆ. ಈ ಔಷಧವನ್ನು ತೆಗೆದುಕೊಳ್ಳುವ ಸಮಯದಲ್ಲಿ ನೀವು ಏದೆ ಉರಿ, ಲೈಂಗಿಕ ಸಾಮರ್ಥ್ಯದಲ್ಲಿ ನಷ್ಟ, ಮಲಬದ್ಧತೆ, ಭೇದಿ ಮತ್ತು ಬಾಯಿ ಒಣಗುವಿಕೆಯನ್ನು ಅನುಭವಿಸಿದರೆ, ನಿಮ್ಮ ವೈದ್ಯರಿಗೆ ಆದರ ಬಗ್ಗೆ ತಿಳಿಸಿ.

ಕ್ವೆಟಿಯಪೈನ್: ಕ್ವೆಟಿಯಾಪೈನ್‌ನ ಆರಂಭಿಕ ಡೋಸ್ ದಿನಕ್ಕೆರಡು ಬಾರಿ 25 ಮಿಗ್ರಾಂನಿಂದ ದಿನಕ್ಕೆ 800 ಮಿಗ್ರಾವರೆಗೆ. ಇದನ್ನು ಮೂಲತಃ ಬೈಪೋಲಾರ್ ಖಿನ್ನತೆಗಾಗಿ ಬಳಸಲಾಗುತ್ತದೆ. ಆತ್ಯಂತ ಸಾಮಾನ್ಯ ಅಡ್ಡಪರಿಣಾಮಗಳೆಂದರೆ ಚಳಿ, ಚಳಿ ಬೆವರಿಕೆ, ಗೊಂದಲ, ತಲೆ ತಿರುಗುವಿಕೆ, ನಿತ್ರಾಣ, ಮಂಪರು ಇತ್ಯಾದಿ.

ಪೂರಕ ಚಿಕಿತ್ಸೆಗಳು ಮತ್ತು ಆಹಾರ ಪೂರಕಗಳು

ಔಷಧೋಪಚಾರವು ಬೈಪೋಲಾರ್ ಚಿಕಿತ್ಸೆಯ ಮೂಲಾಧಾರವಾಗಿದೆಯಾದರೂ, ಆಹಾರ, ದೈಹಿಕ ವ್ಯಾಯಾಮ ಮತ್ತು ಪೂರಕ ಚಿಕಿತ್ಸೆಗಳೂ ಸೇರಿದಂತೆ ಆರೋಗ್ಯವಾಗಿರುವುದರಲ್ಲಿ ಅನೇಕ ಅಂಶಗಳಿವೆ. "ಪಾಶ್ಚಿಮಾತ್ಯ" ಶೈಲಿಯ ಆಹಾರವನ್ನು ಸೇವಿಸದಿರುವುದು. ರಕ್ಷಣಾತ್ಮಕ ಮತ್ತು ಪೌಷ್ಟಿಕಾಂಶ-ಸಮೃದ್ಧ ಸರಿಹೊಂದಿಸಿದ ಆಹಾರಗಳನ್ನು ಸೇವಿಸಿ. ಈ ಆಹಾರಗಳಲ್ಲಿ ತಾಜಾ ಹಣ್ಣುಗಳು, ತರಕಾರಿಗಳು, ದ್ವಿದಳ ಧಾನ್ಯಗಳು, ಪೂರ್ಣ ಧಾನ್ಯಗಳು, ಕೊಬ್ಬುರಹಿತ ಮಾಂಸಗಳು, ತಣ್ಣೀರಿನ ಮೀನು, ಮೊಟ್ಟೆಗಳು, ಕಡಿಮೆ ಕೊಬ್ಬಿನ ಕ್ಷೀರೋತ್ಪನ್ನಗಳು, ಸೋಯಾ ಉತ್ಪನ್ನಗಳು, ಮತ್ತು ಕರಟಕಾಯಿಗಳು ಮತ್ತು ಬೀಜಗಳು ಸೇರಿವೆ.

ಅಧಿಕ ಮಾಹಿತಿಗಾಗಿ ದಯವಿಟ್ಟು ಸಂಪರ್ಕಿಸಿ:

ಫಾರ್ಮಸಿ ಪ್ರಾಕ್ಟೀಸ್ ವಿಭಾಗ
ಕೆಎಲ್‌ಇಎಸ್ ಡಾ. ಪ್ರಭಾಕರ್ ಕೋರೆ ಆಸ್ಪತ್ರೆ
& ಎಂಆರ್‌ಸಿ, ನೆಹರು ನಗರ, ಬೆಳಗಾವಿ.
ದೂರವಾಣಿ: 2473777- ವಿಸ್ತರಣೆ 1768

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ನಿಮಗೆ ಬೈಪೋಲಾರ್ ಇದೆಯೆಂದು ಪತ್ತೆಯಾಗಿದೆ – ನೀವು ಅದನ್ನು ಹೇಗೆ ನಿರ್ವಹಿಸಬಹುದು

ಬೈಪೋಲಾರ್, ಕೆಲವು ಸಲ ಉನ್ಮಾದಗ್ರಸ್ತ ಖಿನ್ನತೆ ಎಂದು ತಿಳಿಯಲಾಗುವ, ಒಂದು ಗಂಭೀರವಾದ ಮಾನಸಿಕ-ಆರೋಗ್ಯ ಕಾಯಿಲೆಯಾಗಿದ್ದು, ಅದರ ಲಕ್ಷಣಗಳೆಂದರೆ ಮನಃಸ್ಥಿತಿಯಲ್ಲಿ ತೀವ್ರ ಬದಲಾವಣೆಗಳು - ಅತೀವ ಉನ್ಮಾದ ಮತ್ತು ಅತೀವ ಖಿನ್ನತೆ

ಫಾರ್ಮಸಿ ಪ್ರಾಕ್ಟೀಸ್ ವಿಭಾಗ
ಕೆಎಲ್‌ಇಎಸ್ ಡಾ. ಪ್ರಭಾಕರ್ ಕೋರೆ ಆಸ್ಪತ್ರೆ
& ಎಂಆರ್‌ಸಿ, ನೆಹರು ನಗರ, ಬೆಳಗಾವಿ.
ದೂರವಾಣಿ: 2473777- ವಿಸ್ತರಣೆ 1768

ನಿಮ್ಮಲ್ಲಿ ಹೀಗಾದಲ್ಲಿ ವೈದ್ಯರಿಗೆ ವರದಿ ಮಾಡಿ:

- ನಿದ್ರಾಹೀನತೆ.
- ಡಾಂಭಿಕತೆ.
- ಅತಿ ಆತ್ಮವಿಶ್ವಾಸ.
- ಹೆಚ್ಚಿದ ಲೈಂಗಿಕ ಮಗ್ನತೆ.
- ಧರ್ಮದಲ್ಲಿ ಹೆಚ್ಚಿದ ಆಸಕ್ತಿ.
- ಅನುಚಿತ ಖರ್ಚು.
- ಅಸಹನತೆ.
- ಹೆಚ್ಚಿದ ಧೂಮಪಾನ, ಮದ್ಯಪಾನ.
- ಫೋನ್ ಬಳಕೆಯಲ್ಲಿ ಹೆಚ್ಚಳ.
- ನಿದ್ರೆಯ ಕಡಿಮೆ ಅವಶ್ಯಕತೆ.
- ಕಿರಿಕಿರಿ ಮತ್ತು ಹೆಚ್ಚು ವೇಗವಾಗಿ ಮಾತನಾಡುವುದು.

ಬೈಪೋಲಾರ್ ಅನ್ನು ಗುಣಪಡಿಸಬಹುದೇ?

ಇನ್ನೂ, ಈ ಪ್ರಶ್ನೆಗೆ ಯಾವುದೇ ಸ್ಪಷ್ಟ ಉತ್ತರ ಇಲ್ಲ. ಆದರೆ ಬೈಪೋಲಾರ್‌ಗೆ ಏಂಡಿತವಾಗಲೂ ಯಾವುದೇ ಚಿಕಿತ್ಸೆ ಇಲ್ಲ.

ಬೈಪೋಲಾರ್ ಔಷಧಗಳು.

ನಿಮಗೆ ಗುಣವಾಗುತ್ತಿಯೆಂದು ಅನಿಸಿದರೂ ಸಹ, ನೀವು ನಿಮ್ಮ ಎಲ್ಲಾ ಮಾತ್ರೆಗಳನ್ನು ತೆಗೆದುಕೊಳ್ಳುವುದು ಮುಖ್ಯವಾಗಿರುತ್ತದೆ. ಇದು ನಿಮ್ಮ ಜೀವನದ ಗುಣಮಟ್ಟವನ್ನು ಕಾಪಾಡಿಕೊಳ್ಳಲು ಸಹಾಯಮಾಡುತ್ತದೆ.

ಅಡ್ಡ ಪರಿಣಾಮಗಳು:

ಕೆಲವು ಜನರು ಅಡ್ಡ ಪರಿಣಾಮಗಳನ್ನು ಹೊಂದುತ್ತಿದ್ದು, ಅವನ್ನು ವೈದ್ಯರಿಗೆ ವರದಿ ಮಾಡಲೇಬೇಕು . ಒಂದು ವೇಳೆ ಅಡ್ಡ ಪರಿಣಾಮವು ತೀವ್ರವಾಗಿದ್ದರೆ, ನಿಮ್ಮ ವೈದ್ಯರು ನಿಮ್ಮನ್ನು ಮತ್ತೊಂದು ಔಷಧಿಗೆ ಬದಲಾಯಿಸಬಹುದು ಅಥವಾ ನಿಮ್ಮ ಬೈಪೋಲಾರ್ ಔಷಧಿಯ ಡೋಸ್ ಅನ್ನು ಬದಲಾಯಿಸಬಹುದು.

- ತೂಕದಲ್ಲಿ ಹೆಚ್ಚಳ
- ಮಂಪರು
- ವಿಪರೀತ ಬಾಯಾರಿಕೆ
- ಕೊಲೆಸ್ಟ್ರಾಲ್ ಮಟ್ಟದಲ್ಲಿ ಏರಿಕೆ
- ದೌರ್ಬಲ್ಯ ಅಥವಾ ಆಯಾಸ
- ನಡುಕ
- ಹೊಟ್ಟೆ ನೋವು
- ಥೈರಾಯ್ಡ್ ಸಮಸ್ಯೆ
- ಪಾಕರಿಕೆ
- ತಲೆತಿರುಗುವಿಕೆ
- ಅತಿಸಾರ
- ತಲೆಸುತ್ತು
- ಒಣ ಬಾಯಿ
- ಲೈಂಗಿಕ ಅಪಸಾಮಾನ್ಯ ಕ್ರಿಯೆ
- ಮಲಬದ್ಧತೆ
- ಮಂಜು ದೃಷ್ಟಿ43

ಲಿಥಿಯಮ್ ಲಿಥಿಯಂ ಬಿಳಿ ಬಣ್ಣದಲ್ಲಿ ಲಭ್ಯವಿದೆ. ಲಿಥಿಯಂನ ಆರಂಭಿಕ ಡೋಸ್ ಸಾಮಾನ್ಯವಾಗಿ 250-2000 ಮಿಗ್ರಾಂ ಮಾತ್ರೆ ಪ್ರತಿದಿನ ಎರಡು ಮೂರು ಬಾರಿ ಆಹಾರ ಮತ್ತು ಒಂದು ಲೋಟ ನೀರಿನ ಜೊತೆ ತೆಗೆದುಕೊಳ್ಳಿ . ದಿನಕ್ಕೆ 2 ಲೀಟರ್ ನೀರನ್ನು ಸಾಮಾನ್ಯ ಸಮತೋಲನ ಆಹಾರದೊಂದಿಗೆ ಶಿಫಾರಸು ಮಾಡಲಾಗುತ್ತದೆ. ಇದನ್ನು ಮನಸ್ಥಿತಿ ಸ್ಥಿರಕಾರಿಯಾಗಿ ಬಳಸಲಾಗುತ್ತದೆ, ಈ ಔಷಧವನ್ನು ತೆಗೆದುಕೊಳ್ಳುವಾಗ, ನಿಮ್ಮ ಥೈರಾಯ್ಡ್ ಅನ್ನು 3 ತಿಂಗಳುಗಳ ಅವಧಿಯಲ್ಲಿ ತಪಾಸಿಸಬೇಕು.

ಕಾರ್ಬಮಝಪೈನ್: ಇದು ದಿನಕ್ಕೆ 600-1500 ಮಿಗ್ರಾ ಡೋಸ್‌ನಂತೆ ಮಾತ್ರೆ ಮತ್ತು ಸಸ್ಪೆನ್ಷನ್ ರೂಪದಲ್ಲಿ ಲಭ್ಯವಿದೆ. ನೀವು ಈ ಔಷಧವನ್ನು ಊಟದ ಮೊದಲು ತೆಗೆದುಕೊಳ್ಳಬೇಕಾಗುತ್ತದೆ. ಇದನ್ನು ಉನ್ಮಾದದ ಅಥವಾ ಮಿಶ್ರ ಘಟನೆಗಳನ್ನು ನಿಯಂತ್ರಿಸಲು ಬಳಸಲಾಗುತ್ತದೆ. ಸಾಮಾನ್ಯ ಅಡ್ಡ ಪರಿಣಾಮಗಳೆಂದರೆ ಸೆರೆಬೆಲ್ಲೊವೆಸ್ಟಿಬ್ಯುಲರ್, ಒಕಿ-ಮೊಟುರ್ ಅಪಸಾಮಾನ್ಯತೆ, ಅಪ್ಲೆಕ್ಸಿಯಾ ಇತ್ಯಾದಿ

ವಾಲ್‌ಪ್ರೋಯೇಟ್ ಸೋಡಿಯಂ : ಇದು ನಂಗಿನ ಮಾತ್ರೆಯ ರೂಪದಲ್ಲಿ ದಿನಕ್ಕೆ 500-2000 ಮಿಗ್ರಾ ಡೋಸ್‌ನಲ್ಲಿ ಲಭ್ಯವಿದೆ. ವಾಲ್‌ಪ್ರೋಯೇಟ್ ತೀವ್ರ ಉನ್ಮಾದಕ್ಕಾಗಿ ಒಂದು ಪರಿಣಾಮಕಾರಿ ಚಿಕಿತ್ಸೆಯಾಗಿದೆ. ಯಾವುದೇ ಔಷಧವನ್ನು ತೆಗೆದುಕೊಳ್ಳುವಾಗ ಅದು ನಿಮ್ಮ ವಾಹನ ಚಲಾಯಿಸುವ ಅಥವಾ ಯಂತ್ರಗಳನ್ನು ಸುರಕ್ಷಿತವಾಗಿ ನಡೆಸುವ ನಿಮ್ಮ ಸಾಮರ್ಥ್ಯದಲ್ಲಿ ಹಸ್ತಕ್ಷೇಪ ಮಾಡಬಹುದು ಎಂಬುದು ನಿಮಗೆ ತಿಳಿವು ಇರಬೇಕು. ಇದು ಸೌಮ್ಯ ಜೀರ್ಣಕ್ರಿಯೆಯಲ್ಲಿ ತೊಂದರೆ, ತೂಕ ಹೆಚ್ಚಳ, ಸೂಕ್ಷ್ಮ ನಡುಕ ಮತ್ತು ನಿದ್ರೆ ಸ್ಥಿತಿಗೆ ಕಾರಣವಾಗಬಹುದು.

ಓಲಂಝಪೈನ್: ಇದೊಂದು ಅಸಾಮಾನ್ಯ ಮನೋವಿಕಾರ-ನಿರೋಧಕ ಔಷಧ. ದಿನಕ್ಕೆ ಗರಿಷ್ಠ 20 ಮಿಗ್ರಾವರೆಗಿನ ಡೋಸ್‌ನಲ್ಲಿ ಮಾತ್ರೆಯ ರೂಪದಲ್ಲಿ ಲಭ್ಯವಿದೆ. ನೀವು ಇದನ್ನು ಪ್ರತಿದಿನ ಸುಮಾರು ಒಂದೇ ಸಮಯದಲ್ಲಿ ಆಹಾರದೊಂದಿಗೆ ಅಥವಾ ಅಲಿಲದೆ ತೆಗೆದುಕೊಳ್ಳಬೇಕು. ನಿಮ್ಮ ವೈದ್ಯರ ನಿರ್ದೇಶನದ ಪ್ರಕಾರದಂತೆಯೇ ತೆಗೆದುಕೊಳ್ಳಿ; ನಿಮ್ಮ ವೈದ್ಯರ ಅನುಮತಿಯಿಲ್ಲದೆ ನಿಮ್ಮ ಔಷಧವನ್ನು ನಿಲ್ಲಿಸಬೇಡಿ.

एसिटॅलोप्राम: पांढऱ्या रंगाच्या टॅबलेट स्वरुपात उपलब्ध, 10-20 मिग्रॅ/दिवस मात्रा, एक विषण्णतारोधक कारक म्हणून याचा उपयोग. हे औषध घेत असताना, जर आपल्या छातीत जळजळ झाली, लैंगिक क्षमता कमी झाली, बद्धकोष्ठता, अतिसार व तोंडात कोरड पडणे असे झाले तर आपल्या डॉक्टरांना सांगा.

क्विटायापिन: क्विटायापिनचा प्रारंभीक डोस हा 25 मिग्रॅ दररोज दोनदा ते 800 मिग्रॅ/ दिवस पर्यंत असेल. हे मुख्यतः बायपोलर विषण्णतेसाठी वापरले जाते. याचे नेहमी होणारे आनुषंगिक परिणाम म्हणजे थंडी भरणे, घाम येणे, संभ्रम, गरगरणे, भोवळ येणे, गुंगी येणे हे आहेत.

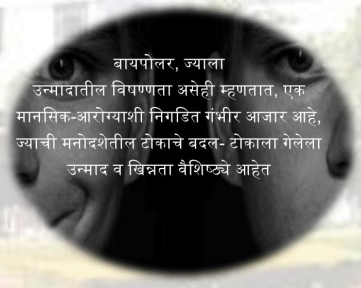
संपूरक उपचार आणि आहार पूरके

बायपोलरवरील इलाजाची औषधोपचार ही कोनशिला आहे, परंतु यात प्रकृती चांगली राहण्यासाठी आहार, शारीरिक व्यायाम व पूरक उपचार प्रणाली सारख्या इतर अनेक बाबींचा समावेश आहे. "पाश्चिमात्य" पद्धतीचा आहार वर्ज करणे संरक्षणात्मक, भरपूर पौष्टिक पदार्थांचे संतुलित सेवन करा. ताजी फळे, भाज्या, डाळी, पूर्ण धान्ये, मांस,गोळ्या पाण्यातील मासे, अंडी, कमी-चरबीयुक्त दुग्धपदार्थ, सोया, आणि शेंगडाणे, बदाम सारखे नट्स व बिया

अधिक माहितीसाठी कृपया संपर्क साधा:
फार्मसी प्रॅक्टिस विभाग
केएलईएस डॉ. प्रभाकर कोरे रुग्णालय
व एमआरसी, नेहरु नगर, बेळगावी.
दूरध्वनी: 2473777, एक्स्टे. 1768

KLES
DR. PRABHAKAR KORE HOSPITAL
Medical Research Centre

आपल्याला बायोपोलर झाल्याचे निदान केले आहे - आपण त्याचा सामना कसा कराल?



फार्मसी प्रॅक्टिस विभाग
केएलईएस डॉ. प्रभाकर कोरे रुग्णालय
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दूरध्वनी: 2473777, एक्स्टे. 1768

डॉक्टरांना कळवा, जर: आपल्याला असं वाटलं

- मोकळेपणाने बोलका.
- मोठेपणाचा आव, आडंबर.
- अति आत्मविश्वास.
- लैंगिक विषयात अतिरुची.
- धर्मात स्वारस्य वाढणे
- अवास्तव खर्च.
- असहिष्णुता
- धूम्रपान, दारु पिणे वाढणे
- फोनचा अत्यधिक वापर
- झोपण्याची गरज कमी होणे.
- चिडचिड व जास्त भरभर बोलणे.

बायपोलर बरा होऊ शकतो का?

अजूनही या प्रश्नाचे स्पष्ट उत्तर मिळाले नाही. खरे पाहता बायपोलर विकार पूर्ण बरा करणारा इलाज नाही.

बायपोलरवरील औषधोपचार.

आपल्याला जरी बरे वाटत असले तरी आपण सर्व गोळ्या घेणे महत्वाचे आहे. याने आपले जीवनमान सुधारेल.

आनुषंगिक परिणाम:

काही लोकांना आनुषंगिक परिणाम होतात जे डॉक्टरांना कळवायला हवेत. जर आनुषंगिक परिणाम हे तीव्र असतील तर, आपले डॉक्टर आपल्याला दुसरे औषध देतील किंवा आपल्या बायपोलरच्या औषधाची मात्रा बदलतील.

- वजनात वाढ
- गुंगी येणे
- अत्यधिक तहान
- कोलेस्टिरॉलच्या पातळीत वाढ
- अशक्तपणा वा थकवा
- कंपन
- पोटदुखी
- थायरॉईड समस्या
- मळमळ
- घेरी येणे
- अतिसार
- गरगरणे
- तोंडाला कोरड पडणे
- लैंगिक निर्बलता
- बद्धकोष्ठता

- धूसर दृष्टी

लिथियम: पांढऱ्या रंगात लिथियम उपलब्ध. लिथियमचा प्रारंभिक डोस प्राय: 250-2000 मिग्रॅ. टॅबलेट जेवणाबरोबर व एक ग्लासभर पाण्यासोबत दररोज दोनदा ते तीनदा आहे. सामान्य संतुलित आहाराबरोबर पाणी 2 लि./दिवस पिणे उचित आहे. ह्याचा वापर मनःस्थिती स्थिर करण्यासाठी होतो, हे औषध घेताना थायरॉइडची 3 महिन्याच्या दरम्यान तपासणी केली गेली पाहिजे .

कार्बमाझेपाईन: हे दोन्ही टॅबलेट आणि द्रव स्वरूपात उपलब्ध आहे, 600-1500 मिग्रॅ / दिवस डोस. हे औषध जेवणाअगोदर घ्यावे लागते. ह्याचा वापर उन्माद वा संमिश्र घटनेचे नियंत्रण करण्यासाठी करतात. याचे सामान्य आनुषंगिक परिणाम सेरेबेलोव्हेस्टिबुलर, ऑक्सिमोटरच्या (डोळ्याच्या हालचालीत) कार्यात विघाड, स्नायुच्या हालचालीत समन्वय नसणे

व्हॅल्प्रोएट सोडियम: हे गिळण्याच्या टॅबलेट स्वरुपात उपलब्ध, 500-2000 मिग्रॅ/ दिवस डोस.व्हॅल्प्रोएट हे तीव्र उन्मादा(वेडा)वर प्रभावी उपचार आहे. कोणतेही औषध घेताना हे लक्षात ठेवावे की याचा आपल्या वाहन चालवण्याच्या वा मशीनवर काम करण्याच्या क्षमतेवर परिणाम होऊ शकतो. यामुळे आपले पोट थोडेसे बिघडू शकते, वजनात वाढ, सूक्ष्म कंपन व झोप येणे असे होऊ शकते.

ओलान्झापाईन:हा एक असाधारण मनोविकाररोधक कारक आहे. टॅबलेट स्वरुपात उपलब्ध जास्तीत जास्त 20 मिग्रॅ/दिवस डोस हे आपल्याला जेवणाबरोबर किंवा जेवणाशिवाय दिवसाच्या एकाच वेळी घ्यावे लागेल. अगदी आपल्या डॉक्टरांच्या सूचनेनुसार घ्यावे; आपल्या डॉक्टरांच्या परवानगी शिवाय आपले औषध घेणे सोडू नका.

Annexure-VI: PCNE Classification

PCNE Classification for Drug related problems

(revised 01-05-06 vm)

V5.01

Contact: jwfvmil@planet.nl

This classification should be referred to as 'The PCNE Classification V 5.01'

Introduction

During the working conference of the Pharmaceutical Care Network Europe in January 1999, a classification scheme was constructed for drug related problems (DRPs). The classification is part of a total set of instruments. The set consists of the classification scheme, reporting forms and cases for training or validation. The classification system is validated and adapted regularly. The current version is V5. It is compatible with previous versions although new items have been added. The numbering of existing items has not been changed.

The classification is for use in research into the nature, prevalence, and incidence of DRPs and also as a process indicator in experimental studies of Pharmaceutical Care outcomes. It is also meant to help health care professionals to document DRP-information in the pharmaceutical care process.

The hierarchical classification is based upon similar work in the field, but it differs from existing systems because it separates the problems from the causes. The following definition is the basis for the classification:

A Drug-Related Problem is an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes.

The basic classification now has 6 primary domains for problems, 6 primary domains for causes and 5 primary domains for Interventions.

However, on a more detailed level there are 21 grouped sub domains for problems, 33 grouped sub domains for causes and 17 grouped sub domains for interventions. Those sub domains can be regarded as explanatory for the principal domains.

In 2003 a scale has been added to indicate if or to what extend the problem has been solved. Zuidlaren, May 2006

N.B. In this version 5.01 an extra Cause is added: *C4.10 Patient takes food that interacts with drugs* and an extra Outcome *O0.0 Outcome not known.*

PCNE Classification scheme for Drug-Related Problems V5.01 -Page 1

The Basic Classification

	Code V5.01	Primary domains
Problems	**P1**	**Adverse reaction(s)** Patient suffers from an adverse drug event
	P2	**Drug Choice Problem** Patient gets or is going to get a wrong (or no drug) drug for his/her disease and/or condition
	P3	**Dosing problem** Patient gets more or less than the amount of drug he/she requires
	P4	**Drug Use Problem** Wrong or no drug taken/administered
	P5	**Interactions** There is a manifest or potential drug-drug or drug-food interaction
	P6	**Other**
Causes	**C1**	**Drug/Dose Selection** The cause of the DRP can be related to the selection of the drug and/or dosage schedule
	C2	**Drug Use Process** The cause of the DRP can be related to the way the patient uses the drug, in spite of proper dosage instructions (on the label)
	C3	**Information** The cause of the DRP can be related to a lack or misinterpretation of information
	C4	**Patient/Psychological** The cause of the DRP can be related to the personality or behaviour of the patient.
	C5	**(Pharmacy) Logistics** The cause of the DRP can be related to the logistics of the prescribing or dispensing mechanism
	C6	**Other**
Interventions	**I0**	**No intervention**
	I1	**At prescriber level**
	I2	**At patient (or carer) level**
	I3	**At drug level**
	I4	**Other**
Outcome of intervention	**O0**	**Outcome intervention unknown**
	O1	**Problem totally solved**
	O2	**Problem partially solved**
	O3	**Problem not solved**

PCNE Classification scheme for Drug-Related Problems V5.01 -Page 2
The Detailed Classification-1

The Problems

Each problem should be coded separately, but there may be more causes or interventions to one problem.

Primary Domain	Code V5.01	Problem
1. Adverse reactions Patient suffers from an adverse drug event	**P1.1**	Side effect suffered (non-allergic)
	P1.2	Side effect suffered (allergic)
	P1.3	Toxic effects suffered
2. Drug choice problem Patient gets or is going to get a wrong (or no drug) drug for his/her disease and/or condition	**P2.1**	Inappropriate drug (not most appropriate for indication)
	P2.2	Inappropriate drug form (not most appropriate for indication)
	P2.3	Inappropriate duplication of therapeutic group or active ingredient
	P2.4	Contra-indication for drug (incl. Pregnancy/breast feeding)
	P2.5	No clear indication for drug use
	P2.6	*No drug prescribed but clear indication*
3. Dosing problem Patient gets more or less than the amount of drug he/she requires	**P3.1**	Drug dose too low or dosage regime not frequent enough
	P3.2	Drug dose too high or dosage regime too frequent
	P3.3	Duration of treatment too short
	P3.4	Duration of treatment too long
4. Drug use problem Wrong or no drug taken/administered	**P4.1**	Drug not taken/administered at all
	P4.2	Wrong drug taken/administered
5. Interactions There is a manifest or potential drug-drug or drug-food interaction	**P5.1**	Potential interaction
	P5.2	Manifest interaction
6. Others	**P6.1**	Patient dissatisfied with therapy despite taking drug(s) correctly
	P6.2	Insufficient awareness of health and diseases (possibly leading to future problems)
	P6.3	Unclear complaints. Further clarification necessary
	P6.4	Therapy failure (reason unknown)

PCNE Classification scheme for Drug Related Problems V5.01 -Page 3

The Detailed Classification-2

The Causes

N.B. One problem can have more causes

Primary Domain	Code V5.01	Cause
1. Drug/Dose selection The cause of the DRP is related to the selection of the drug and/or dosage schedule	**C1.1**	Inappropriate drug selection
	C1.2	Inappropriate dosage selection
	C1.3	More cost-effective drug available
	C1.4	Pharmacokinetic problems, incl. ageing/deterioration in organ function and interactions
	C1.5	Synergistic/preventive drug required and not given
	C1.6	Deterioration/improvement of disease state
	C1.7	New symptom or indication revealed/presented
	C1.8	Manifest side effect, no other cause
2. Drug use process The cause of the DRP can be related to the way the patient uses the drug, in spite of proper dosage instructions (on the label)	**C2.1**	Inappropriate timing of administration and/or dosing intervals
	C2.2	Drug underused/ under-administered
	C2.3	Drug overused/ over-administered
	C2.4	Therapeutic drug level not monitored
	C2.5	Drug abused (unregulated overuse)
	C2.6	Patient unable to use drug/form as directed
3. Information The cause of the DRP can be related to a lack or misinterpretation of information	**C3.1**	Instructions for use/taking not known
	C3.2	Patient unaware of reason for drug treatment
	C3.3	Patient has difficulties reading/understanding Patient Information Form/Leaflet
	C3.4	Patient unable to understand local language
	C3.5	Lack of communication between healthcare professionals
4. Patient/Psychological The cause of the DRP can be related to the personality or behaviour of the patient.	**C4.1**	Patient forgets to use/take drug
	C4.2	Patient has concerns with drugs
	C4.3	Patent suspects side-effect
	C4.4	Patient unwilling to carry financial costs
	C4.5	Patient unwilling to bother physician
	C4.6	Patient unwilling to change drugs
	C4.7	Patient unwilling to adapt life-style
	C4.8	Burden of therapy
	C4.9	Treatment not in line with health beliefs
	C4.10	Patient takes food that interacts with drugs
5. Logistics The cause of the DRP can be related to the logistics of the prescribing or dispensing mechanism	**C5.1**	Prescribed drug not available (anymore)
	C5.2	Prescribing error (only in case of slip of the pen)
	C5.3	Dispensing error (wrong drug or dose dispensed)
6. Others	**C6.1**	Other cause; specify
	C6.2	No obvious cause

PCNE Classification scheme for Drug-Related Problems V5.01 -Page 4
The Detailed Classification-3

The Interventions
N.B. One problem can lead to more interventions

Primary Domain	Code V5.01	Intervention
No intervention	**I0.0**	No Intervention
1. At prescriber level	**I1.1**	Prescriber informed only
	I1.2	Prescriber asked for information
	I1.3	Intervention proposed, **approved** by Prescriber
	I1.4	Intervention proposed, **not approved** by Prescriber
	I1.5	Intervention proposed, outcome unknown
2. At patient/carer level	**I2.1**	Patient (medication) counselling
	I2.2	Written information provided only
	I2.3	Patient referred to prescriber
	I2.4	Spoken to family member/caregiver
3. At drug level	**I3.1**	Drug changed to ….
	I3.2	Dosage changed to ….
	I3.3	Formulation changed to …..
	I3.4	Instructions for use changed to …..
	I3.5	Drug stopped
	I3.6	New drug started
4. Other intervention or activity	**I4.1**	Other intervention (specify)
	I4.2	Side effect reported to authorities

Outcome of intervention
N.B. One problem (or the combination of interventions) can only lead to one level of solving the problem

Primary Domain	Code V5.01	Outcome of intervention
0. Not known	**O0.0**	Outcome intervention not known
1. Solved	**O1.0**	Problem totally solved
2. Partially solved	**O2.0**	Problem partially solved
3. Not solved	**O3.1**	Problem not solved, lack of cooperation of patient
	O3.2	Problem not solved, lack of cooperation of prescriber
	O3.3	Problem not solved, intervention not effective
	O3.4	No need or possibility to solve problem

Annexure VII: ADR Documentation form.

KLE UNIVERSITY COLLEGE OF PHARMACY

DEPARTMENT OF PHARMACY PRACTICE

Dr. PRABHAKAR KORE HOSPITAL & MEDICAL RESEARCH CENTER, BELGAUM

ADR NOTIFICATION AND DOCUMANTATION FORM

Patient's name: Age: Gender:

Weight: I.P/O.P: Dept:

Unit: Consultant:

Reason for admission:

Past medical history:

Patient's background information collected? ☐ Yes ☐ No

Diagnosis:

Drug allergy, if any:

Brief description of reaction:

Date of onset of reaction:

Drug used prior to reaction	Dose	Route and frequency	Date started	Date stopped	Reasons for use

Suspected Drug:

Name of the drug	Brand name	Labeled strength	Batch/lot no.	Exp. Date	Manufacturer

Predisposing Factors:

☐ Age ☐ Gender ☐ Genetic

☐ Intercurrent Disease ☐ Multiple Drug Therapy ☐ Other (specify) ☐ Nil

Other Possible Cause:

Dechallenge: ☐ Yes ☐ No ☐ Not Known

If yes

☐ Definite improvement
☐ No improvement
☐ Unknown

Rechellenge: ☐ Yes ☐ No ☐ Not Known

If yes

☐ Recurrence of symptoms
☐ No recurrence of symptoms
☐ Unknown

Causality:

A) WHO probability scale

☐ Certain ☐ Probable ☐ Possible
☐ Unassessable/unclassifiable ☐ Unlikely ☐ Conditional/unclassified

B) Naranjo's scale

☐ Definite ☐ Probable ☐ Possible ☐ Unlikely

C) Karch & Lasagna's scale

☐ Definite ☐ Probable ☐ Possible ☐ Conditional

Severity:

Mild	**Moderate**	**Severe**
☐ Level 1	☐ Level 3	☐ Level 5
☐ Level 2	☐ Level 4 (a)	☐ Level 6
	☐ Level 4 (b)	☐ Level 7

Predictability: ☐ Predictable ☐ Not Predictable

Preventability: ☐ Definitely Preventable ☐ Probably Preventable ☐ Not Preventable

Management of Adverse Drug Reaction

Fate of Suspected Drug: ☐ Drug withdrawn ☐ Dose altered ☐ No change

Treatment Given: ☐ Specific ☐ Symptomatic ☐ Nil

Outcome: ☐ Fatal ☐ Recovered ☐ Unknown
☐ Permanent Harm ☐ Continuing ☐ Other (Specify)

Patient Interviewed: ☐ Yes ☐ No

Thank you note provided: ☐ Yes ☐ No

Alert card Provided: ☐ Yes ☐ No ☐ N/A

Was supported ADR discussed with concerned physician? ☐ Yes ☐ No

Any appropriate suggestion given? ☐ Yes ☐ No

Follow up:

Reference consulted:

Reporting Doctor Name: **Date:**

Name of pharmacist: **Signature:**

Staff In-charge: **Signature:**

Annexure VIII: Adverse Drug Reaction Notification form & alert card.

KLES Dr. Prabhakar Kore Hospital & Medical Research Center, Belgaum

NOTIFICATION OF A SUSPECTED ADVERSE DRUG REACTION

Patient Name:…….
Age:……Gender:……....
IP/OP No.: …….
Unit:……

Suspected Drug (S):
……..
Date of Suspected Drug (S) Started:
……
Brief Description of Reaction:
…….....
……
……
……

Name of the reported Doctor:
……...
Signature: …….. Date:
……

Note: Please return this to the Department of Pharmacy Practice so that clinical pharmacist can investigate and document the suspected ADR as soon as possible.

ALERT CARD

DEPARTMENT OF PHARMACY PRACTICE
KLEs UNIVERSITY COLLEGE OF PHARMACY

ADVERSE DRUG REACTION ALERT CARD

PATIENT NAME:
AGE: GENDER:
ADDERESS:
ADR: DRUG:

Please produce this card to your doctor at the time of consultation.

Annexure-IX: Naranjo adverse drug reaction probability scale.

The Naranjo adverse drug reaction probability scale; To assess the adverse drug reaction, please answer the following questionnaire and give the pertinent score	Yes	No	Do not know	Score
1. Are there previous *conclusive* reports on this reaction?	+1	0	0	
2. Did the adverse event occur after the suspected drug was administered?	+2	-1	0	
3. Did the adverse reaction improve when the drug was discontinued or a *specific* antagonist was administered?	+1	0	0	
4. Did the adverse reaction reappear when the drug was readministered?	+2	-1	0	
5. Are there alternative causes (other than the drug) that could have on their own caused the reaction?	-1	+2	0	
6. Did the reaction reappear when a placebo was given?	-1	+1	0	
7. Was the blood detected in the blood (or other fluids) in concentrations known to be toxic?	+1	0	0	
8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0	
9. Did the patient have a similar reaction to the same or similar drugs in *any* previous exposure?	+1	0	0	
10. Was the adverse event confirmed by any objective evidence?	+1	0	0	
			Total	

Annexure-X: Hartwig's ADR severity assessment scale.

SEVERITY ASSESSMENT SCALE OF ADR: Hartwig's scale

Level of severity	Description of reaction
Level 1	An ADR occurred but required no change in treatment with the suspected drug.
Level 2	The ADR required that treatment with the suspected drug be held, discontinoued or otherwise changed. No antidote or other treatment required. No increase of LOS (length of stay)
Level 3	The ADR required that treatment with the suspected drug be held, discontinoued or otherwise changed. ADR /OP antidote or other treatment required. No increase of LOS (length of stay)
Level 4	**a)** Any level 3 ADR that increase LOS by at least one day OR **b)** The ADR is the reason for admission
Level 5	Any level 4 ADR which required intensive medical care
Level 6	The adverse reaction either directly or indirectly led the patient
Level 7	The adverse reaction either directly or indirectly led the death of patient.

Annexure-XI: Morisky 8-Item Medication Adherence Questionnaire.

Question	Patient Answer (Yes/No)	Score Y=1; N=0
Do you sometimes forget to take your medicine?		
People sometimes miss taking their medicines for reasons other than forgetting. Thinking over the past 2 weeks, were there any days when you did not take your medicine?		
Have you ever cut back or stopped taking your medicine without telling your doctor because you felt worse when you took it?		
When you travel or leave home, do you sometimes forget to bring along your medicine?		
Did you take all your medicines yesterday?		
When you feel like your symptoms are under control, do you sometimes stop taking your medicine?		
Taking medicine every day is a real inconvenience for some people. Do you ever feel hassled about sticking to your treatment plan?		
How often do you have difficulty remembering to take all your medicine? __ A. Never/rarely __ B. Once in a while __ C. Sometimes __ D. Usually __ E. All the time		A = 0; B-E = 1
	Total score	

Scores:

>2 = low adherence

1 or 2 = medium adherence

0 = high adherence

Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. *Med Care*. 1986;24:67-74.

Annexure-XII: WHOQOL- BREF Health Status Questionnaire.

QUALITY OF LIFE

(World Health Organisation Quality of Life-BREF)

URNumber:

Surname:

Given name:

Dateofbirth:

(Please fill in if no label available)

PURPOSE OF MODULE
To assess the client's perceived quality of life.

WHO CAN ADMINISTER THIS MODULE?
This module can be self-administered by the client if they have the ability or desire to do so, or can be administered by the clinician.

INTRODUCTION FOR CLIENT
"Now I am going to ask you about how you feel about your quality of life, health, or other areas of your life. Please answer all the questions. If you are unsure about which response to give to a question, please choose the one that appears most appropriate. This can often be your first response."

INSTRUCTIONS
1. Introduce module to client.
2. Ask all questions and circle responses on the 5-point scale provided.
3. Score module using the scoring guide.
4. Re-administer to monitor progress.

	VERY POOR	POOR	NEITHER POOR NOR GOOD	GOOD	VERY GOOD
1. How would you rate the quality of your life?	1	2	3	4	5

	VERY DISSATISFIED	DISSATISFIED	NEITHER SATISFIED NOR DISSATISFIED	SATISFIED	VERY SATISFIED
2. How satisfied are you with your health?	1	2	3	4	5

The following questions ask about how much you have experienced certain things in the last two weeks.

	NOT AT ALL	A LITTLE	A MODERATE AMOUNT	VERY MUCH	AN EXTREME AMOUNT
3. To what extent do you feel that physical pain prevents you from doing what you need to do?	1	2	3	4	5
4. How much do you need any medical treatment to function in your daily life?	1	2	3	4	5
5. How much do you enjoy life?	1	2	3	4	5

	NOT AT ALL	A LITTLE	A MODERATE AMOUNT	VERY MUCH	AN EXTREME AMOUNT
6. To what extent do you feel your life to be meaningful?	1	2	3	4	5
7. How well are you able to concentrate?	1	2	3	4	5
8. How safe do you feel in your daily life?	1	2	3	4	5
9. How healthy is your physical environment?	1	2	3	4	5

The following questions ask about how completely you experience or were able to do certain things in the last two weeks.

	NOT AT ALL	A LITTLE	MODERATELY	MOSTLY	COMPLETELY
10. Do you have enough energy for everyday life?	1	2	3	4	5
11. Are you able to accept your bodily appearance?	1	2	3	4	5
12. Have you enough money to meet your needs?	1	2	3	4	5
13. How available to you is the informa- tion that you need in your day-to-day life?	1	2	3	4	5
14. To what extent do you have the op- portunity for leisure activities?	1	2	3	4	5
	VERY POOR	POOR	NEITHER POOR NOR GOOD	GOOD	VERY GOOD
15. How well are you able to get around?	1	2	3	4	5

The following questions ask you to say how good or satisfied you have felt about various aspects of your life over the last two weeks.

	VERY DISSATISFIED	DISSATISFIED	NEITHER SATISFIED NOR DISSATISFIED	SATISFIED	VERY SATISFIED
16. How satisfied are you with your sleep?	1	2	3	4	5
17. How satisfied are you with your ability to perform your daily living activities?	1	2	3	4	5

18. How satisfied are you with your capacity for work?	1	2	3	4	5
19. How satisfied are you with yourself?	1	2	3	4	5
20. How satisfied are you with your personal relationships?	1	2	3	4	5
21. How satisfied are you with your sex life?	1	2	3	4	5
22. How satisfied are you with the support you get from your friends?	1	2	3	4	5
23. How satisfied are you with the conditions of your living place?	1	2	3	4	5
24. How satisfied are you with your access to health services?	1	2	3	4	5
25. How satisfied are you with your transport?	1	2	3	4	5

The following question refers to how often you have felt or experienced certain things in the last two weeks

	NEVER	SELDOM	QUITE OFTEN	VERY OFTEN	ALWAYS
26. How often do you have negative feelings such as blue mood, despair, anxiety, depression?	1	2	3	4	5

WHOQOL-BREF assesses four domains of quality of life: physical health, psychological, social relationships and the environment.

It is possible to derive four domain scores from the WHOQOL-BREF. The four domain scores denote an individual's perception of quality of life in each particular domain.

Calculating domain scores involves two steps

STEP 1

Calculate raw scores for each domain using the table below

DOMAIN	EQUATION FOR COMPUTING DOMAIN SCORES	RAW SCORE
1. Physical Health	(6-Q3) + (6-Q4) + Q10 + Q15 + Q16 + Q17 + Q18	=
2. Psychological	Q5 + Q6 + Q7 + Q11 + Q19 + (6-Q26)	=
3. Social relationships	Q20 + Q21 +Q22	=
4. Environment	Q8 + Q9 + Q12 + Q13 + Q14 + Q23 + Q24 + Q25	=

	+ + + + + + +	

For instance to calculate the Physical Health domain raw score, note down the client's responses to each of the relevant questions.

QUESTION	CLIENTS RESPONSE
Question 3	Very much = 4
Question 4	A moderate amount = 3
Question 10	A little = 2
Question 15	Poor = 2
Question 16	Satisfied = 4
Question 17	Satisfied = 4
Question 18	Very Satisfied = 5

Then add these responses into the equation in the table above. For example:

Physical health domain raw score = (6 - 4) + (6 - 3) + 2 + 2 + 4 + 4 + 5
= 2 + 3 + 2 + 2+ 4 + 4 + 5
= 22

STEP2

Convert raw scores to a transformed scores (on a 0-100 scale) using tables for each domain on the next page (i.e. if a client's raw score on the Physical Health domain is 22 then their transformed score will be 56)

INTERPRETATION

Higher transformed scores on each of the domains indicates higher quality of life in that particular area (i.e. someone who scores 75 on the Social relationships domain has a higher perceived quality of life in relation to Social Relationships than someone who scores 25)

DOMAIN 1: PHYSICAL HEALTH		DOMAIN 2: PSYCHOLOGICAL		DOMAIN 3: SOCIAL RELATIONSHIPS		DOMAIN 4: ENVIRONMENT	
RAW SCORE	TRANSFORMED SCORE	RAW SCORE	TRANSFORMED SCORE	RAW SCORE	TRANSFORMED SCORE	RAW SCORE	TRANSFORMED SCORE
7	0	6	0	3	0	8	0
8	6	7	6	4	6	9	6
9	6	8	6	5	19	10	6
10	13	9	13	6	25	11	13
11	13	10	19	7	31	12	13
12	19	11	19	8	44	13	19
13	19	12	25	9	50	14	19

14	25	13	31	10	56	15	25
15	31	14	31	11	69	16	25
16	31	15	38	12	75	17	31
17	38	16	44	13	81	18	31
18	38	17	44	14	94	19	38
19	44	18	50	15	100	20	38
20	44	19	56			21	44
21	50	20	56			22	44
22	56	21	63			23	50
23	56	22	69			24	50
24	63	23	69			25	56
25	63	24	75			26	56
26	69	25	81			27	63
27	69	26	81			28	63
28	75	27	88			29	69
29	81	28	94			30	69
30	81	29	94			31	75
31	88	30	100			32	75
32	88					33	81
33	94					34	81
34	94					35	88
35	100					36	88
						37	94
						38	94
						39	100
						40	100

This module can be repeated at different time points to monitor progress in quality of life. You can readminister this module in two weeks after the completion of the form. This is the minimum amount of time needed, and the module should not be re-administered before two weeks time.

Annexure-XIII: Young Mania Rating Scale.

1. Elevated Mood

0 Absent
1 Mildly or possibly increased on questioning
2 Definite subjective elevation; optimistic; self- confident; cheerful; appropriate to content
3 Elevated, inappropriate to content; humorous
4 Euphoric; inappropriate laughter, singing

2. Increased Motor Activity/Energy

0 Absent
1 Subjectively increased
2 Animated; gestures increased
3 Excessive energy; hyperactive at times; restless (can be calmed)
4 Motor excitement; continuous hyperactivity (cannot be calmed)

3. Sexual Interest

0 Normal; not increased
1 Mildly or possibly increased
2 Definite subjective increase on questioning
3 Spontaneous sexual content; elaborates on sexual matters; hypersexual by self-report
4 Overt sexual acts (toward patients, staff, or interviewer)

4. Sleep

0 Reports no decrease in sleep
1 Sleeping less than normal amount by up to one hour
2 Sleeping less than normal by more than one hour
3 Reports decreased need for sleep
4 Denies need for sleep

5. Irritability

0 Absent
2 Subjectively increased
4 Irritable at times during interview; recent episodes of anger or annoyance on ward
6 Frequently irritable during interview; short or curt throughout
8 Hostile, uncooperative; interview impossible

6. Speech (Rate and Amount)

0 No increase
2 Feels talkative
4 Increased rate or amount at times, verbose at times
6 Push; consistently increased rate and amount; difficult to interrupt
8 Pressured; uninterruptible, continuous speech

7. Language/Thought Disorder

0 Absent
1 Circumstantial; mild distractibility; quick thoughts
2 Distractible; loses goal of thought; changes topics frequently; racing thoughts
3 Flight of ideas; tangentiality; difficult to follow; rhyming; echolalia
4 Incoherent; communication impossible

8. Thought Content

0 Normal
2 Questionable plans; new interests
4 Special project(s); hyper-religious
6 Grandiose or paranoid ideas; ideas of reference
8 Delusions; hallucinations

9. Disruptive/Aggressive Behavior

0 Absent, cooperative
2 Sarcastic; loud at times, guarded
4 Demanding; threats on ward
6 Threatens interviewer; shouting; interview difficult
8 Assaultive; destructive; interview impossible

10. Appearance

0 Appropriate dress and grooming
1 Minimally unkempt
2 Poorly groomed; moderately disheveled; overdressed
3 Disheveled; partly clothed; garish makeup
4 Completely unkempt; decorated; bizarre garb

11. Insight

0 Present; admits illness; agrees with need for treatment
1 Possibly ill
2 Admits behavior change, but denies illness
3 Admits possible change in behavior; but denies illness
4 Denies any behavior change

Scoring the YMRS

The purpose of each item is to rate the severity of that abnormality in the patient. When several keys are given for a particular grade of severity, the presence of only one is required to qualify for that rating. A severity rating is assigned to each of the eleven items, based on the patient's subjective report of his or her condition over the previous forty-eight hours and the clinician's behavioral observations during the interview, with the emphasis on the latter.

Scoring between the points given (whole or half points) is possible and encouraged after experience with the scale is acquired. This is particularly useful when severity of a particular item in a patient does not follow the progression indicated by the keys.
In scoring the YMRS, the following items are graded on a 0 to 8 scale:

- Irritability
- Speech
- Thought content
- Disruptive/aggressive behavior

The following items are graded on a 0 to 4 scale:

- Elevated mood
- Increased motor activity/energy
- Sexual interest
- Sleep
- Language/thought disorder
- Appearance
- Insight

Annexure-XIV: Hamilton Depression Rating Scale.

1) DEPRESSED MOOD (sadness, hopeless, helpless, worthless)
0 |__| Absent.
1 |__| These feeling states indicated only on questioning.
2 |__| These feeling states spontaneously reported verbally.
3 |__| Communicates feeling states non-verbally, i.e. through facial expression, posture, voice and tendency to weep.
4 |__| Patient reports virtually only these feeling states in his/her spontaneous verbal and non-verbal communication
.

2) FEELINGS OF GUILT
0 |__| Absent.
1 |__| Self-reproach, feels he/she has let people down.
2 |__| Ideas of guilt or rumination over past errors or sinful deeds.
3 |__| Present illness is a punishment. Delusions of guilt.
4 |__| Hears accusatory or denunciatory voices and/or experiences threatening visual hallucinate.

3) SUICIDE
0 |__| Absent.
1 |__| Feels life is not worth living.
2 |__| Wishes he/she were dead or any thoughts of possible death to self.
3 |__| Ideas or gestures of suicide.
4 |__| Attempts at suicide (any serious attempt rate 4).

4) INSOMNIA: EARLY IN THE NIGHT
0 |__| No difficulty falling asleep.
1 |__| Complains of occasional difficulty falling asleep, i.e. more than 1⁄2 hour.
1 |__| Complains of nightly difficulty falling asleep.

5) INSOMNIA: MIDDLE OF THE NIGHT
0 |__| No difficulty.
1 |__| Patient complains of being restless and disturbed during the night.
2 |__| Waking during the night – any getting out of bed rates 2 (except for purposes of voiding).

6) INSOMNIA: EARLY HOURS OF THE MORNING
0 |__| No difficulty.
1 |__| Waking in early hours of the morning but goes back to sleep.
2 |__| Unable to fall asleep again if he/she gets out of bed.

7) WORK AND ACTIVITIES
0 |__| No difficulty.
1 |__| Thoughts and feelings of incapacity, fatigue or weakness related to activities, work or hobbies.
2 |__| Loss of interest in activity, hobbies or work – either directly reported by the patient or indirect in listlessness, indecision and vacillation (feels he/she has to push self to work or activities).
3 |__| Decrease in actual time spent in activities or decrease in productivity. Rate 3 if the patient does not spend at least three hours a day in activities (job or hobbies) excluding routine chores.
4 |__| Stopped working because of present illness. Rate 4 if patient engages in no activities except routine chores,or if patient fails to perform routine chores unassisted.

8) RETARDATION (slowness of thought and speech, impaired ability to concentrate, decreased motor activity)
0 |__| Normal speech and thought.
1 |__| Slight retardation during the interview.
2 |__| Obvious retardation during the interview.
3 |__| Interview difficult.
4 |__| Complete stupor.

9) AGITATION
0 |__| None.

1 |__| Fidgetiness.
2 |__| Playing with hands, hair, etc.
3 |__| Moving about, can't sit still.
4 |__| Hand wringing, nail biting, hair-pulling, biting of lips.

10) ANXIETY PSYCHIC
0 |__| No difficulty.
1 |__| Subjective tension and irritability.
2 |__| Worrying about minor matters.
3 |__| Apprehensive attitude apparent in face or speech.
4 |__| Fears expressed without questioning.

11) ANXIETY SOMATIC (physiological concomitants of anxiety) such as: gastro-intestinal – dry mouth, wind, indigestion, diarrhea, cramps, belching cardio-vascular – palpitations, headaches respiratory – hyperventilation, sighing urinary frequency sweating
0 |__| Absent.
1 |__| Mild.
2 |__| Moderate.
3 |__| Severe.
4 |__| Incapacitating.

12) SOMATIC SYMPTOMS GASTRO-INTESTINAL
0 |__| None.
1 |__| Loss of appetite but eating without staff encouragement. Heavy feelings in abdomen.
2 |__| Difficulty eating without staff urging. Requests or requires laxatives or medication for bowels or medication for gastro-intestinal symptoms.

13) GENERAL SOMATIC SYMPTOMS
0 |__| None.
1 |__| Heaviness in limbs, back or head. Backaches, headaches, muscle aches. Loss of energy and fatigability.
2 |__| Any clear-cut symptom rates 2.

14) GENITAL SYMPTOMS (symptoms such as loss of libido, menstrual disturbances)
0 |__| Absent.
1 |__| Mild.
2 |__| Severe.

15) HYPOCHONDRIASIS
0 |__| Not present.
1 |__| Self-absorption (bodily).
2 |__| Preoccupation with health.
3 |__| Frequent complaints, requests for help, etc.
4 |__| Hypochondriacal delusions.

16) LOSS OF WEIGHT (RATE EITHER a OR b)
a) According to the patient:
0 |__| No weight loss.
1 |__| Probable weight loss associated present illness.
2 |__| Definite (according to patient) weight loss.
3 |__| Not assessed.

b) According to weekly measurements:
0 |__| Less than 1 lb weight loss in week.
1 |__| Greater than 1 lb weight loss with in week.
2 |__| Greater than 2 lb weight loss in week.
3 |__| Not assessed.

17) INSIGHT

0 |__| Acknowledges being depressed and ill.
1 |__| Acknowledges illness but attributes cause to bad food, climate, overwork, virus, need for rest, etc.
2 |__| Denies being ill at all.

Total score: |__|__|

Annexure-XV: Ethical Approval for Study

KLE UNIVERSITY

(Formerly known as KLE Academy of Higher Education & Research, Belagavi)
[Declared as Deemed-to-be-University u/s 3 of the UGC Act, 1956 vide Government of India Notification No.F.9-19/2000-U.3(A)]
'Accredited 'A' Grade by NAAC Placed in **Category 'A'** by MHRD (GoI)

Director, Academic Affairs

JNMC Campus, Nehru Nagar, Belagavi-590 010, Karnataka State, India

☎: 0831-2444444/2493779 **FAX:** 0831-2493777 **Web:** http://www.kleuniversity.edu.in **E-mail:** info@kleuniversity.edu.in

Ref.No.KLEU/Ethic/2015-16/D-93 Date: 6th July 2015.

To,
Mr. Ashish Singh Parihar,
Collage of Pharmacy, Belagavi
Ph.D.Scholar 2014-15

Dear Research Scholar,

Sub:- Regarding Ethical Clearance.

The KLE University **Ethics Committee on Human Subjects** for Ph. D Research Project met on **23rd March 2015** to consider your application for approval of the research project **"Effect of Pharmaceutical care and enhancement of Safety, medication adherence and quality of life in patient with Bipolar disorder: A prospective study in tertiary care hospital".**

As there are no ethical issues involved in your proposed research project, the committee has provided approval for this research project.

You are requested to report to Ethical Committee in case of the following:

1. Any deviation from or change of the protocol.
2. All serious adverse events.
3. Any changes in study documents.

(Dr. Anita Dalal)
Member Secretary,
Ph.D. Ethical Committee(Human),
K.L.E. University,
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CC to: - The Director Academic Affairs, KLE University, Belagavi.
- The Director Research Foundation, KLE University, Belagavi.
- The Registrar, KLE University, Belagavi

Date: 13/July/2015

To,
The Principal,
KLEU J N Medical College,
Belagavi-10.

Through,
Prof. (Dr.) M.S. Ganachari
Professor and Head,
Department of Pharmacy Practice,
Belagavi-10.

Sub.: - Application for permission to conduct Ph.D dissertation work in the Department of Psychiatry in KLES Dr. Prabhakar Kore Hospital & MRC.

Respected Sir,

With respect to the above cited subject, I Ashish Singh Parihar (Ph.D Student, Department of Pharmacy Practice), Full-time research scholar of Doctor of Philosophy (Ph.D.) in Pharmacy, under the guidance of Prof. (Dr.) M. S. Ganachari, would like to take your permission to conduct my Ph.D dissertation work from July 2015 to July 2017 in the department of Psychiatry in KLES Dr. Prabhakar Kore Hospital & MRC. A copy of ethical approval has been attached for your reference. The title of the project is as mentioned below.
Title of the project: - "Effect of Pharmaceutical care and enhancement of safety, medication adherence and quality of life in patient with Bipolar disorder: A prospective study in tertiary care hospital."

Kindly permit for the same and do the needful.

Thanking you,

Yours sincerely,

Ashish Singh Parihar
Ph.D. Full-time Research Scholar
(Reg. No. DO1214008)
Department of pharmacy practice

Permitted
15/7/15
PRINCIPAL
J.N. Medical College
BELGAUM

Research Guide
Prof. (Dr.) M.S. Ganachari
Professor and Head,
Department of Pharmacy Practice

CC: Principal, KLEU College of Pharmacy, Belagavi.

Head, Department of Psychiatry, KLES Dr. Prabhakar Kore Hospital & MRC.

Date: 13/July/2015

To,
The Head
Department of Psychiatry,
KLES Dr. Prabhakar Kore Hospital & MRC,
Belagavi-10.

Through,
Prof. (Dr.) M.S. Ganachari
Professor and Head,
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Research Guide
Prof. (Dr.) M.S. Ganachari
Professor and Head,
Department of Pharmacy Practice

Encl.: Copy of the permission from the Principal, JNMC Belagavi and ethical approval letter.

CC: Principal, KLEU College of Pharmacy, Belagavi.

Permitted
13/7/2015
Dr. N. M. Patil
Professor & Head
Department of Psychiatry
J. N. Medical College,
BELAGAVI-590010

Annexure-XVI: Publication

Original Article

The impact of Clinical Pharmacist Lead Collaborative Care on Quality Of Life of the Patients with Bipolar Disorder: A Unicenter Prospective, Randomization Study

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ABSTRACT

Background: Bipolar disorder is a chronic mental illness, characterized by the presence of manic, depressive and cyclic episodes, usually separated by asymptomatic intervals. Illness significantly affects the patients' quality of life. Hence, clinical pharmacists can contribute to managing the disease condition of the patients, mainly with the use of effective and safe drugs, and improve the patient's quality of life through pharmaceutical care. **Methods/design:** A Randomized, interventional, prospective study was performed on 304 patients, to compare and assess the impact of pharmaceutical care with the usual care. Patients with bipolar disorder, aged 18 to 65 years, who have been discharged from the outpatient department were randomized and enrolled in the study. The intervention group patients' were served with pharmaceutical care, which was provided by clinical pharmacists, Psychiatrists and Nurses, on other hand control group patients were treated with the usual care. Quality of life of the patients was assessed at the baseline level to 3rd, 6th and 9th months of the follow-up. **Result**: Total 266 patients were completed the study. No statistically significant difference was observed at the demographic level and baseline level quality of life ($p = 0.547$) in both the group. After the intervention in the interventional group, significant ($p < 0.001$) improvement in the quality of life were observed during the study period. **Conclusion:** conducted study shows that, clinical pharmacist lead collaborative care can enhance the patients' quality of life in compared to usual care, which is showing that, the participation of clinical pharmacist in psychiatry settings may lead to integration in health care delivery systems.

Keywords: Quality Of Life, Bipolar Disorder, Pharmaceutical Care, Mania, Depression, Psycho-Education, Clinical Pharmacist.

INTRODUCTION

A good quality of life (QOL) is not just only better health status even though it is a sum of good physical health; psychological health; environmental health; socio-economic and spiritual well-being.[1,2] Globally, a good quality of life is an important and broad measure in compared to the health status of the persons' life aspect.[3] As per World Health Organization (WHO) quality of life is an individual perception of their position in life in the context of the culture and value system in which they live and relation to their goal, expectation, standards and concerns,[4] Bipolar disorder impairs quality of life of the patients through mood swings; personal suffering; disturbed familial support and uneven socio-economic functioning.[5] in India, out of 100,000 lack population 200 people are suffering from bipolar disorder in India.[6] Indeed, bipolar disorder is a severe, recurrent and chronic mental suffering, which may represent by the mood swing like dys-

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thymia, depression, euphoria, cyclothymia and mania at different time of interval in the same patient with significant functional and cognitive impairment.[7] Due to cyclic nature of bipolar disorder symptom remission and symptomatic exacerbation can affect the patients' physical; psychological, emotional, economic and social well-being which is directly impaired their overall quality of life.[8]

The usual treatment of bipolar disorder in here pharmacotherapy and psycho-education, many patient responses adequately for such kind of approach but some of do not. They may frequently suffer from the cyclic episode, cognitive impairment, and poor social well-being.[9] Hence multidisciplinary collaboration of health care professionals like a clinical pharmacist, psychiatrist and nurse are needed to optimize the patients' health and good quality of life.[10,11,12]

By the help of this type of study, we planned to assess the impact of clinical pharmacist lead collaborative approach. Our study aim was to measure the effect of pharmaceutical care on various domain of the quality of life of the patients with Bipolar disorder through WHO-BREF QOL. Pharmaceutical care is the care provided by the pharmacist which aim towards patient-centered health and to achieve the desired therapeutic outcome, though patient counseling; interdisciplinary cooperation; improve the medication adherence and ultimately improve the patients' quality of life.[13,14]

METHOD

Ethical Issue: Approval of the study was obtained by the Institutional ethics committee (IEC: KLEU/Ethic/2015-16/D-93). The study protocol was explained to the patients by the investigator orally and the patient information sheet, Informed consent form, patient information leaflets and booklet were issued to the patient. Written consent was obtained from the participants prior to the initiation of the study.

Study Design and Patient Recruitment: Study was initiated at tertiary care hospital. The study was a Prospective, Randomized, open level, comparative study. Total 266 patients completed their follow-up. Patient age between 18 to 65 years of either gender and diagnosed with the bipolar disorder were enrolled in the study. Patients with the history of epilepsy, schizophrenia, obsessive-compulsive disorder, Alcohol-induced psychosis, mental retardation, pregnant and lactating women were excluded from the study.

Study Protocol: Patients, who satisfied the above-cited study criteria were enrolled in the study and randomized through computer-assisted randomization list. The randomization list was prepared by the biostatistician, who was not involved in the study. The allocation was concealed using serial Number.

Selected patients were divided into two groups; control group (n=143) and Interventional group (n=143). Clinical information relevant to the study were collected from the patient and their relatives. Control group patients were on care as usual; whereas, Interventional group patients on pharmaceutical care as well as usual care. Interventional group patient population served with medication-related education, psycho-education, lifestyle modification education along with patient information leaflets and booklets. At each visit patient and their family members knowledge about medicine and disease condition was reinforced and study related data were collected.

Patients' Quality of life (QOL) was measured at the baseline level and at the each visit of follow-up (i.e.3rd, 6th and 9th month). At each visit patients interview were taken place, in which we discuss their medication-related problem and quarries related to the disease condition and medications. After the counseling and interview session, self-reported WHO-BREF QOL questionnaire in Kannada and Marathi was provided to them to mark the option of the question, for same 10 min. time provided to the each patient.

The quality of Life (QOL) Assessment: patients' quality of life was assessed by WHOQOL-BREF; which is a self-reported questionnaire, filled by the patients with bipolar disorder.[15,16] WHOQOL-BREF contain 26 item from which, 2 item represent overall quality of life and health status of the patients and rest of 24 item contain four domain, including physical health domain with 7 item (Domain 1), Psychological health domain with 6 item (Domain 2), Social relationship with 3 item (Domain 3) and Environmental health domain with 8 item (Domain 4).[17] Each of the domain is being rated by 5 points Likert scale and scored from 1 to 5 in response scale. According to WHOQOL guideline, a raw score of each domain was transformed 4 to 20 score. All Domains' score were scaled in ascending direction. The mean score in each domain was obtained by computing the mean of transformed scores converted to a 0–100 scale for each domain. A mean score of <40 in each domain denotes poor, 41–60 indicates moderate and >60 indicates good quality of life.[4,18,19]

Statistical Analysis: The sample size of the study was calculated by the inverse random sampling formula in the order to reject the null hypothesis. An attrition rate of 15% was considered. Probability values of less than 0.05 were considered for statistical significance. Study data were entered and analysed on IBM SPSS, Version

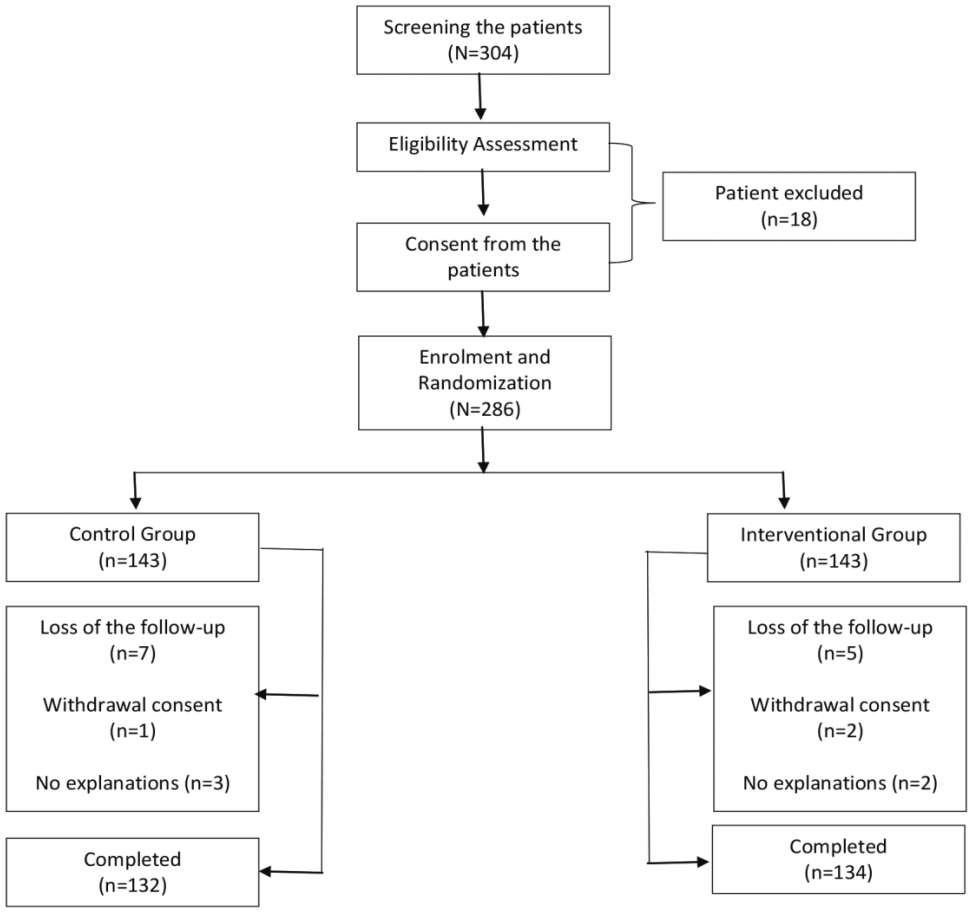

Figure 1: Flowchart showing patients' distribution, a control group receiving usual care and the interventional group receiving pharmaceutical care for a period of 9 months.

20. Socio-demographic data and clinical characteristic of the groups compared with the chi-square test with the frequency, mean, percentage, and degree of freedom. The quality of life both the group was compared and assessed through unpaired student 't' test with mean, standard deviation, 't' value and degree of freedom at 95% confidence interval.

RESULT

Total 304 bipolar disorder patients were screened for the study. Patients who got enrolled after their willingness to informed consent were likewise randomized into two groups, to know the effect of pharmaceutical care in the quality of life (QOL) of the patients. A flowchart representing the patients' distribution, which cited in figure 1. In the control group out of 143 patients, 134 were completed, their follow-up, of which 81 were male and 51 were female; their mean age was 36.6 ± 11.36 years; mean age of onset of the first episode of Bipolar disorder was 26.84 ± 8.47 and mean Body Mass Index (BMI) was 24.11 ± 4.07. Whereas in Interventional group, 84 patients were male and 50 were females; having a mean age of 38.34 ± 12.91 years; mean age of onset of the first BPAD of 27.46 ± 10.09 and mean BMI of 24.36 ± 3.94. No statistically significant differences were observed in mean age, the age of onset of first BPAD and BMI. (Table 1)

In both groups, the majority of the patient population was not shown psychiatry family history. In control group, 86.4% (n=114) had no psychiatry family history; 9.1% (n=12) were shown paternal and 4.5% (n=6) were shown maternal psychiatric family history. On the other hand, in the intervention group, 88.1% (n=118) patients had no psychiatric history; 10.45 (n=14) had paternal and 1.5% (n=2) patients had a maternal psychiatric family history. Childhood adversity is also mentioned

Table 1: Demographic data of the patients.								
Sl. No.	Demographic variable	Control group (n=132)	Interventional group (n=134)	t	df	95% confidence Interval		p
						Lower	Upper	
1	Age	36.6±11.36	38.34±12.91	-1.46	264	-5.123	0.754	0.145
2	Age of onset of first BPAD	24.11±4.07	24.36±3.97	-0.51	264	-1.226	0.715	0.605
3	BMI	26.84±8.47	27.46±10.09	-0.53	264	-2.929	1.685	0.596

Data are represented as mean ± SD
BMI= body mass Index

Table 2: Demographic data of the patients.						
Sl. No.	Demographic variable	Control group (n=132)	Interventional group (n=134)	Total	Chi square test	
					df	p
1	**Gender**					
	Male	81 (61.4%)	84 (62.7%)	165 (62.0%)	1	0.824
	Female	51 (38.6%)	50 (37.3%)	101 (38.0%)		
2	**Religion**					
	Hindu	126 (95.5%)	121 (90.3%)	247 (92.9%)		
	Muslim	6 (4.5%)	12 (9.0%)	18 (6.8%)	2	0.214
	Christian	0 (0.0%)	1 (0.7%)	1 (0.4%)		
3	**Marital Status**					
	Unmarried	35 (26.5%)	29 (21.6%)	62 (24.1%)		
	Married	96 (72.1%)	105 (78.4%)	201 (75.6%)	2	0.337
	Widow	1 (0.8%)	0 (0.0%)	1 (0.4%)		
4	**Socioeconomic Status**					
	Government Job	1 (0.8%)	6 (4.5%)	7 (2.6%)		
	Private Job	29 (22.0%)	27 (20.1%)	56 (21.1%)		
	Daily Basis	2 (1.5%)	2 (1.5%)	4 (1.5%)		
	Homemaker	36 (27.3%)	42 (31.3%)	78 (29.3%)	7	0.616
	Farmer	34 (25.8%)	28 (20.9%)	62 (23.3%)		
	Student	21 (15.9%)	22 (16.4%)	43 (16.2%)		
	Retired	4 (3.0%)	2 (1.5%)	6 (2.3%)		
	Unemployed	5 (3.8%)	5 (3.7%)	10 (3.8%)		
5	**Family History**					
	Nothing Significant	114 (86.4%)	118 (88.1%)	232 (87.2%)		
	Paternal	12 (9.1%)	14 (10.4%)	26 (9.8%)	2	0.332
	Maternal	6 (4.5%)	2 (1.5%)	8 (3.0%)		
6	**Childhood Adversity**					
	Neglect	9 (6.8%)	14 (10.4%)	23 (8.6%)		
	Physical Health	0 (0.0%)	2 (1.5%)	2 (0.8%)	3	0.164
	Loss of Parents	2 (1.5%)	0 (0.0%)	2 (0.8%)		
	Absent	121 (91.7%)	118 (88.1%)	239 (89.8%)		
7	**Smoker**					
	Yes	37 (28.0%)	38 (28.4%)	75 (28.2%)	1	0.953
	No	95 (72.0%)	96 (71.6%)	191 (71.8%)		
8	**Alcoholic**					
	Yes	26 (19.7%)	23 (17.2%)	49 (18.4%)	1	0.594
	No	106 (80.3%)	111 (82.8%)	217 (81.6%)		

Data are presented as % (n)

in Table 2. On the assessment of childhood adversity, in control group, 6.8% (n=9) patients were expressed childhood negligence; 1.5% (n=2) with lost of parents and 91.7% were not expressed any childhood adversity. Whereas in the intervention group, 10.4% (n=14) patients were with childhood negligence; 1.5% (n=2) were with abnormal physical health and 88.1% (n=118) patients were not shown any childhood adversity. In control group 28.0% (n=37) and interventional group 28.4% (n=38) patients were with smoking habit, while 19.7% (n=26) and 17.2% (n=23) patients, in control and interventional group respectively, were with drinking habit. Patient's marital status, socioeconomic status and religion is mentioned in Table 2.

Table 3: Mean total Quality of Life (QOL) of the patients.								
Sl. No.	Baseline and follow-up visit for QOL	Control group (n=132)	Interventional group (n=134)	t	df	95% confidence Interval		*p*
						Lower	Upper	
1	Baseline visit	49.47±4.19	49.79±4.38	-0.60	263.7	-1.353	0.718	0.547
2	Follow-up visit 1	49.54±3.97	54.34±3.79	-10.1	263.0	-5.746	-3.871	0.001
3	Follow-up visit 2	48.93±3.93	55.25±3.90	-13.1	263.8	-7.260	-5.368	0.001
4	Follow-up visit 3	49.11±3.84	56.27±3.56	-15.7	261.8	-8.056	-6.268	0.001

Data are represented as mean ± SD; Baseline versus visit 1, visit 2 and visit 3 in both of groups.
$p < 0.05$ in increasing the quality of life; unpaired student t test.
df = degree of freedom; QOL=quality of life

Table 4: Quality of life of patients in different Domains of WHOQOL-BREF.								
Sl. No.	Domains	Control group (n=132)	Interventio-nal group (n=134)	t	df	95% confidence Interval		*p*
						Lower	Upper	
1	**Physical Health**							
	Baseline visit Follow-up	51.16±7.9	50.21±8.24	0.95	263.85	-1.004	2.9047	0.339
	visit 1 Follow-up visit 2	52.84±5.9	58.16±5.56	-7.51	262.01	-6.709	-3.921	0.001
	Follow-up visit 3	51.31±4.8	59.39±5.07	-13.29	263.71	-9.282	-6.887	0.001
		51.59±5.2	60.85±5.00	-14.74	263.02	-10.48	-8.016	0.001
2	**Psychological Health**							
	Baseline visit Follow-up	50.04±7.2	49.47±6.86	0.664	262.70	-1.129	2.280	0.507
	visit 1 Follow-up visit 2	47.37±5.1	52.92±5.03	-8.323	263.68	-6.418	-3.962	0.001
	Follow-up visit 3	47.18±5.1	53.43±4.92	-10.05	263.46	-7.474	-5.027	0.001
		47.04±4.8	54.70±3.99	-14.00	252.66	-8.732	-6.579	0.001
3	**Social Relationship**							
	Baseline visit Follow-up	48.66±8.1	49.17±7.44	-0.526	260.87	-2.392	1.384	0.599
	visit 1 Follow-up visit 2	49.34±5.6	53.47±5.07	-6.302	260.60	-5.419	-2.838	0.001
	Follow-up visit 3	49.08±5.4	54.94±5.45	-8.744	263.89	-7.185	-4.543	0.001
		48.93±5.0	55.17±4.88	-10.24	263.39	-7.438	-5.040	0.001
4	**Environmental Health**							
	Baseline visit Follow-up	48.02±7.5	50.31±7.54	-2.471	263.91	-4.116	-0.465	0.014
	visit 1 Follow-up visit 2	48.25±6.1	52.81±6.27	-6.009	263.95	-6.058	-3.068	0.001
	Follow-up visit 3	48.17±6.0	53.14±6.08	-6.672	263.95	-6.443	-3.506	0.001
		48.86±5.8	54.28±6.23	-7.327	263.27	-6.876	-3.963	0.001

Data are represented as mean ± SD; Baseline versus visit 1, visit 2 and visit 3 in both of groups.$p < 0.05$ in increasing the quality of life; unpaired student t test.
df = degree of freedom; QOL=quality of life.

The quality of life has been being assessed by WHO-QOL-BREF. Change in the quality of life (QOL) from baseline to the end of the study in both groups are shown in Table 3. It is evidence from the result that, the quality of life in the interventional group, were increased gradually at every follow-up. Whereas in the control group, QOL of patients were on stationary stage. The mean score of QOL at baseline, in control and the interventionalgroup, was 49.475±4.191 and 49.792±4.384. There was no statistical difference (p=0.547) observed at baseline level with 95% confidence interval (CI). After the pharmaceutical care based intervention in the interventional group, it is to be observed that, during the follow-up visit there were statistically significant improvement were observed (p=0.001).

On the assessment of WHOQOL-BREF, in Domain 1 (Physical health) no significant difference (p=0.339) were observed at baseline in both of the groups. But during the follow-up visits, there was a significant improvement (p=0.001) seen Same as in Domain 2 (Psychological health) and Domain 4 (Environmental health) respectively, no significant differences were observed at baseline, but in Domain 3 (Social relationship) significant difference (p=0.014) was observed. On the other hand, in the interventional group, statistically significant improvement (p=0.001) were observed in all Domains. (Table 4)

DISCUSSION

Ours is the first study to evaluate the impact of pharmaceutical care based on collaborative care for the patients with bipolar disorder in India. As per the result of the study, we assessed the positive effect of pharmaceutical care on intervening patient population in compare to patients with care as usual. Lizer M H *et al*[20] assessed the effect of pharmacist assist psychiatry clinic, in the observation statistically significance difference were observed in physical health and psychological health domain ($p<0.001$). Ghazavi Z *et al*[21] conducted a pilot study to compare the effect of psycho-education on quality of life of the patients, there statistically significant difference were observed in the (mean) quality of life of both study group ($p=0.04$) and control group ($p=0.09$). As per the observation of the our study the (mean) quality of life in the interventional group was found $p<0.001$ (Table 3). So, we can concluded that pharmaceutical care-based collaborative approach can enhance the patients' quality of life.

We had taken different measures to improve the quality of our study. Firstly, we included the qualified and trained clinical pharmacist during the study, so that we could provide better education and care to the patients. Secondly, we prepared the selective exclusion criteria for the targeted patient population to get the good accuracy of the study result. Thirdly, we prepared a proper plan for the interventional group patients' population, in which, medication-related education, psycho-education and lifestyle related education were provided along with the structured patient information leaflet and booklets in a local vernacular language like Kannada, Marathi, Hindi and English. Fourthly, we used randomization process so that we could assessed better result for the effect of provided care.[8] Finally, during the follow-up of the study, we were in telephonic contact with the patient so that we could control the attrition rate of the study. Besides these positive points, our study had some limitations. The first limitation of the study was patient biased, which as passed by the patients. Many patients during the manic phase self-report the high quality of life whereas during the depressive phase poor and during euphoric phase shows the normal quality of life.[22]certainly, this kind of bias may change during the cyclic phase of bipolar disorder and mood swing of the patients. The second limitation of the study was to control the attrition rate of the patients due to the patients' psychological condition. Most of the patients left the study without showing any cause. The voluntary withdrawal of the patients may affect the result of study and the third limitation of the study was to control the exposure of patient with other participants during the follow-up, which might alter the result too. Fourthly, we did not assess the symptom improvements of the patients.

Such type of limitation is possible during the study, but most of the patient done follow-up and participate properly in the study. This type of study required for the multicentre level with a high number of patient sample, to show the better effect of care which has provided by the clinical pharmacist as a part of collaborative care team.

CONCLUSION

conducted study shows that, clinical pharmacist lead collaborative care can enhance the patients' quality of life in compared to usual care, which is showing that, the participation of clinical pharmacist in psychiatry settings may lead to integration in health care delivery systems.

ACKNOWLEDGEMENT

I heartily thanks to Department of Psychiatry, Jawaharlal Nehru Medical College, Belagavi, Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi, Karnataka for their great support.

CONFLICT OF INTEREST

There are no conflict of interest .

ABBREVIATION USED

QOL: Quality of life; **BMI:** Body mass index; **BPAD:** Bipolar affective disorder; **WHO:** World health organization.

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SUMMARY

- The authors in this study assessed the effect of pharmaceutical care in the quality of life of the patients with Bipolar disorder between the control group and interventional group. the result of the study indicated that, effective pharmaceutical care can improve the patients quality of life.

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Clinical pharmacist assessment in monitoring and resolving the adverse drug reaction in bipolar disorder patients: A prospective, observational study at tertiary care teaching hospital

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Abstract:

BACKGROUND: Adverse drug reaction (ADR) is a noxious, unintended effect of the drug which may occur due to pharmacotherapy of the disease. Bipolar disorder is a chronic mental illness represented by mania, depression and cyclic episode. The treatment of Bipolar disorder is lifelong. Hence, there are increased chances of ADRs.

METHODOLOGY: An observational, prospective study was performed on 286 patients, to identify, monitor, and resolve the ADR with bipolar disorder patients. The patients aged 18–65 years of either gender or diagnosed with bipolar disorder were enrolled in the study. Patient-related data had been collected from the patient record; probability of ADR was measured by Naranjo scale and severity by Hartwig scale. Descriptive statistics had been used for study data interpretation.

RESULTS: A total of 286 patients were enrolled in the study, of which 27 patients suspected with ADR. Among all the ADR, nonallergic side effect suffered ADR were 88.1%. Of which, the most common ADR were hand tremor and hypothyroidism, which were associated with lithium (81.4%) followed by valproate (11.1%). On causality assessment, 44.4% cases were probable and possible. In most cases, severity of ADR was founded at Level III with 74.7% and Level II with 25.9%. The rate of acceptance of pharmacist intervention by a psychiatrist has been found to be 74.7%. The major cause of ADR was a drug/dose selection (74.07%).

CONCLUSION: ADRs occur most frequently in bipolar disorder. The incidence of drug-related noxious effect can be minimized by the prior identification, monitoring, and reporting. Thus, the clinical pharmacist can play a key role in pharmacovigilance of ADR.

Keywords:

Adverse drug reaction, adverse event, bipolar disorder, drug-related problem, pharmacist intervention

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Introduction

Drug is the active chemical entity which is present in the dosage form for the pharmacotherapy of the patients. The drug response variability from person to person is the major problem of the pharmacological treatment in clinical practice; it can be a therapeutic failure or adverse drug reaction (ADR) in individual or in clusters.[1,2] ADR is the leading cause of morbidity and mortality. The worldwide approximately 5% adult and 3% pediatric hospital admissions are the result of ADR.[3] In India, around 5%–20% patients experience ADR as a result, of which 10% hospital admissions occur every year.[4]

As per the World Health Organization, ADR is "Any response of drug which is noxious

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and unintended and which occurs at dose normally used in human for prophylaxis, diagnosis, or therapy of disease or for the modification of physiological function."[5,6] The monitoring of ADR has been done under the pharmacovigilance program in India (PVPI) runs under the Central Drugs Standard Control Organization.[7] PV is the pharmacological science related to collection, detection, assessment, monitoring, and prevention of ADR and drug-related problems (DRPs).[8] PV is still in infancy and ADR reporting system is below 1% in India against the world rate of 5%.[9]

Bipolar disorder is a severe, recurrent, and chronic mental suffering, which may represent by the mood swings such as dysthymia, depression, euphoria, cyclothymia, and mania at different time of interval in the same patient with significant functional and cognitive impairment.[10] Pharmacotherapy for bipolar disorder is frequently associated with ADR because of its lifelong treatment which impairs the patient quality of life.[11] Hence, multidisciplinary collaboration of health-care professionals such as a clinical pharmacist, psychiatrist, and nurse is needed to optimize the patients' pharmacotherapy for the safety of patients from ADR.

In the present study, efforts were made to encourage the pharmacovigilance program in India. The aim of our study is to monitor, identified, and resolve the ADR associated with patients with bipolar disorder through clinical pharmacist lead collaborative approach.

Methodology

Ethics approval

The study was reviewed and approved by the Institutional Ethics Committee (IEC) (KLEU/Ethics/2015–16/D-93); the study-related documents include protocol, patient data collection form, patient information sheet, informed consent form, and patient information leaflets which were prepared in local language (Kannada, Marathi, and Hindi) and submitted and presented to ethics committee before the study presentation in front of the ethics committee. The study protocol and procedure were explained orally.

Study design and patient recruitment

The study was conducted in 2400-bedded tertiary care hospital at the Department of Psychiatry over a period of 1 year from March 2015 to March 2016 after obtaining the IEC approval. It was prospective, observational study with 286 enrolled patients, those were fulfilled the study criteria like aged between 18 and 65 years of either gender and diagnosed with the bipolar disorder as per the Diagnostic and Statistical Manual of Mental Disorders (DSM-V). Patient with other comorbid psychiatry problem, lactating mothers, and pregnant women were excluded from the study.

Study protocol

Patients those fulfilled the above-cited criteria were enrolled in the study. Enrolled patients were followed for 1-year duration, in which the four observations have been proposed (each observation gap was 3 months). Initially, the patient's demographic data, the chief complaint, past medical and medication history, and a current treatment plan with a drug information were collected at the baseline from the patient records. During the study period, the ADR has been identified and resolved through clinical discussion with the psychiatrist here clinical pharmacist assessed the ADR and reported it to the psychiatrist, the necessary correction has been made by psychiatrists, and ADRs were reported by a clinical pharmacist to PVPI. The type of ADR, clinical suggestions, causes, and outcome of ADR have been collected in the ADR documentation form and pharmacist intervention form.

Causality assessment

Probability of ADR has been assessed by a Naranjo Probability Assessment Scale which relates the list of questionnaires, which consist information of drug administration and event occurrence, alternative causes for the event, drug levels, dose–response relationships, and previous patient experience with the medication.[12]

Severity assessment

The severity of ADR has been assessed by Hartwig's Severity Assessment Scale which is a list of questionnaires related to ADE. Hartwig's scale consists of seven different levels. Among them, Level 1 represents the mild severity of ADR and Level 7 represents the chronic severity of ADR. This scale consists information of suspected drugs, dose, dose change, length of hospital stay, alternative treatment, intensive medical care, and the patient's condition.[13]

Pharmaceutical care network Europe classification

DRPs have been monitored, identified, assessed, and analyzed on a daily basis as per the Pharmaceutical Care Network Europe (PCNE) classification of the drug-related problem's version 5.01. This classification is used to assess the nature, prevalence, incidence of DRPs, and also acts as an indicator of pharmaceutical care outcome.[14]

Statistical analysis and sample size

The data of the study have been segregated and analyzed with the help of IBM SPSS Statistics 20 (IBM Corporation, United State). Presentation of results such as demographic data and severity of ADR, causality

assessment, and outcome assessment was done using descriptive statistics. The sample size of the study was decided with the help of patient flow at the Department of Psychiatry and journal of the previous study.

Results and Discussion

The study was conducted at the Department of Psychiatry of Tertiary Care Hospital. A total of 286 patients were included in the study after taking their and legally acceptable representative a signed consent. It was observed that the male (61.2%) was more prevalent than female (38.8%), aged less than 30 years enrolled in the study. As per collected data, maximum patients were married (75.9%). Among the patients, approximately 86.7% did not have any family history and approximately 90% patients did not have childhood adversity. The patient-related demographic data have been mentioned below [Table 1].

All the selected patients were receiving their treatment as per the DSM-V, of which patients received valproate 9.7% (n = 43), lithium 50% (n = 223), sertraline 0.9% (n = 04), chlorpromazine 1.3% (n = 06), aripiprazole 2.0% (n = 09), olanzapine 20.7% (n = 92), quetiapine 13.0% (n = 58), trifluoperazine 9.2% (n = 41), trihexyphenidyl 10.8% (n = 48), haloperidol 3.6% (n = 16), divalproex 2.9% (n = 13), risperidone 4.2% (n = 19), lorazepam 15.5% (n = 69), and alprazolam 0.4% (n = 02).

Suspected drug for adverse drug reaction

Majority of ADR had been associated with lithium 22 (81.4%) (Lithosun and Lithosun SR, Sun Pharmaceutical Industries Ltd.,) of which 13 patients suffered from hand tremor, 6 with hypothyroidism, 2 with facial muscle twitching, and 1with dry mouth. After the lithium, most of the patients reacted with valproate (Torvate, Torrent Pharmaceuticals Ltd.,)-induced ADR followed by trifluoperazine (Benzyzine, La Pharmaceuticals) and alprazolam (Alprax Torrent Pharmaceuticals Ltd.,). The detail of ADR has been summarized in Table 2 and Figure 1.

Causality and severity assessment

The ADR selection and classification have been done as per the PCNE classification, of which 88.81% (n = 24) were nonallergic side effect suffered and 11.19% (n = 03) were allergic side effect suffered. The probability or causality had been assessed by the Naranjo Probability Assessment Scale in four categories, of which 3.70% (n = 1) were doubtful, 44.4% (n = 12) were possible, 44.4% (n = 12) were probable, and 7.40% (n = 2) were definite. The severity has been assessed by Hartwig's Severity Assessment Scale, and the majority of severity were found at level III 74.07% (n = 20) followed by level II 25.92% (n = 7). The detail of Causality and severity assessment has been summarized in Table 3.

Table 1: Demographic data of the patients

Category	Frequency, *n* (%)
Sex	
Male	175 (61.2)
Female	111 (38.8)
Age (years)	
Under 30	87 (30.4)
30-39	78 (27.3)
40-49	71 (24.8)
50-65	50 (17.5)
Religion	
Hindu	266 (93.0)
Muslim	19 (6.6)
Christian	1 (0.3)
Marital status	
Single	67 (23.4)
Married	217 (75.9)
Divorcee	1 (0.3)
Widow	1 (0.3)
Occupation	
Government	8 (2.8)
Private	61 (21.3)
Daily basis	4 (1.4)
Homemaker	86 (30.1)
Student	44 (15.4)
Unemployed	11 (3.8)
Farmer	66 (23.1)
Retired	6 (2.1)
Family history	
Nothing significant	248 (86.7)
Paternal	29 (10.1)
Maternal	9 (3.1)
Childhood adversity	
Neglect	23 (8.0)
Physical health	2 (0.7)
Sexual abuse	1 (0.3)
Loss of parents	2 (0.7)
Absent	258 (90.2)
Smoking habit	
Yes	77 (26.9)
No	209 (73.1)
Alcoholic	
Yes	52 (18.2)
No	234 (81.8)
BMI	
Underweight	16 (5.6)
Normal weight	176 (61.5)
Over weight	63 (22.0)
Obese	31 (10.8)
Other comorbidity	
Nil	251 (87.8)
Hypothyroidism	16 (5.6)
Hypertension	6 (2.1)
CVS disease	1 (0.3)
Diabetes mellitus	9 (3.1)
Respiratory disease	3 (1.0)

BMI: Body mass index, CVS: Cardio vascular system

Table 2: Suspected drug for adverse drug reaction

Drug	ADR	Number of patients with AE's, *n* (%)
Lithium (Lithosun SR, Sun Pharmaceutical Industries Ltd.)	Hypothyroidism	6
	Hand tremor	13
	Muscle twitching	2
	Dry mouth	1
Total		22 (81.4)
Valproate (Torvate, Torrent Pharmaceuticals Ltd.)	Hand tremor	2
	Thrombocytopenia	1
Total		3 (11.1)
Trifluoperazine (Benzyzine, La Pharmaceuticals)	Bradykinesia	1 (3.7)
Alprazolam (Alprax, Torrent Pharmaceuticals Ltd.)	Impaired co-ordination	1 (3.7)

AEs: Adverse events, ADR: Adverse drug reaction

Table 3: Causality and severity assessment

Variables	ADR		Total (%)
	Side effect suffered (nonallergic)	Toxic effects suffered	
Naranjo ADR probability scale groups			
Doubtful	0	1	1 (3.70)
Possible	10	2	12 (44.4)
Probable	12	0	12 (44.4)
Definite	2	0	2 (7.40)
Total	24	3	27
Hartwig's severity assessment scale			
Level 2	4	3	7 (25.92)
Level 3	20	0	20 (74.07)
Total	24	3	27

ADR: Adverse drug reaction

Management and outcome aspect of adverse drug reaction

Intervention has been proposed at prescriber, patient, and drug level, In which at prescriber level, 77.7% of interventions which were proposed by clinical pharmacist, which, has been approved by the psychiatrist. At patient level, patient counseling and their family member counseling had been done by clinical pharmacist, and at drug level, new drug had been started 70.3% by a psychiatrist to patient those suffered with ADRs. As the outcome of pharmacist intervention, 51.8% problems were completely solved and 48.1% problems were partially solved. The proposed intervention is mentioned in Table 4.

Monitoring of ADR in a psychiatric setting holds a special place of importance due to the less likely reporting of ADR. There is a need to robust the spontaneous ADR reporting system to improve the pharmacovigilance system in India. For the same, Shah *et al*. conducted

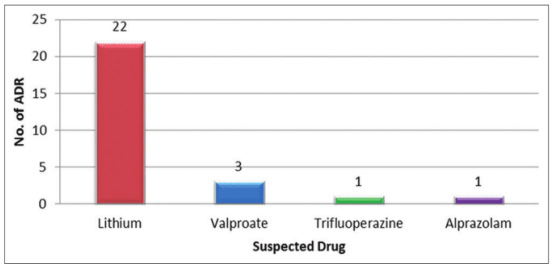

Figure 1: Suspected drug for adverse drug reaction

a prospective study of ADR in patients with bipolar disorder. In this study, 180 patients were enrolled, of which 97.22% patients suffered from ADR which were as follows: asthenia (11.95%), sedation (10.24%), polyuria/polydipsia (10.10%), weight gain (9.25%), and hand tremors were most common assessed ADRs those were associated with lithium, valproate, olanzapine, and clozapine. In this study, the author assessed that the majority of ADRs were probable (56.33%), of which most of were not preventable (64.3%). They concluded that proper reporting of ADRs can help to minimize the drug-induced side effect.[15] A similar study has been conducted by Harichandran *et al.* to assess 53 ADRs on 31 patients of the psychiatry department. The psychotropic drugs such as olanzapine, risperidone, and clozapine were the major suspected drugs for the ADR. The author assessed that most of ADR were dose-dependent and predictable.[16] Khoda *et al.* have monitored and reported the adverse events (AEs) of 32 psychiatric patients, of which they have found a 79.31% incidence in AEs among the psychiatric population. As per the results, the author concluded that effective monitoring by a clinical pharmacist can help to minimize the incidence of AEs[17] and Ujwala *et al*. monitored and reported 92 ADRs of patients with psychiatric conditions, of which overall incidence rate of ADRs was 6.41%. Among all the patients, most common ADRs were tremor (13.04%), somnolence (11.95%), and constipation (9.7%). A majority of ADRs was associated with antipsychotic (46%), an antidepressant (29%), and antiepileptic drugs (12%), of which most of cases were probable and 80.4% were mild.[18]

The conclusion of these all previous studies gives us insight that proper spontaneous reporting of ADR by a clinical pharmacist, psychiatrist, patients, and other health-care professionals can enhance the pharmacovigilance program. For the same, in our study, first, we tried to assess the causes of ADR, which we did not find in other studies. The causes of ADR had been assessed through the help of PCNE classification. We observed that the majority of ADR were caused due to drug/dose selection 74.07% ($n = 20$) and drug use process 25.92% ($n = 7$). Under the primary cause of drug/dose selection, 8.33% ($n = 2$) ADRs were occurring due to pharmacokinetics problem,

Table 4: Management and outcome aspect of adverse drug reaction

Intervention	ADR		Total
	Side effect suffered (nonallergic)	Toxic effects suffered	
At prescriber level			
Prescriber informed only	1	1	2
Prescriber asked for information	3	1	4
Intervention proposed, approved by prescriber	19	2	21
Total	23	4	27
At patient/care level			
Patient (medication) counseling	18	1	19
Written information provided only	3	1	4
Patient referred to the prescriber	1	1	2
Spoken to family member/caregiver	1	1	2
Total	23	4	27
At drug level			
Dosage changed to	4	1	5
Drug stopped	1	2	3
New drug started	18	1	19
Total	23	4	27

ADR: Adverse drug reaction

12.5% (n = 3) due to the requirement of synergistic and preventive drug, 33.3% (n = 8) ADRs occurred due to new symptom revealed, and 45.83% (n = 11) ADRs were occurring due to the manifested side effect of the drug. Under the secondary cause of ADRs drug use process, the most common problem was the unmonitored therapeutic drug level. For the assessed problem, clinical pharmacist proposed the intervention, the causes and problems were resolved with the help of a psychiatrist. Second, we were on the telephonic contact with the patients during follow-up as well as clinical pharmacists reinforced the medication-related knowledge for their better care or quality of life.

As in our study, we also have many limitations, first, this is the unicentric study with a small sample size so we could not represent the incidence of ADR in the region. Second, due to mental stigma, it was difficult to control the attrition rate and follow-up of the patient. Third, many patients belonged to the poor socioeconomic background because of the same they were not able to check the therapeutic level of drugs and laboratory investigation report of the patients.

Conclusion

The study suggested that clinical pharmacist intervention with the collaboration of psychiatrist and other health-care professionals can help minimize the burden of ADRs and its related problem in patients with bipolar disorder. The clinical pharmacist intervention is very important to maximize the drug-related safety and minimize the drug-related noxious effect, which ultimately promotes the patients' quality of life.

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Conflicts of interest

There are no conflicts of interest.

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CLINICAL PHARMACIST ASSESSMENT OF MONITORING AND RESOLVING THE DRUG-RELATED PROBLEMS IN BIPOLAR DISORDER PATIENTS: A PROSPECTIVE, OBSERVATIONAL STUDY AT TERTIARY CARE TEACHING HOSPITAL

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ABSTRACT: Background: Bipolar disorder is a chronic mental illness due to a different interval of manic and depressive phase, the patient may become more prone to DRP, which interfere with the patients' health outcome. Hence, clinical pharmacist can contribute to managing the DRP through proper pharmaceutical care intervention. **Method/Design:** A prospective, observational study had been done with 286 participants to assess, monitor, and resolve the DRP through Clinical Pharmacist intervention. Patients with Bipolar disorder, aged 18 to 65, included in the study except for the patient with other comorbid condition, lactating mothers, and pregnant women. **Results:** DRP in between, all the patients were observed, of which 70.9 % were drug-drug interaction followed by 29.1% ADR. The two major causes of DRP were at drug/dose selection level 95.5%, followed by a drug use process level 4.5%. Pharmacist intervention has been proposed at prescriber level, of which majority of interventions 52.7% had been accepted by the prescriber. **Conclusion:** In our study, the majority of DRP 64.7%, had been resolved due to the clinical pharmacist intervention, which shows that participation of clinical pharmacist in psychiatric setting may help to resolve the DRP and integrate the health care delivery system.

INTRODUCTION: The drug-related problems (DRPs) are the major public health concern because of its consequence on morbidity, mortality, and burden on the patient's pocket [1]. As per PCNE and SFPC classification, DRP is the event or circumstances involving drug therapy that actually or potentially interfere with the desired therapeutic outcome [2, 3].

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There are several studies reported the incidence of DRP is approximately 1.7% to 25.1% of which only 5% of studies had been reported hospital admission [4]. As per the Pharmacy Today report, the DRPs are raising the cost of healthcare expenditure around $177.4 Billion. They estimated that 40% of the cost and 120,000 deaths due to DRP could be preventable through clinical pharmacist effort to assure the proper pharmacological treatment [5].

Almost all the psychiatry diseases or disorders have a temporary cure and long-term pharmacological treatment. Due to their psychiatry condition and long-term treatment, psychiatry patient's population are most susceptible to the DRP [6]. As Bipolar disorder is a severe mental as well as a life-

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long long co-morbid disorder, which is responsible for premature mortality from suicide [7]. Which implies the patients quality of life through mood swings, personal suffering. Uneven sociological behavior and distinguished family relationship [8]. In India, there is 200 bipolar disorder sufferer per 100,000 population [9]. Indeed, bipolar disorder is a severe chronic mental illness which is represented by the mood swing, dysthymia, depression, cyclothymia, euphoria, and mania at a different time interval [10].

Lack of follow-up and reassessment of therapeutic outcome may also contribute toraising the number of DRPs. Clinical pharmacist assists care with other health professional offers to improve health outcome [11]. DRP is a challenge for the healthcare professionals because of its health-related burden on patients, especially psychiatry population like bipolar disorder patient. As a patient with bipolar disorder may undergo through the various phases of mania and depression, in such condition, there are more chances of a drug-related problem.

Aim of the Study: To Identified, Resolve and Report and percentage of DRP of the patient with bipolar disorder (as per DSM-V) at tertiary care hospital.

Ethics Approval: The study was reviewed and approved by the institutional ethics committee (KLEU/Ethics/2015-16/D-93) the study related documents, including study Protocol, Patent data collection form, patient information sheet (PIS), informed consent form (ICF) and patient information leaflets (PIL's) which were prepared in local language (Kannada, Marathi and Hindi) and submitted prior to study presentation. The study protocol and procedure were explained orally to the IEC.

Method:

Study Design and Patient Recruitment: The study was initiated in 2,400 bedded tertiary care teaching hospitals at the Department of Psychiatry. It was prospective, observational study with 286 enrolled patients out of 314 patients, those were fulfilled the study inclusion criteria like aged between 18 to 65 years of either gender and diagnosed with the bipolar disorder as per DSM- V. Patient with other comorbid psychiatry problem, lactating mothers and pregnant women were excluded out from the study.

Study Protocol: Patient those were fulfilled; the above-cited criteria were admitted. In the study, patient demographic data, the chief complaint, past medical and medication history, a current treatment plan with a subscription, inscription, and signature were collected at the time of enrollment. The drug-related problems (DRP's) have been identified through clinical discussion with the psychiatrist.

The type of DRP's, Brief description of DRP's, clinical suggestions, causes, and outcome of DRP's has been collected in the data collection form and pharmacist intervention form.

PCNE Classification: DRP's has been monitored, identified, assessed, and analyzed daily as per the PCNE classification of the drug related problem's version 5.01. This classification is used to assess the nature, prevalence; the incidence of DRP's and also acts as an indicator of pharmaceutical care outcome. As per this classification, DRP's are classified into six major categories [2].

1. **Adverse Reaction (P1):** the Patients those who are suffering or are going to suffer from an adverse drug event such as an ADR or toxicity. This problem might occur due to prescribing error. The ADRs may also immerge at fixed dosages of the appropriate drug. It consists of three major problems; P1.1 Side effect suffered (Non-allergic), P1.2 Side effect suffered (Allergic), and P1.3 Toxic effect suffered.

2. **Drug Choice Problem (P2):** under this domain Patients comes those are getting or are going to get a wrong drug for their disease condition. This may occur due to a prescribing error. It's covered six major problems; P2.1 Inappropriate drug (not most appropriate for indication), P2.2 Inappropriate drug form (not most appropriate for indication), P2.3 Inappropriate duplication of therapeutic group or active ingredient, P2.4 Contra-indication for drug (include Pregnancy/breastfeeding), P2.5 No clear indication for drug use and P2.6 No drug prescribed but clear indication.

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3. **Dosing Problem (P3):** Patient may get a low or high dose of a drug which is not meet with their therapy requires. It can be due to prescribing error or drug use error. This is classified in four categories; P3.1 Drug dose too low or dosage regime not frequent enough, P3.2 Drug dose too high or dosage regime too frequent, P3.3 Duration of treatment too short and P3.4 Duration of treatment too long.

4. **Drug Use Problem (P4):** Under this domain, willingly or unwillingly Patient uses to take a wrong drug or no drug. Such a problem may occur because of drug use or administration errors and filling error in the pharmacy. It consists; P4.1 Drug not taken/administered at all and P4.2 Wrong drug took/administered.

5. **Interactions (P5):** Under this domain, mild, moderate, and major drug-drug or drug-food interaction covered. This may occur because of prescribing or drug use error. Under this P5.1 Potential interaction and P5.2 Manifested interaction comes.

6. **Others (P6):** Problems like P6.1 Patient dissatisfied with therapy despite taking the drug(s) correctly, P6.2 Insufficient awareness of health and diseases (possibly leading to future problems), P6.3 Unclear complaints. Further, clarification necessary and P6.4 Therapy failure (reason unknown) falls under this domain.

The causes of DRP's, intervention and outcome of intervention have been assessed with the help of PCNE V.05.1 classification.

For the suspected DRP's proper interventions are made by the clinical pharmacist. The proposed interventions were provided at Prescriber level (I1), Patient/care level (I2) and Drug level (I3)

1. **At Prescriber Level (I1):** Intervention proposed through the prescriber, under this some of the intervention include Prescriber informed only (I1.1), Prescriber asked for information (I1.2), Intervention proposed, approved by Prescriber (I1.3), Intervention proposed, not approved by Prescriber (I1.4) and Intervention proposed, outcome unknown (I1.5).

2. **At Patient / Care Level (I2):** Intervention at patient level mainly focus on the patient-related issue, and it proposed to the patients, these are Patient counseling (medication) (I2.1), Written information provided only (I2.2), Patient referred to prescriber (I2.3) and Spoken to family member/LAR (I2.4).

3. **At Drug level (I3):** The Intervention directly by altering/substituting the drug or frequency change in the use of the drug. Under this domain proposed intervention was drug change (I3.1), dosage change (I3.2), substitute drug (I3.3), instruction for use (I3.4), drug withdraw (I3.5) and new drug start (I3.6).

During the treatment period, patient data like current medication, altered dose or medication, lab investigation value, and ECG report was collected daily, latter collected data was segregated and analyzed with the help of IBM SPSS V.20.

Causality Assessment: The probability of DRP's was being assessed by Naranjo adverse drug reaction probability scale that is an adverse event (AE) related list of questionnaires, which consist information of drug administration and event occurrence, alternative causes for the event, drug levels, dose-response relationships and previous patient experience with the medication [12].

Statistical Analysis: The sample size of the conducted study was calculated with the help of the prevalence of DRP in previous studies. The probability value (p) was considered p 0.05 as a significant value with the 95% confidence interval (CI). The collected data were analyzed with the help of IBM-SPSS Version 20 software.

RESULTS: The study was conducted at the Department of Psychiatry of tertiary care hospital. Total 314 patients were screened out of which 286 patients were included in the study after their and family member writing signed consent.

The patient related demographic data are mentioned below **Table 1**.

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TABLE 1: DEMOGRAPHIC DATA OF THE PATIENTS

Category		Frequency	Percent %
Sex	Male	175	61.2
	Female	111	38.8
Age	Under 30	87	30.4
	30 To 39	78	27.3
	40 To 49	71	24.8
	50 To 65	50	17.5
Religion	Hindu	266	93.0
	Muslim	19	6.6
	Christian	1	0.3
Marital Status	Single	67	23.4
	Married	217	75.9
	Divorcee	1	0.3
	Widow	1	0.3
Occupation	Government	8	2.8
	Private	61	21.3
	Daily Basis	4	1.4
	Homemaker	86	30.1
	Student	44	15.4
	Unemployed	11	3.8
	Farmer	66	23.1
	Retired	6	2.1
Family History	Nothing Significant	248	86.7
	Paternal	29	10.1
	Maternal	9	3.1
Childhood Adversity	Neglect	23	8.0
	Physical Health	2	0.7
	Sexual Abuse	1	0.3
	Loss Of Parents	2	0.7
	Absent	258	90.2
Smoking Habit	Yes	77	26.9
	No	209	73.1
Alcoholic	Yes	52	18.2
	No	234	81.8
BMI	Under Weight	16	5.6
	Normal Weight	176	61.5
	Over Weight	63	22.0
	Obese	31	10.8
Other Comorbidity	Nil	251	87.8
	Hypothyroidism	16	5.6
	Hypertension	6	2.1
	CVS Disease	1	0.3
	Diabetes mellitus	9	3.1
	Respiratory Disease	3	1.0

TABLE 2: ADVERSE DRUG REACTIONS (ADR)

Drug	ADR	No. of AE's
Lithium	Hypothyroidism	06
	Hand Tremor	13
	Muscle Twitching	02
	Dry mouth	01
Valproate	Hand Tremor	02
	Thrombocytopenia	01
Trifluoperazine	Bradykinesia	01
Alprazolam	Impaired coordination	01

All the selected patients were receiving their treatment as per DSM-V, of which 9.7% (43) Valproate; 50% (223) Lithium; 0.9% (04) Sertraline; 1.3% (06) Chlorpromazine; 2.0% (09) Aripiprazole; 20.7% (92) Olanzapine; 13.0% (58) Quetiapine; 9.2% (41) Trifluoperazine; 10.8% (48) Trihexyphenidyl; 3.6% (16) Haloperidol; 2.9% (13) Divalproex; 4.2% (19) Respiridon; 15.5% (69) Lorazepam and 0.4% (02) were with Alprazolam.

DRP's had been assessed through PCNE classification. In our study, among the DRP's, we had found 29.1% (27) ADR and 70.9% (66) Drug-Drug Interaction. Of which, 88.8% (24) ADR were reported non-allergic side effects suffered and

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11.1% (03) ADR were reported allergic side effect suffered. Whereas, among all drug-drug interactions, minor drug interactions were reported 22.7%; significant drug interaction 87.8% (58) and serious drug interaction 4.5% (3). Drug-related ADR and Interactions have been mentioned in below cited **Table 2** and **Table 3**.

TABLE 3: DRUG-DRUG INTERACTIONS

Drug-Drug interaction		Causality		No. of AE's
		Probable	Suspected	
Minor drug interaction	Haloperidol + chlorpromazine	0	1	1
	Sertraline + lithium	1	2	3
	Sertraline + chlorpromazine	1	0	1
	Total	2	3	5
significant drug interaction	Trihexphenedyl + trifluoperazine	3	1	4
	Lorazepam + trifluoperazine	3	6	9
	Lorazepam + haloperidol	1	3	4
	Lorazepam + quetiapine	1	3	4
	Lorazepam + aripiprazol	0	1	1
	Trihexphenedyl + chlorpromazine	2	0	2
	Lorazepam + olanzapine	7	7	14
	Haloperidol + quetiapine	0	1	1
	Haloperidol + olanzwpine	1	0	1
	Lithium + trifluoperazine	4	5	9
	Lithium + haloperidol	1	0	1
	Quetiapine + trihexyphenidyl	1	1	2
	Sertraline + lithium	1	0	1
	Aripiprazole + quetiapine	1	0	1
	Olanzapine + trifluoperazine	1	0	1
	Olanzapine + quetiapine	2	1	3
	Total	29	29	58
serious drug interaction	Trifluoperazine + chlorpromazine	1	2	3
	Total	1	2	3

DISCUSSION: Globally, there are 140,000 hospitalizations due to DRP's every year. It indicates the problem in current medical practices and service delivery system, which leads the drug-related morbidity and mortality [13]. In this contest for assessment of DRP's, Dahal P *et al*., have assessed the clinical pharmacist intervention in 49 patients with DRP's, of which most were related to inappropriate drug dosing problem (25.3%) followed by drug selection (23.9%). As per the result of their study, an acceptance rate of the proposed intervention was 70.5%. As per their conclusion, clinical pharmacist interventions are helpful to monitor, resolve, and prevent the DRP's [14]. In the same type of study, Vijayalakshmi *et al*., has been found 598 DRP's, of which 55.5% due to drug interactions and 12.7% drug choice problem. The intervention has been proposed by them at prescriber and drug administration level with an 88.5 % acceptance rate [15]. Khoda DA *et al*. has monitored and reported the AE's of 32 psychiatric patients. Of which they have found a 79.31% incidence in AE's among the psychiatric population. As per result, the author concluded that effective monitoring by a clinical pharmacist could help to minimize the incidence of AE's [16].

In our study, cause of DRP had to be found at Drug/Dose selection level 95.5% (85) and Drug use process level 4.4% (4). The majority of DRP cases were at the drug/dose selection level in which 74.1% (63) due to pharmacokinetics problems with the drug, including aging/deterioration in organ function and interactions, 3.5% (3) due to Synergistic/preventive drug required, but not given, 9.4% (8) due to the new symptom or indication revealed/presented and 12.9% (11) due to manifest side effect. Rest of cases were at a drug use process level in which 4 cases were associated with un-monitored therapeutic drug level. As per the assessed causes, we framed our intervention for the patients. The intervention has been proposed at the prescribed level. Total 91 interventions have been proposed, out of which a large number of intervention, *i.e.,* 72.5% (66) has been accepted and 27.4% (25) were not accepted by the prescriber. The number of proposed intervention has been cited in **Table 4**.

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TABLE 4: PHARMACIST INTERVENTIONS

Pharmacist intervention		No. of proposed intervention
At prescriber level	Prescriber informed only	3 (3.2%)
	Prescriber asked for information	8 (8.7%)
	The intervention proposed, approved by Prescriber	48 (52.7%)
	The intervention proposed, not approved by Prescriber	25 (27.4%)
	The intervention proposed outcome unknown	7 (7.6 %)

The outcome of the intervention has been assessed of which, 35.2% (31) were not known, 28.4% (25) were solved, 36.3% (32) were partially solved, and 1.1% (1) was not solved.

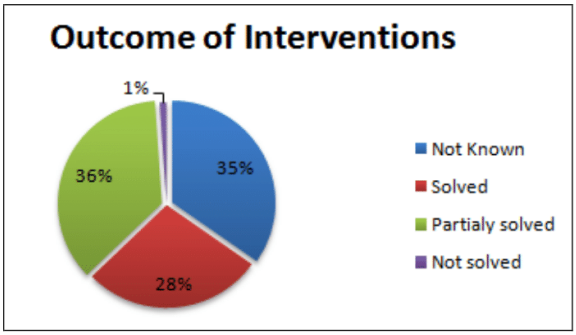

FIG. 1: OUTCOME OF THE PROPOSED PHARMACIST INTERVENTION

For good quality of data, we used PCNE classification for the drug-related problem (V5.01). In the same, we participated in ward round daily basis as well as, we were in contact with the patients during the study period so that we could provide better quality care to the patients. As we also had some limitation during the study of which patient-related barrier was more common. As most of the bipolar affective patients may fall into mania or depression at that time, there may be chances of subjective as well as information related bias. Another challenge was to make them adhere to the medication, as bipolar is a mood disorder so it was difficult to make them agree to adhere to their medication plan. The majority of suggestions has been accepted by the prescriber which helped to resolve the patient's DRP and enhancement of their quality of life.

CONCLUSION: The study result has given us the insight that clinical pharmacist lead a collaborative approach with the Psychiatrist and other health care professionals can help to minimize the DRP's associated with the patient's pharmacotherapy. The result shows that clinical pharmacist intervention is very important in maximizing the beneficiary effect & minimizing the side effect or DRP which ultimately promotes the better quality of life.

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CONFLICT OF INTEREST: There are no conflicts of interest.

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Annexure-XVII: Certificates of Oral & Poster Presentations

National Institute of Mental Health & Neuro Sciences, Bengaluru

MHECON2018

First National Conference on Mental Health Education

April 6th - 7th 2018

Supported by: Indian Council of Social Science Research (ICSSR)

&

Dr. Ramachandra N. Moorthy Foundation

Certificate of Presentation

This certificate is being awarded to Mr. Ashish Singh Parihar *acknowledging the presentation in the session* Poster Presentation *for work titled* A Randomized Prospective study on QOL of Bipolar Affective Disorder Patients *in MHECON2018, First National Conference on Mental Health Education conducted by the Department of Mental Health Education, NIMHANS, 6th - 7th April 2018, Bengaluru.*

Patron
Dr. B. N. Gangadhar
Director & Vice Chancellor
Senior Professor of Psychiatry
NIMHANS

Advisor and Organizing Chairperson
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Dean Behavioural Sciences
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Scientific committee
Dr. Sharmitha Krishnamurthy
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ISPOR India Telangana Chapter

CERTIFICATE FOR BEST PRESENTATION

This is to certify that Mr/Mrs/Ms/Dr. Ashish Singh Parihar

presented the best oral/Poster entitled " Effect of Pharmaceutical Care on medication adherence of Bipolar disorder Patients.

in the Two-day

"International Conference on the use of National Medicines Policy and Biostatistics in Pharmaceutical Sciences",

held on 28th & 29th September 2016.

2nd PLACE

Organized by

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Sri Ch. Sathi Reddy	Mr. Ch. Aditya Reddy	Dr. V. Rama Mohan Gupta	Mr. Subhas Sahoo
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Certificate

THIS IS TO CERTIFY THAT

Dr/Mr/Miss/Mrs. / ASHISH SINGH PARIHAR has participated

as ~~Delegate~~/~~Resource person~~/Presented poster in

I[st] NATIONAL PHARM.D COLLOQUIUM (NPC-2019) organized by Dept. Of pharmacy Practice,

KLE College of Pharmacy, Belagavi on 8[th] & 9[th] March 2019.

Prof. (Dr). M.S. Ganachari
Convener

Prof. (Dr). B.M. Patil
Principal