"HEALTH RELATED QUALITY OF LIFE IN STABLE COPD PATIENTS: A HOSPITAL BASED CROSS SECTIONAL STUDY"

By

REG NO. BR0117002

Dissertation

Submitted to the
KAHER, Belagavi, Karnataka
In partial fulfillment
of the requirements for the degree of

M.D in

RESPIRATORY MEDICINE

DEPARTMENT OF RESPIRATORY MEDICINE,

J. N. MEDICAL COLLEGE,

BELAGAVI- 590010. KARNATAKA

APRIL-2020

KLE ACADEMY OF HIGHER EDUCATION AND RESEARCH, BELAGAVI, KARNATAKA

Endorsement by Head of the Department, Principal/ Head of the Institution

This is to certify that the thesis **"Health Related Quality of Life in Stable COPD patients - A Hospital Based Cross Sectional Study"** is a bonafide research work done by **(REG NO:BR0117002)** .

Dr.Gajanan S Gaude
MD, DNB, FCCP, FAPSR, FICS, FNCCP
Professor and Head,
Department of Respiratory Medicine,
J.N Medical College
Belagavi-10

Date:
Place : Belagavi

Dr.(Mrs.)N S Mahantashetti **MD (Paed.)**
Principal,
J. N. Medical College,
Nehru Nagar,
Belagavi – 10

Date:
Place: Belagavi

PLAGIARISM ACCEPTED LETTER

JAWAHARLAL NEHRU MEDICAL COLLEGE

(A constituent unit of KLE Academy of Higher Education & Research Deemed-to-be University)

Accredited 'A' Grade by NAAC (2nd Cycle) Placed in Category "A" by MHRD (GoI)

Nehru Nagar, Belagavi-590 010, Karnataka-India

Website : http/www.jnmc.edu
E-Mail : Principal@jnmc.edu

☎ Office :+91-(0)831 2471350
FAX :+91 (0)831-2470759

Ref. No. : MDC/Pg/

Date : 17/09/2019

To,

REG NO. BR0117002

Sub: Acceptance Letter

Sir/Madam,

The softcopy of thesis entitled " HEALTH RELATED QUALITY OF LIFE IN STABLE COPD PATIENTS: A HOSPITAL BASED CROSS SECTIONAL STUDY" has been submitted for Anti-Plagiarism check through Turnitin software. The scan has been carried out and the scanned output reveals a match percentage of 3% (Three percentage) which is within the acceptable limits of 10% as per the guidelines given by UGC.

Thanking you,

Yours sincerely,

Coordinator
Dept. of Respiratory Medicine.,
J. N. M. C., Belagavi.

Dr. Bhagyashri Patil
CONSULTANT PULMONOLOGIST
KMC Reg. No.62951
KLES Dr. Prabhakar Kore Hospital,
& MRC, Belagavi -590010

Chairman,
Antiplagiarism Committee

COPD

ORIGINALITY REPORT

3%	3%	3%	%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	kasrimkasrim.blogspot.com Internet Source	1%
2	fr.slideshare.net Internet Source	1%
3	www.dovepress.com Internet Source	1%
4	shodhganga.inflibnet.ac.in Internet Source	1%

Exclude quotes	Off	Exclude matches	< 1%
Exclude bibliography	On		

LIST OF ABBREVIATIONS

COPD	–	Chronic Obstructive Pulmonary Disease
FEV_1	–	Forced Expiratory Volume in 1 second
BMI	–	Body Mass Index
HRQOL	–	Health related quality of life
SGRQ	–	St.George Respiratory Questionnaire
NHP	–	Nottingham Health Profile
6MWT	–	6 Minute Walk Test
6MWD	–	6 Minute Walk Distance
GOLD	–	Global Initiative for Chronic Obstructive Pulmonary Disease
FRC	–	Forced Residual Capacity
RV	–	Residual Volume
DLCO	–	Diffusing Lung Capacity for Carbon monoxide
MMRC	–	Modified Medical Research Council dypnea grading scale
BODE	–	BMI, Obstruction of airways, Dyspnea scale, Exercise capacity
CPET	–	Cardio Pulmonary Exercise Test
PFT	–	Pulmonary Function Test
EL	–	Energy Level component in NHP scale
P	–	Pain component in NHP scale
PA	–	Physical Ability
ER	–	Emotional Reaction
S	–	Sleep component in NHP scale
SI	–	Social Isolation component of NHP scale
SpO_2	–	Peripheral capillary oxygen saturation
PR	–	Pulse Rate

RR	–	Respiratory Rate
RS	–	Respiratory System
BPM	–	Beats per minute
HRQLI	–	Health Related Quality of Life Index
OPD	–	Out Patient Department

ABSTRACT :

Introduction : COPD is an important cause that leads to higher mortality in India and worldwide along with airflow limitation, patients with COPD also have systemic manifestations. Due to persistent symptoms, these patients have a poor health related quality of life (HRQOL). Many subjective and objective scales are designed but they are either complex for use or nonspecific. Hence a simple tool like BODE index is suggested to measure HRQOL in COPD patients.

Objective :

1. To measure health related quality of life in stable COPD patients.
2. To evaluate validity of BODE index as Health relat //ed quality of life index (HRQLI) with SGRQ and NHP scales.

Methods : It was a prospective hospital based cross sectional study. Stable COPD patients who were diagnosed by spirometry based on GOLD guidelines, after considering inclusion and exclusion criteria were enrolled in the study. Demographic details, MMRC dyspnea grading, clinical examination, lung functional tests and oral questionnaires ie SGRQ and NHP were taken and 6 minute walk test was conducted on the same day in the same order. Finally with all BMI, FEV_1, MMRC scale and 6MWD, BODE index was calculated. Pearson correlation coefficient was used to know the association between BODE index, SGRQ and NHP scales. Univariate and multivariate analysis was done to predict validity of BODE index.

Results : 155 stable COPD patients who visited Respiratory medicine OPD in KLEs Dr.Prabhakar Kore Hospital and MRC were evaluated for inclusion in the study. After considering selection criteria, 124 patients were considered for the study. Mean age of

the study population was 67.37± 7.93 years and 64.5% of them were men. Pearson correlation coefficient analysis shows a positive correlation between BODE index, SGRQ (p value = 0.001) and NHP scores(p value = 0.001). Regression analysis shows that BODE index is 54.2% (r^2 = 0.542) valid in comparison to SGRQ scale and 61.1% (r^2= 0.611) valid in comparison to NHP scale to measure HRQOL.

Conclusion : BODE index is a simple and robust tool to measure health related quality of life in stable COPD patients.

Key words : COPD, BODE index, Health related quality of life, SGRQ, NHP.

CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF PHOTOGRAPHS

INTRODUCTION :

Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases.[1]

As per World Health Organization (WHO), 65 million people all around the world are having mild to moderate COPD[2] and COPD is responsible for 30 million of DALYs lost and about 5% of total deaths worldwide.[3]

In India, with the increasing pollution, there is increase in COPD prevalence and due to irreversible airflow limitation, patients have persistent symptoms and it causes poor quality of life. Severity of this illness differs from person to person since it is a complicated heterogenous systemic disorder. Though quality of one's life is affected, progress of this disease is still measured with spirometry values which is an objective test and subjective evaluation is still not a part of treatment line. Hence patient centered outcome measures has to be acknowledged and effective target diagnosis and treatment plans should be varied with each individual patient. Recent GOLD guidelines emphasized the same and focussed about primary aim of treatment which is to lessen symptom rate[4], future exacerbations risk while improving health related quality of life[5].

Health related quality of life (HRQOL) assessment is an important measure in evaluating a COPD patient and there are various scales like St.George Respiratory Questionnaire, Sickness Impact Profile, Nottingham health profile etc. to do this subjective evaluation. Among this, SGRQ is the COPD specific questionnaire[6]. But

most of these questionnaires are long and difficult to implement in COPD patients who are stable and visit OPD. Many scales aren't validated in local languages which creates difficulty in self administration. For a physician to administer such a long questionnaire in OPD is impractical. Hence a simple measure is necessary to know the HRQOL in these patients which can evaluate the patients both subjectively and objectively.

Nottingham Health Profile (NHP) is used to measure health related quality of life. Along with diseased population, it is also used in general population as a screening tool to know their energy level, physical mobility, pain, social isolation, sleep and emotional reaction. Although it is not a disease specific questionnaire, it is one of the most valid and widely accepted scales to see health related quality of life index[7] (HRQLI)

St.George Respiratory Questionnaire (SGRQ) is one of the most widely used COPD specific scale to measure HRQOL. It is purely a subjective scale with three components i.e symptom score, activity score and impact score. Generally COPD patients have a score $\geq$25 and <25 is seen in healthy population. Scores vary according to severity of disease. In comparison to many other scales, this is the most valid subjective index to measure HRQOL[8].

A multidimensional measure named BODE index has four components : BMI, measurement of airway obstruction by FEV_1, measurement of dyspnea by MMRC grading and measurement of exercise capacity by six minute walk test. It is already proved in predicting number of hospitalizations, exacerbations, mortality and evaluating pulmonary rehabilitation programmes. If it predicts HRQOL also then its

usage in regular clinical practise can be increased and it can be used as a regular prognostic tool.

In India, many studies have been done to evaluate treatment options in COPD and there are very few studies that measures HRQOL. There were no studies from South India which has validated BODE index to measure HRQOL. Hence this study is pivotal and it has been done to evaluate the health related quality of life in stable COPD patients with BODE index and to find its predictive validity with SGRQ and NHP.

OBJECTIVES :

Primary objective :

To measure Health related quality of life in stable COPD patients by BODE index.

Secondary objective :

To predict validity of BODE index in comparison to St.George Respiratory Questionnaire and Notingham Health Profile.

REVIEW OF LITERATURE :

DEFINITION OF COPD :

Global initiative for chronic obstructive pulmonary disease (GOLD)[1] defines chronic obstructive pulmonary disease (COPD) as a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and alveolar abnormalities usually caused by significant exposure to noxious particles or gases.

The ATS and ERS[2] define COPD as a preventable and treatable disease state characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and it is associated with an abnormal inflammatory response of the lungs to the noxious particles or gases, primarily caused by cigarette smoking. Although COPD affects lungs, it also produces significant systemic complications.

BURDEN OF COPD :

WHO estimated that worldwide there are 65 million people who are having moderate to severe COPD[3]. By 2020, in mortality ranking, COPD will be in third place[5]. It's prevalence is 2-22% in male and 1-19% in female population across the world[5]. Prevalence of this disease is increasing and now it is almost equal in both men and women. COPD prevalence was estimated by the Burden of Obstructive Lung Disease (BOLD) study all around the world using standardized methods and protocols[9]. They used post bronchodilator spirometry testing with questionnaires about respiratory system, risk factor exposure and their health condition.

Changing trends are seen in developing countries in terms of industrialization, urbanization, socio-economic and lifestyle modifications that is leading to high prevalence of noncommunicable diseases like diabetes, hypertension, COPD etc. Crude estimates suggest there are thirty million Emphysema and chronic bronchitis patients in India[10] with a prevalence of 2.12 – 9.4% in North India and 1.4 – 4.08% in South India[13] which is not very much different from the world scenario. In 1986, Malik[15] reported that this disease has a prevalence of 9.4% in rural males and 3.7% in urban males whereas 4.9% in urban females and 1.6% in urban females in North India. In South India, Ray D et al[16] published that COPD has a lesser prevalence in females than males which is about 4.08% and 2.55% respectively.

A multi-centric study done on 35295 COPD cases in 2006 showed that smokers were effected 2.6 times more than nonsmokers[17]. The INSEARCH trial (Indian Study on Epidemiology of Asthma, Respiratory Symptomatology and Chronic bronchitis, 2006-2009) which was sponsored by Indian Council of Medical Research (ICMR) had varied prevalence rates in chronic bronchitis patients in various regions, ranging from 0.61% to 13.54%[18].

Mortality in COPD patients is immense in developing countries, may be around 90%. This rate is estimated to rise by 30% in the next 10 years making COPD as one of the primereasons for death by 2030[19]. 2.3-8.4% of the world's mortality rateis already because of this disease with a male predominance[7].

Apart from an encompassing influence on disease progression and disease state all around the world, with a hundred billion army of its own, India faces a major economic jolt of the disease as well. The estimated economic loss due to COPD in India is about Rs.35,000 crores for the year 2011 and it is around Rs.48,000 crores for

the year 2016[17]. Few studies assessed the treatment cost in COPD patients and it was understood that patients spent 15% of their annual income on smoking products and 30% on disease management[18]. In a study done in Karnataka, South India, the total direct cost of medicines in a COPD patient accounts to Rs.29,885 ± 11,995.33 and the total mean indirect medical cost was Rs.7,441.25 ± 2,228.90. With comorbidities the cost was around Rs.28,148 ± 2,578 and without comorbidities it was Rs.13,460 ± 1,255. The mean absenteeism from the work was around 193 ± 33 hours in one month[19,20]. Therefore a proper protocol relied management strategies can reduce the mortality, morbidity and economic burden of the disease.

RISK FACTORS :

Knowledge regarding risk factors help in preventing the disease initiation and progression. Risk factors are broadly classified into host factors and environmental factors.

Table 1. Risk factors of COPD

HOST FACTORS	ENVIRONMENTAL FACTORS
Genes	Smoking
Asthma/ airway hyperresponsiveness	Air pollution
Age	Occupational exposure
Gender	Childhood respiratory infections
	Low socioeconomic status

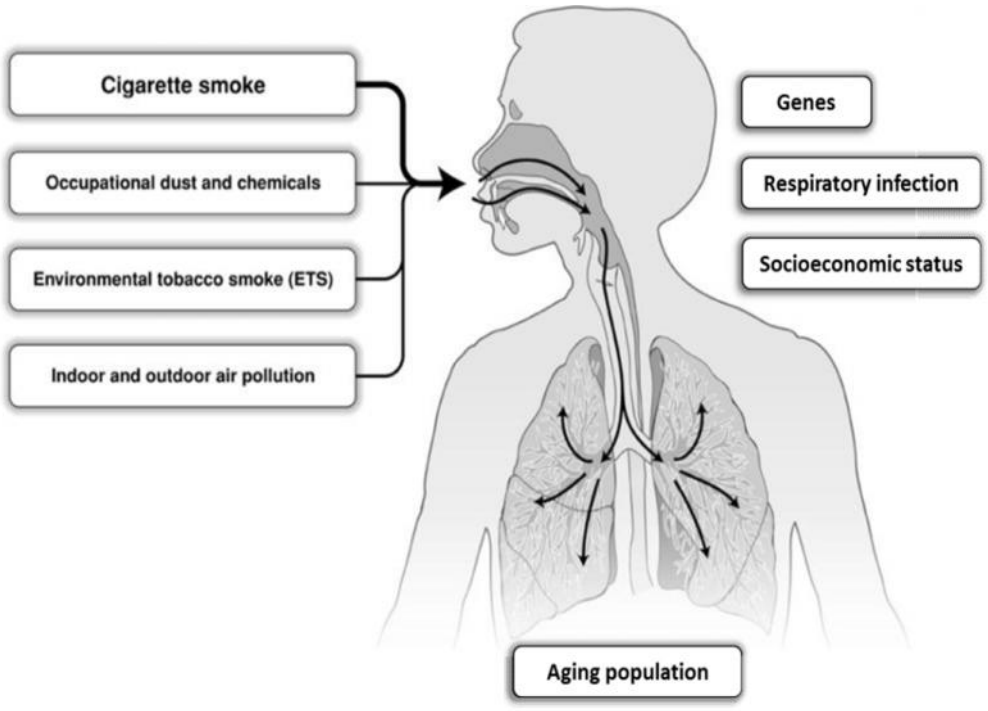


Fig.1 : Risk factors of COPD

1. **Genetic susceptibility :**

COPD develops as a result of complicated gene-environment interaction. Hereditary deficiency of the gene, alpha 1 antitrypsin which is an inhibitor of serpin peptidase, clade A, member 1 (SERPINA1) is the best documented genetic factor of COPD[21]. Other genes like, those coding for Glutathione s transferase[22], Tensin 1 (TNS1), C terminal domain (GSTCD), advanced glycoslylation end product-specific receptor (AGER), Hydroxytryptamine (serotonin) receptor 4 (htr4) and thrombospondin type I domain containing 4 (THSD4)[23], metalloproteinase1 and metalloproteinase 2are also responsible for genesis of COPD.

2. Asthma / Airway hyperresponsiveness

Long time asthma can be a risk factor to cause COPD. In a study done by Vonk et al[24], about 16-20% asthma patients were found to have irreversible airflow limitation.

Bronchial hyperreactivity could be an independent predictor of COPD[1]

3. Age and Gender :

A survey done in USA shows that COPD prevalence increased from 3.2% to 11.6% in patients who were in the age group of <44 years and those of >65 years respectively. Hence it can be said that age is one among the many risk factors for COPD[24]. A decade ago COPD prevalence was more in men than in women but with a changing trend in habits like smoking and tobacco chewing, it is almost equally prevalent in both the groups[25].

4. Smoking :

All around the world, cigarette smoking is the most common cause for COPD. Smokers have alot of symptoms like cough, breathlessness, wheezing etc, greater reduction in FEV_1 and other lung function abnormalities than non smokers[26]. Reasons for nonsmoker COPD could be atmospheric exposure to irritants, organic and inorganic particles, chemicals and gases. Biomass fuels and smoke circulating in ill ventilated kitchens causing indoor pollution are also few important factors causing COPD[21,22]. E-cigarettes are used in deaddiction process of smoking but they also cause COPD, although less than a normal cigarette. Prevalence of COPD in western countries with e-cigarette is about 4.45% as per a recent study[29].

5. Air pollution :

There are primary and secondary air pollutants in the atmosphere which are released from vehicles, industries, burning waste and other sources. These pollutants are responsible for COPD by causing oxidative stress and bronchial hyperreactivity[10]. Independently, second hand smoking or environmental smoke is another risk factor for COPD. It degrades body elastin and causes possible lung injury[30]. However few studies identified that pollutants didn't have much effect on COPD pathophysiology although they affect lung development in childhood and increase exacerbation rate[31].

6. Childhood respiratory infections :

Repeated childhood infections cause reduced lung functions and increased symptoms in adulthood[25]. But role of infections in COPD isn't very clear and tuberculosis is another risk factor of COPD[31].

7. Low socioeconomic status :

Concomitantly outdoor and indoor pollution, overcrowding, bad nutrition, infections can cause COPD. There are no strong evidences suggesting the presence of COPD in low socioeconomic groups[33].

PATHOGENESIS :

COPD is a clinical expression of complex alterations in structure and function of alveolar tissue along with small airways. Smaller airway remodeling and narrowing along with damage to lung parenchyma and alveolar attachments of airways leading to emphysema are the two major causes of COPD. Few major pathogenetic processes leading to this pathway are

1. Inflammation

2. Protease antiprotease imbalance

3. Oxidative stress

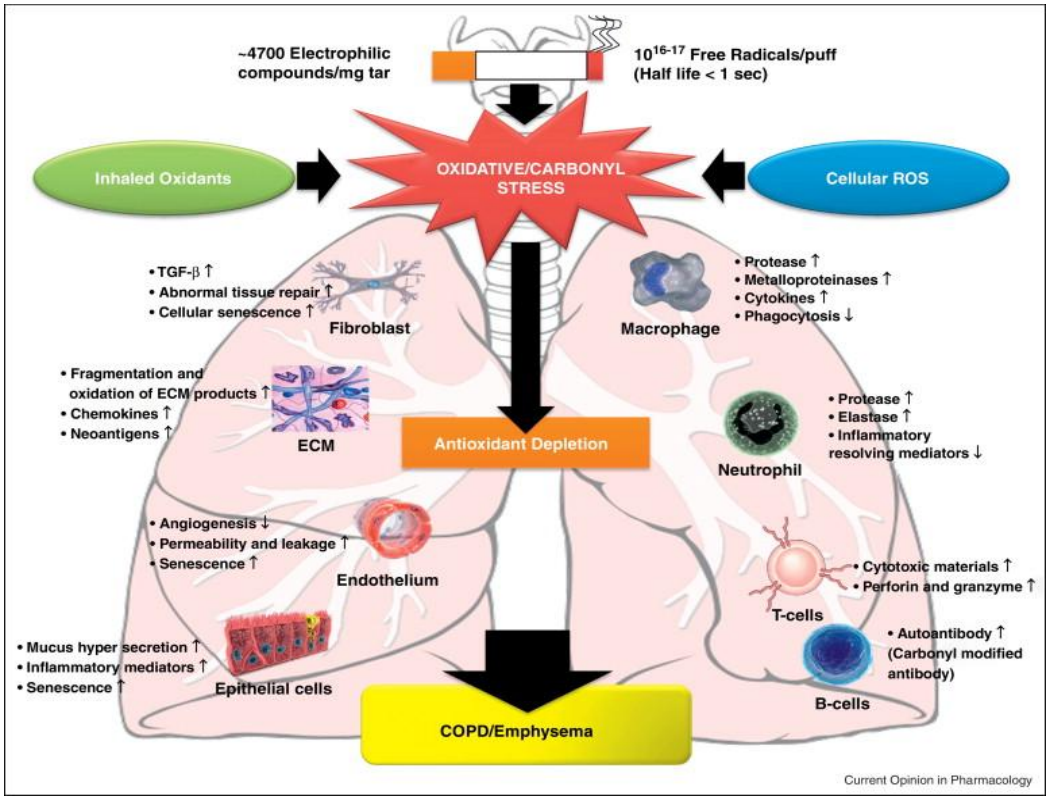


Fig.2 : Pathogenesis of COPD

1. Inflammation :

Irritant inhaled substances like cigarette smoke and air pollutants or gases activate surface macrophages and airway epithelial cells to release multiple chemotactic mediators like chemokines which attract circulating neutrophils, monocytes and lymphocytes in the lung. This inflammation persists explaining a self perpetuating mechanism although this is not elucidated[34].

Tumor necrosis factor alpha (TNF alpha), Interleukin 1 (IL-1), IL-6, IL-8 and Transforming growth factor beta (TGF beta) along with chemokines like CXCL 10 and CXCL 11 which cause small airway fibrosis are few inflammatory mediators released by activated epithelial cells of the airway. They recruit T cells leading to further activation of macrophages and release of metalloproteinases causing further inflammation. Mucous production from goblet cells and production of antioxidants, antiproteases along with defensins which are defense mechanisms of airway epithelial cells are impaired, further worsening the inflammation[34].

Macrophages activated from cigarette smoke or any noxious particles activate inflammatory mediators like TNF alpha, CXCL 1, CXCL 8, reactive oxygen species (ROS) and secrete enzymes like MMP 2, MMP 9, MMP 12 causing pathological destruction.

Direct stimulatory effect on granulocyte production due to various chemotactic factors released by activated macrophages cause neutrophil recruitment to the airways. These neutrophils secrete serine proteases including neutrophil elastase, cathepsin G, MMP 8, MMP 9 which alveolar destruction.

2. <u>Protease Antiprotease imbalance :</u>

Stimuli like cigarette smoke, noxious particles produce oxidative stress and release inflammatory mediators which cause inflammation. Along with this, it inactivates several antiproteases like SLP, alpha 1 antitrypsin by oxidation which causes protease antiprotease imbalance and further leads to the progression of inflammation[35].

3. **Oxidative stress :**

It occurs when excess of ROS is produced in view of antioxidant defense mechanism resulting in harmful effects like damage to lipids, proteins and DNA. Additionally, this oxidative stress decreases the antioxidant level due to down regulation of Nuclear erythroid factor 2 (NRF 2) which helps in the increased production of antioxidants, further reducing antioxidants.

PATHOPHYSIOLOGY :

Inflammatory injury to airways, lung parenchyma and pulmonary vasculature in various combinations leading to airflow obstruction, exaggerated work of breathing and gas exchange abnormalities are the charecteristics of COPD. Advanced COPD causes pulmonary artery hypertension, corpulmonale or right heart failure. Airflow limitation is seen in the expiratory phase is a defining physiologic characteristic in COPD patients and it represents the final expression of diverse derangements of respiratory mechanics.

1. **Airflow limitation and air trapping :**

Airflow limitation in the expiratory phase is the principal physiological defect in COPD. Intrinsic airway factors relate to bronchial wall remodeling/fibrosis and increased mucosal secretions. Extrinsic factors involve the loss of elastic tissue support for small airways and the dynamic expiratory compression of these airways[1].

Hyperinflation in COPD causes increase in functional residual capacity (FRC) which explains about the amount of air remaining in the lung at the end of tidal exhalation. This can lead to gas trapping and a rise in residual volume (RV). As a consequence, there is an upsurge in the work of breathing which turns out to be an

important factor for dyspnea. Since expiratory time is important for lung emptying, factors like increasing respiratory rate during exercise result in progressive increase in FRC or delayed emptying[35].

2. **Ventilation perfusion abnormalities :**

Gas exchange abnormalities result in hypoxemia and hypercapnia. Reduced ventilation could be due to reduced ventilatory drive which causes co_2 retention and it is further increased by exaggerated work of breathing caused by severe airflow obstruction and hyperinflation coupled with ventilatory muscle impairment[1].

3. **Mucous hypersecretion :**

In chronic bronchitis, chronic airflow irritation causes goblet cell hyperplasia and enlarged submucosal gland resulting in chronic productive cough. Many of the inflammatory mediators and proteases stimulate mucous hypersecretion.

4. **Ventilatory muscle dysfunction :**

There are various contributing factors for ventilatory muscle dysfunction in COPD. As a consequence of hyperinflation, muscle strength and endurance[36] of inspiratory muscles are at mechanical disadvantage. Other factors which may further contribute to exercise limitation are nutritional depletion, tissue hypoxia and loss of muscle mass[37,38].

COPD AS A SYSTEMIC DISEASE :

COPD is a respiratory disease with permanent and progressive airflow obstruction with extra pulmonary manifestations which was acknowledged recently[32].

Large clinical trials and many epidemiological studies have helped us in understanding the importance of comorbidities[40].

A study done by Antonelli-Incalzi[4] et al has demonstrated the impact and prognostic role of comorbidities in COPD. In their data analysis from 270 patients discharged after a COPD exacerbation, understood about common comorbidities associated with this disease. Few of them were : hypertension which accounted to 28%, diabetes mellitus which to 14% and ischemic heart disease to 10%. The median survival was 3.1 years and 228 patients out of 270 died during a five year follow up period. Hence, a shift in the targets to manage extrapulmonary abnormalities with airflow limitation management caused by the disease is essential.

DIAGNOSIS :

1. **Medical History :**

A detailed history accentuating vulnerability to risk factors, history of allergy, sinusitis, asthma, repeated childhood infections, any family history of allergic disorders, symptom pattern, history of exacerbations, no.of hospitalizations, other diseases, effects of disease on lifestyle, social and family support along with drug history has to be taken.

2. **Physical Examination :**

It gives an idea about disease severity, hyperinflation, presence of respiratory failure and corpulmonale or congestive cardiac failure.

3. **Spirometry :**

It is essential to diagnose COPD. As per GOLD criteria COPD should have a post bronchodilator value of $\leq$0.7 and it is an objective measure of airflow limitation

4. Imaging :

a) Chest Radiograph:

Routinely chest radiograph is done to rule out other diagnosis rather than diagnosing COPD. Chest X-ray changes of COPD are signs of hyperinflation, flattened diaphragm, tubular heart, increased retro sternal space, hyperlucency of lung fields and pruning of pulmonary vasculature.

b) CT Scan of Thorax :

It is not routinely recommended but it might help in the differential diagnosis and it is more helpful when patient is being considered for surgical options like lung volume reduction surgery[35,41].

5. Static lung volumes and DLCO :

Body plethysmography helps in diagnosing air trapping or static hyperinflation to know the disease severity although it is not a compulsion. Calculation of diffuse lung capacity provides information on functional impact of emphysema in COPD[42].

6. Oximetry and Arterial blood gas analysis :

Pulse oximetry is useful to know the patient's oxygen saturation and need for supplemental oxygen. SpO_2 less than 92% should be evaluated with ABG[43]. ABG gives us an idea about respiratory failure and helps in the further management.

7. Alpha 1 Antitrypsin screening :

It is a genetic disorder. In high prevalence countries of alpha 1 antitrypsin deficiency COPD variants, this screening should be advocated[44]. These patients tend to have an age <45 years and predominantly lower lobe involvement with a serum concentration of alpha 1 antitrypsin level less than 15-20% of normal and such conditions highly suggest homozygous alpha 1 antitrypsin deficiency variants[1].

8. Disease severity assessment:

This is done to determine :

1) Amount of airflow obstruction
2) Impact of airflow obstruction on patient's overall health condition
3) Risk of further events like exacerbations, oxygen requirement, hospital admissions and death.

Determination of above factors helps in guiding the treatment plan.

To achieve above goals, assessment of COPD should be done in the following way

- **<u>Lung function test abnormality and disease severity :</u>**

According to GOLD 2019[1], severity of disease is classified according to PFT and it is as below :

Table.2 : Classification of disease severity according to PFT.

GOLD Staging	Grading	FEV_1 % predicted
1	Mild	≥80
2	Moderate	50-80
3	Severe	30-49
4	Very severe	<30

Various studies have observed a weak correlation is found between FEV1% and symptoms along with impairment of life[45,46].

- **Nature and intensity of patient's current symptoms:**

Initially it was thought that COPD patients have their chief complaint as breathlessness and that is why MMRC dyspnea grading scale was used to know the severity of disease. However this disease is known to have many symptoms apart from breathlessness[48]. Hence comprehensive symptomatology assessment is being done with some other scales like Chronic Respiratory Questionnaire (CRQ)[49], St.George Respiratory Questionnaire (SGRQ). These scales are more sensitive than other short questionnaires like Clinical Assessment Test (CAT) and COPD Clinical Questionnaire (CCQ). But for regular usage these short scales are being used in view of ease of administration. Various scales are explained in further discussion.

- **Assessment of exacerbation risk**:

Exacerbations are acute deterioration of symptoms resulting in additional therapy[50,51] and hospitalizations. Exacerbations which are controlled by short acting bronchodilators (SABA) are grouped as mild; those which require SABA, antibiotics

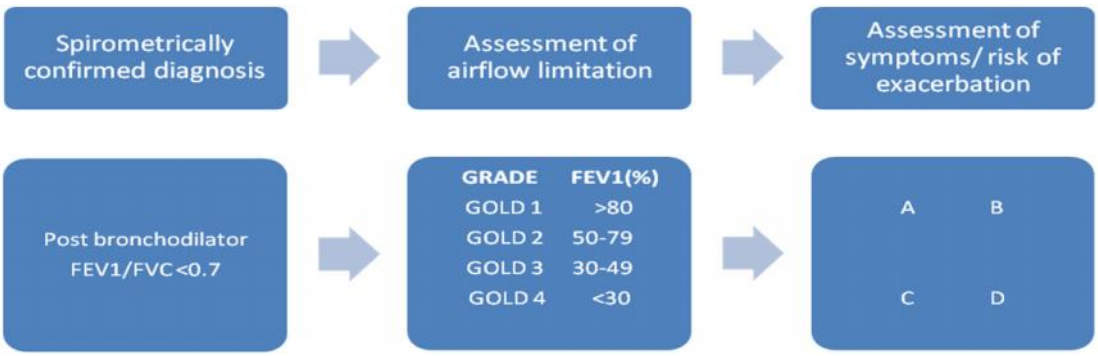
or oral steroids are grouped under moderate exacerbations and those which require hospitalizations or who are in respiratory failure are grouped under severe exacerbations. Few studies explained that exacerbations differ in patients during follow ups[52] .The best way to discover a predictor of frequent exacerbators is by knowing the relevant history of exacerbations[53].

- **Presence of any comorbidities** :

COPD is an important component of multi morbid condition in elderly. Other common coexisting diseases in COPD patients include cardiovascular diseases, skeletal muscle dysfunction, anxiety, depression, metabolic syndrome, osteoporosis and lung carcinoma[54]. COPD itself might escalate the risk for other diseases like lung carcinoma[55,56]. This association might be due to other common risk factors (e.g., smoking), similar gene susceptibility or impaired clearance of carcinogens. Comorbidities are seen in these patients with any amount of airflow obstruction[23], which can influence hospitalizations and mortality independently[57].This deserves specific treatment along with COPD treatment.

Combined COPD assessment as per GOLD 2019[1] :

ABCD Assessment tool :



- Moderate or severe exacerbation history :
  - ≥2 or ≥1 causing hospital admissions
  - 0 or 1 (not causing hospital admission)
- Symptoms (more in A and B) :
  - mMRC 0-1 , CAT < 10 (A and C)
  - mMRC≥2, CAT ≥10 (B and D)

Indices to measure Health related quality of life :

Various questionnaires are used to find HRQOL in COPD patients. They are

A. Generic instruments to measure HRQOL :

1. Dartmouth COOP chart:

It is useful to measure clinical status of disease in primary care[68]. This is a self administered or interviewer based questionnaire. It has 6-9 single item chart. Physical activities, emotional reactions, daily and social activities, pain are various domains of this scale[69,70].

2. EuroQoL (EQ 5D) :

It consists of five domains and this is a visual analog scale. This is a self administered scale which takes around 8 minutes[71]. Mobility of patient, Self-care, usual activities, pain, anxiety & depression are various domains of the scale. Patients who had health problems on EQ-5D had significant low mean SF-12 scores for all the dimensions. Patients who show a health issue on EQ-5D had a significant low mean SF-36 scores for all the dimensions[72]

3. Functional performance inventory :

This is a measure of functional performance developed from explicit framework. Day to day activities, usual roles and wellbeing is identified by this questionnaire. This is a self administered scale with 65 questions under 6 subscales. High scores reflect better functioning of the individual[73].

4. Nottingham Health Profile (NHP) :

This instrument is useful in evaluating perceived distress in various populations. It takes around 8-10 minutes to administer the scale. There are 38 questions under 6 domains.

Physical mobility (8 constituents), pain (8 constituents), emotional reactions (9 constituents), energy (3 constituents), sleep (5 constituents), social isolation (5 constituents). Each constituent is weighted; these weights were derived from patients and healthy individuals. Dimensions score range from 0 to 100, greater health problems have higher scores. Findings are expressed as a profile instead of a overall score. It is one among the most widely used scoring system in subjective evaluation of a disease all over the world[74,75]

There are so many other generic scales like Quality of well being scale, SF 12, SF-36, Measure your medical outcome profile (MYMOP) scale, World Health Organisation QOL assessment instrument, sickness impact profile etc.

A cross sectional study was done by Jans et al[7] in 170 COPD cases, NHP scale was administered and computer scoring of data along with measurement of internal consistency was done by Cronbach's alpha coefficient. With a mean apha of 0.74, this

study was approved for usage in COPD cases to measure HRQOL or psychological and social components.

B. Breathing problem based Quality of life questionnaire :

1. Chronic Obstructive Pulmonary Disease Activity Rating Scale (CARS) :

It is a self reported disease specific scale with 12 questions under 4 sections. The sections are about personal care, household, outdoor activities and social activities. It is a three point scale with a higher score showing less impairement[76].

2. Chronic Respiratory Questionnaire (CRQ) :

It was established by Guyatt et al in 1987. CRQ is an interviewer scale. At a later stage, self administered scale is available. This questionnaire has 20 questions which can be divided into four constituents : fatigue (4 questions), Breathlessness (5 questions), mastery (4 questions), emotion (7 questions). It can be scored on a 7 point scale ranging from one (which indicates maximum impairment) to seven (which doesn't show impairment). These findings are expressed as a mean score for each domain along with overall score[77].

3. COPD Assessment Test (CAT) :

It is a short and simple questionnaire invented in 2009 to calculate COPD impact. It also helps in monitoring long term follow up. It has 8 items, a six point scale (0-5) with a score range of 0-40. High scores indicate a bad HRQOL. It is a self administered scale in 50 languages. It is a reliable scale with good responsiveness. It is endorsed by GOLD for its use in diagnosis and treatment. It predicts future exacerbations[78].

4. The Airway Questionnaire 20 (AQ20) :

It was framed for Asthma and COPD patients to know subjective status of disease. It has 20 questions with scores varying from 0 to 20 and poor HRQOL is evidenced by higher scores. It only takes very less time to complete. It is reliable and valid. It is for both clinical and academic purposes[79].

5. Clinical COPD Questionnaire (CCQ) :

It is a self administered, reliable, validated, specialised score for COPD developed in 2003. It is supposed be used in daily practice. It has 10 items under 3 domains i.e, symptom score, functional score and mental state. They were asked to record experiences in last 7 days. HRQOL is poor with higher scores. It is available in 53 languages[80].

6. St. George Respiratory Questionnaire (SGRQ) :

SGRQ is the most widely documented comprehensive measure. It has 2 parts. Part 1 has 8 questions which has previously 12 month recall of patient's symptomatology although now it is reduced to 1month recall period. Part 2 has 8 questions which measures the patient's level of activity and psycho-social activity subjectively. Hence part 1 has symptom score and part 2 covers impact and activity scores which altogether constitute total SGRQ score. This is a validated scale for COPD and asthma. It has been widely used by clinicians. This is a supervised, self administered scale and it is available in many languages including kannada. Since each question had a specific score, manual calculation becomes clumsy hence the data can be entered in a SGRQ excel sheet and the scores will be obtained[62]. Generally COPD patients have SGRQ scores ≥ 25[60,61] and scores < 25 are usually found in

healthy people[59] Therefore, according GOLD 2019 guidelines,a recommendation is made that SGRQ score ≥ 25 is considered for treatment of symptoms[1].

In a study done by Hana Mullervo et al[58], in 12,043 patients SGRQ predicted exacerbations, HRQOL and mortality. This scale is validated in various Indian languages including Kannada.

Weatherall et al[8] measured HRQOL with SGRQ scale in 3,500 participants in the age group of 25-75 years which included both COPD and Asthma patients. Quantile regression analysis and ROC analysis was done and it proved HRQOL measurement by SGRQ would be of great value to diagnose COPD in addition to GOLD diagnosis.

The scales that are COPD specific are CCQ, CRQ, CAT, CARS and SGRQ, out of which SGRQ has been considered highly specific to measure HRQOL in COPD patients, although it is very long.

BODE Index:

BODE index, a composite index measures BMI, FEV_1, breathlessness and exercise capacity. It's a simple multimodality approach to know the severity of disease[6].

Components of BODE Index are :

1. **Body Mass Index :**

Nutritional deficiency is one of the most common findings observed in advanced COPD patients. Prevalence in loss of weight in COPD patients who visits OPD ranges from 20% and it increases to 35% who are hospitalized[89]. It was also observed that low BMI could be a risk factor for COPD mortality. Less BMI was associated with an increased risk of mortality[90].

2. **Obstruction of airways :**

Obstruction of Airways is an objective test done by spirometry. FEV_1 / FVC <0.7 shows that there is obstruction. Grading is done according to predicted FEV_1% values. As per GOLD 2019 guidelines, it is classified as:

Table 3. FEV_1 and severity of obstruction

Predicted FEV_1%	**Severity of obstruction**
>80	Mild
50-79	Moderate
30-49	Severe
<30	Very severe

3. **Modified MRC dyspnoea scale[47] :**

The most common disabling symptom of COPD is breathlessness.This is the main reason for a patient to seek medical attention[91]. MMRC scale is simple to know the level of breathlessness and disability during an activity. Though this is a good scale,

these days it is considered to be a primitive method of assessing symptoms and HRQOL since breathlessness is not the only symptom of COPD. Weak correlation is found between dyspnea and FEV_1[92]. Since it predicts dyspnea in a better way, it is considered as one among the components in BODE Index. Grading is as follows :

Table 4: MMRC Dyspnea Scale

MMRC 0	I only get breathless with strenuous activity
MMRC1	I get short of breath when hurrying on the level or walking up a slight hill
MMRC 2	I walk slower than people of the same age on the level because of my breathlessness or I have to stop for breath when walking on my own pace on the level
MMRC 3	I stop for breath after walking about 100 metres or after a few minutes on the level
MMRC 4	I am too breathless to leave the house or I am breathless when dressing or undressing

4. <u>Six Minute Walk Distance (6MWD) :</u>

Six Minute Walk Test (6MWT) is a simple and accurate test for understanding the severity of the disease and exercise tolerance in a COPD patient. It gained acceptance because of its simplicity, reliability and standardization[93]. Various factors reduce 6MWD like female sex, shorter height, lack of motivation, impaired cognition, musculoskeletal or cardio pulmonary diseases. It helps in disease severity ranking and helps in predicting survival[94].

The main disadvantage of this test is the measurement of functioning of all muscles rather than measuring the fatigue in individual group of muscles or specific muscles. Milder disease patients may not demonstrate reduced exercise capacity.

Association between 6MWD, peak VO_2 and death rate in COPD patients was studied by Cole and colleagues which showed that 6MWT is one of the better predictors of mortality. It is better than peak VO_2 obtained in CPET test[95].

After measuring all the indices, BODE index will be scored as:

Table 5. BODE scoring system

	BODE SCORES			
BODE COMPONENTS	0	1	2	3
Predicted FEV_1 %	$\geq$65	50-64	36-49	$\leq$35
6MWD (mts)	$\geq$350	250-349	150-294	$\leq$149
Dyspnea scale	0-1	2	3	4
BMI	>21	$\leq$21	-	-

In 2004, Celli et al[65] studied 207 COPD patients in which the predictive validity of above variables were assessed and they quoted that these variables predict mortality in COPD patients.

Claudia et al[66] did a study in 625 COPD patients, a 6 monthly follow up was done till 2 years and BODE index scores which ranged from 0-10 were divided into four quartiles and this was compared with rate of mortality. They observed that 4th quartile which had 7-10 BODE scores yielded more mortality in comparison with

other quartiles. Hence it is proved that composite indices are better predictors of mortality than individual components[67,68].

Marin et al[81] did a prospective cohort study on BODE index for predicting COPD exacerbations risk. He considered 275 patients from two tertiary care centers in Spain. Exacerbations per year was 1.95 and mean time of first exacerbation was inversely proportional to the BODE quartiles. Mean time taken to visit an ER was 6.7, 3.6, 2 and 0.8 years with a significant p value. On application ROC curves, BODE was shown to be a better predictor than $FEV_{1.}$ In another retrospective study done by Hogdev et al[83], 76 COPD cases with a mean age of 59 years and a mean FEV_1 of 35% were taken to compare frequent and infrequent exacerbators with BODE index. Exacerbations were found by patient interview and health database. A total of 178 exacerbations were noted and a significant difference was found between frequent and infrequent exacerbations and BODE index with a p value of 0.002.

32 patients from New South Wales, Australia were divided into two groups ie, <3 hospital admission group and $\geq$3 hospital admission group by McKellar et al[82] to find if BODE score was associated with hospital admission rate or not. He observed that BODE score was not significantly related to hospital admissions in the first group and it was significantly related in the second group with a p value of 0.004. Although sample size is small, he could prove an association between higher BODE scores and more number of hospital admissions.

Celli BR et al[64] in his study about BODE index in COPD. 625 patients were prospectively evaluated for outcomes like death. 25 deaths were reported among 207 patients and 162 deaths were reported in a validation group. 61% had respiratory insufficiency, 14% had MI, 12% had lung cancer, 13% died due to other causes.

Hazard ratio from any of the cause per one-point increase was 1.34 and hazard ratio from any of the respiratory cause was 1.67. Thus this simple system helps in identifying the cause of death from any cause or from respiratory etiology.

Fagenello et al[84] in their prospective study to evaluate utility of BODE index in COPD patients in Brazil with 120 patients has observed that both the scales had similar clinical utility in knowing exacerbation rates. Median per year exacerbation rate was 0.8. Regression analysis showed the risk among moderate to severe exacerbations during a year follow up with GOLD; Odds ratio was 2.08 with 95% CI and odds ratio for BODE index was 0.69. Old age and low Spo_2 were found to be risk factors for an exacerbation by adjusted multiple regression analysis proving their clinical usage in finding out exacerbations, however other variables which aren't present in both scales can be reason for exacerbations.

A study done in 86 COPD cases for 3-5 years in Russia by Karoli et al[85], studied about BODE in COPD cases. Follow up of 86 patients for 3-5 years was done to determine risk factors COPD patient's mortality. Results showed more mortality in >60 year old patients, with breathlessness over 10 years and >50 pack years. <40% FEV_1, SpO_2<90, 6MWD <300 meters, pulmonary artery systolic pressure >40mmHg are found to be predisposing factors. They concluded that mortality risk was more in old age patients more than 40 years of smoking history and higher BODE index.

Ong et al[86] followed up 127 COPD cases in Singapore. Their aim was to followup127 COPD patients for 15 months to evaluate the role of BODE index for hospitalisations in COPD cases and observed that 47% of patients required hoapitalisations in one year and 17% was mortality. Poisson regression analysis showed a positive association in between BODE index and hospitalisations with

incidence rate ratio of 1.2 and 95% CI. Correlation coefficient (r^2) was 0.16 when BODE was used and it was only 0.04 when FEV_1 alone was used. This shows the importance of BODE index in knowing further hospitalisations in a COPD patient. Mahajan et al[87], in a study done in 100 male COPD patients, hospital stay was 3.15 days with 0-5 BODE score and 16 days with a score of 7-10. Among this cohort, it was found that increasing age lead to an increase in BODE index along with a significant association with number of pack years. Average pack years was 16.46. Average duration of hospital stay was 6.43 days in past 2 years. Moderate COPD group had 3.17 days as average hospital durationand severe COPD group had 16 days as hospital COPD duration. BODE index was a reliable method to know the severity of disease and hospitalization.

METHODOLOGY :

This study was a Cross-sectional study conducted in the Department of Respiratory Medicine, KLE'S Dr.Prabhakar Kore Hospital and Medical Research Centre, Belagavi. It was done in stable COPD patients from January 2018 to December 2018.

Design :

Prospective study

Method of data collection:

Data was collected from diagnosed COPD cases as per GOLD 2017 guidelines attending Respiratory Medicine OPD in KLE'S Dr.Prabhakar Kore Hospital and Medical Research Centre, Belagavi.

Sample size:

Universal sample

Selection criteria:

Inclusion criteria:

All stable COPD patients (without exacerbations for atleast 8 weeks prior to study) whose age were >40 years diagnosed by spirometry with FEV_1 / FVC < 0.7 attending out patient department of Respiratory Medicine in KLE'S Dr.Prabhakar Kore Hospital and Medical Research Centre, Belagavi.

Exclusion criteria :

1. Other chronic respiratory diseases like Bronchial Asthma, Tuberculosis, Allergic Rhinitis, and Bronchiectasis.
2. Cardiac patients suffering from congestive cardiac failure, unstable angina or recent MI
3. Any major life threatening illness
4. Patients who were unable to perform PFTor 6 minute walk test.
5. Bronchogenic carcinoma
6. Neurological disorders

Procedure:

With prior approval of Ethical and Research committee of Jawaharlal Nehru Medical College, Belagavi, the selected patients were explained about this study and written informed consent was taken.

It was a prospective hospital based cross sectional study. Stable COPD cases diagnosed by spirometry based on GOLD guidelines, after considering inclusion and exclusion criteria were registered in the study.

A questionnaire with demographic details like age, gender, height, weight, BMI, presenting complaints, past history, habits(smoking, alcohol consumption, tobacco chewing), MMRC dyspnea grading along with duration of COPD was taken.

All patients were subjected to clinical examination, PFT and oral questionnaires on the same day. Within that session, clinical, social and demographic data were collected; then, PFT and 6minute walk test was conducted.

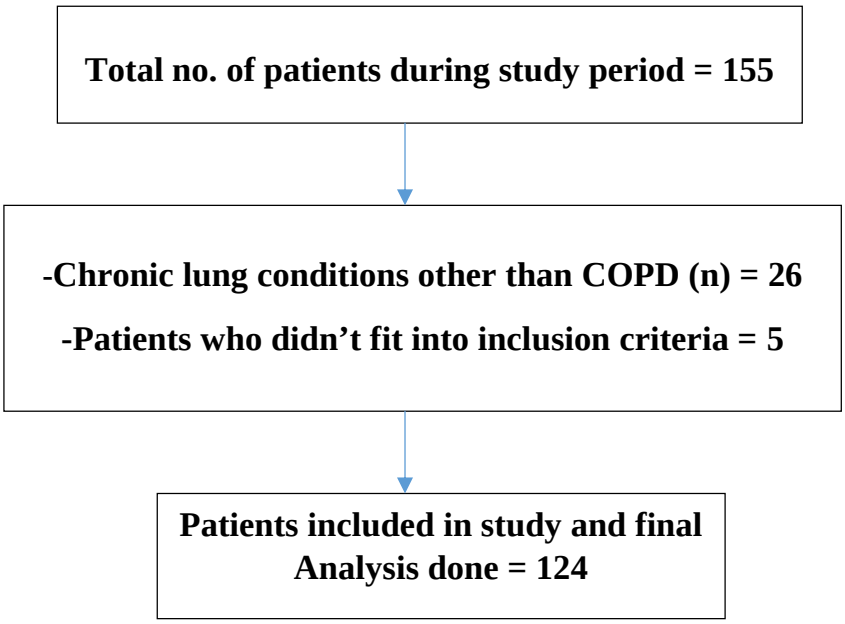
All questionnaires were completed in the same order: first St.George Respiratory Questionnaire (SGRQ) which contains 3 components (Symptom score, activity score and impact score) in 2 parts will be completed first and then Nottingham Health Profile (NHP) questionnaire which has 2 parts with 45 questions was completed. Although second part was not necessary to be filled for this study and first part had various questions assessing Energy level, Pain, Physical disability, Social isolation, Sleep and Emotional reaction. Each question had specific score. Later dyspnea scale (MMRC), BMI and finally BODE index were calculated. SGRQ data was entered in a SGRQ excel sheet and each component score along with total score was thus calculated. NHP component score and total score was calculated by a simple addition of respective individual scores.

Statistical Analysis :

Obtained data was entered into Microsoft Excel Spreadsheet and categorical data were expressed as rates, ratios and percentages. Continous data was expressed as mean +/- standard deviation. Pearson correlations after adjusting gender and age were used to know the association between BODE Index and SGRQ, also with NHP. Univariate and multivariate analysis was done and r^2 was calculated to check the validity of BODE Index as a tool to determine HRQOL. SPSS version 12 software was used. A p-value of <0.05 (two-tailed) was considered statistically significant.

RESULTS:

Fig. 3 : Study design



A total of 155 cases were considered for this study. 26 patients were excluded as they had chronic lung conditions and 5 patients were unable to perform PFT and six minute walk test, hence they were excluded.

Thus a total of 124 cases were considered in the study.

Table 6 :Gender distribution

Gender	No.of Patients	Percentage
Male	80	64.5
Female	44	35.5
Total	124	100

80 males (65%) and 44 females (35%) were present in the study group of 124 patients. There was male gender predominance in the study population.

Fig 4.Gender distribution

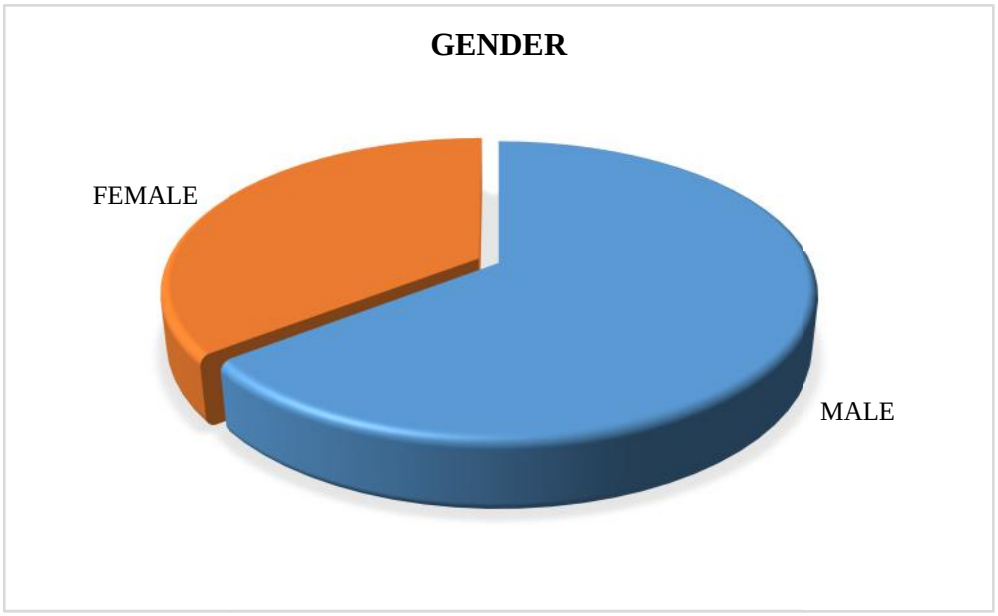


Table 7 :Age distribution

Age Distribution	Male	Female	Total	Percentage
50-60	16	8	24	19.35
61-70	37	22	59	47.58
71-80	23	9	32	25.82
81-90	6	3	9	7.25

Mean age of the study population was 67.37 years and standard deviation was 7.93 years. Most of the patients in this study were between 61-70 years of age that is 47.58%

Fig 5.Age distribution

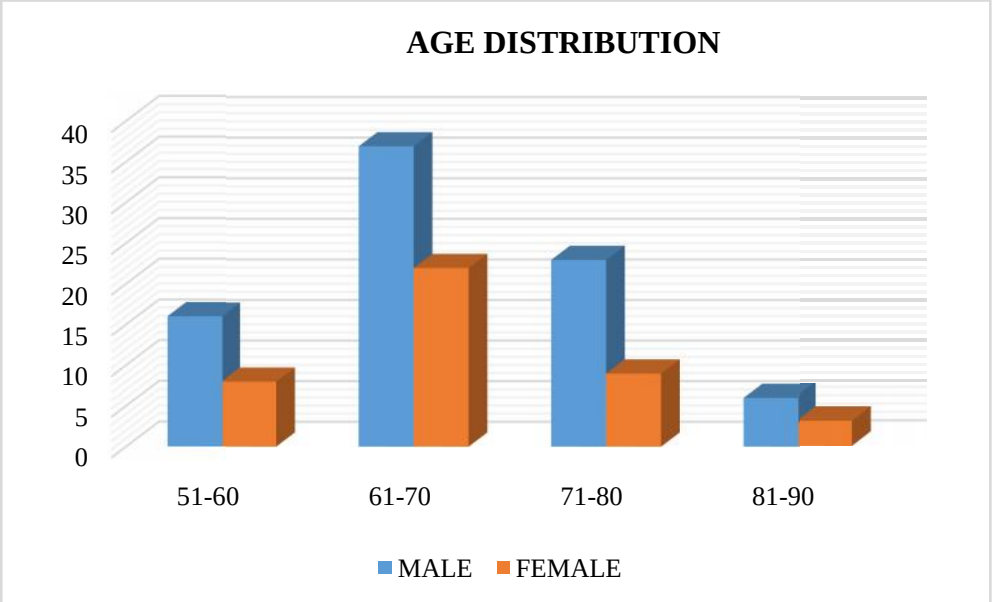
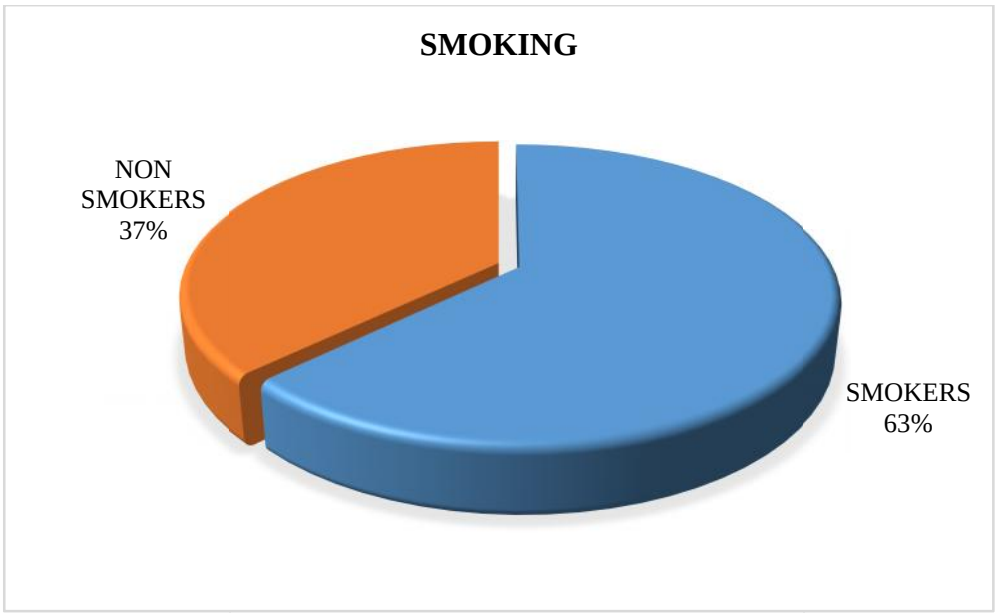
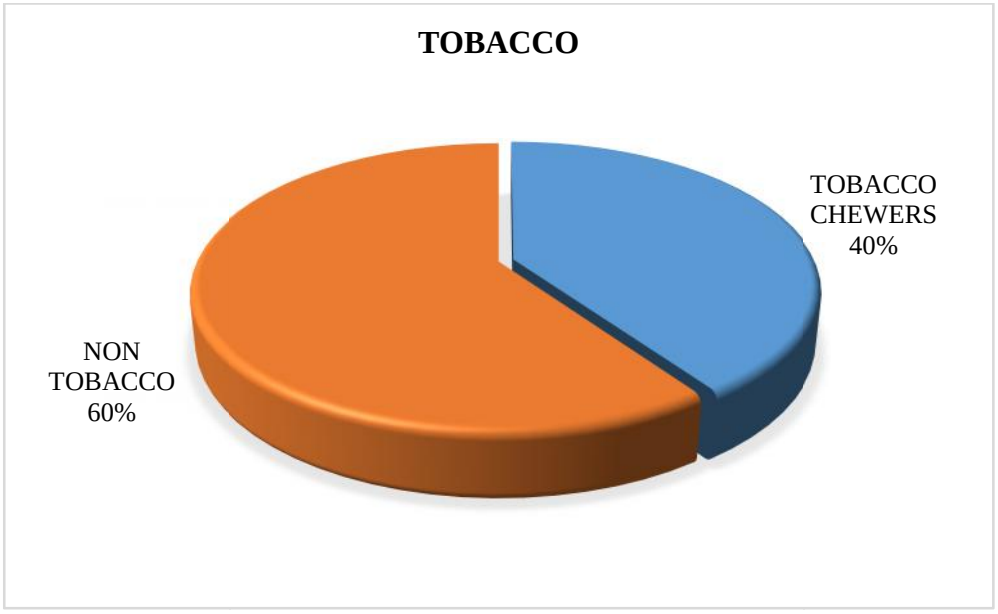


Fig 6 : Smoking population



Out of 124 patients 78 were smokers and 46 patients were non smokers. Hence many patients included in the study were smokers.

Fig 7 :Tobacco chewers :



Out of 124 patients, 74 were tobacco chewers and 50 were non tobacco chewers. Hence majority were tobacco chewers.

Table 8 : Symptomatology

Symptom	No. of Patients	Percentage
Cough	103	83
Breathlessness	121	97.5
Chest pain	39	23.3
Pain abdomen	40	32.2
Others (Leg pains, fever)	15	12.9

Many patients in study population were suffering from breathlessness and cough. Leg pains was another symptom noted in few of the COPD patients in the study population.

Fig8 :Symptomatology

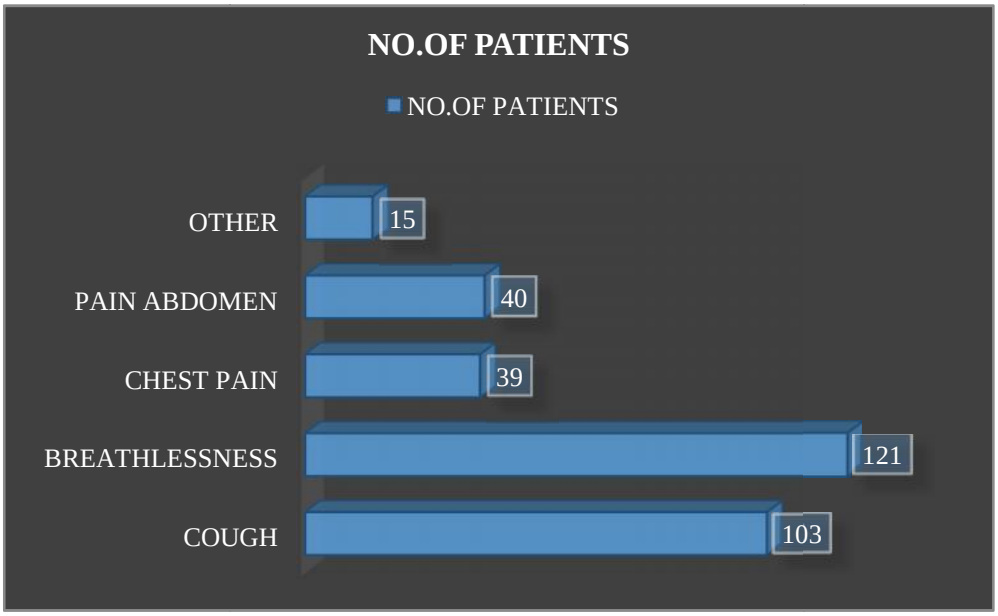


Table 9 : Comorbidities

Comorbidities	No. of Patients	Percentage
Diabetes	43	34.6%
Hypertension	73	58.8 %
IHD	12	9.67%
Other (DVT, Hypothyroidism, Hernia, PAH, Esophageal Varices)	17	13.7%

In this study group, most of the patients suffer from Hypertension. Diabetic patients comprise 34.6% of the study population. Others are IHD, DVT, Hypothyroidism, Hernia, Pulmonary artery hypertension, esophageal varices.

Fig 9 : Comorbidities

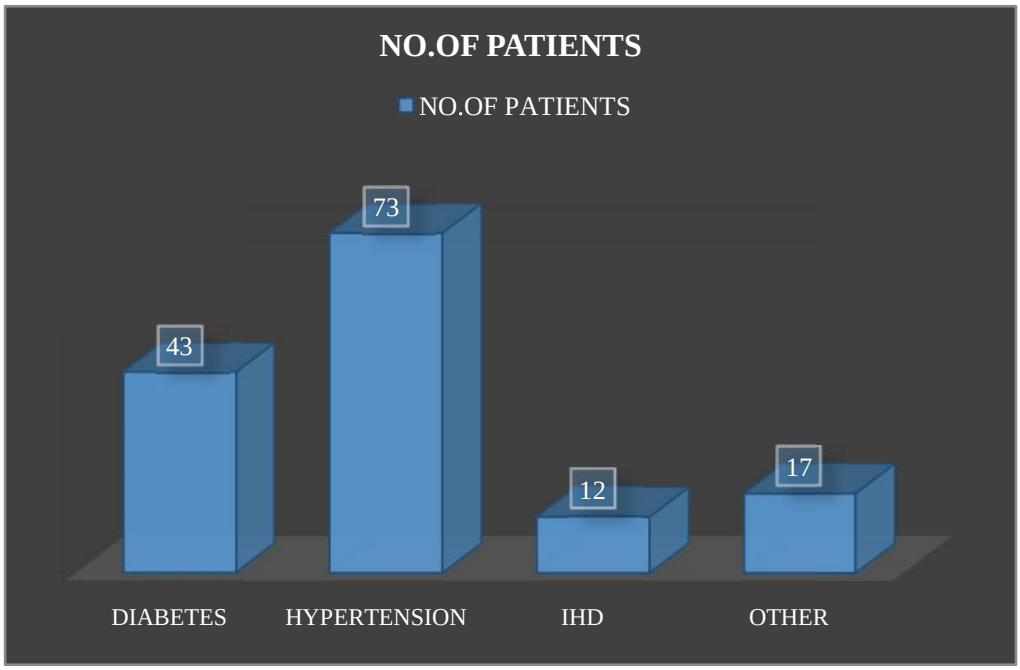


Table 10 : BMI

BMI	Frequency	Percentage
<18.5	21	16.9
18.5-24.9	60	48.4
25-29.9	27	21.8
>30	16	12.9

Maximum numbers of people were in BMI range of 18.5-24.9 which was normal. 16.9% of the patients in this study group were underweight and 12.9% study group patients were obese.

Fig.10.BMI

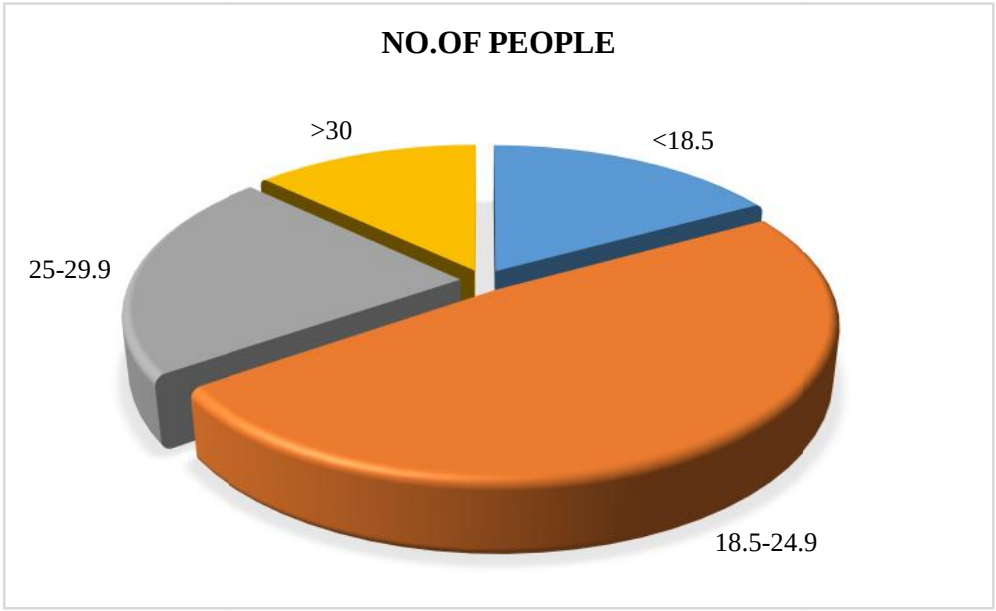


Table 11 :Baseline charecteristics of patients

Variable	**Mean**	**SD**
Age (years)	67.37	7.93
COPD duration (years)	5.12	3.42
No. of hospitalizations	1.52	1.37
FEV_1	1.24	0.76
FEV_1 %	52.04	15.57
FVC	53.82	24.10
FVC %	61.66	15.73
FEV_1/FVC	0.66	0.38
SpO_2 (%)	95.23	2.64
6 MWD (METERS)	282.97	94.28
BMI (KG/M^2)	23.81	5.77
MMRC	1.84	1.22
SGRQ (Percentile)		
Symptom score	46.07	21.38
Activity score	37.91	20.91
Impact score	18.74	15.71
Total score	29.67	16.79
NHP		
Energy (EL)	10.99	16.48
Pain (P)	8.98	8.67
Physical activity (PA)	10.54	11.09
Sleep (S)	13.12	10.27
Social isolation (SI)	6.61	9.50
Emotional reaction (ER)	7.62	7.05
Total score	57.86	2.06

Above table shows the complete demographic details of the study. Age, gender, smokers and tobacco chewers. Other comorbidities and symptomatology were described earlier in detail. Duration of the disease in study group was around 5.12 $\pm$

3.42 years. No.of hospitalizations in the previous years were around 1.52± 1.37 times. FEV_1/FVC ratio was around 0.66 ± 0.38 with most of the study population in moderate and severe groups according to GOLD 2017 guidelines. Mean six minute walk distance was 282.97 meters with a standard deviation of 94.28 meters. On an average, BMI of the study population was normal. Mean MMRC grade was around 1.84±1.22.

There are three components in St.George Respiratory Questionnaire. They are symptom score, activity score and impact score. Individual scores were calculated. Scores were calculated in terms of percentiles. Total score was 29.67 ± 16.79.

Nottingham health profile has 6 components. They are energy level, pain, physical ability to perform activities, sleep, social isolation and emotional reaction. Each component had a total score of 100 and the obtained scores of the study group were mentioned in the above table. Total score sums upto 600 and mean total score of this study group was 57.86 with 2.06 as standard deviation.

Table 12 : BODE Scores

BODE score	No. of patients
0	8
1	17
2	19
3	13
4	15
5	8
6	12
7	9
8	8
9	10
10	5

Depending on BMI, level of airway obstruction calculated by FEV_1, dyspnea measured by MMRC grading system and exercise capacity measured by 6MWT, BODE index was calculated and the scores range from 0-10. Most of the patients in study group had BODE scores of 1-4 which accounts to mild to moderate COPD. Also there are around 10 patients in BODE score 9 which accounts to severe COPD. Hence all grades of COPD severity are covered in the study population.

Table 13 : BODE Quartiles

BODE quartile	BODE indices	No.of patients
1	0-2	44
2	3-5	36
3	6-8	29
4	9-10	15

As per BODE scores, four quartiles were made. First quartile had scores ranging from 0 to 2, second had a range of 3-5, third had a range of 6-8 and fourth had a range of 9 and 10. Though there were good number of patients in third and fourth quartiles, maximum of them were in the first and second quartiles.

Fig .11 : BODE Quartiles

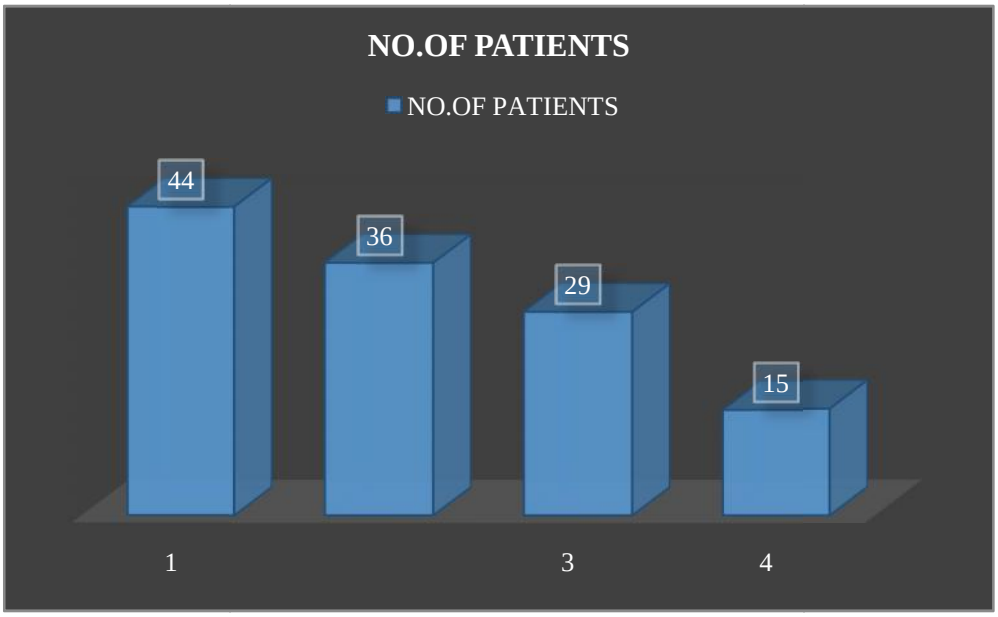


Table 14 : GOLD severity staging

FEV_1 (%)	**No.of patients**
>80	4
51-80	57
30-50	58
<30	5

Patients who are having FEV_1/FVC <0.7 were considered to have obstructive pattern and severity of obstruction depends on FEV_1 %.Four Patients in this study cohort with >80% FEV_1 were considered to have mild obstruction. 57 patients with 51-80% FEV_1 were considered to have moderate obstruction. 58 patients with 30-50 % FEV_1 were considered to have severe obstruction and 5 patients with <30 % FEV_1 were considered to have very severe obstruction. Hence the study group constitutes moderate to severe COPD patients as a major group as per GOLD 2017 severity staging.

Table 15: Classification as per MMRC grading

MMRC Grading	No. of patients
0,1	51
2	35
3	21
4	17

51 patients were found in 0 and 1 scale together, 12 and 39 were in 0 and 1 scales respectively. 2,3,4 scales had 35, 21 and 17 patients respectively. Maximum accounting to 0-2 scales.

Table 16 :Correlation between MMRC grading and BODE quartiles

MMRC GROUP * BODE GROUP Cross tabulation							
			BODE group				Total
			0 TO 2	3 TO 5	6 TO 8	9 TO 10	
MMRC group	0,1	Count	35	12	4	1	52
		% within BODE group	79.50%	33.30%	13.80%	6.70%	41.90%
	2	Count	9	22	5	0	36
		% within BODE group	20.50%	61.10%	17.20%	0.00%	29.00%
	3	Count	0	2	19	0	21
		% within BODE group	0.00%	5.60%	65.50%	0.00%	16.90%
	4	Count	0	0	1	14	15
		% within BODE group	0.00%	0.00%	3.40%	93.30%	12.10%
Total		Count	44	36	29	15	124
		% within BODE group	100%	100%	100%	100%	100%

Chi-Square Tests			
	Value	df	P value
Pearson Chi-Square	191.485	9	.001

*P Value <0.05 is significant

79.5% cases with 0 and 1 MMRC grades belong to 0-2 bode indices, that is first BODE quartile. 61.1% patients with grade 2 of MMRC belong to 3-5BODE indices, i.e., second BODE quartile. 65.5% of patients with MMRC grade 3 belong to 6 to 8 BODE indices that is third BODE quartile. 93.3% of MMRC grade 4 patients belong to 9 and 10 BODE indices that is fourth BODE quartile. Hence BODE quartiles correspond to MMRC grading. Chi square test had a pvalue of 0.001 which is statistically significant. Hence correlation was found in between BODE quartiles and MMRC grading.

Table 17: Correlation between GOLD severity staging and BODE index

FEV1 GROUP * BODE GROUP Cross tabulation							
			BODE GROUP				Total
			0 TO 2	3 TO 5	6 TO 8	9 TO 10	
FEV1GROUP	<30	Count	0	2	1	1	4
		% within BODE GROUP	0.0%	5.6%	3.4%	6.7%	3.2%
	>80	Count	4	0	0	0	4
		% within BODE GROUP	9.1%	0.0%	0.0%	0.0%	3.2%
	30-50	Count	2	21	22	14	59
		% within BODE GROUP	4.5%	58.3%	75.9%	93.3%	47.6%
	51-80	Count	38	13	6	0	57
		% within BODE GROUP	86.4%	36.1%	20.7%	0.0%	46.0%
Total		Count	44	36	29	15	124
		% within BODE GROUP	100%	100%	100%	100%	100%

Chi-Square Tests			
	Value	df	P value
Pearson Chi-Square	66.635	9	0.001

*P Value <0.05 is significant

Many of the patients in all quartiles belonged to moderate and severe COPD groups as per GOLD staging which accounts for 47.6% and 46% respectively. 6.7% of the fourth BODE quartile patients were in very severe COPD group which was high in comparison to other quartiles. 93.3% of fourth quartile and 75.9% of third quartile patients are in severe COPD group. 86.4% of first quartile patients are in moderate COPD group where as 9.1% patients of quartile 1 are in mild COPD group. This is statistically significant since p value is 0.001. it concludes GOLD severity staging is correlated with BODE quartiles.

Table 18 : Correlation between BODE index and demographic details

		Age	COPD Duration	No. of Hospitalisations	BMI	MMRC	FEV_1
BODE	Pearson Correlation (r^2)	-.009	.119	.386	-.403	.866	-.476
	P value	.923	.186	.001	.001	.001	.001

*P Value <0.05 is significant

Demographic details like number of hospitalizations, BMI, MMRC grading and FEV_1 are significantly associated with BODE index whereas age and disease duration of COPD is not statistically significant. Positive correlation was observed between BODE index and no. of hospitalizations. BMI reduces with increase in severity of disease and FEV_1 also reduces with increased severity of the disease. Strong positive correlation is observed between MMRC grading and BODE index.

Table 19 : T Test

	Smoking	N	Mean	Std. Deviation	P value
BODE	Present	78	4.001	2.7775	0.140
	Absent	46	4.804	3.1313	

*pvalue <0.05 is significant

78 smokers were seen in the study group. T Test was done to know the correlation between smoking and BODE index and there was no correlation between the two.

Table 20 : Comparison of MMRC grading with SGRQ scoring

		Symptom score	Activity score	Impact score	Total score
MMRC	Pearson correlation (r^2)	.586	.561	.519	.611
	P value	.001	.001	.001	.001

*pvalue < 0.05 is significant

St.George Respiratory Questionnaire has three components that are symptom score, activity score and impact score. All three components are individually found to have statistical significance. The total score of SGRQ seems to be statistically significant with MMRC grading. Positive correlation is found between MMRC grading and all SGRQ scores.

Table 21 : Correlation between MMRC and SGRQ scale

		NHP	EL	P	ER	S	SI	PA
MMRC	Pearson correlation (r^2)	.627	.389	.518	.424	.328	.480	.310
	P value	.001	.001	.001	.001	.001	.001	.001

*P Value < 0.01 is significant

Nottingham Health Profile (NHP) has two sections and the first section has six components that are energy level (EL), pain (P), emotional reaction (ER), sleep (S), social isolation (SI), physical ability (PA). Each component along with total score is significantly associated with MMRC grading. Section two of NHP is not required to be studied for the current study.

Table 22: Correlation between GOLD severity staging and SGRQ scale

		Symptoms score	Activity score	Impacts score	Total score
FEV_1	Pearson Correlation	-.426	-.371	-.322	-.387
	p value	.001	.001	.001	.001

*p value < 0.05 is significant

Gold severity staging was done according to FEV_1. Negative correlation was seen between FEV_1 and SGRQ components. As FEV_1 reduces, symptom score, impact score, activity score and total score increases.

Table 23: Correlation between BODE index

		Symptom score	Activity score	Impact score	Total score
BODE	Pearson correlation coefficient (r^2)	.682	.643	.612	.698
	p value	.001	.001	.001	.001

*p value < 0.05 is significant

The three components of SGRQ scale along with total score are significantly associated with BODE index. There is a strong positive correlation between total score and BODE index and moderate correlation is seen between symptom score, activity score, and impact score and BODE index.

Fig.12 : Correlation SGRQ symptom score and BODE index

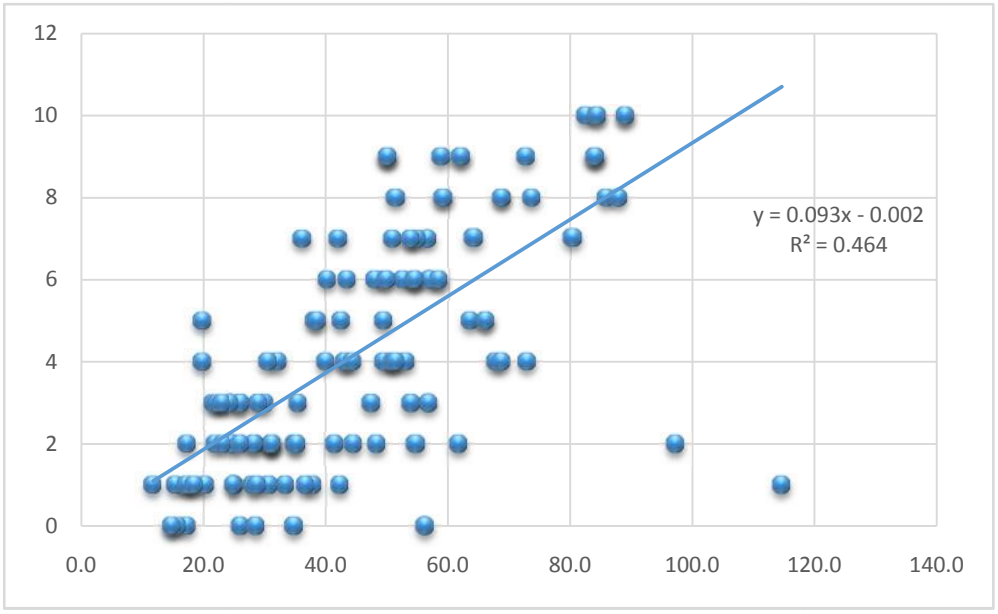


Fig.13: Correlation between SGRQ activity score and BODE index

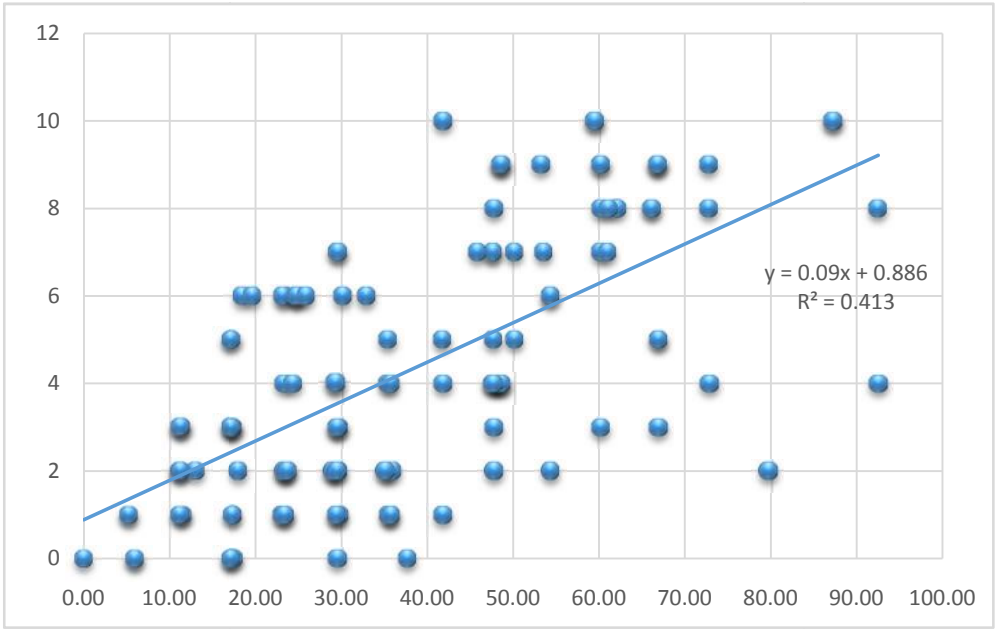


Fig.14 :Correlation between SGRQ impact score and BODE index

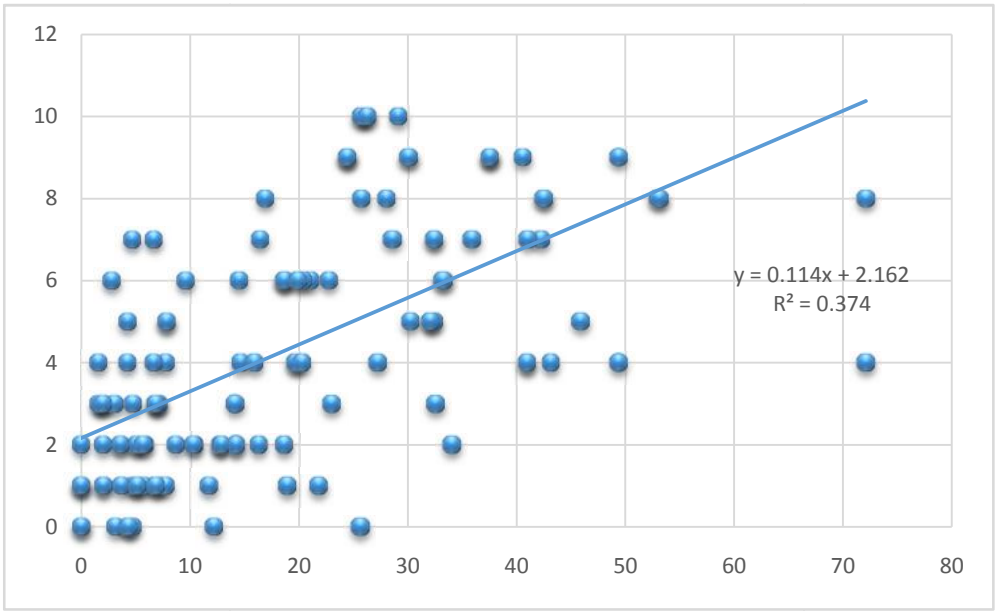


Fig.15: Correlation between SGRQ total score and BODE index

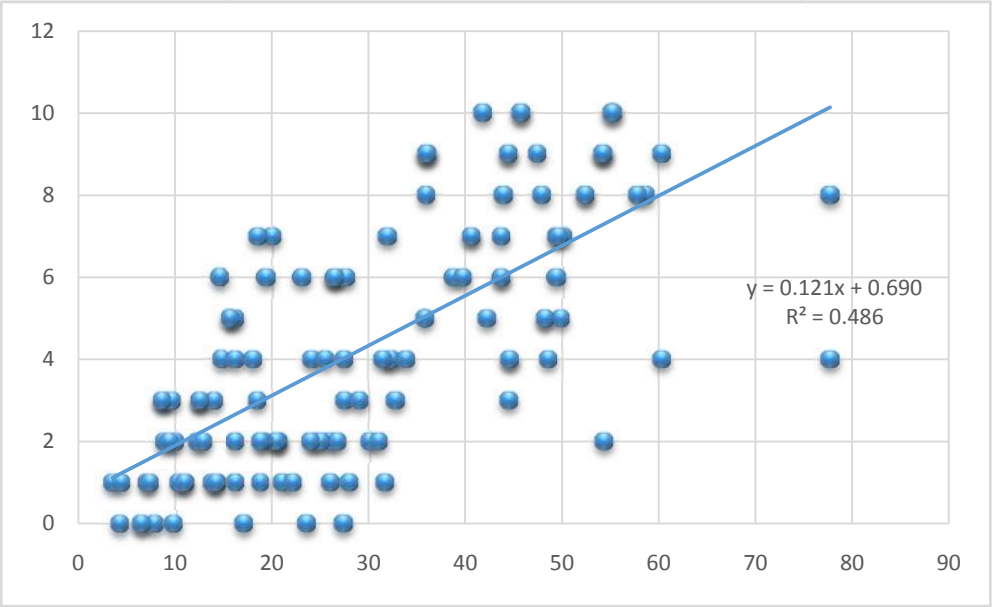


Table 24 :Correlation between NHP and BODE index

		NHP	EL	P	ER	S	SI	PA
BODE	Pearson Correlation coefficient(r^2)	0.677	0.488	0.577	0.422	0.42	0.444	0.353
	p value	0.001	0.001	0.001	0.001	0.001	0.001	0.001

*p value <0.05 is significant

Nottingham Health Profile (NHP) has 6 components that are energy level (EL), pain (P), emotional reaction (ER), sleep (S), social isolation (SI), and physical ability (PA). Physical ability had mild correlation with BODE index and other components along with total score have moderate correlation with BODE index. BODE index has 67.7% correlation with NHP scale.

Fig.16: Correlation between NHP total score and BODE index

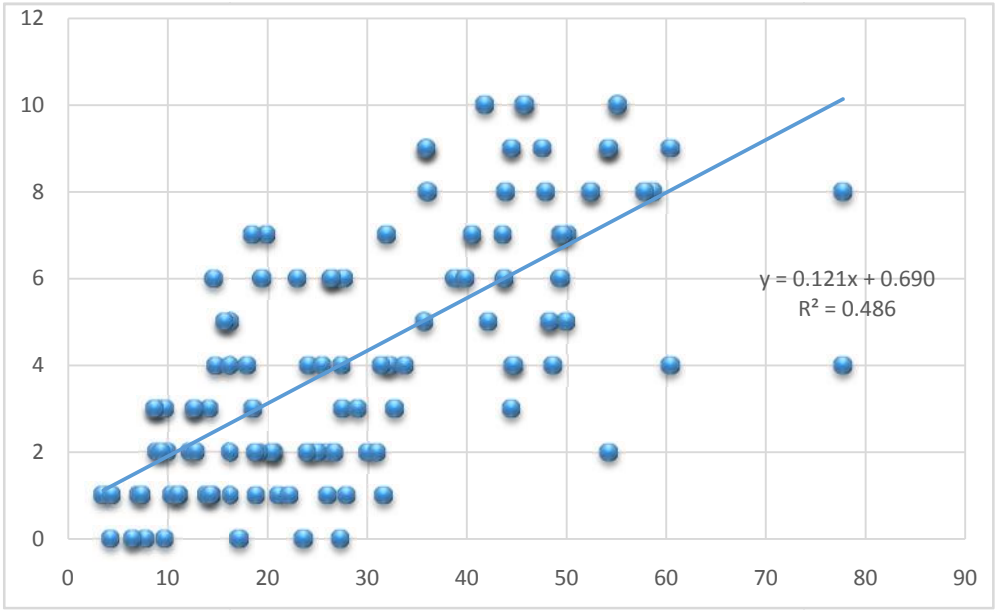


Fig.17: Correlation between energy level component and BODE index

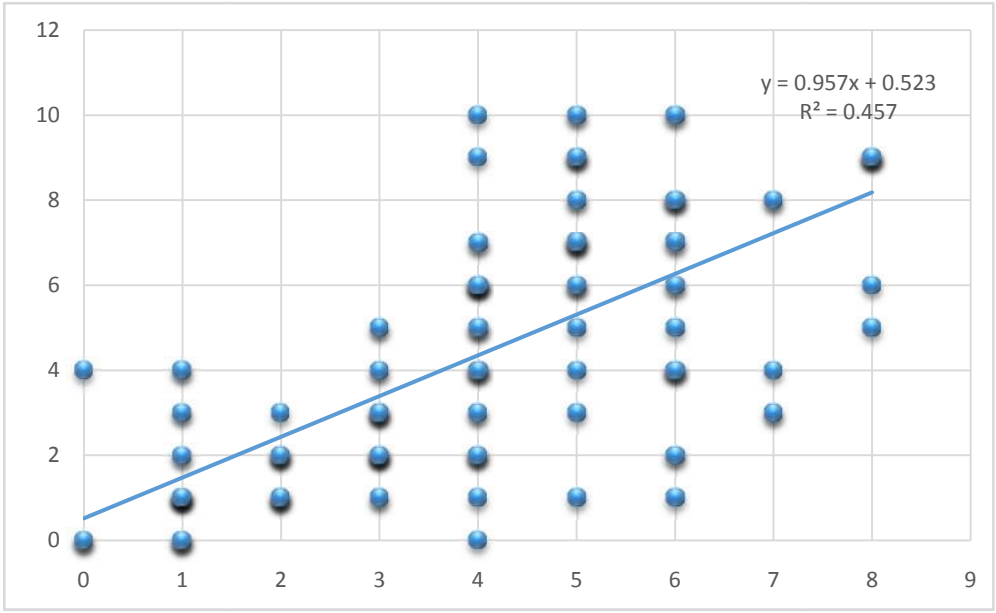


Fig.18: Correlation between pain component and BODE index

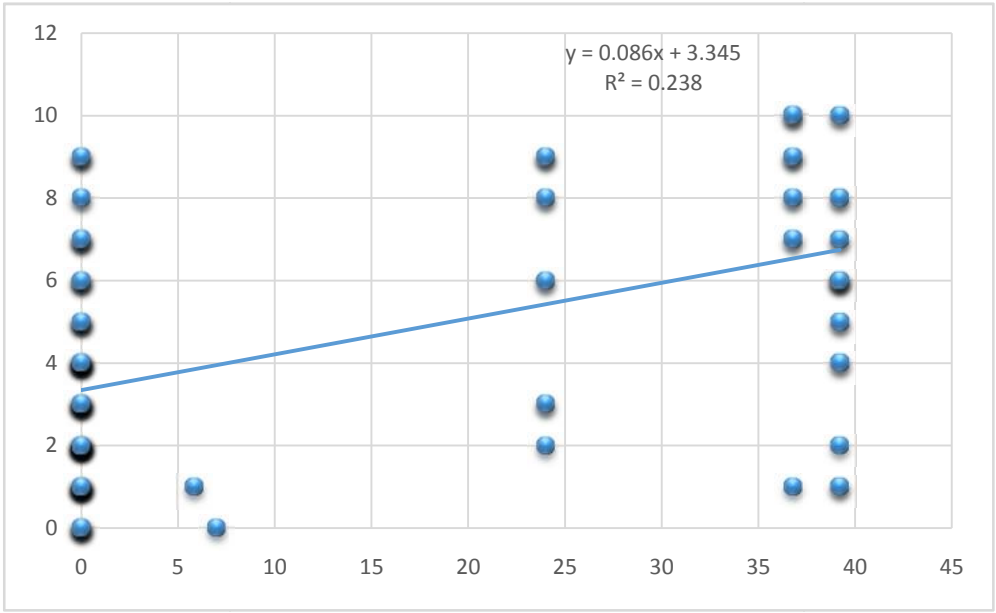


Fig.19: Correlation between emotional reaction component and BODE index

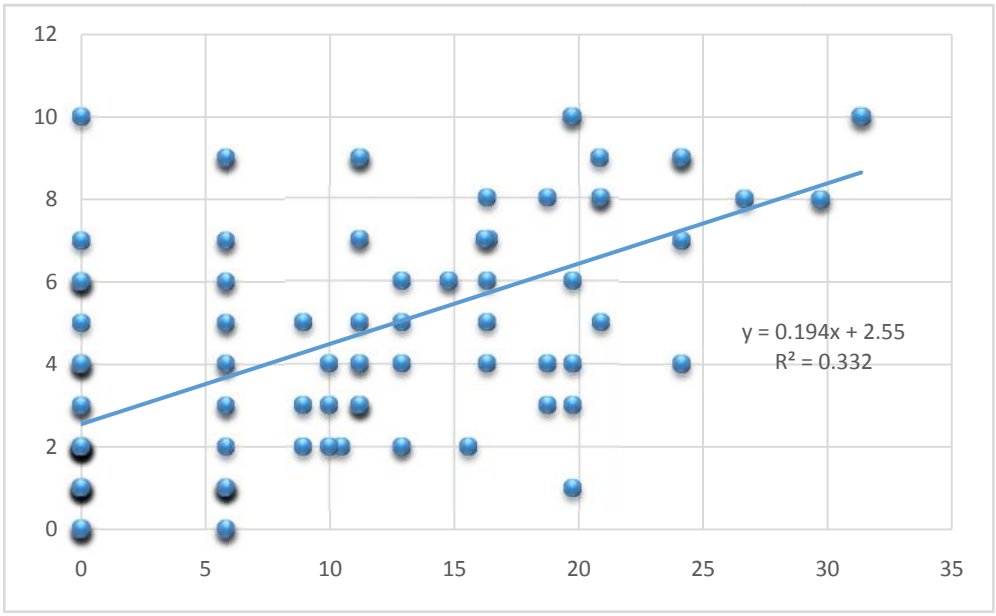


Fig.20: Correlation between sleep component and BODE index

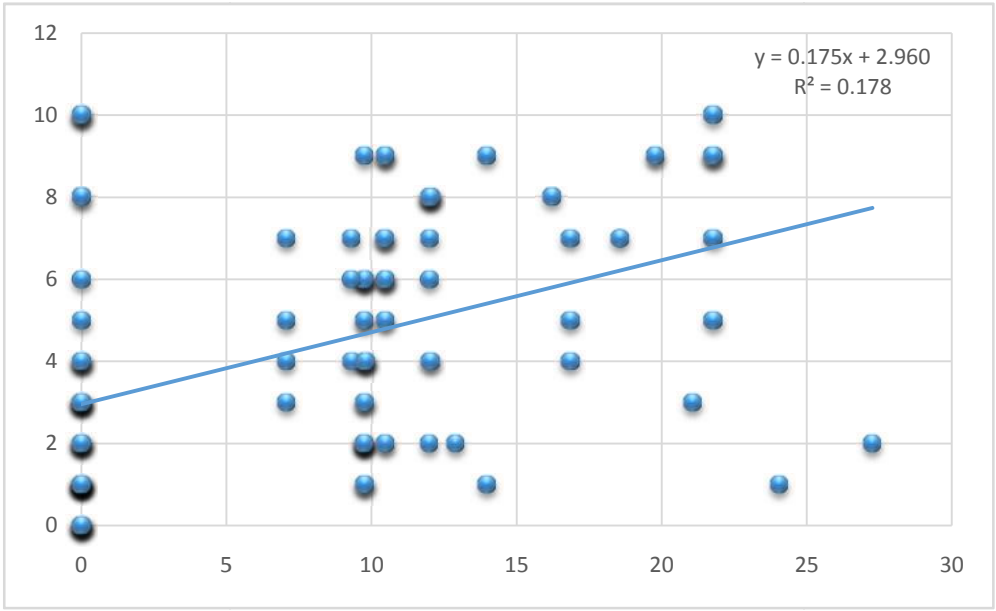


Fig.21: Correlation between social isolation component and BODE index

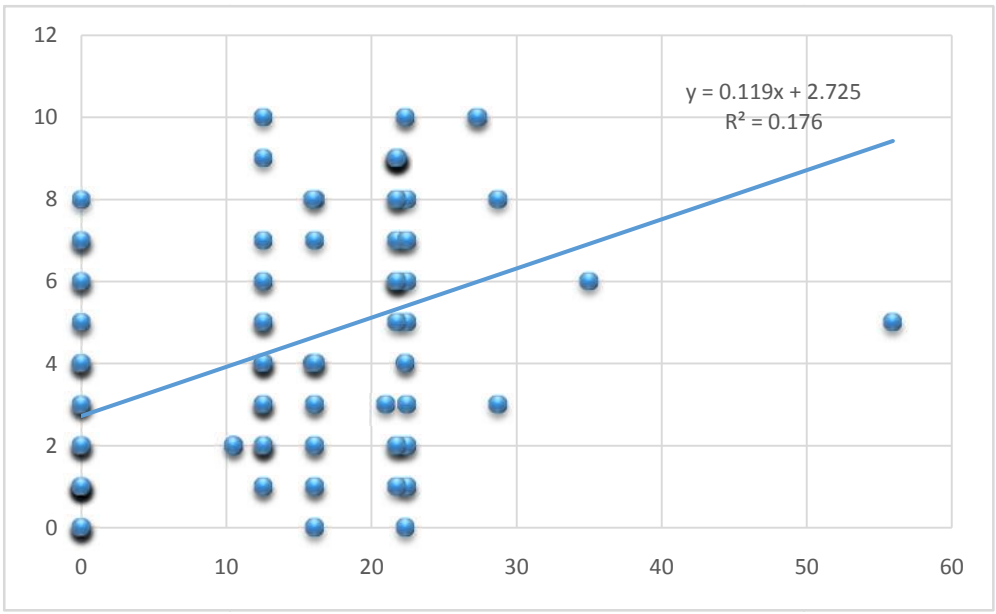


Fig.22: Correlation between physical ability component and BODE index

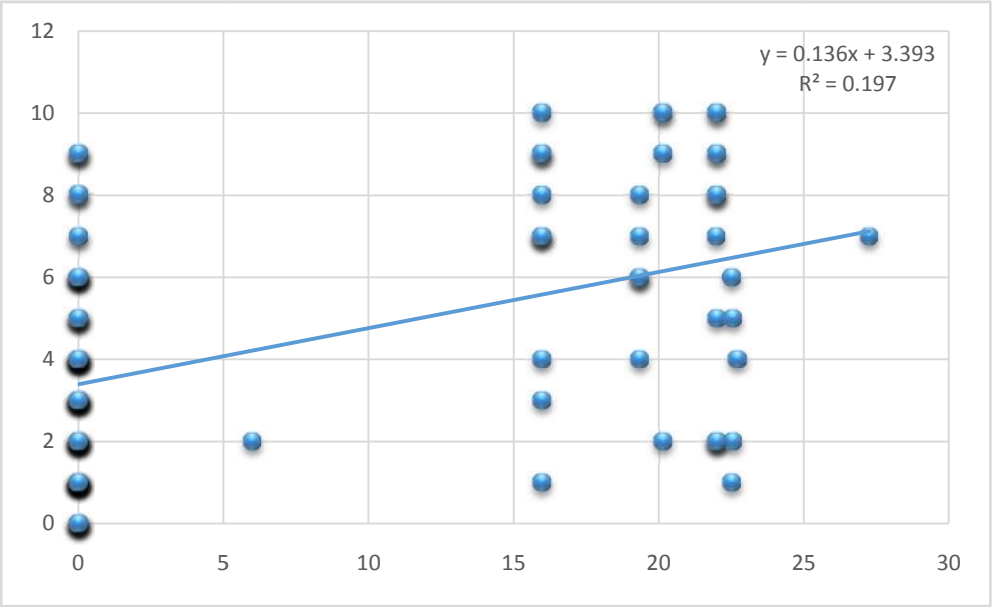


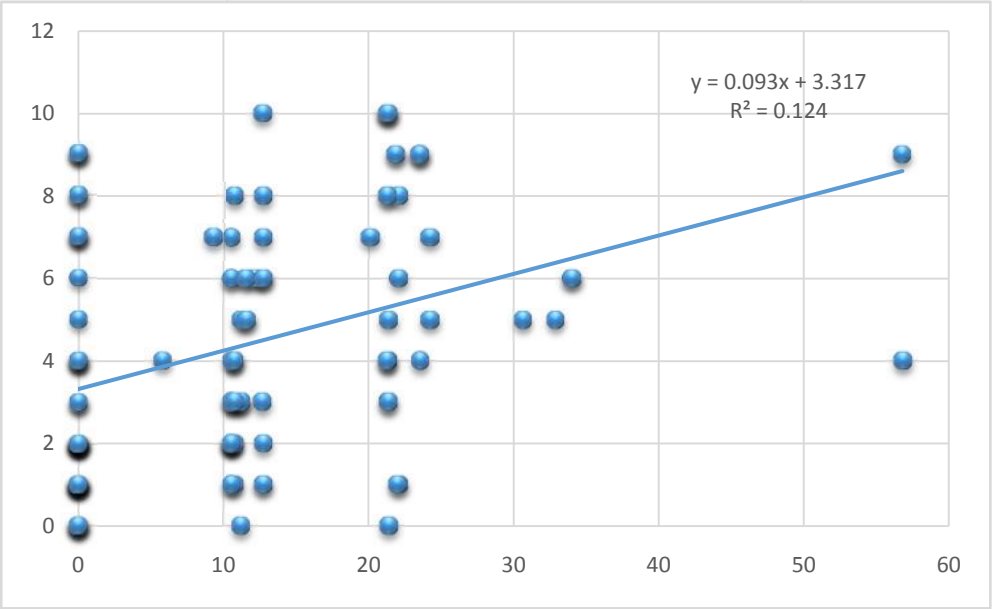
Table 25: Correlation among BODE index, SGRQ and NHP

		SGRQ	NHP
BODE	Pearson correlation coefficient	.698	.677
	P value	.001	.001

***p value < 0.05 is significant**

BODE Index is strongly correlated with SGRQ scale and moderately correlated with NHP scale. There was 69.8% correlation among BODE index and SGRQ scale. 67.7% correlation in between BODE index and NHP scale.

Fig.23 :Correlation among BODE index, SGRQ and NHP



UNIVARIATE AND MULTIVARIATE REGRESSION ANALYSIS :

Table 26: Univariate analysis between BODE index and SGRQ symptom score

Descriptive Statistics			
	Mean	Std. Deviation	N
BODE	4.298	2.9272	124
Symptoms score	46.079	21.3827	124

Model Summary				
Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.682a	.465	.461	2.1501
a. Predictors: (Constant), Symptoms score				

Coefficients a								
Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95.0% Confidence Interval for B	
		B	Std. Error	Beta			Lower Bound	Upper Bound
1	(Constant)	-.003	.460		-.006	.995	-.914	.908
	Symptoms score	.093	.009	.682	10.295	.000	.075	.111
a. Dependent Variable: BODE								

Regression analysis explains the amount of correlation between the two variables and validity of the test scale. In this study, the test scale was BODE index. Regression analysis done between symptom score of SGRQ scale and BODE index shows the validity of BODE index in comparison with symptom score of SGRQ scale was 46.5%

Table.27: Univariate analysis between BODE index and SGRQ activity score

Descriptive Statistics			
	Mean	Std. Deviation	N
BODE	4.298	2.9272	124
Activity score	37.911921776554635	20.917501459338170	124

Model Summary				
Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.643a	.413	.409	2.2510
a. Predictors: (Constant), Activity score				

Coefficients a								
Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95.0% Confidence Interval for B	
		B	Std. Error	Beta			Lower Bound	Upper Bound
1	(Constant)	.887	.420		2.113	.037	.056	1.718
	Activity score	.090	.010	.643	9.274	.000	.071	.109
a. Dependent Variable: BODE								

BODE index was moderately correlated with activity score. It was 41.3% valid when compared with activity score of SGRQ scale.

Table 28.Univariate analysis between BODE index and SGRQ impact score

Descriptive Statistics			
	Mean	Std. Deviation	N
BODE	4.298	2.9272	124
Impacts score	18.740429584088425	15.711800638836250	124

Model Summary				
Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.612a	.374	.369	2.3253
a. Predictors: (Constant), Impacts score				

Coefficients a								
Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95.0% Confidence Interval for B	
		B	Std. Error	Beta			Lower Bound	Upper Bound
1	(Constant)	2.163	.326		6.638	.000	1.518	2.808
	Impacts score	.114	.013	.612	8.539	.000	.088	.140
a. Dependent Variable: BODE								

Regression analysis is done between BODE index and impact score of SGRQ scale. It was found that BODE index is 37.4% valid in comparison with impact score.

Table 29.Univariate analysis between BODE index and SGRQ total score

Descriptive Statistics			
	Mean	Std. Deviation	N
BODE	4.298	2.9272	124
Total score	29.678142914626640	16.795281103216208	124

Model Summary				
Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.698a	.487	.482	2.1062
a. Predictors: (Constant), Total score				

Coefficients a								
Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95.0% Confidence Interval for B	
		B	Std. Error	Beta			Lower Bound	Upper Bound
1	(Constant)	.690	.385		1.792	.076	-.072	1.453
	Total score	.122	.011	.698	10.752	.000	.099	.144
a. Dependent Variable: BODE								

BODE index was strongly correlated with SGRQ total score as Pearson correlation coefficient is 0.698 with p value of 0.0001. Univariate regression analysis shows that BODE index is 48.7% valid in comparison to SGRQ scale.

Table 30. Multivariate analysis between BODE index and SGRQ score

Model Summary				
Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.736a	.542	.527	2.0136
a. Predictors: (Constant), Total score, Symptoms score, Activity score, Impacts score				

Coefficients a								
Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95.0% Confidence Interval for B	
		B	Std. Error	Beta			Lower Bound	Upper Bound
1	(Constant)	-.368	.477		-.772	.441	-1.312	.576
	Symptoms score	.048	.016	.350	2.997	.003	.016	.080
	Activity score	.020	.024	.142	.815	.417	-.028	.068
	Impacts score	-.023	.044	-.126	-.537	.592	-.110	.063
	Total score	.072	.068	.415	1.057	.293	-.063	.208
a. Dependent Variable: BODE								

Multivariate analysis is done in between SGRQ scores and BODE index to know the validity of BODE index with less errors. Constants are symptom score, impact score, activity score and total score. BODE index is the dependant variable. R^2 value in this multivariate analysis is 0.542 which shows BODE index is 54.2% valid in comparison to SGRQ.

Table 31.Univariate analysis between BODE index and energy level component

Descriptive Statistics			
	Mean	Std. Deviation	N
BODE	4.298	2.9272	124
EL	10.9938	16.48159	124

Model Summary				
Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.488a	.238	.232	2.5657
a. Predictors: (Constant), EL				

Coefficients a								
Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95.0% Confidence Interval for B	
		B	Std. Error	Beta			Lower Bound	Upper Bound
1	(Constant)	3.346	.277		12.065	.000	2.797	3.895
	EL	.087	.014	.488	6.173	.000	.059	.114
a. Dependent Variable: BODE								

Nottingham Health Profile (NHP) has five components. Correlation between BODE index and each component of NHP along with validity of BODE index in comparison to NHP scale has been measured. The above table shows that Energy level component of NHP is moderately correlated with BODE index. BODE index is 23.8% valid in comparison to energy level component of NHP scale.

Table 32.Univariate analysis between BODE index and pain component

Descriptive Statistics			
	Mean	Std. Deviation	N
BODE	4.298	2.9272	124
P	8.9856	8.67854	124

Model Summary				
Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.577a	.333	.327	2.4009
a. Predictors: (Constant), P				

Coefficients a								
Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95.0% Confidence Interval for B	
		B	Std. Error	Beta			Lower Bound	Upper Bound
1	(Constant)	2.550	.311		8.199	.000	1.934	3.166
	P	.195	.025	.577	7.800	.000	.145	.244
a. Dependent Variable: BODE								

BODE index was moderately correlated with pain component of NHP scale. It was 33.3% valid in comparison to pain component of NHP scale.

Table 33.Univaraite analysis between BODE index and emotional reaction component

Descriptive Statistics			
	Mean	Std. Deviation	N
BODE	4.298	2.9272	124
ER	7.6244	7.05018	124

Model Summary				
Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.422a	.178	.172	2.6640
a. Predictors: (Constant), ER				

Coefficients a								
Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95.0% Confidence Interval for B	
		B	Std. Error	Beta			Lower Bound	Upper Bound
1	(Constant)	2.961	.353		8.384	.000	2.262	3.660
	ER	.175	.034	.422	5.149	.000	.108	.243
a. Dependent Variable: BODE								

BODE index was moderately correlated with emotional reaction component of NHP scale. It has 17.8% validity in comparison to emotional reaction component of NHP scale.

Table 34. Correlation between BODE index and sleep component

Descriptive Statistics			
	Mean	Std. Deviation	N
BODE	4.298	2.9272	124
S	13.1285	10.27639	124

Model Summary				
Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.420a	.177	.170	2.6667
a. Predictors: (Constant), S				

Coefficients a								
Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95.0% Confidence Interval for B	
		B	Std. Error	Beta			Lower Bound	Upper Bound
1	(Constant)	2.726	.390		6.998	.000	1.955	3.497
	S	.120	.023	.420	5.119	.000	.073	.166
a. Dependent Variable: BODE								

BODE index was significantly associated with sleep component of BODE index. Pearson correlation coefficient was 0.42; hence there was moderate correlation between the two. BODE index is 17.7% valid in comparison to sleep component of NHP scale. The validation in this aspect seems to be low.

Table 35.Univariate analysis between BODE index and social isolation component

Descriptive Statistics			
	Mean	Std. Deviation	N
BODE	4.298	2.9272	124
SI	6.6171	9.50945	124

Model Summary				
Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.444a	.197	.191	2.6334
a. Predictors: (Constant), SI				

Coefficients a								
Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95.0% Confidence Interval for B	
		B	Std. Error	Beta			Lower Bound	Upper Bound
1	(Constant)	3.394	.288		11.764	.000	2.823	3.965
	SI	.137	.025	.444	5.476	.000	.087	.186
a. Dependent Variable: BODE								

Univariate analysis was done in between BODE index and social isolation component of NHP scale. BODE index was 19.7% valid in comparison to social isolation component of NHP scale. Validity seems to be low for this component.

Table 36.Univariate analysis between BODE index and physical ability component

Descriptive Statistics			
	Mean	Std. Deviation	N
BODE	4.298	2.9272	124
PA	10.5443	11.09358	124

Model Summary				
Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.353a	.124	.117	2.7504
a. Predictors: (Constant), PA				

Coefficients a								
Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95.0% Confidence Interval for B	
		B	Std. Error	Beta			Lower Bound	Upper Bound
1	(Constant)	3.317	.341		9.716	.000	2.641	3.993
	PA	.093	.022	.353	4.163	.000	.049	.137
a. Dependent Variable: BODE								

Univariate analysis shows that BODE index in comparison to physical ability component of NHP scale is 12.4% valid.

Table 37.Multivariate analysis between BODE index and NHP

Model Summary				
Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.785a	.616	.593	1.8667
a. Predictors: (Constant), PA, EL, ER, P, SI, S, NHP1				

Coefficients a								
Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95.0% Confidence Interval for B	
		B	Std. Error	Beta			Lower Bound	Upper Bound
1	(Constant)	.489	.369		1.323	.188	-.243	1.220
	NHP	.363	.141	.256	2.566	.012	.083	.642
	EL	.043	.011	.244	3.830	.000	.021	.066
	P	.100	.023	.298	4.327	.000	.054	.146
	ER	.055	.029	.133	1.894	.061	-.003	.113
	S	.017	.020	.061	.879	.381	-.022	.057
	SI	.043	.020	.139	2.088	.039	.002	.083
	PA	.006	.018	.024	.355	.723	-.029	.042
a. Dependent Variable: BODE								

Multivariate regression analysis minimizes the errors and it was better than univariate analysis for comparing two scales with multiple components. BODE index and NHP scale are significantly associated and moderately correlated. R^2 value is 0.616 which explains that BODE index is 61.6% valid in comparison with NHP scale.

DISCUSSION :

COPD is one among the leading causes of death all over the world. Symptoms are persistent with high level of disability. Treatment goals for this disease are mostly palliative like reducing symptoms and increasing functions. As the disease progresses, the HRQOL in these patients worsens because of their poor work ability and declined participation in social and physical activities[96,97]. Nevertheless, diagnosis and monitoring of the disease progression mainly depends on objective tests rather than subjective evaluation leading to poor assessment of HRQOL. For the same reason, over the last decade, research on the development and validation of HRQOL measurement scales are being taken up. Recently, a new multidimensional scoring system named BODE index was proposed to know the prognosis of COPD patients. Present study is done to measure HRQOL in COPD patients and it validates BODE index with other standard scales like St.George Respiratory Questionnaire (SGRQ) and Nottingham Health Profile (NHP)

155 patients were screened for this study, 26 patients had other chronic lung diseases, 5 patients couldn't perform Spirometry or 6 minute walk test, hence they were excluded from this study. Finally, 124 diagnosed cases of COPD were considered for the study. Clinical examination, pulmonary function test, answering questionnaires and performing 6 minute walk test was done on the same day in the same order.

Most of the patients were men (n=80) which accounted to 64.5% of the study group and most of them belonged to the age group of 61-80 years. Women (n=44) accounted to 35.5% and most of them belonged to the age group of 61-70 years. Mean

age of the cases were 67.37 ± 7.93 years. The higher study age is comparable to the mean age in other studies[40,64,98]. Though this study prove. that there is no significant correlation between age and HRQOL. A study done by Corlateanu et al[99] suggests that rather than age the level of obstruction is one of the major determinants of HRQOL. Malik et al[100]observed that the increasing age correlated with declining health related quality of life.

A total of 63% of the study population were smokers and majority of them were men but no statistical significance was found between smoking and BODE index. In a study done by Tan et al[101], which analysed data from BOLD and CanCOLD studies compared obstructive pattern in ever smokers and never smokers. This study group has 5176 general population whose age was >40 years. 47% of the study group were never smokers and 53% were ever smokers with varying smoking indices. The prevalence of obstruction in never smokers was 6.43% and it was 15.28% in ever smokers which was significant. Studies which assessed relation between smoking and HRQOL had mixed results. Study done by Vinay et al[102] in Oklahoma city, USA proved that current smokers had declining health related quality of life unlike ex smokers who had no correlation.

The average disease duration in the present study group was 5.12 ± 3.42 years and there was no significant correlation found between COPD duration and BODE index. Number of hospitalizations during their disease period was 1.52 ± 1.37 and a significant correlation was observed between number of hospitalisations and BODE index. These findings were in co ordinance with study done by Sarioglu et al.[102]

Mean BMI in the study group was 23.81 ± 5.77. A total of 16.9% of patients were underweight and 12.9% of patients were obese. Another 48.4% of patients had

normal BMI. A significant and moderate negative correlation was observed in between BMI and BODE index. In one of the studies done by Sarioglu et al[98], mean BMI of COPD study group was similar to this study and a positive correlation was found in between 6MWT and BMI rather than other components of BODE index. Amoros et al[104]has observed similar findings in their study where majority of the study group had BMI above 21kg/m^2. A study done by Naushad et al[105] had a similar mean BMI in the study population but there was no correlation between BMI and COPD.

A total of 58.8% of the patients in study group were hypertensives and 34.6% were diabetic. They could be confounding factors for poor HRQOL although significance was not found in this study. Cote et al[106] studied 683 COPD patients with comorbidities and observed significance between comorbidities and COPD exacerbations. ECLIPSE (Evaluation of COPD Longitudinally to Identify Predictive Surrogate End-points) study also had similar results[106]. A Pan European study done by Jones et al[108] showed worsening in HRQOL with increase in number of comorbidities especially $\geq$3.

The primary objective of this study is to measure BODE index in stable COPD patients. BODE index constitutes of four components: BMI which has score of 0-1, Obstruction of airways which is measured by FEV_1 (spirometric value) which has a score of 0-3, level of Dyspnea (MMRC grading) with a scores of 0-3 and Exercise capacity (6MWT) with a score of 0-3. The combined score of all four components comes up to 0-10. Most of the patients in this study are in a score range of 1-6. In order to compare with GOLD severity staging, BODE quartiles were made and scores 0-2 were categorised as BODE quartile 1 which had 44 patients. This is the major

group in this study. 2nd BODE quartile had 36 patients and score ranges from 3-5, 3rd quartile ranges from 6-8 with 29 patients and 4th quartile had 15 patients with scores of 9 and 10. It is correlated with mild, moderate, severe and very severe COPD as per GOLD 2017 guidelines. Though all levels of severity of COPD are found in this study, most of them were moderate and severe COPD groups as per GOLD classification and it is mild, moderate and severe COPD patients as per BODE quartiles.

The study done by Elamparithi et al[107] in 250 stable COPD patients had similar results and BODE quartiles were correlated with COPD severity stages (GOLD guidelines)

BODE quartiles were compared with MMRC dyspnea scale. Statistically significant correlation was observed between both the indices. HRQOL in 200 COPD cases were assessed in one of the studies done by Taghreed et al[109] in Tanta, Egypt which showed a strong positive correlation between BODE index and MMRC scale similar to the present study. It is also in co ordinance with the Indian study done by Venugopalet al[110] which observed a strong correlation between MMRC and BODE index.

Secondary objective of the present study was to find out the predictive validity of BODE index to measure HRQOL. St.George Respiratory questionnaire (SGRQ) and Nottingham Health Profile (NHP)were used as tools to validate BODE index. SGRQ is a COPD specific questionnaire. A study done by Ferrer[6] et al in Barcelona, Spain observed high sensitivity and specificity of SGRQ to measure HRQLI in COPD cases. Study done by Mullerova et al[58] in 12043 COPD patients proved that baseline SGRQ can predict outcome of COPD patients like further hospital admissions,

exacerbations and quality of life. In this study, significant positive correlation was observed between SGRQ and MMRC scale which was similar to the present study.

Nottingham Health Profile (NHP) is useful to know the quality of life. In the present study, NHP was found to have moderate correlation with MMRC scale. This is in correlation with the study done in Alonso et al[111].

Secondary objective of the present study was to validate BODE index with SGRQ and NHP. Pearson correlation coefficient analysis was done to know the association between BODE index and HRQOL. Symptom score, activity score and impact score of SGRQ were observed to be moderately and positively correlated with BODE index. Total SGRQ score was strongly and positively correlated with BODE index. A study done by Amoros et al[98], in 67 COPD patients in Spain found moderate positive correlation between individual SGRQ component scores and total score which is in co ordinance with this study. A study done in 97 COPD patients by Shrikar Tripathi et al[112] in UP, India also found to have a moderate positive correlation between all SGRQ scores and BODE index.

Studies done by Sarkar et al[113] and Nonato et al[14] concluded that BODE index had very strong correlation with SGRQ total score, impact score and activity score but it had a moderate correlation with symptom domain unlike this study. Although positive correlation is seen in all the studies, level of correlation varied in various studies.

Performing secondary analysis ie Univariate regression analysis was done in between individual and total score of SGRQ and BODE index. Symptom score had 46.5% correlation, activity score had 41.3% correlation, impact score had 37.4%

correlation with BODE index. Psychological and social impact of the disease appears to be least predicted by BODE index. Total SGRQ score in univariate regression analysis showed 48.7% predictive validity of BODE index which is in co ordinance with the results of a Spanish study done by Amoros et al[98], which had a correlation of 46.1% among BODE index and SGRQ. Unlike our study, their study had a very low correlation between symptom score and activity score with BODE index 19.5% and 30.7% respectively. On a whole, BODE index can predict HRQOL by 54.2% in comparison to SGRQ which was predicted by multivariate regression analysis (minimal errors in comparison to univariate analysis)

Study done by Taghreed et al[109] in 200 stable COPD patients showed that FEV_1, MMRC, GOLD staging, IHD, exacerbations per year and 6MWD were the best predictors of impaired HRQOL that is, a prediction of 81.6% and BODE index had significant correlation with a less r^2 value. Although findings of activity score correlation are in consistency with our study, total score result is not in consistency with our study.

Pearson correlation coefficient analysis was done in between BODE index and each component of NHP. Moderate positive correlation is found in between components like energy level, pain, emotional reaction, sleep, social isolation and BODE index. Univariate regression analysis was done to know the level of correlation. BODE index can predict energy level up to 23.8% in comparison to NHP. It can predict pain up to 33.3%, emotional reaction up to 17.8%, sleep up to 17.7%, social isolation up to 19.7% and physical ability up to 12.4% which is very low. But in multivariate regression analysis, BODE index had a predictive validity of 61.1% in comparison to NHP. Hence it shows overall HRQOL is well predicted with BODE

index although individual components had no much validity. In the present study done by Amoros et al,[98] correlation was found between NHP total score, physical ability and energy level. Other components (pain, sleep, social isolation, emotional reaction) had no correlation with BODE index unlike our study. In their study, BODE index had only 14.8% validity unlike our study which had 61.1% validity in comparison to NHP. Although, low validity of individual components shows similarity with their study.

Strengths of the study :

- This study was a cross sectional study and included all stable COPD patients who visited OPD of a tertiary care centre in one year.
- The study used a structured analytical tool for measuring health related of life in COPD patients
- This is one among the few studies done to predict health related quality of life using BODE index. Limited data was available about predictive validity of BODE index
- This is the first of its kind to compare BODE index with general quality of life questionnaire that is Nottingham Health Profile.

Limitations of the study :

- The samples were selected from a single centre.
- The sample size of 124 is not adequate enough to highlight the importance of BODE index as a measure of HRQOL.
- Since SGRQ was a long, self administered questionnaire, it was difficult to be administered in OPD and most of the times; it was taken on interview basis.
- Most of the questions in SGRQ scale were not suitable in Indian scenario, especially in our setup, like playing golf, swimming on regular basis etc which might have created biased results and this requires to be customised for Indian patients.
- Since missing data doesn't give results in SGRQ excel sheet, such questions had to be replaced by questions apt for Indian scenario which is not validated by any study. This might have created bias in the results.

CONCLUSIONS :

- BODE index is a simple yet a powerful predictor of HRQOL in stable COPD patients.
- Increased score will result in poor HRQOL in stable COPD patients.
- It is simple to apply unlike SGRQ and other lengthy scales.
- It gives both subjective and objective evaluation of the disease.
- It helps the clinicians to predict HRQOL in patients so as to modify treatment and counsel them accordingly.
- Quality of life as a measurement of disease increases and compliments the clinical staging of disease, adding data to the psychological and social well being of these patients at different stages.

SUMMARY

- A total of 155 COPD cases were initially analysed for inclusion in the study. After selection criteria, 124 patients were included in the study to measure HRQOL by BODE index and its validity was checked by comparing it with SGRQ and NHP scales.
- The study cohort had 80 males (64.5%) and 44 females (35.5%) with a mean age of 67.37±7.93 years and mean predicted FEV_1 % of 52.04±15.57.
- Demographic data, clinical examination, PFT, 6MWT and oral questionnaires regarding SGRQ and NHP were taken in all the patients in the same order on the same day.
- After measuring BMI, Obstruction of airways (FEV_1) by PFT, breathlessness by MMRC grading and exercise capacity by 6MWT, BODE index was calculated.
- BODE score ranges from 0-10. Then BODE quartiles were made.
- Most of the patients in study group belonged to moderate to severe COPD groups as per GOLD COPD staging and BODE quartiles correlated with GOLD severity staging.
- BODE index was found to have positive correlation with number of hospitalisations, MMRC grading system and a strong negative correlation is observed with BMI and $FEV_{1.}$
- Smoking didn't affect HRQOL of COPD cases.
- A strong correlation was observed between MMRC grading, SGRQ scoring system and NHP scale.

- Strong positive correlation was observed between BODE index and SGRQ total score.
- Moderate positive correlation was observed in between BODE index and individual components of SGRQ scale ie, symptom score, activity score and impact score.
- Moderate positive correlation was observed between BODE index and NHP components i.e. pain, energy level, emotional reaction, sleep, social isolation and physical ability.
- Univariate regression analysis was done to measure the validity of BODE index. It was found that BODE index had 46.5% validity as compared to symptom score of SGRQ, 41.3% in comparison to activity score and 37.4% in comparison to impact score.
- Multivariate analysis showed that BODE index had 54.2% validity as compared to SGRQ scale.
- Univariate regression analysis was done in between BODE index and NHP scale. BODE index was 23.8% valid in comparison with energy level component, 33.3% valid in comparison with pain component, 17.8% valid in comparison with emotional reaction component, 17.7% valid in comparison with sleep component, 19.7% valid in comparison with social isolation component and 12.4% valid in comparison with physical ability component.
- Multivariate regression analysis showed that BODE index had 61.6% validity as compared to NHP scale.

BIBLIOGRAPHY :

1. Global Initiative for Chronic Lung Disease. Global strategy for the diagnosis, management and prevention of chronic obstructive lung disease.Updated 2017. Available from http:// www. goldcopd. Com (Accessed on August 13th, 2019) .
2. Brooks D, Solway S, Gibbons WJ. ATS Committee on proficiency standards for clinical pulmonary function laboratories. ATS statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med 2002;166:111-17
3. Salvi S, Kumar GA, Dhaliwal RS, Paulson K, Agrawal A, Koul PA, et al. The burden of chronic respiratory diseases and their heterogeneity across the states of India: the Global burden of disease study 1990–2016. Lancet 2018; 96:e1363–74.
4. Antonelli-Incalxi R, Corsonella A, Pedone C. Drawing impairement predicts mortality in severe COPD. Chest 2006;130:1687-94
5. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PLOS Med 2006; 3(11): e442-47.
6. Ferrer M, Villasante C, Alonso J, Sobradillo V, Gabriel R. Interpretation of quality of life scores from the St George's Respiratory Questionnaire. Eur Respir J 2002; 19: 405–13
7. Jans MP, Schellevis FG, Eijk JTV. The Nottingham Health Profile: score distribution, internal consistency and validity in asthma and COPD patients. Qual Life Res 1999; 8(6): 501–07.
8. Weatherall SM, Shirtcliffe P, Williams M, Travers J, Beasley R. Quality of life measured by the St George's Respiratory Questionnaire and spirometry. Eur Respir J 2009; 33:1025–30.

9. Edurado J, Mortani B Jr, Warren BG. Pathophysiological changes in COPD.In:Fishman'sPulmonary Diseases and Disorders.Elias JA, Kotloff RM, Fishman JA, Pack AI, Senior RM(Editors). Chicago: McGrawHill (publication) 2015:412-67.
10. Salvi S, Agarwal A. India needs a national COPD prevention and control program. JAPI 2012;60:5-7.
11. Buist AS, McBurnie MA, Vollmer WM, Gillespie S, Burney P, Mannino DM, et al. BOLD collabarative research group. International variation in the prevalence of COPD (the BOLD study): A population based prevalence study. Lancet2007;370(9589):741-50.
12. Gupta D, Agarwal R, Aggarwal AN, Maturu VN, Dhooria S, Prasad KT, et al. Guidelines for diagnosis and management of chronic obstructive pulmonary disease on behalf of Indian Chest Society and National College of Chest Physicians 2014.Indian J Chest Dis Allied Sci 2014;56:1-54.
13. Murthy KJ, Sastry JG. Burden of diseases in India. Published by National commission on macroeconomic and health. New Delhi: Ministry of Health and Family Welfare; Economic burden of COPD; 264–74.
14. Nonato NL, Díaz O, Nascimento OA, Dreyse J, Jardim JR, Lisboa C. Behaviour of quality of life in COPD patients according to BODE scores. Int J of Thorac Med 2015; 51:315–21.
15. Malik Sk. Profile of chronic bronchitis in North India. The PGI experience (1972-1985).Lung India.1986;4:89-100.
16. Ray D, Abel R, Selvaraj KG. A 5 year prospective epidemiological study of chronic obstructive pulmonary disease in rural South India. Indian J Med Res.1995;101:238-44.

17. Jindal SK, Aggarwal AN, Chaudhry K, Chhabra SK, D'Souza GA, Gupta D, et al. A multicentric study on epidemiology of chronic obstructive pulmonary disease and its relationship with tobacco smoke exposure. Indian J Chest Dis Allied Sci.2006;48:23-29.
18. Jindal SK. Indian study on epidemiology of asthma, respiratory symptoms and chronic bronchitis (INSEARCH) 2006-2009;1:17-20.
19. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030.PLoS Med 2006;3:2011-30.
20. Lakiang, Nair NS, Ramaswamy A, Singhal U. Economic impact of chronic obstructive pulmonary disease. A cross sectional study at a teaching hospital in South India. J Family Med Prim Care 2018;7:1002-6
21. Eriksson S. Pulmonary emphysema and alpha1 antitrypsin deficiency. J of Intern Med 1964;175:197-205
22. Mukherjee B, SalavaggioneOE, Pelleymounter LL, Moon I, Eckloff BW, Daniel J et al. Drug Metab Dispos.2006;34:1237-1246.
23. Repapi E, Sayers I, Wain LV, Burton PR, Johnson T, Obeidat M,et al. Genome wide association study identifies five loci associated with lung function. Nat Genet 2010;42:36-44.
24. Eisner M, Anthonissen N, Coultas D, Kuenzil N, Padilla R, Postma D, et al. Novel risk factors and the global burden of COPD. Am J Respir Crit Care Med 2010;182;693-718.
25. Guzman ED, Manino DM. Epidemiology and prevalence of chronic obstructive pulmonary disease. Clin Chest Med 2014;35(1):7-16.

26. Cohansal R, Martinez CP, Agusti A, Buist AS, Mannino DM, Soriano JB. The natural history of chronic airflow limitation revisited: An analysis of the Framingham offspring cohort. Am J Resp Crit Care Med 2009;180;3-10.
27. Thomsen M, Nordestgaard BG, Vestbo J, LangeP. Characteristics and outcomes of chronic obstructive pulmonary disease in never smokers in Denmark: a prospective population study. Lancet Respir Med 2013; 1: 543–550
28. Arbat S, Arbat A, Agarwal B, Deshpande P. Clinical profile of non-smoker patients with COPD. Chest2019;211:155-64
29. Perez MF, Atuegwu N, Mead E, Oncken C, Mortensen EM. E-cigarette use is associated with emphysema, chronic bronchitis and COPD. Am J Respir Crit Care Med 2018;197:A6245-49.
30. Schikowski T, Mills IC, Anderson HR, Cohen A, Hansell A, Kauffmann F, et al. Ambient air pollution: a cause of COPD. Eur Respir J 2014; 43:250-63.
31. Barker DJ, Godfrey KM, Fall C, Osmond C, Winter PD, Shaheen SO. Relation of birth weight and childhood respiratory infections to adult lung function and death from COPD. BMJ 1991;303:671-5
32. Menezes AM, Hallal PC, Perez PR, Jardim JR, Muino A, Lopez MV, et al. Tuberculosis and airflow obstruction : Evidence from PLATINO study in Latin America. Eur Respir J 2007;30:1180-5.
33. Prescott E, Lange P, Vestibo J. Socioeconomic status , lung functions and admission to hospital for COPD : Result from Copenhagen city heart study. Eur Respir J 1999;13:1109-14.
34. Barnes PJ. Cellular and molecular mechanisms of chronic obstructive pulmonary disease. Clin Chest Med 2014;35(1):71-86.

35. O'Donnel DE, Webb KA. Exertional breathlessness in patients with chronic airflow limitation. The role of lung hyperinflation. Am J Respir Dis 1993;48:1351-57
36. Hughes RL, Katz H, Sahgal V, Campbell JA, Hartz R, Sheilds TW. Fibre size and energy metabolites in five separate muscles from patients with chronic obstructive pulmonary disease. Respiration 1983;20:44-47.
37. Schols AM, Slangen J, Volovics L, Wouters EF. Weight loss is a reversible factor in the prognosis of chronic obstructive pulmonary disease, Am J Respir Crit Care Med 1998;157:1791- 97
38. Calverly PMA, Anderson JA, Celli B, Ferguson GT, Jerkins C, Jones PW, et al. Salmeterol and Fluticasone proprionate and survival in chronic obstructive pulmonary disease. N Engl J Med 2007:356;775-78.
39. Pauwels RA, Buist AS, Calverly PM, Jenkins CR, Hurd SS. Global strategy for diagnosis, management and prevention of chronic obstructive pulmonary disease. NHLBI/WHO global initiative for chronic obstructive pulmonary disease workshop summary. Am J RespCrit Care Med 2001;163:1256-76.
40. Celli BR, Thomas NE, Anderson JA, Ferguson GT, Jenkins CR, Jones PW et al. Effect of pharmacotherapy on rate of decline of lung functions in COPD : Results from TORCH study. Am J RespCrit Care Med 2008;178:332-8.
41. Shah PL, Herth FJ, Van Geffen WH, Deslee G, Slebos DJ. Lung volume reduction for emphysema. Lancet Respir Med. 2017; 95: 147-56
42. Decramer M, Janssens W, Miravitles M. Chronic obstructive pulmonary disease. Lancet2012;379:1341-51.
43. Kelly AM, McAlpine R, Kyle E. How accurate are pulse oximeter in patients with acute exacerbations of COPD. Res Med 2001;95:336-40.

44. Diab N, Gershon AS, Sin DD,Tan WC, Bourbeau J, Boulet LP, et al. Underdiagnosis and overdiagnosis of chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2018;198(9):1130–39.
45. Murray CJ, Barber RM, Foreman KJ, Abbasoglu OA, Abd-Allah F, Abera SF et al. Global, regional, and national disability-adjusted life years (DALYs) for 306 diseases and injuries and healthy life expectancy (HALE) for 188 countries, 1990-2013: quantifying the epidemiological transition. Lancet 2015; 386(10009): 2145-91.
46. Murray CJ, Atkinson C, Bhalla K, Birbeck G, Burstein R, Chou D, et al. The state of US health, 1990-2010: burden of diseases, injuries, and risk factors. JAMA 2013; 310(6): 591-608.
47. Fletcher CM, Elmes PC, Fairbarn AS, Wood CH. The significance of respiratory symptoms and the diagnosis of chronic bronchitis in a working population. BMJ 1960;12:1662-68
48. Hunninghake GM, Cho MH, Tesfaigzi Y, Soto-Quiros ME, Avila L, Lasky-Su J,et al. MMP12, lung function, and COPD in high-risk populations. N Engl J Med 2009; 361: 2599-608.
49. Ding Z, Wang K, Li J, Tan Q, Tan W, Guo G. Association between glutathione S-transferase gene M1 and T1 polymorphisms and chronic obstructive pulmonary disease risk: A meta-analysis. Int J Gen Mol Per Med.2019 Jan;95(1):53-62
50. Lopez VMV, Montes DMM, Halbert RJ, Muiño A, Perez-Padilla R, Tálamo C, et al. Sex-related differences in COPD in five Latin American cities: the PLATINO study. Eur Respir J 2010; 36(5): 1034-41.

51. Tam A, Churg A, Wright JL, Zhou S, Kirby M, Coxson HO et al. Sex differences in airway remodelling in a mouse model of chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2016; 193(8): 825-34.
52. Allinson JP, Hardy R, Donaldson GC, Shaheen SO, Kuh D, Wedzicha JA. Combined impact of smoking and early-life exposures on adult lung function trajectories. Am J Respir Crit Care Med 2017; 196(8): 1021-30.
53. Lawlor DA, Ebrahim S, Davey Smith G. Association of birth weight with adult lung function: findings from the British women's heart and health study and a meta-analysis. Thorax 2005; 60(10): 851-8.
54. Marchetti N, Garshick E, Kinney GL, McKenzie A, Stinson D, Lutz SM et al. Association between occupational exposure and lung function, respiratory symptoms, and high-resolution computed tomography imaging in COPD gene. Am J Respir Crit Care Med 2014; 190(7): 756-62.
55. Hnizdo E, Sullivan PA, Bang KM, Wagner G. Association between chronic obstructive pulmonary disease and employment by industry and occupation in the US population: a study of data from the third national health and nutrition examination Survey. Am J Epidemiol 2002; 156(8): 738-46.
56. Balmes J, Becklake M, Blanc P, Henneberger P, Kreiss K, Mapp C et al. American Thoracic Society statement: Occupational contribution to the burden of airway disease. Am J Respir Crit Care Med 2003; 167(5): 787-97.
57. Orozco LM, Garcia-Aymerich J, Villar J, Ramirez-Sarmiento A, Anto JM, Gea J. Wood smoke exposure and risk of chronic obstructive pulmonary disease. Eur Respir J 2006; 27(3): 542-6.
58. Müllerova H, Gelhorn H, Wilson H, Benson VS, Karlsson N, Menjoge S et al. St George's Respiratory Questionnaire score predicts outcomes in patients with

COPD: Analysis of individual patient data in the COPD biomarkers qualification consortium database. Chronic ObstrPulm Dis. 2017; 4(2): 141-49

59. Agusti A, Calverley PM, Celli B, Coxson HO, Edwards LD, Lomas DAet al. Characterisation of COPD heterogeneity in the ECLIPSE cohort. Respir Res 2010; 11: 122-27.
60. Nishimura K, Mitsuma S, Kobayashi A, Yanagida M, Nakayasu K, Hasegawa Y, et al. COPD and disease-specific health status in a working population. Respir Med 2013; 14: 61-67.
61. Miravitlles M, Soriano J, Garcia-Rio F,Muñoz L, Duran-Tauleria E, Sanchez G,et al. Prevalence of COPD in Spain: impact of undiagnosed COPD on quality of life and daily life activities. Thorax 2009; 64: 863-8.
62. Jones PW, Quirk FH, Baveystock CM. The St George's Respiratory Questionnaire. Respir Med 1991;85: 25–31.
63. Katrin C, Cleary PD, Parker CE, Czeisler CA. The prevalence and health impact of shift work.Qual Life Res 2004;13: 1495-49.
64. Celli R, Cote G, Marin M, Ciro Casinova. The Body-Mass Index, Airflow Obstruction, Dyspnea, and Exercise Capacity Index in Chronic Obstructive Pulmonary Disease.NEngl J Med 2004;350:1005-1012.
65. Claudia GC, Celli BR. BODE Index : A new tool to stage and monitor progression of chronic obstructive lung disease. Advances in Res Med 2009;77:305-313.
66. Ong KC, Earnest A, Lu SJ. A multidimensional grading system (BODE Index)as a predictor for hospitalization of COPD. Chest 2005;128:3810-16.
67. Imfield S, Bloch KE, Weder W, Russi EW. The BODE index after lung volume reduction correlates with survival. Chest 2006;129:835-36.

68. Cote CG, Celli BR. Pulmonary rehabilitation and the BODE Index in COPD. Eur Respir J 2005;26:630-36.
69. Nelson E, Landgraf JM, Hays RD, Wasson JH, Kirk JW. The functional status of patients: How can it be measured in physician's office. Med Care 1990; 28:1111-26.
70. Landgraf JM, Nelson EC, Dartmouth COOP Primary Care Network. Summary of the WONCA/COOP International health assessment field trial. Aust Fam Physic 1992; 21:255-69.
71. Rabin R, Charro F.EuroQol-A new facility for the measurement of health-related quality of life. Health Policy1990; 16:199-208.
72. Brazier JE, Jones N, Kind P. Testing the validity of the EuroQol and comparing it with the SF-36 health survey questionnaire. Quality Life Res. 1993; 2:169-180.
73. Leidy NK. Functional status and the forward progress of merry-go-rounds: Toward a coherent analytical framework. Nurs Res 1994;43(4):196-202.
74. Hunt SM, McEwen J, McKenna SP. Measuring health stats: a new tool for clinicians and epidemiologists. J Royal Coll Gen Pract 1985;35:185-88.
75. Van-Schayck C, Rutten-van MM, van-Doorslaer E, Folgering H, Weel C. Two-year bronchodilator treatment in patients with mild airflow obstruction: contradictory effects on lung function and quality of life. Chest 1992;102 (5):1384-91.
76. Morimoto M, Takai K, Nakajima K, Kagawa K. Development of the chronic obstructive pulmonary disease activity rating scale: Reliability, validity and factorial structure. Nur Health Sci 2003; 5:23-30.

77. Moran LA, Guyatt GH, Norman GR. Establishing the minimal number of items for a responsive, valid, health-related quality of life instrument. J Clin Epidemiol 2001;54(6): 571-9.
78. Lee SD, Huang MS, Kang J, Hsiung C, Park J, Yeon-Mok Oh,et al. The COPD assessment test (CAT) assists prediction of COPD exacerbations in high risk patients. Respir Med 2014;108:600-08.
79. Win T, Pearce L, Nathan J, Cafferty F, Laroche C. Use of the airway questionnaire 20 to detect changes in quality of life in asthmatic patients and its association in St George Respiratory Questionnaire and clinical parameters. Can respir J 2008;15:133-37
80. Vander MT, Willems BWM, Schokker S, Hacken NH, Postma DS, Juniper EF. Development, validity and responsiveness of the clinical COPD Questionnaire. Health related quality of life outcomes BMJ 2003;99:13-20.
81. Marin JM, Carrizo SJ, Casanova C, Martinez-Camblor P, Soriano JB Agusti AG et al. Prediction of risk of COPD exacerbations by the BODE index. Respir Med 2009;103:373-75e8.
82. Mckellar A, Cottrell WN, Whelan A. BODE score is useful predictor of hospital admission in rural patients with chronic obstructive pulmonary disease. Respirology 2008;13(3):438-43.
83. Hodgev VA, Stephan SK, Blagoi AM. Correlation of frequency of exacerbations with the BODE index in COPD patients. Folia Med. 2006;48(2):18-22.
84. Fagenello MM, Suzana ET, Fernanda FS, Nilva RGP, Paulo AL. BODE Index and GOLD staging as predictors of risk factors of 1 year exacerbations in COPD. Am J Med Sci 2010,339(1):10-14

85. Karoli NA, Rebrov AP. The BODE index as a predictor of unfavourable prognosis in chronic obstructive pulmonary disease. Lancet 2007;79(3):11-14
86. Ong KC, Earnest A, Lu SJ. A multidimensional grading system (BODE index) as predictor of hospitalization for COPD. Chest 2005;128:3810-21.
87. Mahajan M, Shah A, Francis S, Shah KV. BODE Index as a predictor of severity in patients with chronic obstructive pulmonary disease. J Dent Med Sci 2016; 15(5):2279-853.
88. Shivakumar BG, Krishna V. Study of BODE index as a predictor of severity and systemic involvement in patients with COPD. Ind J Basic Appl Med Res 2015;4(3): 395-404.
89. Wilson DO. Rogers RM, Wright EC, Anthonisen NR. Body weight in chronic obstructive pulmonary disease: The National institute of health intermittent positive pressure breathing trial. Am J Respir Dis.1988;139:1435-38.
90. Schols AM, Slangen J, Volovics L, Wouters EF. Weight loss is a reversible factor in the prognosis of chronic obstructive pulmonary disease. Am J RespCrit Care Med 1998;157:1791-99.
91. Parshall MB, Schwartzstein RM, Adams L, Banzett RB, Manning HL, Bourbeau J et al. An official American Thoracic Society statement: update on the mechanisms, assessment, and management of dyspnea. Amj Respir Crit Care Med2012;185(4):435-52.
92. Walkove N, Dajczman E, Colacone A, Kreisman H. The relationship between pulmonary function and dyspnea in obstructive lung disease. Chest 1989;96:1247-51.

93. Brooks D, Solway S, Gibbons WJ. American Thoracic Society Statement : Interpretation of six minute walk test. Am J RespCrit Care Med 2002;166:115-17.

94. Cote CG, Pinto-Plata V, Kasprzyk K, Dordelly LJ, Celli BR. The 6 minute walk distance, peak oxygen uptake and mortality in COPD patients. Am J Respir Crit Care Med 2003;167(9):1287-91.

95. Claudia GC, Victoria PP, Kyra K, Luis J, Celli BR. The 6 minute walk distance peak oxygen uptake and mortality in COPD, Chest 2007;132:1778-85.

96. Nyberg A, Saey D. American Thoracic Society. Standards for the diagnosis and care of patients with chronic obstructive pulmonary disease. Definitions, epidemiology, pathophysiology, diagnosis and staging. Am J Respir Crit Care 1995; 152: S78–83.

97. Graydon JE, Ross E. Influence of symptoms, lung function, mood and social support on level of functioning of patients with COPD. Res NursHealt 1995; 18: 525–33.

98. Amorós MM, Alorda C, Renom F, Rubí M, Centeno MJ.Quality of life in patients with chronic obstructive pulmonary disease: the predictive validity of the BODE index. Chron Respir Dis.2005;5(1):7-11

99. Alexandru C,Victor B,Serghei C, Silvia D, Nikolaos S. Predicting health related quality of life in patients with chronic obstructive pulmonary disease: The impact of age. Respiration 2016;92:229–34

100. Ahmed MS, Neyaz A, Aslami AN. Health-related quality of life of chronic obstructive pulmonary disease patients: Results from a community based cross-sectional study in Aligarh, Uttar Pradesh, India. Lung India 2016; 33(2): 148–53.

101. Tan WC, Sin DD, Bourbeau J, Hernandaz P, Chapman KR, Cowie R, et al. Characteristics of COPD in never-smokers and ever-smokers in the general population: results from the CanCOLD study. Thorax 2015;70:822-829.
102. Cheruvu VK, Odhiambo LA, Mowls DS, Zullo MD, Gudina AT. Health-related quality of life in current smokers with COPD: factors associated with current smoking and new insights into sex differences. Int J Chronic Obstruct Pulm Dis 2016;15(11):2211-19.
103. Sarioglu N, Alpaydin AO, Coskun AS, Celik P, Ozyurt BC, Yorgancioglu A. Relationship between BODE index, quality of life and inflammatory cytokines in COPD patients. Multidiscip Respir Med 2010; 5: 84-91.
104. Khan NA, Daga MK, Ahmad I, Mawari G, Kumar S, Kumar N, et al.Evaluation of BODE index and its relationship with systemic inflammation mediated by proinflammatory biomarkers in patients with COPD. J Inflamm Res 2016;9:187–98
105. Cote C, Zilberberg MD, Mody SH, Dordelly LJ, Celli B. Haemoglobin level and its clinical impact in a cohort of patients with COPD. Eur Respir J 2007; 29: 923–29.
106. Agusti A, Calverley PM, Celli B, Coxson HO, Edwards LD, Lomas DA, et al. Evaluation of COPD longitudinally to identify predictive surrogate endpoints (ECLIPSE) investigators. Characterisation of COPD heterogeneity in the ECLIPSE cohort. Respir Res 2010; 11: 122-26.
107. Elamparithi S, Aswin S, Babu KB. Health related quality of life among chronic obstructive pulmonary disease patients and its determinants in a hospital based observational study from south India. J Fam Med Prim Care 2018;17:10-16.

108. Jones PW, Brusselle G, DalNegro RW, Ferrer M, Kardos P, Levy ML,et al. Health-related quality of life in patients by COPD severity within primary care setting. EurRespir Med 2011;101: 57–66.

109. Taghreed SF, Eman SM, Sobh SB, Elsawy BMF. Evaluation of health-related quality of life in patients with chronic obstructive pulmonary disease. Egypt J Bronchol 2018;12:288–94

110. Venugopal KP, Thomas GP, Kiran VN, Jain G. The BODE index and health related quality of life-Is there a correlation in COPD. J Heart Lung Tran 2017; 5: 26251-56

111. Alonso J, Anto J, Moreno C. Spanish version of the Nottingham Health Profile: translation and preliminary validity. Am J Pub Health 1990; 80: 704–8.

112. Tripathi S, Srivastava A, Gupta SS, Agarwal A, Verma A, Srivastava A,et al. To study the interrelationship of COPD assessment test (CAT) score with BODE index and SGRQ in patients of COPD. J Evolution Med Dent Sci 2017;6(19):1489-93.

113. Sarkar SK, Basuthakur S, Das SK, Das A, Das S, Choudhury S, et al. Evaluation of correlation of BODE index with health-related quality of life among patients with stable COPD attending a tertiary care hospital. Lung India 2015; 32:24-27.

ANNEXURE -I

INFORMED CONSENT

HEALTH RELATED QUALITY OF LIFE IN STABLE COPD PATIENTS BY BODE INDEX : A ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY

Objective and purpose of the study :

You are being asked to enroll in this study as you are eligible for this study. All stable COPD patients >40 years of age will be included in this study. During this study, patients will be asked questions regarding their presenting complaints and they are supposed to answer to the best of their knowledge. The principal investigator of the study is Dr.Errabelli Harshini under the guidance of Dr.Gajanan S Gaude (Guide)

The purpose of this study is to study Health related quality of life in stable COPD patients and to find the predictive validity of BODE index. COPD is a chronic airway disease with subjective and objective manifestations and BODE index is a new multidimensional scoring system which can assess both subjective and objective manifestations of patient unlike spirometry which assess objective manifestations alone. Hence it is used to assess Health related quality of life in COPD patients and as it is a new index, its validity is also checked in this study.

Proceedure :

Patients whose symptoms are suggestive of COPD or diagnosed cases of COPD attending the outpatient clinic of KLE's Dr.Prabhakar Kore Hospital and MRC will be

subjected to detailed history taking, clinical examination followed by BODE index application.

BODE index contains 4 components. They are :

1. Body Mass Index which is measured by knowing height and weight.
2. Airflow obstruction will be measured using spirometry which is being performed 15 minutes after inhalation of 400 mcg salbutamol according to ATS guidelines.
3. Dyspnea being measured with the help of MMRC dyspnea grading
4. Exercise capacity is tested by performing the best of two 6minute walk tests performed with a gap of 30 minutes interval.

All patients will undergo clinical examination, lung function tests and oral questionnaire on the same day. Within the same session, the clinical, social and demographic data will be collected and lung function tests along with 6 minute walk test will be performed.

All questionnaires will be completed in the same order : SGRQ questionnaire which contains 3 components in 2 parts, NHP questionnaire which has 45 questions in 2 parts, MMRC scale and BMI calculation will be done. Finally BODE index scoring will be done.

Risks and Benefits :

There will be no risks and benefits involved. During the period of study, the existence or development of any significant findings in terms of respiratory illness will be informed to you/your relative as well as the parent consultant for the appropriate action.

Alternative :

Taking part in this study is voluntary. You may choose not to take part in this study or if you decide to take part now, you can later change your mind and withdraw from the study. Your decision will not change the present or future health care or other services that you receive. The study doctor or sponsor may terminate your participation in this study anytime.

Privacy and confidentiality :

All information collected about you during the course of this study will be kept confidential to the extent permitted by law. The code numbers will identify you in this research record. Information from this study will be published but your identity will be confidential in any publication. No information about you or information provided by you during the research will be disclosed to others without your written permission except :

1. In emergency to protect your rights and welfare
2. If required by law.

Institution/Sponsor's policy :

Does not apply to this research.

Financial incentives for participation :

You will not be paid/offered any gifts/incentives for participating in this study.

Compensation :

In the event of any adverse effects related to the study, treatment will be made available through KLES Hospital and MRC, Belgaum. There is no compensation or payment for such medical treatment by law. For any further queries you may contact Dr.Harshini Errabelli , PG in Department of Respiratory Medicine. Ph. No. 8722865205

Authorization to publish results :

The results of this study would be forwarded to KLE Academy of Higher Education, Belgaum as a part of requirement towards the completion of MD degree, review and publishing.

Questions :

In case you have any questions related to the study, in future or in case of study related injury or illness, you can contact :

- Dr.Harshini Errabelli, PG in Department of Respiratory Medicine, KLE'S Dr.Prabhakar Kore Hospital and MRC. Ph.No. 8722865205
- Dr.Gajanan S Gaude, Professor and Head, Department of Respiratory Medicine, KLE'S Dr.Prabhakar Kore Hospital and MRC, Belgaum. Ph.No.0831 2551376
- If you have any queries about your rights as a subject, you may call Dr.RoopaBellad, Professor, Department of Paediatrics, Chairman of JN Medical College, Institutional Ethical Committee of Human Subjects Research, Ph.no. 9448863866 at Jawaharlal Nehru Medical College, Belgaum.

CONSENT STATEMENT

I voluntarily agree to take part in this study by signing below. I may withdraw at any time. I am not giving up any legal rights by signing this form. My signature below indicates that I have read or it has been read to me, this entire consent form and have had all my questions answered.

In case of any queries during the study or in future you may contact following person.

Principal investigator :

Name of the participant :

Name of the witness :

Name of the investigator :

Name of the Guide :

Date :

Place :

Address :

ANNEXURE II- PROFORMA

Name :

Age :

Sex :

Occupation :

Chief complaints :

Cough / Breathlessness / Chest pain / Pain abdomen

Other symptoms :

MMRC grading of breathlessness :

Past history :

- K/C/O COPD for _____ years
- No.of Hospitalizations :
- History of Diabetes Mellitus / Hypertension / Asthma / Tuberculosis
- Other Comorbidities

Personal History :

Smoking / Alcohol / Tobacco chewer

General Physical Examination

Height : Weight : BMI :

Pulse rate : BP : RR : SpO_2 :

Pallor / Icterus / Cyanosis / Clubbing / Pedal edema / Lymphadenopathy / Koilonychia

Systemic Examination

Respiratory System :

Other Systems :

PFT

FEV_1 / FVC :

FEV_1% predicted :

FVC % predicted :

6MWD :

Nottingham Health Profile

Overview:

The Nottingham Health Profile is intended for primary health care, to provide a brief indication of a patient's perceived emotional, social and physical health problems.

Breakdown of questionaire

(1) Part I: 38 questions in 6 subareas, with each question assigned a weighted value; the sum of all weighted values in a given subarea adds up to 100

- energy level (EL): 3
- pain (P): 8
- emotional reaction (ER): 9
- sleep (S): 5
- social isolation (SI): 5
- physical abilities (PA): 8

(2) Part II: 7 life areas affected

Completing questionaire

- each question answered "Yes" or "No"
- important that all questions are answered
- if the patient is not sure whether to say "yes" or "no" to a problem, s/he are instructed to answer the one more true at that time.

Part I

Question	Yes	No	Section	Weight
I'm tired all the time.			EL	39.20
I have pain at night.			P	12.91
Things are getting me down.			ER	10.47
I have unbearable pain.			P	19.74
I take pills to help me sleep.			S	22.37
I've forgotten what it's like to enjoy myself.			ER	9.31
I'm feeling on edge.			ER	7.22
I find it painful to change position.			P	9.99
I feel lonely.			SI	22.01

Nottingham Health Profile

I can walk about only indoors.			PA	11.54
I find it hard to bend.			PA	10.57
Everything is an effort.			EL	36.80
I'm waking up in the early hours of the morning.			S	12.57
I'm unable to walk at all.			PA	21.30
I'm finding it hard to make contact with people.			SI	19.36

Question	Yes	No	Section	Weight
The days seem to drag.			ER	7.08
I have trouble getting up and down stairs and steps.			PA	10.79
I find it hard to reach for things.			PA	9.30
I'm in pain when I walk.			P	11.22
I lose my temper easily these days.			ER	9.76
I feel there is nobody that I am close to.			SI	20.13
I lie awake for most of the night.			S	27.26
I feel as if I'm losing control.			ER	13.99
I'm in pain when I'm standing.			P	8.96
I find it hard to get dressed by myself.			PA	12.61
I soon run out of energy.			EL	24.00
I find it hard to stand for long (e.g., at the kitchen sink, waiting in a line).			PA	11.20
I'm in constant pain			P	20.86
It takes me a long time to get to sleep.			S	16.10
I feel I am a burden to people.			SI	22.53
Worry is keeping me awake at night.			ER	13.95
I feel that life is not worth living.			ER	16.21

Nottingham Health Profile

I sleep badly at night.			S	21.70
I'm finding it hard to get along with people.			SI	15.97
I need help to walk about outside (e.g., a walking aid or someone to support me).			PA	12.69
I'm in pain when going up or down stairs.			P	5.83
I wake up feeling depressed.			ER	12.01
I'm in pain when I'm sitting.			P	10.49

Part II

Is your persent state of health causing problems with your:	**Yes**	**No**
Work? (that is, paid employment)		
Looking after the home? (cleaning & cooking, repairs, odd jobs around the home, etc.)		
Social life? (going out, seeing friends, going to the movies, etc.)		
Home life? (that is, relationships with other people in your home)		
Sex life?		
Interests and hobbies? (sports, arts and crafts, do it-yourself, etc.)		
Vacations? (summer or winter vacations, weekends away, etc.)		

Interpretation

- number of questions in each section affected
- relative level affected, in which the sum of the relative weights are subtracted from 100%, giving values between 0 and 1, with 0 indicating poor and 1 good health

PART 1

1) Over the last year, I have coughed:
Most 80.6
Several 63.2
A few 29.3
Only 28.1
Not 0.0

2) Over the last year, I have brought up phlegm (sputum):
Most 76.8
Several 60.0
A few 34.0
Only 30.2
Not 0.0

3) Over the last year, I have had shortness of breath:
Most 87.2
Several 71.4
A few 43.7
Only 35.7
Not 0.0

4) Over the last year, I have had attacks of wheezing:
Most 86.2
Several 71.0
A few 45.6
Only 36.4
Not 0.0

5) During the last year, how many severe or very bad unpleasant attacks of chest trouble have you had?
More than three 86.7
3 attacks 73.5
2 attacks 60.3
1 attack 44.2
None 0.0

6) How long did the worst attack of chest trouble last?
a week or more 89.7
3 or more days 73.5
1 or 2 days 58.8
less than a day 41.9

7) Over the last year, in an average week, how many good days (with little chest trouble) have you had?
None 93.3
1 or 2 76.6
3 or 4 61.5
nearly every day 15.4
every day 0.0

8) If you have a wheeze, is it worse in the morning?

No 0.0
Yes 62.0

PART 2

9) How would you describe your chest condition?

The most important problem I have 83 .2

Causes me quite a lot of problems 82.5

Causes me a few problems 34.6

Causes no problem 0.0

10) If you have ever had paid employment?

My chest trouble made me stop work 88.9

My chest trouble interferes with my work or made me change my work 77.6

My chest trouble does not affect my work 0.0

11) Questions about what activities usually make you feel breathless.

Sitting or lying still 90.6

Getting washed or dressed 82.8

Walking around the home 80.2

Walking outside on the level 81.4

Walking up a flight of stairs 76.1

Walking up hills 75.1

Playing sports or games 72.1

12) More questions about your cough and breathlessness.

My cough hurts 81.1

My cough makes me tired 79.1

I get breathless when I talk 84.5

I get breathless when I bend over 76.8

My cough or breathing disturbs my sleep 87.9

I get exhausted easily 84.0

13) Questions about other effects your chest trouble may have on you.

My cough or breathing is embarrassing in public 74.1

My chest trouble is a nuisance to my family, friends or neighbours 79.1

I get afraid or panic when I cannot get my breath 87.7

I feel that I am not in control of my chest problem 90.1

I do not expect my chest to get any better 82.3

I have become frail or an invalid because of my chest 89.9

Exercise is not safe for me 75.7

Everything seems too much of an effort 84.5

14) Questions about your medication.

My medication does not help me very much 88.2

I get embarrassed using my medication in public 53.9

I have unpleasant side effects from my medication 81.1

My medication interferes with my life a lot 70.3

15) Questions about how activities may be affected by your breathing.

I take a long time to get washed or dressed 74.2

I cannot take a bath or shower, or I take a long time 81.0

I walk more slowly than other people, or I stop for rests 71.7

Jobs such as housework take a long time, or I have to stop for rests 70.6

If I walk up one flight of stairs, I have to go slowly or stop 71.6

If I hurry or walk fast, I have to stop or slow down 72.3

My breathing makes it difficult to do things such as walk up hills, carry things up stairs, light gardening such as weeding, dance, play bowls or play golf 74.5

My breathing makes it difficult to do things such as carry heavy loads, dig the garden or shovel snow, jog or walk at 5 miles per hour, play tennis or swim 71.4

My breathing makes it difficult to do things such as very heavy manual work, run, cycle, swim fast or play competitive sports 63.5

16) We would like to know how your chest trouble usually affects your daily life.

I cannot play sports or games 64.8

I cannot go out for entertainment or recreation 79.8

I cannot go out of the house to do the shopping 81.0

I cannot do housework 79.1

I cannot move far from my bed or chair 94.0

17) Tick the statement which you think best describes how your chest affects you.

It does not stop me doing anything I would like to do 0.0 It stops me doing one or two things I would like to do 42.0

It stops me doing most of the things I would like to do 84.2

It stops me doing everything I would like to do 96.7

ANNEXURE-III- ETHICAL CLEARANCE LETTER

K.L.E.UNIVERSITY'S
JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)
(Accredited 'A' Grade by NAAC)

Website: http://www.jnmc.edu
E-Mail : dome@jnmc.edu

Phone: (+91-(0)831 Office : 2471350
Principal: 2471701
Fax No. +91 (0)831 – 2470759

Ref: MDC/DOME/ 55

Date: 22/11/2017

To.

REG NO. BR0117002

Sub: Institutional Ethical Clearance for the study.

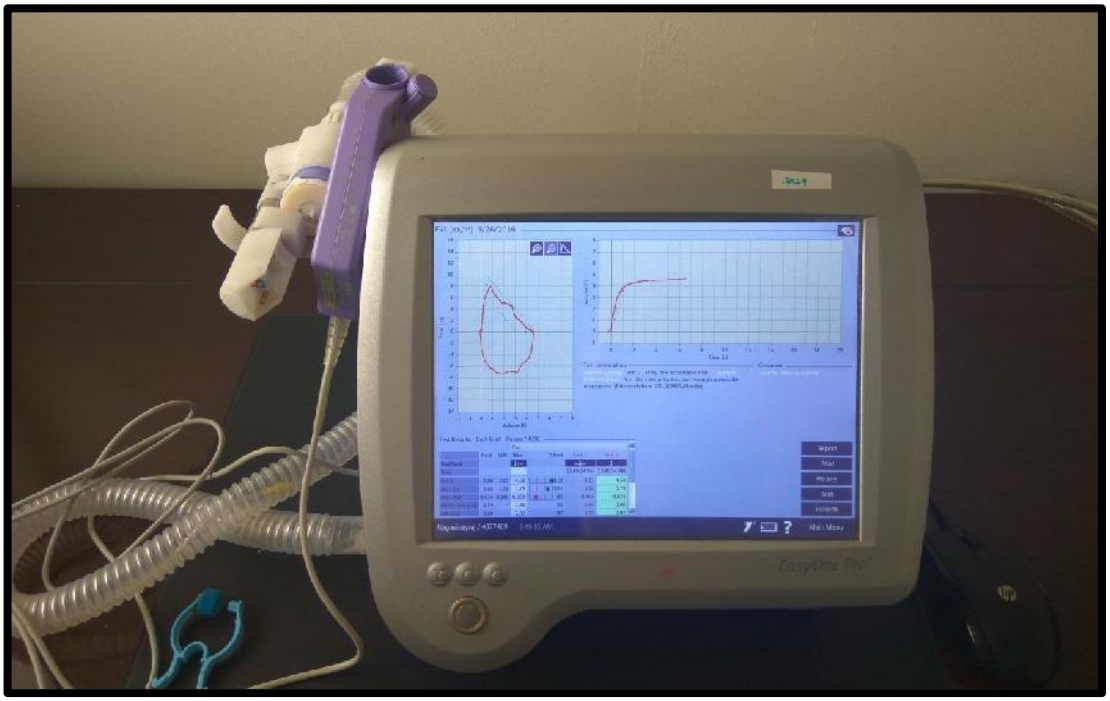
With reference to the above, we wish to inform you that your proposed research project titled **"HEALTH RELATED QUALITY OF LIFE IN STABLE COPD PATIENTS BY BODE INDEX: A ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY",** is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

(Dr. Arathi Darshan)
Member Secretary
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College. Belagavi.

(Dr. Roopa M Bellad)
Chairman,
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

44

ANNEXURE IV – PHOTOGRAPHS



Photograph 1.Spirometer

ANNEXURE-VI

KEY TO MASTER CHART

DM – Diabtes Mellitus

HTN – Hypertension

HT – Height

WT – Weight

BMI – Body Mass Index

PR – Pulse Rate

BP – Blood Pressure

RS – Respiratory System

SpO_2 – Saturation of oxygen

FVL – Ratio of Forced expiratory volume in 1 second and Forced Vital Capacity

FEV_1 – Forced expiratory volume in 1 second

FVC – Forced Vital Capacity

FEV_1%– Forced expiratory volume in 1 second predicted percentage

FVC %– Forced Vital Capacity percentage predicted

6MWT – 6 Minute Walk Test

NHP1 – Nottingham Health Profile section 1 score

EL – Energy Level

P – Pain

ER – Energy Level

S – Sleep

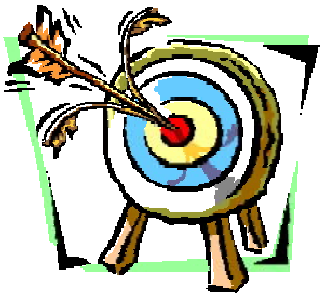
SI – Social Isolation

PA – Physical Ability

NHP2 – Nottingham Health Profile section 2 score

BODE – Total BODE index score

Introduction



Objectives

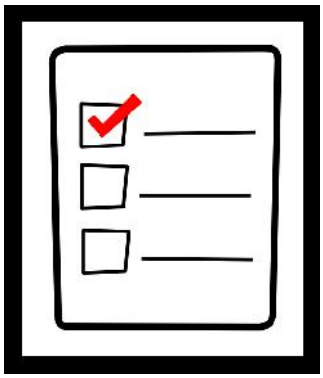
Review of Literature

Methodology

Results

Discussion

Conclusion

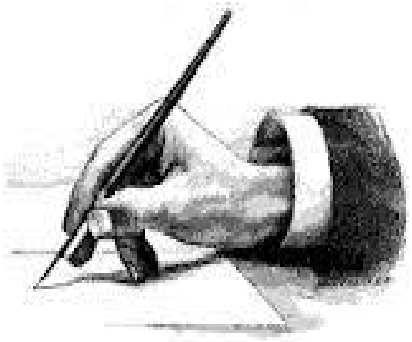


Limitations

Recommendations

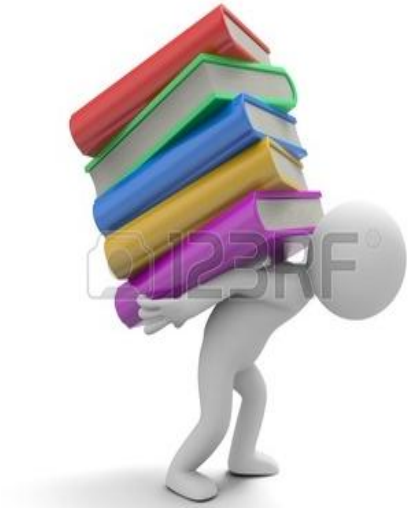
Summary

Bibliography



Annexure-I

Annexure-II



Annexure-III

Annexure-IV

Annexure-V