"PREVALENCE OF VITAMIN D AND SERUM CALIUM DEFICIENCY IN STABLE COPD PATIENTS- A ONE YEAR HOSPITAL BASED OBSERVATIONAL STUDY"

By
REG NO. BR0117003

Dissertation

Submitted to the
KLE Academy of Higher Education and Research,
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 **"Prevalence of Vitamin D and serum calcium Deficiency in stable COPD patients- A One Year Hospital Based Observational Study"**is a bonafide research work done by**REG NO:BR0117003,** Department of Respiratory Medicine, J. N. Medical College, Belagavi.

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

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. : JNMC/PG/2303 Date : 23-9-2019

To,

BR0117003

Sub: Acceptance Letter

Sir/Madam,

The softcopy of thesis entitled "PREVALENCE OF VITAMIN D AND SERUM CALCIUM DEFICIENCY IN STABLE CHRONIC OBSTRUCTIVE PULMONARY DISEASE – A ONE YEAR HOSPITAL BASED OBSERVATIONAL 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 05% (Five percentage) which is within the acceptable limits of 10% as per the guidelines given by UGC.

Thanking you,

Yours sincerely,

Coordinator
Department of Respiratory Medicine
J. N. M. C. Belagavi.

Guide.

Chairman,
Antiplagiarism Committee

KAHER * BELAGAVI * J.N. MEDICAL COLLEGE

LIST OF ABBREVIATIONS

COPD	Chronic Obstructive Pulmonary Disease
25(OH)D	25 Hydroxy vitamin D
FEV_1	Forced Expiratory Volume in 1 second
BMI	Body Mass Index
IL	Interleukin
ILC	Innate Lymphoid Cell
TNF-α	Tumor Necrosis Factor α
FVC	Forced Vital Capacity
UV	Ultraviolet
TLR	Toll Like Receptor
IFN γ	Interferon γ
Th2	T helper 2
RCT	Randomized control trial
GOLD	Global initiative for chronic obstructive pulmonary disease
CCL5	Chemokine ligand 5
PTH	Parathyroid hormone
CHF	Congestive heart failure
DALY	Disability adjusted life year
IHD	Ischemic heart desease
GBD	Global Burden of Disease
ATS	American thoracic society
Nrf2	Nuclear factor erythroid 2
EGFR	Estimated glomerular filtration rate
RANKL	Receptor activator of nuclear factor kappa-B ligand

ABSTRACT

Background and Objectives

COPD is a major burden of chronic morbidity & mortality. Majority of mortality occurs while patient comes in episodes of acute exacerbations. Common triggering factors for exacerbations are infection by respiratory viruses and bacteria, which increases airway inflammation. Vitamin D metabolites enhance the induction of antiviral and antimicrobial effector mechanisms and decreases inflammatory responses. Vitamin D levels decreases with age & aging is potential risk factor for developing COPD. In COPD considering the age and poor nutrition status due to disease or comorbidity there might be an increased prevalence of serum calcium deficiency. Vitamin D plays a crucial role in serum calcium level regulation in the body. This study is aimed to find out the prevalence of deficiency of Vitamin D and hypocalcemia in stable COPD patients and to look for any association between Vitamin D and hypocalcemia in stable COPD patients

Methodology - The study was a one-year observational study done in the Department of Respiratory Medicine, J N Medical College, Belagavi. A total of 100 stable COPD patients were included. All patients underwent clinical examination, spirometry, measurement of serum Vitamin D levels and serum calcium levels. The Vitamin D levels were correlated to age group, gender, BMI, smoking history, calcium levels.

Results- Total of 100 stable COPD patients were enrolled in the study. There were 65 males, 35 females. Mean age of the study population was 67.70± 10.11. Predominant age group of study population was 70-79years. Majority of study population had normal BMI which was in 59 patients. Mean FEV1 of was 55.8±14.33% predicted. Mean vitamin D levels was 19.33±13.84. Mean serum calcium level was 8.68±0.54.

Prevalence of vitamin D was found to be 62% in the study population. Prevalence of hypocalcemia is found to be 44%

Conclusion - Vitamin D deficiency is highly prevalent in stable COPD patients. There was no association between severity and vitamin D levels among study population. Prevalence of hypocalcemia in stable COPD is high.There was no relation between serum calcium levels and vitamin D levels.

Keywords - Vitamin D, bronchial asthma, exacerbations, severity, FEV_1% predicted.

CONTENTS

SL. NO.	TOPIC	PAGE NO.
1.	INTRODUCTION	1-3
2.	OBJECTIVES	4
3.	REVIEW OF LITERATURE	5-19
4.	METHODOLOGY	20-24
5.	RESULTS	25-46
6.	DISCUSSION	46-53
7.	CONCLUSION	54
8.	SUMMARY	55
9.	BIBLIOGRAPHY	56-72
10.	ANNEXURE I - CONSENT FORM	73-76
11.	ANNEXURE II - PROFORMA	77-78
12.	ANNEXURE III - ETHICAL CLEARANCE	79
12.	ANNEXURE III - PHOTOGRAPHS	80
13.	ANNEXURE IV - KEY TO MASTER CHART	81
14.	ANNEXURE V –MASTER CHART	82-83

LIST OF TABLES

Table No.	DESCRIPTION	Page No.
1	BASELINE CHARACTERISTICS OF STUDY POPULATION	25
2	ASSOCCIATION OF VITAMIN D LEVELS WITH SEVERITY OF COPD	31
3	ASSOCCIATION OF VITAMIN D LEVELS WITH GENDER IN COPD PATIENTS	33
4	ASSOCCIATION OF VITAMIN D LEVELS WITH SMOKING HISTORY IN COPD PATIENTS	35
5	ASSOCCIATION OF VITAMIN D LEVELS WITH BMI IN COPD PATIENTS	37
6	ASSOCCIATION OF VITAMIN D LEVELS WITH SERUM CALIUM LEVELS IN COPD PATIENTS	39
7	ASSOCCIATION OF SERUM CALCIUM LEVELS WITH SEVERITY OF COPD	41
8	ASSOCCIATION OF SERUM CALCIUM LEVELS WITH GENDER IN COPD PATIENTS	43

9	ASSOCCIATION OF SERUM CALCIUM LEVELS WITH SMOKING HISTORY IN COPD PATIENTS	45

LIST OF GRAPHS

Graph No.	DESCRIPTION	Page No.
1	BAR GRAPH SHOWING NUMBER OF PATIENTS IN EACH AGE GROUP	27
2	PIE CHART SHOWING GENDER OF THE STUDY POPULATION	27
3	BAR GRAPH DEPICTING BMI OF STUDY POPULATION	28
4	BAR GRAPH DEPICTING COPD SEVERITY OF THE STUDY POPULATION	29
5	PIE CHART DEPICTING VITAMIN D LEVELS OF THE STUDY POPULATION	30
6	BAR GRAPH DEPICTING THE SEVERITY OF COPD AND VITAMIN D DEFICINCY	32
7	BAR GRAPH DEPICTING VITAMIN D LEVELS IN BOTH GENDER GROUP	34
8	BAR GRAPH COMPARING SMOKERS AND NON SMOKERS	36

	VITAMIN D LEVELS	
9	**BAR GRAPH COMPARING BMI AND VITAMIN D LEVELS**	**38**
10	**BAR GRAPH COMPARING SERUM CALCIUM LEVELS AND VITAMIN D LEVELS IN COPD PATIENTS**	**40**
11	**BAR GRAPH COMPARING SERUM CALCIUM LEVELS WITH SEVERITY OF COPD**	**42**
12	**BAR GRAPH COMPARING CALCIUM LEVELS WITH GENDER OF STUDY POPULATION**	**44**
13	**BAR GRAPH COMPARING CALCIUM LEVELS WITH SMOKING HISTORY**	**46**

LIST OF PHOTOGRAPHS

Photograph No.	DESCRIPTION	Page No
1	Spirometer	80

INTRODUCTION

COPD is 4th leading cause of mortality all over the world and predicted to be 3rd by 2020.[1] COPD is a main public health challenge if intervened properly can be prevented and treated. COPD is a major burden of chronic morbidity &mortality. Continuing exposure to risk factors and aging of the population will increase the disease burden in coming years which can be tackled with appropriate interventions.[2]

COPD affected approximately >170 million people worldwide and lead to an estimated death of 3.2 million in 2015.[3] Majority of mortality occurs while patient comes in episodes of acute exacerbations .[4] Common triggering factors for exacerbations are infection by respiratory viruses and bacteria, which increases airway inflammation.[5]

Vitamin D metabolites enhance the induction of antiviral and antimicrobial effector mechanisms and decreases inflammatory responses.[6, 7]Moreover Meta-analyses from RCTs have shown that vitamin D intake decreases the risk of acute respiratory infections and exacerbations of asthma.[8,9] evidence suggest there is an important role for vitamin D supplementation in prevention of COPD exacerbations.[10] Vitamin D deficiency is commoner among COPD patients, but its relation with exacerbation of COPD have not been demonstrated.[11-14,17,18]

Deficient vitamin D status is associated with increased susceptibility to upper respiratory tract infections among COPD patients.[15] Vitamin D metabolites found to have pleiotropic anti-inflammatory & antimicrobial activity in vitro, which might

indicate that vitamin D intake may have a role in preventing exacerbations and upper respiratory tract infections among COPD patients.[16-18]

The results of a single-center trial of inpatients showed that addition of vitamin D reduced exacerbation risk in those with severe vitamin D deficiency.[19] Four double-blind placebo-controlled RCTs have been published, investigating relation of vitamin D supplementation &risk of exacerbation in COPD among them, three studies reported no effect overall[20-22]& one study reported a protective effect overall.[23]

Multicenter RCTs of vitamin D addition to assess prevention of COPD exacerbation, recruited from community& hospital might provide better understanding role of vitamin D and its implicative value in COPD. Vitamin D deficiency is known to speedup bone loss in adults &low vitamin D levels increases prevalence of chronic illnesses including cancers, autoimmune diseases and cardiovascular diseases[24,25,26]

COPD integrates an uncontrolled inflammatory & infectious disease process of the airways with different comorbidities such as osteoporosis, cancer, skeletal muscle dysfunction, and cardiovascular disease, all these domains are potentially may get affected by low vitamin D levels.[27] Vitamin D levels decreases with age & aging is potential risk factor for developingCOPD[28,29]

Increasing age increases the reduction in bone mineralization and increased incidence of osteoporosis. In COPD considering the age and poor nutrition status due to disease or comorbidity there might be an increased prevalence of serum calcium deficiency. Vitamin D plays a crucial role in serum calcium level regulation in the body. Serum

calcium levels in COPD are not studied and their correlation with vitamin D levels was not clearly understood in COPD patients.

Vitamin D levels in stable COPD patients data is lacking in Indian studies and there are not many studies assessing serum calcium levels and Vitamin D levels relation. This study is intended to find out the Vitamin D deficiency and serum calcium deficiency in stable COPD and association between Vitamin D and calcium levels.

OBJECTIVES

PRIMARY OBJECTIVE

- To find out the prevalence of Vitamin D deficiency in stable COPD patients.

SECONDARY OBJECTIVE

- To find out the prevalence of serum calciumdeficiencyin stable COPD patients and to look for any association between vitamin D and serum calcium levels in stable COPD patients.

REVIEW OF LITERATURE

COPD is stated to be the fourth most important cause for death all over the world and is predicted to be the third leading cause by the year 2020.[1]If intervened properly, COPD can be prevented and treated.

Definition

"Global initiative for chronic obstructive pulmonary disease (GOLD) defines COPD as a common preventable and treatable disease that is described by its persistent respiratory symptoms and airflow obstruction that could be either because of airway and/or alveolar abnormalities usually due to exposure to noxious particles or gases"

Characteristic airflow limitation is contributed by small airway disease & parenchymal destruction which have different manifestations in different individuals and could be influenced by the risk factors involved.

COPD is caused by a multifactorial interplay of prolonged exposure to harmful gases and particulate matter along with several host factors such as airway hyper reactivity, genetics and childhood developmental defect.[30-32] Tobacco smoking has a major role in the causation of COPD as evidenced by the increased prevalence of COPD in countries with increased exposure to tobacco smoking. In few countries, exposure to coal mine dust that is occupational exposure & indoor air pollution due to burning of firewood & biomass fuels were also contributing factors.[33,34]

Existing data on COPD prevalence are varied, attributed to differences in methodology, diagnostic criteria, defining COPD, and analyses.[35] Many studies defined COPD by spirometry only and did not consider symptoms into account. Data from most countries reveal that <6 % of the adult populations are identified with COPD. This could be a representation of the under diagnosis of COPD.[36,37]

In spite of these difficulties, there is emerging evidence that is enabling more precise estimates of the prevalence of COPD. Systematic review and meta-analysis of studies conducted in 28 countries between the years of 1990 and 2004 concluded that COPD is more common among those with exposure to smoke compared to those with no exposure to smoke[36], among those with age more than 40 compared to those with age less than 40, and among men compared to women.[38]

COPD leads to a major financial burden. In European countries, 6% of the healthcare budget is spent towards treatment of respiratory disease.[39] Out of this, COPD accounts for a major percentage, 56 % of all respiratory diseases. In United States, indirect costs account for 20.4 billion dollars and direct costs are 32 billion dollars.[40]Acute exacerbations of COPD are responsible for a large portion of total COPD liability in healthcare system. Likewise, there is a salient association among the severity of COPD and cost of care & cost distribution changes as the disease progresses.

Morbidity

Morbidity measure includes emergency department visits, physician visits&hospitalizations. Available data suggests that morbidity because of COPD is more in the elderly population and in the males as compared to females. Comorbidities like musculoskeletal disease, diabetes mellitus & cardiac diseases could also affect the patient's health status and may also hinder with disease progression and management. [41,42]The Global Burden of Disease Study found that COPD is a major cause of disability & mortality all over the world& it is increasing day by day. In 2005 COPD was 8th leading cause of DALYs lost all over the world & by 2013 it became 5th leading cause of DALYs Lost. In United States, COPD is 2nd important cause of decreased DALYs, behind only IHD.

Mortality

COPD is one amongthe foremost causes of mortality in many countries. The GBD Study has estimated that COPD, which ranked 6th among mortality in 1990, in 2011 COPD was 3rd leading cause of mortality in United States.[43]It is estimated that COPD might become the 3rd leading cause of mortality worldwide by 2020. This raised proportion of predicted mortality is possibly due to the expanding population of smokers and varying demographics with increased longevity of most populations.This increased mortality could be due to increased exposure to smoking & change in demographics of the population in many countries including increased life expectancy.

RISK FACTORS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

The commonest encountered risk factor across the world is Tobacco Smoking, Non-smokers might also develop the disease as well.[44,45] COPD is caused by a multifarious interplay of prolonged exposure to harmful gases and particulate matter, along with several host factors such as genetics, airway hyperreactiveness and impaired lung growth in childhood.

i) Tobacco Smoking

Tobacco smoke is highly prevalent in developed countries &numbers of smokers in developing countries is increasing fast. It is estimated that by 2030, tobacco consumption in any form will account for 10 million deaths per year, half of them aged 35-69 years. Not all smokers are equally prone to develop COPD, implying that genetic factors also contribute. Passive smoking also leads to increased respiratory symptoms & COPD by increasing the exposure to noxious gases & inhaled particles. Smoking while pregnant also affect the fetus, by reducing growth of the lung and in-utero development of the lung and also priming of immune system.[46]Smokers have high chances of developing respiratory symptoms and pulmonary function abnormalities, more decline in FEV1 and greater mortality rate compared to nonsmokers. [47]

ii) Indoor air pollution

There are evidences that indoor air pollution because of biomass cooking in poorly ventilated houses is an important risk for development of COPD & it continues to grow.[48-51] The levels of indoor air pollutants encountered in homes that use biomass fuel are several order higher than the levels in the heavily polluted cities across world. These pollutants have the propensity to produce intense oxidative stress in the lungs and the elastocytic effects of these pollutants have been found to be worse than those caused due to tobacco smoke. Biomass smoke exposure induces the same amount of risk of developing COPD as tobacco smoke. As 3 billion people are exposed to biomass smoke globally as compared to 1.1 billion smokes, biomass fuel is likely largest risk factor of COPD.[52,53]

iii) Outdoor air pollution

Air pollution is increasing day by day in most urban cities across the world. Over the last few years air pollution in many cities among the developed countries has reduced due to the advent of strict legislations and improvements in engine technology, but it continues to increase markedly in most of the cities of the developing countries. Both the particulate matter & gaseous components of urban ambient air pollutants have been shown to be associated with increasing respiratory morbidity.[54] Although there is good evidence to suggest that high levels of air pollutants increase COPD exacerbations and worsen preexisting COPD, still there is no conclusive evidence to support the argument that outdoor air pollutants are responsible for causing new cases of COPD.

iv) Occupational exposure.

Studies shown that occupations leading exposures to gases, dusts &fumes as risk factors for COPD.[55,56]ATSfound that occupational exposures lead to 10-20% of symptoms or functional damage with COPD.[57]Dusts appear to be most significant risk factor. Intensity of exposure is directly related to the risk associated, but it varies among different individuals, indicating the significance of host factors. Many less risky occupations may carry an increased risk of COPD which might not have awareness among people. Proper education may likely reduce the risk or prevent COPD.

v) Genetic

Studies have shown variety of genes in pathogenesis of COPD. Resultsof these genetic association studies have been consistent, and functional genetic variants impacting the development of COPD (other than Alfa 1 antitrypsin deficiency) is not identified. The genetic deficiency is best documented in hereditary Alfa 1 antitrypsin deficiency, a major circulatory inhibitor of serine proteases.[58] Airflow limitation is observed among people with siblings of patients with severe COPD who smoke, indicating that genetics may influence along with environmental components in leading to COPD.[59]

vi) Age and Sex

COPD is known to be old age disease, risk increases as age increases. Prevalence is more in above 60years age group. Airway and parenchymal agingshown similar changes as in COPD cases.[60]Studies indicate that the prevalence of the disease is similar in men and women in developed countries, perhaps showing the shifting patterns of tobacco smoking.[61] Few studies shown that women are more vulnerable to properties of tobacco smoke than men. [62,63]

vii) Asthma

There is no clear evidence to define asthma as a risk factor for COPD. In Tucson Epidemiological study of airway obstruction disease, there was a 12 fold risk of adults with asthma developing COPD overtime compared to those without asthma, after modifying for smoking.[64]In a study including asthma patients observed approximately 20% of them having signs of COPD.[65] In a study assessing the lung growth pattern and decline in FEV1 in asthma patients found that 11% had similarities with COPD in spirometric assessment.[66]

viii) Airway hyper responsiveness

Whether Airway hyper responsiveness precedes or follows COPD development is not clearly understood. The pathological features and mechanistic basis for Airway hyper responsiveness in COPD are not known but stopping smoking exposure is found to reduce Airway hyper responsiveness. It has been shown as an independent predictor

of COPD & mortality among COPD in few studies.[67,68]In European community survey airway hyper responsiveness found to be top 2nd risk factor of COPD.[69]

ix) **Socioeconomic status**

There is an association between low socioeconomic status and prevalence of COPD,but It is not clear whether it is due increased smoking exposure, poor nutrition, crowding, air pollutants, etc.[70-72]

x) Childhood respiratory tract infection

Recurrent respiratory infections during childhood are risk factor for COPD. Growth of lung &alveolar development continues till early childhood so respiratory tract infections during childhood might produce permanent damage or impair lung growth and development. There is an association between increase in symptoms during adulthood with history of childhood recurrent infection.[69]

PATHOGENESIS ANDPATHOPHYSIOLOGY

Exposure to smoking or noxious particles including smoke due to biomass fuel burning leads to lung inflammation, which may get enhanced in COPD patients.

This chronic inflammatory response might lead to parenchymal destruction leading to emphysema and destruction of normal defense & repair mechanisms leading to small airway fibrosis. Thus leading to gas entrapment &airflow limitation which is progressive in nature. Characteristic Pathological changes are mainly found in parenchyma,airways, and pulmonary vasculature.[73]

Pathogenesis

The inflammation observed in patients with COPD seems to be alteration of usual inflammatory response to irritants such as smoking. Although few patients develop disease without history of smoking, the inflammatory response among those patients is not clearly understood. Oxidative stress & elevated proteinases in the lung might increase lung inflammation. These processes might lead to classical findings of COPD.

- **Oxidative stress**

Oxidative stress may play a crucial role in COPD.[74,75] Biomarkers indicting oxidative stress are found more in the expired breath, sputum & systemic circulations among COPD patients. During exacerbation oxidative stress is found to increase.Oxidants are liberated by smoking, inhaled particles, activated neutrophils & macrophages.There might be decrease in endogenous antioxidants due to decrease in levels of transcription factor Nrf2 which controls several genes which are coded for antioxidant.[76,77]

- **Protease &anti-protease imbalance.**

There is enough evidence stating there is an imbalance between proteases & anti-proteases among COPD patients.[77] Increased levels of certain proteases are observed in COPD patients which are derived from inflammatory cells & epithelial cells. Protease-mediated destruction of elastin, which is an abundant connective tissue in lung, is thought to be characteristic of emphysema but difficult to establish in airway changes.[78]

- **Inflammatory cells.**

COPD is characterized by increase of macrophages in peripheral airways, parenchyma and pulmonary vessels, along with increased activated neutrophils & increased lymphocytes in few patients increase in Th2, ILC3, eosinophils can be seen. These cells along with epithelial & other structural cells release multiple inflammatory mediators.[79]Which acts as chemotactic,proinflammatory & growth factors.

- **Peribronchiolar & interstitial fibrosis.**

In asymptomatic smoker COPD patients peribronchiolar fibrosis & interstitial opacities are reported.[80-83] Increased production of growth factors may be seen inCOPD patients among smokers or in those with preceding inflammation of airway.[84] This might add to the limitation of small airways &leads to obliteration.

Pathophysiology

- Inflammation & narrowing of peripheral airways leads to decreased FEV1.[85]
- Parenchymal destruction due to emphysema contributes to airflow limitation & decreased gas transfer.

❖ **Airflow limitation and gas trapping**

The amount of Inflammation, fibrosis &intraluminal exudates in the small airways correlates with the reduction in the FEV1, FEV1/FVC ratio & with the progressive decrease in FEV1, which is characteristic of COPD.[85]Limitation of peripheral airway leads to progressive gas trapping in expiration, which leads to hyperinflation. Hyperinflation decreases Inspiratory capacity & associated with dynamic hyperinflation during exercise leading exercise capacity limitation.[86]

- **Gas exchange abnormalities.**

Abnormalities in gas exchange leads to hypoxemia & hypercapnia. Gas transfer for O_2& CO_2 worsens along the progression of disease. Insufficient ventilation might be due to decreasedventilator drive or Increase in dead space,which might lead to CO_2 retention.[87]Defects in alveolar ventilation & decreased vascular bed worsen ventilation &perfusion ratio& gas exchange.[88]

- **Mucus hyper secretion.**

Excessive production of mucus is commonly seen with COPD patients and not always associated with airway limitation. Mucus hyper secretion is a result of goblet cells hyperplasia & submucosal glands hypertrophy mainly due to irritation by smoking & noxious gas exposure.

Certain mediators&proteases stimulate mucus secretion & few act through the activation of EGFR.[89]

VITAMIN D

The first step in the synthesis of Vitamin D is from UV (Ultraviolet) light through sun exposure. Seven- dehydrocholesterol which is distributed in the skin, on exposure to the UV-B spectrum of 290–315 nm frequency, is converted to pre-vitamin D_3, which is then isomerized to Vitamin D_3. Vitamin D_3subsequently undergoes hydroxylation in liver into 25(OH)D_3 by 25(OH) hydroxylase and then into 1,25 $(OH)_2$ D_3 in the kidney by 1α hydroxylase.[25] Studies now indicate 1α hydroxylase is also present in lung epithelial cells.[90,91]

Vitamin D helps in calcium, phosphorus and bone metabolism. Deficiency causes osteoporosis, bone fractures and muscle weakness. Non skeletal actions of Vitamin D include controlling of genes responsible for regulation of cell proliferation, differentiation, apoptosis, and angiogenesis, inhibition of renin synthesis, increasing insulin production and increase in myocardial contractility. Thus, deficiency is related to cancer, autoimmune diseases, osteoarthritis, diabetes mellitus and cardiovascular diseases. Vitamin D deficiency is also related to schizophrenia and poor lung functions.[92]

VITAMIN D EPIDEMIOLOGY

Despite fortification of foods, Vitamin D deficiency is noted in a significant percentage of people. It is highly prevalent in pregnant females and children but can affect all age groups. Women have lower levels than men.[93] Limited outdoor activity

and air pollution also plays a role, with some studies showing urban populations having lower levels compared to rural subjects.[94]

VITAMIN D AND IMMUNE SYSTEM

The role of Vitamin D as an immunomodulator is still debatable. Vitamin D has roles in the maturation of macrophages and this function is impaired in deficiency of Vitamin D.[95]Vitamin D has a role in the regulation of TNF-α secretion by mononuclear phagocytes, and thus can modulate inflammation, immunity, septic shock.[96]A study showed that Vitamin D is a key link between Toll Like Receptor (TLR) activation and antibacterial responses in innate immunity.[97] Vitamin D is a direct regulator of innate immune response by T and B cells, modulates T helper 17 cells, induces monocyte differentiation to macrophages, stimulates phagocytosis and killing of bacteria by macrophages, and decreases the release of inflammatory cytokines (e.g., IFN γ, IL-4, IL-13) and chemokines.[90-101]

Vitamin D and lung functions

A studies showed that mean FEV_1 and FVC were lower in civilians with lower Vitamin D levels.[102-104]

Vitamin D and Calcium

Vitamin D plays an important role in regulating calcium and in bone homeostasis.[105] Decreased levels of vitamin D leads to reduced bioavailability of calcium, which increase secretion of PTH by stimulates parathyroid glands, known as secondary hyperparathyroidism.

PTH reduces reabsorption of phosphate from the proximal tubule while increasing calcium reabsorption in the distal tubule of nephron, leading to increase in calcium & phosphate ratio. More importantly, PTH induces hydroxylation of 25-OHD, and production of active 1,25 (OH)2D. 1,25(OH)2D increases absorption of calcium from intestine.

It acts on the immature osteoblastic cells to stimulate osteoclastogenesis through the RANKL/RANK regulatory system, with increased bone resorption & mobilization of calcium from the bone. Resulting in increased levels of calcium &1,25(OH)2D have a negative feedback on PTH & will limit resorption of bone. In addition, 1,25(OH)2D enhances osteoprotegerin expression in mature osteoblasts, further reducing osteoclastogenesis.[106,107]

Low levels of Vitamin D in COPD might be due to decrease in cutaneous Vitamin D3 production due to smoking & limited exposure of sunlight. Other mechanisms of Vitamin D deficiency could be due to reduced Vitamin D activation in liver & kidneys, increased Vitamin D sequestration in adipose tissue & intestinal malabsorption.

METHODOLOGY

This study was conducted in Respiratory Medicine department of KLE'S Dr. Prabhakar Kore's Hospital & Medical Research Centre, Belgaum.

Study design

Cross sectional observational study.

Study period

January 2018 to December 2018.

Source of Data

The data was collected from COPD patients visiting for consultation to the Respiratory Medicine department of KLE'S Dr. Prabhakar Kore's Hospital & Medical Research Centre, Belagavi.

Sample Size

The sample size in a cross sectional study is calculated by the formula

$$n = \frac{z^2 pq}{d^2}$$

n: Sample size

z: 1.96 rounded off to 2

p: The prevalence of the condition. Here, it is 60%

q :(100-p), 100-60=40

d : The precision of the estimate, 20%

n= 84

A total of 100 subjects were enrolled in the study.

Inclusion criteria

Individuals with a diagnosis of COPD as per GOLD 2018 were enrolled in the study.

Exclusioncriteria

1. Patients in acute exacerbation of COPD
2. Patients on Barbiturates, Bisphosphonates, Sulfasalazine, omega-3 & Vitamin D supplements.
3. Patients with Asthma-COPD Overlap Syndrome.
4. Patients who have a comorbid disease in addition to COPD that affects Vitamin D levels such as Rheumatoid Arthritis, Cystic fibrosis, Multiple sclerosis, Ulcerative Colitis, Crohn's disease, Celiac disease, Osteomalacia, Sarcoidosis, thyroid dysfunction.
5. Chronic liver disease,
6. Chronic kidney disease,
7. Congestive cardiac failure
8. Malignancy
9. Tuberculosis

Procedure

The study was a cross sectional observational study done over a period of one year. Patients who were diagnosed as COPD as perGOLD 2018 guidelines, were subjected to a detailed evaluation of their personal information, present symptoms, history of co-morbidities &smoking history.

Exacerbations of COPD are episodes characterized by a progressive increase in symptoms of shortness of breath, wheezing or chest tightness, cough & progressive decrease in lung function (quantified by FEV_1), from patient's previous lung function or predicted values.

Spirometry was done according to American Thoracic Guidelines[95] and FVC(%predicted),FEV_1(%predicted),FEV1/FVC ratio was recorded

Serum vitamin D and Serum Calcium levels were obtained.

In this study vitamin D levels were categorised as [108]

- Sufficient ($\geq$30 ng/ml)
- Insufficient (20-30 ng/ml)
- Deficient (<20 ng/ml)

In this study serum Calcium levels were categorised as

- Hypocalcaemia (<8.8)
- Hepercalcaemia (>10.2)
- Normal (8.8-10.2)

COPD patients were divided into 3 groups depending on the severity of disease – mild, moderate and severe, as per GOLD guidelines.

- MILD –FEV1 >80 %
- MODERATE – FEV1 50-80 %
- SEVERE – FEV1 30-50 %
- VERY SEVERE – FEV1 <30 %

Investigations:

Chest Radiograph PA view, Spirometry, Serum Vitamin D levels, Serum calcium levels, Routine blood investigations.

Ethical clearance

Ethical clearance was obtained from the Ethical and Research Committee, Jawaharlal Nehru Medical College, Belagavi.

Informed Consent

All the patients fulfilling the selection criteria were explained about the nature of the study and a written informed consent was obtained before enrolment.

Statistical analysis

The data obtained was entered into Microsoft excel spreadsheet. The results of the study were analysed and presented as numbers, percentage or mean ± standard deviation (SD). Comparison of variables is done by Chi square test and p value is calculated.'p' value of < 0.05 was considered as statistically significant

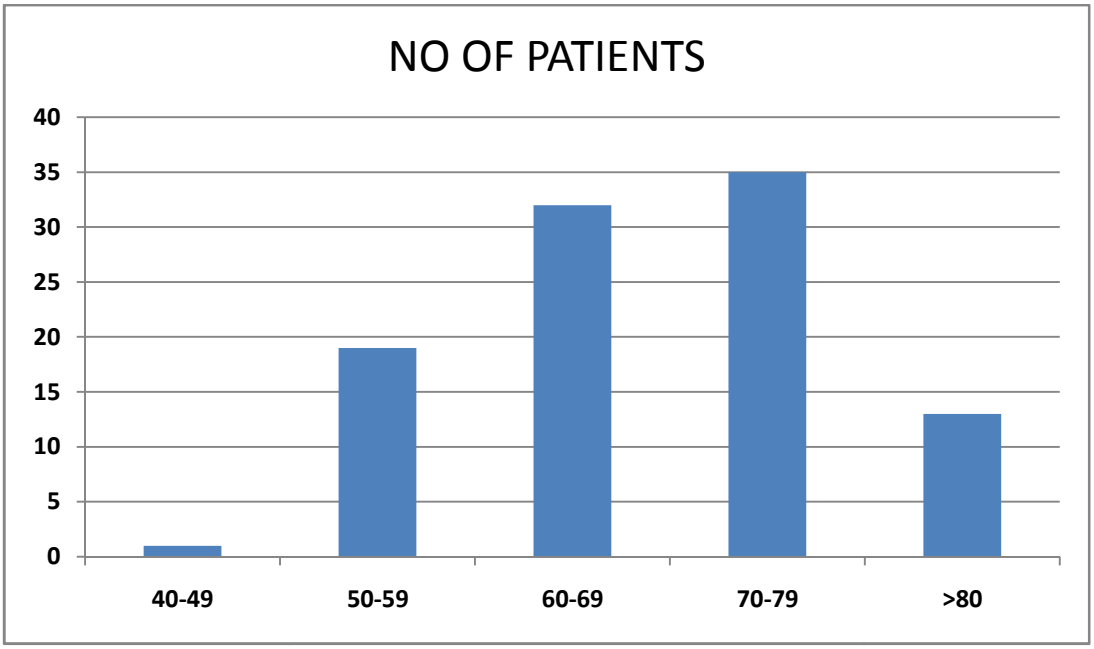
RESULTS

Table -1 BASELINE CHARACTERISTICS OF STUDY POPULATION

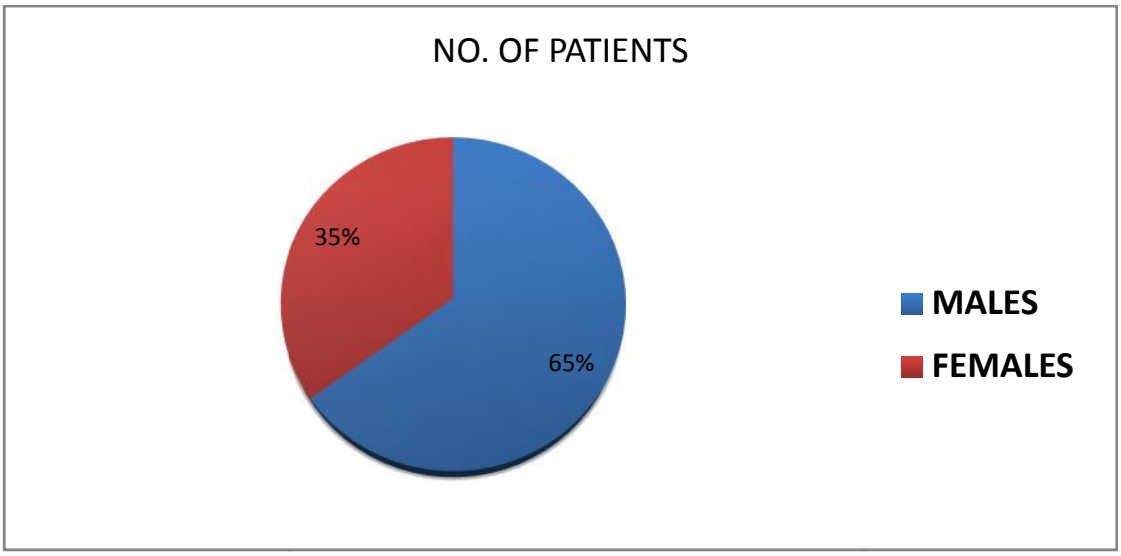
		No. of Patients	Percentage (%)
Age group	40-49	1	1
	50-59	19	19
	60-69	32	32
	70-79	35	35
	>80	13	13
Gender	Male	65	65
	Female	35	35
BMI	Underweight	5	5
	Normal	59	59
	Overweight	28	28
	Obese	8	8
Smoking history	Smokers	52	52
	Non smokers	48	48
Obstruction	Mild	2	2
	Moderate	71	71
	Severe	23	23
	Very severe	4	4
Co-morbidities	Hypertension	25	25
	Diabetes mellitus	28	28
	Ischemic heart disease	14	14
Vitamin D levels	Adequate	19	19
	Insufficient	19	19
	Deficient	62	62
Serum calcium levels	Normal	55	55
	Hypocalcaemia	44	44
	Hepercalcaemia	1	1

Total of 100 patients were enrolled in the study. There were 65 males (65%), 35 females (35%). Age of patients ranged from 49 years to 98 years. Mean age of the study population was 67.70± 10.11. Predominant age group of study population was 70-79years group constituting 35 patients (35%), followed by 60-69years age group constituting 32 patients (32%). BMI of study population ranged from 15.1 to 34.9 with mean BMI of 24.086±4.01. Majority of study population had normal BMI which was in 59 patients (59%). Among study group 52 patients had smoking history & 48 patients were not having any history of smoking. Mean FEV1 of was 55.8±14.33% predicted. Mean vitamin D levels was 19.33±13.84. Mean serum calcium level was 8.68±0.54.

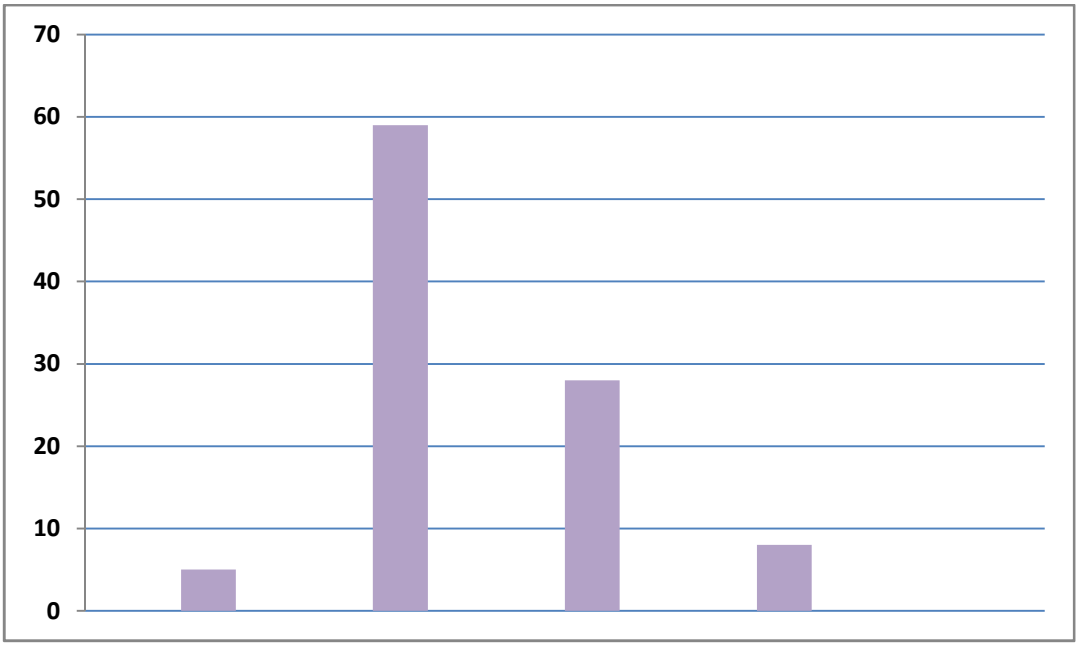
GRAPH –(1)BAR GRAPH SHOWING NUMBER OF PATIENTS IN EACH AGE GROUP



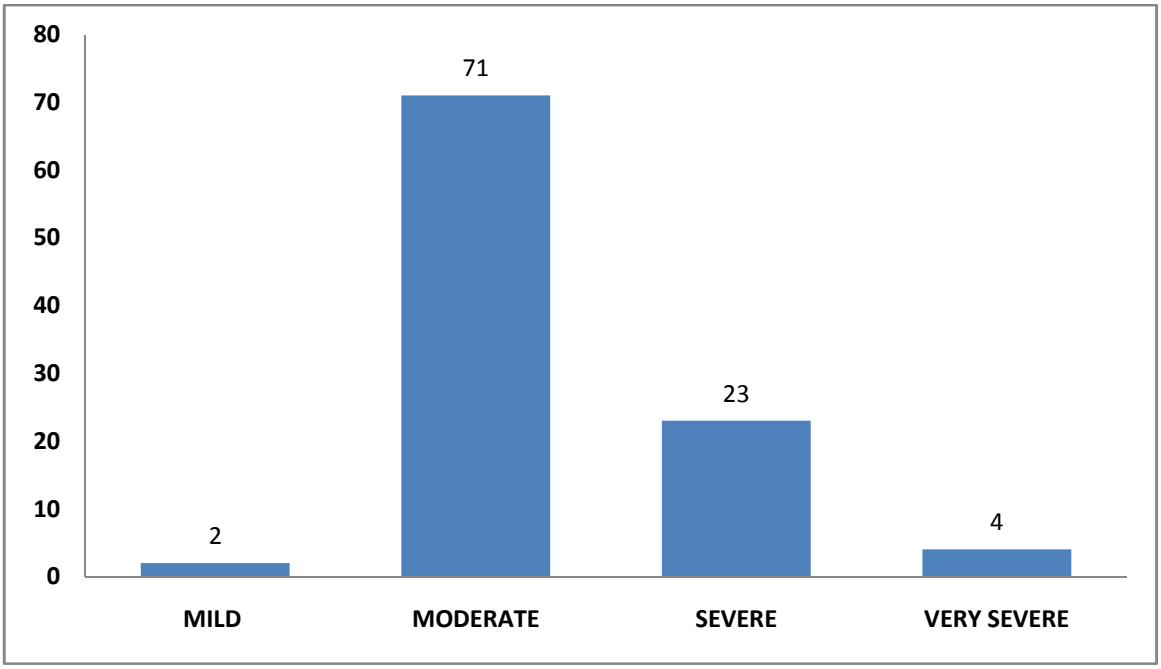
GRAPH-(2) PIE CHART SHOWING GENDER OF THE STUDY POPULATION



GRAPH –(3)BAR GRAPH DEPICTING BMI OF STUDY POPULATION

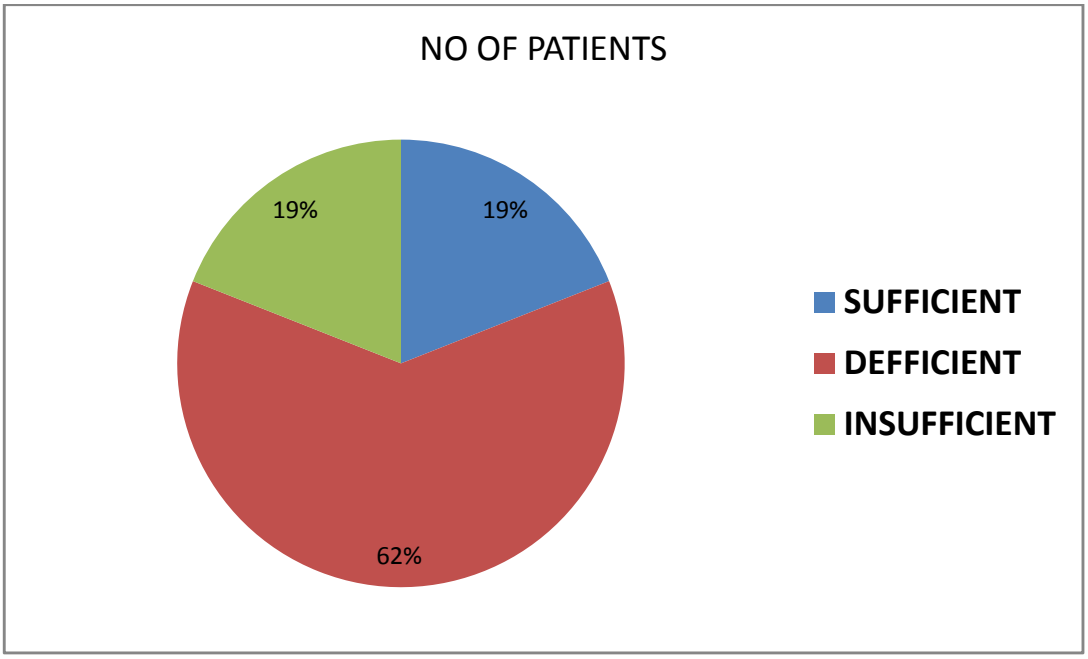


GRAPH-(4) BAR GRAPH DEPICTING COPD SEVERITY OF THE STUDY POPULATION



Majority of the study population were having moderate obstruction in spirometry values constituting 71 patients (71%), followed by severe obstruction that was 23 patients (23%). There are only 2 patients with mild obstruction (2%) in this study, very severe obstructive pattern was seen in 4 patients (4%).

GRAPH- (5) PIE CHART DEPICTING VITAMIN D LEVELS OF THE STUDY POPULATION



Among the study population 62 patients (62%) found to be vitamin D deficient, 19 patients (19%) found to be with insufficient levels of vitamin D and only19 patients (19%) found to be with adequate levels of vitamin D.

Table -2 ASSOCCIATION OF VITAMIN D LEVELS WITH SEVERITY OF COPD

COPD severity	Adequate Vitamin D	Insufficient Vitamin D	Deficient Vitamin D	Total No (%)
Stage 1	**0**	**0**	**2**	**2(2)**
Stage 2	**12**	**14**	**45**	**71(71)**
Stage 3	**6**	**4**	**13**	**23(23)**
Stage 4	**1**	**1**	**2**	**4(4)**
Total	**19**	**19**	**62**	**100(100)**

Chi square = 2.427, p value = 0.877

When comparing COPD severity with vitamin D levels 63.3% of stage 2 patients were having vitamin D deficiency, 56.5% of stage 3 patients were having vitamin D deficiency, stage 1 and stage 4 were having very less number of patients. there was no difference in prevalence of vitamin D deficiency according to stages of COPD.

Only 16.9% of stage 2 patients were having vitamin levels adequate and 26% of stage 3 patients were having adequate vitamin D levels these findings show there is not much difference in prevalence of vitamin D deficiency among stages of the COPD.

There was no statistical significance (p value = 0.877) found in comparing COPD stages with vitamin D levels among stable COPD patients.

GRAPH – (6) BAR GRAPH DEPICTING THE SEVERITY OF COPD AND VITAMIN D DEFICINCY

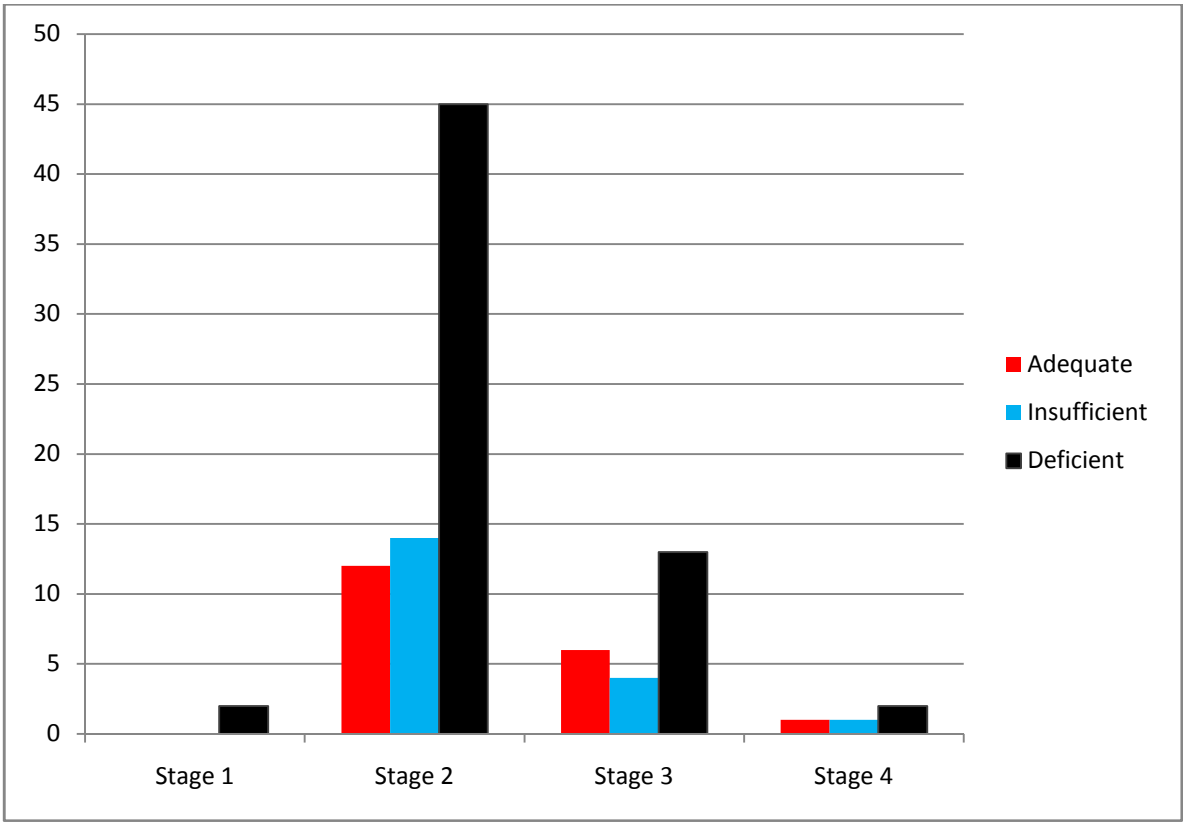


Table -3 ASSOCCIATION OF VITAMIN D LEVELS WITH GENDER IN COPD PATIENTS

Gender	Adequate Vitamin D	Insufficient Vitamin D	Deficient Vitamin D	Total No (%)
Male	**11**	**15**	**39**	**65**
Female	**8**	**4**	**23**	**35**
Total	**19**	**19**	**62**	**100**

Chi square = 2.166, p value = 0.339

Among 62 vitamin D deficient patients, 39 were male comprising to 62.9% and female were 23 comprising 37.1% Stating that male were predominant in deficient group. Among 19 patients with adequate vitamin D levels 11 patients were male (57.8%) and 8 patients were female (42.2%) stating not much difference among both gender in adequate vitamin D patients. In insufficient vitamin D group 78.9% that is 15 patients were male and 4 were female which is 21.1% among 19 patients.

There was no statistical significance (p value = 0.339) found between gender and vitamin D levels among stable COPD patients.

GRAPH –(7) BAR GRAPH DEPICTING VITAMIN D LEVELS IN BOTH GENDER GROUP

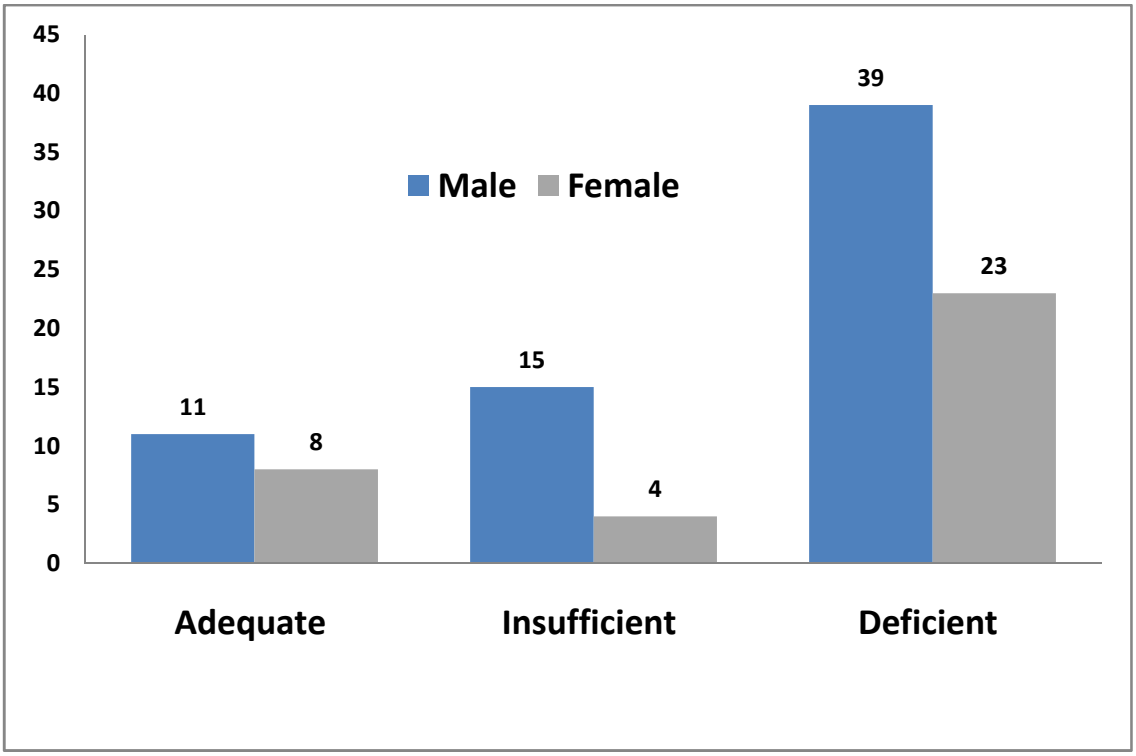


Table -4 ASSOCCIATION OF VITAMIN D LEVELS WITH SMOKING HISTORY IN COPD PATIENTS

	Adequate Vitamin D	**Insufficient Vitamin D**	**Deficient Vitamin D**	**Total No (%)**
Smoker	**8**	**13**	**31**	**52**
Non smoker	**11**	**6**	**31**	**48**
	19	**19**	**62**	**100**

Chi square = 2.897, p value = 0.235

There were 52 patients with smoking history among them 31 had vitamin D deficiency (59.6%). In non smoking group which included 48 patients 31 had vitamin D deficiency (64.5). There was no much difference in prevalence of vitamin D among smokers and non smokers.

There was no statistical significance (p value = 0.235) among smoking history and vitamin D levels in stable COPD patients.

GRAPH-(8) BAR GRAPH COMPARING SMOKERS AND NON SMOKERS VITAMIN D LEVELS

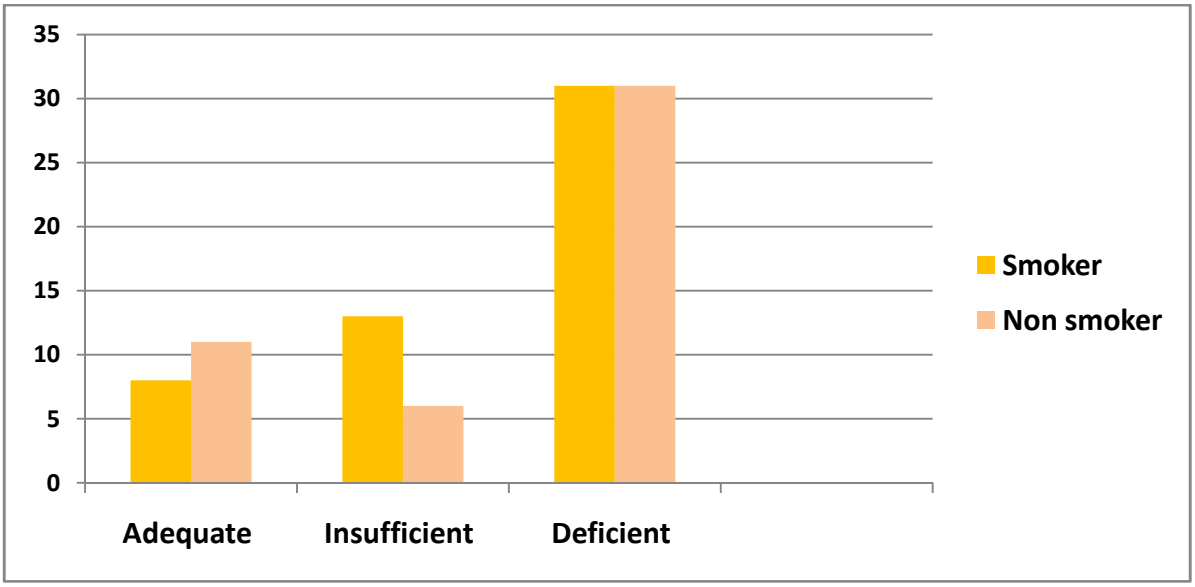


Table -5 ASSOCCIATION OF VITAMIN D LEVELS WITH BMI IN COPD PATIENTS

BMI	Adequate Vitamin D	Insufficient Vitamin D	Deficient Vitamin D	Total No (%)
Underweight	**0**	**1**	**4**	**5**
Normal	**8**	**14**	**37**	**59**
Overweight	**9**	**2**	**17**	**28**
Obese	**2**	**2**	**4**	**8**
TOTAL	**19**	**19**	**62**	**100**

Chi square = 7.946, p value = 0.242

Majority of the patients were having normal BMI which is in 59 patients among them 37 patients were vitamin D deficient which was 62.7%. There were 5 underweight patients and among them 4 had vitamin D deficiency comprising 80%. Among overweight patients which were 28 patients and 17 had vitamin D deficiency which was 60% . there were 8 obese patients and 4 had vitamin D deficiency accounting to 50%.

Numbers show comparatively normal BMI had lesser prevalence of vitamin D deficiency compared to underweight patients but there was no statistical significance (p value = 0.242) in comparing BMI and vitamin D deficiency among stable COPD patients.

GRAPH-(9) BAR GRAPH COMPARING BMI AND VITAMIN D LEVELS

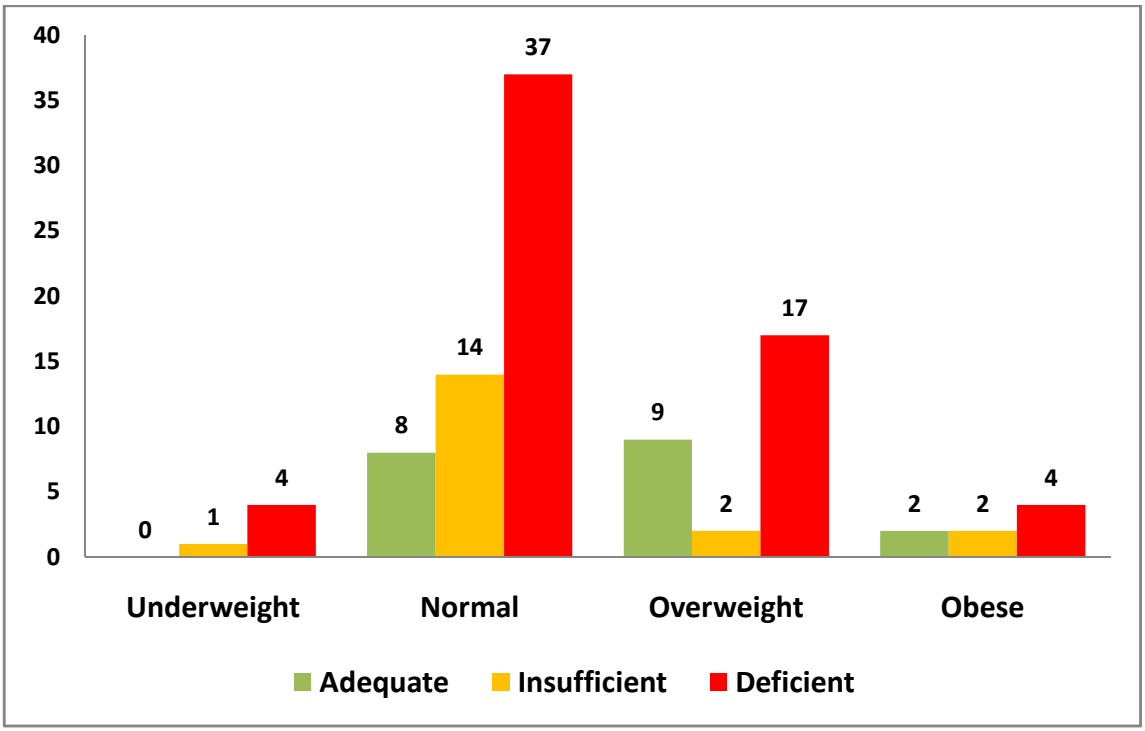


Table -6 ASSOCCIATION OF VITAMIN D LEVELS WITH SERUM CALIUM LEVELS IN COPD PATIENTS

	Adequate Vitamin D	**Insufficient Vitamin D**	**Deficient Vitamin D**	**Total No (%)**
HYPOCACLEMIA	**9**	**10**	**25**	**44**
NORMAL	**9**	**9**	**37**	**55**
HYPERCALCEMIA	**1**	**0**	**0**	**1**
	19	**19**	**62**	**100**

Chi square = 5.473, p value = 0.242

Majority of the patients were having normal serum calcium levels constituting 55 patients among them 67.2% were having vitamin D deficiency which was in 37 patients. In hypocalcemia patients which were 44 vitamin deficiency was found in 25 patients which was 56.8%. There was no much difference among both groups.

There was no statistical significance (p value = 0.242) in serum calcium levels and vitamin D levels among stable COPD patients.

GRAPH–(10) BAR GRAPH COMPARING SERUM CALCIUM LEVELS AND VITAMIN D LEVELS IN COPD PATIENTS

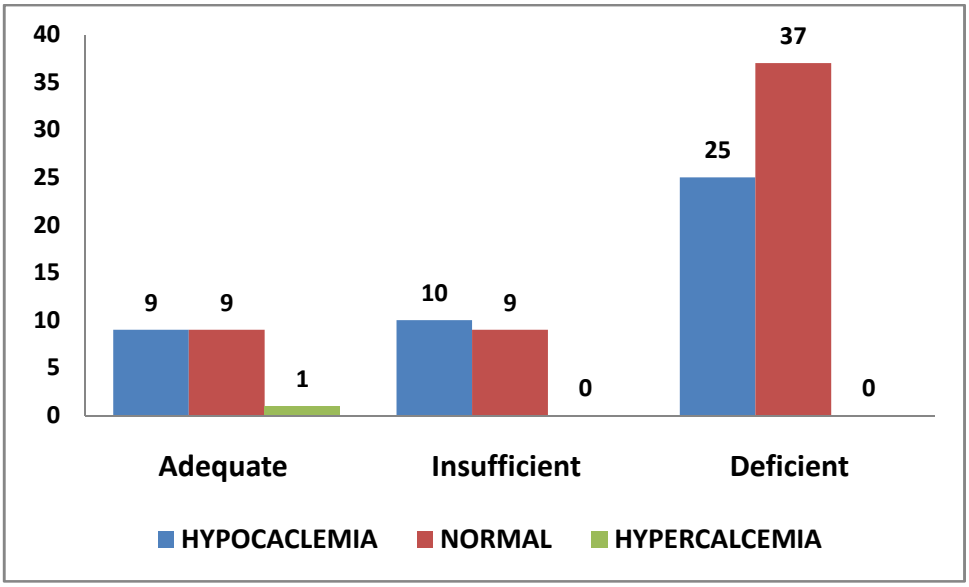


Table -7 ASSOCCIATION OF SERUM CALCIUM LEVELS WITH SEVERITY OF COPD

	HYPOCACLEMIA	NORMAL	HYPERCALCEMIA	Total No(%)
Stage 1	**0**	**2**	**0**	**2(2)**
Stage 2	**32**	**38**	**1**	**71(71)**
Stage 3	**12**	**11**	**0**	**23(23)**
Stage 4	**0**	**4**	**0**	**4(4)**
TOTAL	**44**	**55**	**1**	**100(100)**

Chi square = 5.869, p value = 0.438

71 patients were having moderate obstruction among them 32 patients found to have hypocalcemia accounting to 45% and normal calcium was found in 38 patients that is 53.5% of stage 2 COPD patients. In stage 3 COPD patients which were 23 In number 12 had hypocalcemia accounting to52.1% of stage 3 group. In stage 4 COPD there were 4 patients and 2 were having hypocalcemia accounting to 50% of stage 4 group.

There was no statistical significance (p value = 0.438) in comparing serum calcium and stages of COPD in stable COPD patients.

GRAPH-(11) BAR GRAPH COMPARING SERUM CALCIUM LEVELS WITH SEVERITY OF COPD

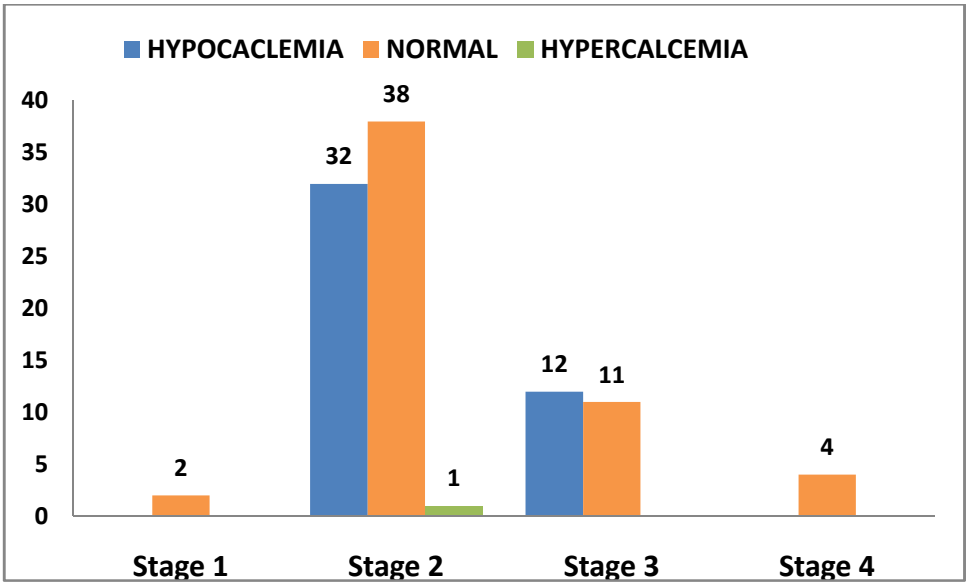


Table -8 ASSOCCIATION OF SERUM CALCIUM LEVELS WITH GENDER IN COPD PATIENTS

	HYPOCALCEMIA	NORMAL	HYPERCALCEMIA	Total No(%)
MALE	**29**	**36**	**0**	**65**
FEMALE	**15**	**19**	**1**	**35**
TOTAL	**44**	**55**	**1**	**100**

Chi square = 1.878, p value = 0.391

Among 65 male patients 29 were having hypocalcemia accounting to 44.6% of male patients. Among 35 females 15 patients were having hypocalcemia accounting to 42.8%. results were similar among both gender.

There was no statistical significance (p value = 0.391) among gender and serum calcium levels in stable COPD patients.

GRAPH-(12) BAR GRAPH COMPARING CALCIUM LEVELS WITH GENDER OF STUDY POPULATION

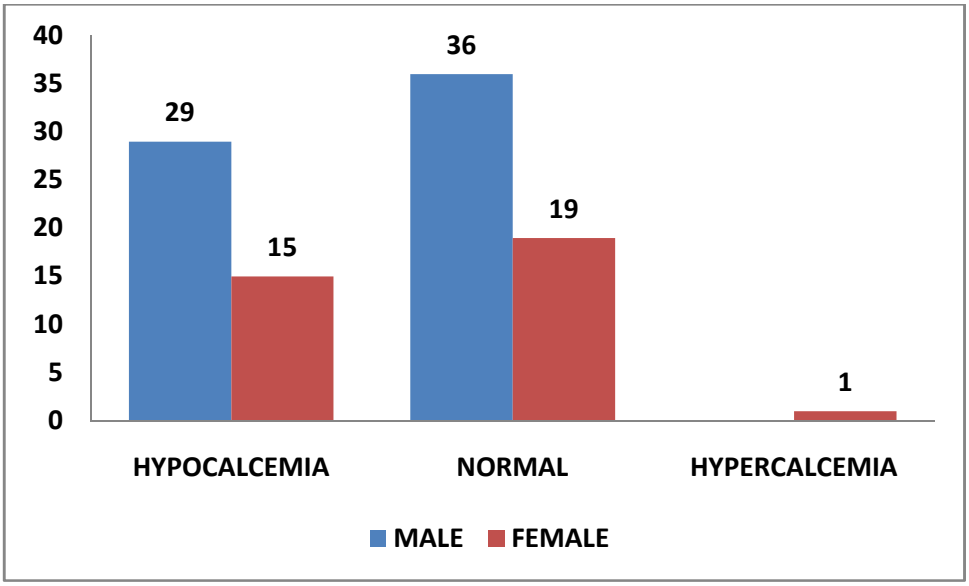


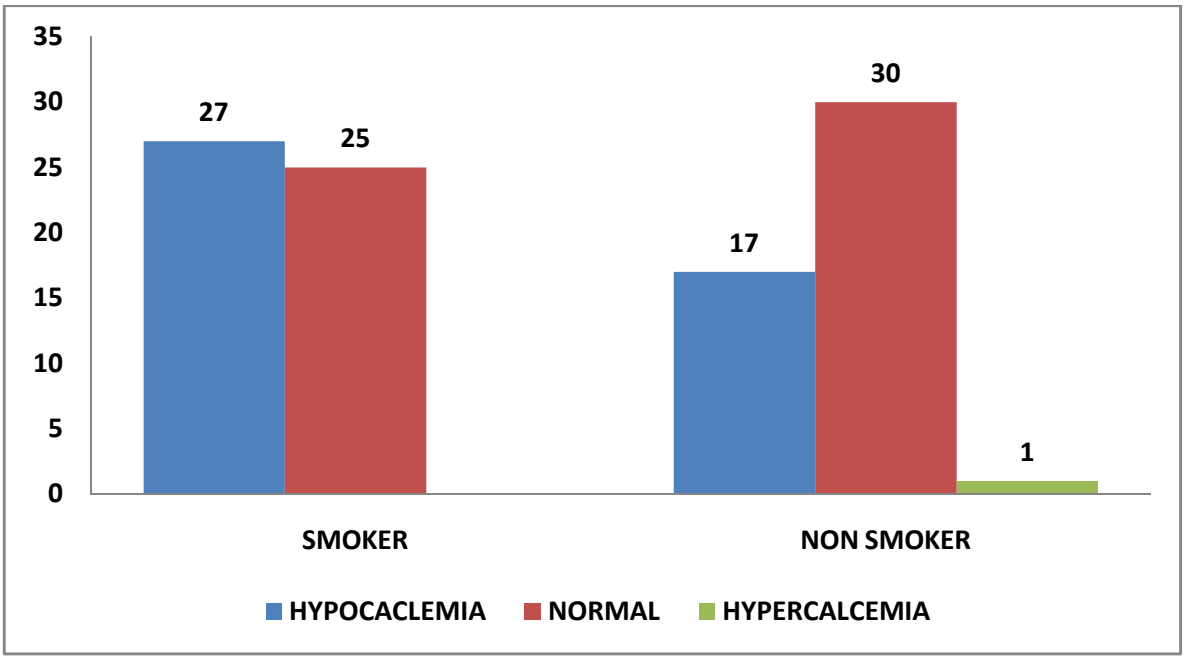
Table -9 ASSOCCIATION OF SERUM CALCIUM LEVELS WITH SMOKING HISTORY IN COPD PATIENTS

	HYPOCACLEMIA	NORMAL	HYPERCALCEMIA	Total
SMOKER	**27**	**25**	**0**	**52**
NON SMOKER	**17**	**30**	**1**	**48**
TOTAL	**44**	**55**	**1**	**100**

Chi square = 3.573, p value = 0.167

Among 52 patients who were having smoking history 27 were found to have hypocalcemia accounting to 51.9%. Among 48 non smoker COPD patients 17 found to have hypocalcemia accounting to 35.4%. numbers depict that non smokers had less prevalence of hypocalcemia but there was no statistical significance (p value = 0.167) comparing smoking history and serum calium levels among stable COPD patients.

GRAPH-(13) BAR GRAPH COMPARING CALCIUM LEVELS WITH SMOKING HISTORY



DISCUSSION

Vitamin D has a significant impact on respiratory system as it can influence immunity & cell functions. The ability of lung epithelial cells to synthesize Vitamin D by 1 alpha hydroxylase & the presence of Vitamin D Receptor polymorphisms support this. Studies have showed relation among Vitamin D deficiency & many lung diseases including respiratory tract infections, rhinosinusitis, COPD, tuberculosis and bronchial asthma. Vitamin D deficiency is widespread issue in adults & is found to be associated with reduced lung function & emphysema [109,110]

The present study included 100 stable COPD patients, among them 65 were male and 35 were female. Majority of the patients belonged to 70-79 year age group. Most of them were having moderate obstruction on spirometry that was 71%. All were subjected for history, general examination, spirometry, vitamin D levels & calcium levels were taken.

Sun exposure is the vital source of Vitamin D. Vitamin D metabolism is affected by many factors including age, skin pigmentation, obesity and chronic illnesses. Sedentary lifestyle and dietary changes have caused increased prevalence of Vitamin D deficiency among the general population.

In the present study, Vitamin D deficiency was found in 62% of patients with stable COPD. The low levels can be attributed to limited sunlight exposure due to outdoor activity limitation and aging skin lacking ability to absorb sunlight in COPD patients. Vitamin D has antimicrobial actions by activating peptides such as cathelicidins and defensins.

Cathelicidin is protective against a range of Viruses, Bacteria, Mycobacteria, and Fungi, and its deficiency increases susceptibility to infection, exacerbations of COPD and in turn leads to decreased quality of life. Viral infections trigger IL-33 release. Vitamin D attenuates IL-33 actions, decreases ILC-2 stimulation and production of IL-5 hence reduces inflammation and exacerbations.

Studies have shown that low Vitamin D levels in COPD patients added to respiratory system infections.[32-37] Observational studies have showed a relation in Vitamin D levels & clinical parameters in COPD.[38-41] In a cohort study which included repeated serum Vitamin D measurements found different values in different seasons.[20]

Vitamin D is discovered as a highly versatile molecule with emerging importance in immunity, cancer, infectious diseases, toxins induced inflammation and fibrosis deficient Vitamin D is well known to speed up bone loss in elderly & increasing evidence links a low vitamin D status to highly prevalent chronic illnesses, including cancers, autoimmune diseases, infectious, and cardiovascular diseases.[111-115]

Observational studies shown that low vitamin D status is associated with increased prevalence of upper respiratory tract infections in COPD patients.[116] The results from a single-center trial of inpatients found that vitamin D addition shown decrease in the exacerbation risk in patients with severe vitamin D deficiency.[19] On the contrary in one of the observational study showed no relation between vitamin D deficiency & exacerbation.[117,118]

In a study done by J. Fernández-Lahera et al which included 70 patients with COPD, mean age was 73years, males were 80%, mean BMI 27, with stage II COPD predominant accounting to 45%, found that 60% of study population were having low vitamin D levels which was similar to the current study prevalence.[119] former study was comparable to current study as both were having predominance in moderate and severe obstruction group COPD patients, having similar age distribution, similar mean BMI and males were predominant in both studies.

In a multi-center observational study done by David A Jolliffe et al[120] including 278 COPD patients with 60.8% male patients which was comparable to present study, with age group ranging from 40 - 90 years which was also almost similar in the present study, with predominant stage II COPD group as in current study, found that prevalence of low vitamin D levels is 61.5% which was similar to the current study. In the former study it was found that low vitamin D levels was found to associate independently with reduced % predicted FEV1 and were associated with lower Socio economic status, increased BMI, but these associations were not found in the current study. It didn't compare vitamin D status in COPD patients with matched control populations. Matched control population is of importance, as deficient vitamin D levels may occur in 40-70% of the elderly in the USA and Europe.[121-123] In contrast to the former study present study did not show any relation among staging which is represented by FEV1 % predicted with vitamin D levels & also there was no statistical significance between BMI of the patients with vitamin D levels as it was found in the former study. This finding could be due to the difference in patient selection as present study considered only stable COPD patients were as former study included exacerbation patients.

In a study done by Peter N. Black, et al. including COPD patients they found that there was a strong association between serum levels of vitamin D and pulmonary functions after adjustment for confounders. They found that there is a positive dose response relation between vitamin D and FEV1, whereas current study did not show any relation between vitamin D and FEV1. The relation between FEV1 and vitamin D levels found to be slightly more in the smoking group but there was no association found in the smoking and vitamin D levels in the current study.[124]

In a study done by Graat-Verboom et al[125] including 255 COPD patients, mean age was 68 years, 62% were men, mean BMI of 27.06, with predominant stage II COPD accounting to 39.2% found that vitamin D deficiency prevalence was 44%. Both the studies were comparable in terms of age distribution, male predominance, mean BMI and stage II COPD predominance. Current study showed more prevalence in comparison i.e. 62% Vs 44% with the above mentioned study.

In a Multicenter trial done by Adrian R Martineau, et al. including 240 COPD patients from hospital & community, mean age was 64.8 years, males were 60%, mean BMI was 27.9, with predominant stage II COPD accounting to 57% of study population, vitamin D deficiency was found in 78.2%(148/240) patients. Both studies were comparable in terms of male predominance, age distribution, mean BMI and prevalence of vitamin D deficiency was higher in the former study in comparison to current study i.e. 78.2% Vs 62%. Vitamin D intervention group comparatively more protected against moderate/severe exacerbation. Especially among those 148 subjects with low baseline vitamin D levels, vitamin D supplementation was related with

decreased risk of moderate/severe exacerbation of COPD; whereas, in patients with baseline adequate vitamin D levels no significant positive effect was noted. Allocation to vitamin D compared with placebo did not show any effect on health service uptake, quality of life due to COPD itself or upper respiratory tract infections. secondary outcomes showed reduced symptom severity for moderate/severe exacerbations in intervention group compared with the control group.Vitamin D supplementation might be of significant benefits so should be offered to patients with low vitamin D levels to reduce the risk of moderate/severe exacerbation.[21]

In a study done by Pourrashid MH et al. including 62 COPD patients 30 in interventional group comprising of vitamin D supplementation and 32 in placebo group they found that Correction of vitamin D levels in the patients of intervention group resulted in statistically significant improvement in patient's health related quality of life among inpatients by day 120 compared to that of placebo group; however, no significant difference was found in days of hospitalization, re-hospitalization, and mortality rates.[126]

Even though studies have shown beneficial effects of vitamin D there is some side effects of vitamin D if supplemented in normal or increased serum vitamin D patients. Vitamin D supplements were associated with decreased serum concentration of PTH. In a randomized control study 73% had a reduced level of PTH at 12 months compared to baseline levels. Analysis of this data by baseline vitamin D concentrations found that most participants had decrease in their PTH levels after vitamin D supplementation, even among those with higher vitamin D levels at baseline.[21]

In the present study it was found that hypocalcemia is common among COPD patients accounting to 44%. There was no association between vitamin D levels and serum calcium levels. Role of serum calcium in COPD is not clearly understood as there is limited data of serum calcium levels in COPD and its relevance.

Symptoms of hypocalcemia depends on severity of hypocalcemia. Mild cases are mostly asymptomatic. classical symptoms include numbness, tingling at upper, lower extremities, perioral region and karpopedal spasm.[127] In severe cases, it may lead to confusion, disorientation, delirium, prolonged QT interval, arrhythmias, CHF & laryngo-bronchospasms which may lead to respiratory failure.[128]This laryngo-bronchospasm can be reversed by correcting calcium levels. In a nutritional study done by Amardeepak Toppo, et al[129] including 75 COPD patients, found that calcium levels were low in COPD patients in comparison to control group. There was no correlation between COPD severity and calcium levels as found in the current study. Role of calcium supplementation in COPD is not evident, it needs further interventional studies.

In the current study we found that there was no relation between vitamin D levels and serum calcium levels in COPD patients. There is limited data in vitamin D and serum calcium levels comparison in COPD patients.

Prevalence of vitamin D and hypocalcemia in COPD is high and evaluating every cases for them might be advisable. In clinical practice supplementing vitamin D and calcium to COPD patients can't be generalized. There is some positive evidence advising supplementation of vitamin D in deficient COPD cases.

Limitations

- Vitamin D levels shown seasonal variations, current study did not take it to account.
- Time spent in daylight by individuals will have direct relation with vitamin D levels which may vary person to person, it was not taken into consideration.
- Vitamin D receptors variability among persons were found in studies which is not considered in the present study.
- Dietary habits of patients were not considered, which might have affected Vitamin D levels.
- The patients included are from a large tertiary care referral center, and therefore might not be a representative of the overall population.
- Obesity affects Vitamin D levels independently, which was not taken into consideration
- Steroid usage will alter calcium levels and vitamin D levels which was not taken into consideration.
- Diseases affecting intestinal absorption will be confounding factor.

CONCLUSION

In the present study including stable COPD patients prevalence of vitamin D deficiency is high which is 62%.There was no association between severity of COPD and vitamin D levels among study population.There was high prevalence of hypocalcemia in study population accounting to 44%.There was no relation between serum calcium levels and vitamin D levels.

As prevalence of vitamin D and hypocalcemia is found to be high in stable COPD patients, treating them might improve overall quality of life.RCTs are required to assess the role of vitamin D and calcium supplements in COPD patients.

SUMMARY

- A total of 100 stable COPD patients were included in the present study,
- Diagnosis of COPD was done by clinical history and PFT. Staging of COPD done as per GOLD guidelines.
- Among them 65 were male, 35 were female patients.
- Study population age ranged from 49 to 98years. Mean age was 67.70±10.11, predominant age group was 70-79 years.
- Mean FEV1 of the study population was 55.8±14.33%
- Majority of the patients were having moderate obstruction accounting to 71%
- Mean vitamin D levels of study population was 19.33±13.84
- Mean calcium levels of study population was 8.68±0.54
- Prevalence of vitamin D deficiency was 62% in the current study.
- Prevalence of hypocalcemia was 44% in the current study.
- Vitamin D and serum calcium levels had no statistical significance in comparing among severity of COPD, gender, smoking history, BMI
- There was no statistical correlation between vitamin D deficiency and hypocalcemia in study population

BIBLIOGRAPHY

1. Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: A systematic analysis for the Global burden of disease study 2010. Lancet 2012; 2095-128.
2. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PLoS med 2006; 3(1):e442.
3. GBD 2015 Chronic Respiratory Disease Collaborators. Global, regional, and national deaths, prevalence, disability-adjusted life years, and years lived with disability for chronic obstructive pulmonary disease and asthma, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet Respir Med, 2017;5:691–706.
4. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management and Prevention of COPD, 2017. http:// goldcopd.org. (accessed on 10june 2019)
5. Wedzicha JA, SeemungalTA . COPD exacerbations: defining their cause and prevention. Lancet, 2007;370:786–96.
6. Reiller CL, Martineau AR. Modulation of the immune response to respiratory viruses by vitamin D. Nutrients, 2015;7:4240–70.
7. Reiller CL, Suri R, Jolliffe DA, Kebadze T, Hirsman AG, Griffiths CJ, et al. Vitamin D attenuates rhinovirus-induced expression of intercellular adhesion molecule-1 (ICAM-1) and platelet-activating factor receptor (PAFR) in respiratory epithelial cells. J Steroid BiochemMolBiol,2019 Mar;187:152-159

8. Martineau AR, Jolliffe DA, Hooper RL, Aloia JF, Susanna Esposito, Gal Dubnov-Raz, et al. Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data. Brit Med J, 2017; 356:65-83.
9. Jolliffe DA, Greenberg L, Hooper RL, Griffiths CJ, Camargo CA, Kerley CP, et al. Vitamin D supplementation to prevent asthma exacerbations: a systematic review and meta-analysis of individual participant data. Lancet Respir Med, 2017;5:881–90.
10. Janssens W, Decramer M, Mathieu C, Korf H. Vitamin D and chronic obstructive pulmonary disease: hype or reality? Lancet Respir Med, 2013;1:804–12.
11. Malinovschi A, Masoero M, Bellocchia M, Ciuffreda A, Solidoro, Mattei A, et al. Severe vitamin D deficiency is associated with frequent exacerbations and hospitalization in COPD patients. Respir Res, 2014;15:131.
12. Kunisaki KM, Niewoehner DE, Connett JE. COPD Clinical Research Network. Vitamin D levels and risk of acute exacerbations of chronic obstructive pulmonary disease: a prospective cohort study. Am J RespirCrit Care Med, 2012;185:286–90.
13. Quint JK, Donaldson GC, Wassef N, Hurst JR, Thomas M and Wedzicha JA. 25-hydroxyvitamin D deficiency, exacerbation frequency and human rhinovirus exacerbations in chronic obstructive pulmonary disease. BMC Pulm Med, 2012;12:28.
14. Puhan MA, Siebeling L, Frei A, Zoller M, Bischoff-Ferrari H, TerRiet G. No association of 25-hydroxyvitamin D with exacerbations in primary care patients with COPD. Chest, 2014;145:37–43.

15. Ginde AA, Mansbach JM, Camargo CA Jr. Association between serum 25-hydroxyvitamin D level and upper respiratory tract infection in the Third National Health and Nutrition Examination Survey. Arch Intern Med,2009; 169: 384–90.
16. Janssens W, Lehouck A, Carremans C, Bouillon R, Mathieu C, Decramer M, et al. Vitamin D beyond bones in chronic obstructive pulmonary disease: time to act. Am J RespirCrit Care Med,2009; 179: 630–36.
17. Kunisaki KM, Niewoehner DE, Connett JE. Vitamin D levels and risk of acute exacerbations of chronic obstructive pulmonary disease: A prospective cohort study. Am J RespirCrit Care Med,2012; 185: 286–90.
18. Quint JK, Donaldson GC, Wassef N, Hurst JR, Thomas M, Wedzicha JA, et al. 25-hydroxyvitamin D deficiency, exacerbation frequency and human rhinovirus exacerbations in chronic obstructive pulmonary disease. BMC Pulm Med,2012; 12: 28.
19. Lehouck A, Mathieu C, Carremans C, Baeke F, Verhaegen J, Van Eldere J, et al. High doses of vitamin D to reduce exacerbations in chronic obstructive pulmonary disease: a randomized trial. Ann Intern Med 2012; 156: 105–14.
20. Jung JY, Kim YS, Kim SK, Kim HY, Oh YM, Lee SM, et al. Relationship of Vitamin D status with lung function and exercise capacity in COPD. Respirology, 2015;20(5):782-9
21. Martineau AR, James WY, Hooper RL, Barnes NC, Jolliffe DA, Greller CL, et al. Vitamin D3 supplementation in patients with chronic obstructive pulmonary disease (ViDiCO): a multicentre, double-blind, randomised controlled trial. Lancet Respir Med, 2015;3:120–30.

22. Rafiq R, Prins HJ, Boersma WG, Daniels JM, den Heijer M, Lips P, et al. Effects of daily vitamin D supplementation on respiratory muscle strength and physical performance in vitamin D-deficient COPD patients: a pilot trial. Int J Chron Obstruct Pulmon Dis, 2017;12:2583–92.
23. Zendedel A, Gholami M, Anbari K, Ghanadi K, Bachari EC, Azargon A. Effects of vitamin D intake on fev1 and COPD exacerbation: A randomized clinical trial study. Glob J Health Sci, 2015;7:243–8.
24. Boonen S, Lips P, Bouillon R, Bischoff-Ferrari HA, Vanderschueren D, Haentjens P, et al. Need for additional calcium to reduce the risk of hip fracture with vitamin D supplementation: Evidence from a comparative metaanalysis of randomized controlled trials. J ClinEndocrinolMetab, 2007; 92:1415–1423.
25. Bouillon R., Bischoff-Ferrari H., and Willett W. Vitamin D and health: Perspectives from mice and man. J. Bone Miner. Res, 2008; 23:974–979.
26. Bouillon R, Carmeliet G, Verlinden L, van Etten E, Verstuyf A, Luderer H. F, et al. Vitamin D and human health: Lessons from vitamin D receptor null mice. Endocr. Rev, 2008; 29:726–776.
27. Janssens W, Lehouck A, Carremans C, Bouillon R, Mathieu C, Decramer M, et al. Vitamin D beyond bones in chronic obstructive pulmonary disease: Time to act. Am J RespirCrit Care Med, 2009; 179:630–636
28. Norman A. W, Bouillon R, Whiting S. J, Vieth R, and Lips P. 13th Workshop consensus for vitamin nutritional guidelines. J. Steroid BiochemMolBiol, 2007; 103:204–205
29. Dawson-Hughes B, Heaney R. P, Holick M. F, Lips P, Meunier P. J, and Vieth R. Estimates of optimal vitamin D status. OsteoporosInt, 2005; 16:713–716.

30. Lange P, Celli B, Agusti A, Boje Jensen G, Divo M, Faner R, et al. Lung Function Trajectories Leading to Chronic Obstmctive Pulmonary Disease. N EngllMed, 2015; 373(2): 111-22.
31. Stern DA, Morgan WJ, Wright AL, Guerra S, Martinez FD. Poor airway function in early infancy and lung function by age 22 years: a non selectivelongitudinal cohort study. Lancet,2007; 370(9589): 758-64,
32. TashkinDP, Ahose MD, Bleecker ER, Connett JE, Kanner RE, Lee WW, et al. The lung health study: airway responsiveness to inhaled memacholinein smokers with mild to moderate airflow limitation. The Lung Health Study Research Group.Am Rev RespirDis 1992; 145: 301-10.
33. Eisner MD, AnthonisenN, CaultasD, Kuenzli N, Perez-Padilla R, Postma D, et al. An official American Thoracic Society public policy statement: Novel risk factors and the Global burden of Chronic Obstructive Pulmonary disease. Am J RespirCritCare Med, 2010; 182(5): 693-718.
34. Salvi SS, Barnes PJ. Chronicobstructive pulmonarydisease in non smokers. Lancet,2009; 374(9691): 733 43.
35. MathersCD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PLoSMed, 2005; 3(11): e442.
36. HalbertRJ,NatoliL,GanoA, BadamgaravE, BuistAS, ManninoDM, et al. Globgtburden of COPD: systematic review and meta analysis. EurRespir,2006; 28(3): 523-32.
37. Quach A, GiovannelliJ, Cherot-Kornobis N, Ciuchete A, Clement G, Matran R, et al. Prevalence and underdiagnosisof airway obstruction among middle-aged adults in northemFrance: The ELISABET study 2011 2013. RespirMed J, 2015; 109(12): 1553-61.

38. Menezes AM, Perez-PadRill, Hallal PC, JaardimJ R, Muino A, Lopez MV, et al. Chronic obstructive pulmonary disease in five Latin American cities, et al(the PLATINO study). A prevalence study. Lancet 2005; 366(9500): 1875-81.
39. American Thoracic Society Foundation. The Global Burden of Lung Disease, 2014. http://foundation.thoracic.org/news/global-burden.php(accessed on 12 june 2019).
40. GuarascioAJ, Ray SM, Finch CK, SeIf TH. The clinical and economic burden of chronic obstructive pulmonary disease in the USA. ClinicoEconomics and outcomes research :CEOR,2013; 5: 235-45.
41. Chen W, Thomas J, Sadatsafavi M, FitzGerald JM. Risk of cardiovascular comorbidity in patients with chronic obstructive pulmonary disease: a systematic review and meta-analysis. The Lancet Respirmed J,2015; 3(8): 631-9.
42. ManninoDM, Higuchi K, Yu TC, Zhou H, LI Y, Tian H, et al. Economic Burden of COPD in the Presence of Comorbidities. Chest, 2015; 148(1): 138-50.
43. Hoyert DL, Xu JO. Deaths: preliminary data for 2011. Natl Wtal Stat Rep,2011; 61(6): 1-65.
44. LamprechtB, McBurnieMA, Vollmer WM, Gudmundsson G, Welte T, Studnicka M, et al. COPD in never smokers: results from the population based burden of obstructive lung disease study. Chest,2011; 139(4): 752-63
45. Rennard SI, Vestbo J. COPD: the dangerous underestimate of 15%. Lancet, 2006; 367(9518): 1216-9.

46. Tager IB, Ngo L, Hanrahan JP. Maternal smoking during pregnancy. Effects on lung function during the first 18 months of life. Am J RespirCrit Care Med, 1995; 152: 977-83.
47. Kohansal R, Martinez-Camblor P, Agusti A, Buist AS, ManninoDm, Soriano JB. The natural history of chronic airflow obstruction revisited: an analysis of the Framingham offspring cohort. AmjRespirCrit Care Med, 2009; 180(1): 3-10.
48. Gan WQ, FitzGerald M, Carlsten C, Sadatsafavi M, Brauer M. Associations of ambient air pollution with chronic obstructive pulmonary disease hospitalization and mortality. AmJRespIr Cat Care Med, 2013; 187(7): 721-7.
49. EzzatiM . Indoor air pollution and health in developing countries. Lancet,2005; 366(9480): 104 6.
50. Zhou V, Zou Y, Li X, Chen S, Zhao Z, He F, et al. Lung function in advance of chronic obstructive pulmonary disease after improved cooking fuels and kitchen ventilation: a 9-year prospective cohort study. PLoSMed, 2014; 11(3): e1001621.
51. Sana A, SomdaSMA, Meda N, Bouland C. Chronic obstructive pulmonary disease associated with biomass fuel use in women: a sys1ematic review and metaanalysis. BMJ open respiratory research 2018; 5(1): e000246.
52. Assad NA, Balmes J, Mehta S, Cheema U, Sood A. Chronic obstructive pulmonary disease secondary to household air pollution. SeminRespirCrit Care Med, 2015; 36(3): 408-21.
53. Sherrill DL, Lebownz MD, Burrows B. Epidemiology of chrome obstructive pulmonary disease. Clin Chest Med,1990; 11(3): 375-87.

54. Gauderman WJ, UrmaRn ,Avol E, Berame K, McConnell R, Rappaport E, et al. Association of improved air quality with lung development in children. N Engl JMed,2015; 372(10): 905- 13.
55. Eisner MD, AnthonisenN, CaultasD, et al. An official American Thoracic Society public policy statement: Novel risk factors and the global burden of chronic obstructive pulmonary disease. AmjRespirCritCare Med,2010; 182(5): 693-718.
56. Paulin LM. Diette GB, Blanc PD, Putcha N, Eisner MD, Kanner RE, et al. Occupational exposures are associated with worse morbidity in patients with chronic obstructive pulmonary disease. Am J RespirCrit Care Med, 2015; 191(5): 557-65.
57. Balmes J, Becklake M, Blanc P, Henneberger P, Kreiss K, MappC,et al. American Thoracic Society Statement: Occupational contribution to the burden of airway disease. Am J RespirCrit Care Med, 2003; 167(5): 787-97.
58. Hospers JJ, Postma DS, Rijcken B, Weiss ST, Schouten JP.Histamine airway hyper-responsiveness and mortality from chronic obstructive pulmonary disease: a cohort study. Lancet, 2000; 356(9238): 1313-7.
59. McCloskey SC, Patel BD, Hinchliffe SJ, Reid ED, Wareham NJ, Lomas DA. Siblings of patients with severe chronic obstructive pulmonary disease have a significant risk of airflow obstruction. RespirCrit Care Med, 2001; 164(8 Pt 1): 1419-24.
60. Mercado N. Ito K, Barnes PJ. Accelerated ageing of the lung in COPD: new concepts. Thorax, 2015; 70(5): 482-9.
61. Landis SH, Muellerova H, Mannino DM, Menezes Am, Han MK, van der Molen T, et al. Continuing to Confront COPD International Patient Survey:

methods, COPD prevalence, and disease burden in 2012-2013. Int J Chron obstruct PulmonDis, 2014; 9: 597-611.

62. Martinez FJ, Curtis JL, Sciurba F, Mumford J, Giardino ND, Weinmann G, et al. Sex differences in severe pulmonary emphysema. AmJRespirCrit Care Med, 2007; 176(3): 243-52.
63. Tam A, Churg A, Wright JL, Zhou S, Kirby M, Coxson HO, et al. Sex Differences in Airway Remodeling in a Mouse Model of Chronic Obstructive Pulmonary Disease. AmjRespCrit Care Med, 2016; 193(8): 825-34.
64. Silva GE, Sherrill DL, Guerra S, Barbee RA. Asthma as a risk factor for COPD in a longitudinal study. Chest, 2004; 126(1): 59-65.
65. VonkJM, Jongepier H, Panhuysen CI, Schouten JP, Bleecker ER, Postma DS, et al. Risk factors associated with the presence of irreversible airway limitation and reduced transfer coefficient in patients with asthma after 26 years of follow up. Thorax, 2003; 58(4): 322-7.
66. McGeachie MJ, Yates KP, Zhou X. Patterns of Growth and Decline in Lung Function in Persistent Childhood Asthma. N Eng J Med, 2016; 374(19): 1842-52.
67. Rijcken B, Schouten JP, Weiss ST, Speizer FE, van der Lende R. The relationship of nonspecific bronchial responsiveness to respiratory symptoms in a random population sample. Am Rev Respir Dis,1987; 136(1): 62-8.
68. Hospers JJ, Postma DS, Rijcken B, Weiss ST, Schouten JP. Histamine airway hyper-responsiveness and mortality from chronic obstructive pulmonary disease: a cohort study. Lancet, 2000; 356(9238): 1313-7.

69. De Marco R, Accordini S, MarconA, Cerveri I, Anto JM, Gislason T, et al. Risk factors for chronic obstructive pulmonary disease in a European cohort of young adults. AmjRespir cri Care Med, 2011; 183(7): 891-7.
70. Townend J, Minelli c, Mortimer K, Daniel O, Ghobian MA, Cherkaski H, et al. The association between chronic airflow obstruction and poverty in 12 sites of the multinational BOLD study. EurRespirJ, 2017; 49(6).
71. Beran D, Zar HJ, Perrin C, Menezes AM, Burney P. Forum of international Respiratory Societies working group c. Burden of asthma and chronic obstructive pulmonary disease and access to essential medicines in low income and middle-income countries. Lancet RespirMed, 2015; 3(2):159-70
72. Gershon AS, Warner L, Cascagnette P, Victor JC. Lifetime risk of developing chronic obstructive pulmonary disease: a longitudinal population study. Lancet,2011; 378(9795): 991- 6.
73. Hogg CT, Timens W. The pathology of chronic obstructive pulmonary disease. Annual review of pathology, 2009; 4: 435-59.
74. Barnes P. Inflammatory mechanisms in patients with chronic obstructive pulmonary disease. J Allergy ClinImmunol2016; 138(1): 16-27.
75. DomejW ,Oettl K, Renner W. Oxidative stress and free radicals in COPD-implications and relevance for treatment. Int J Chron Obstruct PulmonDis 2014; 9: 1207
76. Malhotra D, Thimmulappa R, Vij N, Navas-Acien A, Sussan T, Merali S, et al. Heightened endoplasmic reticulum stress in the lungs of patients with chronic obstructive pulmonary disease: the role of Nrf2- regulated proteasomal activity. Am J RespirCrit Care Med, 2009; 180(12): 1196-207.

77. Stockley RA. Neutrophils and protease/antiprotease imbalance. Am J RespirCrit Care Med, 1999; 160(5 Pt 2): 549-52
78. JohnsonS R. Untangling the protease web in COPD: metalloproteinase in the silent zone. Thorax, 2016; 71(2): 105-6
79. Barnes PJ. Inflammatory mechanisms in patients with chronic obstructive pulmonary disease. J Allergy ClinImmunol,2016; 138(1): 16-27
80. Sze MA, Dimitriu PA, Suzuki M, McDonough JE, Campbell JD, Brothers JF, et al. Host Response to the Lung microbiome in Chronic Obstructive Pulmonary Disease. AmjRespirCrit Care Med, 2015; 192(4): 43845.
81. Katzenstein AL, Mukhopadhyay S, Myers 1L. Diagnosis of usual interstitial pneumonia and distinction from other fibrosing interstitial lung disease. Hum Pathol J, 2008; 39(9): 1275-94.
82. Washko GR, Hunninghake GM, Fernandez IE, Nishino M, Okajima Y, Yamashiro T, et al. Lung volumes and emphysema in smokers with interstitial lung abnormalities. N Engl J Med, 2011; 364(10): 897-906.
83. Putman RK, Hatabu H, Araki T, Gudmundsson G, Gao W, Nishino M, et al. Association Between Interstitial Lung Abnormalities and all cause mortality. Jama, 2016; 315(7): 672-81.
84. Churg A, Tai H, Coulthard T, Wang R, et al. Cigarette smoke drives small airway remodeling by induction of growth factors in the airway wall. Am JRespirCrit Care Med, 2006; 174(12): 1327-34.
85. Hogg JC, Chu F, Utokaparch S, Woods R, Elliott WM, Buzatu L, et al. The nature of small airway obstruction in chronic obstructive pulmonary disease. N Engl J Med, 2004; 350(26): 2645-53.

86. Casaburi R, Maltais F, PorszaszJ, et al. Effects of tiotropium on hyperinflation and treadmill exercise tolerance in mild to moderate chronic obstructive pulmonary disease. AnnAm ThorSoc,2014; 11(9): 1351-61.

87. Elbehairy AF, Ciavaglia CE, Webb KA, Guenette JA, Jensen D, Mourad SM, et al. Pulmonary Gas Exchange Abnormalities in Mild Chronic Obstructive Pulmonary Disease implications for dyspnea and exercise intolerance. Am J RespirCritCare Med, 2015; 191(12): 1384-94.

88. Rodriguez-Roisin R, Drakulovic M, Rodriguez DA, Roca J, Barbera Ja, Wagner PD. Ventilation perfusion imbalance and chronic obstructive pulmonary disease staging severity. J AppIPhysiol, 2009; 106(6): 1902-8.

89. BurgelPR, Nadel JA. Epidermal growth factor receptor mediated innate immune responsesandtheir roles in airway diseases. EurRespir J,2008; 32(4): 1068-81.

90. Sandhu MS, Casale TB. The role of vitamin D in asthma. Ann Allergy Asthma Immunol,2010; 105:191–199.

91. Hansdottir S, Monick MM, Hinde SL, Lovan N, Look DC, Hunninghake GW. Respiratory epithelial cells convert inactive vitamin D to its active form: potential effects on host defense. J Immunol, 2008; 181(10): 7090–99.

92. Holick MF. The vitamin D deficiency pandemic and consequences for nonskeletal health: Mechanisms of action. Mol Aspects Med 2008; 29(6):361-8.

93. Mithal A, Wahl DA, Bonjour JP, Burckhardt P, Dawson-Hughes B, Eisman JA et al. Global vitamin D status and determinants of hypovitaminosis D. OsteoporosInt, 2009; 20:1807–20.

94. Harinarayan CV, Ramalakshmi T, Prasad UV, Sudhakar D, Srinivasarao PV, Sarma KV et al. High prevalence of low dietary calcium, high phytate consumption, and vitamin D deficiency in healthy south Indians. Am J ClinNutr,2007; 85:1062–7.

95. Pludowski P, Holick MF, Pilz S, Wagner CL, Hollis BW, Grant WB, et al. Vitamin D effects on musculoskeletal health, immunity, autoimmunity, cardiovascular disease, cancer, fertility, pregnancy, dementia and mortality- a review of recent evidence. Autoimmun Rev, 2013; 12(10):976-89.

96. Abu- Amer Y, Bar- Shavit Z. Regulation of TNF- α release from bone marrow–derived macrophages by vitamin D. J Cell Biochem, 1994; 55(4):435-44.

97. Liu PT, Stenger S, Li H, Wenzel L, Tan BH, Krutzik SR, et al. Toll-like receptor triggering of a vitamin D-mediated human antimicrobial response. Science, 2006; 311(5768):1770-3.

98. Agrawal DK, Shao Z. Pathogenesis of allergic airway inflammation. Curr Allergy Asthma Rep, 2010; 10(1):39–48.

99. Mak G, Hanania NA. Vitamin D and asthma. CurrOpinPulm Med, 2011;17:1–5.

100. Prietl B, Treiber G, Pieber TR, Amrein K. Vitamin D and immune function. Nutrients, 2013; 5(7):2502-21.

101. Wang T, Nestel FT, Bourdeau V, Nagai Y, Wang Q, Liao J, et al. Cutting edge: 1,25-Dihydroxyvitamin D3 is a direct inducer of antimicrobial peptide gene expression. J Immunol, 2004; 173(5): 2909–12.

102. Black PN, Scragg R. Relationship between serum 25-Hydroxyvitamin D and pulmonary function in the third national health and nutrition examination survey. Chest, 2005; 128(6):3792–98.

103. Larose TL, Langhammer A, Chen Y, Camargo CA, Romundstad P, Mai XM. Serum 25-hydroxyvitamin D levels and lung function in adults with asthma: the HUNT Study. EurRespir J, 2014; 45(4):1019-26.

104. Li F, Peng M, Jiang L, Sun Q, Zhang K, Lian F, et al. Vitamin D deficiency is associated with decreased lung function in Chinese adults with asthma. Respiration, 2011; 81(6):469–475.

105. Lips P. Vitamin D deficiency and secondary hyperparathyroidism in the elderly: Consequences for bone loss and fractures and therapeutic implications. Endocr. Rev, 2001; 22:477–501.

106. Feng X, Lv C, Wang F, Gan K, Zhang M, Tan W, et al. Modulatory effect of 1,25-dihydroxyvitamin D 3 on IL1 β -induced RANKL, OPG, TNF α and IL-6 expression in human rheumatoid synoviocyte MH7A. Clin Dev Immunol, 2013; 160123

107. Baldock PA, Thomas GP, Hodge JM., Baker SU, Dressel U, O'Loughlin PD, et al. Vitamin D action and regulation of bone remodeling: Suppression of

osteoclastogenesis by the mature osteoblast. J. Bone Miner. Res, 2006; 21:1618–1626.

108. Holick MF. Vitamin D deficiency. N Engl J Med, 2007; 357:266–281

109. Black PN, Scragg R. Relationship between serum 25-hydroxyVitamin D and pulmonary function in the third national health and nutrition examination survey. Chest, 2005;128(6):3792-8.

110. Berg I, Hanson C, Sayles H, Romberger D, Nelson A, Meza J, et al. Vitamin D, Vitamin D binding protein, lung function and structure in COPD. Respir Med J, 2013; 107(10):1578-88

111. Akbari M, Ostadmohammadi V, Lankarani KB, Tabrizi R, Kolahdooz F, Heydari ST, et al. The effects of vitamin D supplementation on biomarkers of inflammation and oxidative stress among women with polycystic ovary syndrome: a systematic review and meta-analysis of randomized controlled trials. HormMetab Res, 2018; 50(6):429-440.

112. Chen L, Yang R, Qiao W, Yuan X, Wang S, Goltzman D, et al. 1,25-Dihydroxy vitamin D prevents tumorigenesis by inhibiting oxidative stress and inducing tumor cellular senescence in mice. Int J Cancer, 2018; 143(2):368-382.

113. Lisakovska O, Shymanskyy I, Mazanova A, Khomenko A, Veliky M. Vitamin D3 protects against prednisolone-induced liver injury associated with the impairment of the hepatic NF-kappaB/iNOS/NO pathway. Biochem Cell Biol, 2017; 95(2):213-222.

114. Trepo E, Ouziel R, Pradat P, Momozawa Y, Quertinmont E, Gervy C, et al. Marked 25-hydroxyvitamin D deficiency is associated with poor prognosis in patients with alcoholic liver disease. J Hepatol, 2013; 59(2):344-350.

115. Bouillon, R., Bischoff-Ferrari H and Willett W (2008a). Vitamin D and health: Perspectives from mice and man. J. Bone Miner Res, 2008; 23:974–979.

116. Ginde AA, Mansbach JM, Camargo CA. Association between serum 25-hydroxyvitamin D level and upper respiratory tract infection in the Third National Health and Nutrition Examination Survey. Arch Intern Med, 2009; 169:384–90.

117. Kunisaki KM, Niewoehner DE, Connett JE. Vitamin D levels and risk of acute exacerbations of chronic obstructive pulmonary disease: a prospective cohort study. Am J RespirCrit Care Med, 2012; 185:286–90.

118. Quint JK, Donaldson GC, Wassef N, Hurst JR, Thomas M and Wedzicha JA. 25-hydroxyvitamin D deficiency, exacerbation frequency and human rhinovirus exacerbations in chronic obstructive pulmonary disease. BMC Pulm Med, 2012; 12:28.

119. Fernandez-Lahera J, Romera D, Gómez Mendieta A, MartínezVerdasco A, Fernandez-Bujarrabai A, Santiago A, et al. Prevalence of vitamin D deficiency in patients with chronic obstructive pulmonary disease.European Respiratory Journal, 2015; 46:3977

120. Jolliffe DA, James WY, Hooper RL, Barnes NC, Greiller CL, Islma K, et al. Prevalence, determinants and clinical correlates of vitamin D deficiency in patients with Chronic Obstructive Pulmonary Disease in London, UK.

121. Chapuy MC, Preziosi P, Maamer M, ArnaudS, Galan P, Hercberg S, et al. Prevalence of vitamin D insufficiency in an adult normal population. OsteoporosInt, 1997; 7:439–443

122. Dawson-Hughes B, Heaney RP, Holick MF, Lips P, Galan P, HercbergS,et al. Estimates of optimal vitamin D status. OsteoporosInt, 2005; 16:713–716.

123. Norman AW, Bouillon R, Whiting SJ, Vieth R, and Lips P. 13th Workshop consensus for vitamin D nutritional guidelines. J Steroid BiochemMolBiol, 2007; 103:204–205.

124. Black PN, and Scragg R. Relationship between serum 25-hydroxyvitamin d and pulmonary function in the third national health and nutrition examination survey. Chest,2005; 128:3792–3798

125. Graat-Verboom L, van den Borne BE, Smeenk FW, Spruit MA and Wouters EF. Osteoporosis in COPD outpatients based on bone mineral density and vertebral fractures. J Bone Miner Res, 2011; 26(3): 561-8

126. Pourrashid MH, Dastan F, Salamzadeh J, Eslaminejad A and Edalatifard M. Role of Vitamin D Replacement on Health Related Quality of Life in Hospitalized Patients with "Acute Exacerbation of Chronic Obstructive Pulmonary Disease". Iran J Pharn Res, 2018; 17(2):801-810

127. Cooper MS, Gittoes NJL. Diagnosis and management of hypocalcaemia. Brit Med J, 2008; 336(7656):1298-302

128. Cho KC. Electrolyte & Acid-Base Disorders. In: Maxine A. Papadakis SJM, editor. Current Medical Diagnosis & Treatment McGraw-Hill Education 2015, 861-89.

129. AmardeepakToppo, D. Sudheer, G. S. Rajawat, Thomas Kurian. A study to assess nutritional profile in chronic obstructive pulmonary disease patients. Int J Adv Med, 2017 Apr;4(2):450-456

ANNEXURE I:

INFORMED CONSENT

PREVALENCE OF VITAMIN D AND SERUM CALIUM DEFICIENCY IN STABLE COPD PATIENTS- A ONE YEAR HOSPITAL BASED OBSERVATIONAL STUDY

Purpose of the study:

You are being asked to enroll in the study as you are eligible for participation in this study. All patients who are diagnosed with chronic obstructive pulmonary disease 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.ShrikantDurgeunder the guidance of Dr.BhagyashriPatil.

The purpose of this study is to evaluate the prevalence of deficiency of Vitamin D in patientswith chronic obstructive pulmonary disease and to correlate Vitamin D levels with serum calcium levels of stable COPD patients. There is insufficient evidence to support a causal association between vitamin D status and COPD.

Procedure :

If a patient who is a known case of chronic obstructive pulmonary disease presenting to Dr KLES Prabhakar Kore Charitable Hospital and MRC agrees to enroll himself/herself in the study, he/she will be subjected to detailed history taking, clinical examination, chest Xray PA view, spirometry performed according to American Thoracic Guidelines and serum Vitamin D levels & serum calcium levels will be measured.

Risks and benefits:

There are no risks or benefits involved.

Alternatives:

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 other 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 incentivesfor participation:

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

Authorization to publish results:

The results of this study would be forwarded to the KLE University, 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 orillness, you can contact :

- Dr.ShrikantDurge, Department of Pulmonary Medicine, KLE'S Dr.Prabhakar Kore Hospital and MRC, Ph. No.0831-2551376 or phone number:8495939726
- Dr.BhagyashriPatil, Associate Professor, Department of Pulmonary Medicine, KLE'S Dr.Prabhakar Kore Hospital and MRC, Belgaum Ph.: 0831-2551376
- Dr.Gajanan.S.Gaude, Professor and Head, Department of Pulmonary Medicine, KLE'S Dr.Prabhakar Kore Hospital and MRC, Belgaum Ph.: 0831-2551376

- If you have any queries about your rights as a study subject, you may call Dr. Ganga Pilli,Professor, Department of Pathology, Chairman of J. N. Medical College InstitutionalEthical Committee of Human Subjects Research, Phone No. 9448863866, at J. N.Medical College, Belgaum.

CONSENT STATEMENT

I voluntarily agree to take part in this study by signing below. I may withdraw at any time. I amnot giving up any legal rights by signing this form. My signature below indicates that I haveread, or it has been read to me, this entire consent form, and have had all my questions answered.In case of the queries during the study or in future you may contact following person.

Principle investigator: Dr.ShrikantDurge

Guide : Dr.BhagyashreePatil

Name of the participant: (signature/thumb print)

Name of the witness: (signature)

Name of the investigator: (signature)

Date: Place:

Address :

Phone no:

ANNEXURE II:

PROFORMA

NAME:

AGE: SEX:

OCCUPATION:

PRESENTING COMPLAINTS AND DURATION:

Cough
Breathlessness MMRC
Wheeze
Fever
Chest pain
Other symptoms

PAST H/O :

K/C/O COPD____ yrs

Hospitalizations-

Comorbidity - Diabetes mellitus / Hypertension /Tuberculosis / other comorbidities

HABITS IF ANY -

Smoking / Alcohol / Tobaco

HEIGHT: WEIGHT: BMI:

DIAGNOSIS:

PULMONARY FUNCTION TEST MEASUREMENTS:

FEV1(%predicted)

FVC(%predicted)

FEV1/FVC

Inference

SERUM VITAMIN D LEVELS:

SERUM CALCIUM LEVELS:

INVESTIGATOR'S SIGNATURE **GUIDE'S SIGNATURE**

ANNEXURE III: Ethical Clearance certificate

56

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/56

Date: 22/11/2017

To,

BR0117003

Sub: Institutional Ethical Clearance for the study.

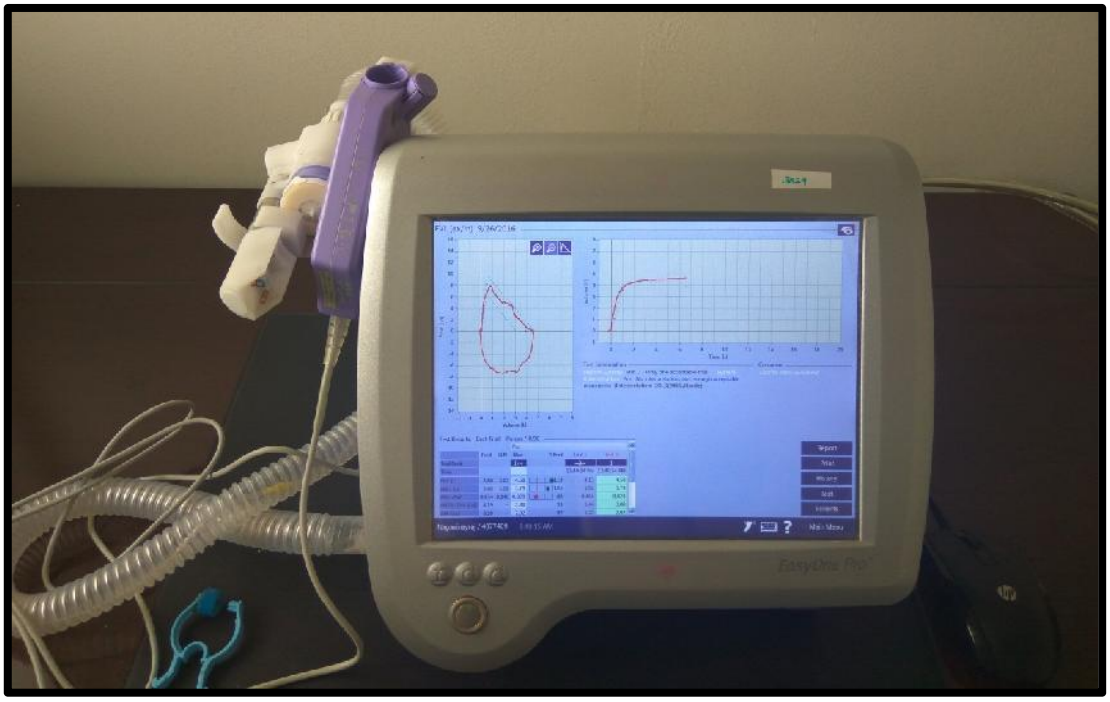
With reference to the above, we wish to inform you that your proposed research project titled **"PREVALENCE OF VITAMIN D AND SERUM CALCIUM DEFICIENCY IN STABLE CHRONIC OBSTRUCTIVE PULMONARY DISEASE A 1 YEAR HOSPITAL BASED OBSERVATIONAL STUDY"**, is ethical and justifiable. The proposed research project 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.

ANNEXURE IV:

PHOTOGRAPHS



Photograph 1.Spirometer

ANNEXURE V:

KEY TO MASTERCHART

- FEV1% : Forced Expiratory Volume in 1 second
- FVC : Forced Vital Capacity
- BMI : Body Mass Index
- F : Female
- M : Male
- HT : Height
- WT : Weight
- S.CA : Serum calcium levels
- S.VIT D : Serum Vitamin D levels

ANNEXURE VI:MASTER CHART

SL. NO	NAME	AGE	SEX	HT	WT	BMI	SMOKING	FEV1	FVC	RATIO	INFERENCE	CO-MORBIDITY	S.VIT D	REMARK	S.CA	REMARK
1	PREMA KAMBLE	61	F	162	70	27	NO	31	36	0.7	SEVERE	HTN,DM	18.2	DEFICIT	8.6	HYPO
2	KRISHNA K	82	M	165	60	22	YES	28	39	0.6	V.SEVERE		27.01	INSUFFICIENT	9.5	NORMAL
3	BHIMANGOUDA D.H	55	M	167	42	15	YES	61	72	0.7	MODERTE	HTN	17.8	DEFICIT	8.9	NORMAL
4	VASANT KAMBLE	70	M	161	81	31	YES	56	59	0.7	MODERTE	HTN	28.6	INSUFFICIENT	8	HYPO
5	GANGAVVA U	75	F	165	72	26	NO	45	58	0.6	SEVERE	HTN	5.8	DEFICIT	8.8	NORMAL
6	PARVATI HARJE	70	F	154	67	28	NO	66	78	0.7	MODERTE	DM	16.4	DEFICIT	8.9	NORMAL
7	DEMAVVA T	57	F	164	54	20	NO	50	59	0.7	MODERTE		28	INSUFFICIENT	8.8	NORMAL
8	VEERBHADRAPPA D	71	M	159	50	20	YES	55	65	0.7	MODERTE	HTN	20.6	INSUFFICIENT	8.4	HYPO
9	BASAVANNA M	70	M	172	75	25	YES	71	91	0.7	MODERTE	HTN	34.5	ADEQUATE	8.4	HYPO
10	GOURAMMA M	65	F	168	59	21	NO	67	71	0.7	MODERTE		42	ADEQUATE	8.8	NORMAL
11	MAHNATAPPA KORI	65	M	140	47	24	NO	35	42	0.7	SEVERE	IHD	28.8	INSUFFICIENT	8.8	NORMAL
12	DATTATRAY H	60	M	146	40	19	YES	57	58	0.7	MODERTE	IHD	16.8	DEFICIT	8.8	NORMAL
13	PARAVATI KORE	65	F	156	75	31	NO	43	54	0.7	SEVERE		32	ADEQUATE	8.9	NORMAL
14	SUNANDABAI P.K	70	F	149	67	30	NO	36	52	0.6	SEVERE		40.1	ADEQUATE	8.8	NORMAL
15	BALAPPA M	70	M	164	62	23	YES	62	78	0.7	MODERTE	IHD	12	DEFICIT	8.9	NORMAL
16	NAGESH PUNED	72	M	157	63	26	YES	55	68	0.7	MODERTE		15	DEFICIT	8.2	HYPO
17	SIDDAPPA P	70	M	160	64	25	YES	65	82	0.7	MODERTE	DM,CVA	12.6	DEFICIT	8.5	HYPO
18	MAHADEV B	55	M	171	61	21	NO	79	78	0.7	MODERTE	DM,HTN	31.6	ADEQUATE	8.9	NORMAL
19	SIDDAPPA M	78	M	166	68	25	NO	70	76	0.7	MODERTE		6.74	DEFICIT	8.1	HYPO
20	SUSHILA KHOT	80	F	140	47	24	NO	58	71	0.7	MODERTE	DM,IHD	4.2	DEFICIT	8.2	HYPO
21	MAHADEV T	70	M	160	74	29	YES	36	48	0.6	SEVERE	HTN,IHD	36.8	ADEQUATE	8.5	HYPO
22	FATIMA JAMADAR	98	F	145	50	24	NO	67	76	0.7	MODERTE		6	DEFICIT	8.6	HYPO
23	NARAYAN N	61	M	173	51	17	YES	60	68	0.7	MODERTE		28	INSUFFICIENT	8.3	HYPO
24	SIDDAPPA P.M	68	M	152	50	22	YES	50	58	0.7	MODERTE	DM	19	DEFICIT	8.4	HYPO
25	SULAVVA KAMBLE	60	F	155	70	29	NO	27	47	0.7	V.SEVERE		32	ADEQUATE	8.2	HYPO
26	RAMACHANDRA K	60	M	157	52	21	YES	56	63	0.7	MODERTE	HTN.DM	8	DEFICIT	8.9	NORMAL
27	BHIMAGOUDA P	65	M	157	52	21	YES	67	69	0.7	MODERTE		24	INSUFFICIENT	8.9	NORMAL

ANNEXURE VI:MASTER CHART

SL. NO	NAME	AGE	SEX	HT	WT	BMI	SMOKING	FEV1	FVC	RATIO	INFERENCE	CO-MORBIDITY	S.VIT D	REMARK	S.CA	REMARK
28	MUDAKAPPA.V.M	80	M	153	49	21	YES	67	76	0.7	MODERTE	HTN	6.6	DEFICIT	9.2	NORMAL
29	BASAYYA .G.D	79	M	163	64	24	NO	54	58	0.7	MODERTE		3	DEFICIT	8.5	HYPO
30	SHOBHA JADHAV	50	F	160	80	31	NO	56	58	0.7	MODERTE	HTN	13.6	DEFICIT	8.3	HYPO
31	BASAPPA S.B	70	M	169	56	20	YES	52	58	0.7	MODERTE		22	INSUFFICIENT	8.2	HYPO
32	SHANTHABAI.Y.G	76	F	163	73	28	NO	55	67	0.7	MODERTE	DM,HTN,IHD	70	ADEQUATE	8.2	HYPO
33	NINGAPPA .B.A	65	M	163	76	29	YES	77	80	0.7	MODERTE	DM	7.9	DEFICIT	8.8	NORMAL
34	PRAKASH GHODKE	63	M	168	90	32	YES	52	55	0.7	MODERTE	DM	28.1	INSUFFICIENT	8.6	HYPO
35	ASHOK VADHE	60	M	162	65	25	YES	63	75	0.7	MODERTE		44	ADEQUATE	8.3	HYPO
36	SUMITRADEVI S.S	70	F	160	65	25	NO	56	71	0.7	MODERTE		58.3	ADEQUATE	11.2	HYPER
37	SHANKAR KOLI	76	M	146	60	28	NO	57	73	0.6	MODERTE	DM.IHD,HTN	12	DEFICIT	9.2	NORMAL
38	BASAVANNEPPAC.K	80	M	159	60	24	YES	49	55	0.7	SEVERE		6	DEFICIT	8.8	NORMAL
39	SATTEVVA M.M	56	F	166	63	23	NO	70	73	0.7	MODERTE	IHD	8.2	DEFICIT	8	HYPO
40	SHIVAJI M.K	64	M	162	54	21	YES	49	64	0.5	SEVERE	DM.HTN	22	INSUFFICIENT	9.4	NORMAL
41	GURUBASAPPA S.P	54	M	145	52	25	YES	59	83	0.6	MODERTE		4.9	DEFICIT	9.2	NORMAL
42	KALLANGOUD B.B	63	M	168	73	26	YES	45	54	0.5	SEVERE		11.9	DEFICIT	8.6	HYPO
43	BABAJI TUPARE	73	M	162	70	27	YES	46	61	0.6	SEVERE	HTN	18	DEFICIT	8.5	HYPO
44	HANUMANTHA D.K	52	M	152	60	26	NO	32	58	0.6	SEVERE		8.3	DEFICIT	8.2	HYPO
45	RAMAYYA D	53	M	165	65	24	YES	34	58	0.5	SEVERE	DM	33	ADEQUATE	8.4	HYPO
46	ARJUN KADEMANI	50	M	169	70	25	YES	27	58	0.4	V.SEVERE	HTN,DM	19	DEFICIT	8.8	NORMAL
47	SHABIR PATEL	49	M	150	66	29	YES	35	45	0.6	SEVERE	DM	10.2	DEFICIT	9	NORMAL
48	CHANNAPPA T	71	M	154	65	27	NO	65	65	0.7	MODERTE	HTN	38	ADEQUATE	8.8	NORMAL
49	SADASHIV H	79	M	159	68	27	NO	70	79	0.7	MODERTE	DM	56	ADEQUATE	8.2	HYPO
50	LAXMIBAI PATIL	71	F	156	45	19	NO	59	83	0.6	MODERTE	HTN,DM	12	DEFICIT	8.6	HYPO
51	RAVIKUMAR PATIL	59	M	143	55	24.8	YES	74	76	0.7	MODERTE		20	INSUFFICIENT	8.5	HYPO
52	BALU DUNDGE	70	M	156	68	27.9	YES	54	61	0.5	MODERTE	IHD,DM	10.1	DEFICIT	8.8	NORMAL
53	SREEPATHIRAO J	75	M	170	60	20.8	YES	74	80	0.7	MODERTE	IHD	11.2	DEFICIT	8.9	NORMAL
54	YASHODA V.T	69	F	166	56	20.3	NO	57	63	0.7	MODERTE		16	DEFICIT	9.2	NORMAL

ANNEXURE VI:MASTER CHART

SL. NO	NAME	AGE	SEX	HT	WT	BMI	SMOKING	FEV1	FVC	RATIO	INFERENCE	CO-MORBIDITY	S.VIT D	REMARK	S.CA	REMARK
55	VISHNU GAVADE	80	M	144	50	24.1	YES	57	62	0.6	MODERTE	HTN,DM	8.1	DEFICIT	8.5	HYPO
56	MAHANTAPPA A.K	65	M	157	70	28.4	NO	72	77	0.7	MODERTE	HTN	26	INSUFFICIENT	8.5	HYPO
57	NAGUBAI CHIKKE	77	F	159	61	24.1	NO	72	77	0.7	MODERTE		3	DEFICIT	8.8	NORMAL
58	SUMITRA S.B	61	F	148	43	19.6	NO	33	51	0.7	SEVERE	IHD,DM	5.8	DEFICIT	7.8	HYPO
59	KAMALA CHOUGLE	61	F	153	56	23.9	NO	56	70	0.7	MODERTE	HTN,DM	14	DEFICIT	9.2	NORMAL
60	SUNANDABAI M	66	F	164	56	20.8	NO	30	36	0.6	SEVERE		22	INSUFFICIENT	8.9	NORMAL
61	YALLAPPA NAIK	85	M	151	47	20.6	YES	63	67	0.7	MODERTE	DM	28	INSUFFICIENT	8.3	HYPO
62	SONAWA S.C	88	F	154	52	21.9	NO	52	67	0.6	MODERTE	DM,IHD	4	DEFICIT	8.8	NORMAL
63	MAHADEVI K	65	F	136	46	24.9	NO	62	69	0.7	MODERTE		23.6	INSUFFICIENT	9	NORMAL
64	PRATIMA MISAL	62	F	144	64	30.9	NO	78	93	0.7	MODERTE		6.3	DEFICIT	9.7	NORMAL
65	BASAPPA GONGADI	85	M	136	46	24.9	YES	80	88	0.7	MILD		10	DEFICIT	8.9	NORMAL
66	MALLAVVA TELI	50	F	147	64	29.6	NO	72	83	0.7	MODERTE		22	INSUFFICIENT	8.3	HYPO
67	LAXMAN PATIL	70	M	167	62	22.2	YES	56	67	0.7	MODERTE		36	ADEQUATE	8.5	HYPO
68	IMAMJAFAR H.J	70	M	165	64	23.5	YES	41	58	0.7	SEVERE		26	INSUFFICIENT	8.9	NORMAL
69	ARJUN SUTAR	55	M	161	60	23.1	YES	62	74	0.7	MODERTE		10	DEFICIT	8.4	HYPO
70	IRAVVA HIREMATH	52	F	153	53	22.6	NO	70	88	0.7	MODERTE	DM	6	DEFICIT	8.8	NORMAL
71	PRAFULL SAWANT	54	M	163	54	20.3	YES	52	68	0.7	MODERTE		48	ADEQUATE	8.3	HYPO
72	RAMACHANDRAPPA R.P	70	M	165	50	18.4	YES	76	80	0.7	MODERTE	DM	13	DEFICIT	8.8	NORMAL
73	SUBHASH KORE	65	M	148	42	19.2	YES	33	41	0.7	SEVERE		34	ADEQUATE	8.9	NORMAL
74	NINGAPPA Y.H	58	M	145	41	19.5	YES	56	70	0.7	MODERTE	IHD	5	DEFICIT	8.8	NORMAL
75	BASAVANI B.J	68	M	148	37	16.9	NO	30	36	0.6	SEVERE		18	DEFICIT	9.2	NORMAL
76	BHIMAPPA M	76	M	170	60	23.5	YES	63	67	0.7	MODERTE		34	ADEQUATE	8.8	NORMAL
77	BHARAMAVVA K	75	F	160	40	15.6	NO	52	67	0.6	MODERTE		13	DEFICIT	8.8	NORMAL
78	MADHUKAR R.H	70	M	156	45	18.5	YES	57	69	0.7	MODERTE	DM	17	DEFICIT	8.8	NORMAL
79	SAVITRI V.K	86	F	143	55	26.9	NO	78	93	0.7	MODERTE	HTN	12	DEFICIT	8.4	HYPO
80	NABISAB F.Y	86	M	162	54	20.6	YES	80	88	0.7	MILD	HTN,DM	6	DEFICIT	8.8	NORMAL
81	ASHOK PATIL	60	M	145	52	24.7	NO	72	83	0.7	MODERTE	HTN	16	DEFICIT	8.9	NORMAL

ANNEXURE VI:MASTER CHART

SL. NO	NAME	AGE	SEX	HT	WT	BMI	SMOKING	FEV1	FVC	RATIO	INFERENCE	CO-MORBIDITY	S.VIT D	REMARK	S.CA	REMARK
82	ABDULKHADAR R.J	72	M	168	63	22.3	YES	60	67	0.7	MODERTE		22	INSUFFICIENT	8.2	HYPO
83	KASHAVVA M.S	60	F	162	70	26.7	NO	61	68	0.7	MODERTE	HTN	32	ADEQUATE	8.8	NORMAL
84	GANGAVVA D	91	F	152	52	22.5	NO	76	72	0.7	MODERTE	HTN	15	DEFICIT	8.3	HYPO
85	ILIYAS MULLA	58	M	165	65	23.9	YES	71	75	0.7	MODERTE		24	INSUFFICIENT	9.2	NORMAL
86	BHARAMAVVA P	65	F	169	70	24.5	NO	38	46	0.7	SEVERE		16	DEFICIT	8.4	HYPO
87	ASHOK K	62	M	150	66	29.3	NO	48	57	0.7	SEVERE		12	DEFICIT	8.1	HYPO
88	SUNANDABAI P.M	75	F	154	65	27.4	NO	47	64	0.6	SEVERE		65	ADEQUATE	9	NORMAL
89	BASAPPA B	70	M	159	85	33.6	YES	69	74	0.7	MODERTE		7.2	DEFICIT	8.8	NORMAL
90	SIDDAPPA R.M	75	M	156	45	18.5	YES	62	67	0.7	MODERTE		6.7	DEFICIT	8.1	HYPO
91	BABAJI KRISHNA	70	M	143	55	26.9	YES	36	43	0.7	SEVERE		14.7	DEFICIT	9.2	NORMAL
92	LAXMIBAI GHODKE	85	F	156	85	34.9	NO	44	49	0.7	SEVERE		5.2	DEFICIT	8.5	HYPO
93	SIDDAPPA M.P	68	M	170	60	20.8	YES	54	82	0.7	MODERTE		9.7	DEFICIT	8.8	NORMAL
94	CHANDRAWWA B	56	F	166	56	20.3	NO	60	83	0.6	MODERTE		16	DEFICIT	8.8	NORMAL
95	PARAVTHI P	78	F	144	50	24.1	NO	16	25	0.5	V.SEVERE		3	DEFICIT	8.1	HYPO
96	RAMAYYA D	53	M	157	70	28.4	YES	73	82	0.7	MODERTE		15	DEFICIT	8.9	NORMAL
97	MAHADEV MANURE	55	M	167	61	21.9	YES	52	66	0.7	MODERTE		14.7	DEFICIT	10	NORMAL
98	SUMITRA B	61	F	148	43	19.6	NO	63	75	0.7	MODERTE	IHD,DM	5.8	DEFICIT	7.8	HYPO
99	KALLANGOUD B	68	M	153	56	23.9	NO	56	71	0.7	MODERTE		12	DEFICIT	8.9	NORMAL
100	BASAPPA PATIL	68	M	153	64	27.3	YES	57	73	0.6	MODERTE		7.8	DEFICIT	8.8	NORMAL