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Demographic Profile of Copd Cases and Their Clinical Correlation with Serum Vitamin D Level

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Background- COPD as a common, preventable, and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation which is due to airway and/or alveolar abnormalities caused by significant exposure to noxious particles or gases. The most common respiratory symptoms include dyspnea, cough with/without sputum production. It is diagnosed by comprehensive history and spirometric data. Vitamin D is traditionally known for its roles in bone health and the homeostasis of calcium and phosphorus.[1,2] However, vitamin D is not just a vitamin. It is recognized as a pleiotropic prohormone with its receptor (vitamin D receptor [VDR]) ubiquitously distributed.[2,3] As an immunomodulatory effector, vitamin D can not only boost innate immune responses upon infection but also regulate adaptive immune response.Amongst 100 COPD cases,majority cases were above 40 years of age and among them, the majority of the cases (34 %), were in the age group 61-70 years, 76%, were males .In our study, 48%, were farmers by occupation.Majority 72% cases were found to be smokers.,out of which 32% were Moderate smokers, In our study, 88% of the cases had a cough and 91% of the cases had dyspnea. In this study, majority of the cases (53%) had COPD Grade 2,and 8%of the cases had COPD Grade 1 Among the grade 1 COPD cases, all 8% cases had normal vitamin D levels and the mean (SD) vitamin D levels among them was 42.62 ± 4.34. Among grade 2 COPD cases, 33% had sufficient vitamin D levels and 19% had insufficient levels and 1% had deficient levels and the mean (SD) vitamin D level among them was 35.82 ± 8.84. Among grade 3 COPD cases 10% had insufficient and 14% cases had deficient levels of vitamin D and the mean (SD) vitamin D level among them was 20.92 ± 5.85. Among grade 4 COPD cases, 27% cases had deficient vitamin D levels and 3% had insufficient levels of vitamin D and the mean (SD) vitamin D level among them was 17.85 ± 2.39. out of the 100 COPD cases, 1 case had ≥5 exacerbations per year and had deficient levels of vitamin D and the vitamin D level in the case was 13.70 ng/ml. Eleven cases had 3-4 exacerbations per year and among them, 6 had deficient levels and 5 had insufficient levels of vitamin D and the mean (SD) vitamin D level among them was 20.17 ± 5.58. Thirty-six cases had 1-2 exacerbations per year and among them, 15 cases had vitamin D deficiency, 14 cases had insufficiency and 7 cases had normal vitamin D levels and the mean vitamin D level among them was 25.05 ± 8.60. The cases with no exacerbations had a mean vitamin D level of 36.01 ± 10.24.

Conclusion- COPD is relatively more common in males than females and more in the older age-group. Smokers , Ex-smokers and people with biomass fuel and dust exposure are in a greater risk of developing COPD.Serum vitamin D deficiency and insufficiency were observed to be very common in patients with COPD and it also correlates with the disease severity and exacerbation

Keywords-COPD-CHRONIC OBSTRUCTIVE PULMONARY DISEASE GOLD--Global Initiative for Obstructive Lung Diseases

I. INTRODUCTION-

Chronic Obstructive Pulmonary Disease (COPD) is a leading cause of morbidity and mortality worldwide including India that induces an economic and social burden that is both substantial and increasing. COPD is the fourth leading cause of mortality worldwide,[1] posing a big threat to public health. It is a progressive disease characterized by persistent airflow limitation, as a consequence of chronic inflammation and structural changes.[2] It is a progressive disease characterized by persistent airflow limitation, as a consequence of chronic inflammation and structural changes

COPD is the result of a complex interplay of long-term cumulative exposure to noxious particles and gases, combined with a variety of host factors including genetics, airway hyper-responsiveness, and poor lung growth during childhood. Often, the prevalence of COPD is directly related to the prevalence of tobacco smoking, although in many countries, especially in

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developing countries, occupational, outdoor, and indoor air pollution (resulting from the burning of firewood and other biomass fuels) are major COPD risk factors. COPD patients suffer from a progressive reduction of lung function, loss of exercise capacity, frequent disease exacerbations, and the development of extrapcomorbidities (such as osteoporosis, infection, and cardiovascular disease).[3]

Global Initiative for Obstructive Lung Diseases (GOLD) defined COPD as a common, preventable, and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation which is due to airway and/or alveolar abnormalities caused by significant exposure to noxious particles or gases. The most common respiratory symptoms include dyspnea, cough with/without sputum production [4]. It is diagnosed by comprehensive history and spirometric data.

Morbidity from COPD may be affected by other concomitant chronic conditions (e.g., cardiovascular disease, musculoskeletal impairment, diabetes mellitus) that are related to smoking, aging, and COPD. These chronic conditions may significantly impair a patient's health status, in addition to interfering with COPD management, and are major drivers of hospitalizations and costs for patients with COPD.[5]

Vitamin D is traditionally known for its roles in bone health and the homeostasis of calcium and phosphorus.[6] However, vitamin D is not just a vitamin. It is recognized as a pleiotropic prohormone with its receptor (vitamin D receptor [VDR]) ubiquitously distributed.[7] As an immunomodulatory effector, vitamin D can not only boost innate immune responses upon infection but also regulate adaptive immune responsesMoreover, vitamin D is related to cell proliferation, cell differentiation, apoptosis, and intercellular adhesion.[8] The majority of vitamin D originates from the skin with sunlight exposure, and the remaining can be obtained from diet or supplements.[9] Epidemiologic studies reported that vitamin D deficiency is a global and important. health issue.[8] Vitamin D deficiency can underpin the etiology of a broad range of diseases, including autoimmune diseases, allergy diseases, endocrine and metabolic disorders, cancer, infections, and cardiovascular disorders.[9,10] Early in life, vitamin D deficiency causes growth retardation and rickets, whereas in adults it is well known to accelerate the process of osteopenia and osteoporosis. Similar to other chronic diseases, it was recently speculated that vitamin D deficiency might also be linked to chronic obstructive pulmonary disease [9] . With a focus on the association between COPD and vitamin D, evidence from some studies indicated a possible link between vitamin D and COPD[11-12] . Vitamin D deficiency and insufficiency are common in patients with COPD and deficiency is associated with pulmonary function deterioration. It was a hospital-based study done in Gauhati Medical College & Hospital where people come from different parts of the state and the north-eastern region

II. AIMS AND OBJECTIVES

Keeping in mind the limitation of the study all efforts were taken to do the study with the following aims and objectives:

1. To study the demographic profile of patients with Chronic Obstructive Pulmonary Disease.
2. To study levels of serum vitamin D in patients with Chronic Obstructive Pulmonary Disease.

INCLUSION CRITERIA:

1) All patients diagnosed with Chronic Obstructive Pulmonary Disease with respiratory symptoms and physical signs and with persistent airflow limitation, Post broncho-dilator forced expiratory volume in one second (FEV1) / Forced Vital Capacity (FVC) ratio < 0.70 in pulmonary function test.
2) Age > 40 years

EXCLUSION CRITERIA

1) Patients with Active Pulmonary Tuberculosis
2) Pregnant women
3) Patients taking vitamin D supplementation
4) Patients with disease that affects Vitamin D and Calcium metabolism like: Chronic Kidney Disease· Osteomalacia· Malignancy· Thyroid disorders· Parathyroid disorders· Inflammatory bowel disease·
5) History of small bowel resection Chronic liver disease· Pancreatitis· Cystic fibrosis· Bronchiectasis· Granulomatous disorder·
6) Patients taking drugs that may affect vitamin D metabolism in long term therapy like: Antibiotics -Rifampicin and Isoniazid· Anti-epileptics- phenobarbital, carbamazepine, phenytoin· Anti-cancer drugs-Taxol· Antifungals-Clotrimazole and ketoconazole· Anti- HIV drugs- Efavirenz
7) **SAMPLE SIZE**

A total of 100 cases attending the outpatient and indoor of the Department of Pulmonary Medicine, Internal Medicine, and its allied specialties were included in this study.

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III. MATERIALS AND METHODS –

STUDY DESIGN - It is a hospital-based observational study. A total number 100 COPD patients who met the inclusion criteria were included in the study. Both indoor and outdoor patients were included in the present study. This study was a hospital-based observational study

Table 1: Age-wise Distribution of Cases

AGE GROUP IN YEARS	Number	Percent
40-50	12	12
51-60	31	31
61-70	34	34
71-80	18	18
>80	5	5
Total	100	100

In the present study, all the cases were above 40 years of age. The majority of the cases (34 %) were in the age group of 61-70 years, followed by 31% cases, in the age- group of 51-60 years, the lowest number of cases (5%) were observed in the age group of > 80 years, whereas 18% cases were observed in 71-80 years age group. The mean (SD) age of the cases was 63.44 ± 10.11 years.

Table 2:Gender-wise Distribution of Cases

SEX	Number	Percent
Male	76	76
Female	24	24
Total	100	100

In the present study, it was observed that the majority of the cases (76%) were males, while 24% were females. The male to female ratio is 3.1:1.

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Table 3: Occupation

OCCUPATION	Number	Percent
Business	14	14
Farmer	48	48
House wife	12	12
Service	11	11
Daily Labourer	15	15
Total	100	100

In the present study, it was observed that the majority of the cases 48% were farmers by occupation, followed by 15% of cases who were daily labourers.Twelve percent of the cases were house-wives whereas 14% of the cases were businessmen and 11% of the cases were in service.

Table 4: Smoking Status

SMOKING STATUS	Number	Percent
Never Smoker	28	28
Smoker	72	72
Total	100	100

Out of the total 100 cases, the majority (72%) were smokers and 28% were non- smokers.

Table 5: Frequency of smoking

SMOKING FREQUENCY	Number	Percent
NEVER SMOKER	28	28
LIGHT SMOKER	16	21
MODERATE SMOKER	32	45

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HEAVY SMOKER	24	14
TOTAL	100	100

In the present study, it can be observed that out of all the smokers, the majority of the cases (32%) were moderate smokers followed by 24%, were heavy smokers.Sixteen percent of the cases were light smokers.

Table 7: Exposure to Other Risk Factors

EXPOSURE TO RISK FACTORS	**Number**	**Percent**
No	11	11
Yes	89	89
Total	100	100

In this study, in the majority of the cases,89% were exposed to other risk factors for COPD like, environmental tobacco smoke [ETS], biomass fuel smoke, occupational dust, household, and outdoor air pollution, while 11% of the cases were not exposed to risk factors.

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.Table8 : clinical presentation of the patients

SYMPTOMS	**Present**	**Percent**	**Absent**	**Percent**	**Total**
COUGH	88	88	12	12	100
DYSPNEA	91	91	9	9	100

In the present study, 88% of the cases had a cough and 91% of the cases had dyspnea
In the present study, the mean (SD) duration of cough was 7.47 ± 3.48 years and the mean (SD) duration of dyspnea was 5.60 ± 2.96 years.

Table 9 Number of times Hospitalized per year

NUMBER OF HOSPITALIZATION PER YEAR	**Number of Cases**	**Percent**
0	46	46
1	29	29
2	16	16

3	8	8
4	1	1
Total	100	100

In the present study, 52% of the cases had no exacerbations in a year, whereas 26% of cases had one exacerbation in a year. Ten percent of cases had two exacerbations, 6% cases had three exacerbations, 5% cases had four exacerbations and 1% of the cases had five exacerbations in a year.

Table 10: Exacerbation Frequency

EXACERBATION FREQUENCY	**Number**	**Percent**
None	52	52
1-2	36	36
3-4	11	11
≥5	1	1
Total	100	100

In the present study, 52% of the cases had no exacerbations, 36% of the cases had 1-2 exacerbations per year, 11% of the cases had 3-4 exacerbations per year and 1% of the cases had 5 exacerbations per year.

Table 11 Number of cases of dyspnea in relation to mMRC grade

mMRC GRADE	**Number**	**Percent**
0	17	17
1	29	29
2	21	21
3	22	22
4	11	11
Total	100	100

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In the present study, the majority of the cases (29%) had mMRC grade 1, whereas 11% of the cases had mMRC grade 4. Twenty percent of the cases had mMRC grade 2 while 22% cases had mMRC grade 3.
In the present study, it was observed that the mean (SD) no. of hospitalization per year was 1.64 0.80, whereas the mean (SD) no. of exacerbations per year was 1.85 ± 1.12.
The mean mMRC grade among the cases was 2.18 ± 1.60.

Fig 1: COPD Grade

In our study, 8% of the cases had COPD Grade 1, majority of the cases i.e 53% had COPD Grade 2, 24% of the cases had COPD Grade 3, and 15% of the cases had COPD Grade 4.

Table 12 Serum Vitamin D LEVELS

SERUM VITAMIN D STATUS	**Number**	**Percent**
Insufficiency	32	32
Deficiency	27	27
Sufficiency	41	41
Total	100	100

In our study, 32% of the cases had vitamin D insufficiency, 27% had vitamin D deficiency and 41% of the cases had normal levels of vitamin D.

Table13 Mean Vitamin D Level in the cases

Variable	**Minimum level**	**Maximum level**	**Mean**	**Standard Deviation**
SERUM VITAMIN D	13.7	53.2	30.09	11.16

In this study, the mean (SD) vitamin D level in the cases was 30.09 ± 11.1

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Table 14 COPD exacerbations vs Vitamin D status

	SERUM VITAMIN D STATUS			Total
EXACERBATION	**Insufficiency**	**Deficiency**	**Sufficiency**	
None	13	5	34	52
1-2	14	15	7	36
3-4	5	6	0	11
≥5	0	1	0	1
Total	32	27	41	100
Pearson Chi-Square	32.567	**P value**	0.0001	Highly Significant

In the present study, all of the grade 1 COPD cases (8%) cases had normal vitamin D levels. Among grade 2 COPD cases, 33% had sufficient vitamin D levels and 19% had insufficient levels and 1% had deficient levels. Among grade 3 COPD cases 10% had insufficient and 14% cases had deficient levels of vitamin D. Among grade 4 COPD cases, 12% had deficient levels and 3% cases had insufficient levels of vitamin D

P-value was 0.0001, which is statistically highly significant.

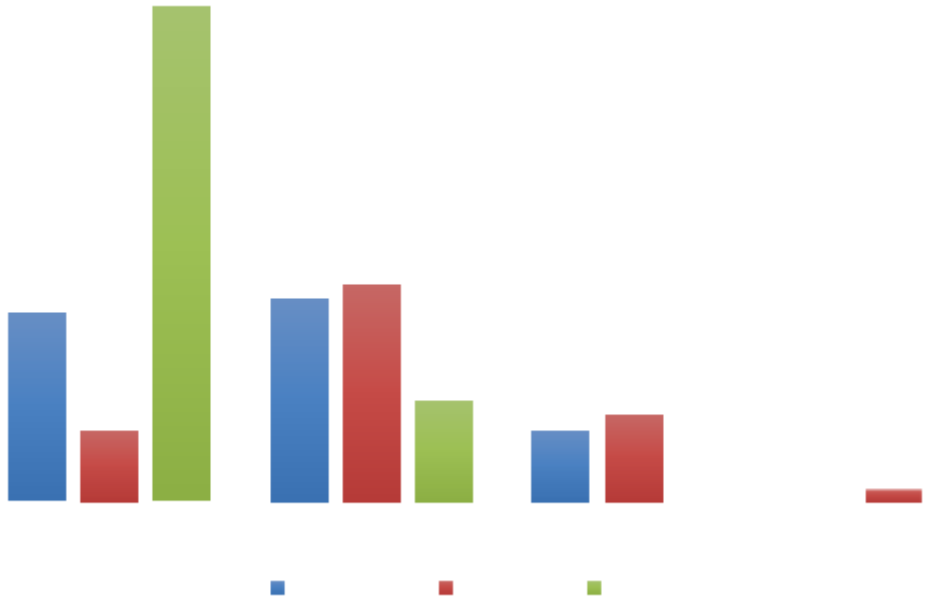

Fig 2 COPD Exacerbations vs Vitamin D status

In the present study, 52% of cases, who had no exacerbations had normal vitamin D levels. Among the 36% cases with 1-2 exacerbations, 15% had vitamin D deficiency and 14% had insufficient levels of vitamin D. Among the 11% cases with 3-4 exacerbations, 6% cases had vitamin D deficiency and 5% had insufficiency. One case who had 5 exacerbations had vitamin D deficiency.

P-value was 0.0001, which is statistically highly significant.

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Table 15. Mean serum Vitamin D level in COPD grades

		SERUM VITAMIN D	
COPD GRADE	**No. of cases**	**Mean**	**Standard Deviation**
1	8	42.63	4.34
2	53	35.83	8.84
3	24	20.92	5.85
4	15	17.85	2.39
Total	100	30.09	11.16
	P value	0.0001	Highly Significant

In the present study, the mean (SD) serum vitamin D level among the grade 1 COPD cases was observed to be 42.63 ± 4.34. Among the cases of grade 2 COPD, it was 35.83 ± 8.84. The mean (SD) serum vitamin D level among the grade 3 COPD cases was 20.92 ± 5.85, while the mean (SD) vitamin D level among the grade 4 COPD cases was 17.85 ± 2.39.P-value was 0.0001, which is statistically highly significant.

Table 16 vitamin d levels and exacerbatiom freequency

		SERUM VITAMIN D	
EXACERBATION	**No. of cases**	**Mean**	**Standard Deviation**
None	52	36.01	10.24
1-2	36	25.05	8.60
3-4	11	20.17	5.58
≥5	1	13.70	.
Total	100	30.09	11.16
	P value	0.0001	Highly Significant

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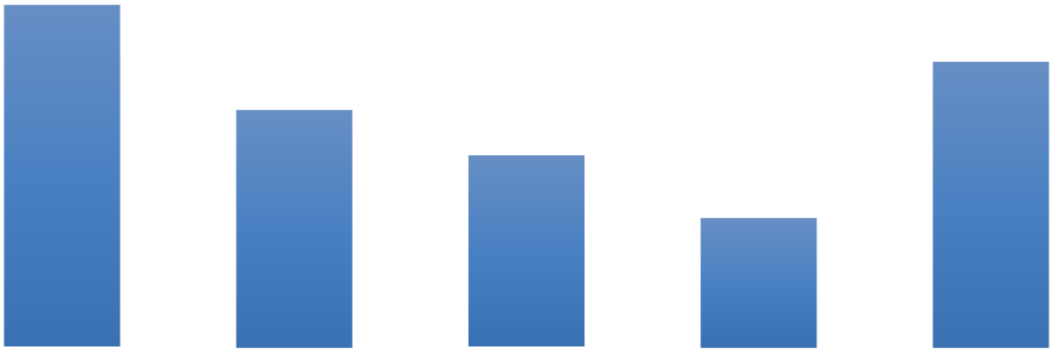
+In the present study, it was observed that the mean (SD) serum vitamin D level in cases with no exacerbations in a year was 36.01 ± 10.24. Cases with 1-2 exacerbations in a year had mean (SD) serum vitamin D level of 25.05 ± 8.60, while cases with 3-4 exacerbations in a year had mean (SD) vitamin D levels of 20.17 ± 5.58. Case with ≥5 exacerbations in a year had serum vitamin D levels of 13.70.

P-value was 0.0001, which is statistically highly significant.



IV. DISCUSSION

In the present study, all the cases were above 40 years of age and among them, the majority of the cases (34 %), were in the age group 61-70 years, while only 5% in age group over 80years age. The mean age is 63.44 ± 10.11 years.Similar to our study, **Persson LJP et al.**[14] in their study stated the mean age of COPD cases as 63.5 ± 6.9. In our study, it is observed that the majority of the patients i.e 76%, were males, while 24% were females. The male to female ratio is 3.1:1. The study done by **Janssens W et al.**[15] found that 82.06% of COPD cases were males and 17.94% were females. A similar study by **Persson LJP et al.**[14] found that 60% of COPD cases were males and 40% of COPD cases were females.

In our study it is observed that the majority of the cases i.e 48%, were farmers by occupation, followed by 15% cases, were daily labourers. Fourteen percent of the cases were businessmen and 11% of the cases were in service. Twelve percent of the cases comprised of housewive the prevalence of COPD was higher in farmers than in nonfarming working control subjects. In another study **Fontana L et al.**[17] also found that farming work was associated with a greater risk of developing COPD. A case-control study by **Dement J et al.**[17] found that construction workers are at increased risk of COPD.

In our study, the majority of the COPD cases, 72% were found to be smokers. Among the 72% smokers, the majority of the cases, 32% were Moderate smokers, 16% were Light smokers,24% were heavy smokers. Twenty-eight percent of the cases were never-smokers. **Janssens W et al.**[15] have shown a strong association between. smoking and COPD* **Sanket S et al.**[18] in their study have shown that chance of having vitamin D deficiency is higher with increased pack-year of smoking.In our study,89% of cases were exposed to other risk factors for COPD like environmental tobacco smoke [ETS], biomass fuel smoke, occupational dust, household, and outdoor air pollution. **Siddharthan T et al.**[19] in their study have found that household air pollution exposure was associated with a higher prevalence of COPD. They found in their study that participants with household air pollution exposure were 41% more likely to have COPD than those without the exposure, and 13.5% of COPD prevalence may be caused by household air pollution exposure. In a case-control study **Weinmann S et al.**[20] have shown a strong association between COPD and occupational exposure like diesel exhaust, irritant gases and vapors, mineral dust, and metal dust. In another study **Sana A et al.**[16] have shown that biomass smoke exposure is associated with COPD in rural and urban women.

In our study, 88%of the cases had a cough and 91% of the cases had dyspnea. In a similar study by **Kornmann O et al.**[21] it was seen that in 210 cases of COPD, cough was present in 84% of cases whereas dyspnea was present in 70% of the cases

In this study, 8% of the cases had COPD Grade 1, majority of the cases (53%) had COPD Grade 2, 24% of the cases had COPD Grade 3, and 15% of the cases had COPD Grade 4. . The mean vitamin D level among all the COPD cases was 30.09 ± 11.16. **Monadi et al.**[22] in their study have

shown that COPD is associated with low vitamin D levels. **Zhu B et al.**[28] found in their study that a high deficiency rate of vitamin D was associated with COPD severity. **Zhu M et al.**[2o] in their study found serum vitamin D levels were inversely associated with COPD risk, severity, and exacerbation.

Vitamin D de1ficiency is associated with an increased risk of COPD and severe COPD. Similarly, **Sanket S et el.**[18] found COPD was associated with an increased risk of vitamin D deficiency, and there was a significant asociation between vitamin D levels and Combined COPD stage severity. **Persson LJP et al.**[14] also showed that there is a reduction of vitamin D level in Grade 3 & Grade 4 severity of COPD. In our study, it was observed that out of the 100 COPD cases, 1 case had ≥5 exacerbations per year and had deficient levels of vitamin D and the vitamin D level in the case was 13.70 ng/ml. Eleven cases had 3-4 exacerbations per year and among them, 6 had deficient levels and 5 had insufficient levels of vitamin D and the mean (SD) vitamin D level among them was 20.17 ± 5.58. Thirty-six cases had 1-2 exacerbations per year and among them, 15 cases had vitamin D deficiency, 14 cases had insufficiency and 7 cases had normal vitamin D levels and the mean vitamin D level among them was 25.05 ± 8.60. The cases with no exacerbations had a mean vitamin D level of 36.01 ± 10.24.The study by **Persson LJP et al**[15] found that the level of vitamin D among cases with exacerbations < 2 episodes per year was 25.4 ± 9.9 and exacerbations ≥ 2 episodes per year was 23.7 ± 10.5. The COPD patients with exacerbations ≥ 2 episodes per year showed a marked reduction in vitamin D levels. One study by **Ferrari R et al.**[24] showed that the association between exacerbation frequency and Vitamin D levels in observational studies remains controversial and meta-analysis revealed a negative association between serum Vitamin D and exacerbation, however, two clinical trials showed that Vitamin D_3 supplementation in COPD patients reduced the risk of moderate and severe exacerbation. **Zhu B et al.**[25] in their study found that low serum levels of vitamin D were not associated with COPD susceptibility, but the high deficiency rate of vitamin D was associated with COPD severity and vitamin D supplementation may prevent COPD exacerbation. vitamin D is an immunomodulator affecting various inflammatory pathways, COPD patients with more severe disease tend to have low levels of vitamin d

V. CONCLUSION

Chronic Obstructive Pulmonary Disease is one of the most common respiratory illnesses and is a major cause of morbidity and mortality among the elderly population in India and around the world. Cough and dyspnea are the most common presenting symptoms and most of the patients remain undiagnosed as people perceive these symptoms as normal occurrences in old age. From our present study, it can be concluded that COPD is relatively more common in males than females and more in the older age-group. Smokers , Ex-smokers and people with biomass fuel and dust exposure are in a greater risk of developing COPD. Serum vitamin D deficiency and insufficiency were observed to be very common in patients with COPD and it also correlates with the disease severity and exacerbations.As this study was carried out in a limited time period and with a small sample size, more elaborate and studies involving large study groups are needed to determine the levels of vitamin D in mild, moderate, and severe COPD and for adding vitamin D as adjuvant therapy in patients with COPD to find out therapeutic & treatment ouput.

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