A Study Of Serum NT-Probnp Levels In COPD Patients - An Observational Study

Bharat Totwani[1], Alok Gupta[2], Amit Sagar[3]

[1](Resident , Department of General Medicine, Dr SN Medical College, Jodhpur, India)
[2](Senior Professor & HOD, Department of General Medicine, Dr SN Medical College, Jodhpur, India)
[3](Associate Professor, Department of General Medicine, Dr SN Medical College, Jodhpur, India)

Abstract:

Background: COPD , Being An Important Cause Of Mortality And Morbidity In India Have Been Recently Associated With Increased NT-Probnp Levels. NT-Probnp Has Been Used Widely As A Marker Of Heart Failure. However, There Are Few Studies That Analyze The NT-Probnp Levels In COPD Patients. So This Study Was Conducted To Know The Concentrations Of Ntprobnp And The Influence Of The Factors That Usually Modify Them, In A Population Of Patients Of Western Rajasthan With COPD During Episodes Of Decompensation, In Order To Know The Future Uses Of This Biomarker In These Type Of Patients.

Materials And Methods: In This Prospective Randomised Observational Study, A Total Of 100 Patients Were Admitted To Department Of Medicine, Mahatma Gandhi Hospital, Jodhpur As COPD According To Criteria Were Taken In The Group & Data Of Patients Were Collected Including ABG, Serum NT-Probnp Of Each Patient Were Recorded. Total Days Of Hospital Stay, Number Of Days Of Mechanical Ventilation (Including Both Non Invasive And Invasive Ventilation) , If Done And Shifts To Intensive/ Critical Care Units Of The Hospital Were Also Taken Into Records. Final Outcome Of The Patient Was Noted Down As Well. Further Data Was Processed And Analysed Using Statistical Tests And Results Were Discussed.

Results: We Found Statistically Significant Relation Of High NT-Probnp Levels With Pco2 Levels, Need For ICU, And Duration Of Hospital Stay. There Was No Relation Of NT-Probnp Levels With Severity Of COPD As Per GOLD Criteria, Ph And Outcome.

Conclusion: Serum NT-Probnp Levels Can Be Used In COPD To Predict Pco2 Levels, Need For ICU And Duration Of Hospital Stay. Therefore NT-Probnp Can Be Used As A Biomarker In COPD For Better Understanding Of The Patient's Condition Which May Help In Better Decision Making In Part Of The Physician.(10)

Key Word: COPD, NT-Probnp, GOLD, Biomarker, Pco2

I. Introduction

Chronic obstructive disease (COPD) is a common disease encountered in daily clinical practice, it is treatable and has significant systemic repercussions. Its prevalence in India is estimated at 7.4% which was higher in males, in urban areas and the northern region[1] . Worldwide, it is the fourth leading cause of mortality and its prognosis is linked to multiple factors, including associated comorbidity. Chronic obstructive pulmonary disease is characterized by a lung airflow limitation and can be due to exposure from harmful substances. The airflow limitation is progressive and is also associated with tissue destruction in response to chronic inflammation. The most common etiology associated with COPD is exposure to noxious particles or gases mainly cigarette smoke. It is associated with decreased lung recoil and progressive narrowing of the airways. The disease often presents with cough , dyspnea and sputum production. Symptoms range from asymptomatic to respiratory failure with impending need for medical intubation and ventilator support in the last stages of the disease.

Brain natriuretic peptide (BNP) is a peptide mainly produced by the ventricle. Although the main producer is the left ventricle, the synthesis and release of the peptide at the level of the right ventricle has also been described. Its synthesis is stimulated by stress phenomenon at that level, such as overload or distension. The physiological actions are diverse and its main use, to date, has been the diagnosis and prognostic stratification of heart failure. Its usefulness, especially prognostic, has also been demonstrated in other pathologies such as pulmonary thromboembolism (PTE), pulmonary hypertension, chronic cor pulmonale, ischemic heart disease or valvular heart disease4,5,6. Both intra- and inter-individual variability of BNP is important, and the following have been described as factors that modify its levels: atrial fibrillation, sex, age, body mass index and kidney failure5. The hypoxemia present in COPD patients frequently implies pulmonary arterial vasoconstriction which,

---

in turn, implies stress for the right ventricle, with long-term development in some patients of right heart failure[7,8]. However, there are few studies that analyze the concentrations of BNP or its amino-terminal fraction in patients with COPD.

The objective of this work is to know the concentrations of NTproBNP and the influence of the factors that usually modify them, in a population of patients of western Rajasthan with COPD during episodes of decompensation, in order to know the future uses of this biomarker in these type of patients.

II. Material And Methods

This study was conducted in the Department of General Medicine, Mahatma Gandhi Hospital affiliated to Dr S. N. Medical College, Jodhpur.

STUDY DESIGN : This was a prospective observational study.

STUDY DURATION : This study was started after Ethics Committee approval, from September 2021 to September 2022.

STUDY POPULATION : Patients admitted in both general ward and ICU till sample size achieved.

INCLUSION CRITERIA : All male and female patients of age above 18 years who were diagnosed as COPD as per GOLD criteria and admitted in hospitals affiliated to Dr S.N. Medical College, Jodhpur.

EXCLUSION CRITERIA :
1. Diagnosed case of heart failure.
2. Hyperthyroidism.
3. Known case of IHD or any other cardiac illness.
4. Serum creatinine >2mg/dl.
5. Neoplasms.
6. Abnormal EKG or Chest Xray showing Cardiomegaly

SAMPLING TECHNIQUE : Consecutive sampling was done, based on the sequence of hospital registration numbers.

METHODOLOGY : After obtaining permission and clearance for the study from the institutional ethics committee, data of patients that meet the inclusion criteria was collected including clinical history, detailed examination, relevant blood investigations, ABG and imaging. Data was collected in a pre-designed pro-forma. Investigations including ABG, Serum NT-proBNP of each patient were recorded. Total days of hospital stay, number of days of mechanical ventilation (including both Non invasive and Invasive ventilation) , if done and shifts to Intensive/ Critical care units of the hospital were also taken into records. Final outcome of the patient was noted down as well. Further data was processed and analysed using statistical tests and results were discussed.

STATSTICAL ANALYSIS : Quantitative data were compared using student t test and presented as mean + /- SD or median (range). While for qualitative variables chi square test were be used andpresented as frequency and percentage. All data was analysed using appropriate software. A p value of <0.05 was considered as statistically significant.

SAMPLE SIZE : Sample size was calculated at 95% confidence interval and 10% absolute allowable error using the formula for sample size for estimation of a single sample proportion –

$$N = \frac{(Z_{1-\alpha/2})^2 \; P\,(1-P)}{E^2}$$

 Where,
N = Standard normal deviate for 95% confidence interval (taken as 1.96)
P = Expected proportion of COPD patients with raised NT-proBNP levels among
all COPD patients (taken as 63% as reported by Muhhamad Adrish et al)
E = Absolute allowable error (taken as 10% of P)
Sample size was calculated to be 91 COPD patients, which was enhanced and
rounded to 100 patients.

III. Result

A total of 100 patients admitted to Department of Medicine, Mahatma Gandhi Hospital, Jodhpur as COPD according to criteria were included in the group.

Table no 1 Shows metabolic parameters of patients of the three groups before treatment. Total cholesterol (TC), 224.3 ±30.8 mg/dl, 226.1 ±35.4&225.3 ±40.7 mg/dl, LDL-C, 158.3 ±22.6 mg/dl, 156.1 ±27.8&157.2 ±26.7 mg/dl, HDL-C, 37.5 ±2.70 mg/dl, 35.5 ±2.21&36.4 ±1.90 mg/dl, Triglyceride165.8 ±30.8 mg/dl, 162.6 ±28.2&166.8 ±35.7mg/dl, Non-HDL-C 180.6 ±31.2 mg/dl, 182.4 ±29.2 & 185.2 ±32.4 mg/dl, , FBG, 142.5 ±25.7 mg/dl, 148.2 ±26.9 & 145.8 ±27. mg/dl4, HbA1c, %, 5.82 ±0.2, 5.62±0.4 & 5.65 ±0.3 respectively of patients of the three groups. The difference in the values of all parameters in respect of three groups was not statistically significant (p>0.05).

Table no 1 : Severity of COPD in cases of Normal NT-proBNP vs High NT-proBNP

| GOLD category	Normal NT-proBNP		Raised NT-proBNP		Total	
	No.	%	No.	%	No.	%
1	2	28.6%	5	71.4%	7	7.0%
2	15	60.0%	10	40.0%	25	25.0%
3	16	36.4%	28	63.6%	44	44.0%
4	6	25.0%	18	75.0%	24	24.0%

P value 0.074
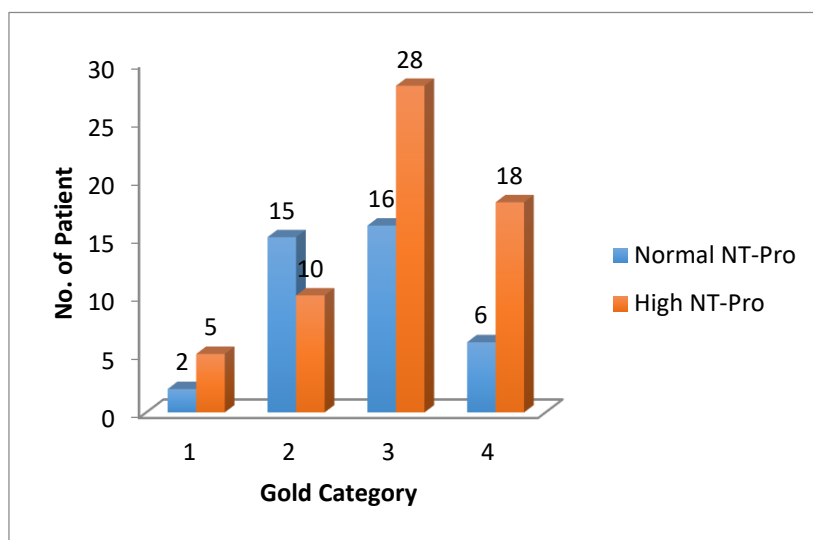
As seen in table 1, total no. of patients in GOLD category 1 were 7, out of which 28.6%(2/7) of patients had normal NT-proBNP levels while 71.4% of them had high levels of serum NT-proBNP levels. Total no. of patients in GOLD category 2 were 25, out of which 60%(15/25) had normal NT-proBNP levels while 40%(10/25) of cases had high levels of serum NT-proBNP. Total no. of patients in GOLD category 3 were 44 out of which patients with normal serum NT-proBNP levels were 36.4% (16/44) and with high levels of serum NT-proBNP levels were 63.6%(28/44). Total no. of patients in GOLD category 4 were 24, out of which 25% (6/24) had normal levels of serum NT-proBNP levels and 75% (18/24) had high levels of serum NT-proBNP levels.

The P value was .074 at 95% confidence limit and therefore there was no statistically significant difference in severity of the two groups and thus no relation was found between severity of COPD as per GOLD criteria and NT-proBNP levels.

Table no2 : Requirement of ICU in cases of Normal NT-proBNP vs High NT-proBNP.

Admissions in ICU	Normal NT-proBNP		Raised NT-proBNP		Total	
	No.	%	No.	%	No.	%
No	28	49.1%	29	50.9%	57	57.0%
Yes	11	25.6%	32	74.4%	43	43.0%

P value -.023
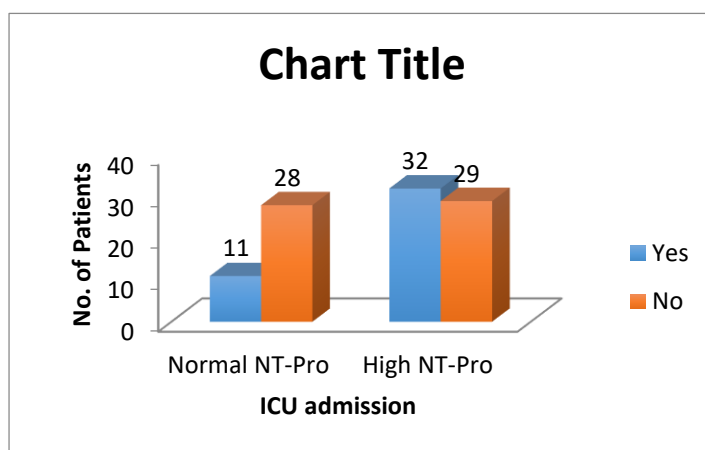
As seen in table 2, total no. of ICU admissions were 43 out of which, cases with normal NT-proBNP levels were 25.6% (11/43) and cases with high levels of serum NT-proBNP levels were 74.4% (32/43). The P value was 0.023 at 95% confidence limit. Therefore, a statistically significant relation was found between high levels of serum NT-proBNP levels and need for ICU admissions in COPD patients.

Table no 3 :pH, pCO2 & pO2 levels in cases of Normal NT-proBNP vs High NT-proBNP.

Parameters	Normal NT Pro BNP					Raised NT Pro BNP					Total					P Value
	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	
PH	7.30	.11	7.26	7.21	7.40	7.29	.11	7.30	7.22	7.38	7.30	.11	7.30	7.22	7.40	.910
pCO2	60	8	57	54	63	67	11	66	60	70	64	11	62	57	68	.045
pO2	69	7	71	64	74	75	10	72	68	84	73	9	72	66	78	.120

As seen in Table 3, mean pH was 7.30 in both groups and there was no statistically significant difference between pH of cases with normal NT-proBNP 3.levels and cases with high levels of serum NT-proBNP levels. Mean pCO2 levels in patients with normal serum NT-proBNP levels was 60 ± 8 mmHg and of patients with high levels of serum NT-proBNP was 67 ± 11 mmHg. Mean pCO2 levels of total cases was 64 ± 11 mmHg. P value is 0.045 at 95% confidence limit which shows that a statistically significant relation was found between serum pCO2 levels and serum NT-proBNP levels. Mean pO2 levels of total cases was 73 ± 9 mmHg. Mean pO2 levels of patients with normal serum NT-proBNP levels was 69 ± 7 mmHg and of patients with high levels of serum NT-proBNP levels was 75 ± 10 mmHg. P value is 0.120 at 95% confidence limit which shows no statistically significant relation between serum pO2 levels and serum NT-proBNP levels.

Table 4: Requirement of intervention in cases of Normal NT-proBNP vs High NT-proBNP

Intervention	Normal NT-proBNP		Raised NT-proBNP		Total	
	No.	%	No.	%	No.	%
MV	4	28.6%	10	71.4%	14	14.0%
NIV	17	44.7%	21	55.3%	38	38.0%

P Value- .541

As seen in Table 4, total patients requiring Mechanical ventilation support were 14 out of which patients with Normal NT-proBNP levels requiring Mechanical ventilation support were 4 (28.6%) while patients with high NT-proBNP levels requiring Mechanical ventilation support were 10 (71.4%).

Also, total patients requiring NIPPV support were 38 out of which patients with Normal NT-proBNP levels requiring NIPPV support were 17 (44.7%) while patients with high NT-proBNP levels requiring NIPPV support were 21 (55.3%).

The p value for intervention required was .541 at 95% confidence interval which implies no statistically significant relation between NT-proBNP levels and intervention required in COPD patients.

Table 5 : Duration of hospital stay in cases of Normal NT-proBNP vs High NT-proBNP.

Duration of hospital stay (days)	Normal NT-Pro		High NT-Pro		Total	
	N	%	N	%	N	%
≤1	9	23.08	10	16.39	19	19.00
2-5	16	41.03	17	27.87	33	33.00
6-10	12	30.77	34	55.74	46	46.00
>10	2	5.13	0	0.00	2	2.00
Total	39	100.00	61	100.00	100	100.00

Chi square 8.160, P value 0.042 (S)
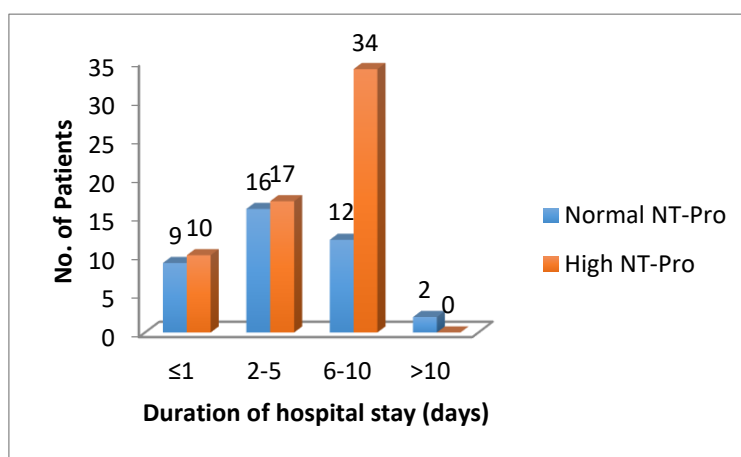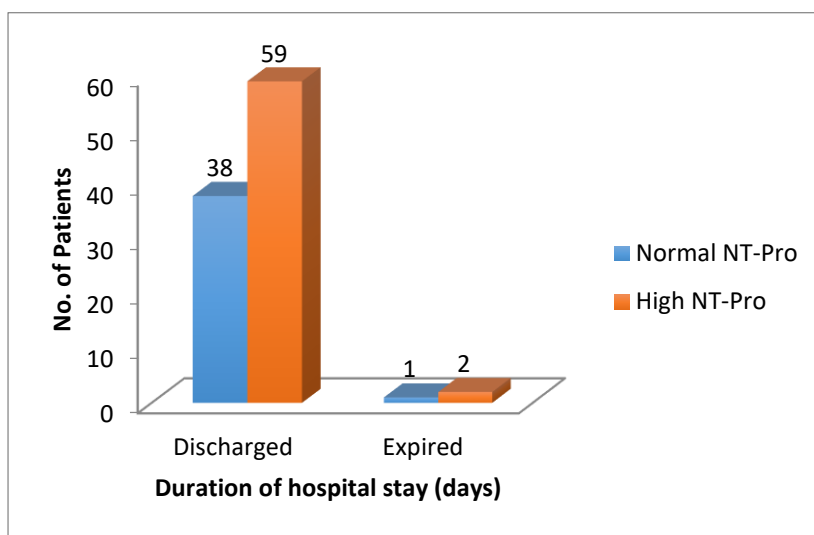
As seen in the Table 5, P value for duration of hospital stay in normal vs high levels of serum NT-proBNP was 0.042, which shows a statistically significant relation between NT-proBNP levels and duration of hospital stay. Mean Duration of hospital stay for patients with normal NT-proBNP levels was 4 days while mean duration of hospital stay for patients with high levels of NT-proBNP levels was 5 days. Mean duration of hospital stay for total cases was 5 days.

Table 6 : Outcome of patients in cases of Normal NT-proBNP vs High NT-proBNP

Outcome	Normal NT-proBNP		Raised NT-proBNP		Total	
	No.	%	No.	%	No.	%
Discharged	38	39.2%	59	60.8%	97	97.0%
Expired	1	33.3%	2	66.7%	3	3.0%

P value – 1.000

Table 6 shows that out of 39 patients of normal NT-proBNP 38 were discharged and 1 patient expired. 59 out of 61 patients with high levels of NT-proBNP discharged and 2 expired. The p value was 1.00 which shows no statistically significant difference between the outcome of patients of normal NT-proBNP levels and high NT-proBNP levels.

Table 7 : Distribution of various variables in cases of Normal NT-proBNP vs High NT-proBNP

Variables		No. of patients	Percentage
Serum NT Pro BNP	Normal NT-Pro	39	39.00
	High NT-Pro	61	61.00
Gold category	1	7	7.00
	2	25	25.00
	3	44	44.00
	4	24	24.00
ICU admission	Yes	43	43.00
	No	57	57.00
NIV/MV	NIV	38	38.00
	MV	14	14.00
Duration of hospital stay (days)	≤1	19	19.00
	2-5	33	33.00
	6-10	46	46.00
	>10	2	2.00
Outcome	Discharge	97	97.00
	Death	3	3.00

IV. Discussion

In a prospective observational study conducted in Department of Medicine, Mahatma Gandhi Hospital affiliated to Dr S.N. Medical College, 100 consecutive patients admitted with diagnosis of COPD were taken to estimate the proportion of raised or normal serum levels of NT-proBNP in COPD patients and to determine any relation of serum NT-proBNP levels with severity of COPD as per GOLD scoring and other parameters such as ABG, duration of hospital stay, need for ICU admission and outcome.

This study shows:- Mean presenting age of total cases was 63 ± 7 years. Mean age of patients with normal serum NT-proBNP levels was 62 ± 6 years and of patients with high serum NT-proBNP levels was 63 ± 7 years. Out of 100 patients, 34 were females and 66 were males. Total no. of cases with Normal NT-proBNP were 39, out of which 28 were males(i.e. 71.79%) and 11 were females(i.e. 11%). Similarly, total no. of cases with high levels of NT-proBNP were 61, out of which 38 were males(i.e. 62.30%) and 23 were females(i.e. 37.70%).

While comparing the two groups in relation to the severity as per GOLD criteria, the p value was .074 at 95% confidence limit and therefore there was no statistically significant difference in severity of the two groups and thus no relation was found between severity of COPD as per GOLD criteria and NT-proBNP levels.

Total no. of ICU admissions were 43 out of which, cases with normal NT-proBNP levels were 25.6% (11/43) and cases with high levels of serum NT-proBNP levels were 74.4% (32/43). The P value was 0.023 at 95% confidence limit . Therefore, a statistically significant relation was found between high levels of serum NT-proBNP levels and need for ICU admissions in COPD patients.

While comparing the two groups in relation to ABG, the p value for pCO_2 was 0.045 at 95% confidence limit which shows that a statistically significant relation was found between serum pCO_2 levels and serum NT-proBNP levels. mean pH was 7.30 in both groups and there was no statistically significant difference between pH of cases with normal NT-proBNP 3.levels and cases with high levels of serum NT-proBNP levels. p value for pO_2 level was 0.120 at 95% confidence limit which shows no statistically significant relation between serum pO_2 levels and serum NT-proBNP levels.

Total patients requiring Mechanical ventilation support were 14 out of wihich patients with Normal NT-proBNP levels requiring Mechanical ventilation support were 4 (28.6%) while patients with high NT-proBNP levels requiring Mechanical ventilation support were 10 (71.4%). Also, total patients requiring NIPPV support were 38 out of which patients with Normal NT-proBNP levels requiring NIPPV support were 17 (44.7%) while patients with hign NT-proBNP levels requiring NIPPV support were 21 (55.3%). The p value for intervention required was .541 at 95% confidence interval which implies no statistically significant relation between NT-proBNP levels and intervention required in COPD patients.

P value for duration of hospital stay in normal vs high levels of serum NT-proBNP was 0.042, which shows a statistically significant relation between NT-proBNP levels and duration of hospital stay. Mean Duration of hospital stay for patients with normal NT-proBNP levels was 4 days while mean duration of hospital stay for patiets with high levels of NT-proBNP levels was 5 days. Mean duration of hospital stay for total cases was 5 days.

Out of 39 patients of normal NT-proBNP 38 were discharged and 1 patient expired. 59 out of 61 patients with high levels of NT-proBNP discharged and 2 expired. There was no statistically significant difference between the outcome of patients of normal NT-proBNP levels and high NT-proBNP levels.

V. Conclusion

COPD remains an important diagnosis in medical outdoors and emergency department. Recently, role of NT-proBNP levels have been implicated in COPD as a tool for determining severity and prognosis. In our study, we took 100 consecutive patients of COPD and estimated their NT-proBNP levels. We found statistically significant relation of high NT-proBNP levels with pCO_2 levels, need for ICU, and duration of hospital stay. There was no relation of NT-proBNP levels with severity of COPD as per GOLD criteria, pH and outcome. Further studies are required to estabilish the role of this biomarker in COPD for better understanding of the patient's condition which may help in better decision making in part of the physician.

References

[1].   Daniel, Roy Arokiam1; Aggarwal, Praveen2; Kalaivani, Mani3; Gupta, Sanjeev Kumar1, Prevalence of chronic obstructive pulmonary disease in India: A systematic review and meta-analysis, Lung India: Nov–Dec 2021 - Volume 38 - Issue 6 - p 506-513doi: 10.4103/lungindia.lungindia_159_21

[2].   Fu, S., Ping, P., Wang, F. et al. Synthesis, secretion, function, metabolism and application of natriuretic peptides in heart failure. J Biol Eng 12, 2 (2018). https://doi.org/10.1186/s13036-017-0093-0

[3].   Rogliani P, Ora J, Puxeddu E, Cazzola M. Airflow obstruction: is it asthma or is it COPD? Int J Chron Obstruct Pulmon Dis. 2016 Nov 30;11:3007-3013. doi: 10.2147/COPD.S54927. PMID: 27942210; PMCID: PMC5137932.

[4].   Janssen R, Piscaer I, Franssen FME, Wouters EFM. Emphysema: looking beyond alpha-1 antitrypsin deficiency. Expert Rev Respir Med. 2019 Apr;13(4):381-397. doi: 10.1080/17476348.2019.1580575. Epub 2019 Feb 22. PMID: 30761929.

[5].   Halbert RJ, Natoli JL, Gano A, Badamgarav E, Buist AS, Mannino DM. Global burden of COPD: systematic review and meta-analysis. The European respiratory journal. 2006;28(3):523-32.

[6].   Prins KW, Markowitz J, Pritzker M, Duval S, Thenappan T. Use of PAH-specific therapy in world health organization group iii pulmonary hypertension: A systematic review and meta-analysis. Journal of Heart and Lung Transplantation. 2016;1):S175.

[7].   Huiart L, Ernst P, Suissa S. Cardiovascular morbidity and mortality in COPD. Chest. 2005;128(4):2640-6.

[8].   Global Initiative for Chronic Obstructive Lung Disease. The Global Strategy for the Diagnosis and Managment of COPD. . 2019