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ORIGINAL ARTICLE

Study of Levels of Plasma Fibrinogen and its Association with Disease Severity in Patients with Chronic Obstructive Pulmonary Disease

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ABSTRACT

COPD has been recognized as a component of the systemic inflammatory syndrome. A commonly used indicator of the severity and progression of the disease in COPD is expiratory volume per second (FEV1). However, it is weakly associated with symptoms and administration difficulties in elderly patients. Therefore, there is a need for other markers that are better and easy to apply to sick and elderly patients. Plasma fibrinogen can be used as a marker of disease severity.

Aim: To estimate the plasma fibrinogen level in patients with COPD and Relationship of levels of plasma fibrinogen with the severity of chronic obstructive pulmonary disease using the BODE classification and GOLD staging.

Place and Duration: In the Medicine Unit-II of Jinnah Hospital Lahore for one-year duration from August 2020 to August 2021.

Methods: In this cross-sectional study, 110 COPD patients were assessed by measuring plasma fibrinogen correlated with disease severity using the GOLD scale, BODE index and the 6-minute walk test.

Results: Plasma fibrinogen is present in all COPD patients. A significant correlation was observed between the BODE index ($r = 0.69$, $p < 0.001$), gold grading ($r = 0.95$, $p < 0.001$) and plasma fibrinogen levels. Most of the 110 subjects (34.5%) were Grade II, then Grade III 30.9%, 18.1% Grade IV and 14.5% Grade I. In our study, it was found that the average level of fibrinogen increased with the increase in the GOLD stage, which was statistically significant, and the p value was 0.01.

Conclusions: Plasma fibrinogen levels are significantly higher in COPD and can be used as a marker correlating with disease severity in COPD.

Keywords: COPD; plasma fibrinogen; GOLDEN stage; BODE index.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is categorized by insistent airflow limitation and respiratory symptoms due to anomalies in the alveoli/ airways, usually instigated by extensive exposure to noxious stimuli that are completely irreversible[1-2]. Chronic obstructive pulmonary disease is the fourth leading reason of death universally, but is predictable to become the third foremost reason of mortality by 2020[3-4]. In 2012, over three million individuals expired from COPD, counting for six percent of all deceases worldwide[5]. Worldwide, the load of COPD is predictable to rise in the coming years due to sustained COPD risk factors and an aging population. A commonly used indicator of the severity and progression of the disease in COPD is expiratory volume per second (FEV1). However, it is weakly associated with symptoms and administration difficulties in elderly patients[6-7]. Therefore, there is a need for other markers that are better and easy to apply to sick and elderly patients. Fibrinogen, an acute phase protein in plasma, is mainly produced in the liver. Thrombin then converts it into fibrin as the blood clots[8]. In COPD there is pneumonia associated with high levels of acute phase reagents. We therefore hypothesize that plasma fibrinogen can be used as an indicator of disease severity and exacerbation in COPD patients[9]. Very little work has been done in this regard in the past. Therefore, the need for a simple laboratory parameter such as plasma fibrinogen to assess the severity of COPD and its exacerbation by chronic systemic inflammation can be considered as a common relationship between plasma fibrinogen in COPD patients[10-11].

The goal of the study is to evaluate the plasma fibrinogen level and its relationship with the severity of chronic obstructive pulmonary disease in patients with COPD by means of GOLD grading and the BODE index.

MATERIALS AND METHODS

This cross-sectional study was held in the Chest Medicine department of Jinnah Hospital Lahore for one-year duration from March 2020 to March 2020

110 COPD patients who consented to the study and met the inclusion criteria were selected for the study

Criteria of Inclusion

- Age group:> 18 years old.
- A case of COPD diagnosed according to GOLD 2017 criteria
- Patients willing to provide informed consent in writing

Exclusion criteria:

- Age <18
- Patients who do not wish to give their informed consent in writing
- Spirometry showed asthma.
- Inability to perform spirometry and the six-minute walk test.
- Active infections.
- Acute kidney injury and chronic kidney disease.
- myocardial infarction and Congestive heart failure.
- Patients using oral steroids.
- Tuberculosis with positive sputum

After gaining the institutional ethics committee approval and written consent, 110 patients diagnosed with COPD in accordance with the GOLDS 2017 criteria and meeting the exclusion and inclusion criteria were registered in the study. Demographic data was collected using a semi-structured questionnaire, clinical trial and questionnaires. Data was collected and analyzed from all patients who met the exclusion and inclusion criteria.

Statistical analysis will be performed using the SPPSS software. The correlation of plasma fibrinogen levels between different stages of COPD patients will be performed using the Pearson correlation test and the ANOVA test, a P value of <0.05 (probability of correct result) is considered statistically significant under all assumptions. SPSS version 22, MS Excel was used for the analysis of data.

RESULTS

Age Distribution Of the 110 participants 87 (79.1%) are male: and 23 (20.9%) were females in this study.

Table 1: Sex and age distribution of the patients

	N	Minimum	Maximum	Mean	Std. Deviation
Age	110	32	87	60.23	10.60

Gold Stage And Subjects: Most of the 110 subjects (34.5%) were Grade II, then Grade III 30.9%, 18.1% Grade IV and 14.5% Grade I. In our study, it was found that the average level of fibrinogen increased with the increase in the GOLD stage, which was statistically significant, and the p value was 0.01.

Table 2: The patients distribution grounded on gold staging (using fev1)

GOLD STAGE	Frequency	Percent
I (MILD FEV1> 80)	16	14.5
II (MODERATE50%< FEV1 <80%)	38	34.5
III (SEVERE30% < FEV1 <50%)	34	30.9
IV (VERY SEVEREFEV1 <30%)	22	18.1
Total	110	100.0

The R value for this correlation was 0.95.

Table 3: The patients distribution grounded on plasma fibrinogen

	Frequency	Percent
350 to 375	39	35.5
375.1 to 390	44	40
390.1 to 400	19	17.3
Above 400	8	7.2
Total	110	100.0

Table 4: relationship between gold staging and mean plasma fibrinogen using Pearson correlation (2 tailed)

Gold staging	N	Minimum	Maximum	Mean	Std. Deviation	R-value	P value
I	16	350	363	355.1	3.6	0.939	0.01
II	38	357	379	372.1	5.2		
III	34	369	400	385.3	5.1		
IV	22	386	408	399.0	4.3		

Table 5: Pearson's association between plasma fibrinogen and bode index

Bode Index	N	Minimum	Maximum	Mean	Std. Deviation
1	16	353	379	359.20	9.2
2	38	355	390	372.23	7.2
3	34	372	405	387.51	9.2
4	22	362	409	393.36	12.4

DISCUSSION

It is a cross-sectional study intended at evaluating plasma fibrinogen in COPD patients and correlating the value with the severity of COPD using GOLD grading and BODE index, as well as assessing its relationship with other parameters such as age, BMI, FEV1[12]. 110 patients were included in our analysis. Of the 110 patients in our study, the maximum number of patients in our study was over 62 years (47.3%), with a mean age of 60.23 (SD 10.60). The lowest age in our current study was 32 years and the oldest patient was 83. The mean age group in this analysis was comparable to the study by Chopra RK et al in 2018 was 63.16 (SD ± 10.4) who conducted a similar study design. This can also be compared to the study by Raheem Hussain et al in 2017 in the Indian population (52.58 ± 11.25) in Hyderabad. In this study, 87 (79.1%) are male: and 23 (20.9%) were females. The female to male ratio was 1: 4.2 with no gender variation, comparable to Raheem Hussain et al. (2017) with a 1: 9 F: M ratio[13-14]. A similar distribution was observed in Chopra. Also RK et al (2018), which has an F: M ratio of 1: 2.57[15]. In our study, no significant variation by gender was found. In this study, the majority (34.5%) of the 110 people were gold in the first degree, then 30.9% in the third stage, 18% in the fourth and 14.5% in the stage I. This is analogous to the Chopr study. R.K et al. As of 2018, it is 6% in stage I, 34% in stage II, 40% in stage III and 20% in stage IV[16-17].

In our study it was found that the average level of fibrinogen increased with the increase of the gold degree, which was statistically significant, and the p value was 0.001. The R value for this correlation was 0.95. Similar to the work done by Sumathy et al. Since 2016, as the Gold Stage at madras Medical School increased, the average fibrinogen level also increased, which was statistically significant, and the p-value was <0.001. Moreover, the ketal chop study showed a similar positive correlation between plasma fibrinogen and the GOLD stage (p <0.0001)[18]. Thomas et al. Showed a similar optimistic association between plasma fibrinogen and the GOLD stage (p <0.001). As in this study, David M et al. conducted a study showing increased levels of fibrinogen associated with disease severity and increased mortality[19-20].

There is a strong and optimistic association between the plasma fibrinogen and Bode index (r = 0.66, p = 0.001), which is statistically significant. In this analysis, it was institute that the average fibrinogen level increased with the increase in the BODE INDEX level, which was statistically significant, and the p value was 0.001. The R value of this correlation was 0.69. A study by Kashifa Ehsan et al. Showed that plasma fibrinogen is a potential marker for disease severity in COPD using the GOLD and BODE index, which is similar to this study. Duvoix A et al. concluded that fibrinogen is a valuable biomarker in patients of COPD, in particular for identifying those most prone to exacerbation, binds to important clinical endpoints, and acts as a surrogate marker for treatment achievement, similar to our current study[21]. In another small cohort of 96 Japanese people with milder COPD (median FEV1 predicted 70%), Higashimoto and colleagues institute that those with high blood levels of fibrinogen showed a negligible tendency to deteriorate lung function more rapidly (p = 0.054)[22]. In contrast, fibrinogen was related with baseline FEV1 rather than a longitudinal decline in FEV1 in the larger multinational cohort of 1,793 patients in the ECLIPSE study. Which is similar to this study.

CONCLUSION

1 Plasma fibrinogen levels are significantly elevated in COPD patients.

2 Plasma fibrinogen values correlated well with FEV1, GOLD grading, BODE index and 6mwt.

3 Age, gender and BMI are not related to each other.

4 Plasma fibrinogen can be used as a biomarker to predict the severity of COPD.

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