



Serum Fibrinogen Level in COPD Patients- A Comparative Study

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Abstract

Introduction: Chronic obstructive pulmonary disease (COPD) is now the third most common cause of death in the world. The severity and progression of COPD is measured by forced expiratory volume in 1 second (FEV₁). However, FEV₁ may not be an ideal surrogate for short-term drug trials. Biomarkers like Fibrinogen, CRP etc could become suitable surrogates in the early detection of disease.

Aims & objectives: To study the association of blood fibrinogen level in COPD and its correlation with the severity of COPD

Methodology: this study was conducted on 50 stable COPD patients and a control group of 50 healthy persons. After the thorough history and clinical examination, all the subjects were investigated with complete Blood Count, chest radiographs, spirometry and serum Fibrinogen levels.

Results: Mean age in test group was 63.16 yr and in control group was 59.86 years. Mean WBC count in the test group was 8795/cmm and in Control group was 6020 /cmm ($p < 0.0001$). Mean fibrinogen level in the test group was 455.38 mg% and in control group was 255.50 mg% ($p < 0.0001$). Fibrinogen levels correlate with severity of COPD

Conclusion: Serum fibrinogen levels can be used as a biomarker in the COPD which correlates with the disease severity.

Keywords: COPD, FEV₁, Serum Fibrinogen.

Introduction

Fibrinogen is an acute phase soluble plasma glycoprotein, synthesised primarily in the liver and converted by thrombin into fibrin during blood coagulation. Normal range is 1.5 and 3.5 g/litre, but can increase threefold during acute phase stimulation in response to increased IL-6 production¹. Fibrinogen has emerged as a promising biomarker in COPD and is currently

being considered for qualification as a drug development tool by the US Food and Drug Administration and the European Medicines Agency². IL 8, IL 6, neutrophils, TNF α are other inflammatory biomarkers which also increase in exacerbation.

The present study aims to evaluate the serum levels fibrinogen as the biomarker of severity of COPD.

Materials and Methods

After obtaining approval of the ethics committee of the Medical institute, we conducted this prospective, observational study at our tertiary care institute.

The study was done over a period of 13 months (April 2013 – May 2014).

The study was carried out in 100 consecutive subjects over the period of 13 months, who visited our OPD and IPD. Out of these 100 subjects, 50 were normal healthy individuals forming control group & rest 50 patients were diagnosed COPD cases as per GOLD guidelines.

Patients with history suggestive of asthma or any other pre-existing pulmonary disease affecting lung function other than COPD as well as patients with other systemic diseases were excluded.

Detailed history and examination of patient, with mMRC scoring of dyspnoea was done. All patients were subjected to spirometry and diagnosis and staging of COPD was made based on GOLD guidelines. All the subjects had blood test done for CBC and serum fibrinogen level. Using standard methods, results were analyzed.

Results

Table 1: Comparison of age in COPD and control group

| | COPD(n-50) | | Control(n-50) | |
|----------|------------|-------|---------------|------|
| | mean | SD | mean | SD |
| Age(yrs) | 63.16 | 10.47 | 59.86 | 6.86 |

p>0.05

Table 2: Sex wise distribution of cases in COPD group

| Sex | COPD |
|--------|------|
| Male | 36 |
| Female | 14 |
| Total | 50 |

Chi-square = 0.48, P>0.05

Table 3: Comparison of WBC in COPD and control group

| | COPD(n-50) | | Control(n-50) | |
|------------------------|------------|------|---------------|------|
| | mean | SD | mean | SD |
| WBC (mm ³) | 8794 | 3619 | 6020 | 1914 |
| | .68 | .27 | 54 | 76 |

p<0.0001

Table 4: Comparison of Fibrinogen level in COPD and control group

| | COPD(n-50) | | Control(n-50) | |
|--------------------|------------|--------|---------------|------|
| | mean | SD | mean | SD |
| Fibrinogen (mg/dl) | 455.38 | 159.71 | 255.50 | 7.98 |

p<0.0001

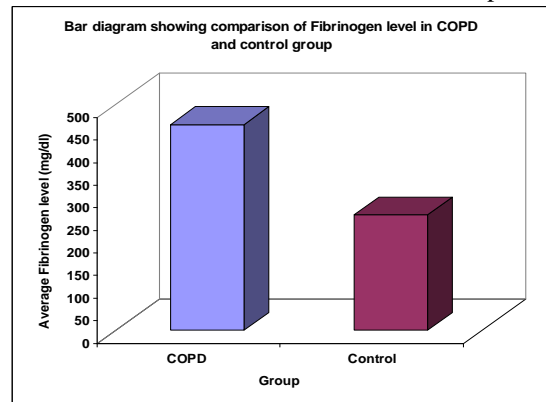


Fig1: Graph of comparison of serum fibrinogen level in COPD & control group

Table 5: Severity of disease wise distribution of cases in COPD

| Severity of disease | COPD | Percentage |
|---------------------|------|------------|
| Mild | 3 | 6% |
| Moderate | 17 | 34% |
| Severe | 20 | 40% |
| Very severe | 10 | 20% |
| Total | 50 | |

Table 6: Comparison of Fibrinogen level according to severity of disease in COPD group

| Severity | n | Fibrinogen (mg/dl) | |
|-------------|----|--------------------|-------|
| | | mean | SD |
| Mild | 3 | 271.7 | 117.7 |
| Moderate | 17 | 387.9 | 113 |
| Severe | 20 | 451.7 | 157 |
| Very severe | 10 | 632.7 | 79.2 |

p<0.0001

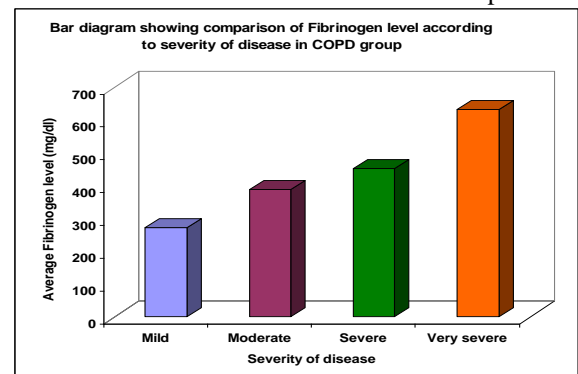


Figure 2: Graph of distribution of fibrinogen level according to severity of COPD

Table 7: Comparison of WBC according to severity of disease in COPD group

| Severity | n | WBC (cells/cmm) | |
|-------------|----|-----------------|---------|
| | | mean | SD |
| Mild | 3 | 7933.33 | 1011.59 |
| Moderate | 17 | 7686.12 | 2124.44 |
| Severe | 20 | 8128.70 | 3047.18 |
| Very severe | 10 | 12269.60 | 5147.14 |

p<0.01

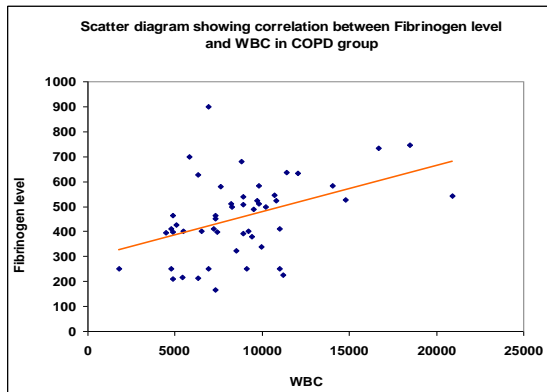


Fig 3: Graph of correlation between serum fibrinogen level & WBC count with severity of COPD

Discussion

Mean age of our patients was 63.16 ± 10.47 yrs with minimum age of 36 yrs and maximum age of 85 yrs, maximum patients were in the age group of 51-60 yrs. In the similar studies conducted by Jain N K et al and Hulya Koksals et al, they found mean age of the patients as 60.61± 10.36 yrs and 65.3±7.39 yrs respectively. This result is consistent with the chronicity of the disease and its presentation being more in the elderly.

In our study we found that WBC count is increased in COPD patient as compare to control group. The mean WBC count in COPD patients was 8794.68x10³ cells/mm³ with SD of 3619.27 (P <0.0001).

Few studies demonstrate elevated level of biomarkers seen in COPD & similar findings were observed in meta-analysis research of W Q Gan³ et al, on fibrinogen level in COPD patients; found that overall, circulating leucocytes along with fibrinogen were higher in patients with COPD than in control subjects. The standardized mean difference was 0.44 units (95% CI 0.20 to 0.67;

test for heterogeneity, p=0.003) or 0.886109 cells/l (95% CI 0.36 to 1.40)

In our study, significant difference was found in the serum fibrinogen level in COPD patients and controls (4.55±1.59 mg/dl versus 2.55±0.76 mg/dl, respectively). P (<0.0001) suggested it as significant

In a study conducted by Groenewegan⁴ and his colleagues in Masstricht University in the Netherlands on 277 patients, the serum levels of inflammatory biomarkers CRP, fibrinogen, and TNFα were higher in COPD patients compared to controls. They say that higher fibrinogen levels are significantly predictive for the occurrence of severe as well as moderate exacerbations. The p value is p< 0.039, which is significant as in our study. In another study performed by Valipour A and co-workers on 30 COPD patients Austria, fibrinogen (p<0.05) was higher in these patients compared to controls, along with other biomarker like CRP, VEGF, WBC & IL-6⁵.

In our study, we found that as severity of COPD increases, there is increase in serum fibrinogen levels. For mild COPD according to GOLD staging.

Deepa valvi & colleagues⁶ in their large population study in US community they found, subject with more advanced COPD (stage 3 & 4) had greater elevation in fibrinogen (24.71 mg/dl,p= 0.0000) than GOLD stage 2 & stage 1 disease (12.04 mg/dl, p =0.0000 & 7.68 mg/dl , p=0.0000), these results are similar to our study. In another Asian study of Yoko Shibata & et al⁷ in 3,257 subjects from Japan, they found that there was correlation between decrease FEV1 & increase serum fibrinogen level in men with Coefficient -0.018, SD 0.006, P<0.007. Moreover, for female this was non-significant.

Conclusion

Serum fibrinogen as a new & novel marker for severity of COPD is found useful according to many studies including landmark study- ECLIPSE study. Our short observational study also concluded its usefulness as a severity marker in

both smoking & non-smoking COPD. As our sample size was small, further studies with larger sample size is recommended.

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