

## Original Research Article

## Retrospective Analysis of D- Dimer and Procalcitonin as the Predictor of DIC in Patients with COVID 19

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**Abstract: Background:** COVID 19 causes growing numbers of severe diseases with systemic abnormalities like organ dysfunction, thrombosis, and mortality. Disseminated Intravascular Coagulation or DIC is associated with the development of systemic fibrin, which may cause due to increased thrombin expression, concomitant physiological anticoagulant suppression and dysfunctional fibrinolysis. **Methods:** This study was a retrospective study that was conducted at the department of Clinical Pathology. The study was carried out during the period of September 2021-February, 2022. The total sample size for this study was 50. **Result:** Most of the respondents 12(24%) were aged from 50-59 years. Most of the respondents 35(70%) were female and 15(30%) were male. D-Dimer findings of most of the patients (44%) were severe. PCT test findings were normal for 34% of the participants, mild for 6%, moderate for 26%, and the remaining 40% had severe PCT levels. Among the 50 cases, both PCT and D-Dimer values were in the normal range for 26% of the participants, while 62% of the participants had raised values (mild, moderate, or severe) in both PCT and D-Dimer tests. **Conclusion:** From this study, it can be said that levels of D-dimer and PCT are directly linked to the disease severity among the patients with COVID 19.

**Keywords:** D- dimer, Procalcitonin, Disseminated Intravascular Coagulation or DIC, COVID 19.

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## INTRODUCTION

Coronavirus disease (COVID-19) which is caused due to Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV2), was spread as an epidemic in Wuhan, China, in December 2019, which later turned into a global pandemic [1]. COVID 19 causes growing numbers of severe diseases with systemic abnormalities like organ dysfunction, thrombosis, and mortality [2, 3]. Studies have found Coagulopathy is commonly present in patients with COVID-19. Coagulopathy is considered to be the most alarming predictive sign of severe COVID-19 infection and also results in an increased incidence of mortality

[4, 5]. Disseminated Intravascular Coagulation (DIC) is associated with the development of systemic fibrin, which may cause due to increased thrombin expression, concomitant physiological anticoagulant suppression and dysfunctional fibrinolysis [6]. A study reported that DIC can develop as a median of 4 days (range: 1-12 days) after the hospitalization of patients with COVID-19 [5]. Another study reported that DIC- associated difficulties may contribute to death after evaluating the acute respiratory distress syndrome (ARDS) related factors in patients with COVID-19 [7]. The common diagnostic measures for predicting DIC in sepsis are reduced platelet counts, sustained PT and increased D-

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dimer levels [8]. However, according to the ISTH DIC scoring system, there are four criteria for DIC scoring these are PLT, PT, fibrinogen, and D-dimer. But D-

dimer and Procalcitonin (PCT) are the most commonly used predictor of DIC.

**Table 1: DIC Scoring System**

| Variable                   | Parameter                   | Score |
|----------------------------|-----------------------------|-------|
| Platelet Count             | >100x10 <sup>9</sup> /L     | 0     |
|                            | (50-100)x10 <sup>9</sup> /L | 1     |
|                            | <50x10 <sup>9</sup> /L      | 2     |
| D-Dimer                    | <1mcg/ml                    | 0     |
|                            | 1.0-5.0 mcg/ml              | 2     |
|                            | >5.0 mcg/ml                 | 3     |
| Prolonged Prothrombin Time | <3 seconds                  | 0     |
|                            | 3-6 seconds                 | 1     |
|                            | >6 seconds                  | 2     |
| Fibrinogen                 | >100 mg/dl                  | 0     |
|                            | <100 mg/dl                  | 1     |

According to the DIC scoring system, a combined score of 5 or higher indicates a higher mortality rate. It is found that D-dimer levels of 2.0 µg/ml had a higher incidence of mortality in COVID-19 patients compared to those with D-dimer levels while the PLT count and Alb were much lower in severe patients [9]. Another study claimed D-dimer > 1 µg/ml is one of the common risk factors for mortality in adult patients with COVID-19 [10]. Whereas Procalcitonin (PCT), also known as the precursor of calcitonin, is commonly secreted by thyroid parafollicular C cells [11]. PCT usually induced by bacterial and viral infections in extrathyroidal tissues and has been used to differentiate these infections [12]. In COVID-19 patients, higher PCT levels indicate bacterial infection and increase complications. A meta-analysis based on four related studies proved that an increased PCT level was independently associated with severe COVID-19 infection [13]. The aim of this study was to assess the links of D-dimer and PCT with DIC among patients with COVID-19 and to determine whether the D-dimer and PCT levels accurately predict the development of DIC in these cases.

## OBJECTIVE OF THE STUDY

The objective of this study was to evaluate the effectiveness of D-dimer and procalcitonin in predicting DIC among patients with COVID 19.

## MATERIALS AND METHODOLOGY

This study was a retrospective study that was conducted at the department of Clinical Pathology. The study was carried out during the period of September, 2021-February, 2022. The total sample size for this study was 50.

### Inclusion Criteria

- The patients who were admitted with the symptoms of COVID 19.

- The Patients who did D-dimer and PCT testing during hospital admission.
- The patients were suspected to be with DIC.

### Exclusion Criteria

- Pregnant patients were excluded from this study.
- The patients having a chronic disease like cancer, hematologic malignancy, chronic liver disease, acute coronary syndrome, surgery or trauma within 30 days, and
- The patients without D-dimer and PCT testing during hospital admission.

According to the recommendation of WHO, the diagnosis of COVID-19 was done using the RT-PCR. The primary symptom onset is determined by the previously recorded clinical history taken upon during hospital admission which was consistent with COVID-19, such as fever, cough, dyspnea, muscle pain, diarrhea, fatigue, etc. Critical illness was defined depending on the condition of the patients like those who needed admittance to the ICU, needed mechanical ventilation, or died. Severe patients were identified through some factors like respiratory distress, respiratory rate ≥ 30 times/minute, below-resting state, oxygen saturation ≤ 93%, and oxygen partial pressure (PaO<sub>2</sub>)/oxygen concentration (FiO<sub>2</sub>) in arterial blood ≤ 300 mmHg. The test items included D-dimer and PCT. D-dimer levels and The PCT level were evaluated using an immunoturbidimetric assay method (Cobas c 501, Germany). D-Dimer values of ≤0.5 mg/l were considered normal, and elevated D-dimer was further divided into two groups, mild-moderate, with D-Dimer values ranging from 0.5-2.0 mg/l, while patients having a D-Dimer range of >2.0 mg/l were categorized as severe.<sup>14</sup> PCT values of <0.1 ng/ml were categorized as normal range, while the remaining findings were divided into mild, moderate, and severe groups of severity. PCT values of 0.1-<0.25 ng/ml were recognized as mild, 0.25-<0.5 ng/ml were recognized as moderate, and PCT values of 0.5 ng/ml or higher were

considered severe cases.<sup>15</sup> The study was approved by the Internal Review Board of our hospital and was performed under the Ethical Standards of the

Declaration of the institution. Data were analyzed using SPSS software version 21.0

## RESULT

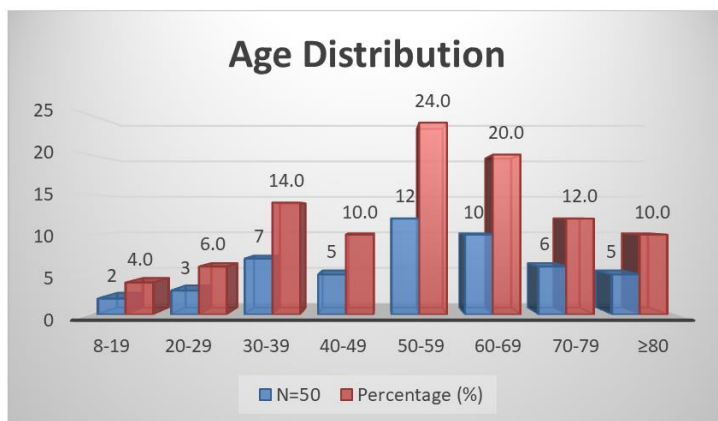


Figure 1: Age Distribution of the Respondents (n=50)

Figure I show the age distribution of the respondents. Most of the respondents 12(24%) were aged from 50-59 years and followed by 2(4%) were 8-19 years, 3(6%) were 20-29 years, 7(14%) were 30-39,

5(10%) were 40-49 years, 10(20%) were 60-69 years, 6(12%) were 70-79 years and the rest 5(10%) were ≥80 years.

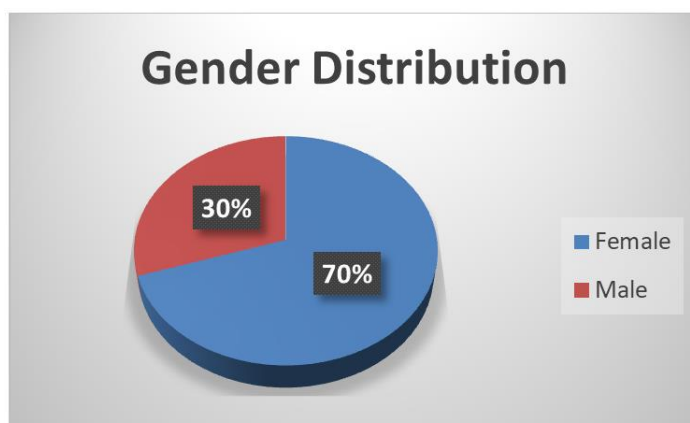


Figure 2: Gender Distribution of the Study People (n=50)

Figure II shows the gender distribution of the study people where most of the respondents 35(70%) were female and 15(30%) were male.

Table 2: Distribution of patients according to Severity of D-Dimer test findings (n=50)

| D-Dimer (mg/l)          | Frequency | Percentage |
|-------------------------|-----------|------------|
| ≤0.5 [Normal]           | 15        | 30%        |
| 0.5-2.0 [Mild-Moderate] | 13        | 26%        |
| >2.0 [Severe]           | 22        | 44%        |

Table 2 shows the result of D-dimer (mg/L) testing among the study patients. D-Dimer findings of most of the patients (44%) were severe, followed by

30% who had normal findings, and the remaining 26% had mild-moderate levels of D-Dimer.

**Table 3: Distribution of patients according to Severity of PCT test findings (n=50)**

| PCT Values (ng/ml)   | Frequency | Percentage |
|----------------------|-----------|------------|
| <0.1 [Normal]        | 17        | 34%        |
| 0.1-<0.25 [Mild]     | 3         | 6%         |
| 0.25-<0.5 [Moderate] | 10        | 20%        |
| ≥0.5 [Severe]        | 20        | 40%        |

Procalcitonin Test or PCT test findings were normal for 34% of the participants, mild for 6%,

moderate for 26%, and the remaining 40% had severe PCT levels.

**Table 4: Combined results of D-dimer and Procalcitonin Testing (n=50)**

| PCT and D-Dimer Combined Findings | Frequency | Percentage |
|-----------------------------------|-----------|------------|
| Both Normal                       | 13        | 26%        |
| Both Raised                       | 31        | 62%        |
| PCT Normal, D-Dimer Raised        | 4         | 8%         |
| D-Dimer Normal, PCT Raised        | 2         | 4%         |

Table 3 demonstrates the combined results of D-dimer and Procalcitonin testing. Among the 50 cases, both PCT and D-Dimer values were in the normal range for 26% of the participants, moderate while 62% of the participants had raised values (mild or severe) in both PCT and D-Dimer tests. For 8% of the participants, PCT was normal and only D-Dimer values were raised, while the remaining 4% had only PCT raised.

## DISCUSSION

Irregularities in coagulation parameters with a higher D-dimer level are generally seen in severe COVID-19 infection [16]. Also, the abnormalities in coagulation are associated with a higher mortality rate, especially among the patients with severe COVID-19 [17]. COVID-19-related coagulation syndromes are categorized as low-grade DIC and pulmonary thrombotic microangiopathy [18]. A study reported that 2.5% of SARS patients had DIC complications which are also linked with mortality [19]. Besides, COVID-19 infection makes the DIC complications worsen [5, 20]. Most of the respondents (24%) were aged from 50-59 years and followed by 4% were 8-19 years, 6% were 20-29 years, 14% were 30-39, 10% were 40-49 years, 20% were 60-69 years, 12% were 70-79 years and the rest 10% were ≥80 years (figure 1). Diego Velasco-Rodriguez *et al.*, in their study reported that most of the respondents 19.48% were aged from ≤50 years and followed by 18.32% were 51-60 years, 19.96% were 61-70 years, 21.12% were 71-80 and the rest 21.12% were >80 years [21]. Most of the respondents 70% were female and 30% were male (figure 2). Hakan Keski in his study found most of the respondents 51% were female and 49% were male [22]. D-Dimer values were severe for 44% of the participants, and only 30% of the 50 participants had normal levels of D-Dimer values (Table 2). According to the procalcitonin test findings, PCT serum was within normal parameters for only 34% of the participants, while 6% had mild PCT values. 20% of the participants had moderate levels of PCT ng/ml, while the remaining 40% had severely high levels of PCT serum (Table 3). Under normal circumstances,

patients with such severe levels of PCT values would be referred to the ICU, but as this was a retrospective study, most of the patients were already admitted to the ICU or NICU at the time of data collection. Zhou *et al.*, in their study reported that COVID-19 patients with an increased D-dimer level (> 1 mg/L) had an 18-times greater risk of mortality (95% CI 2.6- 128.6; p = 0.0033) during hospital admission [23]. On the other hand, Wang *et al.*, carried out a study on 138 COVID-19 patients and found a three-times greater risk of hospitalization in the ICU in patients having higher versus lower PCT levels (75% vs. 22%; p < 0.001) [17]. Generally, patients with mild COVID-19 have lower PCT levels compared with severe COVID-19 [24]. Lippi and Plebani in their study found the association between the increased PCT levels and severe COVID-19 infection [13]. Liu *et al.*, in their retrospective study among 141 COVID-19 patients stated increased PCT levels (> 0.07 ng/mL) at the time of hospital admission in those with severe COVID-19 compared to mild infection [25]. Zhou *et al.*, also confirmed significantly higher PCT levels in patients with critical infection in comparison with severe COVID-19 [26]. Guan *et al.*, proved a significant increase in PCT levels in severe COVID-19 compared to non-severe infection [4]. Among the 50 patients in the present study, only 6 patients in total had either abnormal PCT levels or abnormal D-Dimer levels, but not both. For 62% of the patients, however, both PCT and D-Dimer values were raised above their respective normal range, while 26% had normal values in both PCT and D-Dimer tests (Table 4). A high mortality rate was observed among the patients who had abnormal values in both PCT and D-Dimer findings.

## CONCLUSION

From this study, it can be said that levels of D-dimer and PCT are directly linked to the disease severity among the patients with COVID 19. COVID 19 is an inflammatory disease that has coagulation reactions that causes an increase in thrombotic event rates. Generally, the D-dimer level remains higher in



severe cases and hence, significantly higher levels may be used as a prognostic marker for in-hospital mortality. On the other hand, a higher PCT level can also predict the DIC positivity and identify the severity of COVID-19. Hence, laboratory testing for D-dimer and PCT is needed to categorize the severity of COVID-19 patients. However, early diagnosis of DIC and identification of higher PCT and D-dimer level is required in treating severe cases of COVID-19.

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