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Platelet Count, D- Dimer and NLR Ratio as Biomarkers Predicting the Disease Severity in Covid19 Patients

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Severe acute respiratory syndrome corona virus (SARS Cov2), the cause of ongoing COVID-19 pandemic. Viral induced hematological changes help in diagnostic work up and therapeutic intervention for risk stratification and forecasting intensive care requirements. Though primarily documented as pulmonary disease, emerging research show its multisystem involvement, with significant alteration in hematological and coagulative parameters (1).

The SARS Cov2 enters through ACE2 receptors present on the endothelial cells (2). This triggers various interleukins, growth factors, cytokines and angiogenesis leading on to activation of inflammation, coagulation cascade. Its spectrum of presentation being asymptomatic to Pneumonia, Acute respiratory distress and severe sepsis leading to death involving all age groups with predominance of elderly with co morbidities.

As the disease progresses concordant hematological abnormalities such as leukocytosis, lymphopenia, thrombocytosis, thrombocytopenia, abnormal coagulation profile has been well documented. In this study we explore the platelet count, NLR and D dimer to determine the disease severity in laboratory proven covid positive patients for risk management and stratification of intensive care requirements (3,4). Although several biomarkers have been hypothesized to be involved in the severity of the disease, NLR (NEUTROPHIL LYMPHOCYTE RATIO), D dimer and variation in platelet count may have significant prognostic value in determining disease severity).

MATERIALS AND METHODS

This study was a retrospective observational single center study, started on February 2021 till May 2021. Patients of age 25-75 years admitted in Bhaarath medical college and hospital were included in the study. Patients with underlying conditions such as hypertension diabetes. liver disease. and cerebrovascular disease were excluded. Patients' demographic data and clinical details will be collected and the hematological parameters such as platelets, NLR ratio and D dimer were analyzed in intensive care and non-intensive care COVID 19 patients. Patients will be categorized as severe and non-severe according to WHO protocol version 3 (5). Alteration in hematological parameters were correlated with disease progression.

Disease severity assessed with the following parameters were compared with its progression and outcomes. Platelet count, absolute neutrophil and absolute lymphocyte was measured in five part

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analyser swelab lumi, Boule. D dimer measured using SIA satellite max, Stago analyser.

Neutrophil lymphocyte ratio

Sato et al first used it in 2012 for determining preoperative NLR and therapeutic response in esophageal carcinoma (6). NLR was estimated by using standard formula. The normal NLR should be less than 3.5, any value above 3.5 is considered acute stress in the form of inflammation, infection, cardiovascular disease, cancer or post-operative complications (7).

PLATELET COUNT

There are several studies postulating mechanisms of thrombocytopenia in COVID. The possible mechanisms are decreased production, increased destruction, and removal from circulation. SARS cov2 induced immune reaction causes antibodies production that target platelet and hence remove them from circulation. Further endothelial damage, inflammation, cytokine storm and platelet activation can as well explain the thrombocytopenia (8,9).

D DIMER

Coagulation complications are frequently seen in COVID 19 patients. Elevated Ddimer (>0.5 mg/l) are associated with adverse outcomes especially in ICU patients as previously described in studies done by chen et al with 99 patients in wuhan china. (10).

Statistical analysis

Categorical data were expressed in percentages. Chisquare analysis (X2) was done to compare sex with the severity of the disease. Two sample unpaired t- tests was used to the statistical test of significance of the hematological parameters of ICU and non-ICU patients. A p value of <0.05 was considered statistically significant. SPSS software was used to perform the analysis.

RESULTS

A total of one hundred and fifty patients positive for COVID 19 by rt PCR were included in the analysis. The mean age of these patients was 50.5 ± 10.03 . The mean age of patients admitted in ICU was 54.09 ± 11.58 which was significantly higher than the mean age of non-ICU patients whose mean was 49.56 ± 9.42 (p < 0.05).



Fig 1 Patients admitted in ICU and NON-ICU

Among these 150 patients, 102 were male and 48 were female (Fig1 & 2). Of these 102 male patients 21 required ICU treatment, whereas 10 female patients needed ICU treatment.

Statistical analysis revealed no impact of sex of the patient on the severity of disease (p>0.2).



Fig 2 Distribution of Male and Female patients in ICU and NON ICU

The mean platelet count of all patients were 2.16 \pm 0.72 lakhs. The mean platelet count of ICU patients was 1.81 \pm 0.60 lakhs, whereas the mean platelet count of non- severe disease was 2.24 \pm 0.64 lakhs. The average platelet count was significantly lower in severe illness than non-severe illness (p <0.05).

The average NLR ratio of all 150 patients was 5.27 ± 1.53 . The average NLR ratio of patients who required

intensive care was 5.82 ± 1.32 . This ratio was higher than patients not requiring ICU care whose mean was 5.12 ± 1.55 (p <0.05).

The average d-dimer was 7.37 ± 2.93 . Subgroup analysis revealed that the d-dimer values were significantly higher in ICU patients (10.85 ± 2.47) than non-ICU patients (5.93 ± 1.62) (p <0.05).

	Mean ± SD
Demographic characteristics	
Age (n= 150)	50.5 ± 10.03
Male: Female	102: 48
Hematological parameter	
Platelet count (n= 150)	2.16 ± 0.72
NLR ratio (n= 150)	5.27 ± 1.53
d- dimer	7.37 ± 2.93

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	ICU (n1 = 31)	NON- ICU (n2	p-Value
		=119)	
Demographic			
Characteristics			
Age (n= 150)	54.09 ± 11.58	49.56 ± 9.42	< 0.05
Sex (n= 150)			
Male	21	81	> 0.2
Female	10	38	
Hematological parameter			
Platelet count (n= 150)	1.81 ± 0.60	2.24 ± 0.64	< 0.05
NLR ratio (n= 150)	5.82 ± 1.32	5.12 ± 1.55	< 0.05
d-dimer (n= 48)	10.85 ± 2.47	5.93 ± 1.62	< 0.001

 TABLE 2. Comparison of NLR, Platelet and D dimer among ICU and NON-ICU

DISCUSSION

Aditya Anurag et al (11) found in their study that older age, higher TLC, neutrophilia, lymphopenia, eosinopenia, high NLR and high NMR are associated with severe COVID-19.

In our study comparing hematological parameters between severe and non-severe cases, NLR was mostly found in the range between 3.5 to 6.5. Few patients had NLR greater than 6.5 and their disease severity is compounded by co-morbid factors. Similar result was found by Highboy Javanmand et al (12) who found that the percentage of severe and non-severe patients in NLR range between 3.5 to 6.5 did not differ significantly. However, they found that the percentage of NLR > 6.5 differed significantly (P < 0.0001) between the severe (56.1%) and non-severe cases (20%).

Guan et al (14) found that the percentage of severe (92.6%) and non-severe (82.5%) patients with lymphocytopenia differed significantly (P=0.056). In addition, severe cases presented thrombocytopenia more frequently vs non-severe cases. Huang et al (5) reported similar findings (P=0.45).

Olga Pozdnyakova et al (13) found that more severe disease was associated with significant neutrophilia and lymphopenia, which was intensified in critically ill patients. In addition, they found that all COVID 19 positive patients had abnormal WBC morphology with a wide spectrum of changes.

Giuseppe Lippi et al (17) in a meta-analysis of nine studies with 1799 COVID patients showed that thrombocytopenia was associated with severe coronavirus disease 2019 (COVID-19) infections.

Guan et al (14) found that patients with severe disease (requiring ICU, need for mechanical ventilation or death) presented with elevated D-dimer more frequently than non- severe cases. Lippi et al (16) also found that D-dimer values were considerably higher in COVID-19 patients with severe disease than in those without

CONCLUSION:

The hematological markers known to be altered in the current pandemic were NLR, platelet and D dimer, are directly correlating with disease severity in our study. Although of lesser concern, inflammatory markers and hematological parameters are always an adjunct in facilitating management and monitoring disease severity of patients.

To conclude, close monitoring of hematological and coagulopathic parameters are essential in patients with COVID19.

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