Impact of various hematological and biochemical parameters on mortality in coronavirus disease 2019 (COVID-19): A single-center study from North India

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ABSTRACT

Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes coronavirus disease 2019 (COVID-19), has rapidly evolved into a pandemic, affecting more than 90 million people and more than 1.9 million deaths worldwide. Despite extensive study, the prognostic role of various hematological and biochemical parameters remains unclear. Methods: This study was carried out at a COVID care facility in Delhi. The demographic and clinical information, laboratory parameters (hematological, biochemical, and inflammatory), and the treatment of admitted COVID-19 patients during first wave were collected from electronic medical records and were subsequently analyzed. Results: Between March 2020 and November 2020, a total of 5574 patients were admitted to hospital due to COVID-19. Majority (77.2%) were male and had a mean (standard deviation [SD]) age of 38.9 (14.9) years. The mean (SD) duration of hospital stay was significantly higher in nonsurvivors. Out of the entire cohort, 8.7% of the patients had comorbidities, whereas 47.1% of the patients were asymptomatic at presentation. Compared to the survivors, the nonsurvivors had a significantly higher proportion of comorbidities and were more likely to be symptomatic. Patients who died during hospital stay had significantly higher relative neutrophil percent and neutrophil–lymphocyte ratio and lower lymphocyte percent. The patients who died had significantly higher levels of ferritin, D-dimer, and fibrinogen. Conclusions: Analysis of various hematological and inflammatory parameters can provide useful prognostic information among COVID-19-affected patients. It can also help in identifying patients who merit aggressive institutional care and thereby potentially mitigate the mortality.

KEY WORDS: Biochemical, biomarkers, coronavirus disease 2019, hematological, inflammatory

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes coronavirus disease 2019 (COVID-19), has rapidly evolved into a pandemic, affecting more than 194 million people and more than 4.1 million deaths worldwide.1 Although mainly characterized as a respiratory tract infection, it is now...
considered a systemic disease due to multiple organ involvement.\textsuperscript{[2-4]} Although older age and presence of comorbidities constitute an increased risk of death from COVID-19, younger and previously healthy individuals may also develop lethal complications such as disseminated intravascular coagulopathy and fulminant myocarditis.\textsuperscript{[5,6]}

Although several clinical parameters have been linked with COVID-related outcomes, corresponding information about biochemical parameters is lesser known. Elevation of certain inflammatory markers and cytokines has been associated with poor outcomes in critical COVID-19 disease. However, most data have emerged from relatively smaller studies in intensive care unit settings and in patients with predominantly severe disease. There is limited evidence on the discriminatory ability of initial biochemical parameters between favorable and unfavorable outcomes. This knowledge may help to establish a prediction model based on a combination of routine laboratory tests in COVID-19 patients, thereby providing a simple and feasible approach to predict the outcome of COVID-19 patients in clinical practice.

**MATERIALS AND METHODS**

**Patients**

This study was carried out between March 2020 and November 2020 at a 600-bedded dedicated COVID care facility in Delhi state. The demographic and clinical information, laboratory results, and treatment details of COVID-19 patients were collected from electronic medical records. COVID-19 was diagnosed if patients were positive for SARS-CoV-2 by the reverse transcription–polymerase chain reaction or rapid antigen testing method. As a hospital policy, initially all such patients were admitted irrespective of disease severity. The following laboratory parameters were analyzed: (1) hematological (hemoglobin, total leukocytes, neutrophil percent, lymphocyte percent, neutrophil–lymphocyte ratio [NLR], and platelets), (2) biochemical (aspartate aminotransferase, alanine aminotransferase, albumin, bilirubin, alkaline phosphatase [ALP], and creatinine), and (3) inflammatory (fibrinogen, D-dimer, ferritin, and C-reactive protein [CRP]). The laboratory values were compared between patients who recovered and those who succumbed to their illness.

**Statistical analysis**

The results are presented as mean (standard deviation [SD]) or median (range). Paired t-test or Mann–Whitney U-test was used to compare the difference of continuous variables. Chi-square test was used for categorical data. Statistical significance was determined as $P < 0.05$. Data were analyzed using StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX, USA: StataCorp LP.

**RESULTS**

During the period from March 2020 and November 2020, 5574 patients with COVID-19 were admitted with a mean (SD) age of 38.9 (14.9) years and including 77.2% of males. The mean (SD) duration of hospital stay was 10.9 (2.4) days. Among the total group, 142 (2.5%) patients died in hospital and the remaining 5432 (97.5%) were discharged. The demographic and clinical characteristics of survivors and nonsurvivors are shown in Table 1. The nonsurvivors had a significantly longer duration of hospital stay than survivors (12.2 [5.6] days vs. 10.9 [1.2] days, respectively; $P = 0.03$). Of the total cohort, 8.7% had comorbidities (10.1% diabetes and 8.3% hypertension being the most common), and 47.1% of the patients were asymptomatic at the time of admission. The patients who died had a significantly higher proportion of comorbidities and were more likely to be initially symptomatic. These are highlighted in Table 1.

Compared to patients who recovered, those who died in hospital had significant neutrophilia, lymphopenia, and higher values of NLR. No difference was found among the two groups in hemoglobin and platelet counts [Table 2].

There was no statistically significant difference in bilirubin, serum glutamic-oxaloacetic transaminase, serum glutamic-pyruvic transaminase, serum albumin, ALP, urea, and creatinine between the two groups [Table 2].

The patients who died had significantly higher baseline levels of ferritin, D-dimer, and fibrinogen. However, no significant difference was found with regard to CRP [Table 2].

**DISCUSSION**

In this large observational study, we found that significant differences in several clinical, hematological, and inflammatory parameters between survivors and nonsurvivors of COVID-19. Nonsurvivors were more likely to be initially symptomatic, have comorbidities, and have a longer hospital stay than the survivors. They also have a more severe inflammatory response in the form of higher total leukocyte count, neutrophil percent, NLR, ferritin, D-dimer, and fibrinogen compared to survivors.

Several previous studies have identified clinical predictors of poor outcome in COVID-19,\textsuperscript{[7-9]} although the prognostic contribution of laboratory parameters has been less reported. A few recent studies have shown that NLR is a useful parameter to distinguish severe from nonsevere cases and also to predict mortality, and an NLR value of more than 3.1 in patients aged more than 50 years predicted a higher chance of developing critical illness.\textsuperscript{[10,11]} In our study, the mean NLR among survivors and nonsurvivors was 2.13 and 3.51 and 2.13, respectively. There is also some evidence to suggest that serial measurement of NLR
A meta-analysis has found that elevated levels of D-dimer and fibrinogen among our patients, the mean albumin was significantly higher in the nonsurvivor group. Possibly, these findings were replicated in our cohort as well. The mean D-dimer and fibrinogen levels on admission were significantly higher in the nonsurvivor group. Possibly, such patients with elevated D-dimer could have had a higher incidence of pulmonary thromboembolism leading to higher mortality, although this was not specifically the focus of this study.

We also did not find any significant difference in the liver and renal functions or other biochemical parameters between the two groups. A few studies have reported that the serum albumin level is lower in severe and critically ill patients and may be an independent factor associated with mortality. Among our patients, the mean albumin in the non-survivor group was lower than that of the other, although not statistically. A possible explanation for this fact might be the missing data. A possible explanation for this fact might be that we did not have data for 15 patients in the non-survivor group.

D-dimer is an indicator of activation of the coagulation cascade and the fibrinolytic system. This activation of coagulation cascade is postulated to be due to the viremia, accentuated cytokine levels, infection, and organ dysfunction. Elevated levels of D-dimer and fibrinogen have been associated with severity of COVID-19, higher need for critical care as well as mortality. An elevated D-dimer level above 1 μg/mL on admission was shown to have increased mortality with an odds ratio of 18.42. This can also possibly explain the higher incidence of venous thromboembolism seen in COVID-19 patients. These findings were replicated in our cohort as well. The mean D-dimer and fibrinogen levels on admission were significantly higher in the non-survivor group. Possibly, such patients with elevated D-dimer could have had a higher incidence of pulmonary thromboembolism leading to higher mortality, although this was not specifically the focus of this study.

This study has some limitations; first, it was retrospective in nature, and laboratory data were not available for many patients. Second, we collected and analyzed only a single time point laboratory data and thereby were unable to

**Table 1: Baseline characteristics and comparison between the two groups (n=5574)**

| Parameters                        | Discharged, n (%) | Dead, n (%) | P   |
|-----------------------------------|-------------------|-------------|-----|
| Number of patients                | 5432 (97.5)       | 142 (2.5)   | -   |
| Gender                            |                   |             |     |
| Male                              | 4196 (77.2)       | 111 (21.2)  | 0.09|
| Female                            | 1236 (22.8)       | 31 (27.9)   |     |
| Age, mean (SD)                    | 38.9 (10.71)      | 39.6 (48.8) | 0.63|
| Number of days of hospital stay, mean (SD) | 10.9 (1.2) | 12.2 (5.6) | 0.03*|
| Patients with comorbidities       | 476/5432 (8.8)    | 11/147 (9.4)| 0.03*|
| Asymptomatic at presentation      | 2593/5432 (47.7)  | 38/142 (26.8)| 0.02*|

*P<0.05; all values expressed as n (%) or mean (SD). SD: Standard deviation

**Table 2: Laboratory parameters among COVID survivors and nonsurvivors**

| Biomarkers                        | Survivors, mean (SD) | Nonsurvivors, mean (SD) | P   |
|-----------------------------------|----------------------|-------------------------|-----|
| Hematological markers             |                      |                         |     |
| Hemoglobin (grams per deciliter)  | 13.29 (3.18)         | 13.36 (1.69)            | 0.47|
| Platelet count (platelets per microliter) | 218514 (113177)     | 228115 (31820)          | 0.06|
| Total leukocyte count (WBCs per microliter) | 6252 (5315)         | 6625 (3758)             | 0.04*|
| Relative neutrophil percent       | 55.6 (1.8)           | 58.8 (11.9)             | 0.04*|
| Relative lymphocyte percent       | 30.9 (7.4)           | 28.0 (9.5)              | 0.04*|
| Neutrophil–lymphocyte ratio       | 2.13 (0.26)          | 3.51 (6.60)             | 0.03*|
| Biochemical markers               |                      |                         |     |
| Bilirubin (mg/dL)                 | 1.1 (0.06)           | 0.71 (0.08)             | 0.70|
| SGOT (IU/L)                       | 45.2 (12.7)          | 45.8 (10.6)             | 0.47|
| SGPT (IU/L)                       | 49.8 (17.8)          | 47.3 (19.8)             | 0.75|
| Serum albumin (grams per deciliter) | 4.7 (0.6)             | 4.3 (0.07)             | 0.37|
| Alkaline phosphatase (IU/L)       | 96.7 (20.1)          | 96.2 (24.7)             | 0.11|
| Urea (mg/dL)                      | 23.1 (9.9)           | 24.6 (7.6)              | 0.26|
| Creatinine (mg/dL)                | 0.81 (0.58)          | 0.83 (0.36)             | 0.07|
| Inflammatory markers              |                      |                         |     |
| Ferritin (micrograms per liter)   | 198.9 (205.1)        | 329.1 (381.2)           | 0.01*|
| D-dimer (ng/mL)                   | 165.4 (196.6)        | 333.3 (523.5)           | 0.005*|
| C-reactive protein (milligram per liter) | 1.99 (1.16)       | 2.72 (0.63)             | 0.10|
| Fibrinogen (mg/dL)                | 334.3 (96.2)         | 371.2 (92.6)            | 0.001*|

*P<0.05; all values expressed as mean (SD). SD: Standard deviation, SGOT: Serum glutamic-oxaloacetic transaminase, SGPT: Serum glutamic-pyruvic transaminase

could be more useful and may show a good correlation with other inflammatory markers. Similarly, lymphopenia and neutrophilia have also been correlated with adverse outcomes in COVID-19, including death and development of acute respiratory distress syndrome. Although the effects of SARS-CoV on hematopoiesis are still being explored, it has been proposed that the virus-mediated infection leads to consumption of T-lymphocyte cells, particularly the CD4 and CD8 T-cells, thereby leading to lymphopenia. A meta-analysis has found that thrombocytopenia is significantly associated with disease severity and mortality in COVID-19. The possible reason may be that virus-mediated endothelial damage leads to platelet activation and microthrombus formation in the pulmonary vasculature thereby causing increased platelet consumption. However, we found no significant difference in the platelet count between the survivors and nonsurvivors.
provide information on particular trends of any parameter. Third, due to the existing hospital policy of admitting all COVID patients, the numbers in the survivor and nonsurvivor groups were vastly different, which could have been a source of bias. On the other hand, this study had a large patient number base and collected information on a comprehensive panel of hematological, biochemical, and inflammatory parameters at baseline. As a result, these findings could be potentially useful in a resource-limited setting in enabling triage of patients at baseline and thereby identify the at-risk group.

CONCLUSIONS

Various biochemical parameters measured at baseline can provide useful prognostic information among COVID-19-affected patients. It can also help in early identification of patients who merit aggressive institutional care, thereby potentially mitigating mortality.

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Conflicts of interest

There are no conflicts of interest.

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