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Original Research Article

Association of Haematological and Biochemical Parameters with Severity of COVID-19 Patients: A Retrospective Study

Vikash Bombeshwar[1], Riti Sharma[2], Ruchi Varma[3], Arvind Neral[4], Ramesh Kumar Sahu[5]

[1]Assistant Professor, Department of Pathology, Pt. J. N. M. Medical College & Dr. B. R. A. M. Hospital, Raipur, Chhattisgarh, India.

[2]Assistant Professor, Department of Pathology, Pt. J. N. M. Medical College & Dr. B. R. A. M. Hospital, Raipur, Chhattisgarh, India.

[3]Assistant Professor, Department of Pathology, Pt. J. N. M. Medical College & Dr. B. R. A. M. Hospital, Raipur, Chhattisgarh, India.

[4] Professor & Hod, Department of Pathology, Pt. J. N. M. Medical College & Dr. B. R. A. M. Hospital, Raipur, Chhattisgarh, India.

[5]Third Year Postgraduate Resident, Department of Pathology, Pt. J. N. M. Medical College & Dr. B. R. A. M. Hospital, Raipur, Chhattisgarh, India.

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Corresponding Author: Dr. Vikash Bombeshwar

Conflict of interest: Nil

Abstract:

Background: By affecting 206 countries, the unprecedented health disaster COVID-19 brought about a global emergency. Since SARS-CoV2 is a RNA virus and has a higher mutation rate than DNA viruses, treatment would be challenging. The issue is especially deleterious in India because of the country's large population. The haematological and immunological system are severely affected by the systemic viral infection of COVID-19. It would be crucial to investigate whether the most frequently performed tests could be utilised to help determine a patient's clinical status or anticipate the degree of severity of the disease.

Methods: A cohort of 420 patients of all ages and both sexes having positive COVID-19 RT-PCR test and were admitted to BRAM Hospital Raipur between March 2021 and March 2022 participated in the cross-sectional study. Different hematological and biochemical tests were performed in all cases. Hematological parameters include ALC, TLC, Neutrophil /Lymphocyte ratio, Platelet count and biochemical parameters include Alanine aminotransferase, Aspartate aminotransferase, Lactate dehydrogenase, Serum ferritin and CRP.

Results: Out of 420 cases, 210 were categorised under severe cases and rest 210 were non-severe cases. It is also found that, in severe cases the male patients were more than female patients. The mortality was associated with increased CRP, Neutrophil count, WBC count, AST, ALT and increased LDH.

Conclusion: In conclusion, several laboratory parameters could be associated with the severity and mortality of COVID-19 pandemic. This comparative investigation can help reinforce clinical judgements in the clinical context and increase the survival rate of critically sick patients.

Keywords: COVID-19, Haematological Parameter, Biochemical Parameter, Disease Severity.

Introduction

Due to a novel virus called COVID-19, which destroyed the world's usual way of life and state of health, the beginning of 2020 has been transformed into a terrifying and unforgettable memory [1]. The COVID-19 disease initially emerged in December 2019 in Wuhan, Hubei, China, and it has quickly transformed from an epidemic outbreak into a global pandemic [2]. The World Health Organisation labelled COVID-19 a pandemic on March 11, 2020, and it is an alarming worldwide health problem [3]. By touching 206 nations, the emergence of this novel health disaster plunged the whole world into a state of emergency.

The first SARS-CoV-2 positive case in India was on January 30th, 2020. Subsequently, the number of cases drastically rose. The huge population is India's largest obstacle in the fight against COVID-19. In urban slums where population density may surpass 250000/km2, social isolation may be difficult, the situation may be worse. 10,375,478 cases have been recorded in India overall, of which 9,997,272 have been recovered, and 150,151 have died as of January 6, 2021. As per reports in India, almost all the states are at the risk of COVID-19 infection. The most number of COVID-19 effected cases are recorded in Maharashtra followed by

Tamil Nadu, Delhi, Kerela and Telangana. On the other hand, the maximum number of deaths recorded were from Maharashtra followed by Kerela, Haryana and Uttar Pradesh. [4]

Given that SARS-CoV2 is a RNA virus with a higher mutation rate than DNA viruses, treatment would be challenging [4]. In severe cases, they have manifested with acute respiratory distress syndrome (ARDS), sepsis, acute cardiac dysfunction, acute renal dysfunction, and multiorgan failure followed by death. Early diagnosis and timely management of these patients therefore can considerably reduce morbidity & mortality [5].

Several biomarkers have been linked to the severity of the disease & have been identified to play an important role in the management of COVID-19 patients. Studies have shown that there is a greater increase in inflammatory markers like C-reactive protein (CRP), ferritin, procalcitonin in critically ill patients with COVID-19. Other predictive markers associated with increased mortality were elevated lactate dehydrogenase (LDH) and D-dimer. Similar to individuals with severe illness, those with mild COVID infection showed signs of liver impairment, including elevated levels of the enzymes alanine aminotransferase (ALT), aspartate aminotransferase (AST), and serum bilirubin. [5]

However, there is a dearth of knowledge related to the availability of specific markers that can be used to detect the occurrence of complications in the early stages of the disease. Hence, in this study, we planned to evaluate the clinical utility and the association between the biochemical and hematological parameters as predictors of severity in COVID-19 patients in the Indian population.

Materials and Methods

This study is a cross sectional observational study in a cohort of 420 patients of all age group of both sexes with positive COVID-19 RT-PCR test results who were admitted in BRAM Hospital Raipur from March 2021 to March 2022. For each case, age, sex, past medical history, clinical signs, and immunisations were all gathered. At the time of admission, each patient had a thorough clinical examination as well as regular haematological and biochemical tests, an electrocardiogram (ECG), and a chest x-ray.

The hematological parameters includes Absolute Lymphocyte count (ALC), Total leukocytes count (TLC), Neutrophil /Lymphocyte ratio, Platelet count. A complete blood count (CBC) was performed using the Automatic Hematology Analyzer Beckman Coulter DxH 500. NLR, PLR, MLR were calculated from hematological parameters. The haematological parameters of both positive and negative individuals were compared, including WBCs, lymphocyte count and percentage, monocyte count and percentage, neutrophil count and percentage, haemoglobin, RBCs, and platelet count. Biochemical parameters include Alanine aminotransferase, Aspartate aminotransferase, C reactive protein, Lactate dehydrogenase, Serum ferritin. According to the kit insert, serum biochemistry parameters were determined using samples obtained in a simple vial and a biochemistry auto analyzer.

Statistical Analysis

The data was systematically gathered, compiled and entered in MS Excel version 2016. Statistical Package for Social Sciences IBM SPSS® 24.0 software was used to analyse the data in order to create cross-tabs and reach pertinent findings. Mean and standard deviations were used to compare continuous data to ensure normal distribution using descriptive statistics. To present the results, the median and interquartile range (IQR) were employed. Continuous variable results were presented as mean standard deviation. The frequency and percentage of deviation are provided. Descriptive statistics were made by representing demographic characteristics as frequency and percentage values. Appropriate statistics will be used and $P < 0.05$ will be consider statistically significant.

Analysis of Qualitative Data by Chi-square Test

Qualitative data were analysed in frequency or percentage. The Pearson's χ^2 or Fisher's exact chi-square test was used in the analysis of categorical data.

Ethical Clearance

The Institutional Ethics committee of Pt. J.N.M. Medical College Raipur, Chhattisgarh, India has approved the research work purposed to be carried out at Pt. J.N.M. Medical College Raipur, Chhattisgarh, India Date: 14/03/2022 with reference number MC/Ethics/2022/82.

Observation and Result

420 COVID-19 patients admitted in BRAM Hospital Raipur from March 2021 to March 2022 were divided into two groups according to severity of the patients as severe (n=210) and non-severe (n=210). We compiled a comparison of the 420 patients' haematological and biochemical traits and examined the distinction between severe and non-severe cases.

Distribution of Age among Covid-19 Patients

A total of 420 RT-PCR positive COVID-19 patients were included in the study. In the present study, it is observed that, 11% had belonged to 0-20 age group, 45.7% were belongs 21-40 age group, 31% were belong to 41-60 age group and 12.4% were belongs to > 60 age group among non severe patients. The mean age in non severe pa-

tients was 39.76 ±16.52. In severe patients, 3.3% had belonged to 0-20 age group, 35.7% were belongs 21-40 age group, 42.4% were belong to 41-60 age group and 18.6% were belongs to > 60 age group. The mean age in severe patients was 46.74 ±16.10. Also, it was shown that the association of covid-19 patients among severe and non severe is found to be (p-value=0.001) statistically significant with age, p-value <0.05.

Table 1: Result of Statistical analysis of different hematological and biochemical biomarkers

Parameter		Non-Severe (Mean±SD)	Severe (Mean±SD)	Chi-square	P-value	t-Test
Age		39.76 ±16.52	46.74 ±16.10	17.453	0.001 (significant)	-4.384 (p value 0.000)
Gender	**Female**	45.7%	39.5%	1.645	0.200 (Not-Significant)	-
	Male	54.3%	60.5%			
TLC		11.97±9.75	18.01±9.23	31.027	0.000 (Significant)	-6.519 (P value 0.000)
ALC		20.19±9.67	19.19±11.73	3.365	0.195 (Not-Significant)	0.957 (P value 0.339)
N/L		2.56±0.74	2.78±2.22	11.749	0.003 (Significant)	-1.373 (P value 0.171)
Platelet		205.50±97.17	207.30±119.18	7.238	0.027 (Significant)	-0.170 (P value 0.865)
AST		37.90±36.85	54.47±36.53	27.300	0.000 (Significant)	-4.627 (P value 0.000)
ALT		69.30±103.90	106.80±561.42	5.992	0.014 (Significant)	-0.952 (P value 0.342)
LDH		514.42±439.30	954.42±836.52	40.093	0.000 (significant)	-6.748 (P value 0.000)
Serum Ferritin		253.47±419.35	448.89±424.42	73.512	0.000 (significant)	-4.746 (P value 0.000)
CRP	**< 6**	76.2%	42.4%	49.725	0.000 (Significant)	-
	> 6	23.8%	57.6%			

Distribution of Gender among Covid-19 patients

In the present study, it is observed that, 96 (45.7%) were female and 114 (54.3%) were male among non severe covid-19 patients. Whereas, 83 (39.5%) were female and 127 (60.5%) were male among severe covid-19 patients. Here, the association of covid-19 patients among severe and non severe found to be (p-value=0.200) statistically not significant with gender, p-value <0.05.

Distribution of TLC among Covid-19 patients

In the present study, it is observed that, the maximum non-severe cases i.e. 89 cases (42.4%) showing TLC value ranging between $4x10^3$ - $11x10^3$ cells/mm^3 followed by 102 (48.6%) cases having TLC value greater than $11x10^3$ cells/mm^3 and only 19 (9%) non severe cases were showing less than $4x10^3$ of TLC value. However, the maximum severe cases i.e. 155 (73.8%) were showing greater than $11x10^3$ cells/mm^3 followed by 51 (24.3%) showing normal range i.e. 4-$11x10^3$ cells/mm^3 and only 4 (1.9%) were showing less than $4x10^3$ of TLC value. The mean TLC in non-severe patients was 11.97 ±9.75 and in severe patients was 18.01 ±9.23. Here, the association of covid-19 patients among severe and non-severe is found to be (p-value=0.000) statistically significant with TLC, p-value <0.05.

Distribution of ALC among covid-19 patients

In the present study, it was observed that, the maximum non-severe cases 106 (50.5%) cases were belongs to less than 20% followed by 100 (47.6%) were belongs to normal range i.e. 20-40% and only 4 (1.9%) were belongs to greater than 40% of ALC values. However, maximum severe cases 120 (57.1%) were belongs to less than 20% followed by 83 (39.5%) were belongs to 20-40% and only 7 (3.3%) cases were belongs to greater than 40% of ALC values. The mean ± SD of ALC value for non-severe cases was 20.19 ±9.67, and for severe cases was 19.19 ±11.73. Also, the above table shows that the association of covid-19 patients among severe and non-severe is found to be (p-value=0.195) statistically not significant with ALC, p-value <0.05.

Distribution of N/L among covid-19 patients

In the present study, It is observed that, the maximum 195 (92.9%) non severe cases were belongs to 0.78-3.50 of N/L ratio followed by 15 (7.1%) cases were belongs to greater than 3.50 of N/L ratio. While, the maximum 172 (81.9%) severe

cases were belong to normal range of N/L i.e. 0.78-3.50 followed by 37 (17.7%) belongs to greater than 3.50 of N/L ratio and only 1 (0.5%) cases were belongs to patients less than 0.78 of N/L ratio. The mean ± SD of N/L value for non-severe cases was 2.56 ±0.74, and for severe cases was 2.78 ±2.22. The association of COVID-19 patients among the severe and non-severe is found to be statistically significant with N/L (p=0.003).

Distribution of platelet among Covid-19 patients

In the present study, it is observed that, 61(29.0%) were belongs to < 150 platelet group, 148 (70.5%) were belongs 150 – 450 platelet group and 1 (0.5%) were belong to > 450 platelet group among non-severe patients. The mean platelet in non-severe patients was 205.50 ±97.17. In severe patients, 71 (33.8%) were belongs to < 150 platelet group, 131 (62.4%) were belongs 150 – 450 platelet group and 8 (3.8%) were belong to > 450 platelet group among severe patients. The mean platelet in severe patients was 207.30 ±119. Also, the above table shows that the association of covid-19 patients among severe and non-severe is found to be (p-value=0.027) statistically significant with platelet, p-value <0.05.

Distribution of AST among Covid-19 patients

In the present study, it is observed that, 0 (0.0%) were belongs to < 0 AST group, 156 (74.3%) were belongs 0 – 40 AST group and 54 (25.7%) were belong to > 40 AST group among non-severe patients. The mean AST in non-severe patients was 37.90 ±36.85. In severe patients, 0 (0.0%) were belongs to < 0 AST group, 104 (49.5%) were belongs 0 – 40 AST group and 106 (50.5%) were belong to > 40 AST group among severe patients. The mean AST in severe patients was 54.47 ±36.53. Also, the above table shows that the association of covid-19 patients among severe and non-severe is found to be (p-value=0.000) statistically significant with AST, p-value <0.05.

Distribution of ALT among Covid-19 patients

In the present study, it is observed that, 0 (0.0%) were belongs to < 0 ALT group, 109 (51.9%) were belongs 0 – 40 ALT group and 101 (48.1%) were belong to > 40 ALT group among non-severe patients. The mean ALT in non-severe patients was 69.30 ±103.90. In severe patients, 0 (0.0%) were belongs to < 0 ALT group, 84 (40.0%) were belongs 0 – 40 ALT group and 126 (60.0%) were belong to > 40 ALT group among severe patients. The mean ALT in severe patients was 106.80 ±561.42. Also, the above table shows that the association of covid-19 patients among severe and non-severe is found to be (p-value=0.014) statistically significant with ALT, p-value <0.05.

Distribution of LDH among Covid-19 patients

In the present study, it is observed that, the maximum non-severe cases 88 (41.9%) had 240-480 IU/L LDH values followed by 63 (30%) had <240 IU/L LDH value and 59 (28.1%) had >480 IU/L LDH value. However, the maximum severe cases 123 (58.6%) had >480 LDH value followed by 47 (22.4%) had 240-480 LDH value and 40 (19%) had <240 LDH value. The mean ± SD of LDH value for non-severe cases was 514.42 ±439.30, and for severe cases was 954.42 ±836.52. The association of COVID-19 patients among the severe and non-severe is found to be statistically significant with LDH (p=0.000).

Distribution of Serum ferritin among Covid-19 patients

In the present study, it is observed that, 21 (10.0%) were belongs to < 30 serum ferritin (S-ferritin) group, 143 (68.1%) were belongs 30 – 220 S-ferritin group and 46 (21.9%) were belong to > 220 S-ferritin group among non-severe patients. The mean S-ferritin in non-severe patients was 253.47 ±419.35. In severe patients, 2 (1.0%) were belongs to < 30 S-ferritin group, 79 (37.6%) were belongs 30 – 220 S-ferritin group and 129 (61.4%) were belong to > 220 S-ferritin group among severe patients. The mean S-ferritin in severe patients was 448.89 ±424.42. Also, the above table shows that the association of covid-19 patients among severe and non severe is found to be (p-value=0.000) statistically significant with S-ferritin, p-value <0.05.

Distribution of CRP among Covid-19 patients

In the present study, it is observed that, 160 (76.2%) were belongs to < 6 CRP group and 50 (23.8%) were belong to > 6 CRP group among non severe patients. In severe patients, 89 (42.4%) were belongs to < 6 CRP group and 121 (57.6%) were belong to > 6 CRP group among severe patients. Also, the above table shows that the association of covid-19 patients among severe and non severe is found to be (p-value=0.000) statistically significant with CRP, p-value <0.05.

Discussion

It has been demonstrated in various studies that several biochemical and haematological factors can predict COVID-19 related severity of symptoms and associated mortality. The present study was aimed to assess the association between the haematological and biochemical parameters with severity of covid-19 patients. This comparison can help reinforce clinical judgements in the clinical situation and increase the survival rate of critically sick patients.

From this result, we discovered here that the median age of the COVID-19-dead patients was greater than that of the cohort that survived. These

results are consistent with past studies on COVID-19 patients [6,7]. The frequent reasons cited in prior studies on aged with COVID-19 were that the older population has more comorbidities, restricted organ function, lower lung capacity, compromised immune system, biological ageing, and more severe consequences [8]. In the present study we also found that, males were more effected as compared to females in both non severe and severe cases. The results are comparable with observations made by Khalid et al., 2021; Dubey et al., 2021; Toori et al., 2021; and Patel et al., 2021 [1,9,10,11].

The TLC was significantly different and higher in severely ill patients compared to the cases presented with mild and moderated symptoms[12]. Our result is in accordance with the results reported by Agrawal et al., (2021) and Dubey et al., (2021)[9,13]. The severity of the condition was discovered to be significantly influenced by the T-lymphocyte count, i.e., the lower the lymphocyte count, the more serious the sickness[14]. As per our result, the association of COVID-19 patients among the severe and non-severe patients is found to be statistically not significant with ALC. While some other researchers had reported about the significant difference in the Absolute Lymphocyte Count (ALC) of severe cases as compared to non-severe cases (p value <0.001) [12].

It has been reported that the neutrophil/lymphocyte ratio (NLR) is a reliable indicator of the severity of the illness and mortality in hospitalised patients [15]. In the present study, the association of COVID-19 patients among the severe and non-severe is found to be statistically significant with N/L (p=0.003). Study conducted by Kesari et al. (2021) also shows similar results[12]. The neutrophil (N%) and lymphocyte (L%) counts were also substantially different across groups, according to Dubey et al.'s study from 2021 (p=0.001) [9]. When compared to cases with mild symptoms, the neutrophils lymphocyte ratio (N/L) was higher in cases with moderate symptoms. Higher neutrophils-to-lymphocyte ratio (NLR; p=0.01) were associated with death[14]. According to Agrawal et al. (2021), individuals with severe illnesses had considerably greater platelet to lymphocyte ratios (PLR) and neutrophil to lymphocyte ratios (NLR) than patients with less severe illnesses [13].

One of the most significant variables in SARS-CoV-2 study has been platelets. In this present study, the mean ± SD of platelet count for non-severe cases was 69.30 ±103.90, and for severe cases was 106.80 ±561.42. The association of COVID-19 patients among the severe and non-severe is found to be statistically significant with platelet count (p=0.027). However, as per the reports of Bairwa et al., (2021) and Dubey et al., (2021), the platelet count did not significantly differ amongst individuals who were mildly, moderately, or seriously ill [8,9].

Aspartate aminotransferase (AST) is frequently elevated in COVID-19, and high AST levels have been linked to an increased risk of death in several studies[16]. It was found in the present study that, the mean ± SD of AST and ALT value for non-severe cases was 37.90 ±36.85 and 69.30 ±36.85, and for severe cases was 54.47 ±36.53 and 106.80 ±561.42 respectively. The biochemical parameters of patients, including AST, indicated a statistically significant difference when compared with standard values, according to Khalid et al. (2021) (p-0.001 for all) [1]. However, according to Bairwa et al. (2021), patients who reported abnormal x-ray findings had significantly higher levels of AST (all p 0.05) [8]. Healthcare professionals frequently employ an ALT blood test to assist determine the liver's health since elevated ALT levels in the blood can indicate liver disease. According to Khalid et al.'s study from 2021, ALT displayed a statistically significant variation from standard values [1]. However, according to Kesari et al. (2021), there was no statistically significant difference between severe and non-severe cases for ALT [12].

In the current investigation, it was shown that roughly 40% of patients had elevated LDH levels. Elevated LDH has been linked to an increased risk of death, requirement for intensive care, and ARDS [17]. The biochemical parameters of cases including LDH showed a statistically significant difference compared with standard values[1]. Patients with severe illnesses have considerably greater lactate dehydrogenase (LDH) levels than those with less serious illnesses [13]. Lactic acidosis, which is more prevalent in cancer patients and people with comorbid conditions like heart disease, can be the cause of patients' elevated LDH levels and the subsequent rise in related problems[1].

It is widely known that serum ferritin is an acute phase reactant and a sign of both acute and chronic inflammation. Here, the mean ± SD of serum ferritin value for non-severe cases was 253 ±419.35, and for severe cases was 448.89 ±424.42. The association of COVID-19 patients among the severe and non-severe is found to be statistically significant with serum ferritin (p=0.000). Our results obtained here is similar as reported by Kesari et al. (2021), Khalid et al. (2021) [1,12]. Also Sharma et al. (2021) had observed a higher serum ferritin level in non survivors (NS) as compared to survivors [18].

The liver appears to produce CRP as a nonspecific acute-phase reactant in response to IL-6. Increased serum CRP levels are associated with illness severity and inflammation levels (S. et al., 2022;

Chalmers et al., 2019) [19,20]. Based on the current study, CRP (mg/dL) levels rose as illness severity increased, and COVID-19 individuals with severe and non-severe disease were statistically significantly correlated with CRP levels. Bairwa et al., (2021) in their study had reported that, the mortality was associated with increased CRP [8].

Conclusion

The progression, severity and mortality of COVID-19 infection is influenced by a number of haematological, biochemical and immunological factors . Therefore, for establishment of an early clinical diagnosis of SARS-CoV-2 disease , prompt treatment and monitoring of the severity of the disease , search for haematological, biochemical, or other suggestive laboratory parameters is crucial .These parameters include TLC, ALC, N/L ratio, platelet count, AST, ALT, LDH, CRP and S-ferritin .

In our study , we found some useful parameters like CRP, Neutrophil count, WBC count, AST, ALT and LDH , increased value of which were associated with high mortality. Early Investigations including measurement of these parameter will help in better patient management and increase survival rate .

However further continuing research and studies are required to found more useful parameters to decrease the burden of the disease .

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