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CLINICOPATHOLOGICAL STUDY OF LABORATORY PARAMETERS ASSOCIATED WITH MORTALITY IN COVID 19 PATIENTS: A RETROSPECTIVE STUDY OF 100 DEATHS

Dr. Vipul Jain — Assistant Professor, Department of Pathology, TNMC & BYL Charitable Hospital, Mumbai.

Dr. Arsala Mulla — Junior Consultant, Bharatratna Dr Babasaheb Ambedkar Municipal General Hospital, Mumbai.

Dr. Manish Patil* — Assistant Medical Officer, Department of Pathology, HBT Trauma Care Municipal Hospital, Mumbai. *Corresponding Author

ABSTRACT This study aims to identify critical laboratory parameters and compare the same of 100 covid-19 death cases with the same values at time of admission to prevent mortality through early aggressive clinical intervention.

The clinical records, laboratory findings were collected from medical case records of 100 covid-19 mortalities in Covid ICU from a dedicated public sector covid hospital of Western suburbs in Mumbai, Maharashtra from January 2021 to December 2021. Laboratory Parameters at the time of admission were compared using appropriate statistics with the same on before death.

The age (>60yrs), Gender (Male>Female) and underlying diseases (hypertension, diabetes, asthma, chronic kidney disease etc.) were the most important risk factors for mortality. There was statistically significant increase in WBC count, D-dimer, Ferritin and LDH values and can be used as indicators of fatal disease progression.

KEYWORDS : COVID 19, CRP, D-dimer, Ferritin , LDH

INTRODUCTION:

In December 2019, a cluster of atypical severe pneumonia was described in Wuhan, China [1]. The World Health Organization (WHO) named the novel virus associated with acute respiratory distress syndrome (ARDS) as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), with the associated disease coronavirus disease 2019 (COVID-19) [2]. India has the largest number of confirmed cases in Asia; total officially reported covid 19 cases in Mumbai were 7, 85,110 and 16,376 deaths till December 2021.

COVID-19 is a symptomatically and asymptomatically transmissible disease, with a presumed incubation period of up to 14 days. Since the emergence of SARS-CoV-2 in late 2019 several new variants of concern (VOC) have emerged and been associated with waves of infection across the globe. B.1.1.529 Omicron variant of SARS-CoV-2 that emerged recently in South Africa appears to be highly transmissible and has many substitutions in the spike glycoprotein as well as elsewhere in the genome raising fears that the virus may escape from pre-existing immunity, whether acquired by vaccination or by prior infection [3]. SARS-CoV-2 Omicron has given rise to the fourth wave of the COVID-19 epidemic spreading around the world, following the D614G, Beta/Gamma, and Delta variant of concern.

While originally believed to be a primary lower respiratory infection, as more cases were identified, treated, and examined, hematologic complications were being identified as a significant driver of morbidity and mortality associated with the disease. Approximately 10% of confirmed cases progressed to critical illness [4,5] with acute lung failure and, in some cases, multi-organ failure involving the heart, kidney, and gastrointestinal tract, with a high mortality rate [6]. Reported predisposing factors for severe disease included older age, chronic arterial hypertension, and established cardiovascular disease. Nevertheless, whilst epidemiological data on critically ill patients have been well described, the understanding of disease progression and indicators for mortality in critical ill patients remains scarce. The challenge was to find effective predictors of COVID-19 critical disease and death in order to identify critical patients early. Understanding patient characteristics associated with severe forms of COVID-19 is crucial not only for triage and therapeutic selection in these critically ill patients, but also to generate hypotheses based on the pathophysiology of the disease and to support the design of further trials.

MATERIALS AND METHODS:

This retrospective study was performed by 3 pathologists in a Dedicated Public Sector Covid hospital located in western suburbs of Mumbai. Clinical and laboratory data regarding 100 RT-PCR confirmed Covid-19 cases those who were hospitalised and succumbed between January 2021- December 2021 were included in our study. This study aims to compare critical laboratory parameters of Covid-19 mortality on admission versus death day. We excluded those mortalities in which laboratory records were not available, deaths in which Covid RT-PCR report was negative or inconclusive and, in those cases, where hospital stay was less than 48 hours.

Data comprising white blood cell count (WBC), C-reactive protein (CRP), lactate dehydrogenase (LDH), D-Dimer and Ferritin values was obtained from patients records and analysed using SPSS, version 20.0 software. Appropriate statistical tools were used and P value less than 0.05 was indicated as statistically significant.

RESULTS:

From January 2021 – December 2021, total of 100 covid mortalities were included in our study. In our study we had 71 male subjects and 29 were female. The mean age of our study population was 64years, ranging from 21 years to 85 years, out of which 68% were those with age more than 60 years. The mean duration of hospital stay in our study was 12 days, ranging from 4 days to 41 days, where 68% deaths had hospital stay of more than 7 days. 35 of the 100 deaths were patients without any co-morbidities while rest of them had following underlying diseases, the most common of which was hypertension (47%), followed by diabetes (37%), bronchial asthma (8%), kidney diseases (7%), hypothyroidism (4%). The most common symptoms in our study group were fever, cough followed by breathlessness, weakness and sore throat.

Table no 1: Demonstrating laboratory parameters (CRP, D dimer, ferritin, LDH& WBC count) at the time of admission and at the time of death

Parameter	Mean value at	Mean value at	P value
CRP (mg/L)	74.56	62.28	0.219
D-Dimer (ug/ml)	5.21	11.09	0.001
Ferritin (ng/ml)	1231.34	1993.47	0.001
LDH (U/L)	728.09	1010.09	0.001
WBC Count (per mm^3)	9484	18875	0.001

Statistical significance was found in the values of D Dimer, Ferritin, LDH and WBC count at the time of admission as compared to the values at the time of death. We observed in our study that mean values of D-dimer, Ferritin, LDH and WBC was significantly higher at the time of death as compared to their values at the time of admission. Contrastingly, CRP values were lower at the time of death as compared with the time of admission.

Table no 2: Demonstrating difference between laboratory parameters between male and female at the time of admission and at the time of death.

Parameter	Mean value (at Admission) n=100	Mean value (at Death) n=100

	MALE (n=71)	FEMALE (n=29)	MALE (n=71)	FEMALE (n=29)
CRP (0-5 mg/L)	75.14	73.14	60.00	67.86
D-Dimer (< 1.0 ug/ml)	5.66	4.11	11.43	10.26
Ferritin (ng/ml) Male=22-322 Female=10-291	1455.59	682.31	1983.8	2017.14
LDH (120-246 U/L)	743.48	690.41	1010.8	1011.1
WBC (4000-10000 per mm^3)	9009	10645	18781	19104

There was no statistically significant difference between means of laboratory parameters for males & females except for ferritin levels at admission (P= 0.026). Ferritin levels in men were higher at the time of admission as compared to females.

Table no 3: Demonstrating difference in laboratory parameters in 2 different age groups- above and below 60 years of age, both at the time of admission and at the time of death.

Parameter	Mean value (at Admission) n=100		Mean value (at Death) n=100	
	Age < 60 years(n=32)	Age >60 years (n=68)	Age < 60 years (n=32)	Age >60 years (n=68)
CRP (0-5 mg/L)	80.78	71.63	62.13	62.35
D-Dimer (< 1.0 ug/ml)	4.86	5.38	12.40	10.47
Ferritin (ng/ml) Male=22-322 Female=10-291	1417.81	1143.59	2964.66	1536.44
LDH (120-246 U/L)	731.63	726.43	1124.03	957.68
WBC (4000 - 10000/mm^3)	8852	9781	17794	19383

There was no statistically significant difference between means of laboratory parameters for patients less than 60 years of age and more than 60 years of age except for ferritin levels at death (P= 0.001), CRP at admission (P =0.039) and D-dimer at death (P =0.05). We found that ferritin and d-dimer values at the time of death were higher in patients less than 60 years of age undergoing mortality as compared to those above 60 years of age.

DISCUSSION:

This retrospective study tried to compare the various laboratory parameters which are an important predictor for early intervention in covid-19 patient management to prevent mortality. We found that out of 100 deaths, 71% were males which was a significant proportion of mortality in males as compared to females. Nguyen et al. found that as compared to females, males with COVID-19 had a higher rate of in-hospital mortality[7].

In our study among the coagulation parameter i.e., D-dimer had mean value of 5.21 µg/mL at the time of admission and 11.09 µg/mL at the time of death. Zhang et al. found that patients with D-dimer levels ≥2.0 µg/mL had higher incidence of mortality compared to those with D-dimer values less than <2.0 µg/mL [8]. Zhou et al. found that D-dimer elevation > 1 ug/L was the strongest independent predictor of mortality along with older age [4]. Soni et al. found that median D-dimer value among non-survivors was 6.34 µg/mL and D-dimer level ≥ 2.01 µg /mL was a significant predictor of subsequent deaths [9]. In one of the study D-dimer levels a few days after admission had a stronger correlation with mortality than those at the admission[10].

Serum ferritin is an iron storage protein, but it is also a well-known inflammatory marker [11] and it can be increased significantly in response to inflammation and a variety of diseases. Serum ferritin was another laboratory parameter related to poor prognosis whose mean value at the time of admission in our study was 1231.34 ng/ml and 1993.47 ng/ml at the time of death. Mehta et al.found that other predictors of poor outcome include serum ferritin levels and mean serum ferritin levels of 1297·6 ng/ml was seen in non survivors in their study [12]. Liu et al. reported that, when patients began to recover, the ferritin concentrations decreased [13]. This may confirm that hyperferritinemia is associated with inflammatory states in SARS-CoV-2 infection, and therefore, ferritin can be a useful parameter to predict disease severity and the extent of the cytokine storm.

In our study it can be observed that the mean value of WBC Count at the time of admission was 9,484/mm^3 and it was 18,875/mm^3 at the time of death which was higher than at the time of admission. Significant increase of WBC Count and neutrophils at the time of admission (>6.16 x 10^9/L) is significantly correlated with deaths in Covid 19 patients[14].

LDH is an ubiquitous enzyme in the human tissue that serves as the last step of aerobic glycolysis by catalysing the conversion of pyruvate to lactate reversibly [15]. LDH can be released during tissue damage and is involved in various pathophysiological processes and serve as a non-specific indicator of cellular death in many diseases. We found that LDH levels had mean value of 728.09 U/L at the time of admission and mean value of 1010.09 U/L at the time of death in our study. Vidal-Cevallos et al. found that in Covid 19 patients, LDH greater than 561 U/l on admission were associated with higher odds of in-hospital mortality [16]. Levels of d-dimer, serum ferritin and lactate dehydrogenase were clearly elevated in non-survivors compared with survivors throughout the clinical course, and increased with illness deterioration[4].

CRP is a useful inflammatory marker and indicator that plays an important role in host resistance to invading pathogens and inflammation [17]. In our study, it was found that mean CRP level at admission was 74.56 mg/L and the mean CRP level at the time of death was 62.28 mg/L. Our study observed that CRP at the time of admission was higher than that at the time of death which needs further evaluation. Liu et al. found that CRP can effectively assess disease severity and predict outcomes in patients with COVID-19[18]. Besides, higher CRP has been linked to unfavourable aspects of COVID19 diseases, such as cardiac injury, and ARDS development, and death[19]. Therefore, the detection of CRP levels in COVID19 patients is of great value in assessing the severity of their condition to prevent mortality through early aggressive clinical intervention.

CONCLUSION

This study shows that an elevated WBC counts, D-dimer, LDH and serum ferritin were associated with a composite poor outcome in patients with COVID-19. Various haematological and coagulation parameters and increased inflammatory reactions caused by various cytokines are a globally observed phenomenon in COVID-19 patients. While the clinical status (in particular SpO2levels) and concurrent comorbidities of COVID-19 patients largely determine the need for their admittance to ICUs. It is more likely that the course of the disease will be unfavourable if some or all of these parameters are altered. Clinicians should consider levels of WBC count, CRP, D-dimers, ferritin and LDH, which may be used in risk stratification to predict severe and fatal COVID-19 in hospitalised patients. So deranged laboratory parameters facilitate the assessment of disease severity and rational triaging.

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