

Prognostic markers in haematological and biochemical parameters among COVID-19 patients

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Abstract

Background: Coronavirus 2019(COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has become a global threat. Various biomarkers help us in identifying the severity of the patient. This study was formulated to assess the prognostic factors in these biomarkers conducted on the COVID-19 affected patients. A comparative study was done between the survivors of COVID-19 and non-survivors of COVID-19.

Materials and methods: Detailed investigations of COVID-19 positive patients from January 2021 to December 2021 was collected. Among the 155 cases included in the study, 92 patients had survived COVID-19 and 63 patients had died due to COVID-19. Comparison of values of various biomarkers was done between the survivors and non-survivors. Chi-square test was used as a test of significance for qualitative data. A

P value of <0.05 was considered as statistically significant.

Results: Mean age of survivors was 50 ± 14 and those of non-survivors was 51 ± 13 . Mean sPO₂ was significantly higher in survivors compared to non-survivors ($p<0.05$). Haematological profile showed significant difference ($p<0.05$) in absolute neutrophil count (ANC) and neutrophil to lymphocyte ratio (NLR). C reactive protein (CRP) showed significantly higher values in non-survivors compared to survivors ($p<0.05$). Significantly higher values were seen with serum ferritin in non-survivors compared to survivors ($p<0.05$). SPO₂, ANC, NLR, CRP and ferritin are found to be poor prognostic factors in our study.

Conclusion: Identification of high-risk cases at the earliest with these biomarkers and correlating with clinical details helps clinician in deciding the mode of

management of the COVID-19 affected patient. Hence mortality of the patients can be reduced.

Keywords: COVID-19, biomarkers, prognosis

Introduction

A cluster of cases of pneumonia in Wuhan, China was reported in December 2019. The genetic sequence of COVID-19 was shared in January 2020. In view of human-to-human transmission of the virus, World Health Organization (WHO) declared COVID-19 as pandemic in March 2020.¹

Patients with coronavirus disease presented with various symptoms including fever, cough, breathlessness. Majority of the symptoms were related to respiratory symptoms associated with symptoms related to other systems like gastrointestinal, renal, neuronal, cardiac etc.^{2,3}

Upper and lower respiratory tract specimens were obtained from patients. RNA was extracted and tested by real-time RT-PCR with 2019-nCoV specific primers and probes. If two targets tested positive by specific real-time RT-PCR, the case would be considered to be laboratory confirmed.^{4,5,6}

COVID-19 is a multisystem disease caused by a complex interplay of immunological, inflammatory and coagulation cascades. There are several Haematological and biochemical markers linked with predicting the severity of coronavirus disease.^{7,8} This study aims to evaluate Haematological parameters like total leucocyte count (TLC), absolute neutrophil count (ANC), absolute lymphocyte count (ALC), platelet count, neutrophil to lymphocyte ratio (NLR). Neutrophilia, lymphopenia, thrombocytopenia is known to occur in COVID-19 patients.

Inflammatory markers like C reactive protein (CRP) and serum ferritin play an important role in producing proinflammatory cytokines thus causing in cytokine storm in these patients.^{9,10,11} Lactate dehydrogenase (LDH) and D-dimer indicate ongoing injury to the cells and help in predicting progress of patients to sepsis.^{12,13}

Biochemical parameters like random blood sugar (RBS), blood urea, serum creatinine, aspartate transaminase (SGOT), alanine transaminase (SGPT), electrolytes like sodium and potassium provide no significant relation to mortality and in predicting the severity of the disease. It is unclear whether these markers are raised due to underlying comorbidities or the COVID-19 infection itself.

Materials and methods

This is a retrospective study conducted at Raichur Institute of Medical Sciences (RIMS), Raichur. Clinical details and investigations of RT-PCR positive patients from January 2021 to December 2021 were collected from case files maintained at medical record department. RT-PCR negative and cases with incomplete investigations were excluded from the study.

155 cases with complete patient details and investigations were included in the study. Investigations done at the time of admission were taken into account in the study. Among the 155 cases included in the study, 92 patients had survived COVID-19 and 63 patients had died due to COVID-19. This study compared the Haematological and biochemical parameters between the survivors and non-survivors among patients affected with COVID-19. Prognosis of various biomarkers was thus inferred from the study.

Ethical clearance was obtained from the Institutional Ethics Committee with Reference no. RIMS/IEC/Teach. Staff/2022-23/10. The medical record department was

informed before collecting case details. The need for written consent was deferred considering the study design.

Statistical analysis: Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software (IBM SPSS Statistics, Somers NY, USA). Categorical data was represented in the form of Frequencies and proportions. Chi-square test or Fischer’s exact test (for 2x2 tables only) was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. Independent t test was used as test of significance to identify the mean difference between two quantitative variables P value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

Results

Among the 155 cases included in the study, 92(59.4%) cases had survived and 63 (40.6%) had died due to COVID-19. There was no significant difference in the age and sex distribution of the survivors compared to those of non-survivors. Of the 92 survivors, 41(61.2%) were females and 51(58.0%) were males. Among the non-survivors, 26(38.8%) were females and 37(42.0%) were males. Mean age of survivors was 50±14 and those of non-survivors was 51±13. Median age of non-survivor cases was 55yrs with a range of 24-82 years. Median age of survivors was 50.5 with a range of 10-86 years. Descriptive statistics of various parameters is as shown in table1.

Minimum oxygen saturation(sPO2) observed was 34% and maximum was 100%. Mean sPO2 was significantly higher in survivors compared to non-survivors (p<0.05). Various parameters are compared between the survivors

and non-survivors and P value of respective parameters is tabulated in table 2.

Haematological profile showed significant difference in ANC and NLR(p<0.05). TLC was higher in non-survivors compared to survivors. But there was no significant difference(p>0.05). ALC showed lower limit values in both the groups. There was no significant difference in ALC and platelet count between both the groups(p>0.05).

CRP showed significantly higher values in non-survivors compared to survivors(p<0.05). Mean CRP in survivors observed was 37.03±28.02 whereas in deaths it was 73.73±37.54. Biochemical parameters like RBS, urea, creatinine, SGOT, SGPT, sodium and potassium showed no significant difference between the survivors and non-survivors (p>0.05).

Significantly higher values were seen with serum ferritin in non-survivors compared to survivors(p<0.05). Mean serum ferritin in survivors was 264.99±288.28 compared to 511.89±264.50 µg/L in deaths. Though both the survivors and non-survivors showed higher values of LDH and D-dimer there was no significant difference in LDH and D-dimer values when compared between both the groups(p>0.05).

Parameter	Normal range	Mean ± SD
TLC, x10 ⁹ /L	4-11	10.9±5.7
ANC, x10 ⁹ /L	2.5-6.0	8.5±4.9
ALC, x10 ⁹ /L	1.0-4.8	1.8±1.2
NLR	0.78-3.53	6.1±4.7
Platelet count, x10 ⁹ /L	150-400	215±116
CRP, mg/L	0-5	51.9±36.6
RBS, mg/dl	100-140	149±90.6
UREA, mg/dl	6-24	34.7±26.4
Creatinine, mg/dl	0.5-1.5	1.3±1.5

SGOT, U/L	8-40	32±21.4
SGPT, U/L	5-35	33.8±20.7
Serum sodium, mmol/L	135-145	136.8±3.8
Serum potassium, mmol/L	3.5-4.5	4.2±0.6
LDH, U/L	109-245	595.4±442.7
D-dimer, ng/ml	<250	1557.4±1.82
Serum ferritin, µg/L	20-200	365.3±303.4
SPO2, %	95-100	80.2±18.1

Table 1: Descriptive statistics of various parameters.

Parameter	Mean ±SD		P value
	Survivors	Non-survivors	
TLC, x10 ⁹ /L	10.18±5.3	12.0±6.2	0.060
ANC, x10 ⁹ /L	7.6±4.7	9.8±5.0	0.007
ALC, x10 ⁹ /L	1.9±1.2	1.6±1.1	0.062
NLR	4.8±3.9	7.9±5.2	<0.001
Platelet count, x10 ⁹ /L	228±117	196±113	0.101
CRP, mg/L	37±28	73.7±37.5	<0.001
RBS, mg/dl	144.9±87	155.3±96.1	0.485
UREA, mg/dl	31.9±18.9	38.8±34.3	0.113
Creatinine, mg/dl	1.1±0.64	1.6±2.1	0.066
SGOT, U/L	32.3±22.1	32.6±19.6	0.918
SGPT, U/L	33.6±19.4	34.3±22.8	0.820
Serum sodium, mmol/L	136±4	137±4	0.084
Serum potassium, mmol/L	4.2±0.6	4.2±0.7	0.633
LDH, U/L	582.1±213.6	614.8±647.4	0.652
D-dimer, ng/ml	1597.2±247.1	1499.3±914.9	0.744

Serum ferritin, µg/L	264.9±28	511.9±264.5	<0.001
SPO2, %	89±10	68±20	<0.001

Table 2: Comparison of various parameters According to outcome.

Discussion

The ongoing pandemic of COVID-19 poses several diagnostic and therapeutic challenges to clinicians. Along with initial clinical assessment, these laboratory tests with various biomarkers can help in better management and patient care. The effects of virus on the human body and understanding how the body reacts has uncovered many biomarkers. The study of these biomarkers and comparing their values in COVID-19 survivors and non-survivors helps in better output of health care.¹⁴

Median age of non-survivors was observed to be higher than survivors in our study. This correlated with other studies where similar results were obtained.^{15,16} Sheng et al also divided the cases into mild, moderate and severe based on the clinical features and Xray imaging studies. They found that age of severe group was significantly higher than moderate group.¹⁵ Older age associated with comorbidities such as hypertension, cardiovascular disease, diabetes, chronic respiratory disease, and chronic kidney disease (CKD) are more prone for mortality.¹⁷

SpO2 was significantly lower in non-survivors compared to survivors in our study. Mean SpO2 in non-survivors was 68±20 compared to 89±10 in survivors. This observation was well correlated with other studies where SpO2 less than 90% was categorised into severe cases.^{18,19} Thus low SpO2 at the time of admission is a poor prognostic factor and calls for intensive treatment and care.

Haematological profile showed a significant value for ANC. This was in correlation with other studies where higher neutrophil count was seen among the affected patients.^{15,18,19,20,21} According to a study by Urrea et al, patients requiring ICU admission showed higher frequency and percentage of neutrophils. Hence it can be considered as a poor prognostic factor.²² NLR was found to be a predictive factor for early-stage prediction of patients infected with COVID-19 who are likely to develop critical illness according to a study by Liu J et al.²³ Lymphopenia is one of the findings in predicting severity in some of the studies but our study showed mean values of ALC in the normal range and showed no significant difference between deaths and survivors.^{14,16,24}

CRP is a type of plasma protein produced by the liver that is elevated in response to inflammation. A study by Wang G et al found that elevated CRP level as a valuable marker to predict the possibility of aggravation of no severe COVID-19 patients.²⁵ Few other disease also associate disease severity with raised CRP.^{26,27} Our study also found a significant difference between the COVID-19 non-survivors and survivors.

Serum ferritin was found to be significantly higher in non-survivors than survivors in our study. The same observation was noted in a study by Asghar M et al.²¹ In a study of 21 cases ferritin was noted to be higher in severe cases compared to moderate cases.²⁸ Patients with a poor composite outcome had higher ferritin levels in a meta-analysis study done by Huang I et al.²⁹ A biochemical severity score called covichem was built in a study taking into consideration of 26 variables among which ferritin proved to be one of the independent risk factor for severity.³⁰

Taking into consideration of all the Haematological, biochemical and inflammatory markers that could be compared between the COVID-19 survivors and non-survivors in our study, few of the markers showed higher values in deaths compared to survivors with a significant p value ($p < 0.05$). Thus the parameters indicating poor prognosis in these cases are sPO₂, ANC, NLR, CRP and serum ferritin. A study of how different biomarkers behave during the course of disease could help clinicians in identifying severity of disease earlier and subsequently improve the prognosis of patients.

Conclusion

COVID-19 is an unpredictable multi system viral infection which can be detrimental to high-risk patients. Hence identifying the behaviour of the virus on human body by various laboratory markers helps clinician in deciding the course of management in these patients. Our study compared the haematological and biochemical parameters between the survivors and deaths in COVID-19. SpO₂, ANC, NLR, CRP and serum ferritin were significantly higher in non-survivors than the survivors. Hence these parameters could be considered as poor prognostic markers and higher values of these markers can alarm clinician towards an intensive care management.

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