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Original Artide

A Comparative Analysis of Laboratory Parameters of Hospitalized COVID-19 Patients by Disease Severity and Mortality at a Facility in Ibadan, Nigeria

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Abstract

Background: COVID-19, which is caused by the SARS-CoV-2 virus, is associated with abnormalities of biochemical parameters. There are indications that some of these biochemical parameters can differ according to the severity of the disease and the outcome of the infection. This study describes and compares laboratory findings among COVID-19 patients hospitalized at a facility in Southwestern Nigeria according to disease severity and mortality.

Methodology: Records of 223 patients with COVID-19 disease admitted between March 2020 and May 2021 were retrospectively collected. Socio-demographic characteristics, laboratory parameters, and patient outcomes were obtained. Patients were classified according to COVID-19 severity. Laboratory parameters were compared between patients with severe and non-severe disease and between survivors and non-survivors.

Results: Of the 215 patients with some laboratory data included in the analysis, there were 133 (62%) males, and 56.7% were aged above 60 years. A total of 71.6% had severe COVID-19 and 48.4% died during hospitalization. The severe disease occurred significantly more frequently among non-survivors (*P*0.01). Higher leukocyte and neutrophil counts, urea levels, D-Dimer, and fasting blood glucose levels occurred significantly more frequently in both severe disease and mortality categories. Additionally, elevated GGT and CRP were significantly more common in those with severe than non-severe disease while lower hemoglobin, hematocrit, albumin, and higher creatinine levels were significantly more common in non-survivors.

Conclusion: Our study found that certain readily obtainable biochemical parameters occur more frequently with severe disease and/or mortality amongst patients hospitalized with COVID-19 in sub-Saharan Africa and might be useful for prognostication and allocation of resources.

Keywords: SARS-CoV-2; COVID-19; Biochemical Markers; Hematological Indices.

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Quick Response Code:

Introduction

Since its onset, the Coronavirus disease 2019 (COVID-19) pandemic has placed an enormous toll on health systems and healthcare workers alike. In African countries, this burden though less than initially anticipated has also been substantial.[1,2]As a result of this, resources available to care for hospitalized COVID-19 patients have been scarce. The clinical course of COVID-19 varies widely and clinical or biochemical parameters which could predict severity or mortality would be helpful in allocating resources. Abnormal biochemical parameters have been widely reported for COVID-19 and some have been associated with a more severe disease course.[3–5] Some have also been used in prognostication and to determine the risk for clinical progression to severe disease or death.[3,5–7]For instance, elevated inflammatory markers such as C-reactive protein (CRP) and ferritin have been commonly seen in all categories of patients with COVID-19.[5,8,9] Leukocytosis, neutrophilia, and leukopenia have all been reported in patients with COVID-1,9 and lymphopenia which has also been frequently reported has been associated with higher mortality or more severe disease.[4,9,10]Biochemical parameters of COVID-19 have been well described in all regions of the world including sub-Saharan Africa but to a lesser extent. We set out to describe a wide range of biochemical parameters among hospitalized COVID-19 patients at a tertiary hospital in southwestern Nigeria according to disease severity and survival status.

Materials and Methods

Study Design and Study Population

We performed a retrospective study of consecutive patients managed for COVID-19 at a tertiary healthcare facility in Southwestern Nigeria between March 2020 and May 2021. All patients above the age of 18 years who were laboratory confirmed to have SARS-CoV-2 infection by polymerase chain reaction (PCR) and managed as in-patients at the infectious disease isolation and treatment center of the hospital were included in the study. Patients under the age of 18 years were excluded. The study was approved by the ethics committee responsible for research activities in the facility. Informed consent was waived as de-identified secondary data were used.

Data collection

Data were extracted into a pre-tested standardized proforma from the patients' hospital records by physicians in the managing team. Socio-demographic data, symptoms, classification of disease severity, laboratory parameters and patients' outcomes were obtained. We collected data on hematologic parameters, electrolytes, urea and creatinine, liver function tests, inflammatory markers and glucose levels. Laboratory tests were usually carried out within 48 hours of admission to the COVID-19 isolation center. Disease severity was classified according to the WHO classification of severity of severe acute respiratory illness. [11]Outcomes were classified as death during hospitalization and discharge alive. The extracted data were reviewed following extraction by a second clinician in the managing team. The data were subsequently entered into the Statistical Package for Social Sciences (SPSS 25 version) for analysis.

Data analysis

Descriptive statistics were used to summarize the data. Data were presented using simple percentages, frequency tables, charts, graphs and inferential statistics. Tests of normality were performed on continuous variables. Median, interquartile range and minimum and maximum values were described for continuous variables due to skewness. Categorical variables were summarized using percentages and frequencies. The Chi square statistical test of significance was used to compare categorical variables. Median values of continuous variables were compared using Mann Whitney U test. Associations were deemed to be significant at *P*0.05

Results

Out of a total of 223 COVID-19 patients managed for COVID-19 between March 2020 and May 2021, 215 with laboratory data were included in the study. The median (IQR) age was 62(23) years, with a range of 20 to 93 years of age. There were more (61.9%) male than female patients. No statistically significant differences were found in comparisons of socio-demographic characteristics by disease severity or outcome. Other socio-demographic characteristics are listed in table 1.

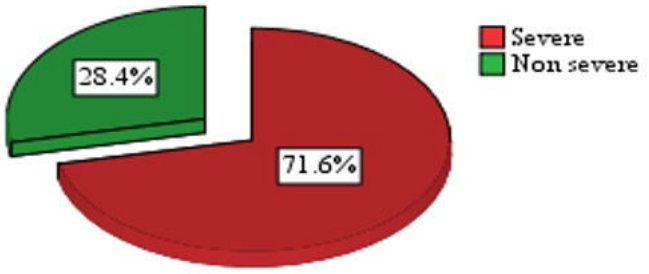
Table 1: Socio-demographic characteristics by disease severity and mortality outcome

Socio-demographic characteristics	Total Number (N)	Severity		*P* value	Clinical Outcomes		*P* value
		Severe (%)	Non-severe (%)		Dead (%)	Survived (%)	
Gender							
Male	133	95 (71.4)	38 (28.6)	0.934	63 (47.4)	70 (52.6)	0.71
Female	82	59 (72.0)	23 (28.0)		41 (50.0)	41 (50.0)	
Age group (years)							
11 – 20	1	1 (100.0)	0 (0.0)		1 (100.0)	0 (0.0)	0.39
21 – 30	4	2 (50.0)	2 (50.0)		1 (25.0)	3 (75.0)	
31 – 40	13	10 (76.9)	3 (23.1)		7 (53.8)	6 (46.2)	
41 – 50	32	19 (59.4)	13 (40.6)	0.66	12 (37.5)	20 (62.5)	
51 – 60	43	31 (72.1)	12 (27.9)		18 (41.9)	25 (58.1)	
61 – 70	56	42 (75.0)	14 (25.0)		27 (48.2)	29 (51.8)	
71 – 80	44	34 (77.3)	10 (22.7)		27 (61.4)	17 (38.6)	
> 80	22	15 (68.2)	7 (31.8)		11 (50.0)	11 (50.0)	
Marital Status							
Married	183	88 (48.8)	95 (51.9)		88 (48.1)	95 (51.9)	
Single	3	2 (66.7)	1 (33.3)	0.94	2 (66.7)	1 (33.3)	0.94
Widowed	23	11 (47.8)	25 (47.2)		11 (47.8)	12 (52.2)	
Divorced/Separated	6	3 (50.0)	83 (55.3)		3 (50)	3 (50.0)	
Level of Education (n = 214)							
No formal Education	2	1 (50.0)	1 (50.0)	0.23	1 (50.0)	1 (50)	0.23
Primary	9	7 (77.8)	2 (22.2)		7 (77.8)	2 (22.2)	
Secondary	53	28 (52.8)	25 (47.2)		28 (52.8)	25 (47.2)	
Tertiary	150	67 (44.7)	83 (55.3)		67 (44.7)	83 (55.3)	

Severity classification and mortality outcomes

One hundred and fifty-four (71.6%) of the patients in the study presented with severe COVID-19 and 104 (48.4%) deaths were recorded as shown in Figures 1 and 2, respectively. There is a significant association between the severity of COVID-19 and mortality (Table 2).

Figure 1: Showing patients disease severity classification



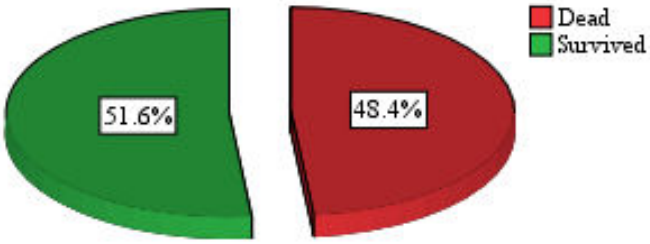


Figure 2: Showing distribution by Clinical outcomes

Table 2: Association between Disease Severity and Clinical Outcomes

Disease Severity at presentation	Outcome of hospitalization		Chi-square (*P* value)
	Dead (%)	Alive (%)	
Severe	91 (59.1)	63 (40.9)	24.971 (0.01)*
Non-severe	13 (21.3)	48 (78.7)	

*Significant at *P*< 0.05

Laboratory Pattern by Severity and Outcome Groups

Mann Whitney analyses were done to compare the median values of the laboratory parameters of patients by severity and by outcome of their hospitalization (Table 3). Significantly higher total white blood cell (WBC) counts, and absolute neutrophil counts (ANC) were reported in the severe compared with the non-severe groups (*P* 0.01 and *P* 0.01respectively). The same finding was noted in the non-survivor compared with the survivor group (*P*0.01 *and P* 0.01). Hemoglobin (Hb) and hematocrit (HCT) values were higher in survivors compared with non-survivors, *P* 0.01, and *P* 0.01 respectively. This was not seen when comparing the severe disease group with the non-severe group, with hemoglobin and hematocrit values being similar in both groups. Other hematological parameters were similar in both disease severity and outcome groups.

Regarding renal biochemical parameters, median urea level was higher (40mg/dL versus 30 mg/dL) in the group with severe COVID-19 compared to the group with non-severe disease (*P* 0.03). However, creatinine was not elevated in the severe cases compared with non-severe cases *(P* 0.31*)*. Bicarbonate levels were lower in non-survivors while both urea and creatinine were higher in non-survivors (*P* 0.01*, P* 0.01, *and P* 0.01 *respectively*).

While D-Dimer was higher in severe disease and among non-survivors than comparator groups*(P*0.03*, P*0.02*),* CRP was only found to be higher in patients with severe disease compared with non-severe disease (*P*0.02*)*and did not significantly differ by survival status *(P*0.23*)*.Fasting blood glucose levels were higher in the group with severe disease (189mg/dL) compared with the non-severe disease (108mg/dL) group*(P*0.01*)* and likewise in non-survivors compared with survivors *(P*0.01*)*.Random blood glucose was not significantly different between severity and outcome groups. Albumin levels were lower in non-survivors, *P* 0.01. Except for GGT, there were no statistically significant differences between liver function test parameters when comparing patients by disease severity and survival status.

Table 3: Comparison of values of laboratory parameters by disease severity and survival status

Laboratory Parameters	Overall Median (IQR)	Severity		*P* value			*P* value
		Severe (IQR)	Non-Severe (IQR)		Non-survivor (IQR)	Survivor (IQR)	
WBC* (cells/mm^3) n = 157	9600 (6840)	9945 (6347.5)	7980 (6670.0)	**0.01†**	11640 (8635)	9375 (5550)	**0.01†**
ANC‡ (cells/mm^3) n = 155	7180 (6205)	7675 (5777.5)	5600 (4560.0)	**0.01†**	9130 (8350)	6580 (6580)	**0.01†**
ALC§ (cells/mm^3) n = 152	1390 (862)	1450 (855.0)	1240 (860)	0.16	1400 (1050)	1390 (820)	0.56
Hb¶ (g/dL) n = 148	11.9 (3.3)	11.9 (3.13)	11.9 (11.4)	0.91	11.4 (3.9)	12.3 (2.7)	**0.01†**
HCT** (%) n = 161	36 (9.3)	36 (9.4)	34.3 (9.3)	0.35	33.7 (10.4)	37.1 (7.2)	**0.01†**
Platelet count (cells/mm^3) n = 150	217000 (165250)	217000 (158500)	216000 (152000)	0.26	201000 (155500)	218500 (175250)	0.59
Sodium (mmol/L) n = 162	136 (7)	135.5 (7.0)	137 (6.5)	0.82	137 (8.75)	135 (6)	0.08
Potassium (mmol/L) n = 162	3.7 (0.8)	3.7 (0.7)	3.5 (0.8)	0.08	3.7 (1.0)	3.7 (0.8)	0.2
Bicarbonate (mmol/L) n = 157	22 (6)	21.8 (6.5)	23 (4.5)	0.64	20 (5)	23 (5)	**0.01†**
Urea (mg/dl) n = 149	36 (52.5)	40 (54)	29.5 (35.5)	**0.03†**	64 (82)	35 (32)	**0.01†**
Creatinine (mg/dl) n = 150	1.1 (1.1)	1.2 (1.4)	1.0 (0.6)	0.31	1.4 (2.0)	1.0 (0.7)	**0.01†**
AST (umol/L) n = 33	64 (66.5)	62 (49)	50.5 (217)	0.72	82 (87)	48 (53)	0.13
ALT (umol/L) n = 34	51.5 (52.8)	58 (62)	36(57.3)	0.19	47 (65)	52 (52)	0.64
ALP (umol/L) n = 30	75 (42.8)	91 (48)	67 (44.8)	0.27	82 (71)	72 (36)	0.54
GGT (umol/L) n = 29	103 (98.5)	134 (86)	53 (34.3)	**0.01†**	134 (106)	75 (105.3)	0.07
Total Bilir ubin (mg/dL) n = 32	0.8 (0.7)	0.7 (0.7)	0.8 (0.8)	0.97	0.8 (0.5)	0.7 (0.7)	0.8

*WBC = White Blood Cell Count, †Significant at $P < 0.05$, § ANC Absolute neutrophil count, || ALC= Absolute neutrophil count, ¶ Hb = Hemoglobin, ** HCT=Hematocrit, †† FBG= Fasting Blood Glucose, ‡‡ RBG = Random Blood Glucose

Discussion

In this study we reported the biochemical parameters of hospitalized patients managed for COVID-19 disease, the majority of which (71.6%) had severe disease at presentation. There was a male predominance in this study, and more than half of the patients were above 60 years of age. Ours is a significantly older cohort of patients than reported by Bowale, Abayomi and Jibrin all in Nigeria but with a similar gender distribution.[12–14] Neither of the first 2 studies reported laboratory data and all had a much smaller proportion of severely ill patients. Jibrin et al did report biochemical parameters which were largely normal values in their cohort of mostly asymptomatic patients. To date, there are relatively fewer (compared to other regions of the world) studies from Nigeria and sub-Saharan Africa that have reported laboratory data in a cohort of hospitalized, mostly severe COVID-19. Not surprisingly, the overall mortality in our study is high because of the high proportion of severe disease at presentation.

Our study found higher total WBC counts and ANC in patients with severe than non-severe disease as well as in non-survivors compared with survivors. The median WBC and ANC counts, reported in this study were within normal limits in severe cases while the median WBC count was above normal limits (>11,000) in non-survivors. Similarly, leukocytosis and sometimes neutrophilia have been associated with severity and/or mortality in other studies.[15–17] A Nigerian study from the same city found higher WBC counts,

neutrophil percentage and lower lymphocyte percentage in COVID-19 patients than in control patients without COVID-19.[18]In our study however, there were higher absolute lymphocyte count (ALC) values in both the severe and non-survivor groups compared with the non-severe and survivor counterparts respectively although neither of these differences was statistically significant. Non-significant differences in comparisons of lymphocyte counts by mortality and severity was also described by Pujani et al in India.[19] Jibrin et al from Bauchi Nigeria reported lymphocytosis in 60% of their patient population of which only3.6% of them had severe disease(14) .It is worthy of note that in all severity and mortality groups in this study, the median ALCs were similar and less than 1,500. It has been previously reported in literature from elsewhere that lower (but normal) ALCs and lymphopenia have been found to be significantly associated with severe disease/mortality.[6,8,9,17,20,21]

This study found higher hemoglobin levels in survivors; higher hemoglobin were also reported by Kantri et al in patients with non-severe disease in Morocco while lower hemoglobin levels were found in patients with severe disease in Japan.[15,17]Of note, median platelet counts were similar, and within normal limits, in both severity and mortality comparison groups and similar to the overall median platelet count of the cohort of patients. Other studies have reported thrombocytopenia as associated with more severe disease and mortality. [22–24] Significantly higher median urea and creatinine levels were found in non-survivors in our study while only urea and not higher creatinine levels were found to occur more frequently with severe disease. Similar findings have been reported previously and it has been postulated that expression of ACE2 receptors (the entry receptor for SARS-CoV-2) in the kidneys might be responsible for worse outcomes.[25]
It has been widely reported that elevated inflammatory biomarkers are a hallmark of the highly inflammatory cytokine storm which is known to be a major pathophysiologic mechanism of severe COVID-19.[26] D-Dimer was accordingly found to be relatively elevated in the severe disease and non-survivor groups in comparisons of severity and survival. This has also been previously reported elsewhere.[15,19]The fact that CRP elevation did not occur more frequently in patients who died(as seen in the severe disease group) might be related to the relatively fewer data points for that particular biochemical parameter or that there was elevation seen in all patients, both severe and non-severe and among non-survivors and survivors.
There were relatively few liver function tests performed on the patients in our cohort and GGT was the only hepatic biochemical parameter found to be significantly different between patients with severe and non-severe disease (*P*0.03); there was no difference found between survivors and non-survivors. Salik et al in Turkey found abnormal liver biochemical parameters to be associated with mortality in COVID-19, our findings were not congruent with this association.[27] Abnormal LFTs have not been found to be widespread in COVID patients but have been seen more commonly in severe cases.[8,9]Again, relatively few data points for liver function test results might be responsible for a lack of difference in our comparisons.

Limitations

The data were incomplete as not all biochemical parameters were assayed in all the patients. This was a single center study and as such, finding may not be generalizable. The laboratory parameters were largely assessed at only one point in time, and this does not allow for an assessment of the evolution or the changes in biochemical parameters throughout the course of illness. The study does not test for risk factors for severe disease or mortality and as such findings cannot be interpreted directly for prognostication.

Conclusion

This study has shown that there are significant differences in certain biochemical parameters by COVID-19 severity and mortality in hospitalized COVID-19 patients in Nigeria. Higher total leukocyte and absolute neutrophil counts, serum urea, GGT, DDimer, CRP and fasting blood glucose levels should be further studied to determine association with severe disease. Except for GGT and CRP, there are statistically significant differences between all of the aforementioned parameters as well as low hemoglobin, hematocrit, albumin and elevated creatinine levels by mortality outcome in COVID-19 and should be further examined. Larger local or regional studies should be done to further evaluate our study findings as well as explore possible reasons for the non-significant differences in lymphocyte counts in between severity and mortality groups that were reported in this study. Development of predictive algorithms using these, and clinical

parameters should be explored to help in risk stratification of COVID-19 patients in the African setting where resources for healthcare are scarce.

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