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ORIGINAL PAPER

Haematological changes and metabolic alterations in SARS-CoV-2 infected patients hospitalised at an Infectious Diseases Center, Ibadan, Nigeria

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ABSTRACT

Introduction and aim. Following the use of repurposing drugs to successfully manage coronavirus disease 2019 (COVID-19) patients in an Infectious Diseases Center (IDC) in Nigeria, it was imperative to assess haematological changes and metabolic alterations in these patients which may inform recommendations for future use.

Material and methods. Blood samples of admitted COVID-19 Nigerian patients during therapeutic management were analysed for haematological- (total white blood cells (WBC), lymphocyte, monocyte, neutrophil, eosinophil, basophil and neutrophil:lymphocyte ratio) and blood chemistry- parameters [total protein, total and conjugated bilirubin, alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine transaminase (ALT), gamma-glutamyl transferase (GGT), albumin, urea, creatinine, total cholesterol, triglycerides, low-density lipoprotein (LDL), high-density lipoprotein (HDL), PO_4^{3-}, Ca^{2+}, uric acid, Na^+, K^+, Cl^- and HCO_3^-] using autoanalysers. The percentages of patients having values below, within and above reference ranges were compared using Chi-square test while the mean values at admission were compared with mean values at discharge using Student *t*-test.

Results. The mean values of total protein, albumin, Na^+, HCO_3^-, uric acid, Ca^{2+}, WBC, platelets, lymphocytes, eosinophils and basophils were significantly increased in COVID-19 patients at discharge compared with COVID-19 patients at admission. Also, more percentages of COVID-19 patients at discharge compared with COVID-19 patients at admission had albumin, ALP, total bilirubin, HDL, Na^+, K^+, Cl^-, HCO_3^-, urea, creatinine, WBC, lymphocytes, neutrophils, monocytes, eosinophils and basophils within normal reference intervals.

Conclusion. This study showed that most metabolic and haematological derangements were normalised by repurposing drugs in most of the COVID-19 patients at this IDC, thus supporting the continuous use of this therapeutic option.

Keywords. COVID-19, laboratory tests, reference interval, repurposed drugs, therapeutic action

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Introduction

Studies have reported abnormal systemic or cellular metabolisms in several disorders, but such report is not available in COVID-19 Nigerian patients before and after therapeutic intervention.[1,2] Metabolic functions which are integrated, balanced and homeostatic pathways have been demonstrated to be altered by several virus infections, leading to viral escape from immune attack, causing tissue inflammation and multiple organ damage in COVID-19 patients.[2,3] The entry of SARS-CoV-2 depends on the interaction between virus Spike protein and angiotensin-converting enzyme 2 (ACE2) receptors on epithelial cells in the lungs and other organs with ACE2 receptors to become a multi-organ disease.[4] The exact mechanisms involved in multi-organ disease during COVID-19 have not been clear, but probably multi-factorial.

It was reported that viral infection affects lipid signalling and synthesis which adversely distorts protective host immune response and other metabolisms.[5] Another study demonstrated that interruption in lipid synthesis impairs virus replication, suggesting that lipid pathways can represent a relevant target in the investigation of viral disorders.[6] Higher levels of diglycerides, free fatty acids, and triglycerides were identified in higher amounts in the severe COVID-19 patients.[4] Furthermore, studies reported increased viral replication in cells with excessive intracellular lipid accumulation.[7] These findings suggested altered systemic and lipid metabolisms in COVID-19 patients.[5,6]

The index case of the COVID-19 in Nigeria was recorded on the 27 February 2020 and within 5 months (by the 7 July 2020), all 36 states and the Federal Capital Territory (FCT) had reported at least a case of the disease, with a total number of 29,789 cases and 669 deaths. As at 10 August, 2022, the total cases of COVID-19 in Nigeria was 262,000 with 3,157 deaths while there were 586,000,000 cases and 6,400,000 deaths worldwide.[7]

A recent study showed that between 3.4% to 51.7% newly admitted COVID-19 Nigerian patients had one or more abnormal values of renal function parameters.[8] Most COVID-19 patients (51.7%) had abnormal levels of chloride and 37.8% of the patients had abnormal levels of creatinine.[8] Another study recorded that COVID-19 patients with elevated creatinine had a significantly higher rate of AKI and associated mortality.[9] These observations suggested an association between COVID-19 severity and renal injury.[8,9]

Abnormal liver function tests (LFTs) are frequently observed in patients with COVID-19, of which the underlying pathogenesis is incompletely understood. Though LFTs are not necessarily liver specific but it has been suggested that elevated aminotransferases in COVID-19 could originate from myositis rather than liver injury.[10] Hypoalbuminemia reported in 55% of hospitalised COVID-19 patients was associated with disease severity to predict mortality.[3] Plasma ALT and AST were elevated more frequently and to a greater extent in patients with severe COVID-19 compared to those with mild disease and are associated with increased disease severity and mortality, whereas other studies did not find an association with mortality, disease progression, ICU admission, or length of hospital stay.[3,11] Several case reports have described severe LFT abnormalities or acute or chronic liver failure in patients with COVID-19. Elevated ALP was reported in 2%-5% of patients, and elevated GGT was reported in 13%-54% of patients (weighted average: 23%).[12] The prevalence of total bilirubin elevations ranged between 1% and 18% of patients with COVID-19 on admission.[3] The prevalence of total bilirubin elevations ranged between 1% and 18% of patients with COVID-19 on admission.[3] Despite extensive studies of LFTs in COVID-19 patients, the prognostic value of abnormal LFTs in COVID-19 is unclear.

COVID-19 is a respiratory disease which also affects multiple systems including the cardiovascular, neurological, haematopoietic and immune system among others.[3,10] Leukopenia, leukocytosis, neutropenia and lymphopenia are among the most common laboratory abnormalities in COVID-19.[13,14] Tan et al. showed that lymphocyte percentage was inversely related to the severity and prognosis of COVID-19 patients.[13] Although, reports on haemocytometric changes in COVID-19 infection at different stages of the disease are many, the roles of these changes in indicating disease prognostication is still poorly understood especially, in Nigerian COVID-19 patients.[15]

Demographic- and immune- parameters in COVID-19 Nigerian patients were previously reported. Moreso, repurposed medication used for COVID-19 patients at IDC, Ibadan, Nigeria are combinations of vitamin D, vitamin C, Zn, azithromycin, hydroxychloroquine and chloroquine (as an alternative to hydroxychloroquine).[14,16-20] The treatment options for COVID-19 at this center are largely supportive as there is no universally agreed protocol of care. In addition, these medications were not used in the context of a trial but the positive outcomes encouraged their continued use. However, it was reported that despite patient's toleration of these medications without a risk of bacterial and malarial super-infection, there is need for further evaluation.[20] However, Arinola and Edem emphasised the need for public enlightenment on the dangers inherent in micronutrient supplement abuse.[21]

Aim

The present study therefore assessed the haematologic- and metabolic- alterations in admitted COVID-19 patients on repurposing drugs in an IDC in Ibadan, Nigeria.

Material and methods

The study was conducted after obtaining institutional ethical approval (UI/EC/20/0233) and informed consent from each study participant. Confirmed cases of COVID-19 (n=195) were recruited from an Infectious Diseases Centre, Olodo, Ibadan, Nigeria between May 2020 and August 2020. They were confirmed to be infected with SARS-CoV-2 using nucleic acid Reverse-Transcriptase Polymerase Chain Reaction (RT-PCR) on nasal and pharyngeal swab specimens.[8] On the day of admission, the patients were commenced on the following medication: vitamin D, vitamin C, Zn^{2+}, azithromycin, hydroxychloroquine and chloroquine (as an alternative to hydroxychloroquine). Ten ml of blood sample was collected from each patient and analysed for haematological parameters (total white blood cell (WBC), lymphocyte, monocyte, neutrophil, eosinophil, basophil, red blood cell and platelets counts as well as haematocrit and haemoglobin levels) using haematology autoanalyser (Sysmex XN-450, Norderstedt, Germany). Blood chemistry parameters such total-bilirubin (Bil-T) and conjugated- bilirubin (Bil-D), alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyltransferase (GGT), albumin, urea, uric acid creatinine (Cr), total cholesterol (TC), sodium (Na^+), potassium (K^+), chloride (Cl^-) and bicarbonate (HCO_3^-) using an autoanalyser (Erba XL-200, Mannheim, Germany). The values of biochemical- and haematological- parameters obtained were compared with normal reference ranges to determine the proportion of patients having parameters below, within and above reference ranges. Data were represented as frequencies and percentages. Chi-square test was used to determine the differences between the frequencies while the differences in the mean of variables of COVID-19 patients at admission and discharge were compared using Student *t*-test on the SPSS statistical software (IBM, Chicago, IL, USA), version 21 for windows. *p*-value less than 0.05 was considered as statistically significant.

Results

As shown in Table 1, most COVID-19 patients (69%) in IDC, Olodo, Ibadan were males, 63% of the patients were less than 40 years of age, 47% were privately employed, 70% of them spent less than 10 days on admission, none had severe COVID-19 and 68% of them were hypertensive.

As shown in Figure 1, the mean values of total protein and albumin were significantly increased while ALT, AST, ALP, GGT, total bilirubin and direct bilirubin were not significantly different in COVID-19 patients at discharge compared with COVID-19 patients at admission.

As shown in Table 2, the TC, triglycerides (TG), high density lipoprotein (HDL) and low density lipoprotein (LDL) were significantly increased in COVID-19 patients at discharge compared with COVID-19 patients at admission. The mean levels of Na^+, HCO_3^-, uric acid and Ca^{2+} were significantly increased in COVID-19 patients at discharge compared with COVID-19 patients at admission (Figure 2).

Table 1. Demography and length of hospital admission of COVID-19 patients

Variables	Frequency	Percentage (%)
Gender		
Male	134	69
Female	61	31
Age (years)		
<40 years	122	63
≥ 40 years	73	37
Occupation		
Self employed	53	27
Private	91	47
Civil servant	31	16
Unemployed	29	10
Days on admission		
≤10 days	137	70
>10 days	58	30
Severity		
Mild	117	60
Moderate	78	40
Severe	0	0
Co-morbidity types		
Hypertension	134	68
Peptic Ulcer Disease	39	20
Diabetes mellitus	19	10
Sickle Cell Disease (HbSS)	3	2

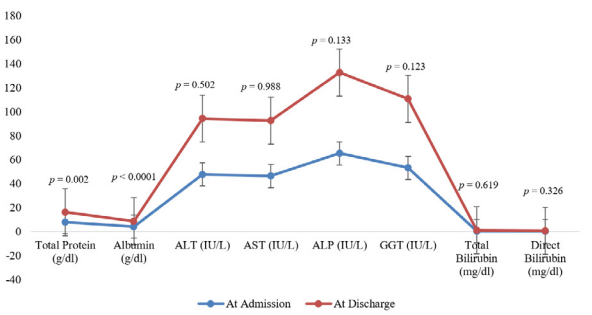

Fig. 1. Liver function parameters in COVID-19 patients at admission and at discharge, AST – aspartate transferase; ALT – alanine transferase; ALP – alkaline phosphatase; GTT – gamma-glutamyl transferase

Table 2. Mean values of lipid profile in COVID-19 patients at admission compared with values at discharge*

Parameters	At Admission	At Discharge	t	p
TC (mg/dl)	176.49±49.50	196.98±49.18	7.835	<0.0001
TG (mg/dl)	103.06±49.21	126.04±64.03	4.366	<0.0001
HDL (mg/dl)	49.72±16.54	56.64±15.06	5.973	<0.0001
LDL (mg/dl)	104.08±41.33	111.46±43.13	2.991	0.003

*TC– total cholesterol; TG– triglycerides; HDL– high density lipoprotein; LDL– low density lipoprotein

As shown in Figure 3, the mean values of WBC, platelets, lymphocytes, eosinophils and basophils

were significantly increased while HGB, HCT, neutrophils, monocytes and NLR were significantly reduced in COVID-19 patients at discharge compared with COVID-19 patients at admission.

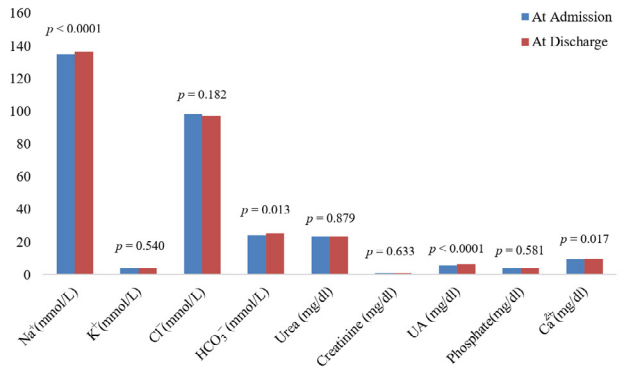

Fig. 2. Renal function parameters in COVID-19 patients at admission and at discharge

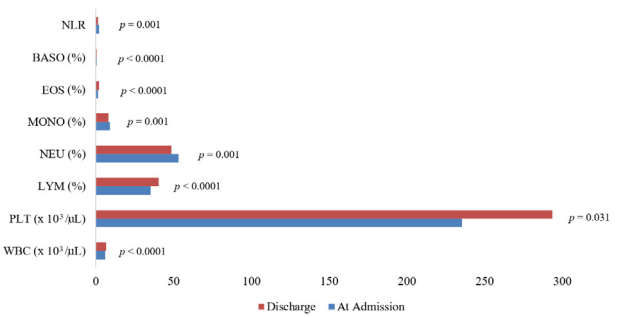

Fig. 3. Haematological parameters in COVID-19 patients at admission and at discharge, WBC – white blood cells; PLT – platelets; LYM – lymphocytes; NEU – neutrophils; EOS– eosinophils; BASO – basophils; NLR –netrophil:lymphocyte ratio

More percentages of COVID-19 patients at discharge compare with COVID-19 patients at admission had albumin, ALP, total bilirubin, HDL, Na^+, K^+, Cl^-, HCO_3^-, urea, creatinine, WBC, lymphocytes, neutrophils, monocytes, eosinophils and basophils (88%vs. 86%, 88% vs. 85%, 94% vs. 93%, 91% vs. 80% , 93% vs. 88%, 89% vs. 72%, 79% vs. 77%, 82% vs. 81%, 87% vs. 76%, 96% vs. 92%, 89% vs. 65%, 61% vs. 43%, 80% vs. 57%, 73% vs. 55%, 42% vs. 27% and 100% vs. 99% respectively) within normal reference intervals (RI). However, more percentages of COVID-19 patients at admission compare with COVID-19 patients at discharge had total protein, ALT, AST, GGT, direct bilirubin, total cholesterol, triglycerides, LDL, uric acid, PO_4^{3-}, calcium and platelets (58% vs. 46%, 45 vs. 41%, 39% vs. 28%, 52% vs. 46%, 96% vs. 95%, 72% vs. 51%, 86% vs. 83%, 40% vs. 37%, 77% vs. 68%, 84% vs. 83%, 75% vs. 68%and 78% vs. 76% respectively) within normal reference intervals (Tables 3-6).

Table 3. The frequencies (percentages) of COVID-19 patients at admission compared with frequencies (percentages) of COVID-19 patients at discharge having liver function parameters within and outside normal reference intervals*

Parameters	Category	At Admission n (%)	At Discharge n (%)	Chi-square	p
Total protein	Below RI	2 (1.1)	0 (0)	4.127	0.127
	Within RI	109 (57.7)	87 (46)		
	Above RI	78 (41.3)	102 (54)		
Albumin	Below RI	21 (11.1)	8 (4.2)	42.471	<0.0001
	Within RI	163 (86.2)	166 (87.8)		
	Above RI	5 (2.6)	15 (7.9)		
ALT	Below RI	0 (0)	0 (0)	13.187	<0.0001
	Within RI	85 (45.2)	77 (41)		
	Above RI	103 (54.8)	111 (59)		
AST	Below RI	0 (0)	0 (0)	0.192	0.662
	Within RI	57 (30.3)	52 (27.7)		
	Above RI	131 (69.7)	136 (72.3)		
ALP	Below RI	3 (1.8)	2 (1.2)	42.843	<0.0001
	Within RI	138 (84.7)	144 (88.3)		
	Above RI	22 (13.5)	17 (10.4)		
GGT	Below RI	1 (0.8)	0 (0)	32.665	<0.0001
	Within RI	63 (51.6)	56 (45.9)		
	Above RI	58 (47.5)	66 (54.1)		
Total Bil	Below RI	0 (0)	0 (0)	13.899	<0.0001
	Within RI	175 (93.1)	176 (93.6)		
	Above RI	13 (6.9)	12 (6.4)		
Direct Bil	Below RI	0 (0)	0 (0)	37.696	<0.0001
	Within RI	181 (95.8)	180 (95.2)		
	Above RI	8 (4.2)	9 (4.8)		

* ALT – alanine transferase; AST – aspartate transferase; ALP – alkaline phosphatase; GTT – gamma-glutamyl transferase; Bil - bilirubin

Table 4. The frequencies (percentages) of COVID-19 patients at admission compared with frequencies (percentages) of COVID-19 patients at discharge having lipid profile within and outside normal reference intervals*

Parameters	Category	At Admission n (%)	At Discharge n (%)	Chi-square	p
TC	Below RI	0 (0)	0 (0)	42.831	<0.0001
	Within RI	136 (72)	97 (51.3)		
	Above RI	53 (28)	92 (48.7)		
TG	Below RI	0 (0)	0 (0)	11.846	0.001
	Within RI	162 (85.7)	156 (82.5)		
	Above RI	27 (14.3)	33 (17.5)		
HDL	Below RI	33 (17.5)	13 (6.9)	19.318	0.001
	Within RI	151 (79.9)	171 (90.5)		
	Above RI	5 (2.6)	5 (2.6)		
LDL	Below RI	54 (29)	46 (24.7)	77.808	<0.0001
	Within RI	75 (40.3)	69 (37.1)		
	Above RI	57 (30.6)	71 (38.2)		

* TC – total cholesterol; TG – triglycerides; HDL – high density lipoprotein; LDL – low density lipoprotein

Table 5. The frequencies (percentages) of COVID-19 patients at admission compared with frequencies (percentages) of COVID-19 patients at discharge having renal function parameters within and outside normal reference intervals

Parameters	Category	At Admission n (%)	At Discharge n (%)	Chi-square	p
Na^+	Below RI	19 (10.9)	10 (5.7)	9.486	0.050
	Within RI	153 (87.9)	162 (93.1)		
	Above RI	2 (1.1)	2 (1.1)		
K^+	Below RI	32 (18.4)	16 (9.2)	6.124	0.190
	Within RI	126 (72.4)	155 (89.1)		
	Above RI	16 (9.2)	3 (1.7)		
Cl^-	Below RI	35 (20.1)	35 (20.1)	43.795	<0.0001
	Within RI	134 (77)	138 (79.3)		
	Above RI	5 (2.9)	1 (0.6)		
HCO_3^-	Below RI	22 (12.6)	13 (7.5)	2.353	0.671
	Within RI	141 (81)	143 (82.2)		
	Above RI	11 (6.3)	18 (10.3)		
Urea	Below RI	26 (13.8)	15 (7.9)	48.896	<0.0001
	Within RI	144 (76.2)	165 (87.3)		
	Above RI	19 (10.1)	9 (4.8)		
Creatinine	Below RI	1 (0.5)	1 (0.5)	16.459	0.002
	Within RI	174 (92.1)	182 (96.3)		
	Above RI	14 (7.4)	6 (3.2)		
Uric acid	Below RI	1 (0.5)	0 (0)	16.470	<0.0001
	Within RI	145 (77.5)	127 (67.9)		
	Above RI	41 (21.9)	60 (32.1)		
Phosphate	Below RI	3 (3.4)	1 (1.1)	12.280	0.015
	Within RI	73 (83.9)	72 (82.8)		
	Above RI	11 (12.6)	14 (16.1)		
Ca^{2+}	Below RI	0 (0)	0 (0)	2.674	0.102
	Within RI	21 (75)	13 (67.9)		
	Above RI	7 (25)	9 (32.1)		

Table 6. The frequencies (percentages) of COVID-19 patients at admission compared with frequencies (percentages) of COVID-19 patients at discharge having haematological parameters within and outside normal reference intervals*

Parameters	Category	At Admission n (%)	At Discharge n (%)	Chi-square	p
WBC	Below RI	41 (21.7)	7 (3.7)	60.024	<0.0001
	Within RI	123 (65.1)	164 (86.8)		
	Above RI	25 (13.2)	18 (9.5)		
PLT	Below RI	26 (13.8)	13 (6.9)	20.201	<0.0001
	Within RI	148 (78.3)	144 (76.2)		
	Above RI	15 (7.9)	32 (16.9)		
LYM	Below RI	45 (23.8)	11 (5.8)	22.185	<0.0001
	Within RI	81 (42.9)	115 (60.8)		
	Above RI	63 (33.3)	63 (33.3)		
NEU	Below RI	45 (23.8)	31 (16.4)	24.577	<0.0001
	Within RI	107 (56.6)	152 (80.4)		
	Above RI	37 (19.6)	6 (3.2)		
MONO	Below RI	15 (7.9)	14 (7.4)	10.380	0.034
	Within RI	104 (55)	137 (72.5)		
	Above RI	70 (37)	38 (20.1)		
EOS	Below RI	130 (70.3)	98 (53)	39.523	<0.0001
	Within RI	50 (27)	79 (42.7)		
	Above RI	5 (2.7)	8 (4.3)		
BASO	Below RI	0 (0)	0 (0)	0.011	0.917
	Within RI	183 (98.9)	184 (99.5)		
	Above RI	2 (1.1)	1 (0.5)		

* WBC – white blood cells; PLT – platelets; LYM – lymphocytes; NEU – neutrophils; MONO – monocytes; EOS – eosinophils; BASO – basophils

Discussion

Our study is the first and most comprehensive report on the haematologic- and biochemical-alterations in Nigerian patients with COVID-19managed at an Infectious Disease Center (IDC) in Oyo State. Previous reports demonstrated the importance of metabolism on the outcomes of viral infections.[1,2,11] The severity of COVID-19 has been reported to be high in patients with underlining metabolic conditions and this demonstrated that metabolic changes could be related to the prognosis of COVID-19.[1,16] It is well established that one of the critical phases of COVID-19 is the cytokine storm generated by the host response, causing extreme inflammatoryprocess.[14,19,22] Patients with existing chronic inflammation often present with accentuated cytokine storm, causing physiological imbalance and aggravated health problems in different organs.[22] An *in silico* study demonstrated the interaction of the spike protein (S protein) from SARS-CoV-2 with human innate immune receptor (Toll-like receptors, TLRs).[23] TLR4 activation has been associated with inflammatory conditions and alteration of lipid and glycolytic homeostasis.[23] The molecular mechanisms involved in metabolic dysfunction in COVID-19 are still sparsely described and not completely understood.[11] Since S protein of SARS-CoV-2 interacts with host TLR to induce inflammation, therefore raised NLR, monocyte and neutrophil counts in our COVID-19 patients at admission may be indicators of the existence of inflammatory phenomenon, and thus alterations in metabolic parameters are expected. This present study revealed one form of abnormal metabolic parameters in 11–72% of COVID-19 patients and haematologic derangements in 1–73% of COVID-19 patients.

Besides altered glycolytic and gluconeogenic pathways in COVID-19, lipid and mitochondrial metabolisms is also affected, demonstrating that altered energy metabolism in renal cell may lead to development of kidney injury affecting systemic metabolism during SARS-CoV-2 infection.[14,24,25] Fatty acids act as mitochondrial substrates for oxidative metabolism and lipid excess induces reactive oxygen species production, apoptosis, inflammation, profibrotic factors release, and organelle damage.[26] Excess LDL levels in 31% of COVID-19 patients at admission and in 32% COVID-19 of patients at discharge may account for inflammation and production of reactive oxygen species in COVID-19 patients as previously pointed out.[11,14,18,19]

Patients infected with SARS-CoV had dysregulated levels of serum free fatty acids and altered lip-

id profile was observed in SARS-CoV infection, even 12 years after recovery from the disease.[3] However, cellular and molecular mechanisms that orchestrate lipid metabolism during SARS-CoV-2 infection are poorly described as recently pointed out.[28] It has also been observed that lipid bodies are localised in monocytes from SARS-CoV-2 infected patients and these lipid bodies are sources of energy and inflammatory mediators for virus replication and virus escape from immune system elimination.[30,31] Thus, normal lipid profile is found in 14–60% of COVID-19 patients at admission compared with 11–72% COVID-19 patients at discharge.

Liver function tests include measures of hepatocyte injury (AST and ALT), bile duct injury or cholestasis (ALP and GGT), markers of hepatic clearance/biliary secretion capacity (bilirubin), as well as measures of synthetic capacity (prothrombin time and albumin). Lower levels of pre-albumin in patients with severe COVID-19 were reported, suggesting decreased hepatic synthesis[3], thus supporting higher level of albumin in COVID-19 patients at discharge compared with COVID-19 patients at admission. In the context of inflammation, hypoalbuminemia in COVID-19 at admission may also reflect albumin extravasation as a consequence of increased capillary permeability. Additional factors that could explain the observed hypoalbuminemia in newly admitted COVID-19 patients are increased catabolism and malnutrition. Plasma ALT and AST were elevated more frequently and to a greater extent in patients with severe COVID-19 compared to those with mild disease.[11] This was also the case for the present study where ALT and AST above normal reference limits were found in 54.8% vs. 59% and 69.7% vs. 72.3% of COVID-19 patients at admission and discharge respectively.

SARS-CoV-2 uses the angiotensin-converting enzyme 2 (ACE2) as docking and entry receptor on host cells while Transmembrane serine protease 2 (TMPRSS2) is also involved in its cellular entry.[4] ACE2 is highly expressed on the brush border of small intestinal enterocytes and SARS-CoV-2 infection was observed in human small intestine organoids.[32] SARS-CoV-2 nucleocapsid was detected in the cytoplasm of intestinal biopsies of a patient with COVID-19.[32] Theoretically, direct virus-induced cytopathic effects could play a role in LFT abnormalities in COVID-19. Assuming brisk viral replication in the intestine, it appears plausible that viruses could enter the portal circulation to reach the liver. Hepatic Kupffer cells would attempt to clear the virus and initiate an inflammatory response. It is also possible that inflammatory mediators from the intestine could enter the portal system and sinusoids.

Previous reports suggested that some changes in the peripheral blood in COVID-19 patients provide clue or guidance for diagnosis, treatment, and prognosis of the disease.[11,14,27] A study indicated that the total number of peripheral white blood cells was normal or the lymphocyte count was reduced in patients at the early stage of COVID-19 and that lymphocyte percentage was inversely related to the severity and prognosis of patients with COVID-19.[13] Other studies reported that WBC, neutrophil count, NLR and PLR in the severe group were significantly higher than those in the moderate group; meanwhile, lymphocyte number and eosinophil count in the severe group were significantly lower than those in the moderate group.[11,14,29] The present finding of lymphopenia in our COVID-19 patients at admission may be related to persistent infection and prolonged hypoxia leading to compensatory hyperplasia of the bone marrow to release more granulocytes or continuous lymphocytes destruction through invasion by SARS-CoV-2 and constant removal of these destroyed lymphocytes by the spleen and other immune organs. However, lymphopenia was conjectured to because by depletion of T lymphocyte subpopulation.[33]

Both NLR and platelet lymphocyte ratio in patients with severe COVID-19 disease were significantly higher and showed that this is probably the best single parameter for differential diagnostic efficacy.[34] Liu et al. also suggested that NLR was helpful for early detection of severe COVID-19 patients with high prediction accuracy, which is consistent with the conclusion of Wang et al.[11,27,34] Our present study showed significantly increased NLR in newly admitted COVID-19 patients compared with discharged patients, thus supporting the usefulness of NLR in COVID-19 prognostication.

The findings of this study has implication on the potential mechanisms of hepatic-kidney injury in patients with SARS-CoV-2, which is capable of binding specifically to ACE2 on hepatocytes, bile duct cells, and liver endothelial cells to cause viral injuries. Besides apoptotic liver cells, fatty change is more frequent in COVID-19 patients while immune-mediated inflammation and drug toxicity may also lead to hepatic injuries. Thus, the risk of severe COVID-19 could be higher for liver transplant recipients using immunosuppressive drugs and especially for those with metabolic complications.[35] In addition, SARS-CoV-2 could infect kidney tissues by ACE2, CD147, and GRP78 with the assistance of TMPRSS2 and furin-like cleavage on spike protein directly to induce kidney injury. Acute kidney disease during COVID-19 can also be caused by activation of Complement system, cytokine storm, abnormal coagulation, rhabdomyolysis or possible direct injury to renal vascular caused by virus.[35] Dysregulation of intestinal microbiota, increase risk of cytokine storms and damage to mucosal immune system were proposed possible mechanisms of injury caused by SARS-CoV-2 on gastrointestinal tract causing abdominal pain and vomiting.[36]

Conclusion

This study found that the repurposed drugs used for the management of COVID-19 patients at the IDC, Olodo, Ibadan, Nigeria normalised certain haematological- and metabolic-parameters which were abnormal at the point of admission. Thus, the use of these repurposed drugs in the management of COVID-19 patients show promising results and should be considered for use in poor resource settings.

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Declarations

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Author contributions

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Conflicts of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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