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# COVID-19-induced Dyslipidemia and Disease Severity: Perspectives from Southern Nigeria

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## ABSTRACT

***Background:*** **The relationship between dyslipidemia and the severity of coronavirus disease 2019 (COVID-19) has extensively been characterized in the Western population with a dearth of data among Nigerians. Hence, the current study evaluated the lipid/lipoprotein disorders inherent in COVID-19 and its relationship with disease severity among Nigerians.**

***Methods:*** **This was a retrospective study conducted among 600 patients with RT-PCR-confirmed COVID-19 at the Eleme COVID-19 treatment facility in Port Harcourt, Southern Nigeria. Data were obtained from medical records using validated acquisition templates and analyzed based on lipid/lipoprotein abnormalities and disease severity status.**

***Results:*** **Among those studied, 54.7% had dyslipidemia while others were normolipidemic. HDL-C dyslipidemia was the most common with a preponderance of hypoalphalipoproteinemia (84.4%). Dyslipidemia afflicted mostly middle-aged, males, urban dwellers, the overweight, and those with classic COVID-19-induced respiratory symptoms. Dyslipidemic cohorts had higher pro-calcitonin, C-reactive protein, D-dimer, total white cell count, and neutrophils, but lower albumin, lymphocyte, and platelet counts compared to the normolipidemic cohorts. Dyslipidemic cohorts with concurrent severe COVID-19 had lower levels of TChol, Tg, HDL-C, and LDL-C levels compared to patients with the less-severe disease. HDL-C was the only lipid/lipoprotein parameter that was associated with severe COVID-19 on crude (OR:8.65; CI:5.96-11.44; p<0.001) and adjusted (OR:8.11; CI:5.65-10.87; p<0.001) regression models compared to other lipid/lipoprotein indices. At 96.77% sensitivity and 89.20% specificity, HDL-C had robust predictive potentials (AUC:0.97; CI:0.84-1.00; p<0.001) over COVID-19 severity.**

**Conclusion: Dyslipidemia is frequent among those presenting with COVID-19 in association with disease severity, especially among the HDL-C dyslipidemic cohorts. Hence, these findings should be factored in during COVID-19 treatment among Nigerians with the disease.**

**Keywords:** COVID-19, COVID-19 severity, dyslipidemia.

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## I. Introduction

Despite all the global efforts channeled towards the current novel coronavirus disease 2019 (COVID-19) pandemic induced by the acute respiratory syndrome coronavirus-2 (SARS-COV-2), the spread of the causative virus remains a cause for concern in some regions of the world including economic powerhouse countries like China and the United States [1]. Though the mortality attributed to the disease is currently on the decline due to the rapid vaccination deployment and more refined management protocols in most countries, the disease has continued to impact negatively on both the global economy and healthcare systems [1], [2]. Ever since the disease evolution from Wuhan City, Hubei province, China in the latter part of 2019, the precise pathogenesis of the disease has continued to evolve on a daily basis but remains an area of debate by several medical professionals in the literature [3], [4]. However, while most patients present with majorly mild variants of the disease that can rapidly progress, others can present with severe and critical conditions with catastrophic consequences [5].

Based on available data, numerous epidemiologic, demographic, pre-existing comorbidities, clinical, radiological, biochemical, and hematological factors have been associated with the severity of COVID-19 [6]. With the

unprecedented surge of COVID-19-related research and as the pandemic continues to evolve, some other factors in association with the disease severity continue to emerge [7]. Recently, several reports have demonstrated the preponderance of dyslipidemia among patients presenting with COVID-19 and these reports have also associated it with adverse outcomes [8]-[11]. Consequently, converging opinions have indicated the incrimination of COVID-19-induced dyslipidemia in association with the disease severity [8], [10]. However, some of these previous reports have been characterized mostly among COVID-19 patients with varied comorbid conditions that may have influenced the outcome of these previous observations. Moreover, the impact of COVID-19-induced dyslipidemia in the Nigerian setting is yet to be exhaustively investigated to date.

Herein, we evaluated the lipid/lipoprotein status and its relationship with disease severity among COVID-19 patients who are devoid of any pre-existing comorbid conditions, in Rivers State, Nigeria.

## II. Materials and Methods

### A. Study Location/Site

The study was conducted at the COVID-19-designated treatment facility located in Eleme Local Government Area of Rivers State, Nigeria. The facility is one of the facilities set up by the Rivers State Government at the peak of the COVID-19 pandemic and it has a side laboratory well-equipped with standard chemistry/hematology auto analyzers. COVID-19 patients presenting at the facility are usually referred from a COVID-19 holding area at the Rivers State University Teaching Hospital (RSUTH) following a positive nasopharyngeal and/or oro-pharyngeal swab reverse-transcriptase polymerase chain reaction (RT-PCR) test for COVID-19-related antigens at the RSUTH molecular laboratory.

### B. Study Design

This was a retrospectively designed cross-sectional observational study to actualize its study's primary aim and specific objectives.

### C. Ethical Considerations

Approval was sought/obtained by the Research Ethics Committee of Rivers State Hospital Management Board (RSHMB) before commencement. The study was subsequently conducted with strict adherence to the RSHMB Research Ethics protocols and per the principles embodied in the Helsinki Declarations of 1964, and as revised recently in 2013. The anonymity of patients was respected/maintained throughout the study. Informed consent was not deemed necessary due to the solely data-base study design which did not involve direct interface with the patients.

### D. Study Materials/Population

This was solely archived data of patients with RT-PCR-confirmed COVID-19 who were managed at the treatment facility during 2020-2022.

### E. Sample Size Determination

The minimum sample population required was approximately 268. This was calculated using the sample size formula for evaluating variables in a population of ≥10,000, at a 95% confidence interval and 5% margin of error, using a recently reported prevalence rate of 22.4% [12]. Though the calculation yielded 268 sample size population. However, due to the availability of data, 600 eligible patients' data were selected to enhance the study power.

### F. Eligibility Criteria

The criteria for inclusion are as follows: age ≥18 years at the time of diagnosis, stable health status before COVID-19 infection/diagnosis, and having lipid profile parameters done within 24 hours of presentation at the treatment facility. Excluded patients were based on pregnancy, being on recent lipid-lowering drugs, unconsciousness, history of previous COVID-19 infection, and pre-existing comorbid conditions (aged ≥65 years, lipid/lipoprotein disorders, cardiovascular disease, hypertension, chronic lung disease, asthma, sickle cell disease, HIV/AIDS, diabetes, cancer, obesity, chronic kidney disease, chronic liver disease, cigarette smoker, transplant recipient, and receiving immunosuppressive therapy), and incompleteness of relevant data.

### G. Infection Prevention/Control

Adequate infection prevention and control measures as recommended by the Nigeria Center for Disease Control (NCDC) were strictly adhered to during the data acquisition, specimen collection, and laboratory analysis [13].

### H. Sampling Method

To avail every patient's data an equal chance of inclusion, a probability-type sampling technique (simple random) was used to recruit the required sample size population from a sampling frame of an eligible 751 population.

### I. Data Collection

This was done by trained research assistants, who are authorized staff at the treatment facility, using validated data collection templates from various hard/soft medical records (case notes, medical review charts, nurses' charts, and laboratory records). Relevant data obtained from each participant were age (years), sex, body mass index (BMI), vital signs including body temperature (BT), respiratory rate (RR), pulse rate (PR), oxygen saturation ($SpO_2$), symptoms, pre-existing comorbidities, and relevant laboratory data. The laboratory data included total cholesterol (TChol), low-density lipoprotein (LDL-C), high-density lipoprotein (HDL-C), triglyceride (Tg), electrolyte, urea, creatinine, random plasma glucose (RPG), albumin, total protein, inflammation-related markers including C-reactive protein (CRP), D-dimer, and hematological parameters including full blood count (FBC)/differentials, and platelet counts.

### J. Specimen Acquisition, Processing, and Laboratory Analysis

Specimen acquisition/analysis was handled while adhering to standard protocols at the treatment facility. Heparin tube-derived plasma was analyzed for plasma electrolytes on an ion-selective electrode chemistry analyzer (SFRI 6000, SFRI Diagnostics, Berganton, France) including the analysis for

urea, creatinine, albumin, total protein, TC, LDL, HDL, Tg, and CRP on an automated chemistry analyzer (BS200, Mindray, Shenzhen, China). EDTA tube-acquired whole blood was analyzed for FBC, and platelet counts on an automated hematology analyzer (BC10, Mindray, Shenzhen, China). Plain-tube processed serum was analyzed for pro-calcitonin, and D-Dimer on an automated immunoassay analyzer (Mini Vidas, Biomerieux, France).

### *K. Definitions/Stratifications*

#### *1) Disease severity*

COVID-19 severity was classified based on the Nigerian Centre for Disease Control National (NCDC) case management guideline as less severe or severe [13]. The disease severity was defined as the presence of fever >38 °C or suspected respiratory infection, plus one of respiratory rate >30 breaths/min; severe respiratory distress; oxygen saturation (SpO2) of ≤ 93% on room air and the presence of co-morbid conditions such as diabetes, asthma, hypertension in adults and cough or difficulty in breathing and at least one of the following central cyanosis or SpO2 < 92%; severe respiratory distress e.g. grunting breathing, very severe chest in-drawing and signs of pneumonia in children.

#### *2) Dyslipidemia Definitions/Categorization*

This was defined based on the United States National Cholesterol Education Program Adult Treatment Panel 111 (NCEP-ATP 111) guidelines if any of the following lipid/lipoprotein parameter cut-off values is exceeded [14]:

i. TChol </> 5.2 mmol/L (TChol dyslipidemia: hypercholesterolemia or hypocholesterolemia)

ii. Tg</> 1.7 mmo/L (Tg dyslipidemia: hypertriglyceridemia or hypotriglyceridemia)

iii. HDL-C </>1.0 mmol/L in males/>/>1.3 mmol/L in females (HDL dyslipidemia: hyperalphalipoproteinemia or hypoalphalipoproteinemia)

iv. LDL-C </> 3.36 mmol/L (LDL-C dyslipidemia: hyperabetalipiproteinemia or hypoabetalipoproteinemia)

#### *3) Age groups/BMI Class Strata*

Age was categorized as young adults (18-44 years) or middle-aged (45-64 years). While BMI was categorized as normal weight (18.5-24.9 kg/m$^2$) or overweight (25.0-29.9 k/m$^2$).

### *L. Data Management/Statistical Analyses*

Data were managed/analyzed using the Statistical Package for Social Sciences software version 25.0 (IBM Co., Armonk, NY, USA). The continuous variables were initially evaluated for conformity to a normal distribution using statistical parameters. Continuous data not fitting normal patterns were log-transformed before analysis, summarized using means ± standard deviations, and compared with independent student t-test. Categorical data were summarized using proportions as counts/percentages and compared using the Chi-square test. Logistic regression models were used to determine the magnitude of the relationship between variables. Receiver operating characteristics analysis was used to evaluate the predictive potentials of parameters. A p-value ≤0.05 was deemed statistically significant.

## III. Results

During the studied period, 893 RT-PCR-confirmed COVID-19 patients presented, and 751 met the eligibility criteria from which 600 eligible patients' data were randomly selected for analysis.

Among those studied (n=600), 328 (54.7%) had dyslipidemia while others (n=272;45.3%) had normolipidemia. HDL-C dyslipidemia (n=154) was the most common dyslipidemia documented among the patients with a preponderance of hypoalphalipoproteinemia (n=110;84.4%) (Table I). This was followed by triglyceride dyslipidemia (n=134) with preponderance of hypertriglyceridemia (n=90;80.6%), LDL-C dyslipidemia (n=122) with preponderance of hypoabetalipoproteinemia (n=82;68.9%), and total cholesterol dyslipidemia (n=118) with a preponderance of hypocholesteronemia (n=78;66.1%) (Table I).

Middle-aged patients, males, those in marital unions, urban dwellers, majorly Christians, and overweight patients predominated among those with established dyslipidemia in the current study (Table II). The dyslipidemic patients also had higher body temperature, systolic blood pressure, respiratory rate, and severe disease frequency but lower oxygen saturation level at presentation (Table II). In addition, those with dyslipidemia had higher proportions of the classic respiratory and other-related symptoms (fever, cough, dyspnea, loss of taste, loss of smell, fatigue/lethargy, congested/runny nose, sneezing, sore throat, and arthralgia/myalgia) of COVID-19 compared to those with normolipidemic status at presentation (Table II).

TABLE I: Categories and Sub-categories of Lipid/Lipoprotein Status among Study Population

| Panel | Description, n (%) | Total Number | Percent | p-value |
|---|---|---|---|---|
| A | Lipid/Lipoprotein Status, n=600 (100%) | | | 0.004* |
| | Dyslipidemia | 328 | 54.7 | |
| | Normolipidemia | 272 | 45.3 | |
| B | Dyslipidemia Sub-Categories, | | | |
| B1 | TChol Dyslipidemia, n=118 (19.6%) | | | 0.002* |
| | Hypercholesterolemia | 40 | 33.9 | |
| | Hypocholesterolemia | 78 | 66.1 | |
| B2 | Tg Dyslipidemia, n= 134 (22.3%) | | | <0.001* |
| | Hypertriglyceridemia | 108 | 80.6 | |
| | Hypotriglyceridemia | 26 | 19.4 | |
| B3 | HDL-C Dyslipidemia, n= 154 (25.7%) | | | <0.001* |
| | Hyperalphalipoproteinemia | 24 | 15.6 | |
| | Hypoalphalipoproteinemia | 110 | 84.4 | |
| B4 | LDL-C Dyslipidemia, n= 122 (20.3%) | | | 0.006* |
| | Hyperabetalipoproteinemia | 38 | 21.1 | |
| | Hypoabetalipoproteinemia | 84 | 68.9 | |

*Statistically significant; TChol: Total cholesterol; Tg: Triglyceride; HDL-C: High-density cholesterol: LDL-C: Low-density cholesterol

TABLE II: DESCRIPTIVE ANALYSIS OF THE NON-LABORATORY VARIABLES BY LIPID/LIPOPROTEIN STATUS

| | Normolipidemia n = 272 | Dyslipidemia n = 328 | p-values | Entire Cases n = 600 |
|---|---|---|---|---|
| Demographic/Clinical Variables | Mean ± SD/n | Mean ± SD/n | | Mean ± SD/n |
| Age, mean, years | 41.98 ± 6.11 | 43.66 ± 6.79 | 0.084 | 42.33 ± 6.23 |
| Age group: young adults/middle-aged | 212/60 | 28/300 | 0.013* | 240/360 |
| Gender: male/female | 72/200 | 228/100 | <0.001* | 300/300 |
| Marital status: married/single | 192/80 | 268/60 | <0.001* | 260/140 |
| Residential area: urban/rural | 252/20 | 288/40 | <0.001* | 540/60 |
| Religion: Christian/Moslem | 256/16 | 320/8 | <0.001* | 576/24 |
| Alcohol intake: Positive/Negative | 28/244 | 104/224 | 0.114 | 132/468 |
| Mean BMI, kg/m$^2$ | 27.92 ± 4.55 | 28.78 ± 5.11 | 0.075 | 28.33 ± 4.64 |
| BMI class: Ideal weight/overweight | 168/104 | 84/244 | <0.001* | 252/348 |
| Body temperature, ºC | 37.44 ± 1.17 | 38.86 ± 1.26 | 0.013* | 37.71 ± 1.60 |
| SBP, mmHg | 136.77 ± 7.24 | 139.67 ± 7.47 | 0.022* | 137.86 ± 7.28 |
| DBP, mmHg | 83.56 ± 5.13 | 84.01 ± 5.33 | 0.076 | 85.51 ± 5.63 |
| HR/minute | 76.47 ± 4.23 | 77.08 ± 4.56 | 0.089 | 77.22 ± 4.42 |
| RR/minute | 23.77 ± 3.50 | 29.78 ± 3.84 | 0.017* | 23.45 ± 3.34 |
| Oxygen saturation ($SpO_2$), % | 92.75 ± 6.20 | 88.97 ± 5.65 | <0.001* | 93.86 ± 6.34 |
| Severe disease, Positive/Negative | 48/224 | 120/208 | 0.011* | 148/452 |
| Presenting Symptoms | | | | |
| Fever with/without chills or rigor | 260 | 324 | <0.001* | 584 |
| Cough | 262 | 326 | <0.001* | 588 |
| Dyspnea | 256 | 322 | <0.001* | 578 |
| Loss of taste | 130 | 202 | 0.014* | 332 |
| Loss of smell | 120 | 218 | 0.002* | 338 |
| Fatigue/lethargy | 226 | 310 | <0.001* | 336 |
| Congested/runny nose | 68 | 156 | 0.012* | 224 |
| Sneezing | 144 | 206 | 0.027* | 350 |
| Sore throat | 68 | 176 | <0.001* | 244 |
| Arthralgia/myalgia | 62 | 144 | 0.022* | 206 |
| Chest pain | 90 | 132 | 0.070 | 222 |
| Abdominal pain/discomfort | 66 | 92 | 0.457 | 158 |
| Nausea/vomiting | 76 | 102 | 0.304 | 178 |
| Anorexia | 72 | 80 | 0.311 | 152 |
| Diarrhea | 68 | 96 | 0.266 | 164 |
| Headache | 92 | 118 | 0.571 | 210 |
| Confusion/disorientation | 82 | 104 | 0.071 | 186 |
| Malaise | 62 | 84 | 0.361 | 146 |

*Statistically significant; M ± SD: mean ± standard deviation; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart rate; RR: respiratory rate; ICU: Intensive Care Unit.

TABLE III: DESCRIPTIVE ANALYSIS OF LABORATORY PARAMETERS BY LIPID/LIPOPROTEIN STATUS

| | Normolipidemia n = 272 | Dyslipidemia n = 328 | p-value | Entire Cases N=600 |
|---|---|---|---|---|
| Parameters, Reporting Units | Mean ± SD/n | Mean ± SD/n | | |
| Plasma/Serum Biochemical parameters | | | | |
| Sodium, mmol/L | 134.11 ± 8.15 | 133.85 ± 7.67 | 0.301 | 135.17 ± 8.55 |
| Potassium, mmol/L | 3.65 ± 1.11 | 3.34 ± 1.06 | 0.077 | 3.56 ± 1.40 |
| Chloride, mmol/L | 96.74 ± 6.78 | 95.79 ± 6.59 | 0.344 | 95.64 ± 6.70 |
| Bicarbonate, mmol/L | 23.05 ± 4.32 | 22.90 ± 4.14 | 0.560 | 23.66 ± 4.63 |
| Urea, mmo/L | 6.40 ± 1.43 | 6.70 ± 1.57 | 0.061 | 6.60 ± 1.41 |
| Creatinine, µmol/L | 110.34 ± 9.27 | 119.33 ± 10.02 | 0.055 | 117.43 ± 10.16 |
| Albumin, g/L | 35.78 ± 4.60 | 33.33 ± 4.46 | <0.001* | 34.82 ± 4.58 |
| Total protein, g/L | 65.02 ± 5.46 | 64.91 ± 5.65 | 0.460 | 64.34 ± 5.56 |
| Pro-calcitonin, µg/L | 1.70 ± 0.32 | 2.80 ± 0.89 | <0.001* | 1.80 ± 0.50 |
| C-reactive protein, nmol/L | 141.51 ± 9.88 | 278.72 ± 11.64 | <0.001* | 166.21 ± 9.66 |
| Hematological/Coagulation parameters | | | | |
| D-Dimer, µg/L FEU | 714.77± 96.64 | 2,231 ± 99.88 | <0.001* | 772.51 ± 99.62 |
| Total WBC x $10^9$/L | 14.11 ± 2.65 | 18.07 ± 3.67 | <0.001* | 15.14 ± 3.91 |
| Neutrophil count x $10^9$/L | 11.64 ± 2.57 | 16.11 ± 2.84 | <0.001* | 12.65 ± 2.76 |
| Lymphocyte count x $10^9$/L | 1.62 ± 0.56 | 1.09 ± 0.33 | 0.011* | 1.63 ± 0.77 |
| Platelet count x $10^9$/L | 143.63 ± 7.81 | 119.06 ± 6.55 | <0.001* | 139.51 ± 7.04 |

TABLE IV: DESCRIPTIVE ANALYSIS OF LIPID PARAMETERS BY COVID-19 SEVERITY AMONG COVID-19 PATIENTS WHO HAD DYSLIPIDEMIA

| | DYSLIPIDEMIC COHORTS, n=328 | | | |
|---|---|---|---|---|
| Parameters, Reporting Units | Less Severe Disease n = 208 (63.4%) | Severe Disease n = 120 (36.6%) | p-value | Entire Cases n=164 |
| | Mean ± SD | Mean ± SD | | Mean ± SD |
| TChol, mmol/L | 5.33 ± 1.25 | 3.27 ± 1.04 | <0.001* | 5.05 ± 1.34 |
| Tg, mmol/L | 1.67 ± 0.45 | 1.01 ± 0.05 | <0.001* | 1.75 ± 0.67 |
| HDL-C, mmol/L | 1.22 ± 0.23 | 0.91 ± 0.14 | <0.001* | 1.00 ± 0.85 |
| LDL-C, mmo/L | 2.96 ± 1.13 | 1.84 ± 0.76 | <0.001* | 2.88 ± 1.22 |

*Statistically significant; TChol: Total cholesterol; Tg: Triglyceride; HDL-C: High-density cholesterol: LDL-C: Low-density cholesterol

TABLE V: EVALUATION OF LIPID/LIPOPROTEIN PARAMETERS AS RISK FACTORS FOR COVID-19 SEVERITY

| | Severity of COVID-19 | | | |
|---|---|---|---|---|
| | Crude logistic regression | | Adjusted logistic regression** | |
| Lipid/lipoprotein Parameters | OR; 95% CI | p-values | OR; 95% CI | p-values |
| TChol, mmol/L | 1.13 (0.56 - 1.47) | 0.107 | 1.06 (0.50 – 1.66) | 0.177 |
| Tg, mmol/L | 1.46 (0.86 – 1.94) | 0.090 | 1.20 (0.67 – 1.83) | 0.121 |
| HDL-C, mmol/L | 8.65 (5.96 – 11.44) | <0.001* | 8.11 (5.65 – 10.87) | <0.001* |
| LDL-C, mmol/L | 1.49 (0.81 – 1.95) | 0.122 | 1.18 (0.68 – 1.80) | 0.161 |

*Statistically significant; TChol: Total cholesterol; Tg: Triglyceride; HDL-C: High-density cholesterol: LDL-C: Low-density cholesterol; OR: odds ratio; CI: confidence interval; **Adjusted for age, gender, marital status, residential area, religion, overweight, body temperature, systolic blood pressure, oxygen saturation, fever, plasma albumin levels, pro-calcitonin, C-reactive protein, D-dimer, total white cell count, neutrophil, and lymphocyte counts.

TABLE VI: PREDICTIVE POTENTIALS OF LIPID/LIPOPROTEIN PARAMETERS AS RISK FACTORS FOR COVID-19 SEVERITY USING THE RECEIVER OPERATING CHARACTERISTICS CURVE (ROC) ANALYSIS

| Lipid/lipoprotein Parameters | Sensitivity, % | Specificity, % | AUC | 95% CI | p-value |
|---|---|---|---|---|---|
| TChol, mmol/L | 36.20 | 44.40 | 0.31 | 0.12 - 0.67 | 0.220 |
| Tg, mmol/L | 41.62 | 68.33 | 0.29 | 0.10 - 0.57 | 0.307 |
| HDL-C, mmol/L | 96.77 | 89.20 | 0.97 | 0.84 -1.00 | <0.001* |
| LDL-C, mmol/L | 28.90 | 66.32 | 0.36 | 0.18 - 0.75 | 0.188 |

*Statistically significant; TChol: Total cholesterol; Tg: Triglyceride; HDL-C: High-density cholesterol: LDL-C: Low-density cholesterol; AUC: area under the curve; CI: confidence interval.

The dyslipidemic cohorts had higher pro-calcitonin, C-reactive protein, D-dimer, total white cell count, and neutrophils concentration/levels, but lower albumin concentration, lymphocyte, and platelet counts compared to the normodyslipodemic cohorts (Table III).

Among the COVID-19 patients who had dyslipidemia (n=328), 120 (36.6%) had severe disease while 208 (63.4%) had less severe disease variants (Table IV).

The dyslipidemic COVID-19 patients with severe disease had lower levels of TChol, Tg, HDL-C, and LDL-C levels compared to dyslipidemic patients with less severe disease (Table IV).

HDL-C was the only lipid/lipoprotein parameter that was significantly associated with severe COVID-19 disease on unadjusted logistic regression analysis (OR: 8.65; CI: 5.96-11.44; p<0.001) which was mildly attenuated but maintained statistical significance following adjustment for confounders (OR: 8.11; CI: 5.65-10.87; p<0.001) compared to Tchol, Tg and LDL-C (Table V).

At 96.77% sensitivity and 89.20% specificity, HDL-C had robust/significant predictive potentials (AUC: 0.97; CI: 0.84 -1.00; p<0.001) over COVID-19 severity compared to TChol, Tg, and LDL-C using the receiver operating characteristics curve (ROC) analysis (Table VI).

## IV. DISCUSSION

### *A. Principal Findings*

The study had some interesting findings which corroborate and strengthen previous reports that have explored this subject within the existing literature. Among the population studied, majority (54.7%) had dyslipidemia. HDL-C dyslipidemia is the most common with a preponderance of hypoalphalipoproteinemia. Dyslipidemia afflicted mostly the the middle-aged, males, urban dwellers, the overweight, and those with a higher preponderance of the classic COVID-19-induced respiratory symptoms.

The dyslipidemic cohorts had higher pro-calcitonin, C-reactive protein, D-dimer, total white cell count, and neutrophils, but lower albumin levels, lymphocyte and platelet counts compared to the normolipidemic cohorts. In addition, dyslipidemic cohorts with concurrent severe COVID-19 had lower levels of TChol, Tg, HDL-C, and LDL-C levels compared to COVID-19 patients with less severe disease. HDL-C was the only lipid/lipoprotein parameter that was associated with severe COVID-19 on crude and adjusted regression models compared to other lipid/lipoprotein parameters. At 96.77% sensitivity and 89.20% specificity, HDL-C had robust predictive potentials over COVID-19 severity.

### *B. Relationship with Existing Literature*

Frequencies of dyslipidemia among COVID-19 patients have differed dramatically in recent times within existing literature. Frequencies as low as 2.8%, 32.5%, 28%, and 80.5% have been documented among Asians, Americans, Europeans, and Africans, respectively [15]-[18]. These diverse rates may be related to environmental and genetic factors that tend to define the population distribution of lipid/lipoproteins [18]. Hence, the rate observed in the current study seems to align with reports of these previous studies. In contrast, these previous studies had recruited mostly patients with varied comorbid conditions that may have also contributed to the variations in these differing frequencies [15]-[18]. The preponderance of dyslipidemia among middle-aged, males, the urban-dwellers, and those with the classic symptoms of COVID-19 may indicate the severity of the disease and reinforces the relationship between dyslipidemia and COVID-19 severity, as recently documented [19]. A recent exhaustive review of existing literature on this subject does indicate that dyslipidemia enhances COVID-19 severity and this relationship was stronger among the older age groups and the males [19].

Additionally, various studies have been documented on the hyper-inflammatory responses to COVID-19 [20]-[23]. Consequently, COVID-19-induced dyslipidemia has been implicated in the tendency to develop hyper-inflammatory responses among patients with the disease. Recent research evidence has shown that lipid parameters decreased with increasing severity of COVID-19 in association with inflammatory markers [24]. This finding is consistent with the conclusions of the current study where dyslipidemic cohorts had an increasing trend of various biomarkers consistent with inflammatory processes compared to the normolipidemic cohorts. The inherent hyper-inflammatory

responses in COVID-19 may well explain the lower lipid/lipoprotein parameters observed among the dyslipidemic patients with severe COVID-19 in the current study, which has previously been documented [24]. However, among the lipid/lipoprotein parameters evaluated and in line with previous studies, HDL had the most significant association with, and predictor of, severe COVID-19 disease [8]-[11], [25]-[27].

### C. Relevant Pathomechanisms

Consistent with previous reports [8]-[11], [25]-[29], lower levels of plasma TC, LDL-C, HDL-C, and higher plasma Tg levels in association with COVID-19 severity were observed in the current study. These lipid/lipoprotein patterns and the associated COVID-19 severity have been hinged on both the quantitative and qualitative changes that accrue to lipid/lipoprotein parameters, especially HDL-C molecule, following the inherent hyper-inflammatory responses in COVID-19 [8]. The various cytokines, inflammatory mediators, modified lipids (oxidized HDL-C/LDL-C), and intermediate lipid classes (smaller LDL) generated during the infection interfere with several steps of lipid metabolism by reducing cholesterol synthesis and absorption, decreasing triglyceride-rich lipoprotein clearance (via inhibition of lipoprotein lipase enzyme) or reducing HDL-C-associated apolipoprotein A1 synthesis, increased HDL clearance (due to enhanced uptake of inflammatory biomarker such as serum amyloid A protein by the HDL-C molecule) [8].

As documented in the current study, the impact of COVID-19-induced lipid/lipoprotein indices is disproportionately tilted toward HDL-C dyslipidemia. HDL-C exhibits antioxidant, anti-inflammatory, antithrombotic, an immune-modulating roles, and may neutralize pathogen-associated lipids that mediate an exaggerated immune response in several infective conditions including COVID-19 [8]-[11], [28],[29]. This may well account for the preponderance of HDL-C dyslipidemia associated with severe COVID-19 in the current study.

### D. Relevance to Clinical Practice and Future Research

The analysis of lipid/lipoprotein parameters should be contemplated as another clinical tool to evaluate the SARS-CoV-2 infection status, prognosis, clinical course, and severity. As therapeutic targets, efforts should be intensified toward clinical trials for effective lipid-raising agents or agents that may ameliorate the impact of COVID-19 and its associated consequences on lipid/lipoprotein metabolism.

### E. Strength and Limitations

The study was strongly strengthened by the recruitment/analysis of only patients with RT-PCR-confirmed COVID-19 without any pre-existing comorbid conditions. Yet, the study was limited by a few factors which are potential areas for improvement in future research. As with most observational studies, its conclusions do not infer causal links but associations. Secondly, it was a single-center study with predominantly black populations, so, its findings may not be reflecting the larger population of other races.

## V. Conclusion

Dyslipidemia was frequent among those presenting with COVID-19 in the current study, especially the HDL-C dyslipidemia subtype. It afflicted mostly middle-aged, males, urban dwellers, the overweight, and those with a higher preponderance of the classic COVID-19-induced respiratory symptoms, inflammatory markers, and severe disease variants. These findings should be factored in during COVID-19 treatment among Nigerians with the disease. However, further studies are recommended.

## Ethical Statements

The ethical approval of the study was obtained from the Research Ethics Committee of RSHMB following the review of the study protocols and the study was subsequently executed in compliance with the principles embodied in the Helsinki Declaration.

## Author Contributions

All the authors were involved substantially in the concept and design of the study, data acquisition, analysis and interpretation of the data, drafting the article, revising the article critically for its intellectual content, and in the final approval of the version to be published.

## Data Availability

The data that support the findings of this study are not publicly available due to their containing information that could compromise the privacy of research participants but are available from the corresponding author (CA) upon reasonable request.

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## Conflict of Interest

Authors declare that they do not have any conflict of interest.

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