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Original Research Article

Characteristics of Lipid Metabolism Disorders in Type 2 Diabetic Patients with COVID-19 in Pointe Noire

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Abstract: ***Introduction*:** Chronic diabetes leads to dyslipidaemia. Patients with dyslipidaemia, the most common risk factor for cardiovascular disease, also have a higher risk of severe evolution of COVID-19. ***Objective*:** To study the characteristics of lipid profile disorders in COVID-19 positive type 2 diabetic patients in Pointe-Noire. ***Methods*:** We recruited a total of 206 participants for this study. Detailed information on age, gender, and health status of participants was collected from medical records. Biomarkers were quantified from blood samples and the sars cov-2 virus was identified using the PCR technique on nasopharyngeal swabs. ***Results***: The majority of patients were male (70.39%), COVID-19 severe symptoms (67%) and comorbidities (57.77%) were more common. CT↑39%, LDL↑36%, HDL↓77% and TG↑68% in non-survivors were found in patients with severe disease severity. A positive correlation between atherogenic indices (AIP, CRR and AC) with TC, LDL and TG then, an inverse linear relationship with HDL. There was also a negative correlation between CPI and HbA1c. ***Conclusion*:** The results of our study show that T2DM with severe signs of COVID-19 have high levels of harmful lipids (TG, CT and LDL) and high atherogenic indices (AIP, CRR and AC), while low levels of HDL, a cholesterol-trapping lipoprotein, and low CPI correlate negatively with HbA1c.

Keywords: Lipid disorders, type 2 diabetes, COVID-19, Pointe Noire.

1-INTRODUCTION

The chronic nature of diabetes can lead to a number of complications, including dyslipidaemia. Dyslipidaemia is a metabolic abnormality caused by the body's inability to manage triglyceride (TG) metabolism correctly. Numerous studies suggest that defective serum triglyceride metabolism results from insulin resistance (Austin MA *et al.,* 1998). It establishes a situation in which cholesterol metabolism is also strongly influenced. This involves quantitative and qualitative changes affecting all the lipoprotein subclasses, due to the metabolic links between them. The changes induced by defective triglyceride metabolism make lipoproteins more atherogenic and facilitate additional pathological changes caused by the diabetic environment (oxidation, glycosylation) (Assmann G *et al.,* 1998).

SARS-CoV-2 is an enveloped virus surrounded by a lipid bilayer, with a genome of around 30,000 nucleotides, encoding four structural proteins: the spike protein (S), the envelope protein (E), the membrane protein (M) and the nucleocapsid protein (N) (Zeng W *et al.,* 2020). Of these, the S protein plays the most important roles in virus attachment, fusion and entry. It ensures viral entry into host cells by binding its receptor binding domain (RBD) in the S1 subunit to angiotensin converting enzyme 2 (ACE2) as a host receptor, then fusing the viral and host membranes via the S2 subunit (Li GM *et al.,* 2020). Viral infectivity depends on interactions between host cell plasma membrane components and the virus envelope (Surma, S *et al.,* 2021).

Coronavirus 2019 (COVID-19) disease has resulted in significant morbidity and mortality globally, particularly in people with underlying co-morbidities such as diabetes. (Huang *et al.,* 2020). Some studies suggest a bidirectional interaction between T2DM and COVID-19 (Rey-Reñones *et al.,* 2022). In fact, in patients with dyslipidaemia, systemic cholesterol levels are increased, which may lead to an increase in the number of ACE2 receptors in the lipid rafts of cells and facilitate the penetration of SARS-CoV-2 into these cells. It has been suggested that lipids, including fatty acids, interact with SARS-CoV-2 and could constitute a potential intervention strategy against COVID-19 (Toelzer C *et al.,* 2020). Furthermore, it has been shown that cholesterol, by influencing the configuration of the SARS-CoV-2 spike protein (S), could increase the affinity for ACE2 and therefore the infectivity of this coronavirus (Shoemark DK *et al.,* 2021).

As lipid profile disorders are major risk factors for cardiovascular complications in T2DM, understanding how COVID-19 specifically affects the lipid profile of type 2 diabetic patients is crucial for clinical management and prevention of complications.

The aim of this study was to investigate the characteristics of lipid profile disorders in COVID-19 positive type 2 diabetic patients in Pointe-Noire.

2-MATERIAL AND METHOD

2-1-Study Population

We conducted a descriptive cross-sectional study and the study population consisted only of T2DM patients with COVID-19 hospitalized at the Clinique Guenin, Louise Michel and Hôpital Général Adolphe sicé in Pointe-Noire.

2-2-Clinical Survey:

Data such as age, sex, covid-19 symptoms and comorbidities were collected from medical records.

2-3-Biological Survey:

Laboratory analyses were performed in the Laboratoire d'Analyses Biomédicales HDL of the Polyclinique Fondation Marie Madeleine Gombes in Pointe noire.

2-3-1-Sampling:

- Blood samples were taken on EDTA and heparinized tubes after a strict fasting period of at least 12 hours, and stored at -20°C until use.
- Nasopharyngeal sampling was performed by swabbing by gently pushing the swab deep into the nostril (up to the nasopharynx: approximately half the length from nose to ear) and detaching as many cells as possible by scraping the inner surface of the nostril using the virus collections and transport kit type citoswab (W/3ML VTM) supplied by CITOTEST LABWARE MANUFACTURING CO., LTD Haimen city 226100, China.

2-3-2-Analysis of Blood Biomarkers:

The Cobas C 311 automatic biochemistry analyzer (Roche Diagnostics, HITACHI, Germany) was used for biochemical analyses: fasting blood glucose (Gly), glycated hemoglobin (HbA1c), total cholesterol (TC), triglycerides (TG), high-density cholesterol (HDLc), low-density cholesterol (LDLc). And the Plasma Atherogenic Index (PAI): TG/HDLc, the Atherogenic Coefficient (AC): (CT-HDLc)/HDLc, the Cardiac Risk Ratio(CRR): CT/HDL, then the Cardioprotective Index(CPI): HDLc/LDLc were obtained by calculation.

2-3-3-Molecular Analysis:

a)-Extractions

We extracted RNA from nasopharyngeal secretions using Total RNA Purification Insert PI12200-37, Norgen Biotek Corp (CANADA), in accordance with the manufacturer's recommendations.

b)-Amplifications

➢ **Procedure:**

- First step: Mix preparation
  - 10µl 2x One-step RT-PCR (Master Mix Dx)

- 1.5 µl Enzyme
- 3.5 µl nuclease free water
- 5µl total RNA

- Step 2: Programming the Mic thermal cycler

Amplification parameters were as follows: initial reverse transcriptase at 50°C for 20 minutes, then denaturation at 95°C for 03 minutes followed by 45 cycles of denaturation at 95°C for 15 seconds and 30 seconds of hybridization at 58°C.

- Choice of fluorochromes and targets:
  - FAM (E-gene Sars-cov-2)
  - HEX (Internal Control).

2-4- Ethical Considerations:

This study was carried out in accordance with the guidelines of the Declaration of Helsinki and was approved under number 125/CERS/FMMG-2021/PNR by the Health Research Ethics Committee (CERS) of the Marie Madeleine Gombes Foundation in Pointe Noire.

2-5: Statistical Analysis:

Categorical data are expressed as numbers (percentage). Participants' characteristics were described by means and standard deviations. We checked the relationship between the indexes (AIP, CA, ICP, RRC) and the glucido-lipid profile, measured using Pearson correlation tests. Statistical analysis was performed using SPSS (version 26.0; IBM). In all calculations, $p < 0.05$ was considered statistically significant.

3-RESULTS

3-1-Sociodemographic and Clinical Characteristics:

Figures 1, 2 and 3 show that the study population consisted of 206 T2DM subjects with 70% (145) male subjects and 30% (61) female subjects. The sex ratio (M/F) was 2.37%. The mean age was 56.33 ± 12 years, with extremes ranging from 30 to 82 years. The most frequent symptoms were fatigue (97.57%), fever (97.08%), dyspnoea (96.11%) and cough (91.26%). Over 50% of our study population had loss of smell, taste and anorexia. 67.0% of our patients had severe symptoms. Over 57% of patients had a co-morbidity, of which hypertension was present in 33%. And 66% of our population were overweight. The clinical course showed that the proportion of non-survivors was 26%.

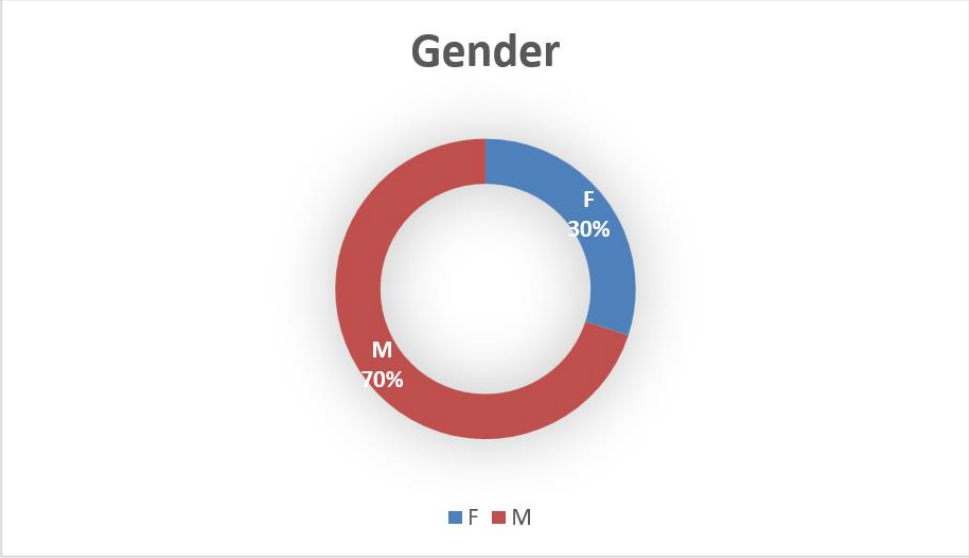

Figure 1: Breakdown of study population by gender

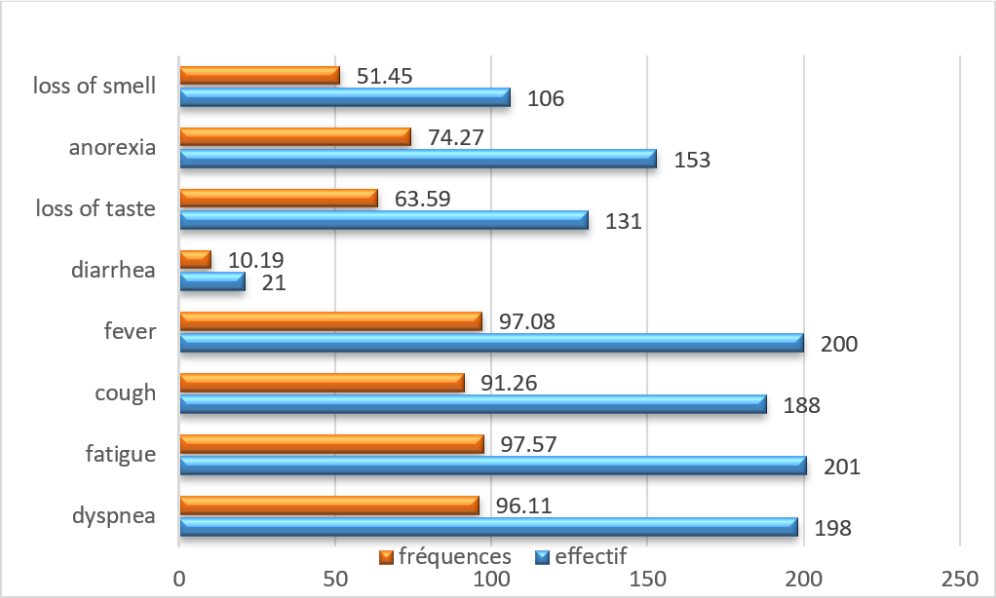

Figure 2: Symptoms of the study population

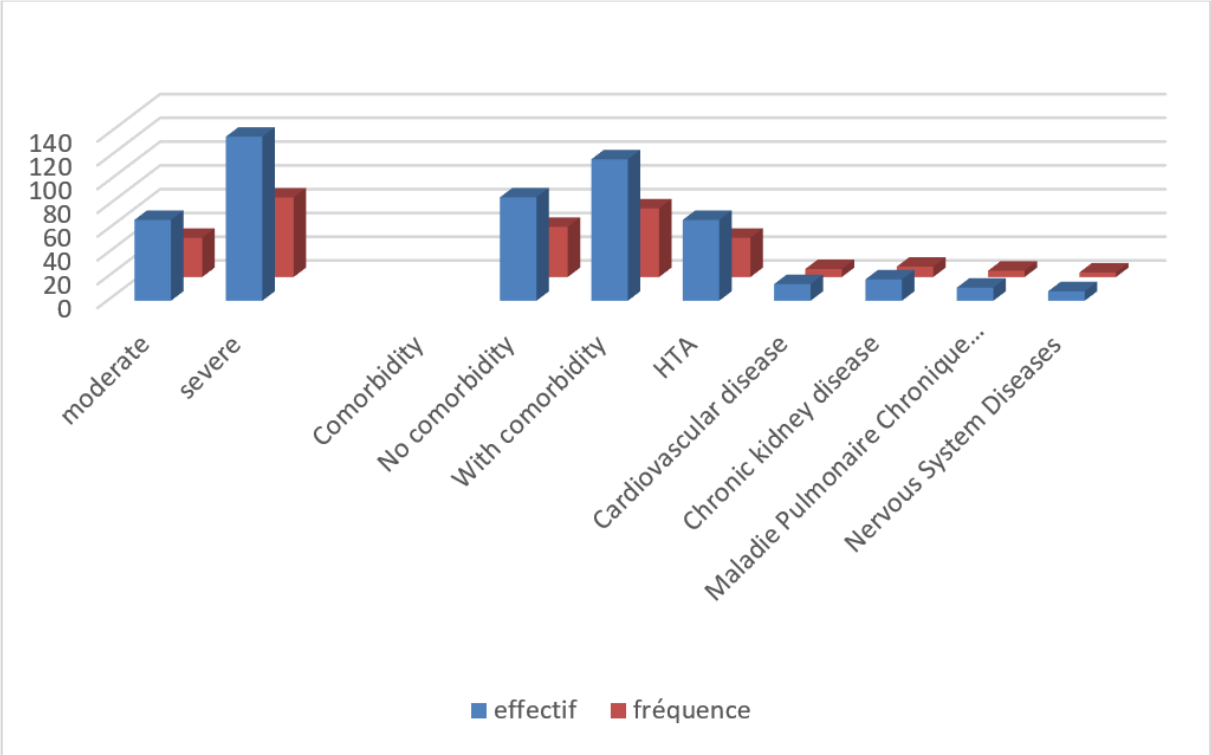

Figure 3: Health status of the study population

3-2 - Biological Characteristics According to Severity and Clinical Course

The results presented in Tables 1 and 2 show the descriptive statistics of carbohydrate metabolism in diabetics, blood lipid measurements and atherogenic indices according to the severity of signs and disease progression.

Table 1: Descriptive statistics of the comparison between moderate and severity

Characteristics	Moderate severity (Mean±SD), n=70	Severity (Mean±SD), n=136	p
AGE	54.11±11.04	55.49±1.,77	0.077
GLY	2.59±1.06	2.26±0.97	<0.001
HBA1c	7.92±1.89	8.56±1.88	0.8
TC	2.04±0.58	2.24±0.47	<0.001

Characteristics	Moderate severity (Mean±SD), n=70	Severity (Mean±SD), n=136	p
HDLc	0.53±0.13	0.41±0.29	<0.001
LDLc	1.26±0.51	1.49±0,54	0.006
TG	1.63±0.54	1.95±1.27	0.2
AIP	3.35±1.61	7.22±6.69	<0.001
AC	2.15±1.01	4.13±1.77	0.006
CRR	4.45±1.34	7.68±4.29	<0.001
CPI	0.64±0.68	0.36±0.49	<0.001

Table 2: Descriptive statistics of the comparison between survivors and non-survivors

Characteristics	No-survivor (Mean±SD), n=46	Survivor (Mean±SD), n=160	p
AGE	61.17±15,41	53.25±11,54	<0.001
GLY	2.83±1,14	2.25±0,93	0.002
HBA1c	7.98±1,84	7.89±2,10	<0.001
CT	2.17±0,39	2.18±0,55	0.9
HDLc	0.45±0,45	0.46±0,20	0.11
LDLc	1.32±0,37	1.44,57	0.12
TG	2.05±1,45	1.78±0,96	0.2
AIP	8.50±9,55	5.16±3,79	0.2
AC	5.15±0,37	3.6±0,77	0.12
CRR	7.71±4,87	6.08±3,59	0.2
CPI	0.47±0,77	0.45±051	0.4

3-3- Frequencies and types of dyslipidemia between moderate and severe severity according to clinical outcome

3-4-1: Dyslipidemia in Moderate COVID-19+DT2: This group includes 02 non-survivors and 68 survivors. Figure 4 shows the dyslipidemia in subjects with moderate severity. It can be seen that CT↑ and LDL↑ have zero proportion then HDL↓ 100% and TG↑50% in non-survivors.

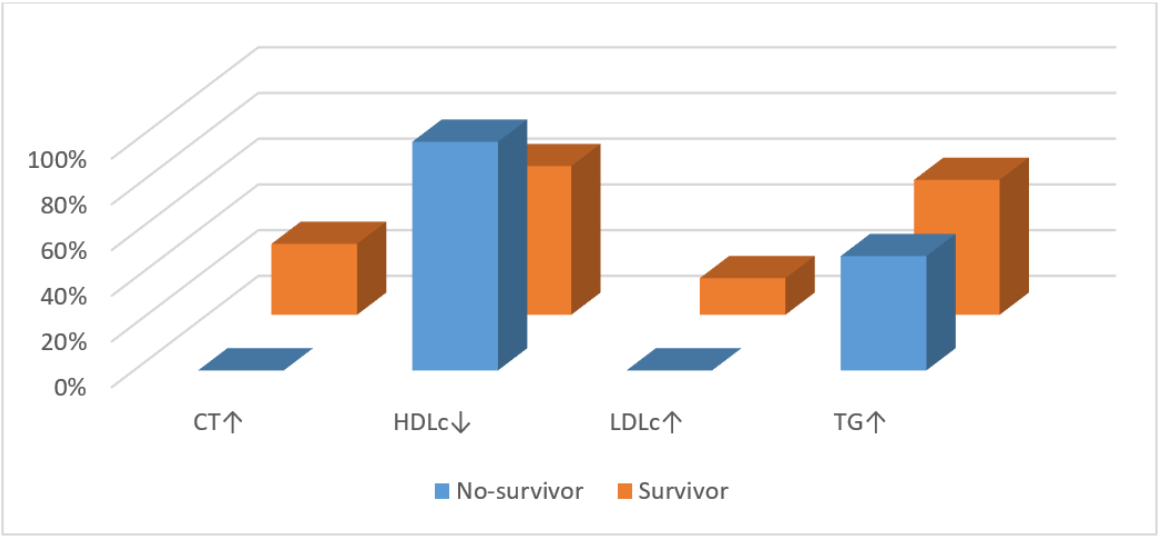

Figure 4: Frequency of moderate COVID-19+DT2 dyslipidemia between survivors and non-survivors

3-4-2: Dyslipidemia in severe COVID-19+DT2: This group comprises 44 non-survivors and 92 survivors. Figure 5 shows dyslipidemia in subjects with moderate severity. It can be seen that CT↑39%, LDL↑36%, HDL↓77% and TG↑68% in non-survivors.

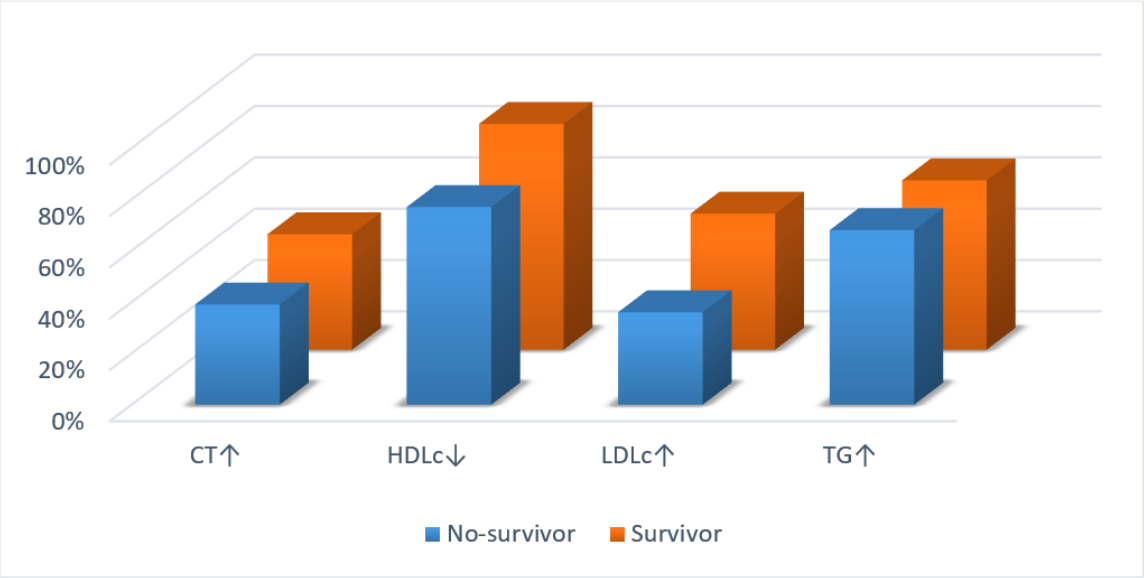

Figure 5: Frequency of dyslipidemia in severe COVID-19+DT2 between survivors and non-survivors

3-4- Relationship between Atherogenic Indices and Plasma Lipidemia

Table 3 shows a strong correlation between AIP and TG (r =0.86, p<0.001) and inversely with HDL (r= -0.56, p<0.0001). A strong association between AC with LDL(r=0.79, p<0.001) and TC (r=0.68, p<0.001). A strong inverse linear correlation of CRR with HDL(r= -0.79, p<0.001) and positive with TC(r=0.53, p<0.001). A strong correlation coefficient of between CPI with HDL(r=0.69, p<0.001) and negative with CT(r= -0.46, p<0.001) and, an inverse relationship with HbA1c(r= -0.22).

Table 3: Correlation between atherogenic indexes and lipids

Parameter 1	Parameter 2	r	95% CI	p
AIP	CT	0.27	[0.13, 0.39]	0.003**
AIP	TG	0.86	[0.81, 0.89]	< 0.001***
AIP	LDL	0.10	[-0.04, 0.23]	0.971
AIP	HDL	-0.56	[-0.65, -0.46]	< 0.001***
AIP	HBA1C	0.14	[0.00, 0.27]	0.793
AC	CT	0.68	[0.60, -0.75]	< 0.001***
AC	TG	0.13	[0.01, 0.26]	0.830
AC	LDL	0.79	[0.73, 0.83]	<0.001***
AC	HDL	0.23	[0.10, 0.35]	0.021*
AC	HBA1C	0.43	[0.31, 0.53]	< 0.001***
CRR	CT	0.53	[0.43, 0.63]	< 0.001***
CRR	TG	0.41	[0.29, 0.52]	< 0.001***
CRR	LDL	0.51	[0.40, 0.60]	< 0.001***
CRR	HDL	-0.72	[-0.78, -0.65]	< 0.001***
CRR	HBA1C	0.03	[-0.10, 0.17]	> 0.999
CPI	CT	-0.46	[-0.56, -0.35]	< 0.001***
CPI	TG	-0.25	[-0.37, -0.11]	0.008**
CPI	LDL	-0.62	[-0.70, -0.53]	< 0.001***
CPI	HDL	0.69	[0.61, 0.75]	< 0.001***
CPI	HBA1C	-0.22	[0.34,-0.08]	0.036*

4-DISCUSSION

The findings of numerous studies indicate that people with co-morbidities, such as hypertension, diabetes, obesity and underlying cardiovascular disease, are particularly vulnerable to the severe progression of COVID-19. Available data also suggest that patients with dyslipidemia, the most common risk factor for cardiovascular disease, are also at higher risk of severe progression of COVID-19. (Surma, S *et al.*, 2021). Thus, we conducted the present study whose aim was to Study the Characteristics of lipid profile disorders in COVID-19 positive type 2 diabetic patients in Pointe-Noire.

In our study, men predominated 145(70%) versus women 61(30%). Our results corroborate those of other studies carried out in Congo (Poaty H *et al.*, 2021; L.M.A. Boumba *et al.*, 2022). In reality, SARS-CoV-2 affects both sexes, with a male predominance; according to the literature, women have a greater immunological advantage than men (Wang J *et al.*, 2016). Several hypotheses may explain this inequality; male subjects express ACE2 receptors more than female subjects (Gebhard C *et al.*, 2020). The immune response to viruses is more developed in females (Sabra L *et al.*, 2022).

Our results show that fever, fatigue, dyspnea and cough were the most frequent severe symptoms in over 91% of the study population. We also observed that in 67% of cases these symptoms were severe. Our results are in line with most studies in the literature. (Plaçais & Richier, 2020 and Hadjadj *et al.*, 2023). Indicating that diabetic patients are more likely to develop a severe form of COVID-19.

The clinical course showed 46 (26.21%) deaths, and over 57.77% of our population had comorbidities, including 33% of hypertensive cases in our study population (Fig. 3). These results corroborate those presented in SITREP N°233 of 2022 concerning the 50-69 age group in the Republic of Congo. Global epidemiological data also show that patients aged 50-64 had 25 times greater risk of complications (CDC, 2020), severity and increased mortality. According to Marco Alifano *et al.*, 2020 Those most at risk of severe illness and death were those aged over 60 and with underlying diseases such as hypertension, diabetes, cardiovascular disease, chronic respiratory disease and cancer.

Comparing the lipid profiles of COVID-19 patients between severity groups, there were no significant differences in cholesterol levels between survival groups (Table 2). Mean cholesterol and TG levels were comparable in all groups, with patients with severe signs having slightly higher levels than those with moderate involvement. Similarly, the study found no significant difference in HDL-c levels between survival groups. Values were closely matched in all groups, with patients with moderate severity and survivors being slightly higher than their counterparts. These results are contrary to those found in the study by Yongli Yan *et al.*, 2020, whose lipid profiles were balanced. The study found slightly higher median LDL-c values in severe patients than in patients with moderate severity, and this difference was significant. This result differs with studies by Zhang *et al.*, 2020 and Ochoa-Ramírez *et al.*, 2024, which found that LDL-c levels were lower in COVID-19 patients with severe disease than in those with mild disease. This difference is justified by the fact that our study population consists solely of diabetic subjects.

The present study also assessed the frequency and Types of dyslipidaemia, we found that CT↑ and LDL↑ have zero proportion then HDL↓100% and TG↑50% in non-survivors in the group with moderate severity. In the group with severe severity the TC↑39%, LDL↑36%, HDL↓77% and TG↑68% in non-survivors. This suggests a potential association between elevated triglycerides, reduced HDL-c levels and an increased risk of mortality in patients with T2+COVID-19. Additional studies suggest that elevated triglycerides and low HDL-c are predictors of severity and mortality in COVID-19 (Malik, J *et al.*, 2021; Mahat, RK *et al.*, 2021; Masana, L. *et al.*, 2021). Indeed, dyslipidaemia is associated with damage to the immune, respiratory and cardiovascular systems, as well as elevated levels of pro-inflammatory cytokines. In addition, dyslipidaemia is associated with an increased risk of thrombotic complications, endothelial dysfunction and higher platelet activity (Sorokin AV *et al.*, 2021). Thus, lipid dysregulation may contribute to the morbidity and mortality associated with COVID-19 infection. However, the characteristics and dynamic changes in lipid profiles in patients with COVID-19, as well as their predictive value for disease severity and mortality, remain largely unknown. Compared with mild or asymptomatic COVID-19 patients, those with severe complications have a higher prevalence of comorbidities. People with severe complications have a higher prevalence of comorbidities such as arterial hypertension, cardiovascular disease and type 2 diabetes (Zheng Z *et al.*, 2020). What these comorbidities have in common are metabolic alterations such as insulin resistance and dyslipidaemia.

This study also shows an AIP↑ in severe cases and those with a poor prognosis; and there is a strong correlation between AIP with TG ($r = 0.86$, $p<0.001$) and an inverse linear relationship with HDLc ($r = -0.56$, $p<0.0001$). According to the work of Mei-Yueh Lee *et al.*, 2018 an AIP↑ ratio was significantly associated with albuminuria, coronary heart disease, Stroke) Vand peripheral arterial occlusive disease (PAOD) in T2DM and is also considered by Nwagha U.I *et al.*, 2010 to be a highly sensitive predictor of cardiovascular disease risk. There is a strong association between AC with LDL($r=0.79$, $p<0.001$) and CT ($r=0.68$, $p<0.001$) in addition to AC↑ in hard cases with T2DM+COVID-19. A strong inverse linear correlation of CRR with HDL($r= -0.79$, $p<0.001$) and positive with CT($r=0.53$, $p<0.001$). Subjects with CRR↑ are more likely to suffer from stroke or atherosclerosis (Saleh Elmezoughi1 *et al.*, 2024). We observe a CPI↓in severe cases, then, a strong correlation coefficient between CPI with HDL($r=0.69$, $p<0.001$) and negative with CT($r= -0.46$, $p<0.001$) and Hba1c($r= -0.22$, p: 0.036), this pattern shows that our T2+COVID-19 are fragile and susceptible to cardiovascular complications.

These indices are invaluable in assessing the risk of developing cardiovascular disease; the more precise the increase in AIP, AC and CRR and the decrease in IPC, the greater the predisposition to cardiovascular disease (Saleh Elmezoughi1 *et al.*, 2024).

5- CONCLUSION

The results of our study show that T2DM patients with severe signs of COVID-19 have high levels of harmful lipids (TG, TC and LDL) and high atherogenic indices (AIP, CRR and AC) and, on the other hand, low levels of HDL, cholesterol-scavenging lipoprotein and low CPI correlating negatively with HbA1c. As a result, these patients have a clear risk of death. Serum lipid ratios (AIP, CA, CPI, and RRC) can be used alongside lipid parameters in clinical practice to assess cardiovascular risk, even when lipid profiles are apparently normal. Better identification of patients at high risk of lipid metabolism disorders, such as COVID-19-positive diabetics, is important. This could make it possible to reduce mortality induced by the disease, and to optimise hypolipidemic treatment.

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