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Epidemiological and Clinical Aspects of Simple Steatosis and Non-Alcoholic Steato- Hepatitis Among Newly Diagnosed Type 2 Diabetes Patients at The Central Hospital in Yaoundé, Cameroon

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Abstract

Non-alcoholic fatty liver disease (NAFLD) is associated with metabolic comorbidities like type 2 diabetes mellitus (T2DM). The aim of this study was to determine the proportion of simple steatosis and non-alcoholic steatohepatitis, which are components of NAFLD, among newly diagnosed T2DM patients. This cross-sectional study was undertaken at the Central Hospital, Cameroon from March 2020 to September 2020 and it included all recently diagnosed T2DM patients, who had an alcohol consumption <140g (14 drinks/week) for women and <210g (21 drinks/week) for men, and without any signs of liver cirrhosis on abdominal ultrasound. All patients underwent a clinical examination with blood samples taken for lipid profile and transaminases measurements and an abdominal ultrasound assessment using a LOGIQ V5 Expert ultrasound machine. A total of 98 (53 males and 45 females) out of 128 eligible patients consented to participate in the study. The mean age was 50.31±10.51. NAFLD was present in 56.1% (55/98) patients; with mild and homogeneously diffused in 92.7% (51/55) and 94.5% (52/55) respectively. There were no significant differences in lipids profiles and transaminases between those with or without steatosis. Factors associated with fatty liver disease were body mass index ≥ 30 kg / m^2 (P = 0.0002), waist circumference ≥ 94 cm for men or ≥ 80cm for women (P = 0.004). In conclusion, NAFLD is a common feature in newly diagnosed T2DM in our setting. There is a need for more attention towards NAFLD by primary care physicians, specialists and health policy makers.

Introduction

Background and rationale

Non-alcoholic fatty liver disease (NAFLD) is defined as the presence of liver fat in the absence of excessive alcohol consumption; it encompasses a wide range of histological manifestations from simple steatosis, non – alcoholic steato hepatitis (NASH) to fibrosis or cirrhosis . The global prevalence of hepatic steatosis is increasing, likely as a result of the various components of metabolic syndrome, including type 2 diabetes mellitus which are risk factors of this disease and are present on a large population (T2DM)[2].

Hepatic steatosis is associated with many known complications including cardiovascular diseases or progression to liver cirrhosis, and its co- existence with unbalanced T2DM in a patient may be responsible of higher morbidity and mortality. As there is a current data gap on the epidemiology of hepatic steatosis among African patients with T2DM, we aimed at establishing whether it is a major prevalent condition among patients recently diagnosed with T2DM in Cameroon.

Our focus was on patients naive to treatment or recently initiated on treatment (less than 6 months), as they were less likely to have a metabolic profile modified by treatment, thus providing a true representation of the magnitude of this condition among T2DM patients.

Objectives

Our objectives were to determine the frequency of non-alcoholic simple steatosis and non-alcoholic steatohepatitis among patients recently diagnosed of type 2 diabetes (less than 6 months), and to describe their sociodemographic, clinical and paraclinical characteristics.

Methods

Study design and setting

We conducted a cross-sectional study over a period of 7 months from March 2020 to September 2020 at the Yaoundé Central hospital in Cameroon. This is the main and largest hospital for diagnosis and management of patients with type 2 diabetes in the city of Yaoundé (capital city of Cameroon), routinely following up a yearly average of 7,000 patients with type 2 diabetes. We enrolled all eligible newly diagnosed type 2 diabetic patients who consented for the study. We performed clinical exam, abdominal ultrasound and blood samples were collected for fasting blood sugar, lipid profile and liver enzymes tests.

Study population

we included in our study patients meeting all the following criteria:

- Type 2 diabetes mellitus diagnosed within the last 6 months before study start.

- Diagnosis of diabetes made according to 2020 criteria of the American Diabetes Association (ADA) [3].

- Patients followed-up at the Central hospital of Yaoundé.

- Not known alcoholic. This was defined as a reported weekly average of alcohol consumption <140g or 14 drinks / week for women and <210g or 21 drinks / week for men [4]

We excluded patients with any of the following criteria:

- Pregnant women or nursing mothers.

- Liver cirrhosis.

- Refusal to participate to the study.

Study procedures

- We used hospital records and logbooks to systematically identify all patients diagnosed of diabetes type 2 within the past 6 months of study start. Diabetes was diagnosed following the 2020 ADA diagnosis criteria [3]. These patients were approached for consenting procedures and for verification of eligibility criteria and were invited to the study site.

- At the site, we recorded socio-demographic data, diabetes history and other known comorbidities, we conducted a routine clinical examination, we collected blood samples for biochemistry analysis, and we performed an abdominal ultrasound.

- The socio-demographic data consisted of sex (Male or Female) age in years, profession and the region the patient lived in. Age ,was presented as mean± standard deviation or as a categorical variable with 4 groups: (≤ 40 years, between 41 years - 50 years, between 51 years - 60 years, ≥ 61 years.

- Diabetes history and known comorbidities: We recorded the number of months since diagnosis of diabetes, the glycated hemoglobin (HbA1C) levels performed within last 3 months (recorded as <7% or >=7%) and any known history of hypertension and antihypertensive treatment.

- Clinical examination: We measured the blood pressure (BP) of all patients using an OMRON® M3 intellisense brand electronic blood pressure adapted to the size of the patient's arm. BP was measured on patients after 3 to 5 minutes of resting in a calm room and in a seated position. On each arm, 3 measurements spaced 1 minute apart were performed in a row, and the average of readings was recorded.

- We performed anthropometrics measurements on partially clothed patients: we measured the standing height in centimeters using a stadiometer, the standing weight in kilograms using a bathroom scale and the waist circumference in centimeters using a regular flexible and non-elastic tape. The tape was applied directly on the skin of the patient standing, feet together, with the arms relaxed on each side of the body and at the end of a normal exhalation. The circumference was measured halfway between the anterosuperior iliac spine and the inferior costal margin. The Body Mass Index in kilograms per square meter was calculated, and categorized into: ≤ 25: normal, between 25 - 29.99: overweight, ≥ 30: obesity; The waist circumference was grouped into 2 categories: normal if <94 cm for men or <80cm for women and pathological if ≥ 94 cm for men or ≥ 80cm for women.

- Biochemistry analyses: Blood samples were collected after a fasting period of 8 hours (usually on the next morning). Analyses included fasting blood sugar, liver function tests (alanine aminotransferase or ALT) and lipid profile. ALT levels were presented into 3 categories: normal, if <40 IU / L for male or < 35 IU / L for female, 1× normal, if 40-80 IU / L for male or 35 - 70 IU / L for female, and 2× normal if > 80 IU / L for male and > 70 IU / L for female. The values of the lipid profile were considered abnormal if total triglycerides> 1.5 g / l, or LDL cholesterol> 1g / l, or total cholesterol> 2g / l, or HDL cholesterol <0.4g / l. [5]

- Abdominal ultrasound: This was done using a LOGIQ V5 Expert brand ultrasound machine, with a low frequency convex probe at 4MGZ. The patient was in supine position, with the stomach uncovered to the bottom of the pelvis and a contact gel was applied on the patient's skin. The size of the right liver in the mid-clavicular sagittal section and the size of the left liver (normal ≤ 10 mm) in axial section were measured. The renal parenchyma was used as reference to assess the echogenicity of the liver on a hepato-renal section, to visualize the walls of the portal trunk and the diaphragm as a whole and for the detection of hepatic nodules. The abdominal ultrasound reported the presence of homogeneous hepatomegaly if right liver:> 15 mm and / or left liver> 10 mm, the presence or absence of hepatic nodule, and a hepatic steatosis score based on a 4 points scale ranging from 0-3: The score was 0 if steatosis was absent (Normal liver ultrasound); score1 when mild steatosis was observed(a slight and diffuse increase of hepatic echogenicity with normal visualization of the diaphragm and portal vein wall); score 2 in case of moderate steatosis (i.e. moderate increase in hepatic echogenicity with a slightly altered appearance of the wall of the portal vein and the

diaphragm) and score 3 in case of severe steatosis (a marked increase of hepatic echogenicity with little or no visualization of the wall of the portal vein, of the diaphragm) [6]

- Two experienced radiologists were involved in performing the ultrasounds and scoring. In order to minimize the variability of the results, a KAPPA coefficient was estimated to measure the degree of agreement between the two radiologists in relation to chance [7]. The calculation was performed after interchanging 20 ultrasound results between the two radiologists. Thus, the result of the coefficient obtained was K = 0.79 which is equivalent to 79% agreement and therefore a good extent of agreement between the two practitioners.

Statistical Methods

Data analysis was performed using R-studio software version 1.1.414. Comparison of categorical variables was carried out using the Chi-square test or the Fisher exact test. Comparison of means of quantitative variables was performed using Student's test or Wilcoxon's test. Significance was set at 5% for all statistical testing. The frequency was obtained after the ratio of the number of newly diagnosed type 2 diabetic patients with uncomplicated fatty liver disease and non-alcoholic steatohepatitis to the total number of type 2 diabetic patients included, who had agreed to participate until the end of the study. It was expressed as a percentage.

Results

- A total of 127 patients were diagnosed of diabetes type 2 at the Yaoundé Central Hospital. Among these patients, 20 did not provide consent, 07 did not complete study procedures, 02 patients were excluded for hepatic cirrhosis. We included a total of 98 patients in the study.

Descriptive data

- The age of participants ranged from 27 to 72 years with a mean (± SD) of 50.31 ± 10.51 years. A total of 61.2% (60/98) patients were between 41 and 60 years old and 54.1% (53/98) were male (M/F ratio was 1.17). As profession, the patients were mostly traders, with a proportion of 21.4% (21/98) and they were mostly from the Center region of Cameroon 41.8% (41/98).

- The median time since diabetes had been diagnosed on the patients was 1 month, with an interquartile range of 1 to 2 months. A total of 34/98 patients (34.7%) were obese and 21/98 (21.4%) had a normal waist measurement.

Main Results

The frequency of non-alcoholic fatty liver disease was 56.1% (55/98). The level of Mild hepatic steatosis was the most represented group (92.7% or 51/55). The homogeneous and diffuse distribution of hepatic steatosis was the most frequent ultrasound presentation in these diabetic patients (94.5% or 52/55).

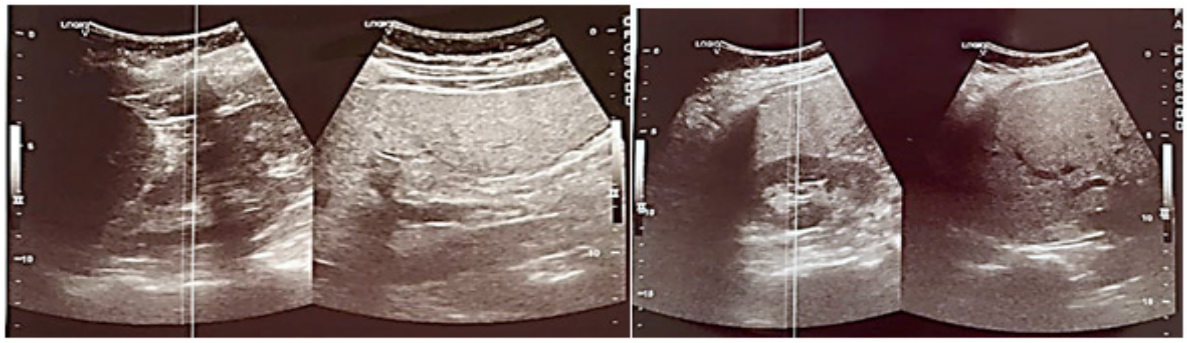

Figure 1 : Images of a patient with moderate hepatic steatosis (score of 2)

Table 1: Socio demographics characteristics

	Fattyliverdisease		
Socio demographics characteristics	**Presence (%)**	**Absence (%)**	**p-value**
Age (year)			
≤ 40 41 - 50 51 - 60 > 61	(22) (33) (33) (13)	(19) (28) (28) (26)	0.48
Sex			
Female Male	(53) (47)	(37) (63)	0.12

Table 2: Clinical and paraclinical characteristics of patients with non-alcoholic fatty liver disease

Clinicalfeatures	Presence of steatosis (%)	Absence of steatosis (%)	P - Value
Average duration of diabetes (months)	1.81	2.20	0.24
Known High blood pressure - Yes - No	 (24) (76)	 (12) (88)	0.12
Diabetes balance (HbA1c) - ≤7% - > 7%	 (7) (93)	 (21) (79)	0.23
Body mass index - < 25 : - 25 – 29.99 : overweight - ≥ 30 : Obesity	 (20) (31) (49)	 (56) (28) (16)	0.0002
Waist size - Normal - Abnormal	 (11) (89)	 (35) (65)	0.0041
ALAT (ui/l) - Normal - Greater than once normal - More thantwice normal	 (64) (35) (2)	 (77) (16) (7)	0.06
Ratio ALAT/ ASAT - < 1 normal - > 1 Abnormal	 (47) (53)	 (63) (37)	0.12
Abdominal ultrasound:			
- Right liver size: ≤15 mm normal > 15 mm abnormal	 (64) (36)	 (81) (19)	0.05
- Left liver size: ≤ 10 mm normal > 10 mm abnormal	 (53) (47)	 (63) (37)	0.32

- Fatty liver disease predominated in diabetic patients aged 41 to 60 years (66% or 36/55) and in women (53% or 29/55), though these differences were not significant.

- In our study population, almost half of the diabetic patients with non-alcoholic fatty liver disease were obese. And nine out of ten diabetic patients who presented with fatty liver disease had abnormal waist circumference.

- ALT results showed that two out of three diabetic patients who had normal ALT levels presented with fatty liver disease, although this result was not significant.

- Ultrasound results revealed that 36% (20/35) of diabetic patients with right hepatomegaly had a significant hepatic steatosis (P = 0.05). Also, close to half of the diabetic patients who had left hepatomegaly (47% or 25/55) presented with non-alcoholic fatty liver disease, though this association was not significant association (P = 0.32).

Discussion

Keys results

- Our study observed a high prevalence of non-alcoholic fatty liver disease (NAFLD) among patients newly diagnosed of T2DM. This is similar to the results of Afolabi et al [8], and Shahjamal et al [9], which observed prevalence of 68.8% and 69% respectively. These results can be justified by the main pathophysiological mechanisms of T2DM which include insulin resistance and increased lipolysis, leading to de novo hepatic lipogenesis and fat accumulation in the liver.

- The predominant age group among patients with NAFLD was 40-60 years, which was similar to the result of Shahjamal et al and Kalra et al [10]. This age group represents the period with peak diagnosis of type 2 diabetes and the onset of its complications, including non-alcoholic fatty liver disease.

- NAFLD was more prevalent in men than in women, likely as a result of the higher prevalence of obesity among women. In our study population, the mean Body Mass Index (BMI) for females

was 32.34 kg / m^2 and was higher than the BMI for males at 28.92 kg / m2. Additionally, NAFLD was observed to be more frequent among obese patients with an abnormal waist circumference. Abnormal waist circumference is an indicator of an increased risk of ectopic white adipose tissue deposits leading to NAFLD.

- We also observed that close to two out of three diabetic patients with normal transaminase levels presented with NAFLD; Similarly, Shahjamal et al [9] found that 78% of diabetic patients who presented with NAFLD had normal values of hepatic transaminases. Although chronic hepatic cytolysis with a slight increase in aspartate aminotransferase (ASAT) or alanine aminotransferase (ALAT) is the main reason of diagnosis non-fatty liver disease according to literature, our findings suggest that liver enzymes levels are not a sensitive screening test for non-alcoholic fatty liver disease, thus, supporting the current recommendations [7].

Limitations of the study

As this was a hospital-based study, the study was likely subject to a selection bias.

Our sample size was limited, mainly as a result of the Covid-19 epidemic which led to a reduction of the number of patients seeking care in the hospital facility.

Generalisability

The results of our study can be generalized to patients recently diagnosed of T2DM and followed-up in referral hospitals in low to middle income countries.

Conclusion

Among the newly diagnosed diabetic patients in our study, 56.1% had non-alcoholic fatty liver disease diagnosed by abdominal ultrasound and the most common form of the disease was mild fatty liver disease with homogeneous and diffuse distribution of hepatic steatosis.

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