The Prevalence of Non-Alcoholic Fatty Liver Disease and its Association with Glycemic Control in Type 2 Diabetes Mellitus Patients at the Batangas Medical Center – Out-Patient Department

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Abstract

Background: Diabetes mellitus is a chronic disease which has been increasing both in incidence and global impact. In the Philippines, cases of diabetes mellitus increase at an alarming rate. Previous study in Nigeria among Type 2 Diabetic patients with non-alcoholic fatty liver disease (NAFLD) has observed an increased prevalence of 69%. However, there is no definite association between severity of NAFLD and glycemic control (HbA1c).

Objectives: To investigate the prevalence of NAFLD and its association with glycemic control of Type 2 Diabetes Mellitus (T2DM) patients at Batangas Medical Center (BatMC) – Out Patient Department (OPD).

Methods: A single center, cross sectional study was performed on 80 T2DM patients, who underwent OPD consultation between November 2020 to October 2021. Clinicodemographic profile, duration of T2DM, diagnostic tests including HbA1c and ultrasound of the liver were taken. *Chi-Square test* of homogeneity and *Fisher's Exact test/Fisher-Freeman-Halton test* were utilized for comparison of categorical variables from a single population to determine whether there is a significant association between the severity of NAFLD and patients characteristics and glycemic control.

Results: 80 T2DM patients were included in the analysis, there was an equal number of male (50%) and female (50%). Majority of the patients were in the age of 50 – 59 years old (33%), with a BMI of 25 and above (81%), had been diagnosed with T2DM for > 5 years (72%) and maintained with oral hypoglycemic agents (68%). The prevalence of NAFLD by ultrasonography among T2DM patients was 81%. 80% of these patients had mild NAFLD and 20% had moderate NAFLD; but none had severe NAFLD. The average HbA1c level of 8.9% had a mild NAFLD compared to patients with moderate NAFLD with an average HbA1c level of 10.1%. With a $p=0.053$, NAFLD severity and glycemic control do not show any statistically significant association. Subgroup analysis was not performed in the study due to limited sample size. In addition, results of association are not sufficient evidence for any conclusion; hence, there appear to be no group of interest.

Conclusion: The result of this study confirmed that the prevalence of NAFLD in T2DM was high at 81% but there is no sufficient evidence to conclude a statistically significant association between the level of glycemic control and the severity of NAFLD.

Keywords: Type 2 Diabetes Mellitus, Non-Alcoholic Fatty Liver Disease, NAFLD, Glycemic control, HbA1c, Dyslipidemia, Obesity, Metabolic Syndrome

Introduction

Type 2 Diabetes Mellitus is a chronic disease which has been increasing both in its incidence and global impact. In the Philippines, one out of every five Filipinos could potentially have diabetes mellitus or pre-diabetes.[1] Based on previous population-based research, cases of diabetes increase at an alarming rate of 16.3% in Asian countries including the Philippines. Diabetes is one of the primary causes of mortality among the Filipinos based from the Philippine Health Statistics in the year 2013.[2] The WHO projects that it will be the seventh leading cause of death by 2030.[3] In addition, in 2017, the Philippine Center for Diabetes Education Foundation stated that over 3.5 million Filipino adults are suffering from the disease.[4] Uncontrolled diabetes leads to more serious complications such as liver disease, cerebrovascular disease, myocardial infarction, and kidney disease.

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Fatty liver is characterized as the presence of deposits of excess fat in the liver. The two classifications of fatty liver disease are non-alcoholic fatty liver disease (NAFLD) and alcoholic fatty liver disease (AFLD), differentiated by amount of alcohol consumption. NAFLD is mostly recognized in patients who are obese and diagnosed with diabetes, hypertension, and dyslipidemia.[5] It is now identified as one of the most prevalent liver diseases in the United States with about 5% in the general population and reaching 25-75% in individuals with T2DM and obesity.[6] In a research conducted at the Philippine General Hospital from January 1999 to December 2004, there were 134 out of 1,102 patients diagnosed both clinically and histologically with NAFLD.[7] Moreover, there is a notable upturn in the presence of NAFLD among individuals with T2DM. A study in Nigeria among T2DM patients with NAFLD observed an increased prevalence of 69%.[8] Another study in India using ultrasound demonstrated that among 200 patients with T2DM, NAFLD had a prevalence of 64%.[9] While there is a well-cited association between the presence of T2DM and NAFLD, at present there is still no established association between level of glycemic control and severity of NAFLD. Also, it is important to define which factors are associated with the presence of NAFLD in diabetic patients and particularly, whether the presence and severity of NAFLD are related to diabetic metabolic status or to the occurrence of chronic microvascular and macrovascular degenerative complications.[10]

T2DM continues to burden Filipinos today with its increasing rate, myriad complications, and associated comorbidities. Among these comorbidities, NAFLD adds further disease burden by increasing risk to develop liver cirrhosis, liver cancer, and subsequent mortality among diabetics, compared to non-diabetics with NAFLD. In our local setting, there is a lack of data on the prevalence of NAFLD among T2DM and how glycemic control can be an important factor in the development of NAFLD. Moreover, the association of glycemic control and severity of NAFLD is not well established. Hence, to address this gap, the researchers aim to identify the prevalence of NAFLD and its association with glycemic control for early detection that will help clinicians make better and rational decisions in the disease management that will greatly improve the quality of life among patients with T2DM.

General Objective. To investigate the prevalence of NAFLD and its association with glycemic control among T2DM patients seen at BatMC – OPD.

Specific Objectives. 1) To determine the prevalence of NAFLD in patients with T2DM, 2) To determine the association between patient characteristics and the severity of NAFLD, 3) To determine the association between the duration of T2DM and NAFLD, and 4) To determine the association between the severity of NAFLD and glycemic control among T2DM patients.

Methods

Study setting, design and duration. This study was conducted in Batangas Medical Center, a tertiary government hospital located at Kumintang Ibaba, Batangas City, Philippines. A cross-sectional study was performed on 80 T2DM patients, who underwent OPD consultation from November 2020 to October 2021. The study protocol was approved by the Department of Internal Medicine Technical Review Board followed by the Batangas Medical Center Research Ethics Review Committee (BATMC RERC 2020-033).

$$X = \frac{z^2_{\alpha/2} * p * (1-p)}{e^2}$$

where, α = level of significance = 0.05
$z_{\alpha/2}$ = critical value of the normal distribution at alpha = 1.96
p = estimated true proportion = 12.2%
e = margin of error = 0.02

Figure 1. Formula for Sample Size Calculation used in this Study.

Participants. Considering the decreased number of diabetic patients who consulted at the BatMC-OPD during the pandemic, the minimum sample size was computed using the formula as shown in *Figure 1*.

Apart from this, taking into account the total T2DM patients during the pandemic, the level of significance ($p<0.05$), margin of error (0.02), and the prevalence rate of NAFLD (12.2%) as an estimate of true proportion from the local study of De Lusong et al, it was sufficient for this study to push through.[7] A total of 92 T2DM patients were included. They met the criteria based on UNITE for Diabetes Philippines: Philippine Practice Guidelines on the Diagnosis and Management of Diabetes Mellitus and American Diabetes Association.[11,12] Patients should also have available laboratory results such as complete blood count, liver aminotransferases, lipid profile, HBsAg, serum creatinine, HbA1c level as well as liver or whole abdominal ultrasound done at Batangas Medical Center within the previous 3 months.

Among these subjects, 12 were excluded from the study due to the following factors: (1) patients with current and history of significant alcohol consumption, greater than 140 g/week for males and 70 g/week for females; (2) patients with anemia and chronic blood loss (hemoglobin < 120 g/L for males and < 110 g/L for females); (3) recently transfused patient (last 120 days); (4) subjects diagnosed with Chronic Kidney Disease stage IV and V; (5) pregnant women; (6) presence of other identifiable causes such as but not limited to viral liver disease; (7) patients who currently or previously used a drug known to cause fatty liver including amiodarone, corticosteroids, tamoxifen, methotrexate and high dose estrogen, and; (8) all autoimmune medical condition by history.

Thus, the final sample consisted of 80 T2DM patients (*Figure 2*). Written informed consent was obtained from each subject and the study procedures explained before the study was started.

Data collection procedure. All eligible subjects were

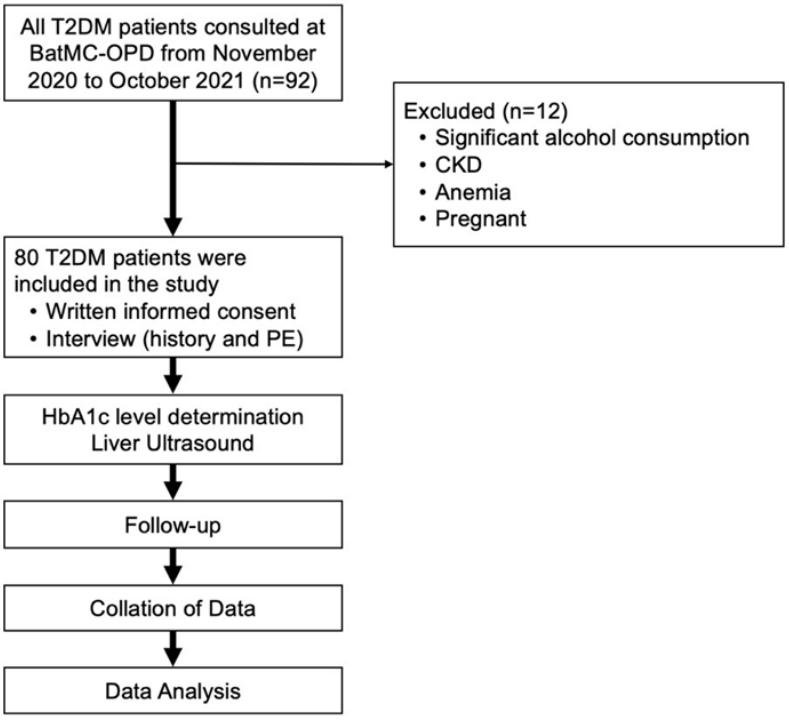

Figure 2. Study Procedure

invited to participate in the study. Those who gave their written informed consent were enrolled and interviewed where detailed history and physical examination were done. The following information were gathered: age, sex, duration of T2DM (≤ 5 years and > 5years), diabetes regimen being used (Insulin alone, oral hypoglycemic alone or combination of insulin and oral hypoglycemic agent), waist circumference (cm), weight (kg) and height (m). BMI was subsequently calculated in kg/m^2.

The HbA1c level test done at Batangas Medical Center Laboratory used calibrated D-10 hemoglobin system and accessories. In D-10 system, HbA1c was reported based on National Glycohemoglobin Standardization Program (NGSP), modelled after the Cholesterol Reference Method Laboratory Network program ranging from 3.9% to 18.8%, with the normal value of 4.3% to 6.4%. In the study, the researchers categorized the HbA1c level into three (<7%, 7 to 9% and >9%) based on the study of Fonseca on the management of diabetes looking into the degree of glycemic control.[13]

Liver ultrasonography using *Samsung Medison*™ ultrasound machine with a curvilinear probe at a frequency of 3.5-5.0 MHz was performed by the Radiology residents and/or fellow. This was verified by the consultant expert in the field of ultrasound. They were blinded of the HbA1c levels. A diagnosis of fatty liver was made using the standard sonographic grading, as described by the Radiology Department based on their reference book of Fundamentals of Diagnostic Radiology by William Brant and Clyde Helms. Grade I or Mild fatty liver was defined as having an increased echogenicity of liver, normally seen diaphragm and intrahepatic vessels; Grade II or Moderate fatty liver, moderate increase echogenicity, mildly obscured visualization of diaphragm and intrahepatic vessels; and Grade III or Severe fatty liver, marked increase in echogenicity, obscured penetration, poor or non-visualization of diaphragm and intrahepatic vessels.

Statistical Analysis. All data collected were encoded and organized in 2019 *Microsoft Excel* for Mac version 16.30. Descriptive statistics was used to secure categorical data which was presented as frequency and percentages of total samples. *Chi-Square test* of homogeneity and *Fisher's Exact test/Fisher- Freeman-Halton test* were utilized for comparison of categorical variables from a single population. It was used to determine whether there is a significant association between the NAFLD and its risk factors and the patient's glycemic control. Statistical analyses were performed using *SPSS version 26*. A $p < 0.05$ was considered statistically significant. Subgroup analysis was not performed in the study due to limited sample size. In addition, results of association are not sufficient evidence for any conclusion; hence, no group of interest was tested.

Ethical Considerations. The study adhered to ethical principles and declare no conflict of interest**.**

Privacy and Confidentiality. The protocol of this study was reviewed and approved by the BaTMC RERC 2020- 033 and monitored the progress thereto. Also, the study was accomplished in accordance with the Data Privacy Act of 2012. The primary investigator did not disclose the identity of the included patients; instead, they were pooled and anonymized to maintain the privacy and confidentiality. All data obtained were kept confidential and only the primary investigator had access to it. Moreover, the master list of the pertinent information was placed in a secured folder stored in a cabinet with safety lock, for hard copy materials. While, all encoded data (soft copies) were stored in a password-protected application and laptop. All obtained data were discarded and deleted once the primary investigators interpreted the results and made a conclusion.

Informed Consent Process. An informed consent form was given to the eligible patients or to their representative for those patients who cannot give their consent (a detailed discussion regarding representative who will give consent is under vulnerability and illiterate section). All details of the consent form were explained

Table I. Patient Demographics

Parameters	Frequency (n=80)	%
Age in years		
30 to 39	12	15%
40 to 49	16	20%
50 to 59	26	33%
60 to 69	18	23%
> 70	8	10%
Sex		
Male	40	50%
Female	40	50%
BMI* (kg/m^2)		
Underweight [<18.5]	1	1%
Normal range [18.5 to 22.9]	2	3%
Overweight [23 to 24.9]	12	15%
Obese I [25 to 29.9]	48	60%
Obese II [>30]	17	21%
Waist Circumference (cm)		
Elevated (Male=>90; Female=>80)	53	66%
Normal	27	34%
Duration of T2DM**		
5 years and less	22	28%
Above 5 years	58	72%
Diabetes regimen		
Injectable Insulin	25	31%
Oral hypoglycemic agent	54	68%
Injectable Insulin + Oral hypoglycemic agent	1	1%

**BMI: body mass index; based on World Health Organization – Asia-Pacific guidelines*
***T2DM: Type 2 Diabetes Mellitus*

Table II. Prevalence of NAFLD in T2DM Patients at BatMC-OPD

Severity of NAFLD	Present	Absent
	65 (81%)	15 (19%)
Mild	52 (80%)	
Moderate	13 (20%)	
Severe	0	

thoroughly and all questions regarding the study were entertained.

Voluntary Participation and Right to Refuse. The participation in the study was entirely voluntary. Whether the patient chooses to participate or not, all services they received and will be receiving at BatMC will be continued and no changes shall be made.

In case the patient chooses not to participate in the study, the same standard of care for T2DM and NAFLD were given. Patients who changed their mind during the course of the research study were allowed to withdraw with their care being continued. Those who refused to participate in the study did not affect their treatment at BatMC-OPD. The participants continue to receive all the benefits.

Vulnerability and Illiteracy. Elderly patients with T2DM were considered part of the vulnerable group who are subjected to unnecessary exposure during this COVID-19 pandemic; hence, the primary investigator scheduled their follow-up to limit the number of patients per clinic visit and maintained the observation of social distancing to minimize the risk of acquiring the disease.

For participants who are illiterate, demented or otherwise cannot give their consent, the primary investigator explained the purpose, risks and benefits of the study to the representative of the participant provided that they are of legal age (≥ 18 years old) and must sign the informed consent. If possible, this person should be selected by the participant and should have no connection to the research team. For participants who are illiterate, thumbprints are included in the informed consent.

Risk and Benefits. All included subjects had no greater risk in participating in this study since no medicines were administered and no invasive procedures were done that will put more risk of causing potential complication. Also, the participants had the potential benefit of early detection of NAFLD and associated glycemic control. There may be no benefit to the society at this stage of the research, but future generations are likely to gain from this.

Incentives, Compensation and Reimbursement. All expenses were shouldered by the participants including laboratory and diagnostic work-ups as well as the transportation or travel expenses. All participants were referred to the medical social service to get an out-patient discount in all tests done at BatMC. The primary investigator did not reimburse any expenses. No money or tokens were given to the participants for taking part in this research study.

Results

The characteristics of the participants in the study are shown in *Table I*. Among the 80 enrolled subjects, there was an equal number of male (50%) and female (50%) patients. Majority of the patients were aged 50 – 59 years old (33%), followed by those aged 60 – 69 years old (23%). A large majority of the study population had a BMI of 25 and above, totaling 65 subjects out of 80 (81%). Finally, 72% of the patients had been diagnosed with T2DM for longer than 5 years and majority were being treated with oral hypoglycemic agents (68%) for their maintenance medication.

The prevalence of NAFLD by ultrasonography among T2DM patients who consulted at BatMC-OPD was 81% (65 of 80) as shown in *Table II*. Of the 65 patients, 52 (80%) had mild NAFLD and 13 (20%) had moderate NAFLD; but none had severe.

As shown in *Table III*, the distributions of the clinicodemographic profiles of T2DM patients in terms of whether they had NAFLD were not statistically different at $p=0.05$ level of significance. All age groups had higher distribution of patients with NAFLD. The same was observed in terms of the sex of patients. The only underweight patient had no NAFLD, however all other BMI categories had higher distribution of patients with NAFLD. Seventy six percent (76%) of patients with elevated waist circumference, which may signify the presence of abdominal obesity, had NAFLD. Moreover,

Table III. Clinicodemographic profile of T2DM patients at BatMC – OPD with and without NAFLD by ultrasonography

Parameters	Present	Absent	p Value
Age in years‡			
30 to 39	12 (100%)	0	0.298
40 to 49	11 (69%)	5 (31%)	
50 to 59	21 (81%)	5 (19%)	
60 to 69	14 (78%)	4 (22%)	
> 70	7 (88%)	1 (12%)	
Sex†			
Male	32 (80%)	8 (20%)	0.775
Female	33 (83%)	7 (17%)	
BMI* (kg/m^2)‡			
Underweight [<18.5]	0	1 (100%)	0.123
Normal range [18.5 to 22.9]	2 (100%)	0	
Overweight [23 to 24.9]	12 (100%)	0	
Obese I [25 to 29.9]	37 (77%)	11 (23%)	
Obese II [>30]	14 (82%)	3 (18%)	
Waist Circumference [cm]†			
Elevated [Male=>90; Female=>80]	40 (76%)	13 (24%)	0.064
Normal	25 (93%)	2 (7%)	
Duration of T2DM†			
5 years and less	18 (82%)	4 (18%)	0.936
Above 5 years	47 (81%)	11 (19%)	
Diabetes regimen‡			
Injectable Insulin	19 (76%)	6 (24%)	0.626
Oral hypoglycemic agent (OHG)	45 (83%)	9 (17%)	
Injectable Insulin + OHG	1 (100%)	0	

**BMI: body mass index; based on World Health Organization – Asia-Pacific guidelines*
†Chi-square test of independence
‡Fisher's Exact test / Fisher-Freeman-Halton test

almost 93% of patients who had normal waist circumference also had NAFLD. There was an equal distribution of patients with and without NAFLD in terms of the duration of their T2DM. In addition, majority of patients with different diabetes regimen also had NAFLD.

Statistically, all the variables considered as risk factors in the development of NAFLD show that there is no evidence to conclude a significant association between these risk factors and NAFLD (*Table IV*).

At $p<0.05$ level of significance, there was insufficient evidence to conclude that there is an association between the duration of T2DM and the severity of NAFLD ($p=0.662$) as presented in *Table V*.

The HbA1c level was not significantly different between T2DM patients with NAFLD compared to those without NAFLD, as shown in *Table VI* with $p=0.066$. Older adults who are otherwise healthy with few coexisting chronic illness and intact cognitive function and good functional status are able to achieve the lower glycemic goal of <7%.

Measurement of HbA1c is used as the standard biomarker for glycemic control in all T2DM patients.[12] In the study of Fonseca, it suggested that all aspects of glucose metabolism shown to be clinically relevant must be monitored for effective diabetes management including the postprandial glucose.[13] Hence, the goals of treatment can be based on HbA1c level as used in this study. In the study population shown in *Table II*, 81% had NAFLD and 80% of the same had mild NAFLD. The association between NAFLD severity with glycemic control, as presented in *Table VII*, shows an average mean of HbA1c level of 8.9% with mild NAFLD. A higher distribution of T2DM patients with mild NAFLD (93%) with HbA1c level of 7% to 9% followed by patients having HbA1c of <7% had mild NAFLD (80%). The same was observed in patients with HbA1c of >9%, however only 67% of patients had mild NAFLD, while the remaining 33% had moderate NAFLD. With a resulting $p=0.053$, there is insufficient evidence to conclude that there is a significant association between the severity of NAFLD and glycemic control among T2DM patients.

Discussion

NAFLD is one of the most common liver diseases with an estimated global prevalence of 25–35%, affecting both men and women equally.[14] At present, it is also becoming prevalent in Asia.[2,3] NAFLD is also reported commonly in T2DM patients with high prevalence of up to 70%. Our cross-sectional study found 81.25% prevalence of T2DM

Table IV. Risk factors in the development of NAFLD among T2DM patients

Risk Factors	NAFLD by Ultrasonography		p Value
	Present (n=65)	Absent (n=15)	
Dyslipidemia			
Total Cholesterol†			0.652
< 200 mg/dL [5.2 mmol/L]	22 (79%)	6 (21%)	
> 200 mg/dL [5.2 mmol/L]	43 (83%)	9 (17%)	
Low-density lipoprotein [LDL]†			0.491
< 100 mg/dL [2.6 mmol/L]	20 (75%)	6 (23%)	
> 100 mg/dL [2.6 mmol/L]	45 (83%)	9 (17%)	
High-density lipoprotein [HDL] †			0.569
< 40 mg/dL [1 mmol/L] in male	52 (83%)	11 (17%)	
< 50mg/dL [1.3 mmol/L] in female	13 (77%)	4 (23%)	
> 40 mg/dL [1 mmol/L] in male	19 (83%)	4 (17%)	
> 50mg/dL [1.3 mmol/L] in female	46 (81%)	11 (19%)	
Triglycerides†			0.843
<150 mg/dL [1.7 mmol/L]	19 (83%)	4 (17%)	
>150 mg/dL [1.7 mmol/L]	46 (81%)	11 (19%)	
Obesity‡			0.508
Not Obese	14 (93%)	1 (7%)	
Overweight [25.0 to 29.9]	37 (77%)	11 (23%)	
Obesity Class I [30.0 to 34.9]	8 (73%)	3 (27%)	
Obesity II [35.0 to 39.9]	4 (100%)	0	
Extreme Obesity III [>=40]	2 (100%)	0	
Hypertension‡			0.862
Without hypertension	32 (78%)	9 (22%)	
Stage I (BP 130 to 139/ 80 to 89 mm Hg)	22 (85%)	4 (15%)	
Stage II (BP >140/90 mm Hg)	11 (85%)	2 (15%)	

BP: Blood Pressure
†*Chi-square test of independence*
‡*Fisher's Exact test / Fisher-Freeman-Halton test*

Table V. Association of the Duration of T2DM and NAFLD

Duration of T2DM	Normal (n=15)	Mild (n=52)	Moderate (n=13)	Severe (n=0)	p Value
≤5 years	4 (18%)	13 (59%)	5 (23%)	0	0.662
>5 years	11 (19%)	39 (67%)	8 (14%)	0	

Table VI. Glycemic Control with and without NAFLD

HbA1c‡	Ultrasonographic findings		p value
	Present (n=65)	Absent (n=15)	
< 7%	10 (63%)	6 (37%)	0.066
≥ 7%	55 (86%)	9 (14%)	

‡*Fisher's Exact test / Fisher-Freeman-Halton test*

Table VII. Association between Severity of NAFLD with Glycemic Control Among T2DM patients.

HbA1c	NAFLD by Ultrasonography			p Value
	Mild (n=52)	Moderate (n=13)	Severe (n=0)	
Mean ± SD	8.9% ± 2.35	10.1% ± 2.45	-	0.053
<7%	8 (80%)	2 (20%)	0	
7% to 9%	26 (93%)	2 (7%)	0	
>9%	18 (67%)	9 (33%)	0	

SD: standard deviation

patients had a NAFLD, as shown in *Table II*, with equal sex distribution. This is comparable to the findings from other studies.

Some risk factors were included in the study. However the included risk factors, namely dyslipidemia, obesity and hypertension were not significantly associated with the presence of NAFLD. The same was observed in the local study done by Manuel et al., that the NAFLD distribution among T2DM with dyslipidemia were not significant with *p=0.634*. But in terms of NAFLD and obesity, this was found to be statistically significant with *p=0.001*. Possibly, they only have two groups, either obese or normal and if obese they categorized it into two either Obese I or Obese II, unlike in our study where we categorized obesity into four, based on the WHO international classification of obesity. Furthermore, T2DM and obesity, which are part of the metabolic syndrome, seemed to be closely related to the development of NAFLD and suggested links to insulin resistance.[14,15,17]

There is an equal distribution of patients with and without NAFLD with regards to the duration of T2DM but this is not statistically significantly associated (*p=0.662*) similar to the study of Manuel et. al. in the Philippines and Afolabi et al. in Nigeria.[8,15] The small sample size may be a reason for the lack of statistical significance.

T2DM is an independent risk factor for the development of NAFLD and progression to liver fibrosis, cirrhosis, and hepatocellular carcinoma.[15] Development of NAFLD and its progression into advanced liver disease and cancer has been reported to greatly impair the quality of life of diabetics.[3,8,14]

Optimal glycemic control is fundamental to the management of diabetes. There is compelling evidence that improved glycemic control reduces the risks of development and/or progression of complications in T2DM

including NAFLD.[8,11,12,14,15] HbA1c is a known predictor for different complications related to T2DM and can give a gauge as to the duration of the patient's hyperglycemia.[11] According to the population-based study of Yu et.al, HbA1c level is related to the severity and presence of NAFLD, independent of potential confounders.[16] It was found that in patients with NAFLD, the level of HbA1c is increased with increasing NAFLD Fibrosis Score (NFS).[17] The results of the study indicate that HbA1c level is correlated with the presence of NAFLD in Chinese adults. Moreover, elevated levels of HbA1c are also independently linked with greater risks of fibrosis in patients with NAFLD without T2DM, supporting a practical approach of assessing HbA1c in managing NAFLD patients.[18]

Poor glycemic control was an independent predictor of NAFLD on logistic regression.[8] Prevalence of NAFLD is significantly higher among those with poor glycemic control (77%) than those with good glycemic control (55%), exhibiting significant association between NAFLD and glycemic control among T2DM.[8,12]

Similarly, a prevalence of 60.4% and 43.1% of NAFLD in those patients with uncontrolled and controlled T2DM, respectively, were reported in a study on about 147 Filipinos. Another study likewise showed that diabetics who had poor glycemic control are about 3.5 times more likely to have NAFLD compared to those with good glycemic control.[15]

This study showed that among diabetics with NAFLD, there was no statistically significant association between the level of glycemic control and severity of NAFLD, as shown in *Table VII*. The results of this study are similar to the study conducted by Afolabi et al, where among 55 diabetic patients with diagnosed NAFLD, HbA1c level was not significantly associated with severity of NAFLD.[8] Compared to that study, this study has a larger sample of patients with diagnosed NAFLD and the levels of glycemic control are more well-defined since Afolabi et al. only used two groups to define level of glycemic control, those with HbA1c < 7% (controlled) and those who are not controlled. But still, it is important to identify the diabetic patients with NAFLD to manage and prevent a possible worst outcome and address an important endocrine health problem.

This study involves several limitations. First, it is a single-center study performed in the out-patient department of a tertiary government hospital in CALABARZON that may have caused selection bias as only those who consulted had the opportunity to be enrolled. Second, due to the COVID-19 pandemic, there was a decrease in the number of consultations in the OPD compared from the previous years prior to the COVID-19 pandemic. Follow-up rates are also observed to be decreased, hence, there is a relatively small sample size which affects the study's ability to show statistically significant association of NAFLD, T2DM and other variables with each other. Third, the specific oral hypoglycemic agents (OHA) were not included in the study. Furthermore, patients' adherence to the OHA and insulin, which may have an impact on the level of the glycemic control, were not included in the study. Fourth, HbA1c levels and liver ultrasound were not taken on the same day in most of the patients, although we strictly followed the exclusion criteria which is within three months. Lastly, we relied solely on the history provided by the patients to record the amount of alcohol consumption which may be inaccurate. Also, the patients' diet and physical activities that might predispose to steatosis were not included in the study.

Conclusion

In conclusion, the study revealed that the prevalence of NAFLD in T2DM was high as 81.25%. However, there is insufficient evidence that the glycemic control can remarkably affect the severity of NAFLD in patients with T2DM. It is worth mentioning that it is important to control the progression of NAFLD in patients with T2DM to prevent the potential development of liver cirrhosis, liver failure or even liver malignancy.

Recommendations

The investigators recommend further studies with adjusted and larger samples or even a multi-center study to better investigate the prevalence of NAFLD in T2DM and determine the association of glycemic control in general. Liver biopsy is the gold standard in the diagnosis of fatty liver; however due to its invasiveness, the researcher recommends to utilize the fatty liver index through laboratory and physical examination findings. This may be able to identify the risk of having fatty liver and NFS based on the estimate of the amount of liver scarring. This score can be used to reliably predict which patient is likely to have cellular evidence of fibrosis on biopsy. Also, supplementary research analyzing the effect of cholesterol level is recommended.

Disclosure. The views expressed in the submitted research study are the author's own and do not reflect the views of the institution to which they are affiliated. The information gathered throughout this research will remain confidential, and protected from unauthorized disclosure, tampering, or damage. The author declares that there were no conflicts of interest that arose from the conduct and publication of this study.

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