

Prevalence of Non Alcoholic Fatty Liver Disease in middle aged patients with Type 2 Diabetes Mellitus¹Dr Vijant Singh Chandail, Associate Professor, Postgraduate Department of Medicine, Govt Medical College Jammu²Dr Vinu Jamwal, Associate Professor, Postgraduate Department of Medicine, Acharya Shree Chander College of Medical Sciences, Jammu**Corresponding Author:** Dr Vijant Singh Chandail, Associate Professor; Postgraduate Department of Medicine, Govt Medical College Jammu**How to citation this article:** Dr Vijant Singh Chandail, Dr Vinu Jamwal, “Prevalence of Non Alcoholic Fatty Liver Disease in middle aged patients with Type 2 Diabetes Mellitus”, IJMACR- January - February - 2021, Vol – 4, Issue -1, P. No. 41 – 51.**Copyright:** © 2021, Dr Vijant Singh Chandail, et al. This is an open access journal and article distributed under the terms of the creative commons attribution noncommercial License 4.0. Which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.**Type of Publication:** Original Research Article**Conflicts of Interest:** Nil**Abstract**

Introduction: Non-alcoholic fatty liver disease (NAFLD) is a spectrum of clinical and pathological conditions characterized by excessive fat deposition in the form of triglycerides in the liver parenchyma (>5% of hepatocytes histologically), in the absence of significant alcohol consumption [1]. It is a leading cause of liver dysfunction worldwide and is an alarming health problem. In the past decade, NAFLD has gained worldwide prominence as an important public health condition because of the enhanced risk of progressive end-stage liver disease, liver failure and hepatocellular carcinoma [2,3]. Current evidence suggests that NAFLD is the hepatic component of the metabolic syndrome, a syndrome that also includes central obesity, dyslipidemia, hypertension and insulin resistance/impaired glucose tolerance [3-5].

Materials and methods: This is a retrospective analysis of patients who presented to the outpatient services of the department of medicine, at Government Medical College

Jammu wef April 2016 to February 2020. Included were patients with age group of 30-60 years with established T2DM.

Results: A total of 1250 patients, of T2DM presented to our medical outpatient department at Government medical college Jammu from April 2016 to February 2020 and their data were retrospectively analysed. Out of these 725 (58%) were males and 525 (42%) were females. The maximum number of patients were in the age group of 40-50 years (619, 49.5%) followed by 50-60 years (404, 32.3%), and then the least number were in the age group of 30-40 years (227, 18.2%). Out of total 1250 patients, 973 (77.8%) had evidence of fatty liver on USG and 277(22.2%) had normal liver on USG. Out of the total 973 patients who had evidence if fatty liver, maximum patients had grade I fatty liver (476, 48.9%), and grade II fatty liver in 340 (34.9%), and grade III fatty liver in 157 (16.2%) patients. The maximum patients had history of T2DM of 10-15 years duration of diabetes (556, 44.4%)

out of which 523 were having fatty liver and 33 had normal liver. This was followed by T2DM duration of 5-10 years (380, 30.4%) out of which only 205 were having fatty liver and 175 had normal liver. A total of 248 (18.8%) patients were having T2DM duration of more than 15 years out of which 241 had fatty liver and only 7 had normal liver on USG. The least number of patients had duration of T2DM of less than 5 years (66, 5.2%) out of which only 4 patients had fatty liver and 62 had normal liver.

Conclusion: The prevalence of NAFLD in patients with Type 2 DM was 77.8%. Prevalence of NAFLD was significantly higher in males. Prevalence of NAFLD was highest in the age group of 40-50 years and was more in T2DM patients with duration of diabetes 10-15 years.

Keywords: Type 2 Diabetes Mellitus, Non Alcoholic Fatty Liver Disease, Ultrasonography, Prevalence

Introduction

Non-alcoholic fatty liver disease (NAFLD) is a spectrum of clinical and pathological conditions characterized by excessive fat deposition in the form of triglycerides in the liver parenchyma (>5% of hepatocytes histologically), in the absence of significant alcohol consumption [1]. It is a leading cause of liver dysfunction worldwide and is an alarming health problem. In the past decade, NAFLD has gained worldwide prominence as an important public health condition because of the enhanced risk of progressive end-stage liver disease, liver failure and hepatocellular carcinoma [2,3]. Current evidence suggests that NAFLD is the hepatic component of the metabolic syndrome, a syndrome that also includes central obesity, dyslipidemia, hypertension and insulin resistance/impaired glucose tolerance [3-5]. When examined histologically, e.g., in a liver biopsy specimen, excess accumulation of lipids (representing predominantly triglycerides) is evident within hepatocytes. In some cases, NAFLD may progress

from steatosis to steatohepatitis (with evidence of inflammation and cell injury), cirrhosis (hepatic fibrosis), and ultimately liver failure. In assessing disease severity and risk of progression to cirrhosis, it is useful to divide NAFLD into two categories: non-alcoholic fatty liver (NAFL) and non-alcoholic steatohepatitis (NASH). The difference between the two entities is histologic. In NASH, there is the presence of hepatic inflammation in contrast to NAFL, which involves only steatosis. NAFL and NASH occur as part of a continuum in which the histology often is not exclusively steatosis or steatohepatitis (6). The overall prevalence of NAFLD in Western countries varies from 15-40% and in Asian countries from 9-40% (7). The prevalence of NAFLD among people with Type II Diabetes Mellitus (T2DM) is significantly higher than reported in the general population and ranges from 21%-78% [4,8-10].

India is evolving into the diabetic capital of the world and NAFLD is emerging as an important cause of liver disease. Even physically lean Indians may be metabolically obese. Epidemiological studies suggest the prevalence of NAFLD to be around 9-32% in general Indian population. The real prevalence is unknown since NAFLD is often undiagnosed and most subjects with NAFLD, even those with diabetes, have normal liver aminotransferases and clinicians do not suspect the potential presence of NAFLD.

The prevalence of NAFLD has doubled during last 20 years and the current epidemics of diabetes and obesity in both developed and developing countries suggest that numbers will continue to rise, indicating that NASH will become an increasingly common liver problem in both rich and poor countries and thus increasing the global burden of liver disease

In T2DM, NAFLD pursues a more aggressive clinical course with necro-inflammation and fibrosis and progression to end-stage chronic liver disease. Beyond these hepatic consequences, NAFLD is being increasingly associated with an excess risk of cardiovascular disease, coronary artery disease, as well as peripheral vascular disease in patients with T2DM [11-13]. There however remains a dearth of epidemiological and clinical evidence on NAFLD in patients with type 2 diabetes mellitus. The aim of this study was to determine the prevalence and risk factors for NAFLD in our patients with T2DM. The findings from this study will provide an opportunity to determine the prevalence of NAFLD in T2DM in our part of the world and ultimately enhance awareness of this condition and contribute to the evaluation and clinical management of the patients with NAFLD with T2DM and consequently prevent the dreaded complications of liver diseases in patients with T2DM.

Materials and methods

This is a retrospective analysis of patients who presented to the outpatient services of the department of medicine, at Government Medical College Jammu wef April 2016 to February 2020.

Included were patients with age group of 30-60 years with established T2DM diagnosed according to the American Diabetes Association (ADA) diagnostic criteria [16] (ie symptoms of diabetes plus random plasma glucose concentration ≥ 200 mg/dl or fasting Plasma Glucose (FPG) ≥ 126 mg/dl, or Two-hour Plasma Glucose > 200 after a 75g glucose load or HbA1c $> 6.5\%$). Exclusion criteria included alcohol intake in excess of 20 grams per day, history of jejunoileal bypass surgery or extensive small bowel resection, usage of drugs known to cause secondary steatosis like corticosteroids, methotrexate, and amiodarone. Pregnant women and subjects with severe comorbidities such as malignancies, congestive heart failure

and chronic kidney disease were excluded. A structured questionnaire was administered to each subject to obtain information such as bio-data, alcohol intake, current medications as well as family history of diabetes and liver disease. All patients were clinically evaluated and weight (kg) and height (m) were measured. The Body Mass Index (BMI=weight (kg) /height (m²) was calculated and classified based on World Health Organisation (WHO) criteria [17]. BMI cutoff points (Asian) was taken as follows; BMI < 18.5 kg/m² (lean or underweight), between 18.5 and 22.9 kg/m² (normal), between 23 and 27.49 kg/m² (overweight) and 27.5 kg/m² or above as (obese).[14]. Waist circumference was measured from the right side in the mid-axillary line, midway between the lower margin of the least palpable rib and the top of the iliac crest (highest point of the hip bone on the right side) as the point of reference. Hip circumference measurement (HC) in centimetres was done at the point of widest circumference of the buttocks with the tape parallel to the floor. Both waist and hip circumference was taken twice and the average was calculated. The cutoffs points for Asians used (0.95 in men and 0.80 in women) denote abdominal obesity. Average of two readings was used for analysis [15,18]. The average of three BP readings was calculated. Hypertension was considered at a blood pressure reading of more than or equal to 140/90 mmHg or current intake of anti-hypertensive or both [19]. Blood samples were taken for evaluation of serum alanine transaminase (ALT), aspartate transaminase (AST), fasting lipid profile including total cholesterol (TCHOL), high-density lipoprotein cholesterol (HDL-C), triglyceride (TG) Low-density lipoprotein cholesterol (LDL-C) was calculated using Friedwald formulae $LDL = (TCHOL - HDL - C) - TG/5$ [20]. Dyslipidemia was defined as having one or more of the criteria: LDL-C ≥ 100 mg/dL, total cholesterol ≥ 200 mg/dL, triglycerides ≥ 150 mg/dL, or

HDL-C < 40 mg/dL in males and <50 mg/dL in females [19]. Samples were also analysed for detection of antihepatitis C virus and hepatitis B surface antigen. Abdominal Ultrasound scan (USG) evaluation was performed (Aloka Pro-sound 3500, Japan) using a 3.75 MHz probe. Findings suggestive of hepatic steatosis included "bright liver" with increased echogenicity, hepato-renal contrast and attenuation of the diaphragm. The USG will assess the severity of fatty liver as grade I, II or III. [20,21]. The diagnosis of NAFLD was based on the absence of alcohol consumption (or alcohol intake less than 20 grams per day) and the presence of hepatic steatosis on USG evaluation.

Results

A total of 1250 patients, of T2DM presented to our medical outpatient department at Government medical college Jammu from April 2016 to February 2020 and their data were retrospectively analysed. Out of these 725 (58%) were males and 525 (42%) were females (Table 1, Figure 1). The maximum number of patients were in the age group of 40-50 years (619, 49.5%) followed by 50-60 years (404, 32.3%), and then the least number were in the age group of 30-40 years (227, 18.2%) (Table 1, Figure 2). Out of total 1250 patients, 973 (77.8%) had evidence of fatty liver on USG and 277(22.2%) had normal liver on USG. Out of the total 973 patients who had evidence of fatty liver, maximum patients had grade I fatty liver (476, 48.9%), and grade II fatty liver in 340 (34.9%), and grade III fatty liver in 157 (16.2%) patients (Table 1, Figure 3).

The duration of T2DM was also categorised as less than 5 years, 5-10 years, 10-15 years and more than 15 years. The maximum patients had history of T2DM of 10-15 years duration of diabetes (556, 44.4%) out of which 523 were having fatty liver and 33 had normal liver. This was followed by T2DM duration of 5-10 years (380, 30.4%)

out of which only 205 were having fatty liver and 175 had normal liver. A total of 248 (18.8 %) patients were having T2DM duration of more than 15 years out of which 241 had fatty liver and only 7 had normal liver on USG. The least number of patients had duration of T2DM of less than 5 years (66, 5.2%) out of which only 4 patients had fatty liver and 62 had normal liver (Table 1, Figure 4).

Our study revealed maximum number of patients who had NAFLD were in the overweight group, with BMI 23 - 27.49 (Kg/M^2) (629/973, 64.6%), whereas (285/973, 29.3%) NAFLD patients had normal BMI (18.5- 22.9 Kg/M^2) and (59/973, 6.1%) NAFLD patients had obesity with BMI $\geq 27.5 \text{ kg}/\text{m}^2$ (Table 2,).

The waist hip ratio suggestive of abdominal obesity with values >0.95 in Males and

>0.80 in Females were found in all patients with T2DM with NAFLD and in 31 patients without NAFLD (Table 2).

The liver function tests done in all the patients were almost normal regardless of their NAFLD status. Our study found no significant difference in the levels of Bilirubin, AST, ALT, GGT and triglyceride levels in patients of T2DM with NAFLD or without NAFLD

Discussion

Non-alcoholic fatty liver disease is a common lifestyle disease all over the world and is a matter of concern in view of sedentary habits and lack of awareness of this common disease. The most important aspect of this NAFLD is that once detected early, this condition is reversible and patient can live a healthy life after proper control of his dietary and ambulatory habits. NAFLD is the most serious liver disorder and the most common cause of cirrhosis among patients with T2DM. Our study was intended to assess the prevalence of NAFLD in patients with T2DM, rather than a sample of general population.

In our study, overall prevalence of NAFLD in T2DM was found to be 77.8%. Our prevalence is in accordance of the study done by Shivananda Pai et al (22), where they documented a prevalence of 75%. However in a study by Gupte et al (23), it was seen that mild moderate and severe NAFLD was seen in 65.5%,12.5% and 9.35% of asymptomatic T2DM patients respectively. Prashanth et al (24), reported that 87% had NAFLD on histology with 62.6% steatohepatitis and 37.3% fibrosis. They further observed that age, duration of diabetes mellitus, degree of glycemic control, body mass index, waist circumference, family history of diabetes mellitus, did not predict the presence or severity of NAFLD or fibrosis.

Our prevalence is higher than the other studies. In a larger, multicentre study by Kalra et al (25), prevalence of NAFLD was found to be 56.5%. In another study by Banerjee et al (26), they observed that, on histology, only fatty change was present in 43%, NASH in 40% and more advanced disease in 23%.

Our study revealed significantly more NAFLD in males (60%) as compared to females (40%). Our findings are in accordance with most of the studies in India where they have shown higher prevalence of NAFLD in males than in female population (27,28).

Our study documented that the maximum number of patients were in the age group of 40-50 years (619, 49.5%) followed by 50-60 years (404, 32.3%), and then the least number were in the age group of 30-40 years (227, 18.2%). The previous studies have also shown that the prevalence of NAFLD increases with age, with the most cases occurring between the age of 40-60 years (29)

Our study revealed maximum number of patients who had NAFLD were in the overweight group, with BMI 23 - 27.49 (Kg/M²) (629/973, 64.6%), whereas (285/973,29.3%) NAFLD patients had normal BMI (18.5-

22.9 Kg/M²) and (59/973, 6.1%) NAFLD patients had obesity with BMI ≥ 27.5 kg/m².

The waist hip ratio suggestive of abdominal obesity with values >0.95 in Males and >0.80 in Females were found in all patients with T2DM with NAFLD and in 31 patients without NAFLD. Our findings are in accordance with the study by Federico A et al(30)

Our study found no significant difference in the levels of Bilirubin, AST, ALT, GGT and triglyceride levels in patients of T2DM with NAFLD or without NAFLD. Infact a study by Targher et al, reported that most of the patients with NAFLD had normal Liver function tests, thus making it an insensitive marker of NAFLD(11).

Several studies have suggested relationship of NAFLD with features of the Metabolic syndrome. In this study majority of patients in the NAFLD group were overweight/obese (688/973, 70%). So, we can assume that T2DM patients with these co-morbid conditions, definitely have a higher risk of NAFLD. A peculiar observation of our study was that 29% (285/973) of our patients with T2DM with NAFLD were having normal BMI. This represents the patients who can be labelled as lean NAFLD. This sub-phenotype of NAFLD patients has been described across populations of different ethnicity, particularly in Asia, but it can be diagnosed in 10 to 20% of nonobese Americans and Caucasians. Pathophysiological mechanisms underpinning the "lean" phenotype are not completely understood, but they may include a more dysfunctional fat (visceral obesity, differences in adipocyte differentiation and altered lipid turnover), altered body composition (decreased muscle mass), a genetic background, not limited to patatin-like phospholipase domain-containing protein 3 (PNPLA3) C > G polymorphisms, epigenetic changes occurring early in life and a different pattern of gut microbiota. Lean

subjects with NAFLD have milder features of the metabolic syndrome when compared with obese patients. Nonetheless they have a higher prevalence of metabolic alterations (e.g., dyslipidemia, arterial hypertension, insulin resistance, and diabetes) compared with healthy controls. Data on histological severity are controversial, but they can develop the full spectrum of liver disease associated with nonalcoholic steatohepatitis NASH. Since lean NAFLD usually present with less obesity-related comorbidities, it is commonly believed that this group would follow a relatively benign clinical course but recent data challenge this concept. A call for more studies to understand the natural history of the disease but also for greater awareness among practitioners about the potential health risks associated with lean NAFLD is the need of the hour.

It is important that we donot focus on just one-off evaluation or short term studies on NAFLD, but rather regular long term follow up of these patients over a period of 7-10 years and encourage these patients to change their dietary habits and change their sedentary life style by regular exercise and weight loss. In fact Zelber Sagi S et al , published on prevalence and 7 years development of NAFLD in a cohort of > 200 healthy individuals with no previous history of liver disease. All the patients were counceled for weight loss and it was observed that one thirds of the patients who had NAFLD at admission, had complete regression of NAFLD after 7 years (31).

It is important to emphasise here that a proper identification of NAFLD risk factors and their undelayed control can not only reduce the prevalence of this reversible condition, but also the complications related to NAFLD and also reduce the systemic conditions related to this disease like coronary heart disease, stroke,peripheral vascular diseases, chronic kidney disease. So the authors would like to emphasise that

further research should be undertaken in our part of the country, in order to know the exact pathogeneisis and identify the actual effective treatment options relating to NAFLD.

Conclusion

The prevalence of NAFLD in patients with Type 2 DM was 77.8%. Prevalence of NAFLD was significantly higher in males. Prevalence of NAFLD was highest in the age group of 40-50 years and was more in T2DM patients with duration of diabetes 10-15 years. A proper education and the awareness of the natural history of NAFLD should be provided to the healthcare workers at the primary care level, so that such a condition is diagnosed early and the required interventions should be implemented early to take care of this reversible health issue.

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Legend Table and Figure

Table 1: Table showing the baseline characteristics and findings of the study group

Variable	Characteristics	Frequency (N=1250)	Percentage (%)
Sex	Males	725	58%
	Females	525	42%
Age	30-40 years	227	18%
	40-50 years	619	50%
	50-60 years	404	32%
Duration of T2DM	< 5 years	66	5.2%
	5-10 years	380	30.4%
	10-15 years	556	44.4%
	>15 years	248	19.8%
Liver status on USG	Normal	277	22.2%
	Grade I Fatty Liver	476	38.1%
	Grade II Fatty Liver	340	27.2%
	Grade III Fatty Liver	157	12.5%

Table 2: Table showing comparative data with regards to sex, Body mass index, abdominal circumference in the study group patients

Parameter	All patients (N=1250)	Patients with NAFLD (N=973)	Patient's without NAFLD (N=277)	p value
Male/Female (No)	725/525	584/389	141/136	<0.05
BMI (Kg/M ²)				
18.5- 22.9 (normal)	481(38.5%)	285	196	<0.05
23 - 27.49 (overweight)	706(56.5%)	629	77	
≥ 27.5 kg/m ² (obese)	63(5%)	59	4	
Abdominal obesity				
>0.95 Males	1004	973	31	<0.05
>0.80 Females				

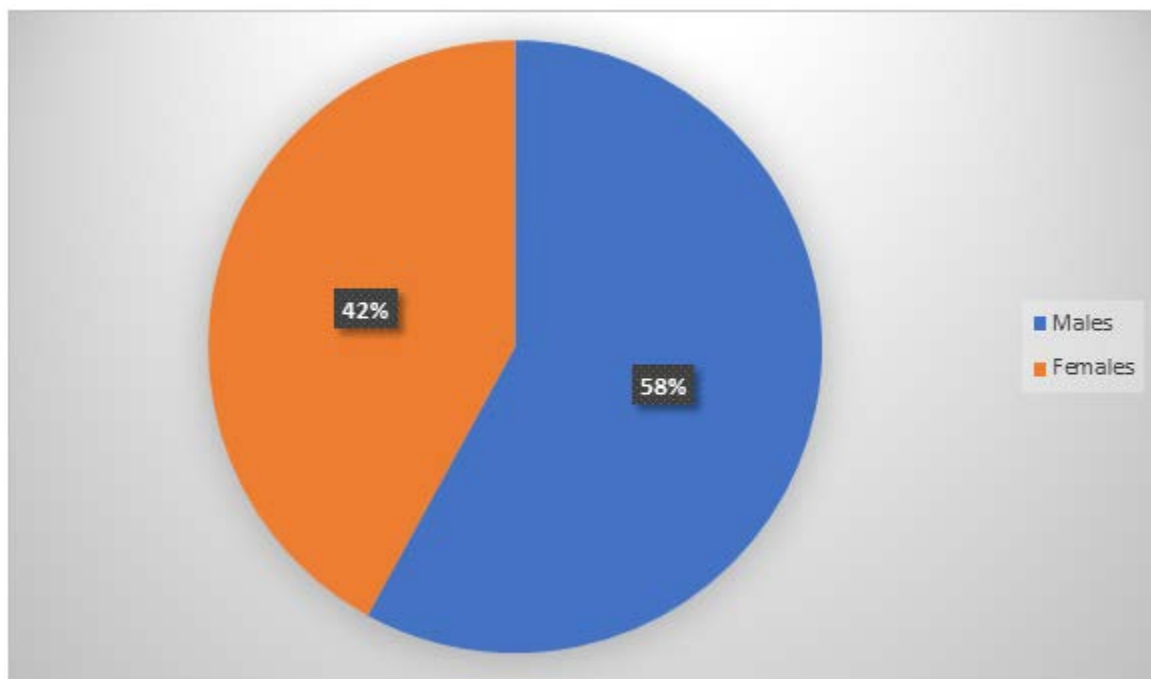


Figure 1: Pie Diagram showing the gender distribution of the study group

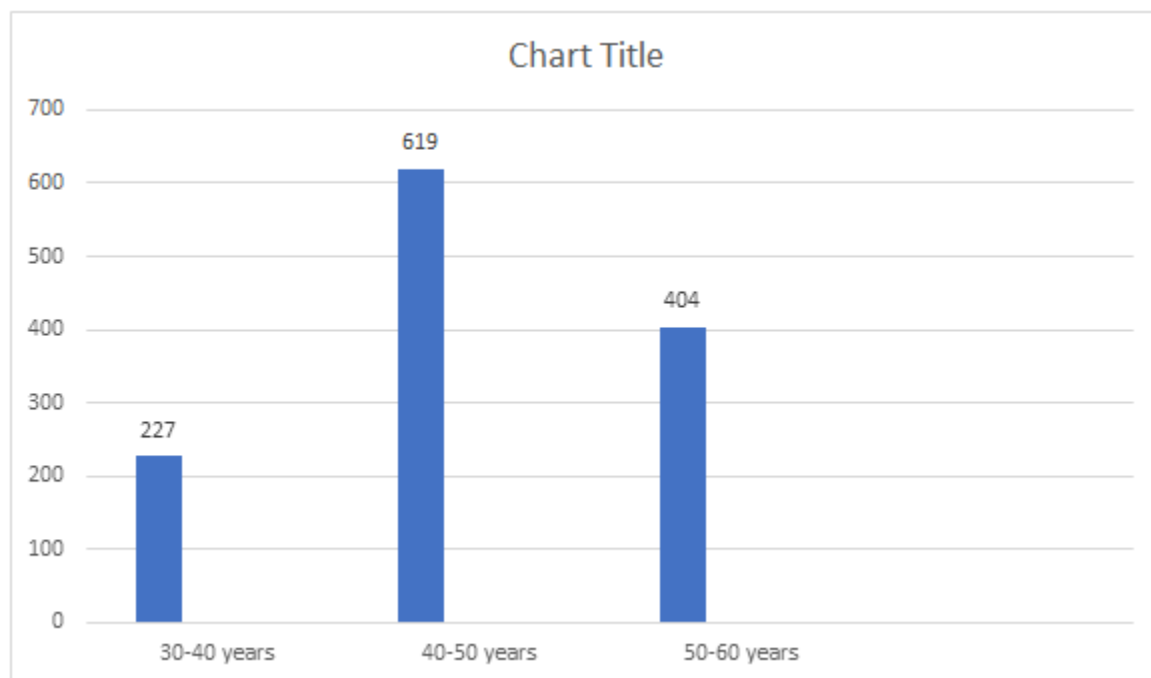


Figure 2: Bar Diagram showing the age wise distribution of the study group

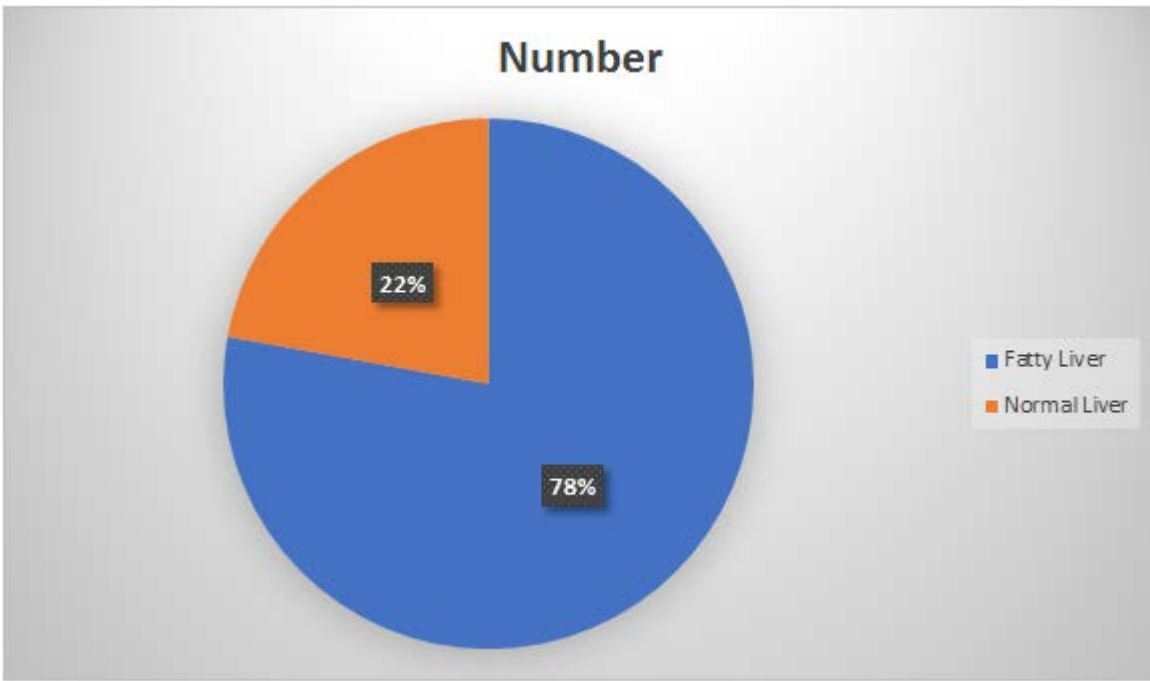


Figure 3: Pie Chart showing the prevalence of NAFLD in patients with T2DM

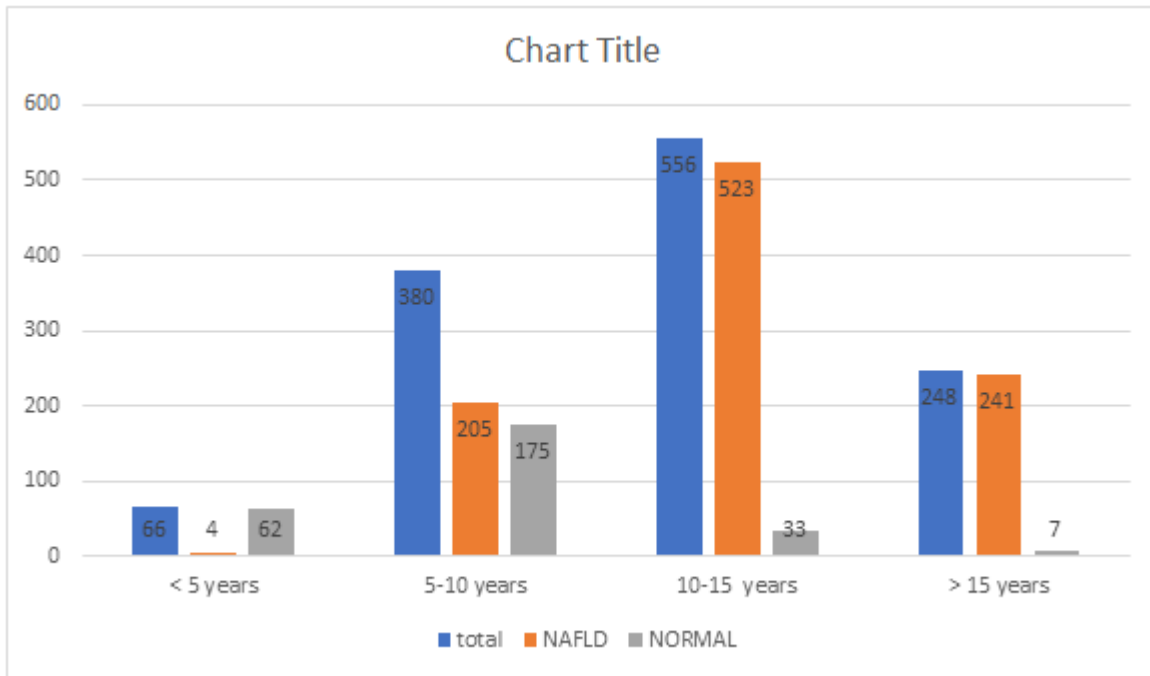


Figure 4: Bar diagram revealing the relationship of duration of T2DM with NAFLD