A Prospective Observational Study on Prevalence of Diabetes with Nonalcoholic Fatty Liver Disease in Gastroenterology Department of Tertiary Care Hospital

[1]Sreenu Thalla [*]R. Kamaraj, [2]A. Kavitha

[1]Department of Pharmacology, SRM College of Pharmacy, SRMIST, Kattankulathur, Kancheepuram, Tamil Nadu – 603203

[*]Professor, SRM College of Pharmacy, SRMIST, Kattankulathur, Kancheepuram, Tamil Nadu – 603203

[2]Professor, Department of Gastroenterology, Guntur Medical College, Guntur, Andhra Pradesh

Corresponding author: Dr. R. Kamaraj, Professor, SRM College of Pharmacy, SRMIST, Kattankulathur, Kancheepuram, Tamil Nadu – 603203. **E-mail:** kamarajr@srmist.edu.in

ABSTRACT

Non-alcoholic fatty liver disease (NAFLD), the majority universal source of hepatic abnormalities with fat accumulation with results in abnormal function of liver may cause change in metabolism. The aim of this study is prevalence of diabetes patients suffering with chronic liver disease as it is observational study. A total of 150 patients who were diagnosed as NAFLD are included in the study in which 71 patients were males and 79 patients were females. Out of 150 patients participated in the study, 106 patients were found to have NAFLD with DM and 44 were NAFLD without Diabetes Mellitus (DM). The highest prevalence was recorded in the age group of >60 years and it was more prevalent among females than males. The majority of the patients were found in the age group of >60 years followed by 40-60 years and least in 20-40 years of age. The patients diagnosed with NAFLD with a duration of >3 years were found in 90 patients followed by 1-3 years in 42 and 0-1 year in 18 patients respectively. The most common Ultrasonography (USG) Abdomen grade of NAFLD was Grade I (73 patients) followed by Grade 2 (58 patients), and least in Grade 3 (16 patients) and Grade 4 (3 patients).Whereas NAFLD patients with DM have elevated prevalence of Non-Alcohoic Steato Hepatitis (NASH) and advanced fibrosis, the probable risk of severe NAFLD cannot be ignored in patients without DM since both NASH and advanced fibrosis occur in a substantial proportion of these patients

Key Words: Chronic Liver Diseases, Diabetes, NAFLD, Steatosis, NASH

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INTRODUCTION

Non-Alcoholic Fatty Liver Disease (NAFLD) is the accumulation of triglycerides within hepatocytes that exceeds 5% of liver weight.Nonalcoholic fatty liver disease (NAFLD) is an umbrella term that encompasses multiple progressive liver disorders, ranging from simple hepatic steatosis, often called nonalcoholic fatty liver (NAFL)(Jacob M Kneeman, 2012), to nonalcoholic steatohepatitis (NASH) which is marked by hepatocyte inflammation and ballooning. Around 35% of NASH cases progress to liver fibrosis and potentially to end-stage liver disease or hepatocellular carcinoma (HCC) (Singh S, 2015 & Crespo M, 2016). The growing epidemicof NAFLD in western societies is estimated to affect around20 to 30% of the overall population and 45 to 75% of patientswith type 2 diabetes (Masarone M, 2014 & Younossi ZM, 2019). Over the last two decades,the high prevalence rates of NAFLD have been parallelingthe rapidly progressing epidemic of obesity and type-2 diabetes(Estes C, 2018). In fact, we see NAFLD and type-2 diabetes atthe intersection of similar risk factors, epidemiology, andpathophysiology. In the metabolic syndrome consists of following features like central obesity, impaired blood

glucose levels, elevated triglycerides, low HDL levels and hypertension(Kanwal F, 2018 & Lavekar A, 2015). The severity of NAFLD is associated with the severity of the metabolic syndrome with NASH and fibrosis being more prevalent in patients with more metabolic risk factors especially in Type 2 diabetes patients have insulin resistance, which links NAFLD and the metabolic syndrome. Liver stiffness measurements ranged from 2.4 to 75.4 kPa (median 6.8) in fibroscan(Jessica KD, 2014). In Utrasonography, grading of non-alcoholic fatty liver disease in following manner; Grade 1,2,3,4 depending on the visualization and diffuse status of vessel borders with penetration segment of the liver(Harman DJ, 2018).

METHODS

Source of Data

- Data was collected from Prescriptions of the patients inGastroenterology department of in-patient and out-patientsand evaluation of patient medication charts in follow-upcases, along with the clinical laboratory data, USG abdomen scan and fibroscan in Amaravathi Institute of Medical Sciences (AIMS), Amaravathi Hospital, Guntur

Study site

- Gastroenterology clinic in Amaravathi Institute of Medical Sciences (AIMS), Amaravathi Hospital, Guntur. It is a hospital based prospective observational study.

Sample size

- A total of 150 patients who fulfilled the inclusion and exclusion criteria were selected the study. Out of 150, 71 male patients and 79 female patients

Study Duration

- The study was conducted over a period of 9 months from October 2018 to June 2019

Study Criteria

The study was considered the following criteria

Inclusion Criteria

- The study included patients 18 years of age and above with NAFLD with type-2 DM & without DM

Exclusion Criteria

- Patients who are alcohol consumption, type 1 DM, hepatotoxic drug history, viral hepatitis, hemochromatosis, autoimmune hepatitis, Wilson's disease or alpha-1-antitrypsin disease were excluded

DataAnalysis

All the collected data was analyzed to assess the age, gender, Body Mass Index (BMI), duration of DM, glycemic control (HbA1C), lipid profile, co-morbidities, USG abdomen for grading of disease, fibroscan to know status of fibrous tissue of liver were determined through the analysis. Most common reasons for developing the disease were determined. All patients were monitored from the day of admission to the day of discharge. The patient data was collected and documented.

Statistical Analysis

Standard statistics were used to describe patient demographics and test manually using the Microsoft Excel 2007

RESULTS

Table 1: Age and Sex (71M + 79F)

Age	No. of patients	Percentage (%)
20-40	31(17M+14F)	20.67
40-60	43(21M+22F)	28.67
>60	76 (33M+43F)	50.66

Table 2: Duration of Diabetes

Duration	No of Patients	Percentage (%)
0-1 years	18 (7M+11F)	12.0
1-3 years	42(28M+14F)	28.0
>3 years	90 (36M+54F)	60.0

Table 3: DM with NAFLD & NAFLD without DM

DM with NAFLD	NAFLD without DM
106 (47M+59F)	44 (24M+20F)

Table 4: NAFLD with DM with duration – 106 (47M+59F)

Duration	No of Patients	Percentage (%)
0-1 years	1 (1M+0F)	0.94
1-3 years	15 (6M+9F)	14.1
3-6 years	32 (10M+22F)	30.18
> 6 years	58 (30M+28F)	54.71

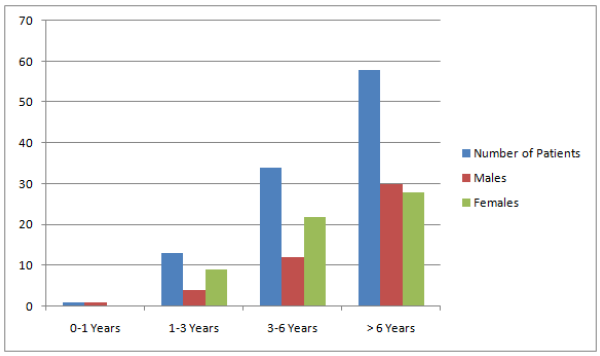

Figure 4: NAFLD with DM with duration

Table 5: NAFLD with DM with age – 106 (47M+59F)

Age	No. of patients	Percentage (%)
20-40	4 (2M+2F)	3.78
40-60	34 (13M+21F)	32.07
>60	68 (32M+36F)	64.15

Table 6: NAFLD without DM (Co-morbidities) – 44 (24M+20F)

Disease	No of Patients	Percentage (%)
Hypothyroidism	10 (6M+4F)	22.73
Cardiovascular Diseases	8 (3M+5F)	18.18
Hypertension	11 (4M+7F)	25.0
Neurological Diseases	15 (11M+4F)	34.09

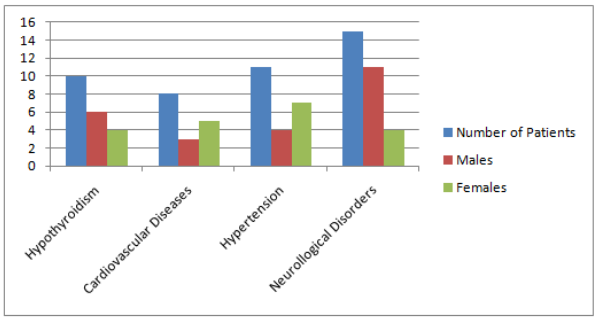

Figure 1: NAFLD without DM (Co-morbidities)

Table 7: NAFLD without DM with age – 44 (24M+20F)

Age	No. of patients	Percentage (%)
20-40	27 (15M+12F)	61.37
40-60	9 (8M+1F)	20.45
>60	8 (1M+7F)	18.18

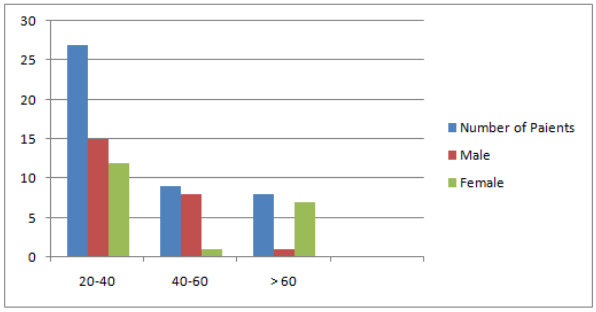

Figure 2: NAFLD without DM with age

Table 8: Body Mass Index (BMI)

Body Mass Index	No. of patients	Percentage (%)
Normal (18.5-25)	18 (7M+11F)	12.0
Over Weight (25-30)	37 (14M+23F)	24.67
Obese Class 1 (30-35)	63 (41M+22F)	42
Obese Class 2 (35-40)	24 (7M+17F)	16
Obese Class 3 (> 40)	8 (2M+6F)	5.33

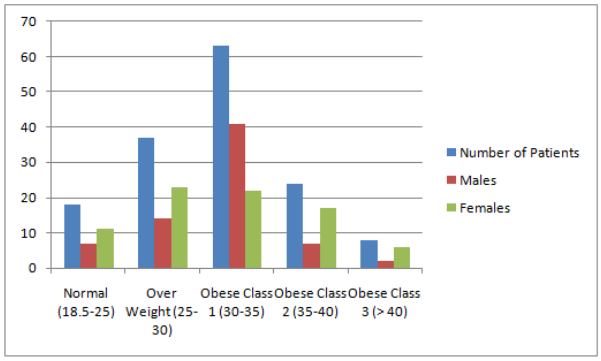

Figure 3: Body Mass Index (BMI)

Table 9: Glycaemic Control (HbA1C)

HbA1C Value	No of patients	Percentage (%)
Normal or Good Control (4-6)	33 (19M+14F)	22
Prediabetes (6-6.5)	11 (5M+6F)	7.33
Diabetes (7-8)	93 (44M+49F)	62
Poor Control (> 8)	13 (3M+10F)	8.67

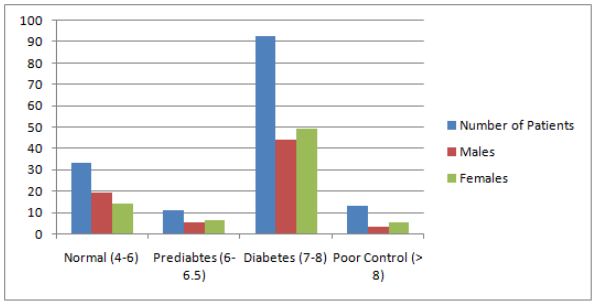

Figure 4: Glycaemic Control (HbA1C)

Table 10: Abnormal Lipid Profile

Lipid Profile	No of patients		
	Mild	Moderate	Severe
Triglycerides	5 (3M+2F)	8 (2M+6F)	3 (2M+1F)
Total Cholesterol	4 (1M+3F)	12 (8M+4F)	7 (4M+3F)
HDL	6	8	2
	(4M+2F)	(5M+3F)	(2M+OF)
LDL	12 (8M+4F)	9 (4M+5F)	4 (2M+2F)
VLDL	7 (3M+4F)	5 (3M+2F)	2 (1M+1F)

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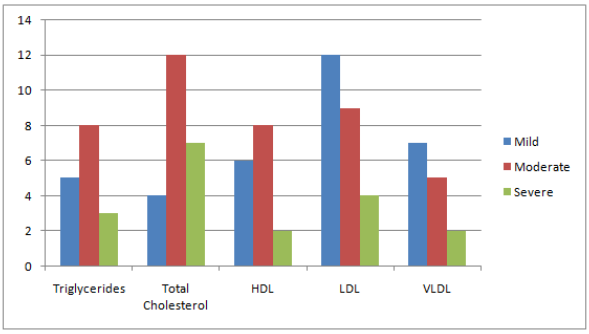

Figure 5: Abnormal Lipid Profile

Table 11: Liver Function Tests (Abnormal)

Parameter	No of Patients	Percentage (%)
Total Bilrubin	114 (53M+61F)	76
AST	64 (26M+38F)	42.67
ALT	87 (54M+33F)	58
ALP	36 (15M+21F)	24
Total Proteins	92 (53M+39F)	61.33
Albumin	71 (32M+39F)	47.33

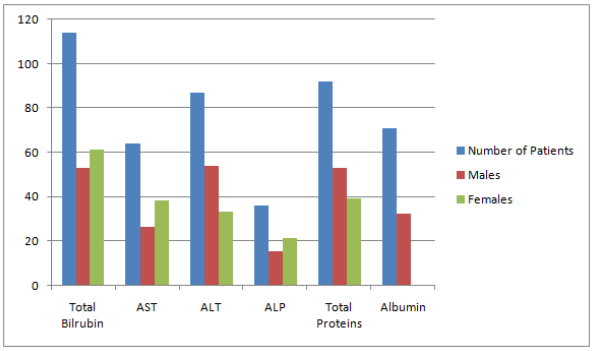

Figure 6: Liver Function Tests (Abnormal)

Table 12: USG Abdomen with grades

Grade	No of patients	Percentage (%)
1	73 (39M+34F)	48.67
2	58 (26M+32F)	38.67
3	16(5M+11F)	10.66
4	3(1M+2F)	2

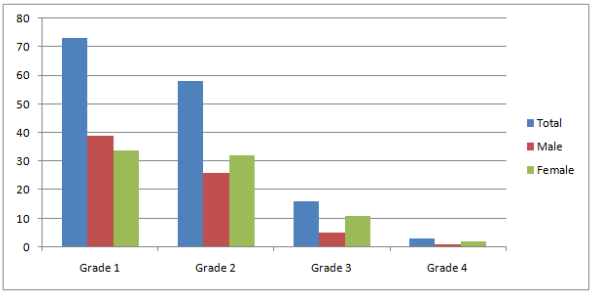

Figure 7: USG Abdomen Grades

Table 13: Fibroscan with grades

Fibroscan Grade (kPa)	No of patients	Percentage (%)
F0 – Normal (2)	0	0
F1 – Mild (2-7)	21 (9M+12F)	14
F2 – Moderate (7.5-10)	67 (38M+29F)	44.67
F3 – Severe (10-14)	52 (18M+34F)	34.67
F4 – Advanced (14-75)	10 (6M+4F)	6.66

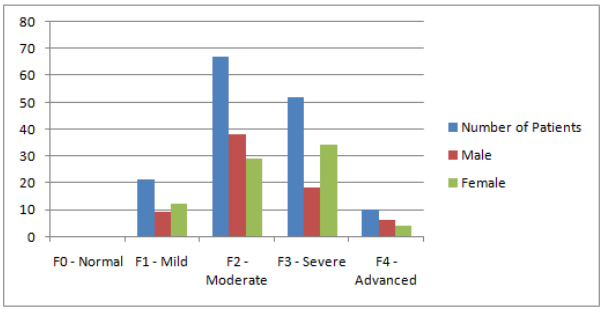

Figure 8: Fibroscan with grades

DISCUSSION

A total of 150 patients who were diagnosed as NAFLD are included in the study in which 71 patients were Male and 79 patients were females. The highest prevalence was recorded in the age group of>60 years and it was more prevalent among females than males. The majority of the patients were found in the age group of >60 years followed by 40-60 years and least in 20-40 years of age (Table 1). The patients diagnosed with NAFLD with a duration of >3 years were found in 90 patients followed by 1-3 years in 42 and 0-1 year in 18 patients respectively (Table 2). Out of 150 patients participated in the study, 106 patients were found to have NAFLD with DM around 70.67percentage and 44 were NAFLD without DM around 29.33 percentage (Table 3).Among 106 patients who were NAFLD with DM, diagnosed patients had more with duration of > 6years were found 58 approximately 54.71 percentage, followed by 3-6 years duration of DM (Table 4).Patients diagnosed NAFLD with DM>60years age had more prevalent compared to other age groups (Table 5 & Figure 1). NAFLD without diabetes patients were 44 had co-morbidities like hypertension 11, hypothyroidism 10, cardiovascular diseases 8 and neurological disorders were 15 (Table 6 & figure 2) and the age group 20-40 had the more prevalence than the other age groups according to our data (Table 7 & figure 3). Based on the body mass index (BMI), obese class 1 patients had highest prevalence 63, followed by overweight and obese class 2 groups (Table 8 & figure 4). Based on the HbA1C (Glycaemic control), poor control were only 13 patients, remaining diabetic patients were under control of their blood glucose levels with their medication (Table 9 & figure 5). Lipid profile of the patients were analysed, majority of patients had mild to moderate levels and very few patients had elevated and severe levels (Table 10 & figure 6).Liver function tests were analysed among all the patients, total bilrubin elevated in 114 patients, AST in 64 patients, ALT in 87 patients, ALP in 36 patients, whereas total protein and albumin levels reduced in 92 and 71 patients respectively (Table 11 & figure 7). Based on the USG Abdomen grades of NAFLD were detected. The most common USG Abdomen grade of NAFLD was Grade I, 73 patients followed by Grade 2, 58 patients and least in

Grade 3, 16 patients and Grade 4, 3 patients (Table 12 and figure 8). Based on the fibroscan grades of NAFLD were detected. The most common grade of NAFLD was Grade 2, 67 patients followed by Grade 3, 52 patients and least in Grade 1, 21 patients and Grade 4, 10 patients (Table 13 and figure 13). We obtain the results using Microsoft Excel 2007.

In our study, the highest prevalence was found in the age group of > 60 years age group followed by 40-60 and 20-40 years of age groups. NAFLD is common among elderly patients and it is associated with components of metabolic syndrome.The Natural history NAFLD suggests that the elder age is the predictor of advanced fibrosis and mortality. The prevalence among females was higher when compared to males may be due to there will be a hormonal change among the post-menopausal women. In this study, NAFLD with DM was found to be more in number 106 patients, when compared to NAFLD without DM was 44 patients (Table 3 and figure 3). As NAFLD is a metabolic disorder there will be a prevalence pattern of NAFLD with DM. Based on the USG Abdomen the severe Steatosis reported in 4 patients. The duration of NAFLD >3 years may suggest the cumulative mortality risk among the elder people.

In a study that followed 11,448 subjects for 5 years, incidence of NAFLD documented by ultrasound was 12% (n=1,418) (Harman DJ, 2018). In a study of 635 Nagasaki atomic bomb survivors who were followed for 11.6 years, incidence of NAFLD documented by ultrasound was 19.9 per 1,000 person-years (Fattahi MR, 2016). In 565 subjects, the incidence of NAFLD at 3-5years, diagnosed using magnetic resonance imaging (MRI) was estimated to be 13.5% (Dhumal UM, 2013). Another cohort study, for an average of 4.5years free of NAFLD at baseline in 77,425 subjects was documented, during 10,340 participants developed NAFLD predictable by ultrasound, translating to an incidence rate of 29.7% (Wong VW, 2015). A study from England, reported an incidence rate for NAFLD of 29/100,000. Given the erroneousness of managerial coding such as ICD-10, this study most likely underestimates the true incidence of NAFLD (Chang Y, 2016). Other study commencing Israel reported an incidence rate of 28/1,000 (Younossi ZM, 2016). A meta-analysis estimated that the collective regional incidence of NAFLD from Asia to be 52.34/1,000, whereas the incidence rate from the West is estimated to be approximately 28/1,000. The highest number of publications describing significance of incidence in contrast with prevalence of NAFLD, the metaanalysis of NAFLD: The meta-analysis estimated that the on the whole global prevalence of NAFLD diagnosed by imaging is around 25.24%. The maximum prevalence of NAFLD is reported from the Middle East 31.79% and South America 30.45% whereas the lowest prevalence rate is reported from Africa 13.48%. The prevalence of NASH amongst NAFLD patients who had liver biopsy for a clinical implication is expected to be 59.10%. The prevalence of NASH among NAFLD patients who had liver biopsy without a specific clinical indication is predictable from 6.67% and the prevalence of NASH in the population ranges between 1.5% and 6.45% (Naga C, 2018). In this context, the prevalence of NAFLD may vary conventional conditions like obesity, type 2 diabetes, hypertension, and dyslipidemia and emerging conditions, age, sex and ethnicity. In fact, both the prevalence of NAFLD and stage of liver disease emerge to amplify with age. Males have major risk when compared with females and the prevalence of NAFLD in men is two times higher than in women (Dongiovanni P, 2013). Lifestyle adaptationbeforemostkey in which consisting of diet, exercise and weight loss to treat patients with NAFLD(Anusha V, 2020). Unfortunately, data of diet,exercises on NAFLD areinadequate. The availability of simple diagnostictests that can be widely used by practitioners,in combination with access tolow-cost, safe, and more effective medications in the near future, will radicallychange disease management in the nearfuture(Fernando B, 2017).Liver stiffness measurement is a goodmethod for the diagnosis of fibrosis and cirrhosis, irrespectiveof the cause of liver disease(Foucher J, 2006). The potency of this study include the hefty number of patients with proven NAFLD in addition to the wide range of available demographic, USG Abdomen, fibroscan, clinical laboratory data had limited number of patient's data, so the further studies required.

CONCLUSION

Whereas NAFLD patients with DM have elevated prevalence of NASH and advanced fibrosis, the

probable risk of severe NAFLD cannot be ignored in patients without DM since both NASH and advanced fibrosis occur in a substantial proportion of these patients

LIST OFABBREVATIONS

NAFLD – Non Alcoholic Fatty Liver Disease

NASH – Non Alcoholic Steato Hepatitis

USG – Ultra Sono Graphy

DM – Diabetes Mellitus

CLD – Chronic Liver Disease

HCC – Hepato Cellular Carcinoma

HDL – High Density Lipoprotein

LDL – Low Density Lipoprotein

VLDL – Very Low Density Lipoprotein

ICD – International Classification of Diseases

BMI – Body Mass Index

HbA1C – Glycalated Hemoglobin

IP – In-Patient

OP – Out-Patient

AST – Aspartate Transaminase

ALT – Alanine Aminotransaminase

ALP – Alkaline Phosphate

DECLARATIONS

ETHICAL APPROVAL AND CONSENT TO PARTICIPATE

Written informed consent was signed by all study participants. The study approval was taken from the Institutional Ethical Committee (IEC), AM Reddy Memorial College of Pharmacy, Narasaraopeta; Guntur held on 24thSeptember 2018 with Ethical Committee number – **ARMN/PP5/2018/H/03.**

CONSENT FOR PUBICATION

Not applicable

AVAILABILITY OF DATA AND MATERIAL

All data generated or analyzed during this study are included in this published article

COMPETING INTEREST

The author declares that they have no competing interests.

FUNDING

Nil

AUTHORS CONTRIBUTIONS

AK and RK contributed for the idea of study and work proposal and supervision, ST collected the patient data, consent for the study and documentation and the contributors for analyzing, interpretation and writing the manuscript. "**All authors read and approved the manuscript**".

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