Original Research Article

Prevalence and risk factors for metabolic-dysfunction associated fatty liver disease in South Indian population

ABSTRACT

Background: Metabolic associated fatty liver disease (MAFLD) is a new definition proposed by the global consensus panel in 2020 for liver disease associated with known metabolic dysfunction. Based on new diagnostic criteria, we aimed to investigate its prevalence and risk factors in Indian population.

Methods: This was a cross-sectional study and included 2290 adult subjects where the socio-demographic details along with their clinical history, examination and other relevant findings were noted and anthropometric details were measured. Blood samples for the required investigations were collected. A diagnosis of MAFLD was made if imaging showed presence of hepatic steatosis along with any of the MAFLD factors. Age under 18, a history of cancer, oophorectomy/ hysterectomy, liver surgery or nephrectomy, and incomplete data were the exclusion criteria. The data were analysed by using SPSS software of version 22.

Results: Out of 2290 subjects, 940 (41%) were females and 1350 (59%) were males with the mean age of 43.8 years (SD ±13.6). Overall, 640 (27.94%) participants were diagnosed with MAFLD and there were significant difference noted between participants of age 40 and above with less than 40 years (P <0.05). In addition, there were also higher significant difference noted in participants with comorbidities such as diabetes mellitus and hypertension (P<0.05). After applying Independent t test, there were statistically significant difference noted between MAFLD and non-MAFLD in all parameters such as age, BMI, WHR, SBP, FPG, TG, HDL, LDL and ALT except uric acid (P<0.05).

Conclusion: We found a prevalence of MAFLD of 27.9% among the study population. Further, the actual significant predictors were age, BMI, WHR, SBP, FPG, TG, LDL and ALT.

Keywords: Nonalcoholic fatty liver disease, metabolic syndrome, metabolic-dysfunction associated fatty liver disease, risk factors

1. INTRODUCTION

Fatty liver disease is described as the accumulation of fat in the liver, and is frequently linked to metabolic syndromes (MS) such as obesity, diabetes, hypertension, and dyslipidaemia. Alcoholic fatty liver disease and nonalcoholic fatty liver disease (NAFLD) are the two primary forms of fatty liver disease [1]. NAFLD has become the most prevalent liver disease worldwide. It considerably raises the risk of cirrhosis, liver failure, and hepatocellular cancer and affects 25–30% of people worldwide [2]. NAFLD is more common in those with diabetes

(55.5%–59.7%) [3-5], overweight or obesity (64.6%–95%) [6-8], and metabolic syndrome (73%) [9].

The prevalence of NAFLD in India has been observed to range from 6.7% to 55.1% [10, 11]. It may be the cause of nearly one-third of all cases with an asymptomatic increase of liver enzymes [12]. Additionally, liver transplant centres' explant histology data indicate that NAFLD was present in two-thirds of patients with "cryptogenic" cirrhosis [13]. In India, the prevalence of prediabetes, diabetes, and metabolic syndrome is rising in both urban and rural areas, with rates of 19–22%, 15%–19%, and 30%, respectively, among adults [14, 15]. It is anticipated that the prevalence of NAFLD will rise along with the prevalence of diabetes, obesity, and metabolic syndrome, placing a greater strain on health resources.

NAFLD, which can range from hepatic steatosis to steatohepatitis, fibrosis, or cirrhosis, is usually thought to be intimately associated with obesity and a number of metabolic diseases. It is recognised as the hepatic manifestation of multisystem metabolic dysfunction [16]. As studies has advanced, NAFLD has been discovered to be derived from the potential state of multiple metabolic dysfunctions with complex pathophysiological characteristics. Additionally, due to its high prevalence in the general population, it is common for NAFLD to coexist with other liver diseases, indicating that the exclusion criteria can no longer meet the current requirements for the diagnosis of the disease [17].

In 2020, a global consensus panel proposed the term metabolic (dysfunction)-associated fatty liver disease (MAFLD) and a set of diagnostic criteria to highlight the pathophysiology. Regardless of concurrent liver disease, the diagnosis of MAFLD is predicated on the presence of metabolic dysregulation, which includes obesity and type 2 diabetes mellitus [18]. Alcohol use and the co-occurrence of other liver conditions, such as viral hepatitis, are no longer ruled out for the diagnosis of MAFLD, unlike NAFLD. Reevaluating the epidemiology of MAFLD is necessary due to a paradigm shift in the definition of fatty liver disease. However, real-world MAFLD research is still in its early stages, and it will take a long time to gather enough data to evaluate the incidence of MAFLD on a global basis. Additionally, the range of MAFLD appears to extend well beyond NAFLD, and data from the great majority of prior studies on NAFLD are ineligible for easily measuring MAFLD prevalence [19].

In order to better understand the relationship between MAFLD and various metabolic disorders and to offer a more precise reference for the management and prevention of MAFLD, this study intends to examine the prevalence and risk factors for MAFLD based on the new diagnostic criteria.

2. METHODOLOGY

This cross-sectional study included 2290 adult subjects who attended the Outpatient unit of Gastroenterology Department at Tirunelveli Super Speciality Hospital, Tamil Nadu from February 2023 to September 2023. The study was conducted after obtaining Institutional ethical committee clearance of register no. ECR/1227/Inst/TN/2019 and informed consent was obtained from all participants before enrolling in this study.

The socio-demographic data of the participants (age, sex, lifestyle habits such as smoking, alcohol and comorbid conditions) along with their clinical history, examination and other relevant findings were noted in a structured proforma. Anthropometric details such as height, weight, waist circumference (WC), body mass index (BMI), and hip circumference (HC) were measured. Blood samples for the required investigations such as fasting plasma glucose (FPG), alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase

(ALP), triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and uric acid (UA) were collected. A diagnosis of MAFLD was made if imaging showed presence of hepatic steatosis along with any of the following conditions such as overweight or obesity, diabetes and metabolic dysfunction. Subjects with age under 18, a history of cancer, a history of oophorectomy or hysterectomy, a history of liver surgery or nephrectomy, and incomplete data were the exclusion criteria.

The primary outcome of this study was to estimate the prevalence of MAFLD among patients attending medical gastroenterology out-patient department. The secondary outcome was to determine the screening indices for predicting the individuals who are at risk for developing MAFLD in a community.

Statistical analysis

The data were analysed by using Statistical Package for the Social Sciences (SPSS) software of version 22. Mean and standard deviation was calculated for continuous variables and percentage was calculated for categorical variables. Odds ratio and relative risk was calculated for risk factors of fatty liver. Chi-square test was done to find the association of risk factors with MAFLD. Independent t test was done to find difference in all parameters between MAFLD and non-MAFLD group of patients. The p-value of less than 0.05 was considered significant.

3. RESULTS

Of these 2290 subjects enrolled in this study, 940 (41%) were females and 1350 (59%) were males with the mean age of 43.8 years (SD ±13.6). There were male dominance noted in this study. The distribution of age group was described in Figure 1, with the majority of participants came in the age group of 41-50 years of 28% respectively. About 30% of the subjects were smoking, 33.6% of them were alcoholic. Further, 71.6% of the subjects have diabetes mellitus, 76.4% of them have hypertension and 72% of them have MAFLD. The clinical characteristics of the participants such as age, height, weight, BMI, WC, HC, waist to hip ratio (WHR), systolic blood pressure (SBP), FPG, TG, HDL, LDL, ALT and UA were detailed in Table 1. In addition, the ultrasonography (USG) findings of the study subjects highlighted that 20% of the subjects have grade 1 fatty liver and 7.86% of them had grade 2 fatty liver (Figure 2).

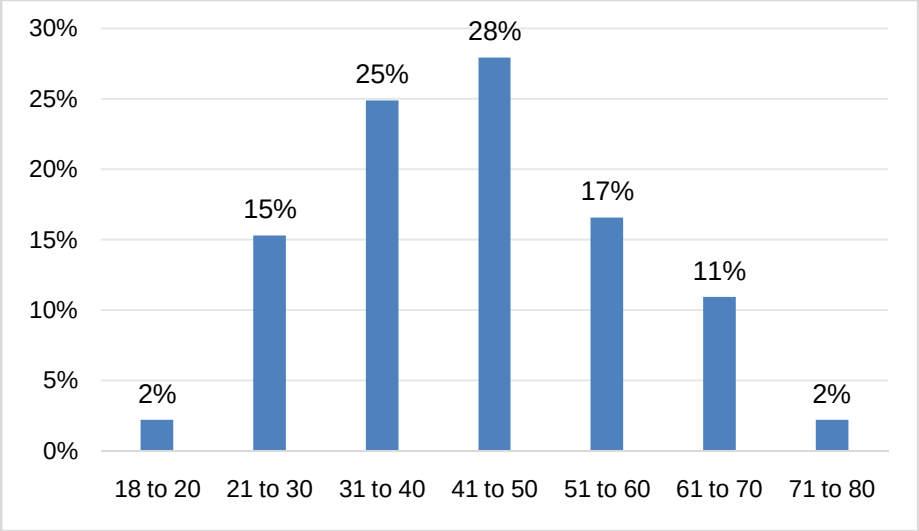

Figure 1. Distribution of subjects based on their age group

Table 1. Clinical characteristics of the study participants

Variables	Mean	Std. Deviation	Median	Std. Error of Mean
Age (Years)	43.83	13.6	43	0.899
Height (Cms)	161.38	4.46	162	0.295
Weight (Kg)	63.33	5.36	63	0.354
BMI (Kg/m^2)	23.78	2.04	22.9	0.1354
WC (Cms)	80.03	5.01	80	0.332
HC (Cms)	94.81	3.97	96	0.263
WHR	0.8412	0.0405	0.8400	0.0026
SBP (mm Hg)	119.34	10.12	120	0.669
FPG (mg/dL)	103.35	28.54	96	1.887
TG (mg/dL)	142.77	42.66	135	2.820
HDL (mg/dL)	44.88	4.15	45	0.274
LDL (mg/dL)	99.38	10.40	98	0.688
ALT (U/L)	40.05	17.65	35	1.166
UA (mg/dL)	6.91	0.8081	6.90	0.0534

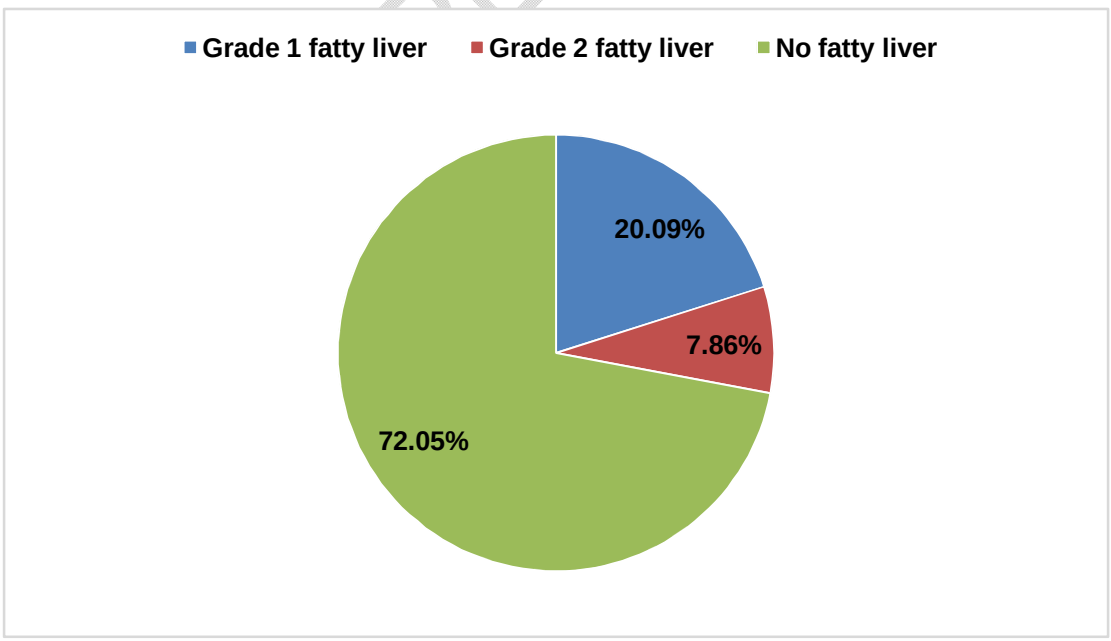

Figure 2. The USG findings of study participants

Prevalence of MAFLD and stratification by age, sex, social history, and comorbidities

Out of 2290 participants, 640 (27.94%) participants were diagnosed with MAFLD and there were significant difference noted between participants of age 40 and above with less than 40 years (P <0.05). In addition, there were also higher significant difference noted in participants with comorbidities such as diabetes mellitus and hypertension (P<0.05) (Table 2). This indicates that the risk of getting MAFLD is more in those who smoke, consume alcohol, diabetics, hypertensives, those with age more than 40 and in females.

Table 2. Prevalence of MAFLD stratified by age, sex, social history, and comorbidities

Parameters		MAFLD		Total	Odds Ratio	Relative Risk	p value
		Yes (N=640)	No (N=1650)				
Age	**40 and Above**	550	810	1360	6.337	4.179	<0.05
	Less than 40	90	840	930			
Sex	**Female**	300	640	940	1.392	1.267	0.264
	Male	340	1010	1350			
Smoking	**Yes**	250	430	680	1.819	1.518	0.053
	No	390	1220	1610			
Alcohol	**Yes**	230	540	770	1.153	1.107	0.644
	No	410	1110	1520			
Diabetes Mellitus	**Yes**	390	260	650	8.34	3.936	<0.05
	No	250	1390	1640			
Hypertension	**Yes**	270	270	540	3.73	2.365	<0.05
	No	370	1380	1750			

Comparison of the relationship between MAFLD and other related risk factors

On applying Independent t test, there were statistically significant difference noted between MAFLD and non-MAFLD in all parameters such as age, BMI, WHR, SBP, FPG, TG, HDL, LDL and ALT except uric acid (P<0.05) (Table 3).

Table 3. Comparison of the association between MAFLD and other related risk variables

Variables	MAFLD	N	Mean	Std. Deviation	Std. Error of Mean	p value
Increased Age	**No**	1650	40.48	12.722	0.990	<0.05
	Yes	640	52.48	11.943	1.493	
Increased BMI	**No**	1650	23.1436	1.35004	0.10510	<0.05
	Yes	640	25.4391	2.57044	0.32131	
Increased WHR	**No**	1650	0.8305	0.03661	0.00285	<0.05
	Yes	640	0.8688	0.03723	0.00465	
Elevated SBP	**No**	1650	116.78	8.090	0.630	<0.05
	Yes	640	125.97	11.778	1.472	
Increased FPG	**No**	1650	92.38	14.964	1.165	<0.05
	Yes	640	131.64	35.193	4.399	
Increased TG	**No**	1650	126.50	22.859	1.780	<0.05
	Yes	640	184.72	52.421	6.553	
Decreased HDL	**No**	1650	45.52	4.013	0.312	<0.05
	Yes	640	43.25	4.090	0.511	
Increased LDL	**No**	1650	96.96	8.867	0.690	<0.05
	Yes	640	105.61	11.502	1.438	
Increased ALT	**No**	1650	32.48	10.865	0.846	<0.05
	Yes	640	59.55	16.858	2.107	
Increased UA	**No**	1650	6.9364	0.76238	0.05935	0.545
	Yes	640	6.8641	0.92021	0.11503	

4. DISCUSSION

The prevalence of MAFLD steadily rises as a result of economic growth, dietary and lifestyle changes, urbanisation, advancements in screening and diagnostic tools, and research methodologies. It has been estimated that 15-20% of patients with MASH will have liver cirrhosis within 10-20 years and the number of liver-related deaths due to MASH will increase 178% by 2030. As the prevalence of MAFLD increases, the incidence of its complications such as decompensated cirrhosis and hepatocellular carcinoma will also increase progressively. MAFLD is the second most common cause for liver transplantation, but it is probable that it will soon be the first one [20]. Despite awareness of the progressive increase in the incidence of the disease, there has been no significant progress in treatment and management in the last few years.

In this present study, the prevalence and risk factors for MAFLD were investigated among the South Indian population to help in identifying the patients at an earlier stage for better management of the patients, and significant differences in the prevalence of MAFLD between groups according to age, sex, BMI, and other characteristics were found. To our knowledge, this is the first large scale population based study done in South India with focus

on prevalence and metabolic factors associated with fatty liver disease since the inception of the new definition of MAFLD in 2020.

In this study, the mean age of the subjects was 43.83, with age range from 18 to 80 years and majority were seen in 41 to 50 age group of 28%. The gender distribution revealed that males were predominant in the study population (59%). This was in line with Chen YL et al. where there were majority of the subjects in the age group of 41-50 years and male predominance in their study [16]. Around 28% of study population have MAFLD with a slight preponderance among males than females. This showed that approximately about one-third of the population had fatty liver disease. Furthermore, we found that middle-aged men were more likely to have MAFLD than older men. The following are some potential explanations for this outcome: In contrast to older men who usually retire, middle-aged men who are at the height of their careers may face greater pressure and participate in social behaviours that may result in unhealthy lifestyles, which can raise their risk of developing metabolic disorders. Some people may die of other diseases at older ages because fatty liver can significantly increase overall mortality [21]; therefore, these people are not included in the MAFLD population.

The impact of alcohol use on MAFLD has not yet been determined. While our study identified no significant difference between alcohol intake and the prevalence of MAFLD, prior research indicates that alcohol consumption may be positively or adversely related with MAFLD when compared to abstinence [22]. Because alcohol intake was linked to certain MAFLD risk variables, which were not taken into account in the studies, the existence of this result did not rule out the possibility of confounding factors.

The percentages of aberrant metabolic features were all considerably greater in MAFLD patients than in non-MAFLD patients, indicating a strong correlation between MAFLD and MS components such as central obesity, hypertension, dyslipidaemia, and dysglycemia. Obesity causes profound changes in the metabolic profile which results in insulin resistance and increased inflammation which predisposes an individual to metabolic disorders [18]. Our study also showed a positive correlation between increased BMI and waist to hip ratio in the development of MAFLD. Additionally, it was found that people with MAFLD have a higher percentage of impaired liver function than people without MAFLD, as seen by the fact that they are more likely to have raised liver enzymes, especially elevated ALT. Furthermore, prior research has demonstrated that high ALT is linked to the development of steatohepatitis and even liver fibrosis in NAFLD [23], suggesting that elevated ALT may also have significant clinical significance for MAFLD.

Among the study participants, in addition to increased BMI and elevated waist circumference, the most significant difference was found in elevated TG, LDL and decreased HDL were also shown to be significantly associated with MAFLD, which suggests that impaired lipid profile tests may be an important risk factor for MAFLD. Moreover, the difference in the proportion of individuals with elevated fasting glucose was also highly significant, and fasting glucose was also significantly associated with MAFLD and was consistent with a previous study that showed a correlation between fatty liver and dyslipidaemia and dysglycaemia [24], indicating that elevated fasting glucose may also be an important risk factor for MAFLD.

Changes in a number of biochemical markers typically accompanied the onset and progression of fatty liver. In this investigation, we discovered that MAFLD patients had greater levels of lipid metabolism indices, such as ALT, TG, LDL-C, and lower HDL-C, as well as liver function enzymology indexes. These findings suggested that MAFLD subjects were more susceptible to dyslipidaemia and abnormalities of hepatic function. Increased

levels of lipid metabolism markers might be the outcome of steatosis and pathological damage caused by excessive fat deposition in the liver cells. The metabolic syndrome, which has a significant and independent connection with MAFLD, includes elevated TG, decreased HDL-C, and a greater prevalence of hypertension and diabetes mellitus [25].

The strength of our present study is that it included a large number of subjects predominantly from the rural population. Furthermore, only very few studies have reported the biochemical parameters of individuals with MAFLD in the general population. The findings of this study can be used to corroborate the blood biochemical results in the general population. However, it has certain limitations. Since it is a cross-sectional design, there could be a recall bias as some habits such as smoking and drinking were based on the self assessment of the participants. USG was used to diagnose MAFLD rather than liver biopsy and histology as ultrasound was much more feasible as the study included a large number of subjects. Further studies are needed for determining the use of non invasive methods for diagnosis of fatty liver and liver function tests to correlate with ultrasound staging of hepatic steatosis severity with follow-up of the lifestyle determinants.

5. CONCLUSION

This study found a prevalence of MAFLD of 27.9% among the study population. Moreover, the actual significant predictors for MAFLD were age, BMI, WHR, SBP, FPG, TG, LDL and ALT. Identifying high-risk groups is the key to establish effective screening strategies. Furthermore, the need of the hour is to design and implement local care pathways in order to improve access to effective treatments and help identify interventions with sustained effect. So, this study could set a baseline for future references and help in tackling the metabolic problems in an effective way.

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