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## INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/13093

DOI URL: <http://dx.doi.org/10.21474/IJAR01/13093>



### RESEARCH ARTICLE

#### RISK FACTORS ASSOCIATED WITH TYPE 2 DIABETES MELLITUS AND THE FREQUENCY OF NAFLD AFFECTED PATIENTS

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#### Manuscript Info

##### Manuscript History

Received: 05 May 2021

Final Accepted: 10 June 2021

Published: July 2021

##### Key words:-

Non-Alcoholic Fatty Liver Disease, type 2 Diabetes Mellitus, BMI, Duration of Diabetes Mellit

#### Abstract

Diabetics have a higher risk of developing nonalcoholic fatty liver disease (NAFLD) and associated complications than the general population. The purpose of this study was to determine the prevalence of Non-Alcoholic Fatty Liver Disease (NAFLD) in patients with type 2 diabetes, as well as the demographic, metabolic, and biochemical features associated with it.

**Material and methods:** This was a prospective, observational, descriptive (cross-sectional), and non-interventional research on a cohort of type 2 diabetes mellitus patients conducted in a hospital setting. Over the course of 18 months, this study was done (August 2019 to March 2021).

**Results:** A total of 100 patients were enrolled, with 63 (63%) being Females and 37 (37%) being men. Age, BMI, and diabetes duration all had statistically significant positive correlations with the prevalence of nonalcoholic fatty liver disease. Overall prevalence of NAFLD was 63 percent (63/100). In this investigation, gender, age > 48, BMI > 25 kg/m<sup>2</sup>, and diabetes mellitus duration > 10 years were all risk variables linked with the existence of NAFLD (p=0.0002).

**Conclusion:** Present study highlighted the significant burden of Non-Alcoholic Fatty Liver Disease in cohort of type -2 Diabetes Mellitus. About half of the subjects had NAFLD (63%). In present study high BMI, and duration of diabetes > 10 years were positively correlated with NAFLD.

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#### Introduction:-

Non-Alcoholic Steato Hepatitis (NASH) was coined by Ludwig and colleagues at the Mayo Clinic in 1980 to characterise a kind of liver disease seen in middle-aged individuals with abnormal liver biochemical test results and histologic indications of alcoholic hepatitis with no history of alcohol norm(Adams, 2013).NAFLD is a condition in which the liver accumulates surplus fat in the form of triglycerides (steatosis) (> 5% of hepatocytes histologically)(Yki-Järvinen, 2020). In addition to the excessive fat, a reasonablepercentage of NAFLD patients have liver cell damage and inflammation (Steatohepatitis),A medical condition, is known as NASH, and is

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histologically very identical to alcoholic steatohepatitis (ASH)(Greuter et al., 2017). While simple steatosis in NAFLD is not associated to an elevated risk of short-term morbidity or death, progressing to NASH substantially raises the risk of cirrhosis, liver failure, and hepatocellular cancer (HCC).

In absence of any significant alcohol consumption, NAFLD can vary from simple steatosis to steatohepatitis (NASH), cirrhosis, and hepatocellular carcinoma (HCC). NAFLD is closely linked to obesity, Type 2 diabetes mellitus (T2DM) or insulin resistance, hypertension, and dyslipidemia, all incorporated in diseases of affluence(Mishra & Younossi, 2012). It is perceived to be the metabolic syndrome hepatic manifestation with 20-33 percent of the general population suffering from this multi-faceted ailment. In Western nations, the prevalence of NAFLD ranges from 15 to 40%, while in Asian countries the range figures between 9 to 40%. As the progression of disease is connected to insulin resistance (IR), its prevalence parallels the increasing rates of obesity and type 2 diabetes worldwide. The available literature estimates 70- 75% of type 2 diabetic patients with some form of NAFLD(Younossi et al., 2018).

India is becoming the world's diabetic capital, and NAFLD a major concern causes of liver disease. According to epidemiological research, the incidence of NAFLD in general Indian population is reported between 9 and 32 percent(Praveenraj et al., 2015). The true frequency is however unclear since NAFLD is frequently misdiagnosed and most people with NAFLD, including those with diabetes, have normal liver aminotransferases, hence clinicians do not suspect the potential presence of NAFLD(Bellentani & Marino, 2009).

The occurrence of NAFLD has doubled during last 20 years, whereas the frequency of other chronic liver diseases has remained stable or even decreased(Asrani et al., 2019). The current epidemics of diabetes and obesity in both developed and developing countries suggest that numbers will continue to rise, an indication of NASH becoming a common liver problem in both rich and poor countries, thereby increasing the global burden of liver disease(Anstee et al., 2019).

### **Methods:-**

Patients with type 2 diabetes mellitus diagnosed and admitted at SKIMS,(medical college and hospital) Srinagar were selected for the study. The study was prospective and observational, conducted between August 2018 to March 2021. Patients satisfying the inclusion criteria were enrolled in the study, after proper informed consent in writing. A thorough medical history and physical examination was performed for each patient, which included measurement of weight and height, BMI, waist/hip ratio. serum samples were obtained from all the participating patients for liver function tests, serum lipid profile, Overweight was defined as BMI between 25-29.99 Kg/m<sup>2</sup>. Obesity as BMI  $\geq$ 30 kg/m<sup>2</sup>. Patients were considered centrally obese if the waist circumference was greater than  $>80$  cm in females and  $>90$  cm in males.

### **Statistical Analysis**

The data were analysed applying  $\chi^2$  -test, univariate logistic regression analysis of significance, using SPSS software. Chisquare test and student t test is used. Data calculated in MS excel 2007, p value is given. Value less than 0.05 was taken as statistically significant.

### **Results:-**

A total of 250 participants took part in our research (100 NAFLD patients and 150 healthy controls). The patient group had 63 females and 37 males, whereas the control group included 63 females and 87 males, the average age of inpatients was 46.8 years. There were 37 males and 63 females among the 100 patient subjects, with 12 males having normal USG, 9 grade 1st fatty liver, 12 grade 2nd fatty liver and 3-grade 3rd fatty liver. Among the 63 female patients, 12 had normal USG, 13 had Grade 1st fatty liver, 13 had Grade 2nd fatty liver, and three had grade 3rd fatty liver. NAFLD was shown to be strongly related to gender ( $p=0.01$ ). The prevalence, severity, and grades of NAFLD were statistically and significantly related to diabetes and BMI in subjects of 45 years' age ( $p=0.05$ ) with diabetic complication (10 years). The occurrence of NAFLD was statistically linked to patients above 45 years of age.

The majority of individuals with NAFLD who seek medical help are diagnosed of incidentally discovering high liver enzymes (ALT, AST). Aminotransferases are only mildly increased (1.5–2 times the upper limit of normal) and ALT is generally greater than AST. Recent investigations revealed that many people with NASH might have severe fibrosis and even cirrhosis with normal liver enzymes, suggesting the incidence of disease is considerably higher

than previously thought. NASH is commonly observed in combination with other elements of the metabolic syndrome (hypertension, diabetes, increased lipids, and obesity) with NAFLD being the hepatic expression of this disease. [6,7] Insulin resistance is the underlying connection between both diseases, and almost all patients with NASH have insulin resistance. According to several research 50 percent of individuals with NASH show abnormal ferritin levels, and raised ferritin levels may be a sign of insulin resistance in NASH.

### Discussion:-

NAFLD (non-alcoholic fatty liver disease) is a form of hepatic illness that was significantly linked to insulin resistance and type 2 diabetes mellitus (Mu et al., 2019). NAFLD has become a major public health concern across the world. The metabolic syndrome is becoming more linked to NAFLD (Lazarus et al., 2020). There is little research on the epidemiology and natural history of NAFLD in people with diabetes. A total of 100 participants of both genders were included in the current cross-sectional observational study, including 37 (37%) male and 63 (63%) females (p-value=0.01). NAFLD was found prevalent in 63 percent of the population with NAFLD found to be present in 25% of males and 38% of females. Diabetes mellitus (DM), BMI and age > 45 years were statistically substantially related to the severity and grades of NAFLD. Aimed various criteria for enrolling research subjects, different criteria for diagnosing NAFLD, community-based, distinct geographic region, and genetic composition of the study population, the current study cannot be directly compared to other studies from India and elsewhere. This prevalence is low in comparison to the current study since it was a hospital-based study that included patients with type 2 diabetes only.

According to Younossi ZM et al, the prevalence of NAFLD varies between 9 and 40 percent in Asian countries and 15 to 40 percent in Western countries. NAFLD was shown to be prevalent in 9-32 percent of the general population in India, but 12.5- 87.5 percent among those with type 2 diabetes (Atri et al., 2020). These findings are in coherence to our study (63 percent). Mujumdar A et al. (2016) investigated 176 people with NAFLD. The prevalence of NAFLD was relatively high (63%) in this study, which might be related to the fact that only type-2 diabetes patients were included. In a study of 100 type 2 diabetes patients, (Bhatt et al., 2017). These findings are comparable to the current study. According to Prabhakar A et al. (2017), the prevalence of NAFLD in the study group (n=114) was 41.2 percent, which is similar to our study. The prevalence of NAFLD was shown to be strongly related to HbA1c, diabetes duration, and obesity in a research that was similar to ours. In a hospital-based observational descriptive research (n=150) of T2DM patients, Gupta M et al (2017) found that 104 (69.33%) had fatty liver on USG, 42.67 percent had grade 1, 24 percent had grade 2, and the remaining 2.67 percent had grade 3 fatty alterations in the liver (Gupta et al., 2017). These findings are again comparable to our study, which found a 63 percent prevalence of NAFLD. NAFLD was shown to be prevalent in 61 percent of type 2 diabetic patients in cross-sectional research (n=100) by Bhardwaj et al (2016). There is a lack of information about the prevalence of NAFLD in the general population. The frequency and risk factors of NAFLD in the general population were compared to the findings of this study. All these isolated works and the results pooled in the scientific literature concerning the NAFLD were largely found in coherence to our study.

### Tables:

Gender distribution and prevalence of NAFLD in cohort of type-2 DM

Variables

Variables	Total=100	% age
Males	37	37%
Females	63	63%
Total	100	
Chi square =6.760		p-value=<0.01

Variables	Normal	Grade 1st	Grade 2nd	Grade 3rd	Chi - square	p-value
Females(63)	25	18	13	7	1.010	>0.05

Males(37)	12	13	9	3	
Total	37	31	22	10	

#### Relation of BMI, age > 45 years and duration of diabetes to NAFLD

Duration of DM	Normal USG (n=37)			NAFLD (n=63)
≤ 10 yrs (n=74)	23			51
>10(n=26)	14			12
O-Ratio=0.387	Relative risk =0.577		p-value<0.05	
BMI (n=37)	Normal USG	Grade-1 fatty liver(n=31)	Grade-2 fatty liver(22)	Grade-3 fatty liver (n=10)
Male(n=37)	12	13	9	3
Female(n=63)	25	18	12	7
Age	Normal USG (n=37)			NAFLD (n=63)
<45 yrs (n=45)	22			23
>45 yrs (n=55)	15			40
O-Ratio =2.511	relative risk=1.793		p-value=<0.05	

#### Conclusion:-

The current investigation revealed a large burden of Non-Alcoholic Fatty Liver Disease in a type-2 diabetes mellitus cohort; about half of the individuals had NAFLD (63 percent). NAFLD and type 2 diabetes appear to be an expensive combo of disease risk factors. High BMI, diabetes duration > 10 years, and age > 45 years were all seen to be strongly associated with the existence of NAFLD in this research.

#### Acknowledgements:-

We acknowledge the Department of Gastroenterology, of Sher-I- Kashmir Institute of Medical Sciences for their Support. We also acknowledge our patients for their participation in the study.

#### Conflict of Interest:

The manuscript has been seen and approved by all the listed authors, all of whom have contributed significantly to the work and there is no conflict of interest between authors.

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