

Development of Diabetes Mellitus in MAFLD- Decompensated Cirrhotic are at Most Risk

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Abstract

Background: Metabolic dysfunction-associated steatotic liver disease (MASLD), formerly called NAFLD, is the leading cause of chronic liver disease (CLD) globally. It occurs when excess fat builds up in the liver and is closely linked to metabolic conditions like obesity, type 2 diabetes, and high blood pressure. MASLD encompasses a continuum of conditions ranging from simple fatty liver to severe, progressive liver damage. Simple Steatosis (Fatty Liver) is excess fat accumulation in the liver but there is little to no inflammation or damage. MASH (Metabolic Dysfunction-Associated Steatohepatitis) is more severe form where fat accumulation is accompanied by liver inflammation and cell damage. Fibrosis is ongoing inflammation leads to the buildup of scar tissue in the liver, graded on a scale from F1 (mild) to F4 (cirrhosis). The aim is to estimate prevalence of development of Diabetes Mellitus in Metabolic dysfunction associated steatotic liver disease patients at tertiary care center of Northern India. **Material and Methods:** This study was conducted at Medical Gastroenterology Department at PGIMS, Rohtak. It was a prospective study done over six years, from 01.04.2020 to 31.03.2026, during which 300 confirmed Metabolic dysfunction associated steatotic liver disease (MAFLD) were investigated for development of diabetes mellitus. For better understanding 100 patients each of F0-F1 fibrosis, F2-F3 fibrosis and F4 (cirrhotic) patient on were enrolled. All these 300 patients were followed up for at least three to five years after being diagnosed of MAFLD for development of diabetes mellitus. The three-to-five-year time period was helpful in determining the late effect of MAFLD in causing pre-diabetic and diabetic stage. Out of total pool of 300 MAFLD patients, 142 (47.33%) were male and 158 (52.67%) were female. The age group was between 20 yrs- 78 yrs with mean age of 45 years. Patient were labelled diabetic, if blood sugar fasting and post prandial were more than 126mg% and 200 mg% respectively or HbA1C was more than 6.5. Pre-diabetic was defined as blood sugar fasting and post prandial was 100-126mg% and 140-200 mg% respectively or HbA1C was between 5.7-6.5. All MAFLD patients were diagnosed after ruling out viral infections including HBV, HCV, HAV, HEV, HIV, normal autoimmune & Wilson profile, ultrasonogram abdomen showed fatty liver or cirrhotic changes, with transaminitis on liver function test and fibrosis or cirrhosis was graded on fibroscan. The written informed consent was taken before enrollment in the study. **Results:** Our department is Model treatment Center (MTC) under National Program on Non-communicable diseases, of which Fatty liver is integral part. Our center is one of the high flow centers in India. On daily basis, 3-4 new and 25 follow up patients of MAFLD/MASH or cirrhosis come for consultation and till date 2000 patients have been enrolled in last thirteen years. Out of total pool of 300 MASH related cirrhotic patients, 100 patients each of F0-F1 fibrosis, F2-F3 fibrosis and F4 (cirrhosis) were enrolled. The new onset diabetes mellitus was seen in 18 patients (6%) with F0-F1 fibrosis, 36 (12%) of F2-F3 fibrosis and 66 (22%) of cirrhotic patients. In cirrhotic also, majority were decompensated. On Pre-diabetic analysis, 10 patients (3.33%) were seen in F0-F1 fibrosis group, 19 (6.33%) in F2-F3 fibrosis and 30 (10%) in cirrhotic patients, predominantly in decompensated stage. **Conclusion:** MAFLD and MASH, especially in cirrhotic stage have high risk of developing diabetes mellitus, hence life-long surveillance is required for the same. The development of DM in these cases is detrimental as fastens the rate of progression of fibrosis as well as cirrhosis. Hence, strict control of blood sugar levels, along with regular treatment of cirrhosis and its complications is mandatory.

Keywords: Diabetes Mellitus, HbA1C level, Fibrosis, Cirrhosis, MAFLD, MASH.

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INTRODUCTION

Metabolic dysfunction-associated steatotic liver disease (MASLD), formerly called NAFLD, is the leading cause of chronic liver disease (CLD) globally. It occurs when excess fat builds up in the liver and is closely linked to metabolic conditions like obesity, type 2 diabetes, and high blood pressure. MASLD encompasses a continuum of conditions ranging from simple fatty liver to severe, progressive liver damage. Simple Steatosis (Fatty Liver) is excess fat accumulation in the liver but there is little to no inflammation or damage. MASH (Metabolic Dysfunction-Associated Steatohepatitis) is more severe form where fat

accumulation is accompanied by liver inflammation and cell damage. Fibrosis is ongoing inflammation leads to the buildup

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of scar tissue in the liver, graded on a scale from F1 (mild) to F4 (cirrhosis). Cirrhosis (F4) is extensive and largely irreversible scar tissue permanently damages the liver's structure.^[1] This can eventually lead to liver failure or hepatocellular carcinoma (HCC). MASLD develops slowly over many years, it is frequently asymptomatic in its early stages. It is diagnosis of exclusion, hence detailed biochemical tests including liver & renal function tests, viral screen, autoimmune & Wilson profile, lipid & thyroid profile, blood sugar & HbA1C levels are done. Imaging modalities include ultrasounds, CT scans, or specialized fibroscan (to measure liver fat and stiffness). Liver biopsy is rarely needed these days and is done in doubtful diagnosis only. There are no specific pharmacological agents universally approved for MASLD, early-stage disease can often be slowed or completely reversed. Management is primarily lifestyle-driven with primary aim of weight loss. The modest weight loss (even 5-10%) can significantly reduce liver fat and inflammation. Dietary adjustments include adopting diets low in refined sugars and saturated fats i.e. Mediterranean diet is highly recommended. Regular physical activity helps improve insulin sensitivity and reduce overall metabolic syndrome. MASLD is strongly associated with cardiovascular disease, managing blood sugar, cholesterol, and blood pressure is equally critical to overall health. MASLD and Diabetes Mellitus (Type 2) share a highly intertwined, bidirectional relationship. Diabetes acts as a powerful catalyst for liver disease progression, while the presence of MASLD significantly increases the risk of developing diabetes and worsens overall blood sugar control.

Aim of Study - To estimate prevalence of development of Diabetes Mellitus in Metabolic dysfunction associated steatotic liver disease patients at tertiary care center of Northern India.

MATERIALS AND METHODS

This study was conducted at Medical Gastroenterology Department at PGIMS, Rohtak. It was a prospective study done over six years, from 01.04.2020 to 31.03.2026, during

which 300 confirmed Metabolic dysfunction associated steatotic liver disease (MAFLD) were investigated for development of diabetes mellitus. For better understanding 100 patients each of F0-F1 fibrosis, F2-F3 fibrosis and F4 (cirrhotic) patient on were enrolled. All these 300 patients were followed up for at least three to five years after being diagnosed of MAFLD for development of diabetes mellitus. The three-to-five-year time period was helpful in determining the late effect of MAFLD in causing pre-diabetic and diabetic stage. Out of total pool of 300 MAFLD patients, 142 (47.33%) were male and 158 (52.67%) were female. The age group was between 20 yrs- 78 yrs with mean age of 45 years. Patient were labelled diabetic, if blood sugar fasting and post prandial were more than 126mg% and 200 mg% respectively or HbA1C was more than 6.5. Pre-diabetic was defined as blood sugar fasting and post prandial was 100-126mg% and 140-200 mg% respectively or HbA1C was between 5.7- 6.5. All MAFLD patients were diagnosed after ruling out viral infections including HBV, HCV, HAV, HEV, HIV, normal autoimmune & Wilson profile, ultrasonogram abdomen showed fatty liver or cirrhotic changes, with transaminitis on liver function test and fibrosis or cirrhosis was graded on fibroscan. The written informed consent was taken before enrollment in the study.

RESULTS

Our department is Model treatment Center (MTC) under National Program on Non-communicable diseases, of which Fatty liver is integral part. Our center is one of the high flow centers in India. On daily basis, 3-4 new and 25 follow up patients of MAFLD/MASH or cirrhosis come for consultation and till date 2000 patients have been enrolled in last thirteen years. Out of total pool of 300 MASH related cirrhotic patients, 100 patients each of F0-F1 fibrosis, F2-F3 fibrosis and F4 (cirrhosis) were enrolled. The new onset diabetes mellitus was seen in 18 patients (6%) with F0-F1 fibrosis, 36 (12%) of F2-F3 fibrosis and 66 (22%) of cirrhotic patients. In cirrhotic also, majority were decompensated. On Pre-diabetic analysis, 10 patients (3.33%) were seen in F0-F1 fibrosis group, 19 (6.33%) in F2-F3 fibrosis and 30 (10%) in cirrhotic patients, predominantly in decompensated stage.

Table 1: Showing Gender and Residential distribution in total pool of MAFLD Patients

Total MAFLD Patients	Males	Females	Rural Background	Urban Background
300	142 (47.33%)	158 (52.67%)	126 (42%)	174 (58%)

Table 2: Showing prevalence of Development of Diabetes Mellitus and Pre-Diabetic Stage in various groups of MAFLD Patients

Total MAFLD Patients	MASH- F0-F1 Fibrosis	MASH- F2 -F3 Fibrosis	MASH Related Cirrhosis- F4
300	100	100	100
Developed Diabetes Mellitus	18 (6%)	36 (12%)	66 (22%)
Developed Pre-Diabetic Stage	10 (3.33%)	19 (6.33%)	30 (10%)

DISCUSSION

In 2020, Eslam et al,^[2,3] proposed the new term 'metabolic dysfunction-associated fatty liver disease (MAFLD),' which could be diagnosed in adults with hepatic steatosis detected by imaging techniques, blood biomarkers, or liver histology, when overweight or obese, or in the presence of T2DM or at least two metabolic risk abnormalities. This

was endorsed by the Asian Pacific Association for the Study of the Liver (APASL),^[4] multiple national societies including the Malaysian Society of Gastroenterology and Hepatology,^[5,6] and various stakeholders globally.^[7] In June 2023, a multi-society Delphi consensus statement on a new fatty liver disease nomenclature was published, introducing the term metabolic dysfunction-associated steatotic liver disease (MASLD) and effectively retiring the term NAFLD.^[8] The terms MAFLD and

MASLD have more in common than not and are more appropriate for the condition. Up to 70% of people with Type 2 Diabetes have MASLD. In diabetic patients, MASLD progresses much faster and is associated with a higher risk of developing advanced liver fibrosis, cirrhosis, and hepatocellular carcinoma (HCC). MASLD independently increases a patient's risk of developing Type 2 Diabetes by 2 to 5 times. Ectopic fat deposits in the liver impair hepatic glucose regulation, increase insulin resistance, and drive systemic hyperinsulinemia. Zahoor et al concluded that MASLD is significantly associated with T2DM, regardless of gender and BMI of patients.^[9] Yamada T et al. demonstrated in their study that fatty liver constitutes an independent risk factor for impaired fasting glucose and T2DM, exerting a more significant impact on Japanese individuals with a lower BMI undergoing health check-ups.^[10] Our study is in alignment with other previous studies highlighting the strong association of development of *denovo* diabetes mellitus in patients of MAFLD or MASH related cirrhosis.^[9,10]

CONCLUSION

MAFLD and MASH, especially in cirrhotic stage have high risk of developing diabetes mellitus, hence life-long surveillance is required for the same. The development of DM in these cases is detrimental as fastens the rate of progression of fibrosis as well as cirrhosis. Hence, strict control of blood sugar levels, along with regular treatment of cirrhosis and its complications is mandatory.

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Conflicts of interest

There are no conflicts of interest.

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