

Review Article

Burden of Metabolic Dysfunction-associated Steatotic Liver Disease in India and the way forward

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Liver disease is a significant public health issue in India and the burden of the disease is rapidly growing. Liver-related deaths in India account for 3.17% of all deaths and 18.3% of global liver-related deaths. Metabolic Dysfunction-associated Steatotic Liver Disease (MASLD) accounts for 8 to 20% of all Chronic Liver Disease (CLD). Progressive adoption of western diet and sedentary lifestyle, along with increasing prevalence of Obesity, Type 2 diabetes and other components of metabolic syndrome will further increase the prevalence of MASLD and corresponding health care expenditure in near future. Unfortunately, there are limitations in the quality of the available epidemiological data resources in India. Better screening strategies, more effective linkage to care for early-stage liver disease and improved awareness on preventive steps in an integrated way could be useful interventions.

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Key words : Metabolic Dysfunction-associated Steatotic Liver Disease, Type 2 Diabetes, Prevalence, Screening.

The burden of Liver Disease in India is high, since it accounted for 18.3% of the two million fatalities Worldwide attributable to liver disease in 2015¹. Cirrhosis and its consequences, commonly known as Chronic Liver Diseases (CLDs), have been growing as a cause of death in India since 1980. However, the quality of the available epidemiological data on liver disease is limited in this country. There has been a recent rise in the cases of Metabolic Dysfunction-associated Steatotic Liver Disease (MASLD) as cause of liver disease in addition to viral factors and alcoholic etiology. Adoption of sedentary lifestyle, lack of exercise, unhealthy dietary habits, increasing prevalence of obesity and metabolic syndrome, rising life expectancy are significant demographic factors influencing this development. MASLD is rapidly becoming recognised as an important public health issue. In accordance with this, India has established encouraging health system response methods. A nationwide MASLD control programme including actions that incorporate liver disease control into other non-communicable disease control measures was established in 2021^{2,3}.

The Burden of MASLD :

Complications of MASLD and its associated metabolic syndrome are important cause of mortality in India. The Global Health Estimates (GHE) 2018

Editor's Comment :

■ In India, MASLD is progressively becoming an issue that is given emphasis in terms of public health. In order to battle the burden of MASLD, the magnitude of the problem and the obstacles in implementing effective care need to be identified. In a strategic shift, the Government of India has incorporated non-communicable diseases into its comprehensive primary healthcare approach for universal health coverage.

dataset documented that MASLD accounted for 10.9% of all deaths due to Cirrhosis and 9.6% of all deaths due to liver cancer⁴. MASLD is intricately related to several metabolic (like obesity, type 2 diabetes) and environmental factors (such as physical inactivity). These are common in the Indian population⁵. According to community-based studies, the prevalence of MASLD on ultrasonography in urban areas varied between 18.9% to 32%, and in rural areas between 8.7% to 30.7%⁶⁻⁹. In hospital-based studies, this prevalence was between 25.3% to 32.2%^{10,11}. Indian studies have also shown high prevalence of fatty liver disease in patients with type 2 diabetes (10-5-88%) or amongst obese people (50-80%)^{12,13}. Overall, 11-32% of patients with MASLD had a normal Body-mass Index (BMI)¹⁴. Table 1 shows the epidemiological studies on MASLD done in India over last two decades.

Over the years, India has witnesses a disproportionate increase in the number of overweight and obese adults and it nearly doubled to 18.6% in 2015-16 from 9.3% in 2005-06 in men, and to 20.7% from 12.6% in women¹⁵. Additionally, there are currently more than 70 million adults with type 2

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Table 1 — Epidemiological study on prevalence and risk factors of MASLD (NAFLD) in India

Study, year, reference	Setting	Total population screened	Prevalence of MASLD	Main findings	Risk factors
Amrapurkar, <i>et al.</i> 2007 [6]	Community-based, urban	1168	16.6%	Mean age 39.08 ± 12.3 years, 4% had diabetes, 57% had central obesity	Age > 40 years, male gender, central obesity, high BMR > 25, elevated FPG, raised AST, ALT
Mohan, <i>et al.</i> 2009 [7]	Community-based, urban	541	32%	Mean age: 42 ± 13 BMI 22.9 ± 3.6 years, AST 21.9, ALT 22.2	Type 2 diabetes (OR:2.9) and metabolic syndrome (OR:2.0)
Das, <i>et al.</i> 2010 [8]	Community-based, rural	1911	11%	75% had BMI <25 kg/m ² , 54% neither over weight nor had abdominal obesity	BMI > 25, Abdominal obesity, dysglycemia, elevated HOMA
Majumdar, <i>et al.</i> 2016 [9]	Community-based, rural	216	30.7%	No significant difference in the calorie intake and average total physical activity in population with and without NAFLD	Hypertension (OR: 2.3), increased waist circumference (OR: 4.9)
Siraj, <i>et al.</i> 2012 [10]	Hospital-based	300	25.3%	Most subjects were males, between 36-45 years of age, from urban areas	High energy, protein and fat intake
Bajaj, <i>et al.</i> 2009 [11]	Hospital-based	121	32.2%	Subjects with NAFLD have significantly higher values of BMI, waist circumference, hip circumference, FBG, fasting insulin, total cholesterol and serum triglycerides	High BMI (OR 4.3), FPG (OR 5.4), and fasting insulin (OR 2.4)
Jali, <i>et al.</i> 2015 [12]	Hospital-based, patients with T2DM	1750	10.51%	Prevalence of obesity (65% vs 41%), hypertension (86% vs 58%), dyslipidemia higher	Increasing age (>60 years) increasing duration (>9 years) of DM
Kalra, <i>et al.</i> 2015 [13]	Hospital-based, patients with T2DM	924	56.5%	Prevalence higher in females, in northern states, highest (61.8%) in 61-70 years' age group. mean AST 54.8 ± 36.1 IU/L and mean ALT 55.6 ± 39.8 IU/L	Dyslipidemia, hypertension, obesity (had 38%, 17% and 14% higher risk of NAFLD respectively)

diabetes aged 20-79 years, and this population is likely to increase to 123.5 million by 2040, which would probably lead to an increase in the burden of MASLD¹⁶. One hospital-based study had shown that nearly half of patients with MASLD with increased aminotransferase concentrations had histologically confirmed Metabolic Dysfunction-associated Steatohepatitis (MASH) on liver biopsy, although majority (80-98%) had only stage 1 or stage 2 changes¹⁷. There is scarcity of prospective follow up data on the natural history of MASLD and MASH in India. In hospital-based studies between 2003 and 2011, cryptogenic cirrhosis, believed to be largely due to MASLD progression, accounted for 15.8-48.8% of patients with Cirrhosis¹⁸. Moreover, 4.6-19% of patients with liver cancer had no risk factor for liver disease (like HBV, HCV or Alcohol)^{19,20}.

Current Challenges :

India's epidemiological statistics are insufficient, making it challenging to estimate liver disease burden. Limitations of resources, hepatologists and healthcare facilities; cultural beliefs; dependence on untested and unproven traditional medicines and herbal supplements; lack of awareness of diseases and their modes of transmission – all contribute to making

management of these conditions difficult²¹. Moreover, due to rapid urbanization, industrialization and upwards movement of society in terms of affordability, the prevalence of diabetes, obesity and metabolic syndrome are increasing all over the country.

The number of health care personnel like doctors, nurses, technicians trained to manage liver disease and its complication at secondary/ tertiary care level is grossly insufficient in India. We also lack adequate number of health care personnel at primary level who are appropriately trained for detection and initial management of liver diseases and referral of those at risk of progressive disease to specialised centres. There are very few dedicated liver institutes, and the facilities for management of paediatric liver diseases are available in only a few centres.

The number of liver transplantation in India is much less compared to the large number of patients of decompensated chronic liver disease who die on waiting list. The facilities for transplantation are available only in a limited number of institutes. Most such institutes are private hospitals, situated in the metropolitan cities and beyond the reach of common people. Cadaveric transplantation has not yet gained momentum in this country.

Screening for MASLD in Primary Care :

Although the gold standard for diagnosing MASLD and MASH with and without fibrosis is liver biopsy, this method is often impractical, expensive and not without risk. Because laboratory values alone are not a reliable indicator of MASLD, a three-pronged approach is suggested to screen for MASLD in high-risk patients.

First, patients should be screened for MASLD with abdominal ultrasound. Second, if fatty liver is present on ultrasound, patients should be assessed for the severity of liver fibrosis using clinical prediction rule(s). A commonly used system is FIB-4 score (a composite of age, alanine transaminase, aspartate transaminase and platelet count) as it has been shown to have the best diagnostic accuracy of the non-invasive scores in detecting advanced fibrosis and are simple to calculate in the clinic. Further, patients showing indeterminate values should be referred for transient elastography (Fibroscan of liver). Finally, patients who are at high risk for advanced fibrosis or who are found to have this condition should be referred to a hepatologist for further evaluation (Fig 1).

Therapeutic Considerations for MASLD in India:

Lifestyle interventions including dietary calorie restriction and exercise constitute the central pillar of MASLD management. There is a dose-response relationship with weight loss of (3-5)%, 7% and 10% being associated with improvement in steatosis, steatohepatitis and fibrosis, respectively²². Even in lean individuals, exercise helps in improving hepatic triglycerides and insulin resistance. In India, INASL recommends daily calorie restriction by 30% or (500-1000) kcal to achieve the target weight loss⁵. It also recommends moderate intensity aerobic or resistance exercises 30-45 min/day at least 5 days in a week (at least 200 min per week) in all patients with MASLD irrespective of body weight. In the absence of randomized clinical trials, bariatric surgery cannot be recommended as a primary treatment for MASLD in India.

The choice of drugs for MASH pharmacotherapy should be individualized on the basis of age, gender and the presence/absence of diabetes/dyslipidemia, cost and availability.

Vitamin E is recommended as pharmacotherapy for MASH with or without hepatic fibrosis (F1-F3) in nondiabetic adult and pediatric patients; pioglitazone and saroglitazar in those with or without hepatic fibrosis (F1-F3) (in both diabetic and nondiabetic adult patients). In patients in whom liver biopsy is not available, NASH specific pharmacotherapy can be used in those having significant fibrosis on noninvasive assessment (like Fibroscan of liver). Obeticholic acid as pharmacotherapy is not recommended in India. Two recent meta-analyses by Indian authors have established the role of saroglitazar and injectable semaglutide in improving hepatocellular inflammation and to a smaller extent liver fibrosis, in MASLD patients^{23,24}. Studies on oral semaglutide are underway. The use of pharmacotherapy in MASH-related cirrhosis is not recommended⁵.

Government's Initiatives to Curb MASLD :

With an aim to curtail the burden of non-communicable diseases including MASLD, the Government of India has taken many initiatives. The Indian Ministry of Health and Family Welfare has reduced the diagnostic threshold of overweight to a

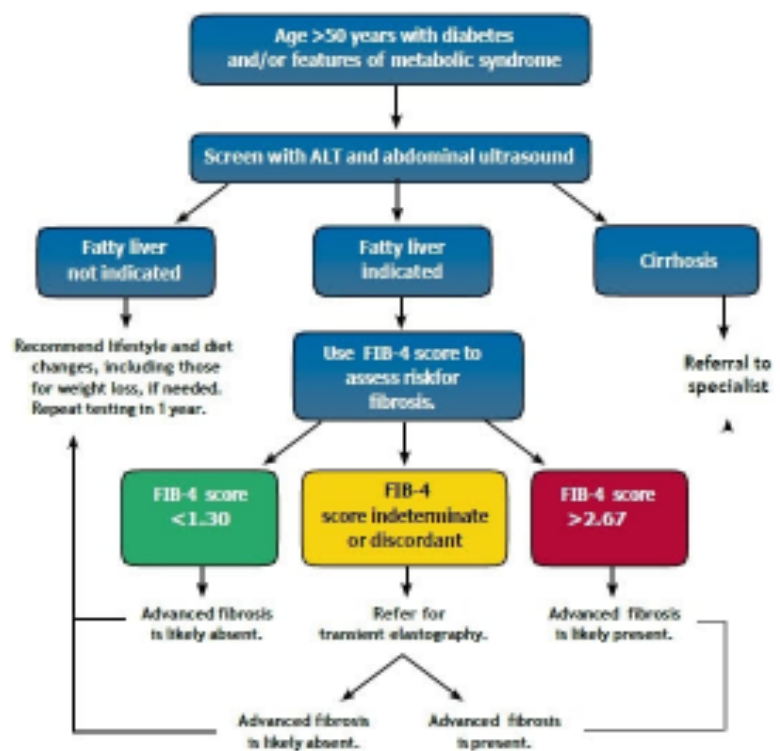


Fig 1 — Clinical care pathway for screening and evaluation of MASLD

BMI of 23 kg/m² (from 25), and the standard waist circumference diagnostic of abdominal obesity to 90 cm in men and 80 cm in women (internationally accepted values are 102 cm in men and 88 cm in women). This is a timely response to ameliorate the risk of death and burden of disability due to non-communicable diseases, as projected by Global Disease Burden (GBD) statistics in 2015. These standards have been published in the ministry's Consensus Guidelines for the Prevention and Management of Obesity and Metabolic Syndrome²⁵.

The Government of India also initiated the integrated National Programme for Prevention and Control of Diabetes, Cardiovascular Disease and Stroke (NPCDCS) in 2017 and since 2021, MASLD is also included in it²⁶. This is the recognition of the shared risk factors between these lifestyle-related diseases. The major objectives of NPCDCS are: (i) health promotion, awareness generation and promotion of healthy lifestyle, (ii) self-testing, screening and early detection, (iii) affordable point-of-care diagnosis, (iv) access to affordable treatment, and finally, (v) rehabilitation.

In India, there are no specific laws that regulate the marketing and advertising of fast foods. However, the State Governments of Delhi and Uttar Pradesh had taken small initiatives and instructed schools not to allow the sale of junk foods in their canteens. Local food vendors are also prevented from selling such items in the vicinity of educational institutions. The Food Safety and Standards Authority of India (FSSAI) had also produced guidelines to control the objectivity and accuracy of food advertisements. However, all of these measures are recommendations rather than mandatory and hardly any punishment is meted out for failure in compliance²⁷. Amendments regarding packaging and labelling of food under part VII of the Prevention of Food Adulteration Rules of 1955 mandate the disclosure of health claims alongside nutritional labelling. However, stricter policies are required to prevent misleading information. In 2010, the FSSAI expert group formulated guidelines that recommend less than 10% trans fats in food products²⁸. The state of Kerala has already imposed 14.5% fat tax on the consumption of certain foods²⁹.

The Way Forward :

We need dedicated public awareness campaigns to increase knowledge about MASLD, its risk factors, and preventive measures. Community health programmes may be arranged or digital media may be utilized to disseminate information.

Another way to prevent the menace of MASLD is to provide nutritional counselling services to individuals with MASLD on every consultation to promote healthy eating habits and weight management. Nutritionists can offer support groups or online resources for individuals to share experiences and seek guidance.

In the past decade, India has developed liver transplantation, largely from donors, with results comparable to Western countries. The newly established Indian Liver Transplant Registry (ILTR) may soon provide prospective and transparent countrywide statistics. As there is gross mismatch in the demand and supply of organs, liver transplantation from deceased brain-dead donors needs to be encouraged. Even in deceased donors, the organ-sharing policies should change from current rotational policy to a more pragmatic severity-based system.

To address the challenges of MASLD collectively, we need to foster collaborations between healthcare institutions, research organizations and community groups. Engaging with international experts and organizations to share best practices may be an innovative idea. Research priorities in India need to focus on the quality of data collection regarding the incidence and prevalence of MASLD and associated risk factors, as well as morbidity and mortality related to Cirrhosis and Liver Cancer in this condition. The effectiveness of potential interventions to prevent and treat MASLD needs to be investigated in longitudinal studies.

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