PUBLIC HEALTH
OpenJournal
Openventio PUBLISHERS

Review Article

Changing Paradigm of Fatty Liver Management

Musarrat Mahtab[1], Rokshana Begum[2], Ahmed Lutful Moben[3], Sheikh Mohammad Noor E Alam[4], Md. Abdur Rahim[5], Sakirul Khan[6], Sheikh Mohammad Fazle Akbar[7], Mamun Al Mahtab[8]

[1]Clinical Research Organization Ltd., Dhaka, Bangladesh
[2]Department of Hepatology, Shaheed Suhrawardy Medical College, Dhaka, Bangladesh
[3]Department of Hepatology, Kurmitola General Hospital, Dhaka, Bangladesh
[4]Department of Hepatology, Bangladesh Medical University, Dhaka, Bangladesh
[5]Department of Hepatology, International Medical College, Gazipur, Bangladesh
[6]Department of Microbiology, Faculty of Medicine, Oita University, Yufu, Oita, Japan
[7]Department of Gastroenterology and Metabology, Ehime University Graduate School of Medicine, Ehime, Japan
[8]Department of Hepatology, Bangladesh Medical University, Dhaka, Bangladesh

Corresponding Author
Mamun-Al-Mahtab
Email: shwapnil@agni.com

Article Information:
Received: 18 January 2025 | Revised: 15 February 2026 | Accepted: 16 March 2026 | Published: April 21, 2026

Cite this article:
Musarrat Mahtab, Rokshana Begum, Ahmed Lutful Moben, Sheikh Mohammad Noor E Alam, Md. Abdur Rahim, Sakirul Khan, Sheikh Mohammad Fazle Akbar, Mamun Al Mahtab (2026). Changing Paradigm of Fatty Liver Management *Public Health Open Journal*. 11(1):348–352. https://doi.org/10.17140/PHOJ.11.01.348

Abstract
Metabolically-dysfunction-associated fatty liver disease is a major health concern globally and is on the rise worldwide. It is a form of chronic liver disease with potentials of progression to liver cirrhosis and hepatocellular carcinoma. For long, lifestyle modification remained the only effective intervention for the management of this disease. However, the scenario is now gradually changing. Not only newer drugs are showing promise in the management of metabolic dysfunction-associated fatty liver disease, but some have also already been approved by different regulatory bodies. These include semaglutide, resmetirom and saroglitazar. Therefore, a shift in the of paradigm of management of patients presenting to us with metabolic dysfunction-associated fatty liver disease, metabolic dysfunction-associated steatohepatitis and complications is also gradually becoming visible.

Keywords: *Metabolic dysfunction-associated fatty liver disease, metabolic dysfunction-associated steatohepatitis, lifestyle modification*

1. Introduction

It has been estimated that approximately 25% patients who have metabolic dysfunction-associated fatty liver disease (MASLD) i.e. fatty liver, suffer from metabolic dysfunction-associated steatohepatitis (MASH), i.e. chronic hepatitis. The spectrum of MASLD also includes liver cirrhosis (LC) and hepatocellular carcinoma (HCC). More importantly these patients are at risk of progressing to LC at a rate of 25% over a period of 7-8 years [1]. Liver decompensates also at a 25% rate over 10 years, while the rate of development of HCC is 1% per annum [2]. In Asia, MASLD affects 27.4% of the population and the situation back home, i.e. in Bangladesh, is indifferent, where the prevalence of MASLD is estimated at 18.5% [3]. MASLD is more common among diabetics and in obese and is seen in up to 70%-75% of them [4, 5].

Why only lifestyle modification may not be the final answer to MASLD?

Lifestyle modification has 3 main components, namely diet control, exercise and weight reduction [1]. Exercise can be of many times including brisk walking, swimming, aerobic exercise, cycling etc. [6]. Losing more than 7% body weight leads to resolution of fatty liver, while more than10% makes hepatic fibrosis due to MASH disappear [7]. Adhering to lifestyle modifications, however, remains challenging due to variety of reasons. Not only is reducing body weight a tough cry, but rebound weight gain is also a natural phenomenon [8]. It is also an established fact that in many cases patients are unable to adhere to lifestyle modification due to co-morbidities or other reasons [9, 10]. These make lifestyle modification questionable as an effective intervention. Nutrition transition, particularly in the Indian sub-continent poses a huge challenge. This includes obesity, physical inactivity and unhealthy food habits due to the socio-economic shift and makes adhering to lifestyle modification more difficult by the days thus adding to our burden of MASLD and/or MASH [11, 12]. Another challenge is ultra-processed foods (UPFs). These are industrial food formulations that contain ingredients not commonly included in home-cooking e.g. emulsifiers, colorants, flavor enhancers, preservatives etc. These foods now constitute up to 50%-80% calory intake in high income countries partly because they extend shelf-life of foods, are hyper-palatable and convenient [13]. According to the United Kingdom National Diet and Nutritional Survey, UPFs contribute 53% of the dietary calory intake [14]. It is therefore no wonder that they are often replacing minimally processed and home-prepared meals in modern diets [15]. Confectionary and sugar-sweetened beverages are among the top of the list of UPFs that dominate modern diets [16]. UPFs have led to increased dietary energy density and calory consumption. However, this comes at the cost of compromised nutritional quality as compared to fresh and minimally processed foods, UPFs have high content of added sugar, unhealthy fat and sodium, while there is less fiber, vitamins and minerals [17]. Interestingly UPFs are more frequently consumed by vegans [18]. Global rise in MASLD parallels increased consumption of UPFs. According to the United Kingdom National Diet and Nutritional Survey, UPFs have direct association with prevalence of obesity [14]. A review of 9 studies that included 60000 participants, revealed that UPFs intake significantly increases the risk of developing MASLD [19]. Similar observation was made by another study that reviewed 27 studies [20]. A UK-Biobank study that included a cohort of 143073 individuals, observed that high consumption of UPFs-rich diet is associated with 26% increased risk of severe MASLD, defined by hospitalization and/or death [21]. The observation of another prospective cohort study is indifferent and established strong correlation between UPFs intake and visceral fat deposition and MASLD [22]. Like UPFs, trans fat (TFA) remains another major concern. TFA is a harmful type of unsaturated fat present in foods processed via partially hydrogenated oils (PHOs) and also in some animal products. TFA increases low density lipoproteins (LDL) or 'bad' cholesterol, while lowering high density lipoproteins (HDL) or 'good' cholesterol. TFA has been directly linked to metabolic dysfunctions including cardiac comorbidities. While, WHO recommends restricting TFA to less than 2 grams per 100 grams of total fat, the United States Food and Drug Administration (USFDA) has banned PHOs in the USA. One important issue is that, TFA formation is directly related to high temperatures and duration of heating food. Repeated heating of oil above 180C-200C or reusing oil more than 2-3 times or continuous heating for more than 2 hours lead to TFA formation [23]. Polyunsaturated fats like sunflower oil remain particularly vulnerable. While, oil dominates curries that are integral part of the Indian sub-continental cuisines, with current high pace of life it is nearly impossible for most urban Indian sub-continental families to avoid reusing or repeated heating of oil for all practical reasons thus adding to the increasing burden of MASLD/MASH and other metabolic dysfunctions in our region, like in many other parts of the world. Rapid urbanization is further adding to the challenge. According to urban planning studies and recommendations, an ideal city should have at least 25% of it's total area dedicated to open spaces and greenery [24]. The World Health Organization (WHO)

recommends 9 square meters of green space per capita, though many experts consider 50 square meters per capita as ideal. Green space ration above 30% is considered healthy for supporting biodiversity and urban livability. Modern standard dictates that residents should see at least 3 trees from their home, live in a neighborhood with 30% tree canopy coverage and be within 300 meters of a high-quality park [24]. However, the unfortunate reality is that these are not the case in many major cities. Dhaka city can be a perfect example. According to a recent United Nations (UN) report, Dhaka is now the second most populous city of the world, next only to Jakarta. Approximately 36.6 million people now call Dhaka their home [25]. Dhaka structure plan recommends that the city should have at least 25% open space, which is already below the global standard. However, the unfortunate reality is that the city's total open space, including green cover and water bodies, is less than 15% at present. Studies further suggest that when looking at designated public open spaces, this figure comes down to as low as 0.9%-1.26%. In contrast to WHO recommendation of 9 square meters of green space per capita, Dhaka's residents enjoy only 0.5-1 square meter of green space per capita [26]. This clearly shows that like many other major urban centers across the globe, residents of the second largest city on the face of the earth in terms of population, hardly have enough space to modify their lifestyle in order to enjoy a healthy liver and healthy living. As already mentioned, it has been estimated that MASLD is commoner among those who are obese and/or suffer from diabetes and can be seen in up to 75% of them [5]. The other side of the story is that as in the global perspective, both diabetes and obesity are on the rise, therefore we will surely encounter MASLD/-MASH more frequently in the coming days [27, 28]. At the same time, there is no reason to anticipate that lifestyle modification 'alone' will be our answer to this emerging health threat, given the fact that it has failed to halt the diabetes and obesity pandemic.

What's in our armory?

In recent times pharmacologic interventions for MASLD/MASH have been revolutionized. While there are several drugs in the pipeline, we already have a few very useful ones in our hands to be prescribed to the benefit of our MASLD/MASH patients. One such drug is resmetirom, a partial activator of liver-directed thyroid hormone receptor-, which has been approved recently by the USFDA for MASLD/MASH management. When activated by resmetirom, the thyroid hormone receptors reduce hepatic steatosis [29]. Multiple studies have established the safety as well as efficacy of resmetirom in improving liver enzymes, hepatic steatosis and most importantly hepatic fibrosis [30, 31]. A 36-week, phase 2 clinical trial observed mean reduction and mean relative reduction of magnetic resonance imaging - proton density fat fraction (MRI-PDFF) to be -11.1% and -52,3%, respectively on 80 mg and 100 mg resmetiron orally, daily for 36 weeks, compared to placebo in liver biopsy adults having MASLD ($p<0.001$) [31]. Another phase 3, randomized control trial found that by the end of 52 weeks, MASH resolution with no worsening of fibrosis was achieved in 25.9% patients on resmetiron 80 mg orally, daily and in 29.9% taking the drug 100 mg, orally, daily compared to only 9.7% in the placebo group ($p<0.001$) [30]. Fibrosis improvement by at least 1 stage with no worsening of MASLD activity score was achieved in 24.2% and 25.9% patients taking resmetirom at a dose of 80 mg and 100 mg orally, daily as opposed to only 14.2% taking a placebo ($p<0.001$) [30]. Initial findings of our ongoing prospective, observational, real-world study with resmetirom in MASLD are also encouraging, which we hope to publish shortly. Next there is semaglutide, which is a glucagon-like peptide-1 (GLP-1) receptor agonist. The drug has received accelerated approval from the USFDA in August 2025 for the management of MASLD/MASH [32]. Findings of the ESSENCE trial show that semaglutide 2.4 mg/week subcutaneously for 72 weeks resulted in resolution of MASH (62.9% vs 34.3%, $p<0.001$) and lowering of hepatic fibrosis by >1 stage (36.8% vs 22.4%, $p<0.001$) compared to placebo. There was no worsening of MASH. The drug is also recommended for use in MASH-related compensated LC patients under careful monitoring [32]. There are handful of drugs that are also promising. One such drug is saroglitazar, a peroxisome proliferator activated receptor (PPAR)- and agonist. Central Drugs Standard Control Organization (CDSCO), which is the Indian drug regulatory authority has approved saroglitazar for treatment of MASLD/-MASH [33]. PPAR- receptors are present in hepatocytes. Saroglitazar inhibits hepatic fat accumulation by acting on these receptors. Besides, saroglitazar also acts on the PPAR- receptors in adepocytes to improve insulin sensitivity and lipid oxidation, thus reducing hepatic fat availability [33]. Saroglitazar is effective in reducing hepatic fat content, inflammation and fibrosis [34, 35, 11]. Several studies have observed the beneficial role of saroglitazar in fatty liver. A prospective, observational, real-world study of saroglitazar at a dose of 4 mg, orally, daily for 24 weeks led to reduction of liver stiffness from 8.4 kPa (7.1 kPa - 9.3 kPa) to 7.5 kPa (6.4 kPa -8 .4 kPa) on fibroscan compared to placebo [36]. Another randomized controlled, double blind, phase 2 trial showed that compared to placebo, saroglitazar 4 mg, orally, daily for 16 weeks improved liver fat content

4.1% vs -19.7% [37]. Our own observation has been indifferent. In one of our recent prospective, observational, real-world study, we found that saroglitazar in 'combination' with lifestyle modification, led to lowering of both hepatic steatosis and fibrosis in MASLD patients compared to lifestyle modification 'only'. At 24 weeks following saroglitazar 4 mg, orally, daily liver fat reduction was 293.0+33.4 vs 319.0+34.9 dB/m) and liver stiffness reduction was 6.5+2.8 vs 5.5+1.0 kPa) on fibroscan respectively [38]. Another promising drug is obeticholic acid (OCA), which is a synthetic farnesoid X receptor (FXR) analogue. FXR, in turn, is a member of the bile acid-activated-receptor (BAR) superfamily and is present predominantly in hepatocytes and stellate cells [8]. OCA regulates several hepatic metabolic, inflammatory and fibrotic pathways thus benefiting MASLD [1]. Although not approved by the USFDA, OCA has been shown to be beneficial for MASLD patients in several studies. A phase 2b clinical trial (FLINT) reported significant improvement of hepatic histopathology on oral, daily OCA compared to placebo [39]. Improvement of hepatic histology was also seen with oral OCA at 72 weeks compared to placebo (45% vs 23%) in another clinical trial [39]. Similarly, one more large, international, multi-centre, phase 3 clinical trial (REGENERATE) observed 1-stage reversal of hepatic fibrosis, without worsening of MASH in 23% vs 18% vs 12% MASLD patients either taking OCA 25 mg, orally, daily or 10 mg, orally daily and placebo respectively [40]. Our recent prospective, observational, real-world experience yielded that when 'combined' with lifestyle modification, OCA is superior to lifestyle modification 'only' in improving hepatic steatosis. At 24 weeks OCA 20 mg, orally daily led to reduction of liver fat (274.7+45.3 vs 294.1+36.8 dB/m) as well as liver stiffness (5.38+1.00 vs 5.46+1.05 kPa) on fibroscan [41]. We also recently concluded a prospective, observational real-world study in MASLD patients where we used 'combination' of OCA, saroglitazar and lifestyle modification and compared the results with those who were advised 'only' lifestyle modification. We not only observed improvement of hepatic steatosis in the 'combination' arm, but most strikingly hepatic fibrosis, which is the key concern in any chronic liver disease management, also came down significantly among the patients in this group. At 24-48 weeks following saroglitazar 4 mg, orally, daily plus OCA 20 mg, orally daily, liver fat reduction was 239.4+43.0 vs 289.9+38.9 dB/m and liver stiffness reduction 5.7+2.4 vs 8.9+7.6 kPa on fibroscan respectively ($p<0.001$) [1]. This study is unique, as it is one of rare clinical studies where the effect of dual pharmacologic agents has been evaluated for MASLD/MASH management.

Conclusion

MASLD/MASH is an ongoing non-communicable pandemic that already poses significant threat to human health as well as to the health infrastructure and budget globally. Till long, lifestyle modification remained the mainstay of treatment of MASLD/MASH in the absence of any effective pharmacologic intervention. However, although effective, lifestyle modification is associated with multiple challenges. With the advent of newer drugs, our emphasis is gradually switching to 'combining' drugs with lifestyle modification in order to contain this global health threat.

References

1. Noor-E-Alam SM, Moben AL, Begum R, Rahim MA, Rahman MA, Saha M, Mahtab M, Khan S, Akbar SMF, Mahtab MA (2025) Dual drug therapy for fatty liver: A prospective real-life study from Bangladesh. *Int J Med Pharm Res* 6:253–258. https://doi.org/10.5281/zenodo.17589078
2. Asrani S, Devarbhavi H, Eaton J, et al (2019) Burden of liver diseases in the world. *J Hepatol* 70:151–171. https://pubmed.ncbi.nlm.nih.gov/30266282/
3. Rahman MM, Kibria MG, Begum H, Haque M, Sultana N, Akhter M, Rowshon AHM, Ahmed F, Hasan M (2020) NAFLD in rural South Asia. *BMJ Open Gastroenterol* 7:e000535. https://doi.org/10.1136/bmjgast-2020-000535
4. Williamson R, Price J, Glancy S (2011) Hepatic steatosis in T2DM. *Diabetes Care* 34:1139–1144.
5. Hazlehurst JM, Woods C, Marjot T, Cobbold JF, Tomlinson JW (2016) NAFLD and diabetes. *Metabolism* 65:1096–1108.
6. EASL, EASD, EASO (2016) Clinical practice guidelines for NAFLD. *J Hepatol* 64:1388–1402.
7. Hannah WN Jr, Harrison SA (2016) Weight loss and NAFLD. *Clin Liver Dis* 20:339–350.
8. Roy PP, Mahtab MA, Rahim MA, Yesmin SS, Islam SB, Akbar SMF (2022) Obeticholic acid in NASH. *Euroasian J Hepatogastroenterol* 12:S46–S50.
9. Bellentani S, Dalle Grave R, Suppini A, Marchesini G (2008) Behavioral therapy in NAFLD. *Hepatology* 47:746–754.
10. Musso G, Gambino R, Cassader M, Pagano G (2010) Meta-analysis of NAFLD treatments. *Hepatology* 52:79–104.
11. Pawlak M, Lefebvre P, Staels B (2015) PPAR and lipid metabolism. *J Hepatol* 62:720–733.
12. Foucher J, Chanteloup E, Vergniol J, et al (2006) FibroScan diagnosis of cirrhosis. *Gut* 55:403–408.
13. Monteiro CA, Cannon G, Moubarac JC, et al (2018) Ultra-processed foods and nutrition. *Pub-*

lic Health Nutr 21:5–17.
14. Adams J, White M (2015) UK diet and food processing. *Int J Behav Nutr Phys Act* 12:160.
15. Singh AK, Gandotra A, Kumar S, Singh A, Kochhar R, Manrai M (2025) Ultra-processed foods and gut health. *World J Gastroenterol* 31:109143.
16. Martini D, Godos J, Bonaccio M, Vitaglione P, Grosso G (2021) Ultra-processed foods meta-analysis. *Nutrients* 13:3390.
17. Pagliai G, Dinu M, Madarena MP, Bonaccio M, Iacoviello L, Sofi F (2021) UPF consumption and health. *Br J Nutr* 125:308–318.
18. Gehring J, Touvier M, Baudry J, et al (2021) UPF consumption patterns. *J Nutr* 151:120–131.
19. Henney AE, Gillespie CS, Alam U, Hydes TJ, Cuthbertson DJ (2023) UPF and NAFLD meta-analysis. *Nutrients* 15:2266.
20. Grinshpan LS, Eilat-Adar S, Ivancovsky-Wajcman D, et al (2023) UPF and metabolic risk. *JHEP Rep* 6:100964.
21. Zhang YF, Qiao W, Zhuang J, et al (2024) UPF and NAFLD UK Biobank. *J Nutr Health Aging* 28:100352.
22. Konieczna J, Morey M, Abete I, et al (2021) UPF and adiposity. *Clin Nutr* 40:4290–4300.
23. Szabo Z, Marosvölgyi T, Szabo E, et al (2022) Heating oils and fatty acids. *Foods* 11:192.
24. UN-Habitat (2020) Public space indicator training module. https://unhabitat.org
25. United Nations (2020) Urbanization data. https://www.un.org
26. Rahman SH, Islam M (2022) Urban green space in Dhaka. *Bangladesh J Environ Res* 13:1–12.
27. Estes C, Razavi H, Loomba R, Younossi Z, Sanyal AJ (2018) NAFLD burden modeling. *Hepatology* 67:123–133.
28. Marchesini G, Bugianesi E, Forlani G, et al (2003) NAFLD and metabolic syndrome. *Hepatology* 37:917–923.
29. FDA (2024) First treatment for liver fibrosis due to fatty liver. https://www.fda.gov
30. Harrison SA, Bedossa P, Guy CD, et al (2024) Resmetirom phase 3 trial. *N Engl J Med* 390:497–509.
31. Harrison SA, Bashir M, Moussa SE, et al (2021) Resmetirom phase 2 study. *Hepatol Commun* 5:573–588.
32. Bansal MB, Patton H, Morgan TR, et al (2025) Semaglutide therapy update. *Hepatology*.
33. Jaiswal A, Jain K, Singh AK (2021) Saroglitazar in NAFLD. *J Clin Diagn Res*. https://doi.org/10.7860/JCDR/2021/52065/15738
34. Jain MR, Giri SR, Bhoi B, et al (2018) Saroglitazar experimental study. *Liver Int* 38:1084–1094.
35. Sosale A, Saboo B, Sosale B (2015) Saroglitazar in T2DM. *Diabetes Metab Syndr Obes* 8:189–196.
36. Goyal O, Nohria S, Goyal P, et al (2020) Saroglitazar real-world study. *Sci Rep* 10:21117.
37. Gawrieh S, Noureddin M, Loo N, et al (2021) Saroglitazar RCT. *Hepatology* 74:1809–1824.
38. Moben AL, Begum R, Noor E Alam SM, et al (2025) Generic Saroglitazar study. *UKR J Med Med Res*. https://doi.org/10.5281/zenodo.18047012
39. Neuschwander-Tetri BA, Loomba R, Sanyal AJ, et al (2015) FLINT trial. *Lancet* 385:956–965.
40. Younossi ZM, Ratziu V, Loomba R, et al (2019) Obeticholic acid phase 3 trial. *Lancet* 394:2184–2196.
41. Begum R, Moben AL, Noor E Alam SM, et al (2025) Generic Obeticholic acid study. *J Med Med Res*. https://zenodo.org/records/17962328