UTJMS 2025 June 30, 13(S3):e1-e4

Effect of Pemafibrate, a Selective Peroxisome Proliferator-activated Receptor? Modulator (SPPARM?), on the Lipid Profile, Liver Function, and Liver Fibrosis among Patients with Non-alcoholic Fatty Liver Disease: A Systematic Review and Meta-Analysis

Mona Hassan¹, Nooraldin Merza^{2*}, Yusuf Nawras³, Halah Alfatlawi², Hasan Al-Obaidi⁴, Omar Saab⁵, Khalid Al Zubaidi⁶, Daniah Al-Sabbagh⁷, Sarmed Mansur⁸, Marwah Algodi⁹, Omer Al Najafi¹⁰, Rand Matbachi⁹, Tamarah Al Hamdany¹¹, Zainab Noori⁶, Abdallah Kobeissy¹²

¹Assistant Professor and Associate Program Director Gastroenterology Fellowship, Division of Gastroenterology, Department of Medicine, 3000 Arlington Avenue, The University of Toledo, Toledo OH 43615

²Fellow, Division of Gastroenterology, Department of Medicine, 3000 Arlington Avenue, The University of Toledo, Toledo OH 43615

³College of Medicine and Life Sciences, 3000 Arlington Avenue, The University of Toledo, Toledo OH 43615

⁴Jamaica Hospital Medicine Center, Internal Medicine Department, Queens NY 11435

⁵Cleveland Clinic, Internal Medicine Department, Cleveland OH 44115

⁶University of Al-Mostansiryah College of Medicine, Internal Medicine Department, Baghdad, Iraq

⁷Al-Kindy College of Medicine – University of Baghdad, Internal Medicine Department, Baghdad, Iraq

⁸Assistant Professor, Division of Internal Medicine, Department of Medicine, 3000 Arlington Avenue, The University of Toledo, Toledo OH 43615

⁹University of Baghdad College of Medicine, Internal Medicine Department, Baghdad, Iraq

¹⁰Zucker School of Medicine / Northwell Health at Mather Hospital, Internal Medicine Department, Hempstead NY 11540

¹¹University of Michigan, Internal Medicine Department, Ann Arbor MI 48109

¹²Associate Professor and Associate Program Director Gastroenterology Fellowship, Division of Gastroenterology, Department of Medicine, 3000 Arlington Avenue, The University of Toledo, Toledo OH 43615

Dr. Lance D. Dworkin Department of Medicine Research Symposium

UTJMS 2025 June 30, 13(S3):e1-e4

Email: nooraldin.merza@utoledo.edu

Received: 2024-08-16

Accepted: 2024-09-16

Published: 2025-06-30

Background: Metabolic dysfunction associated steatotic liver disease (MASLD) and Metabolic dysfunction associated steatohepatitis (MASH) are prevalent conditions linked to obesity and metabolic disturbances, with potential complications such as cirrhosis and cardiovascular risks (1). This systematic review and meta-analysis aimed to evaluate the efficacy of Pemafibrate, a drug targeting fat and sugar metabolism genes, in treating patients with MASLD/MASH.

Methods: Databases such as MEDLINE, Web of Science, Cochrane Library, and Scopus were searched until September 2023 to identify relevant studies. Selected studies underwent a thorough quality assessment using tools like ROB-2 and the NIH Quality Assessment Tools. Comprehensive Meta-analysis software was used for statistical evaluations, with a focus on lipid profiles, liver function tests, and fibrosis measurements.

Results: A total of 13 studies were included; 10 of them were included in the quantitative analysis. Our findings showed that pemafibrate significantly decreased LDL-C (ES= -9.61 mg/dL, 95% CI: -14.15 to -5.08), increased HDL-C (ES= 3.15 mg/dL, 95% CI: 1.53 to 4.78) (2,3-13), and reduced triglycerides (TG) (ES= -85.98 mg/dL, 95% CI: -96.61 to -75.36). Additionally, pemafibrate showed a marked reduction in liver enzyme levels, including AST, ALT, GGT, and ALP, with significant effect sizes and p-values. For liver stiffness outcomes, pemafibrate decreased APRI (ES= -0.180, 95% CI: -0.221 to -0.138).

Conclusion: Pemafibrate, with its enhanced selectivity and safety profile, presents as a pivotal agent in MASLD/MASH treatment. Its lipid-regulating properties, coupled with its beneficial effects on liver inflammation markers, position it as a potentially invaluable therapeutic option.

Keywords: MASLD, MASH, Pemafibrate, PPARS, Lipid profile, Liver fibrosis, Liver stiffness

References

- 1. Hsu C, Caussy C, Imajo K, Chen J, Singh S, Kaulback K, Le M-D, Hooker J, Tu X, Bettencourt R, Yin M, Sirlin CB, Ehman RL, Nakajima A, Loomba R. *Magnetic Resonance vs Transient Elastography Analysis of Patients With Non-alcoholic Fatty Liver Disease: A Systematic Review and Pooled Analysis of Individual Participants*. Clin Gastroenterol Hepatol Off Clin Pract J Am Gastroenterol Assoc, 2019. **17**:630-637.e8. https://doi.org/10.1016/j.cgh.2018.05.059
- 2. Yamashita S, Masuda D, Matsuzawa Y. *Pemafibrate, a New Selective PPAR? Modulator: Drug Concept and Its Clinical Applications for Dyslipidemia and Metabolic Diseases*. Curr Atheroscler Rep, 2020. **22**:5. Doi:10.1007/s11883-020-0823-5

Dr. Lance D. Dworkin Department of Medicine Research Symposium

UTJMS 2025 June 30, 13(S3):e1-e4

- 3. Ikeda S, Sugihara T, Hoshino Y, Matsuki Y, Nagahara T, Okano JI, Kitao S, Fujioka Y, Yamamoto K, Isomoto H. *Pemafibrate dramatically ameliorated the values of liver function tests and fibrosis marker in patients with non-alcoholic fatty liver disease*. Yonago Acta Med, 2020. **63**:188–197. Doi:10.33160/yam.2020.08.009
- 4. Ikeda S, Sugihara T, Kihara T, Matsuki Y, Nagahara T, Takata T, Kitao S, Okura T, Yamamoto K, Isomoto H. *Pemafibrate ameliorates liver dysfunction and fatty liver in patients with non-alcoholic fatty liver disease with hypertriglyceridemia: A retrospective study with the outcome after a mid-term follow-up*. Diagnostics, 2021. **11**. Doi:10.3390/diagnostics11122316
- 5. Hatanaka T, Kosone T, Saito N, Takakusagi S, Tojima H, Naganuma A, Takagi H, Uraoka T, Kakizaki S. *Effect of 48-week pemafibrate on non-alcoholic fatty liver disease with hypertriglyceridemia, as evaluated by the FibroScan-aspartate aminotransferase score*. JGH Open, 2021. **5**:1183–1189. Doi: 10.1002/jgh3.12650
- 6. Nakajima A, Eguchi Y, Yoneda M, Imajo K, Tamaki N, Suganami H, Nojima T, Tanigawa R, Iizuka M, Iida Y, Loomba R. *Randomised clinical trial: Pemafibrate, a novel selective peroxisome proliferator-activated receptor? modulator (SPPARM?), versus placebo in patients with non-alcoholic fatty liver disease.*Aliment Pharmacol Ther, 2021. **54**:1263–1277. Doi:10.1111/apt.16596
- 7. Hatanaka T, Kakizaki S, Saito N, Nakano Y, Nakano S, Hazama Y, Yoshida S, Hachisu Y, Tanaka Y, Kashiwabara K, Yoshinaga T, Tojima H, Naganuma A, Uraoka T. *Impact of pemafibrate in patients with hypertriglyceridemia and metabolic dysfunction-associated fatty liver disease pathologically diagnosed with non-alcoholic steatohepatitis: A retrospective, single-arm study*. Intern Med, 2021. **60**:2167–2174. Doi:10.2169/INTERNALMEDICINE.6574-20
- 8. Shinozaki S, Tahara T, Lefor AK, Ogura M. *Pemafibrate decreases markers of hepatic inflammation in patients with non-alcoholic fatty liver disease*. Clin Exp Hepatol, 2020. **6**:270–274. Doi:10.5114/ceh.2020.99528
- 9. Seko Y, Yamaguchi K, Umemura A, Yano K, Takahashi A, Okishio S, Kataoka S, Okuda K, Moriguchi M, Okanoue T, Itoh Y. *Effect of pemafibrate on fatty acid levels and liver enzymes in non-alcoholic fatty liver disease patients with dyslipidemia: A single-arm, pilot study.* Hepatol Res, 2020. **50**:1328–1336. doi:10.1111/hepr.13571
- 10. Shinozaki S, Tahara T, Lefor AK, Ogura M. *Pemafibrate improves hepatic inflammation, function and fibrosis in patients with non-alcoholic fatty liver disease: A one-year observational study*. Clin Exp Hepatol, 2021. **7**:172–177. Doi:10.5114/ceh.2021.106864
- 11. Shinozaki S, Tahara T, Miura K, Kawarai Lefor A, Yamamoto H. *Pemafibrate therapy for non-alcoholic fatty liver disease is more effective in lean patients than obese patients*. Clin Exp Hepatol, 2022. **8**:278–283. Doi:10.5114/ceh.2022.120099

Dr. Lance D. Dworkin Department of Medicine Research Symposium

UTJMS 2025 June 30, 13(S3):e1-e4

- 12. Sugimoto R, Iwasa M, Eguchi A, Tamai Y, Shigefuku R, Fujiwara N, Tanaka H, Kobayashi Y, Ikoma J, Kaito M, Nakagawa H. *Effect of pemafibrate on liver enzymes and shear wave velocity in non-alcoholic fatty liver disease patients*. Front Med, 2023. **10**:1–8. Doi:10.3389/fmed.2023.1073025
- 13. Iwadare T, Kimura T, Kunimoto H, Tanaka N, Wakabayashi SI, Yamazaki T, Okumura T, Kobayashi H, Yamashita Y, Sugiura A, Joshita S, Umemura T. *Higher Responsiveness for Women, High Transaminase Levels, and Fat Percentage to Pemafibrate Treatment for NAFLD*. Biomedicines, 2022. **10**:2–13. Doi:10.3390/biomedicines10112806