EURASIAN EXPERIMENT JOURNAL OF SCIENTIFIC AND APPLIED RESEARCH
(EEJSAR) ISSN: 2992-4146
©EEJSAR Publications Volume 7 Issue 3 2025

Oxidative Stress, Liver Dysfunction, and Urological Complications: Mechanistic Insights and Therapeutic Opportunities in Benign Prostatic Hyperplasia

Kamanzi Ntakirutimana G.

School of Natural and Applied Sciences Kampala International University Uganda

ABSTRACT

Benign Prostatic Hyperplasia (BPH) is a non-malignant enlargement of the prostate gland commonly affecting aging men and is a leading cause of lower urinary tract symptoms (LUTS). Increasing evidence highlights the pivotal role of oxidative stress (OS) in driving the pathophysiological processes underlying BPH, including chronic inflammation, cellular proliferation, and fibrosis. Notably, liver dysfunction, especially in the context of non-alcoholic fatty liver disease (NAFLD), often coexists with BPH due to shared metabolic risk factors and systemic oxidative-inflammatory processes. The liver-prostate axis represents a critical yet underexplored pathway through which hepatic injury and oxidative stress exacerbate urological complications. This review provides mechanistic insights into the interplay between oxidative stress, liver dysfunction, and BPH development. Furthermore, emerging therapeutic opportunities focusing on antioxidant-based interventions, hepatoprotective agents, and integrative systems medicine approaches are discussed as promising strategies for the management of patients with concurrent liver and prostatic disorders.

Keywords: Benign Prostatic Hyperplasia; Oxidative Stress; Liver Dysfunction; Urological Complications; Antioxidant Therapy

INTRODUCTION

Benign Prostatic Hyperplasia (BPH) is one of the most common urological disorders affecting aging men globally [1]. It is a progressive, non-malignant enlargement of the prostate gland characterized by hyperplasia of both stromal and epithelial cells [2]. This pathological growth leads to compression of the prostatic urethra, resulting in bladder outlet obstruction and the development of lower urinary tract symptoms (LUTS) [1]. These symptoms include increased urinary frequency, nocturia, weak urine stream, incomplete bladder emptying, and urinary hesitancy [3]. The prevalence of BPH increases with advancing age, affecting approximately 50% of men over 50 years and nearly 90% of men over 80 years of age [2]. With increasing global life expectancy and aging populations, the healthcare burden associated with BPH is expected to escalate further [4]. Traditionally, BPH pathogenesis has been associated with age-related hormonal changes, particularly the role of androgens such as dihydrotestosterone (DHT), which promotes prostatic cell proliferation [5]. However, contemporary research has identified additional pathogenic drivers beyond hormonal factors. Notably, oxidative stress (OS) and chronic inflammation have gained significant attention as central mechanisms involved in prostatic tissue remodeling and hyperplasia [6]. OS results from an imbalance between the generation of reactive oxygen species (ROS) and the body's antioxidant defense mechanisms, leading to cellular damage and dysfunction [7]. In BPH, excessive ROS production in prostatic tissues contributes to inflammatory signaling, extracellular matrix remodeling, and stromal-epithelial proliferation, promoting disease progression and symptom severity [8]. Parallel to the increasing burden of BPH, liver dysfunction — particularly non-alcoholic fatty liver disease (NAFLD) and its progressive form non-alcoholic steatohepatitis (NASH) — has emerged as a leading global health challenge [9]. NAFLD affects approximately 25-30% of the global population and is closely linked to metabolic syndrome components such as obesity, insulin

resistance, type 2 diabetes, and dyslipidemia [9,10]. Like BPH, NAFLD is strongly influenced by oxidative stress and chronic inflammation, which contribute to hepatocyte injury, lipid accumulation, mitochondrial dysfunction, and the progression of hepatic fibrosis [11]. Recent studies have highlighted a significant pathophysiological link between liver dysfunction and BPH through a dynamic interplay of metabolic, hormonal, and inflammatory pathways — often referred to as the liver-prostate axis [12]. Both conditions share common risk factors, including metabolic syndrome, obesity, insulin resistance, and chronic low-grade systemic inflammation. Importantly, liver dysfunction amplifies systemic oxidative stress, leading to the release of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and C-reactive protein (CRP) into the circulation [13]. These inflammatory mediators can reach the prostate gland, exacerbating oxidative stress and inflammatory responses within the prostate microenvironment, thus promoting prostatic enlargement and worsening LUTS [6].

Furthermore, liver dysfunction influences bile acid metabolism, lipid homeostasis, and hormonal regulation, all of which have downstream effects on prostatic tissue growth and function [14]. For instance, hepatic insulin resistance leads to hyperinsulinemia, which promotes insulin-like growth factor-1 (IGF-1) activity — a potent driver of prostatic cell proliferation and hyperplasia [15]. Additionally, altered lipid metabolism associated with NAFLD contributes to changes in androgen and estrogen levels, further influencing the hormonal milieu within the prostate [16]. Given the overlapping pathophysiology between BPH and liver dysfunction, there is growing recognition of the need for therapeutic strategies that target oxidative stress and inflammatory signaling within both organs simultaneously. Such an integrated approach could offer substantial benefits in managing patients with concurrent BPH and liver disease, particularly those with underlying metabolic syndrome. This review synthesizes current mechanistic insights into the role of oxidative stress and liver dysfunction in urological complications, focusing on BPH. It further explores emerging therapeutic opportunities that leverage antioxidant-based interventions, hepatoprotective agents, and personalized medicine approaches within this interconnected pathophysiological framework. Addressing the systemic nature of oxidative stress and inflammation across both the liver and prostate may hold the key to developing more effective, holistic management strategies for BPH and its associated comorbidities.

The Liver-Prostate Axis: Pathophysiological Interactions

The liver-prostate axis represents an emerging concept in understanding the systemic interplay between liver dysfunction and benign prostatic hyperplasia (BPH) [17]. Increasing evidence suggests that metabolic, hormonal, and inflammatory mediators originating from liver dysfunction can exacerbate prostatic pathology, highlighting the systemic nature of BPH pathogenesis [1]. One of the primary mechanisms by which liver dysfunction influences prostate health is through dysregulated bile acid metabolism [18]. The liver is the key organ responsible for bile acid synthesis and homeostasis [19]. Alterations in bile acid profiles due to hepatic injury or non-alcoholic fatty liver disease (NAFLD) can influence androgen receptor signaling pathways in prostatic tissues, potentially promoting cellular proliferation and hyperplasia [20]. Additionally, hepatic insulin resistance, commonly associated with NAFLD and metabolic syndrome, leads to systemic hyperinsulinemia [21]. Elevated insulin levels enhance insulin-like growth factor-1 (IGF-1) signaling, which plays a critical role in stimulating prostatic stromal and epithelial cell proliferation [22]. This hormonal disturbance accelerates prostate growth and contributes to lower urinary tract symptoms (LUTS). Hepatic inflammation also results in the systemic release of pro-inflammatory cytokines such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and C-reactive protein (CRP) [23]. These mediators not only promote systemic oxidative stress but also reach the prostate, amplifying local inflammation, extracellular matrix remodeling, and fibrosis [8]. Moreover, altered lipid metabolism associated with liver dysfunction further contributes to hormonal imbalances, including dysregulated testosterone and estrogen levels [24]. These hormonal disturbances favor prostatic hyperplasia and disease progression. Thus, liver dysfunction acts as a systemic amplifier of oxidative stress, chronic inflammation, and hormonal dysregulation — all of which converge to exacerbate prostatic remodeling, fibrosis, and LUTS severity. This understanding highlights the importance of therapeutic strategies that target the liver-prostate axis for more effective management of BPH in patients with coexisting hepatic conditions.

Therapeutic Opportunities Targeting Oxidative Stress and Liver Dysfunction in BPH

Given the strong pathophysiological link between liver dysfunction, oxidative stress, and BPH, there is a growing interest in therapeutic strategies that can simultaneously modulate oxidative damage and inflammation within both the liver and prostate. Dual-targeted interventions hold significant promise for managing patients with coexisting urological and hepatic complications [25].

Antioxidant Therapy

Natural antioxidants derived from dietary and plant-based sources have demonstrated substantial hepatoprostatic benefits. Compounds such as lycopene (from tomatoes), curcumin (from turmeric), resveratrol (from grapes), and

silymarin (from milk thistle) exert potent antioxidant and anti-inflammatory effects [26]. These antioxidants neutralize reactive oxygen species (ROS), suppress NF-κB-mediated inflammatory signaling, enhance insulin sensitivity, and inhibit fibrosis in both the liver and prostate tissues 27]. Antioxidants also modulate redox-sensitive transcription factors and improve mitochondrial function, thereby restoring cellular homeostasis [28].

Hepatoprotective Agents

Specific hepatoprotective agents, including silymarin and N-acetylcysteine (NAC), have shown the ability to reduce liver-derived oxidative stress and inflammation [29]. These agents stabilize hepatocyte membranes, enhance hepatic detoxification pathways, and promote antioxidant enzyme activity [30]. By improving liver function, hepatoprotective agents indirectly benefit prostate health by reducing systemic inflammatory and oxidative mediators that contribute to BPH progression.

Combination Therapies

A rational therapeutic strategy involves combining antioxidants with prostate-specific medications, such as alpha-adrenergic blockers and 5-alpha-reductase inhibitors, which improve urinary flow and reduce prostate volume [31]. Simultaneously incorporating hepatoprotective interventions addresses liver dysfunction, ensuring a holistic approach to managing dual organ involvement.

Gut Microbiota Modulation

Emerging evidence suggests that the gut-liver-prostate axis plays a critical role in modulating systemic inflammation and oxidative stress [32]. Modulating the gut microbiota through probiotics, prebiotics, dietary fibers, and polyphenol-rich diets can enhance intestinal barrier function, reduce endotoxin translocation, and improve antioxidant capacity [33]. Gut microbiota-targeted interventions represent a promising adjunctive therapy for patients with BPH and liver dysfunction, capable of restoring systemic metabolic and inflammatory balance [34].

Future Research Directions

Future research should prioritize the development and clinical validation of dual-targeted therapeutic strategies that address both benign prostatic hyperplasia (BPH) and liver dysfunction, particularly in patients with underlying metabolic syndrome. Well-designed clinical trials evaluating the efficacy and safety of antioxidant therapies in BPH patients with concurrent liver disease are urgently needed. These trials should focus on the use of natural antioxidants such as lycopene, curcumin, resveratrol, and silymarin, in combination with hepatoprotective agents and conventional prostate-specific medications. Such integrative approaches could offer superior clinical benefits compared to monotherapies. Another promising research avenue involves the application of systems pharmacology models to predict patient-specific responses to dual-targeted therapies. By integrating data from genomics, proteomics, metabolomics, and liver-prostate axis biomarkers, these models can facilitate the design of precision medicine frameworks tailored to individual patient profiles. Predictive modeling can also guide the selection of optimal antioxidant formulations, dosing regimens, and therapeutic combinations based on the metabolic and inflammatory status of each patient. Further research is warranted to identify novel molecular targets within redox-regulated pathways that mediate the liver-prostate axis. Targeting transcription factors such as NF-κB, Nrf2, or signaling mediators involved in oxidative stress and fibrosis may yield new therapeutic agents for the management of BPH with liver comorbidities. Additionally, the exploration of gut microbiome signatures in patients with BPH and liver disease represents an innovative frontier. Understanding how gut microbial composition and function influence systemic inflammation, oxidative stress, and hormonal regulation could lead to microbiota-targeted interventions, including probiotics, prebiotics, and dietary strategies, to improve therapeutic outcomes in this patient population.

CONCLUSION

Oxidative stress serves as a unifying mechanistic link between liver dysfunction and urological complications, particularly BPH. Understanding the molecular interplay between the liver and prostate opens new avenues for integrated therapeutic interventions. Dual-targeted antioxidant strategies, combined with hepatoprotective agents and personalized medicine approaches, hold significant promise for improving patient outcomes in BPH complicated by liver dysfunction. Future research should emphasize the development of precision medicine frameworks that address the systemic nature of oxidative stress-mediated diseases across organ systems.

REFERENCES

1. Edyedu I, Ugwu OP, Ugwu CN, Alum EU, Eze VHU, Basajja M, Ugwu JN, Ogenyi FC, Ejemot-Nwadiaro RI, Okon MB, Egba SI, Uti DE, Aja PM. The role of pharmacological interventions in managing urological complications during pregnancy and childbirth: A review. Medicine (Baltimore). 2025 Feb 14;104(7):e41381. doi: 10.1097/MD.0000000000041381. PMID: 39960970; PMCID: PMC11835077.
2. Ibiam, U. A., Uti, D. E., Ejeogo, C. C., Orji, O. U., Aja, P. M., Ezeaani, N. N., Alum, E. U., Chukwu, C., AlokeC., Chinedum, K. E., Agu, P. and Nwobodo, V. In Vivo and in Silico Assessment of Ameliorative Effects of Xylopia

aethiopica on Testosterone Propionate-Induced Benign Prostatic Hyperplasia. *Pharmaceut Fronts.* 2023;5: e64–e76. DOI:10.1055/s-0043-1768477

3. Uhuo EN, Egba SI, Obike CA, Anyiam PN, Alaebo PO, Okeke PM, et al. Combined extracts of Syzygium aromaticum (Clove) and Xylopia aethiopica (Negro pepper) seeds inhibit testosterone propionate-induced benign prostatic hyperplasia in Wistar rats. All Life [Internet]. 2024 Dec 5;17(1). Available from:https://www.tandfonline.com/doi/epdf/10.1080/26895293.2024.2435277
4. Ibiam U. A., Uti, D. E., Ejeogo, C.C., Orji, O. U. Aja, P. M., Ezeani, N. N., Alum, E. U., Chukwu, C., Aloke, C., Itodo, M. O., Agada, S. A., Umoru, G. U., Obeten, U. N., Nwobodo, V. O. G., Nwadum, S. K., Udoudoh, M. P. Xylopia aethiopica Attenuates Oxidative Stress and Hepatorenal Damage in Testosterone Propionate-Induced Benign Prostatic Hyperplasia in Rats. Journal of Health and Allied Sciences. 2024, 01: 1-148. https://doi.org/10.1055/s-0043-1777836.
5. Obeagu, E.I., Alum, E.U., Obeagu, G.U. and Ugwu, O. P. C. Benign Prostatic Hyperplasia: A Review. *Eurasian Experiment Journal of Public Health (EEJPH).* 2023; 4(1): 1-3.
6. Ugwu, CE., Sure, SM., Dike, CC., Okpoga, NA and Egba, SI. Phytochemical and *in vitro* antioxidant activities of methanol leave extract of *Alternanthera basiliana*. Journal of Pharmacy Research, 2018; 12(6): 835-839
7. Alum, E. U., Ibiam, U. A., Ugwuja, E. I., Aja, P. M., Igwenyi, I. O., Offor, C. E., Orji, O. U., Ezeani N. N, Ugwu, O. P. C., Aloke, C., Egwu, C. O. Antioxidant Effect of *Buchholzia coriacea* Ethanol Leaf Extract and Fractions on Freund's Adjuvant-induced Arthritis in Albino Rats: A Comparative Study. *Slovenian Veterinary Research.* 2022; 59 (1): 31–45. doi: 10.26873/svr-1150-2022.
8. Uroko Robert Ikechukwu, Fatima Amin Adamude, Egba Simeon Ikechukwu, Chinedu Paulinus Nwuke, Chidinma Lilian Asadu and Peter Anyaorah. Effect of combined ethanol extract of Funtumia Africana and Abutilon mauritanium leaves on prostate biomarkers and serum mineral levels in prostatic hyperplasia induced in rats. J. Renal Endocrinol 2021; 7:e06
9. Dong X, Li JM, Lu XL, Lin XY, Hong MZ, Weng S, et al. Global burden of adult non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH) has been steadily increasing over the past decades and is expected to persist in the future. Translational Gastroenterology and Hepatology. 2024;9:33. doi:10.21037/tgh-23-118
10. Godoy-Matos AF, Júnior WSS, Valerio CM. NAFLD as a continuum: From obesity to metabolic syndrome and diabetes. Diabetology & Metabolic Syndrome. 2020;12(1). doi:10.1186/s13098-020-00570-y
11. Robert I. Uroko., Charles N. Chukwu., Simeon I. Egba., Fatima A. Adamude andJoy C. Ajuzie Combined ethanol extract of *Funtumia africana* and *Abutilon mauritianium* leaves improves the lipid profile and kidney function indices of benign prostatic hyperplasia in rats. Acta Sci. Pol. Technol. Aliment. 2020; 19(4): 395-404
12. IR Uroko, F A Adamude, S I Egba, C N Chukwu, C L Asadu, E C Okwara. Effects of combined ethanol extract of *Funtumia africana* and *Abutilon mauritianum* leaves (FAAM) on liver function indices of benign prostatic hyperplasia (BPH) induced rats, Herba Polonica,2020; 66 (3): 24-35
13. Bhol NK, Bhanjadeo MM, Singh AK, Dash UC, Ojha RR, Majhi S, et al. The interplay between cytokines, inflammation, and antioxidants: Mechanistic insights and therapeutic potentials of various antioxidants and anti-cytokine compounds. Biomedicine & Pharmacotherapy. 2024;178:117177. doi:10.1016/j.biopha.2024.117177
14. Fuchs CD, Simbrunner B, Baumgartner M, Campell C, Reiberger T, Trauner M. Bile acid metabolism and signaling in liver disease. Journal of Hepatology. 2024. doi:10.1016/j.jhep.2024.09.032
15. Wang Z, Olumi AF. Diabetes, growth hormone-insulin-like growth factor pathways and association to benign prostatic hyperplasia. Differentiation. 2011;82(4–5):261–71. doi:10.1016/j.diff.2011.04.004
16. Song MJ, Choi JY. Androgen dysfunction in non-alcoholic fatty liver disease: Role of sex hormone binding globulin. Frontiers in Endocrinology. 2022;13. doi:10.3389/fendo.2022.1053709
17. Chung GE, Yim JY, Kim D, Kwak MS, Yang JI, Park B, et al. Nonalcoholic fatty liver disease is associated with benign prostate hyperplasia. Journal of Korean Medical Science. 2020;35(22):e164. doi:10.3346/jkms.2020.35.e164
18. Wang Y, Xu H, Zhou X, Chen W, Zhou H. Dysregulated bile acid homeostasis: Unveiling its role in metabolic diseases. Medical Review. 2024;4(4):262–83. doi:10.1515/mr-2024-0020
19. Chiang J. Liver physiology: Metabolism and detoxification. In: Elsevier eBooks. 2014. p. 1770–82. doi:10.1016/B978-0-12-386456-7.04202-7
20. Chávez-Talavera O, Haas J, Grzych G, Tailleux A, Staels B. Bile acid alterations in nonalcoholic fatty liver disease, obesity, insulin resistance and type 2 diabetes: What do the human studies tell? Current Opinion in Lipidology. 2019;30(3):244–54. doi:10.1097/MOL.0000000000000597

21. Paschos P, Paletas K. Non alcoholic fatty liver disease and metabolic syndrome. 2009. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC2633261/
22. Matsushita M, Fujita K, Hatano K, De Velasco MA, Uemura H, Nonomura N. Connecting the dots between the gut–IGF-1–prostate axis: A role of IGF-1 in prostate carcinogenesis. Frontiers in Endocrinology. 2022;13. doi:10.3389/fendo.2022.852382
23. Tangvarasittichai S, Pongthaisong S, Tangvarasittichai O. Tumor necrosis factor-alpha, interleukin-6, C-reactive protein levels and insulin resistance associated with type 2 diabetes in abdominal obesity women. Indian Journal of Clinical Biochemistry. 2015;31(1):68–74. doi:10.1007/s12291-015-0514-0
24. Kasarinaite A, Sinton M, Saunders PTK, Hay DC. The influence of sex hormones in liver function and disease. Cells. 2023;12(12):1604. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC10296738/
25. Mitchell MC, Kerr T, Herlong HF. Current management and future treatment of alcoholic hepatitis. 2020. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC8132686/
26. Issinger OG, Guerra B. Phytochemicals in cancer and their effect on the PI3K/AKT-mediated cellular signaling. Biomedicine & Pharmacotherapy. 2021;139:111650. doi:10.1016/j.biopha.2021.111650
27. Uhuo E N, Egba S I, Nwuke P C, Obike C A and Kelechi G K. Antioxidative properties of Adansonia digitata L. (baobab) leaf extractexert protective effect on doxorubicin induced cardiac toxicity in Wistar rats. Clinical Nutrition Open Science 2022; 45:3-16
28. Ochulor Okechukwu C., Njoku Obioma U., Uroko Robert I and Egba Simeon I**.** Nutritional composition of *Jatropha tanjorensis* leaves and effects of its aqueous extract on carbon tetrachloride induced oxidative stress in male Wistar albino rats. Biomedical Research 2018; 29(19): 3569-3576
29. De Andrade K, Moura F, Santos JD, De Araújo O, De Farias Santos J, Goulart M. Oxidative stress and inflammation in hepatic diseases: Therapeutic possibilities of N-acetylcysteine. International Journal of Molecular Sciences. 2015;16(12):30269–308. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC4691167/
30. Aja, P. M., Igwenyi, I. O., Ugwu, O. P. C., Orji, O. U., Alum, E. U. Evaluation of Anti-diabetic Effect and Liver Function Indices of Ethanol Extracts of *Moringa oleifera* and *Cajanus cajan* Leaves in Alloxan Induced Diabetic Albino Rats. Global Veterinaria 2015; 14(3): 439-447. DOI: 10.5829/idosi.gv.2015.14.03.93129.
31. McVary KT. A review of combination therapy in patients with benign prostatic hyperplasia. Clinical Therapeutics. 2007;29(3):387–98. doi:10.1016/S0149-2918(07)80077-4
32. Fujita K, Matsushita M, De Velasco MA, Hatano K, Minami T, Nonomura N, et al. The Gut-Prostate Axis: A new perspective of prostate cancer biology through the gut microbiome. Cancers. 2023;15(5):1375. doi:10.3390/cancers15051375
33. Rodríguez-Daza MC, Pulido-Mateos EC, Lupien-Meilleur J, Guyonnet D, Desjardins Y, Roy D. Polyphenol-mediated gut microbiota modulation: Toward prebiotics and further. Frontiers in Nutrition. 2021;8. doi:10.3389/fnut.2021.689456
34. Liu J, Yang D, Wang X, Asare PT, Zhang Q, Na L, et al. Gut microbiota targeted approach in the management of chronic liver diseases. Frontiers in Cellular and Infection Microbiology. 2022;12. doi:10.3389/fcimb.2022.774335

CITE AS: Kamanzi Ntakirutimana G. (2025). Oxidative Stress, Liver Dysfunction, and Urological Complications: Mechanistic Insights and Therapeutic Opportunities in Benign Prostatic Hyperplasia. EURASIAN EXPERIMENT JOURNAL OF SCIENTIFIC AND APPLIED RESEARCH. 7(3):66-70