J Nephropharmacol. 2025; 14(1): e12695.

https://jnephropharmacology.com DOI: 10.34172/npj.2024.12695

Journal of Nephropharmacology

Renal dysfunction after hematopoietic cell transplantation; a mini-review study

Saeed Hoseininia, Sousan Mohammadi Kebar*

Department of Internal Medicine, Faculty of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran

ARTICLE INFO

Article Type:
Mini-Review

Article History:
Received: 28 May 2024
Accepted: 30 Jun. 2024
ePublished: 10 Aug. 2024

Keywords:
Bone marrow transplantation, Chronic renal failure, Bone marrow transplant nephropathy, Acute kidney injury, Hematopoietic cell transplantation

ABSTRACT

Bone marrow transplantation (BMT) can lead to renal manifestations, including acute kidney injury (AKI) and long-term renal dysfunction. Late-onset kidney disturbance can detect in around 20% of the BMT survivors. This condition is defined as bone marrow transplant nephropathy (BMTN). Total body irradiation is a main parameter in this syndrome, though concurrent or previous chemotherapies may aggravate the effect of radiation on the renal function and structure. BMT is characterized by inappropriate azotemia, anemia and hypertension while renal function may deteriorate acutely or more slowly. Other renal manifestations of BMT include hemolytic-uremia-like syndrome, which may manifest later (3-6 months or more), and membranous nephropathy, which is a rare complication of BMT.

Mini-Review

Implication for health policy/practice/research/medical education:
Bone marrow transplant is a life-saving procedure for various hematological malignancies and non-malignant disorders. However, one of the significant complications associated with BMT is bone marrow transplant nephropathy, which can lead to significant morbidity and mortality.

Please cite this paper as: Hoseininia S, Mohammadi Kebar S. Renal dysfunction after hematopoietic cell transplantation; a mini-review study. J Nephropharmacol. 2025;14(1):e12695. DOI: 10.34172/npj.2024.12695.

Introduction

Hematopoietic cell transplantation (HCT) is a procedure used to treat various hematological disorders, such as leukemia, lymphoma, and certain genetic diseases (1). While HCT can be life-saving, it can also lead to various complications, including kidney disease. Understanding the mechanisms of kidney disease following HCT is crucial for early detection and management of this condition (1,2). Several mechanisms contribute to the development of kidney disease after HCT. Prior to HCT, patients undergo a conditioning regimen that includes high-dose chemotherapy and/or total body irradiation (1,2). These treatments can cause direct kidney damage by inducing inflammation and oxidative stress in the renal tissue (3). Graft-versus-host disease (GVHD) is a common complication after HCT, where donor immune cells attack the recipient's organs, including the kidneys. GVHD-related kidney injury can manifest as acute or chronic kidney disease (CKD) and is characterized by immune-mediated inflammation and tissue damage (4,5). Patients undergoing HCT often receive nephrotoxic medications such as calcineurin inhibitors (e.g., cyclosporine or tacrolimus) to prevent graft rejection. Prolonged use of these medications can lead to nephrotoxicity and subsequent kidney dysfunction. Infections are common after HCT due to immunosuppression (6,7). Certain infections like viral (e.g., cytomegalovirus) or bacterial (e.g., urinary tract infections) can directly affect the kidneys and contribute to kidney injury (8). Thrombotic microangiopathy (TMA) is a condition characterized by microvascular thrombosis in various organs, including the kidneys. It can occur after HCT due to endothelial injury triggered by conditioning regimens or GVHD, leading to impaired blood flow and subsequent kidney dysfunction (9). The recent study by Abudayyeh et al showed that acute renal injury is detected inside the first

***Corresponding author**: Sousan Mohammadi Kebar, Email: Drsousanmk@gmail.com, s.mohammadi@arums.ac.ir

one hundred days of HCT and has an incidence ranging among 12 and 73%, with the highest rate in myeloablative allogeneic stem cell transplantation. Importantly, an outsized subset of cases following stem cell transplantation showed chronic renal failure. The can etiology of chronic renal failure was calcineurin toxicity, TMA and nephrotic syndrome. Meanwhile, dialysis necessity after necessity was accompanying with mortality of more than 80% (10). Moreover, Madsen et al, considered the frequency of acute renal failure and its effect on transplant consequences amid 408 cases of allogeneic HCT. They showed the whole rate of acute renal failure at first 100 days was 64.2%. This study also showed, individuals who established acute renal failure had below two years of overall survival (11). Patients with pre-existing kidney diseases, such as diabetic nephropathy or glomerulonephritis, may experience disease progression or exacerbation following HCT due to the aforementioned mechanisms (12). This mini-review aims to provide an overview of bone marrow transplant nephropathy (BMTN), including its pathophysiology, clinical presentation, diagnosis, and management strategies. Additionally, recent advancements in the understanding of BMTN and potential future directions for research are discussed

Search strategy

For this review, we searched PubMed, Web of Science, EBSCO, Scopus, Google Scholar, Directory of Open Access Journals (DOAJ) and Embase, using different keywords including; bone marrow transplantation, chronic renal failure, bone marrow transplant nephropathy, acute kidney injury, hematopoietic cell transplantation, thrombotic microangiopathy, immunosuppression, graft-versus-host disease, endothelial injury and radiation nephritis

Bone marrow transplant nephropathy

Bone marrow transplantation (BMT) is a procedure used to replace damaged or destroyed bone marrow with healthy stem cells. While BMT can be life-saving for many patients, it can also have several renal manifestations (13). Acute kidney injury (AKI) is a common complication following BMT. It can occur due to various factors such as sepsis, nephrotoxic medications, graft-versus-host disease (GVHD), and high-dose chemotherapy or radiation therapy used before transplantation (14). Nephrotic syndrome is characterized by the presence of proteinuria, hypoalbuminemia, edema, and hyperlipidemia. It can occur as a result of GVHD affecting the kidneys or due to certain medications used during BMT (15,16). Renal thrombotic microangiopathy (TMA) is a condition characterized by the formation of blood clots in small blood vessels within the kidneys. It can occur as a result of conditioning regimens used before BMT, infections, GVHD, or certain medications (17,18). BMT can lead to renal tubular dysfunction, which affects the ability of the kidneys to reabsorb and excrete various substances properly. This dysfunction can result in electrolyte imbalances, acid-base disturbances, and impaired kidney function (19,20). Long-term complications following BMT may include CKD, which is characterized by a gradual loss of kidney function over time. CKD can develop due to various factors such as chronic GVHD affecting the kidneys, long-term use of nephrotoxic medications, or recurrent infections (12,21).

BMTN versus radiation nephritis

Bone marrow transplant nephropathy and radiation nephritis are both renal manifestations that can occur following BMT and radiation therapy, respectively. As mentioned, BMTN is defined by disproportionate hypertension, anemia and azotemia and may manifest later (3–6 months or post-). Total body irradiation is a major factor in this syndrome. Previous or concurrent chemotherapy may potentiate the effect of radiation on the kidney. Kidney function may decline acutely or more gradually, with eventual long-term stabilization (22,23). In radiation nephritis, kidney injury induced by the ionizing radiation. Histopathologic features include vascular, glomerular, and tubulointerstitial damage. The clinical course of radiation nephropathy includes a latent period of six months after irradiation, followed by the onset of clinical damage. Radiation is a major cause of this syndrome (24).

Treatment of BMTN

Bone marrow transplant nephropathy is a slowly progressive condition that can lead to chronic renal failure. The BMTN treatment focuses on managing the underlying risk factors and preventing further kidney damage. Hypertension is a common symptom of BMTN, and controlling blood pressure can help prevent further kidney damage (23,25). Angiotensin-converting enzyme inhibitors or angiotensin receptor blockers can help control blood pressure and reduce proteinuria. Diuretics can help reduce edema and control blood pressure (26). Certain medications, such as aminoglycosides and nonsteroidal anti-inflammatory drugs, can be toxic to the kidneys and should be avoided in patients with BMTN (27). Anemia is a common symptom of BMTN, and treatment with erythropoietin-stimulating agents or blood transfusions may be necessary. In severe cases of BMT NP, kidney transplantation may be necessary to restore kidney function (28).

Conclusion

Bone marrow transplant nephropathy is a popular complication of BMT that can lead to kidney dysfunction and failure. It is thought to be caused by a combination of factors, including chemotherapy, radiation therapy, and the use of immunosuppressive medications

Authors' contribution

Conceptualization: Sousan Mohammadi Kebar, Saeed Hoseininia.
Data curation: Sousan Mohammadi Kebar, Saeed Hoseininia.
Investigation: Sousan Mohammadi Kebar, Saeed Hoseininia.
Resources: Sousan Mohammadi Kebar, Saeed Hoseininia.
Supervision: Sousan Mohammadi Kebar.
Validation: Sousan Mohammadi Kebar, Saeed Hoseininia.
Visualization: Sousan Mohammadi Kebar.
Writing–original draft: Sousan Mohammadi Kebar, Saeed Hoseininia.
Writing–review and editing: Sousan Mohammadi Kebar, Saeed Hoseininia.

Conflicts of interest

The authors declare that they have no competing interests.

Declaration of generative AI and AI-assisted tools in the writing processes

During the preparation of this work, the authors utilized ChatGPT—a chatbot developed by OpenAI— to refine grammar points and language style in writing. Subsequently, the authors thoroughly reviewed and edited the content as necessary, assuming full responsibility for the publication's content.

Ethical issues

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

Funding/Support

None.

References

1. Hatzimichael E, Tuthill M. Hematopoietic stem cell transplantation. Stem Cells Cloning. 2010;3:105-17. doi: 10.2147/SCCAA.S6815.
2. Vinothkumar G, Venkataraman P. Current advances and challenges in stem cell–based therapy for chronic kidney disease. In: Pathak S, Banerjee A, eds. Stem Cells and Signaling Pathways. Elsevier; 2024:399-413.
3. Vuong KT, Joseph C, Angelo JR. Review of acute kidney injury and progression to chronic kidney disease in pediatric patients undergoing hematopoietic cell transplant. Front Oncol. 2023;13:1161709. doi: 10.3389/fonc.2023.1161709.
4. Choi SW, Levine JE, Ferrara JL. Pathogenesis and management of graft-versus-host disease. Immunol Allergy Clin North Am. 2010;30:75-101. doi: 10.1016/j.iac.2009.10.001.
5. Justiz Vaillant AA, Modi P, Mohammadi O. Graft-Versus-Host Disease. [Updated 2022 Oct 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK538235/.
6. Miyata M, Ichikawa K, Matsuki E, Watanabe M, Peltier D, Toubai T. Recent Advances of Acute Kidney Injury in Hematopoietic Cell Transplantation. Front Immunol. 2022;12:779881. doi: 10.3389/fimmu.2021.779881.
7. Kogon A, Hingorani S. Acute kidney injury in hematopoietic cell transplantation. Semin Nephrol. 2010;30):615-26. doi: 10.1016/j.semnephrol.2010.09.009.
8. Prasad N, Patel MR. Infection-Induced Kidney Diseases. Front Med (Lausanne). 2018;5:327. doi: 10.3389/fmed.2018.00327.
9. Rosenthal J. Hematopoietic cell transplantation-associated thrombotic microangiopathy: a review of pathophysiology, diagnosis, and treatment. J Blood Med. 2016;7:181-6. doi: 10.2147/JBM.S102235.
10. Abudayyeh A, Wanchoo R. Kidney Disease Following Hematopoietic Stem Cell Transplantation. Adv Chronic Kidney Dis. 2022;29:103-115.e1. doi: 10.1053/j.ackd.2021.11.003.
11. Madsen K, Pelletier K, Côté G, Kitchlu A, Chen S, Mattsson J, et al. Acute kidney injury within 100 days post allogeneic hematopoietic cell transplantation is associated with increased risk of post-transplant complications and poor transplant outcomes. Bone Marrow Transplant. 2022;57:1411-1420. doi: 10.1038/s41409-022-01744-0.
12. Cohen EP, Pais P, Moulder JE. Chronic kidney disease after hematopoietic stem cell transplantation. Semin Nephrol. 2010;30:627-34. doi: 10.1016/j.semnephrol.2010.09.010.
13. Bishop MM, Welsh H, Coons M, Wingard JR. Blood and marrow transplantation. In: Biopsychosocial Perspectives on Transplantation. Boston, MA: Springer US; 2001. p. 19-37 .
14. Krishnappa V, Gupta M, Manu G, Kwatra S, Owusu OT, Raina R. Acute kidney injury in hematopoietic stem cell transplantation: a review. Int J Nephrol. 2016;2016:5163789. doi: 10.1155/2016/5163789.
15. Chien YH, Lin KH, Lee TY, Lu MY, Tsau YK. Nephrotic syndrome in a bone marrow transplant recipient without chronic graft-versus-host disease. J Formos Med Assoc. 2000;99:503-6.
16. Sato N, Kishi K, Yagisawa K, Kasama J, Karasawa R, Shimada H, et al. Nephrotic syndrome in a bone marrow transplant recipient with chronic graft-versus-host disease. Bone Marrow Transplant. 1995;16:303-5.
17. Changsirikulchai S, Myerson D, Guthrie KA, McDonald GB, Alpers CE, Hingorani SR. Renal thrombotic microangiopathy after hematopoietic cell transplant: role of GVHD in pathogenesis. Clin J Am Soc Nephrol. 2009;4:345-53. doi: 10.2215/CJN.02070508.
18. Seaby EG, Gilbert RD. Thrombotic microangiopathy following haematopoietic stem cell transplant. Pediatr Nephrol. 2018;33:1489-1500. doi: 10.1007/s00467-017-3803-4.
19. Heering P, Degenhardt S, Grabensee B. Tubular dysfunction following kidney transplantation. Nephron. 1996;74:501-11.
20. Kintzel PE. Anticancer Drug—Induced Kidney Disorders: Incidence, Prevention and Management. Drug Safety. 2001;24:19-38.
21. Sedhom R, Sedhom D, Jaimes E. Mini-review of kidney disease following hematopoietic stem cell transplant. Clin Nephrol. 2018;89:389-402. doi: 10.5414/CN109276.
22. Cohen EP, Bedi M, Irving AA, Jacobs E, Tomic R, Klein J, et al. Mitigation of late renal and pulmonary injury after hematopoietic stem cell transplantation. Int J Radiat Oncol Biol Phys. 2012;83:292-6. doi: 10.1016/j.ijrobp.2011.05.081.
23. Cohen EP, Lawton CA, Moulder JE. Bone marrow transplant nephropathy: radiation nephritis revisited.

Nephron. 1995;70:217-22. doi: 10.1159/000188587.
24. Klaus R, Niyazi M, Lange-Sperandio B. Radiation-induced kidney toxicity: molecular and cellular pathogenesis. Radiat Oncol. 2021;16:43. doi: 10.1186/s13014-021-01764-y.
25. Ichida S, Okada K, Itoh M, Okada R, Katoh N, Kasai M, et al. Bone marrow transplant nephropathy successfully treated with angiotensin-converting enzyme inhibitor. Clin Exp Nephrol. 2006;10:78-81. doi: 10.1007/s10157-005-0394-3.
26. Herman LL, Padala SA, Ahmed I, et al. Angiotensin-Converting Enzyme Inhibitors (ACEI) [Updated 2023 Jan 28]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK431051/
27. Elseviers MM, De Broe ME. Analgesic abuse in the elderly. Renal sequelae and management. Drugs Aging. 1998;12:391-400. doi: 10.2165/00002512-199812050-00005.
28. Malyszko J, Glowinska I, Mysliwiec M. Treatment of anemia with erythropoietin-stimulating agents in kidney transplant recipients and chronic kidney disease-another drawback of immunosuppression? Transplant Proc. 2012;44:3013-6. doi: 10.1016/j.transproceed.2012.06.070.