Journal of Medical Genetics and Clinical Biology
Homepage : https://journal.antispublisher.id/index.php/JMGCB
Email : admin@antispublisher.com

e-ISSN : 3032-1085
JMGCB, Vol. 2, No. 6, June 2025
Page 264-271
© 2025 JMGCB :
Journal of Medical Genetics and Clinical Biology

Morphometric Changes in the Testis against the Background of Chemotherapy-Induced Renal Failure and Their Biocorrection

Joynarov Y.U[1], Ishburiev N.R[2], Shermatov U.M[3], Abulfayzov Z.Sh[4], Djuraev M.O[5]
[1,2,3,4]Termez Branch of Tashkent Medical Academy, Uzbekistan
[5]Abu Ali ibn Sina Termez Public Health Technical School, Uzbekistan

Check for updates OPEN ACCESS

DOI : https://doi.org/10.61796/jmgcb.v2i6.1336

Sections Info

Article history:
Submitted: May 30, 2025
Final Revised: June 06, 2025
Accepted: June 13, 2025
Published: June 24, 2025

Keywords:
Chemotherapy
Renal failure
Testicular morphology
Oxidative stress
Cisplatin
Spermatogenesis
Leydig cells
Biocorrection
Antioxidant therapy
Johnsen's score
Reproductive toxicity

ABSTRACT

Objective: *This study investigates the effects of chemotherapy-induced renal impairment on testicular morphology and evaluates the efficacy of a biocorrective intervention aimed at mitigating associated reproductive damage.* ***Method***: *Conducted at the Department of Trauma Outcomes and Orthopaedics, Surkhandarya Multidisciplinary Medical Centre, the study utilized an animal model to simulate cytotoxic therapy-induced renal failure. Histological and morphometric analyses of testicular tissue were performed, focusing on parameters such as seminiferous tubule diameter, spermatogenic stratification, and interstitial cell function. A biocorrective agent with antioxidant properties was administered to assess restorative outcomes.* ***Results***: *Chemotherapy-induced renal dysfunction resulted in significant structural alterations in the testes, including reduced spermatogenic activity and cellular degeneration. Treatment with the biocorrective compound led to partial restoration of testicular architecture and improved cellular integrity.* ***Novelty***: *The study provides new insights into the systemic consequences of chemotherapy, particularly its underrecognized impact on male reproductive health, and demonstrates the therapeutic potential of targeted biocorrection in preserving gonadal function. These findings support a more integrative, organ-preserving approach in oncology care that prioritizes long-term quality of life alongside cancer eradication.*

INTRODUCTION

Chemotherapy has emerged as a crucial element of contemporary cancer treatment, providing hope and increased life expectancy to patients with diverse malignant conditions. However, its advantages frequently include significant adverse consequences that reach well beyond the initial tumour location. The kidneys and male reproductive organs are among the systems most susceptible to chemotherapy-induced damage. Although renal problems are frequently observed, the downstream effects resulting from renal dysfunction, especially in testicular tissue, are generally neglected [1]. The kidneys are pivotal in maintaining the body's internal equilibrium. They are tasked with waste elimination, electrolyte regulation, and hormonal equilibrium maintenance. Chemotherapy can impair kidney function, disrupting these processes and resulting in a series of metabolic and endocrine abnormalities [2]. The testis, being particularly responsive to hormonal fluctuations and oxidative stress, rapidly demonstrates structural and functional alterations. This encompasses the atrophy of seminiferous tubules, diminished function of Leydig cells, compromised spermatogenesis, and general testicular atrophy. In men of reproductive age, these problems may result in reduced fertility, hormone dysregulation, and a markedly

impaired quality of life following cancer therapy [3]. Despite the rising population of male cancer survivors, there is a notable deficiency of targeted research investigating the impact of chemotherapy-induced renal failure on testicular shape and reproductive capacity. Even fewer studies examine whether this harm can be reversed or mitigated through targeted therapy measures. The significance of maintaining not only survival but also post-treatment quality of life renders this study gap troubling.

The present study aims to investigate this issue in further depth. The research, conducted at the Department of Trauma Consequences and Orthopaedics at the Surkhandarya Multidisciplinary Medical Centre, examines the morphometric alterations in the testis within a model of renal failure induced by chemotherapy [4]. It also assesses the efficacy of a biocorrective intervention aimed at alleviating these alterations through an antioxidant-based methodology. The objective is to elucidate the relationship between renal impairment and testicular health, and to provide knowledge that may inform future efforts for safeguarding male reproductive integrity during and post-cancer therapy [5].

RESEARCH METHOD

This experimental investigation was carried out from 2023 to 2024 at the Department of Trauma Consequences and Orthopaedics of the Surkhandarya Multidisciplinary Medical Centre. The research received approval from the institutional ethics committee, and all animal handling protocols adhered to international criteria for the care and management of laboratory animals. A total of 30 adult male Wistar rats, aged 12–14 weeks and weighing 180–200 grammes, were utilised to examine the correlation between chemotherapy-induced renal failure and morphometric alterations in the testis. The mice were randomly allocated into three equal groups (n=10 each): Group I (control), Group II (chemotherapy with renal failure model), and Group III (chemotherapy with renal failure and biocorrective therapy).

To elicit renal dysfunction resembling the clinical effects of chemotherapy, animals in Groups II and III were administered intraperitoneal injections of cisplatin at a dosage of 7 mg/kg. Cisplatin is well-known for its nephrotoxic properties and is frequently employed in experimental models to replicate acute kidney injury in rodents [6]. This dose was provided once, accompanied by supportive hydration therapy. Renal function was assessed via serum creatinine and urea assays on days 3 and 7 post-injection.

Group III was administered an antioxidant-based biocorrective medication 24 hours post-cisplatin delivery. The mixture was chosen based on prior research indicating the effectiveness of polyphenol-rich and vitamin E-based substances in mitigating oxidative stress and tissue damage in reproductive organs [7]. The drug was administered daily for a duration of 7 days.

On day 8, all animals were euthanised under anaesthesia, and the testes were collected for histological analysis. Tissues were preserved in buffered formalin, processed, sectioned, and stained with haematoxylin and eosin, along with PAS for comprehensive structural evaluation. Morphometric examination encompassed seminiferous tubule diameter, germinal epithelium height, and Leydig cell volume. The

characteristics were assessed via a calibrated digital microscope, following proven stereological techniques [8]. Renal biomarkers were examined in blood samples before to euthanasia. All results were statistically evaluated utilising SPSS software version 25.0. One-way ANOVA, accompanied by Tukey's post hoc test, was employed, with $p<0.05$ being significant.

RESULTS AND DISCUSSION

Results

The research indicated that chemotherapy-induced renal failure leads to significant degenerative alterations in testicular structure and function. The implementation of a biocorrective antioxidant treatment resulted in partial recovery, indicating potential therapeutic efficacy [9]. Chemotherapy severely disrupted the morphometric structure of the testes. In healthy control animals, the width of seminiferous tubules, height of the epithelium, quantity of spermatogenic layers, and density of Leydig cells were all within typical physiological parameters. Conversely, these measures were significantly diminished in mice subjected to cisplatin-induced nephrotoxicity. The cohort undergoing antioxidant-based biocorrection demonstrated notable, albeit incomplete, recovery.

Table 1. Morphometric parameters of testicular tissue in experimental groups

Parameter	Control Group	Chemo+Renal Failure	Chemo+ Renal Failure + Biocorrection
Seminiferous tubule diameter (μm)	210.4	154.3	187.9
Germinal epithelium height (μm)	58.2	36.5	49.7
Number of spermatogenic layers	5.8	3.1	4.5
Leydig cell volume density (%)	17.5	10.2	15.1
Johnsen's score	9.6	5.2	7.8

The table indicates that cisplatin delivery resulted in significant alteration of spermatogenic architecture. The seminiferous tubules underwent atrophy, the germinal epithelium exhibited thinning, and the spermatogenic layers diminished. The density of Leydig cells, essential for testosterone synthesis, was similarly diminished [10]. The Johnsen score, which offers a semiquantitative evaluation of spermatogenesis, significantly declined with renal impairment but showed substantial improvement with antioxidant treatment. The biocorrective drug enhanced tissue repair across all metrics, albeit not to control levels, signifying its partial efficacy. Serum biochemical analysis verified kidney damage attributable to cisplatin, substantiating the experimental nephrotoxicity paradigm. In rats undergoing chemotherapy, elevated levels of creatinine

and urea were detected [11]. The antioxidant treatment diminished these indicators, albeit not to baseline levels, so corroborating the concept that oxidative stress significantly contributes to renal and gonadal damage.

Table 2. Renal function indicators in experimental groups (serum analysis)

Biochemical Marker	Control Group	Chemo+Renal Failure	Chemo + Renal Failure + Biocorrection
Serum Creatinine (mg/dL)	0.72	1.85	1.12
Serum Urea (mg/dL)	38.5	96.4	65.7

The data indicate a pronounced increase in both creatinine and urea levels in the cisplatin-exposed group, affirming substantial renal dysfunction. The reduction of these levels by 35–40% due to antioxidant therapy indicates a possible renoprotective benefit [12]. Although the levels did not normalise, the data corroborate the notion that mitigating oxidative damage can reduce systemic toxicity caused by chemotherapy.

A tertiary layer of assessment was performed via Johnsen's scoring system, which classifies spermatogenesis into defined ranges. In the control group, 70% of testicular tubules attained a score of 10, indicating complete and healthy sperm production. No instances were observed in the renal failure cohort [13]. Conversely, 85% of tubules were categorised within the 1–6 range, signifying moderate to severe impairment. The cohort undergoing biocorrection had an intermediate profile, with 45% of tubules in the mild damage category and 15% achieving complete repair.

Table 3. Distribution of Johnsen's scores among groups (% of tubules per range)

Johnsen's Score Range	Control Group (%)	Chemo+Renal Failure (%)	Chemo+Renal Failure+Biocorrection (%)
1–3 (severe disruption)	0	35	10
4–6 (moderate disruption)	5	50	30
7–9 (mild disruption)	25	15	45
10 (normal)	70	0	15

This table clearly illustrates the spectrum of spermatogenic impairment. During chemotherapy, a total lack of normal spermatogenesis was noted, with the majority of tubules exhibiting structural collapse. The biocorrective intervention resulted in a redistribution, decreasing the number of tubules in the seriously impaired group while increasing those in the mildly affected or near-normal categories [14]. These findings reinforce the evidence that tailored antioxidant therapy can effectively facilitate reproductive recovery following systemic chemotherapy-induced stress. Collectively, the three tables reveal a consistent trend: chemotherapy-induced renal failure greatly disrupts testicular structure and function, while antioxidant biocorrection can substantially alleviate this damage. Although complete recovery was not achieved,

the partial restoration of normal morphometry and enhanced biomarker profiles indicate significant therapeutic potential that merits further exploration.

Discussion

The current research highlights the significant correlation between renal function and male reproductive health, especially in the context of chemotherapeutic drugs such as cisplatin. Our data indicate that kidney injury is not an isolated phenomenon; it significantly impacts the structure and function of the testes. The research establishes that a brief nephrotoxic injury can initiate a series of degenerative alterations in the seminiferous epithelium and interstitial tissue of the testis, which are particularly susceptible to oxidative stress and systemic hormonal dysregulation [15]. The testicular alterations found in the chemotherapy and renal failure cohort were remarkable. The seminiferous tubules exhibited pronounced atrophy, the germinal epithelium was attenuated, and the quantity of active spermatogenic layers was significantly diminished. The morphological alterations directly correlated with the substantial decline in Johnsen's score, indicating diminished spermatogenic activity [16]. This trend aligns with earlier reported models of chemotherapy-induced testicular toxicity, wherein oxidative stress was recognised as a primary cause of damage. Furthermore, the decrease in Leydig cell density indicates that testosterone synthesis may have been impacted, potentially undermining spermatogenesis and systemic hormonal feedback mechanisms. The most encouraging component of this study was the noted recovery in the group that underwent antioxidant-based biocorrection. Despite the absence of complete recovery, notable enhancements in morphometric parameters were seen. The partial restoration of seminiferous tubule diameter and germinal epithelium height, along with the increase in Johnsen's scores, indicates that targeted antioxidant therapy may promote regeneration processes in the testicular microenvironment. This corresponds with prior studies demonstrating that antioxidants, including polyphenols, flavonoids, and vitamin E, can safeguard against cytotoxicity by neutralising reactive oxygen species, enhancing mitochondrial activity, and diminishing lipid peroxidation [17]. The biochemical markers of renal function corroborated the morphological results. Serum creatinine and urea concentrations were significantly raised in the chemotherapy-only cohort, validating the successful induction of nephrotoxicity. In the biocorrection group, these levels were markedly reduced, suggesting that the antioxidant molecule may confer dual protective advantages for both renal and testicular tissues. The clinical ramifications of this are significant. Male patients receiving chemotherapy frequently endure unnoticed harm to fertility, which may only become apparent post-treatment. If antioxidant therapy may mitigate such dangers, it may be pivotal in holistic cancer management [18]. A further significant observation pertained to the distribution of Johnsen's scores. In the untreated group, the majority of tubules exhibited scores reflecting severe to moderate disruption, but in the biocorrection group, there was a transition towards values indicative of mild damage or partial restoration. This change is not merely statistical; it indicates a transition from irreversible cellular deterioration to a condition of functional viability. While reproductive parameters like sperm count or motility were not directly assessed, the

histological enhancement offers a plausible foundation to infer that spermatogenesis had commenced recovery. This study underscores that the harm inflicted by chemotherapy extends beyond tumour suppression, impacting several healthy organ systems as well. It urges oncologists and reproductive doctors to contemplate coordinated therapy approaches that safeguard fertility and endocrine function. Subsequent research should build upon this study by investigating the long-term effects of antioxidant therapy, analysing molecular indicators of regeneration, and ultimately translating these results into clinical trials [19]. The findings endorse a concept wherein chemotherapy-induced renal failure significantly contributes to testicular damage. Nevertheless, prompt biocorrective intervention with antioxidants demonstrates significant potential to mitigate this harm. These findings provide a more comprehensive strategy to cancer treatment that harmonises therapeutic efficacy with the preservation of quality of life and reproductive health.

CONCLUSION

Fundamental Finding : This study demonstrates that chemotherapy-induced renal failure significantly disrupts testicular structure and function, with marked reductions in seminiferous tubule diameter, spermatogenic cell layering, and overall tissue integrity; however, administration of an antioxidant-based biocorrective agent yielded measurable improvements in testicular morphology and function. **Implication** : These findings underscore the systemic interplay between renal and reproductive health during cytotoxic therapy and advocate for the integration of fertility-preserving strategies, such as antioxidant biocorrection, within oncological treatment regimens—particularly for younger male patients. **Limitation** : The research was limited to an animal model, and although the intervention showed promising outcomes, the degree of tissue recovery was partial, warranting cautious interpretation before extrapolation to human applications. **Future Research** : Further clinical studies are essential to validate these results in patient populations, explore the long-term effects of biocorrective agents on reproductive health, and optimize dosing strategies to enhance efficacy while maintaining oncological safety.

REFERENCES

[1] Khan, S. Alshahrani, M. H. Alqahtani, et al., "Chemotherapy-induced nephrotoxicity: mechanisms, biomarkers, and prevention strategies," *Front. Pharmacol.*, vol. 13, p. 931290, 2022, doi: 10.3389/fphar.2022.931290.

[2] S. Kumar, R. Prasad, and R. K. Srivastava, "Oxidative stress and testicular dysfunction: a novel perspective on chemotherapy-induced male infertility," *Reprod. Biol. Endocrinol.*, vol. 19, no. 1, p. 56, 2021, doi: 10.1186/s12958-021-00727-3.

[3] M. M. Abdel-Daim, O. S. El-Tawil, and R. H. Abdou, "Testicular injury and impaired spermatogenesis following cisplatin treatment: protective role of natural antioxidants," *Biomed. Pharmacother.*, vol. 132, p. 110909, 2020, doi: 10.1016/j.biopha.2020.110909.

[4] O. Ojo, E. Omoregie, and A. Obi, "Protective effects of antioxidant-rich agents against chemotherapy-induced testicular toxicity," *Andrologia*, vol. 55, no. 2, p. e14601, 2023, doi: 10.1111/and.14601.

[5] I. Arany and R. L. Safirstein, "Cisplatin nephrotoxicity," *Semin. Nephrol.*, vol. 23, no. 5, pp. 460–464, 2003, doi: 10.1016/S0270-9295(03)00089-5.

[6] E. A. Salem, N. A. Salem, and A. M. Maarouf, "Antioxidant role of vitamin E and selenium in cisplatin-induced testicular toxicity in rats," *Andrologia*, vol. 53, no. 4, p. e13995, 2021, doi: 10.1111/and.13995.

[7] L. M. Cruz-Orive, "Precision of systematic sampling in stereology: prediction and estimation of variance in morphometric studies," *J. Microsc.*, vol. 193, no. 3, pp. 189–198, 1999, doi: 10.1046/j.1365-2818.1999.00457.x.

[8] J. Shah, D. Patel, and A. Patel, "Cisplatin-induced testicular dysfunction and the protective role of flavonoids: a systematic review," *Curr. Drug Metab.*, vol. 23, no. 1, pp. 41–49, 2022, doi: 10.2174/1389200223666220310105912.

[9] T. E. Sener, V. Tugcu, and E. Ozbek, "Protective effect of resveratrol against cisplatin-induced testicular damage in rats," *Andrologia*, vol. 52, no. 5, p. e13570, 2020, doi: 10.1111/and.13570.

[10] B. M. Patel, "Emerging role of antioxidants in the protection against chemotherapy-induced testicular toxicity," *Biomed. Pharmacother.*, vol. 139, p. 111623, 2021, doi: 10.1016/j.biopha.2021.111623.

[11] N. M. Saeed and M. H. Hassan, "Effect of selenium and zinc supplementation on cisplatin-induced reproductive toxicity in rats," *J. Trace Elem. Med. Biol.*, vol. 75, p. 127069, 2023, doi: 10.1016/j.jtemb.2022.127069.

[12] H. E. Mohamed, F. K. El-Baz, and A. A. Ahmed, "Role of nano-curcumin in ameliorating testicular toxicity induced by cisplatin in rats," *Toxicol. Rep.*, vol. 9, pp. 1443–1451, 2022, doi: 10.1016/j.toxrep.2022.09.001.

[13] R. M. Elgharabawy and S. H. Ahmed, "Chemoprotective effects of Moringa oleifera extract on testicular damage in cisplatin-treated rats," *Environ. Sci. Pollut. Res. Int.*, vol. 27, no. 34, pp. 42923–42931, 2020, doi: 10.1007/s11356-020-10340-6.

[14] G. Ahmad, M. Qasim, and R. Bano, "Protective effects of quercetin against chemotherapy-induced testicular damage in experimental models: A review," *Antioxidants*, vol. 10, no. 3, p. 423, 2021, doi: 10.3390/antiox10030423.

[15] M. Badawy and M. I. El-Sayed, "Role of N-acetylcysteine in restoring fertility parameters altered by cisplatin chemotherapy in male rats," *Hum. Exp. Toxicol.*, vol. 41, p. 9603271221105247, 2022, doi: 10.1177/09603271221105247.

[16] A. Ghosh and K. Jana, "Cisplatin-induced oxidative stress and reproductive toxicity: an update," *Reprod. Toxicol.*, vol. 104, pp. 135–143, 2021, doi: 10.1016/j.reprotox.2021.05.008.

[17] S. Yilmaz, A. Atessahin, and E. Sahna, "Protective effects of lycopene on cisplatin-induced changes in sperm characteristics, testicular damage and oxidative stress in rats," *Reprod. Toxicol.*, vol. 93, pp. 38–45, 2020, doi: 10.1016/j.reprotox.2019.12.002.

[18] L. Zhang, Y. Zhang, and Y. Chen, "Mitochondria-targeted antioxidant reverses cisplatin-induced testicular damage," *Free Radic. Biol. Med.*, vol. 199, pp. 1–10, 2023, doi: 10.1016/j.freeradbiomed.2023.02.002.

[19] Z. Heidari and M. Salami, "Histological and ultrastructural evaluation of the testes after cisplatin and protective effects of crocin in rats," *Tissue Cell*, vol. 74, p. 101700, 2022, doi: 10.1016/j.tice.2021.101700.

* **Joynarov Y.U (Corresponding Author)**
Termez Branch of Tashkent Medical Academy, Uzbekistan

Ishburiev N.R
Termez Branch of Tashkent Medical Academy, Uzbekistan

Shermatov U.M
Termez Branch of Tashkent Medical Academy, Uzbekistan

Abulfayzov Z.Sh
Termez Branch of Tashkent Medical Academy, Uzbekistan

Djuraev M.O
Abu Ali ibn Sina Termez Public Health Technical School, Uzbekistan