



Histological and Physiological Changes in The Kidneys of Female Albino Rats Treated with Levothyroxine



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Abstract

Background: Levothyroxine is a common medication used to treat hypothyroidism. Administering it in high doses for extended periods can affect many organs in the body. **Objective:** The objective of the study was to evaluate the physiological and histological effects of levothyroxine at different doses on kidney tissue in female albino rats. **Methodology:** This experimental study was conducted at the University of Karbala, College of Education for Pure Sciences, Department of Biology, from October 2025 to April 2026. The effect of levothyroxine was investigated at three concentrations. The study was performed on 20 female albino rats, and the drug's effect on the physiological and histological aspects of the kidneys was examined. **Results:** The renal cortex had obvious pathological alterations, including structural and vascular anomalies as well as inflammatory infiltration, according to histological analysis. The control group's physiological results revealed normal values for urea (32.80 ± 3.17) and creatinine (0.28 ± 0.03). At $50 \mu\text{g/kg}$, these values rose to 1.08 ± 0.08 for creatinine and 54.40 ± 2.22 for urea; at $100 \mu\text{g/kg}$, they rose to 1.84 ± 0.18 and 82.80 ± 2.00 , respectively. The highest values of creatinine (2.44 ± 0.12) and urea (104.40 ± 5.41) were recorded at the $150 \mu\text{g/kg}$ dose, suggesting a progressive decline in kidney function with increasing dosage. **Conclusion:** Levothyroxine leads to negative effects on the kidney, represented by increased levels of urea and creatinine and the occurrence of pathological tissue changes. [Bangladesh Journal of Infectious Diseases, June 2026;13(1):144-152]

Keywords: Levothyroxine, kidney, nephrotoxicity, urea, creatinine

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Introduction

Levothyroxine is one of the most prescribed medications in the world, but its absorption is affected by many factors, including medications, overlapping foods, diseases, or concomitant medications, which may lead to persistent hypothyroidism even with high doses of levothyroxine¹. Normal thyroid function is essential for maintaining the body's internal balance in most

patients diagnosed with hypothyroidism, as treatment is lifelong with thyroid hormone substitutes. Levothyroxine is the most common medication used to treat hypothyroidism².

Thyroid hormones can directly affect the kidneys, and impaired kidney function may contribute to thyroid disorders³. The renal manifestations of thyroid disorders depend on hemodynamic changes and the direct effects of thyroid hormones. The

renin-angiotensin system plays a crucial role in the thyroid-renal interaction, and primary and subclinical hypothyroidism, as well as triiodothyronine (T3) deficiency syndrome, are common features in patients with chronic kidney disease⁴. The kidneys play a role in regulating the metabolism and elimination of thyroid hormones. Thyroid hormones are essential for kidney growth and development and for maintaining body water balance. Both hypothyroidism and hyperthyroidism affect renal blood flow, glomerular filtration rate, renal tubular function, ion balance, and kidney structure⁵. Elevated TSH levels, exceeding the upper limit of normal, are associated with an increased risk of kidney dysfunction or exacerbation of chronic kidney disease (CKD) in a US study^{6,7}.

Patients with subclinical thyroid dysfunction exhibit endothelial dysfunction, suggesting a possible link between thyroid dysfunction and CKD⁶. Since hyperthyroidism accelerates kidney deterioration, levothyroxine (LVT) has a narrow therapeutic range and may pose a risk of treatment-induced hyperthyroidism. Levothyroxine may also increase protein catabolism and cardiac arrhythmias⁷. Thyroid hormones affect kidney growth, renal hemodynamics, glomerular filtration rate, and sodium and water balance. Hypothyroidism and hyperthyroidism affect kidney function through direct renal effects, as well as systemic hemodynamic, metabolic, and cardiovascular effects. Thyroid dysfunction is associated with elevated serum creatinine levels and decreased glomerular filtration rate⁸. Our study was aimed to evaluate the histological and physiological effects of levothyroxine at different doses on kidney tissue in female albino rats by studying pathological changes and measuring the levels of some kidney biochemical parameters.

Methodology

Study Design and Settings: This experimental study was conducted at the University of Karbala, College of Education for Pure Sciences, Department of Biology, from October 2025 to April 2026. Sexually mature females weighing between 170 to 240 grams and aged between 7 to 12 weeks. The animals were obtained from special breeding farms in Babylon Governorate and further used in the experiments.

Experimental Animals: Sexually mature females weighing between (170 to 240) grams and aged between (7 to 12) weeks. They were obtained from special breeding farms in Babylon Governorate.

They were placed in special plastic cages with dimensions of (40×60×25) cm for width, length, and height, respectively, covered with special metal covers and in a suitable laboratory atmosphere in terms of a temperature ranging between 20-25 degrees Celsius, appropriate lighting (12 hours of light - 12 hours of darkness), and good ventilation⁹. The animals were provided with free access to water and standard feed throughout the rearing period. The rats were left for two weeks before the start of the experiment to acclimatize and ensure they were free of disease¹⁰.

Preparation of levothyroxine: Levothyroxine, produced by Merck KGaA (Darmstadt, Germany) under the trade name Euthyrox, was used. The tablets of this drug are available in several therapeutic concentrations. In this study, a concentration of (50-100-150) µg/kg was used, and the required dose was prepared after dissolving it in Distilled Water. The animals were given the dose according to their weights, and the dose was calculated according to the equation for transferring the therapeutic dose from humans to animals.

Experimental Groups: The study was conducted on 20 female albino rats, which were divided into (4) groups of 5 animals each, as follows¹¹. The control group (G1) was without treatment; females were provided with water and feed only 5 animals. The second group was treated with levothyroxine at a concentration of 50 µg/kg of body weight in 5 animals. The third group was treated with levothyroxine at a concentration of 100µg/kg of body weight in 5 animals. The fourth group was treated with levothyroxine at a concentration of 150 µg/kg of body weight in 5 animals.

Blood Sample Collection: The animals were anesthetized by placing them in a sealed container with a cotton ball soaked in chloroform. After a few minutes, the animals would become anesthetized. Blood was then drawn directly from the heart using a sterile 5 mL syringe to obtain the maximum amount of blood. The blood samples were then placed directly into sterile, anticoagulant-free gel tubes. The tubes were then centrifuged at 3000 rpm for 15 minutes to obtain serum. The serum was collected in clean, dry, labeled Eppendorf tubes for identification and stored in a refrigerator at -20°C until biochemical analysis.

Collection of tissue samples: After blood was withdrawn, the animals were immediately dissected by making an incision in the lower abdominal cavity towards the heart. The kidneys were removed, and after removing the surrounding tissue, they were washed with water to remove any remaining blood.

They were then dried on filter paper and cut into small pieces both lengthwise and crosswise to facilitate preservation while ensuring the preservative penetrated the tissue. The pieces were then preserved in 10% formalin in clean, sealed, and labeled plastic containers for 48 hours until histological dissection. If the pieces were not prepared for histological dissection, the formalin should be changed after this time.



Figure I: The study specimen appears during dissection (kidneys)

Measuring Renal Function Parameters:

1.6.2-Measuring Serum Creatinine Levels
Creatinine levels were measured according to the¹². Method, and serum urea levels were measured according to the method described in the estimation kit. Preparation of tissue sections according to the method¹⁴.



Figure II: Microtome Device and Tissue Sectioning Process

The staining of the samples was carried out based on the method indicated by¹⁵. The glass slides were examined to identify changes in the studied tissue sections using a light microscope at different magnification powers. The glass slides were photographed using a light microscope equipped with a high-resolution digital camera connected to a computer at 20X and 40X magnifications.

Statistical Analysis Used in the Study: All results of the current study were statistically analyzed to determine the significant differences between the means of the studied criteria. The Statistical

Analysis System (SAS) software was used for this purpose.

Ethical Consideration: All animal procedures were conducted in accordance with institutional and national guidelines for the care and use of laboratory animals. The study protocol was reviewed and approved by the appropriate Animal Ethics Committee before the commencement of the experiment. Female rats were housed under standard laboratory conditions with free access to food and water, and all efforts were made to minimize stress, pain, and discomfort throughout the study. The animals were monitored regularly for signs of distress or illness, and humane endpoints were applied when necessary. The number of animals used was kept to the minimum required to obtain valid and reliable results, in line with the principles of the 3Rs: replacement, reduction, and refinement.

Results

Histological Study of the Kidney: Histological Study of the Kidney in the Control Group Figure III shows a normal histological section of the renal cortex of female rats in the control group. The glomeruli appear to be of normal size and shape with a regular distribution of capillaries, without any congestion or shrinkage. Bowman's capsule is also clearly visible with regular borders. The proximal convoluted tubules (PCTs) appear as cuboidal cells with dark pink acidic cytoplasm and a narrow lumen, while the distal convoluted tubules (DCTs) appear as smaller cuboidal cells and a wider tubular lumen without inflammatory infiltration or fibrosis, indicating the integrity of the renal structure in this group.

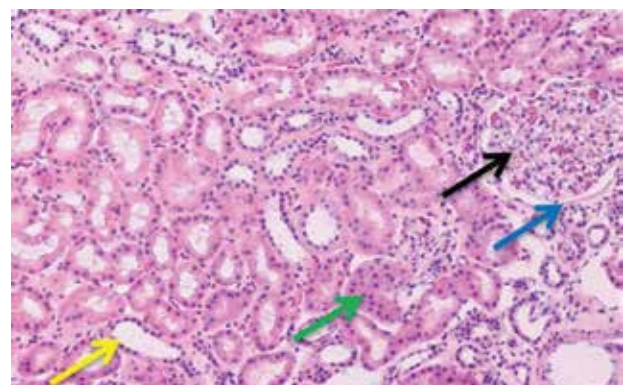


Figure III: A cross-section of the renal cortex of female albino rats from the control group showing the glomerulus (—→) surrounded by Bowman's capsule (—→), the proximal convoluted tubule (PCT) (—→) and the distal convoluted tubule (DCT) (—→) (400X H & E)

Histological Examination of the Kidneys in the Group Treated with Levothyroxine At A Concentration of 50 µg/kg compared to the control group: Figure IV, a microscopic image taken at 10x magnification, shows an overview of the extensive histopathological changes in the renal cortex resulting from the administration of levothyroxine at a concentration of 50 µg/kg. The overall histological analysis reveals a clear disruption of the normal structural integrity of the kidney. The yellow arrows directly indicate the glomeruli, which have suffered significant shrinkage and atrophy with enlargement of the surrounding glomerular lumen. The blue arrows show areas of degeneration and necrosis in the convoluted tubules. A black arrow in the center indicates severe hemocongestion and intensive accumulation of red blood cells within the vessels. This comprehensive histological section reflects a state of acute cellular and vascular stress in the renal cortex due to the levothyroxine dose used. These indicators together confirm that the increased metabolic effect of the hormone has caused damage to tubular cells and disruption of normal blood flow.

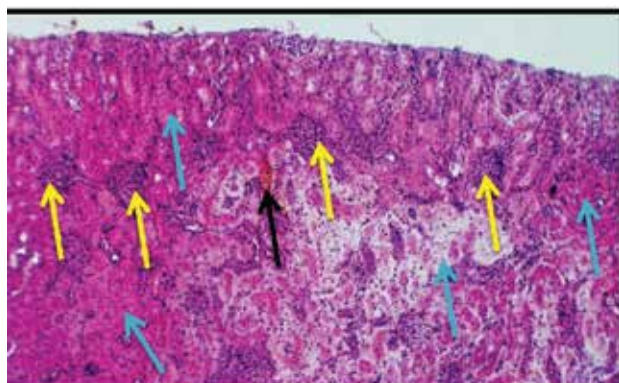


Figure IV: Cross-section of the renal cortex in female albino rats doused with levothyroxine at a concentration of 50 µg/kg. It shows vascular congestion (→) and initial signs of tubular injury, characterized by loss of distinct tubular borders and formation of cytoplasmic vacuoles (→) and glomerular congestion (→). (00X) 1 (H & E)

Figure V shows a cross-section of a female rat kidney treated with levothyroxine at a dose of 50 µg/kg. The microscopic section, photographed at 400X magnification, delves into the cellular depths to document the microdegenerative lesions affecting the cellular components of the renal cortex. The section focuses precisely on the cytoplasmic and nuclear changes within the cells

lining the renal tubules. Multiple black arrows indicate vacuolar degeneration and marked swelling of the tubular epithelial cells, resulting in the loss of their brush-like margins. Nuclei reduction, shrinkage, and disappearance are also clearly visible in some necrotic areas, confirming apoptosis or programmed cell death. On the other side, blue arrows highlight microvascular abnormalities, with the upper arrow indicating glomerular congestion. The effect extends, as the lower blue arrow indicates severe congestion and extravascular hemorrhage between the renal tubules. The cells in this section appear to have lost their ability to maintain internal osmotic and ionic balance as a result of severe oxidative stress.

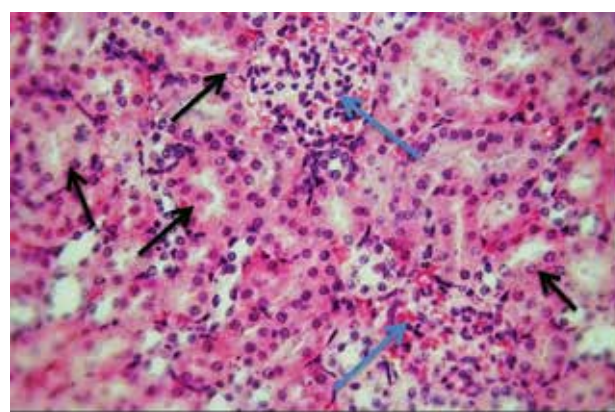


Figure V: shows a cross-section of the renal cortex in female albino rats treated with levothyroxine at a concentration of 50 µg/kg. It reveals vacuole degeneration and swelling of the aponeurotic epithelial cells (→), leading to partial narrowing of the tubular lumen. Slight intraglomerular congestion is also observed (→). (400x) (H & E)

Histological examination of the kidneys in the group treated with levothyroxine at a concentration of 100 µg/kg compared to the control group: Figure IV, stained with hematoxylin and eosin (H&E) at 100x magnification, clearly shows the effects in the renal cortex of female albino rats. It accurately indicates the presence of intense, focal inflammatory cellular infiltration, an immune response to ongoing cellular damage, as shown by the black arrows. The blue arrows clearly illustrate the marked vasodilation and significant congestion of the large renal blood vessels. In addition, the multiple yellow arrows show extensive degenerative changes in the glomeruli and proximal and distal tubules, ranging from vacuolar degeneration to cellular atrophy, reflecting the dysfunction caused by oxidative stress and metabolic disturbances induced by levothyroxine at

a dose of 100 μg .

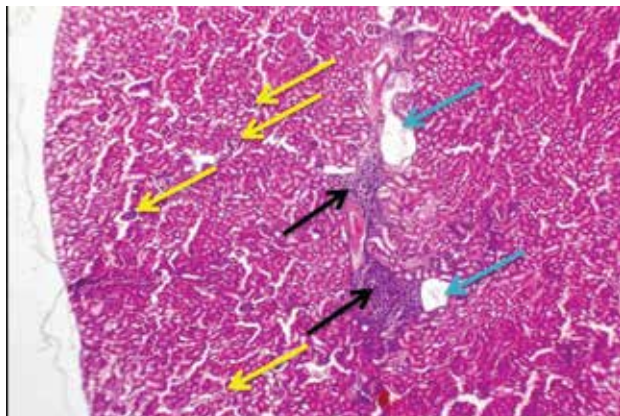


Figure VI: shows a cross-section of the renal cortex in female albino rats doused with levothyroxine at a concentration of 100 $\mu\text{g}/\text{kg}$. It reveals moderate tissue damage, characterized by infiltration of inflammatory cells in the interstitial spaces and around the vessels (→) and damaged renal tubules adjacent to the inflamed area (→), while the glomeruli remain unchanged (→). (100X) (H & E)

Figure VII taken at 400x magnification, shows the fine details of the cellular and structural damage to the tubular and glomerular units of the kidney. The black arrow indicates marked glomerular shrinkage and atrophy accompanied by cellular proliferation, along with a marked dilation of Bowman's capsule, as indicated by the blue arrow. The green arrows reveal severe tissue necrosis and vacuoleic degeneration of the cells lining the renal tubules,

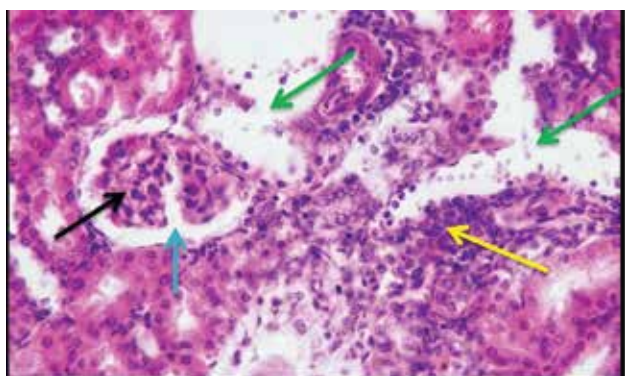


Figure VII: Cross-section of the renal cortex in white females treated with levothyroxine at a concentration of 100 $\mu\text{g}/\text{kg}$ showing tissue damage characterized by glomerulosclerosis (→) accompanied by marked enlargement of Bowman's space (→), acute tubular necrosis (→), and focal infiltration of inflammatory cells (→). (400X) (H & E)

destroying their brush margins, loss of cellular features, and their lysis within the tubular lumen. The yellow arrow also indicates a clear focus of inflammatory cell infiltration between the damaged tubules. This histological panel illustrates the direct toxic effect of a 100 $\mu\text{g}/\text{kg}$ dose of levothyroxine, which disrupted the renal structure, induced apoptosis, and destroyed the nephron structure.

Histological examination of the kidneys in the group dosed with levothyroxine at a concentration of 150 $\mu\text{g}/\text{kg}$ compared to the control group: Figure (8) at 100x magnification clearly shows the nephrotoxicity resulting from dosing with levothyroxine at a concentration of 150 $\mu\text{g}/\text{kg}$. The renal cortex appears as an acute vascular and structural disorder, mainly characterized by severe vascular congestion and thrombosis, indicated by the black arrows. In parallel, intense infiltration of mononuclear inflammatory cells is observed in the interstitial tissue surrounding the tubules and glomeruli, indicated by the yellow arrow. This infiltration represents a cellular immune response and signs of cellular damage induced by oxidative stress. The renal glomeruli, indicated by the blue arrows, appear to suffer from marked narrowing or atrophy of the Bowman's capsule lumen. This glomerular change is due to hypertrophy of the glomerular cells and the retention of fluid and blood within them, which impairs the normal ultrafiltration process. This integrated histological picture reflects an advanced stage of extensive tissue damage affecting the vascular and interstitial components of the renal

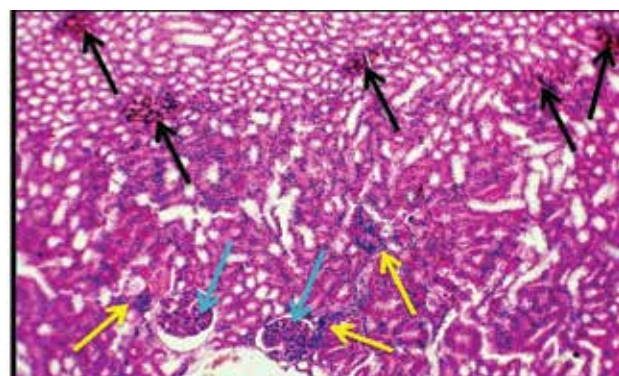


Figure VIII: Cross-section of the renal cortex in female albino rats doused with levothyroxine at a concentration of 150 $\mu\text{g}/\text{kg}$, showing severe and diffuse infiltration of inflammatory interstitial cells (→), cellular hemorrhage in the medulla (black arrow), and severe glomerular congestion (→). (100X) (H & E)

cortex. Taken together, these indicators confirm that a dose of levothyroxine at a concentration of 150 µg/kg caused widespread functional and structural impairment in the renal tissue of female rats.

Figure IX magnified at 400x, shows more detail of the degenerative and necrotic changes occurring at the level of the cells lining the tubules and the glomerulus. The black arrows indicate dense capillary congestion within the cytoplasm of the convoluted tubules. The yellow arrows indicate tubules suffering from cellular necrosis and severe vacuolar degeneration, accompanied by loss of the brush edge. This cytoplasmic degeneration results from impaired cellular ion pump function and programmed cell death due to membrane lipid peroxidation. The blue arrow shows a markedly enlarged glomerulus with severe capillary congestion. This severe glomerular congestion leads to increased filtration pressure, which directly contributes to the degeneration of the associated renal tubules. These results demonstrate the extent of tissue damage at the cellular level, explaining the physiological decline in kidney function under the influence of levothyroxine, which was at its highest concentration of 150 µg/kg.

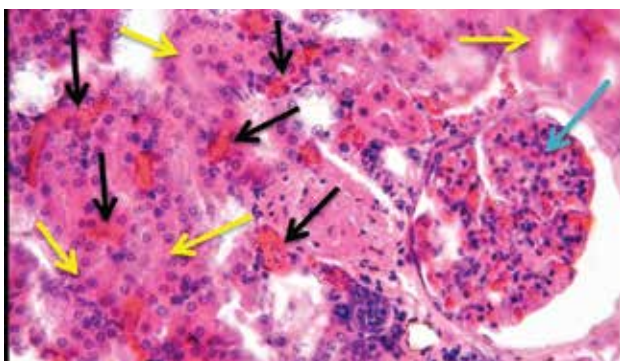


Figure IX: shows a cross-section of the kidney in female albino rats treated with levothyroxine at a concentration of 150 µg/kg. Extensive hemorrhage and capillary congestion are visible (→). The glomerulus exhibits hyperplasia and capillary congestion (→), and acute tubular necrosis and degeneration are characterized by cellular swelling (→) and cellular degeneration (→). (400X) (H & E)

Physiological Study Related to Kidney Function (Urea and Creatinine):

The results of the statistical analysis shown in Table (1) revealed a clear and direct increase in the levels of nitrogenous waste products (urea and creatinine) in the blood serum of laboratory animals, directly proportional to the dose of levothyroxine

administered (50, 100, and 150 µg/kg), compared to the control group. A detailed breakdown of the physiological changes in each group is provided below.

Control Group: The results in this group showed normal indicators of kidney function, with creatinine concentrations remaining stable at (0.28 ± 0.03) and urea at (32.80 ± 3.17). These figures are marked with the statistical letter (D). These results reflect the high efficiency and structural integrity of the nephrons and the normal glomerular filtration rate in the absence of any toxic or exogenous oxidative stress from levothyroxine.

Treatment Group with 50 µg/kg Levothyroxine: When animals were exposed to a 50 µg/kg dose of levothyroxine, a significant increase was observed in both indices compared to the control group. Creatinine increased to (1.08 ± 0.08) and urea increased to (54.40 ± 2.22). This group was designated as C. This initial increase, despite the small dose, provides an early indication of the sensitivity of the renal tubular epithelium to levothyroxine.

The group treated with 100 µg/kg levothyroxine: With the dose doubled to 100 µg/kg, the vital signs continued to rise significantly, with a statistically significant difference compared to the previous groups. The result under study was designated as (B). Creatinine concentration increased to (1.84 ± 0.18), while urea concentration rose to (82.80 ± 2.00). This marked increase in the numbers demonstrates a strong dose-dependent effect between levothyroxine and tissue damage, indicating an increased area of cellular damage in the renal cortex.

Group treated with the high dose of 150 µg/kg of levothyroxine: This group exhibited the highest levels of toxicity and physiological risks. Treatment with 150 mcg/kg resulted in a sharp increase in serum levels, achieving the statistical designation (A), which represents the highest statistical significance in the trial within the kidney parameters. Creatinine concentration reached (0.12 ± 2.44) and urea levels rose to (5.41 ± 104.40). These extremely high values reflect kidney damage and confirm extensive necrosis of the renal tubules, completely impairing the kidney's ability to filter and eliminate these nitrogenous toxins. The statistical variance assigned by the letters (A, B, C, D), supported by the LSD values of 0.3547 for creatinine and 10.439 for urea, conclusively demonstrates that the toxic effect of levothyroxine is cumulative and progressive, directly proportional to the dose administered. The underlying

physiological mechanism for this deterioration in kidney function can be explained by two main axes: Glomerular Filtration Failure and Decreased GFR: Creatinine is the most accurate indicator of glomerular filtration efficiency because it is completely excreted without reabsorption in the tubules. Therefore, the jump from the normal concentration of 0.28 in the control group to 2.44 at the maximum dose physiologically signifies either constriction of the afferent renal arteries or glomerular atrophy, leading to creatinine retention in the bloodstream.

Oxidative Stress and Acute Tubular Necrosis:

The parallel increase in urea from 32.80 in the control group to 104.40 at the highest dose supports the hypothesis of renal failure. Biochemically, the introduction of this substance at high doses depletes the natural antioxidants within kidney cells, such as glutathione (GSH) and SOD, leading to a state of overwhelming oxidative stress. This stress results in a massive influx of free radicals that attack the cell membranes lining the renal tubules, leading to programmed cell death. As a result of the accumulation of these dead cells within the tubules, a mechanical obstruction occurs, causing nitrogenous waste (urea) to leak and be passively reabsorbed back into the bloodstream instead of being excreted in the urine.

Table 1: Kidney Function Criteria for the Study Groups (Means±stderr)

Group	Creatinine	Urea
Control	0.28±0.03 D	32.80±3.17 D
50 µg/kg	1.08±0.08 C	54.40±2.22 C
100 µg/kg	1.84±0.18 B	82.80±2.00 B
150 µg/kg	2.44±0.12 A	104.40±5.41 A
L.S.D	0.3547	10.439

Discussion

The results of this study are consistent with those of 16, which showed clear pathological changes in the kidney tissues of female rats treated with levothyroxine. Degeneration and necrosis were observed in the renal tubules, along with hemorrhage in the interstitial tissue and narrowing of the tubular space. Signs of necrosis were also present in the cells lining the glomerular capsule, along with enlargement of Bowman's area and atrophy of the glomerular capillaries. These combined changes indicate that

administering high doses of levothyroxine leads to significant kidney damage involving the glomeruli and tubules, with hemorrhage and tissue degeneration. These findings are also consistent with the study by 17, in which histological sections showed glomerular shrinkage and congestion, as well as the presence of inflammatory cells in the interstitial tissue. Accumulation of cellular debris was also observed within the interstitial space of some renal tubules, along with vacuole degeneration in the cytoplasm of the cells. Signs of cell death were also present in some cells. This finding is also consistent with the study by 18, which demonstrated that high doses of levothyroxine leading to hyperthyroidism cause an increase in glomerular filtration rate (GFR). While this increase may initially appear beneficial, it can later lead to kidney stress and the appearance of tissue damage such as renal convoluted tubule degeneration. However, these results differ from other study 19 which investigated the effects of thyroid disorders, both hyperthyroidism and hypothyroidism, on renal vascularity in rats. Their results showed increased capillary density in the renal cortex and medulla in both conditions compared to the control group. No differences in the number of glomeruli were observed, but the glomerular area was larger in the hyperthyroid condition. No obvious tissue lesions were noted in the kidneys, suggesting that the changes are more related to function than direct damage.

The current study is consistent with that of another study 20 which confirms that hyperthyroidism or excessive doses of levothyroxine lead to increased protein and tissue breakdown in the body due to hypermetabolic processes. This often results in elevated blood urea levels, a hallmark of hyperthyroidism. The study by 21. Confirmed that hyperthyroidism with high doses of levothyroxine leads to accelerated glomerular filtration rate, causing a decrease in serum creatinine levels in rats. Conversely, these doses lead to elevated urea levels due to increased protein breakdown in the body. This means that it agrees with the current study regarding the increase in urea but differs regarding the decrease in creatinine.

The results of the current study are consistent with those of the other study 22 which confirmed that hypothyroidism significantly increases serum creatinine levels and decreases the urea-to-creatinine ratio. The decrease in glomerular filtration rate (GFR) was corrected after treatment of hypothyroidism with levothyroxine, as hyperthyroidism leads to a slight increase in serum creatinine levels and an increase in urea.

This study is consistent with another study²³ which followed patients with hyperthyroidism after treatment with levothyroxine. The results showed that serum creatinine and urea levels increased significantly after treatment. The restoration of hormonal balance by levothyroxine directly affects kidney function indicators. Thus, it can be said that levothyroxine restores hormonal balance but leads to an increase in creatinine and urea with a decrease in GFR, which necessitates close monitoring of kidney function during treatment. The results of this study are consistent with the study by²⁴. Which assessed kidney function indicators in hypothyroid patients and found that creatinine was elevated. Urea levels did not show a significant or statistically significant change after treatment, suggesting that the effect of levothyroxine on them is limited. The results of this study indicate that creatinine is more sensitive to treatment-induced changes than urea. Thus, levothyroxine is considered a significant factor affecting kidney function in patients with hypothyroidism.

This study is consistent with the study by²⁵. which compared hypothyroidism and hyperthyroidism and showed that serum creatinine levels increased significantly in hyperthyroidism, as did serum urea levels. These changes demonstrated that creatinine and urea levels rise, while glomerular filtration rate (GFR) decreases. Our results differ from those of the study by²⁶. Serum creatinine levels decreased significantly. Regarding urea, the results showed only minor changes, indicating that urea is less sensitive to treatment-induced changes than creatinine. Thus, it can be concluded that levothyroxine improves kidney function in cases of renal failure by lowering creatinine levels, while its effect on urea levels remains limited. The results of this study differed from another study²⁷ which showed that hyperthyroid patients had lower creatinine levels.

Conclusion

Levothyroxine leads to negative effects on the kidney, represented by increased levels of urea and creatinine and the occurrence of pathological tissue changes. These effects increase with increasing doses, which confirms the need for caution when using high doses of it and monitoring kidney function periodically.

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None

Conflict of interest:

The Author has declared no conflict of interest in this work.

Financial Disclosure

The author(s) received no specific funding for this work.

Authors' contributions

The whole work was done by Waleed Khalid Hussein, under the supervision of Dr. Shaymaa Malik yasir.

Data Availability

Any questions regarding the availability of the study's supporting data should be addressed to the corresponding author, who can provide it upon justifiable request.

Ethics Approval and Consent to Participate

All experimental procedures for animals were conducted in accordance with approved ethical controls and after obtaining approval from the Institutional Animal Care and Use Committee (IACUC) at the University of Karbala - College of Veterinary Medicine, under approval number: UOK.VET.BI.2026.177, in full compliance with the animal welfare standards applicable in experimental studies.

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