# HISTOPATHOLOGICAL INVESTIGATION OF GENTAMICIN ACUTE TOXICITY IN EQUIDAE

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**Abstract:** Nephrotoxicity is regarded as one of the most important limitations of gentamicin used, in which it appears in 10–25% of patients treated with gentamicin therapeutic doses, beside gentamicin nephrotoxicity has been considered to result widely from tubular type damage of the kidney, therefore, this study performed on ten animals were divided into two groups equally; the animals of the first group inject gentamicin (100mg / KG BW for ten days twice daily, then the treated animal was euthanized on the day 11th of the experiment and samples from internal organs were obtained for histopathological examination; the histopathological analysis of the treated animals showed that In kidney ; there is area of dilated and vacuolated cortical tubules and increased cellularity of glomeruli with prominent mesangial cells ,while in the livers were had early septal and per portal fibrosis, and centrilobular enlargement of hepatocytes; In the thyroid gland there is the presence of micro follicles, also the follicles characterized by large cells and small lumen, some with proliferation; in testis; there are some seminiferous tubules with vacuolation of spermatogonea and reduced spermatogenesis, as well as there is a papillary projection in the epithelial lining of the epididymis, in addition, there is suppression of spermatogenesis and presence of spermatids in the center of the lumen; in the spleen; the red pulp is rich in cellularity with some pigment with prominent trabeculae and hemosiderin pigment; there are atrophic lymphoid follicles of white pulp; while in the lungs there are dilated alveoli with an area of cystic alveoli suggesting emphysema. In conclusion, gentamicin can cause harmful pathological changes in the vital organs of donkeys based on its therapeutic doses.

**Keywords:** Histopathological, gentamicin, acute toxicity, equidae.

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## INTRODUCTION

Uremia regards a clinical phenomenon related to fluid, electrolytes, and hormone disturbance associated with certain metabolic abnormalities which developed deterioration of renal function; besides, the uremia is defined as urine in the blood which is commonly developed with chronic renal failure (CRF) and may occur with chronic kidney disease (CKD) and can also occur with acute renal failure (ARF) (Andrew and Jack, 2006). This syndrome is resulting from the holding of nitrogen waste products, due to imbalance in the body water and electrolytes contents from an irregularity of hormones function as a concern of renal failure, in which most noticed is features of the uremic phenomenon is nitrogen retention that's related to the products of protein metabolism associated with increased plasma concentration which including urea; moreover preservation of metabolites is related to an opposite clinical symptom like weakness and anorexia, as well as to many other systemic findings like anemia and acidosis (Al-Mosawi, 2006) .

It once all the signs and symptoms of uremia present that lead to advanced renal failure, hypertension due to volume overload, tetanic hypocalcemia as well as the anemia resulted in lack of erythropoietin that regarded as a risk sign of uremia; while uremia term describes the diseases associated renal failure that can't be referred to an imbalance of extracellular volume, inorganic ions concentration or drop of known kidneys products, it seems like uremic disease is resulted in largely to the increased of organic waste product (Meyer and Hostetter, 2007).

Uremia is associated with increased oxidative stress at the plasma and decreased level of antioxidants (Himmelfarb et al., 2002); also, it is associated with hypertension and metabolic turbulences like anemia, hyperphosphatemia, hyperparathyroidism, micro-inflammation, and activation of the Renin-angiotensin system that might lead to heart diseases (Amann et al., 2006).

## MATERIALS AND METHODS

Ten animals were included in this study in which adapted for 14 days in the animal's house at the college of veterinary medicine, university of Basrah, and then divided into two groups (5 animals per each); the animals of the first group was injected gentamicin (gentamicin sulfate, 10% Acdevit, Syria) that dosed100 mg/kg BW for 10 days twice daily for 10 days. Treated animals were euthanized on the day 11th of the experiment and samples from internal organs were obtained for

histopathological examination according to procedures described by Luna, (1993).

## RESULTS

The kidney showed an area of dilated and vacuolated cortical tubules (figures 1,2 and 3), with loss of epithelial lining (figure 4); there is an increase in cellularity of glomerulus with prominent mesangial cells (figure 5); there is also vacuolated of cortical tubules with vacuolated endothelial cells (figures 6 and 7).

The liver showed early septal and periportal fibrosis (figure 8 and 9) and centrilobular enlargement of hepatocytes (figure 10).

The thyroid gland showed the presence of microfollicles (figure 11), there are also small follicles characterized by large follicular cells and small lumen, some with proliferation (figure 12).

The testis showed some seminiferous tubules with vacuolation of spermatogonia and reduce spermatogenesis (figure 13) there is a papillary projection in the epithelial lining of the epididymis (figure 14), there is suppression of spermatogenesis and presence of spermatids in the center of the lumen (figure 15).

The spleen showed the red pulp rich in cellularity with some pigment (figure 16) with prominent trabeculae (figure 17) and haemosiderin pigment (figure 18); there are atrophic lymphoid follicles of white pulp (figure 19).

The lung showed dilated alveoli (figure 20) with an area of cystic alveoli suggesting emphysema (figure 21).

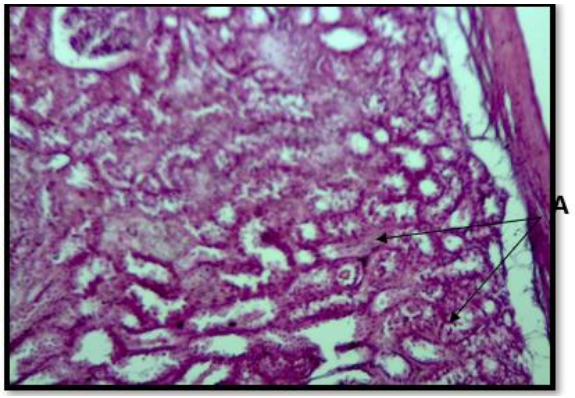


**Figure 1. Kidney showed A. Area of dilated cortical tubules (H&E 100X).**

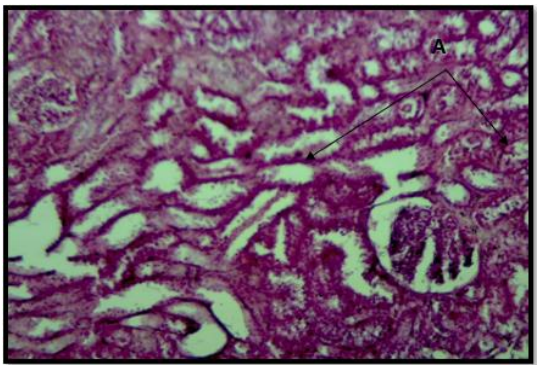


**Figure 2. Kidney showed A. area of vacuolated cortical tubules(H&E 100X).**

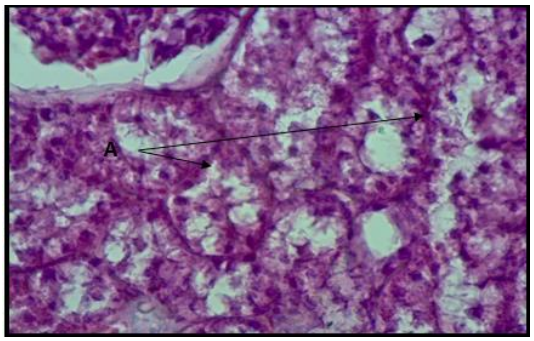


**Figure 3. Kidney showed A. area of vacuolated cortical tubules (H&E 400X).**

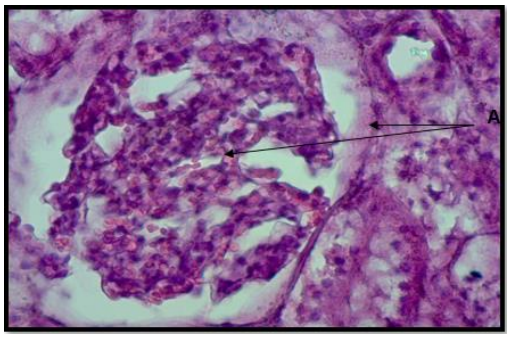


**Figure 4. Kidney showed A. increased cellularity of glumeruli with prominent mesengeal cells (H&E 400X).**

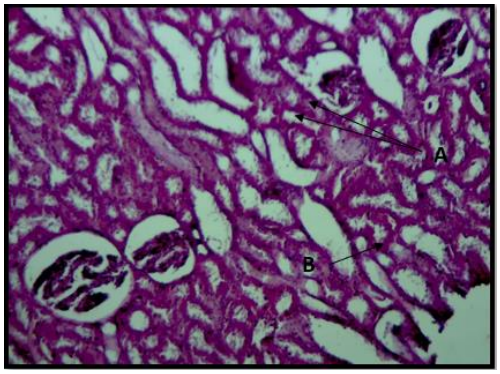


**Figure 5. Kidney showed A. area of dilated cortical tubules. B. loss of epithelial lining of tubules.(H&E 100X).**

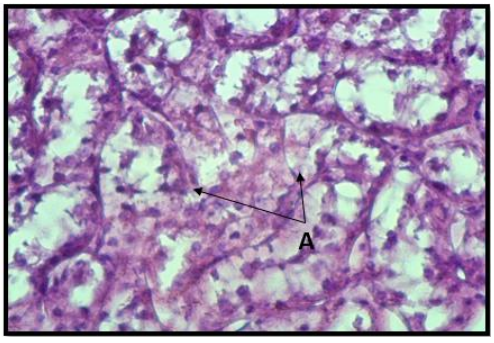


**Figure 6. Kidney showed A. vacuolated cortical tubules (H&E 400X).**

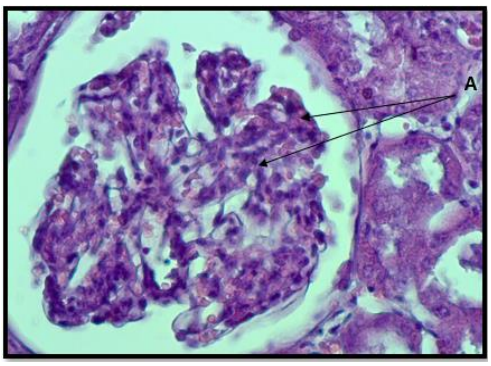


**Figure 7. Kidney showed A. a glomerulus with vacuolated mesengeal cells. (H&E 400X).**

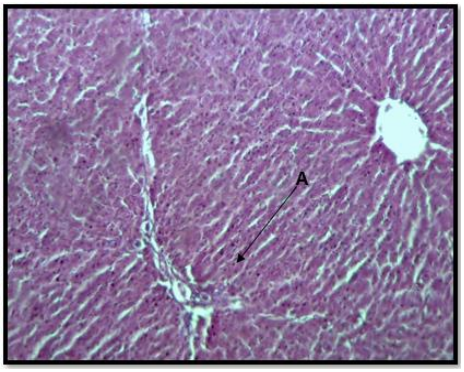


**Figure 8. Liver showed A. early septal fibrosis (H&E 100X)**

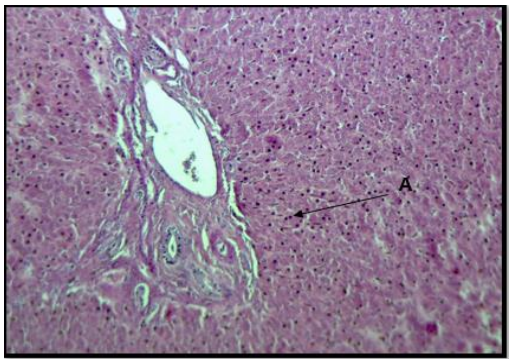


**Figure 9. Liver showed A. periportal fibrosis (H&E 100X).**

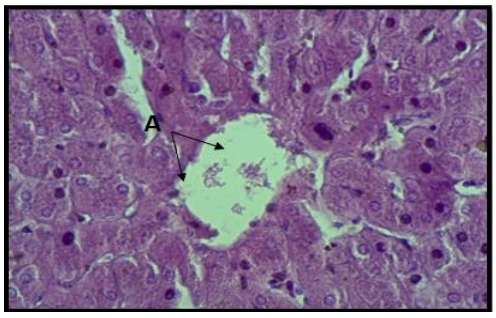


**Figure 10. Liver showed A. centrilobular enlargement of hepatocytes (H&E 100X).**

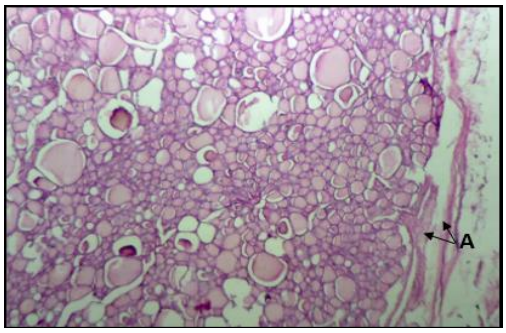


**Figure 11. Thyroid gland showed A. Microfollicles (H&E. 100X).**

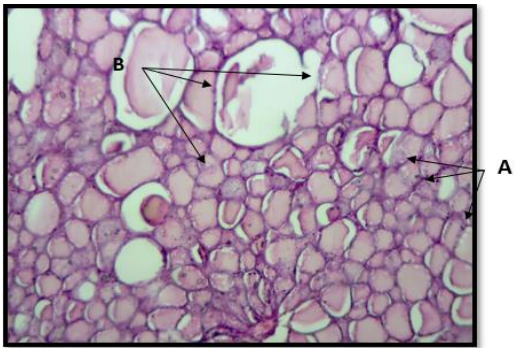


**Figure 12. Thyroid follicles showed A. small follicles and B. large follicles.(H&E 400X)**

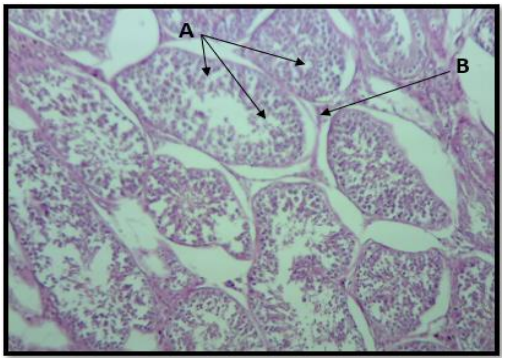


**Figure 13. Testis showed A. Vacuolation of seminiferous tubules. B. suppression of spermatogenesis. (H&E. 100X).**

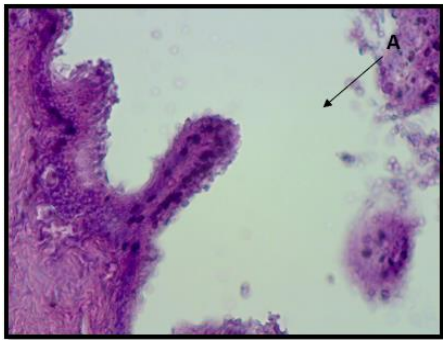


**Figure 14. Epididymis showed A. papillary projection in the epithelial lining. (H&E. 400X).**

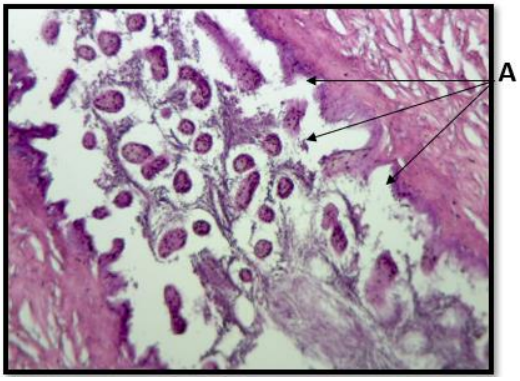


**Figure 15. Epididymis showed A. multinucleated spermatids (H&E. 400X)**

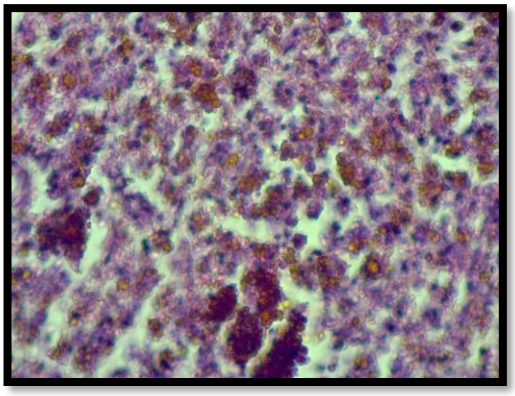

**Figure 16. Spleen showed red pulp rich in cellularity (H&E 400X).**

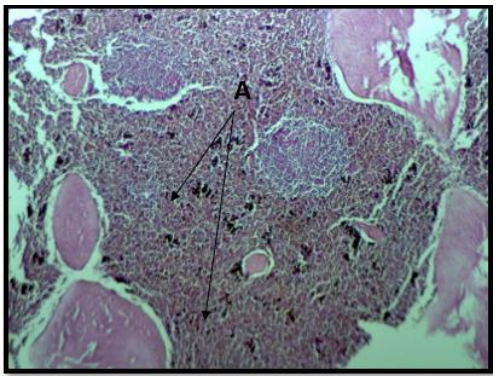


**Figure 17. Spleen showed A. Trabiculi**

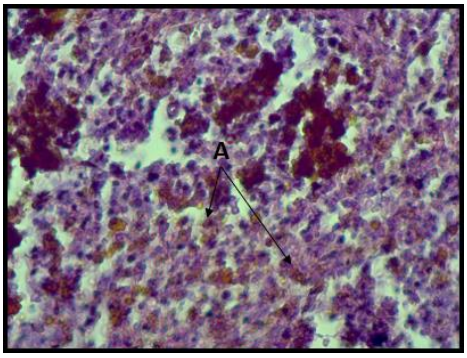


**Figure 18. Spleen showed A. Hemosiderin pigment in red pulp (H&E. 400X).**

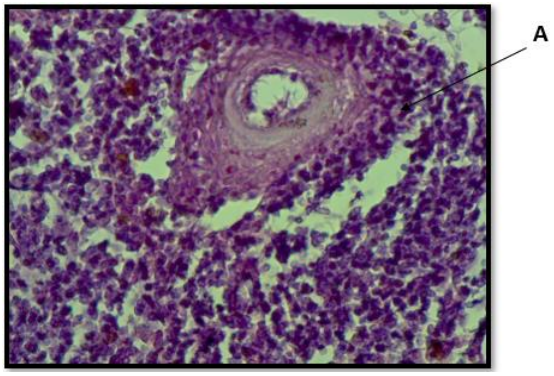


**Figure 19. Spleen showed A. Atrophy of white pulp. (H&E. 400X).**

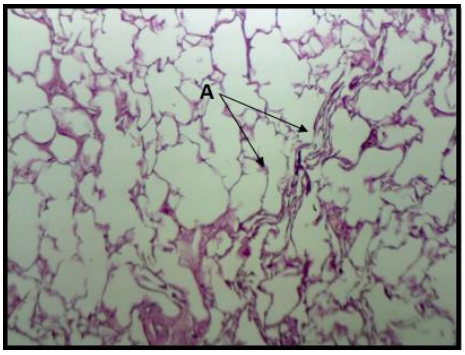


**Figure 20. Lung showed A. dilated alveoli.(H&E 100X).**

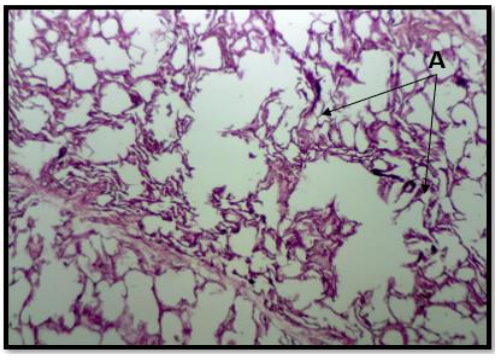


**Figure 21. Lung showed A. emphysema (H&E 40X).**

## DISCUSSION

Gentamicin can cause kidney damage, liver disease, skin irritation also allergic reactions, sensitivity, diarrhea, and vomiting in dogs and cats (Hollinger, 2020; Zadeh et al.,2022; Bokov et al.,2022). The gentamicin works by interrupted or mistranslation and synthesis inhibition of the protein of the bacteria (Ying et al, 2019; Huldani et al.,2022). Vestibulotoxic and ototoxic could be noticed after long-term and high-dose systemic use of gentamicin, While the toxic effects when current use have not been informed in animals (Papich, 2015). Also, it showed a complicated granulation tissue formation in the corneal stroma when used in pigeons (Abdulsamad, et al., 2021).

Udupa and Prakash, (2018) reported that gentamicin could be a reason for nephrotoxicity in rats is usually noticed in serum marker and histopathology of the kidney; which is known as acute kidney deterioration renal biomarkers, and it's used in the diagnosis of early renal damage; there were factors such as BUN and serum creatinine that were significantly elevated on day 8 at a dose of 100 mg/kg BW of gentamicin.

However, the reduction in BUN in a dose of gentamicin that was 100 mg per kg BW daily was associated with serious histological findings, it was connected with weight elevation of the organs and tubular epithelial degeneration and necrosis as well as tubular epithelial cell regeneration, basophilic finding in the renal cortex as well as medulla on the day 8 of treatment associated with paleness coloration of the kidney (Alarifi et al., 2012 and Gautier et al., 2014; Hafsan et al.,2022).

Gentamicin causes elevations in plasma ALT, AST, creatinine, and BUN moreover, the Na and K excretion were elevated while the urine flow rate, as well as the clearance of creatinine, were decreased in the gentamicin treated animals; besides, the liver and kidney tissues MDA were increased in which this test is beneficial to assess the excess formation of free radicals as reactive oxygen species and reactive nitrogen species that caused damages to the cellular renal membranes (Ahmed, 2017); in addition, the glutathione reduced in the gentamicin treated animal's which it seemed apoptosis in liver and kidney in those animals (Khaksari et al., 2021).

Gentamicin causes necrosis and inflammation in the liver parenchyma; Liver enzyme and inflammatory cytokine levels were significantly increased in the GM group (Naser et al 2021). The uses of gentamicin cause a decrease in glutathione and an increase in MDA so it is reflected as ROS, although being one of the major injuries to beings' wellness and condition (Gabriele, 2017).

Aly, (2019) revealed that the testis of male reproductive system histopathological changes showed loss of spermatogenesis and increase of the morphological abnormalities of the testis after treatment with gentamycin. The degenerative effect, decease the spermatogenesis with atrophy of the seminiferous tubules were observed by Hamdy et al, (2018).

Gentamicin showed to cause an increase in congestion in blood vessels but increases the thickness of epithelium of certain organs (Abdulsamad, et al., 2021).

On the other hand, the outcomes of this study indicate that gentamicin creates oxidative stress associated with the weakening of spermatogenesis, in addition to apoptosis; these results revealed the mode of action of gentamicin-induced weakening of spermatogenesis in the rat testis.

## CONCLUSION

The histopathological findings that were studied suggest that gentamicin induced nephrotoxicity, hepatotoxic, and another organ effect due to its mode of action and due to its oxidative effect on the Equidae organs and tissues.

## COMPLIANCE WITH ETHICAL STANDARDS STATEMENTS

**I. Ethical approval:**

The manuscript is written in original and all the data, results pertaining to this manuscript are original according to the research performed. The authors followed academic integrity and have not copied any content/results from another source.

**II. Funding details (In case of Funding):**

The authors of this manuscript did not receive any funding to perform the present research

**III. Conflict of interest**

The authors of the study do not have any conflict of interest

**IV. Informed Consent:**

The authors of the manuscript agrees to publish this research in the journal if it's considerable by the editors of the journal. The authors provide full consent for reviewing and publishing this manuscript.

**V.** All the authors of this study contributed equally in terms of performing the research as well as in preparing the manuscript. All the authors of the study followed the guidelines of the corresponding author. Any query/suggestion related to the manuscript can be reached to the corresponding author

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