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Original Research Article

Histological Effect of Vitamin D3 Overdose on Liver, and Kidney in Female Albino Rats

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Abstract: Vitamin D is a crucial element in the body that plays a pivotal role in health and disease, and it can be obtained either through food or direct exposure to sunlight. This study aimed to detect the histological effect of vitamin D3 overdose on liver and kidney tissues. The experiment included sixteen female rats which were distributed into four groups, each group containing 4 rats, Group1: control was given only olives oil Group2: 0.5ml of D3 + 9.5ml olives oil, Group3: 1ml D3+9ml olives oil Group4: 2ml D3+8ml olives oil, the experiment continued for30days, After end the period, the rats were sacrificed and obtained the organs. The results showed High doses of Vitamin D3 can cause pathological histological changes in the liver and kidneys due to increased calcium deposition and inflammatory effects. The most elevations were in group 4 which was considered high dose. This elevation included: Tubular Calcification and tubular Degeneration, of the kidney, and for the liver the results showed Congestion of Liver Blood Vessels and Hepatocellular Degeneration.

Keywords: Vitamin d3, overdose, Histological elevation, liver and kidney tissue.

INTRODUCTION

One of the fat-soluble vitamins, vitamin D is also known as the sunshine vitamin because it is produced by the body when exposed to ultraviolet light from the sun. Sunlight is thought to be the most significant factor in the body's production of vitamin D, which comes in two basic forms: D2 and D3 (Prakash *et al.*, 2017). Some plant and animal sources contain vitamin D2. It is frequently advised to select vitamin D3 supplements because the liver's metabolic processes for the two types of vitamins D2 and D3 are different, and because vitamin D3 is the form that the body naturally produces when exposed to sunlight, its effectiveness is likely to be higher than that of vitamin D2 (Tebben *et al.*,2016). Vitamin D comes from a variety of sources, both natural and artificial, however, it is best to get it from natural sources. (Ewa Marcinowska- and, Paweł, 2016)

The primary source of vitamin D is the sun. Under the effect of ultraviolet light, adequate exposure to it every day for at least 15 minutes helps to stimulate the skin's production of vitamin D3 (cholecalciferol). (Jones, 2008) A low blood level of vitamin D is a risk factor for several serious illnesses, including cancer, heart disease, fractures, falls, and more, making vitamin D deficiency (VDD) a significant public health issue. Several skeletal and no skeletal disorders can be prevented and treated with vitamin D. (Holick, 2015)

In recent years, the public has become more aware of vitamin D deficiency, leading to a rise in the usage of vitamin D supplements and high dosages of vitamin D prescribed by doctors to treat the condition. (Tebben, 2016) Hypervitaminosis D, vitamin D toxicity (VDT), and other conditions may become more likely as a result of the general public's increased usage of vitamin D supplements and the rising number of therapeutic dose prescriptions written without any monitoring. When someone is exposed to high levels of vitamin D for an extended length of time, they may develop hypervitaminosis D, a rare but potentially dangerous illness (Hawkes *et al.*, 2015). Megadoses of vitamin D medication, rather than food or sun exposure, are typically the source of vitamin D toxicity. This is because even fortified foods do not

contain significant levels of vitamin D, and the human body controls the quantity of pre-vitamin D generated by UVB (Hawkes *et al.*, 2015).

When there are significantly elevated 25(OH)D levels (> 150 ng/mL) along with hypercalcemia, hypercalciuria, and very low or even undetectable PTH activity, the condition is known as VDT. Nonetheless, the main clinical concerns associated with VDT typically center on hypercalcemia, or increased calcium levels, and a range of vague symptoms. Holick (2015)

The vital involvement of calcium in several tissues and organs, such as bone, the circulatory system, neurons, and cellular enzymes, is reflected in the diverse clinical manifestations of hypervitaminosis D, which is primarily caused by hypercalcemia. Generalized weakness and weight loss are among the early symptoms of hypervitaminosis D that can resemble those of other hypercalcemic conditions (Prakash 2010).

MATERIALS AND METHODS

Animal Model and Treatment Protocol

Female Wistar rats (180-200g) were used in this study, obtained from the animal house of the College of Veterinary Medicine, University of Tikrit. The rats were housed in standard laboratory conditions and had free access to food and water. The rats were divided into 4 groups, each group had 4 rats, a total 16 rats, for one month, received vitamin D3 daily orally at a dose of:
G1: olives oil, G2:0.5ml vitD3+9.5ml olives oil, G3:1ml vitD3+9ml olives oil, G4:2ml vit D3+8ml olives oil.

Sample Collection

At the end of the treatment period, Liver and kidney tissues were rapidly excised, washed with saline, and dissected for further analysis. Tissue samples were either fixed in 10% formalin for histological analysis.

Histological Sections Preparation:

Histological sections were prepared following the method described by Luna's method (1968).

RESULTS AND DISCUSSION

1. The kidney:

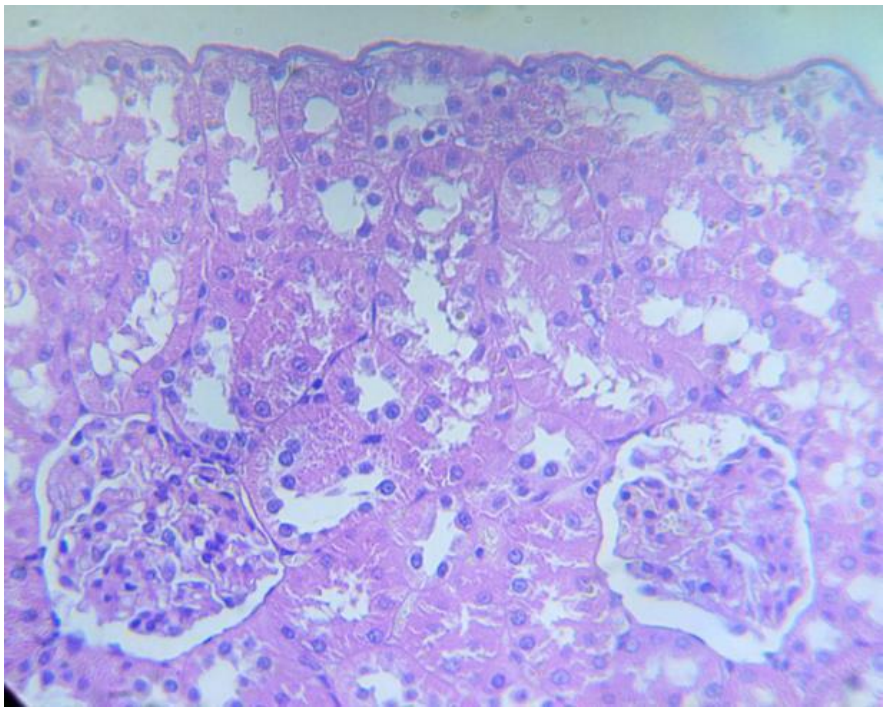

Figure 1: Section of Kidney control1-A: The cortex of kidney had spherical glomeruli surrounded by capsules space and Bowman's capsules, the proximal convoluted tubule were lined by pyramidal cells and the distal convoluted tubule were lined by simple cuboidal cells fig 11 x 40)

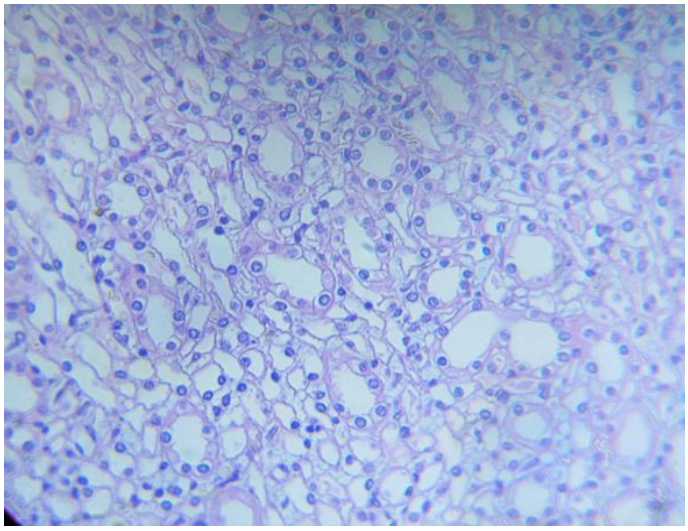

Figure 2: Section of Kidney control -B: The renal medulla was consist of renal tubules and collecting tubules lined with simple cuboidal cells with white cytoplasm and spherical nuclei, also there was thin segments of Henle loops lined with simple squamous cells fig 12)

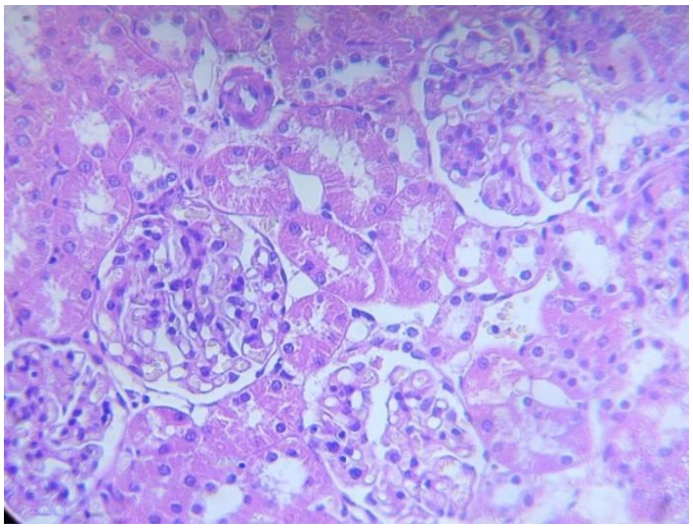

Figure 3: Section of kidney group 2-A; The cortex of kidney had spherical glomeruli, surrounded by bowman's capsules and also surrounded by proximal and distal convoluted tubules fig1x 40)

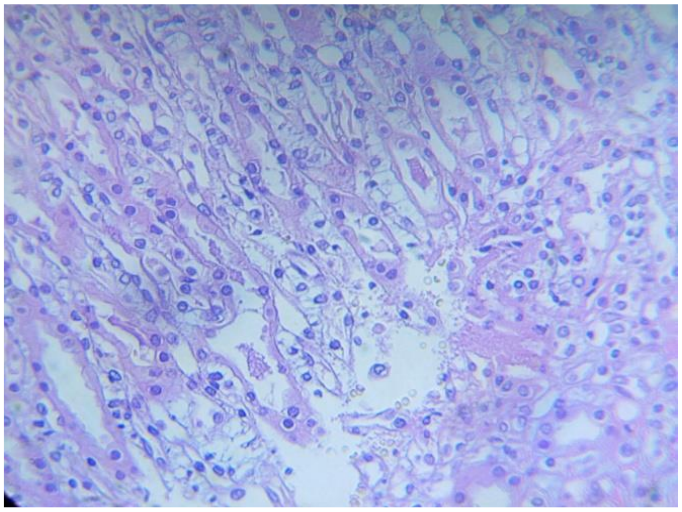

Figure 4: Section of kidney group 2-B: The renal medulla had collecting tubules lined by simple cuboidal cells and henle loops surrounded by simple squamous cells fig2 x 40)

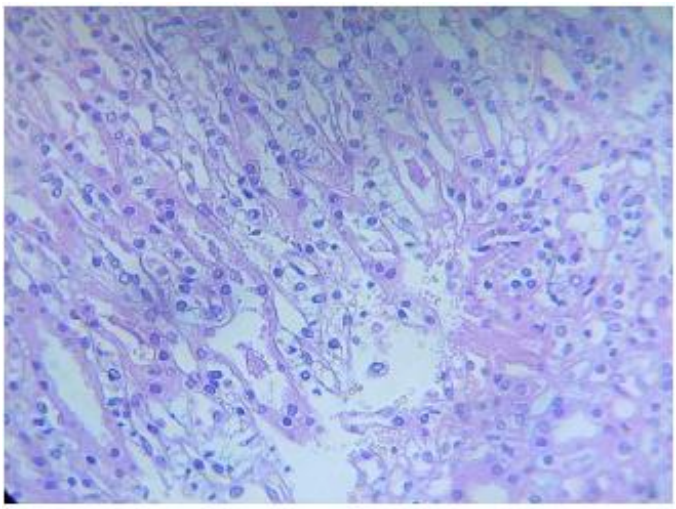

Figure 5: Section of kidney group the renal cortex had glomeruli with hyperplasia of glomerular cells on its surface (A), also hyper trophy of cells lining the proximal and distal convoluted tubules, (B) blood congestion was present H &E x 40)

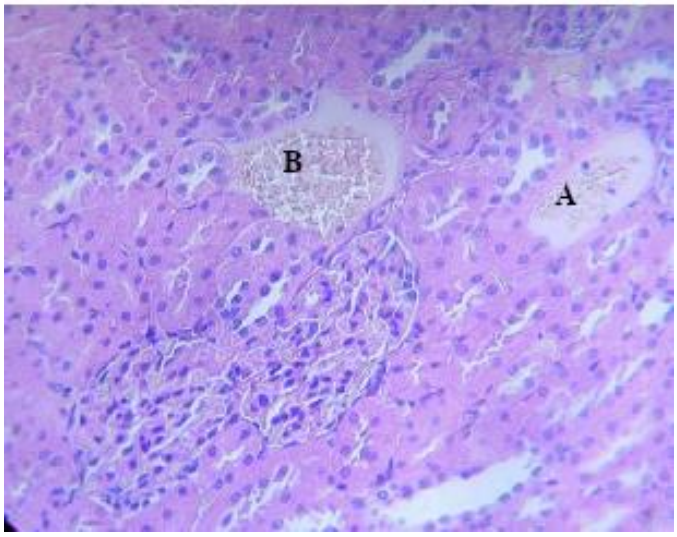

Figure 6: The renal medulla had multiple number of collecting renal tubules, lined with hypertrophic epithelial cells (A)and there was focal aggregation of WBC H &E x 40)

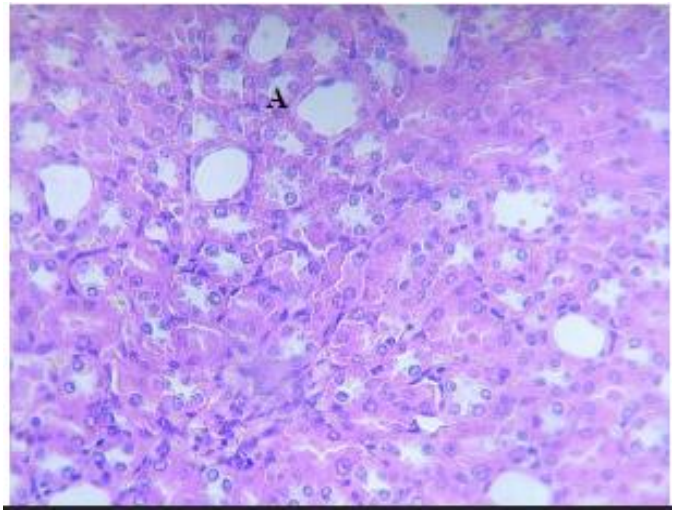

Figure 7: Section of kidney group 4-A: The tissue of renal cortex was demonstrating the presence of atrophied glomeruli (A) and shrinkage of bowman's capsule around glomeruli (B) also there was sloughing of tubules with blood hemorrhage in the interstitial C.T (H &E x 40)

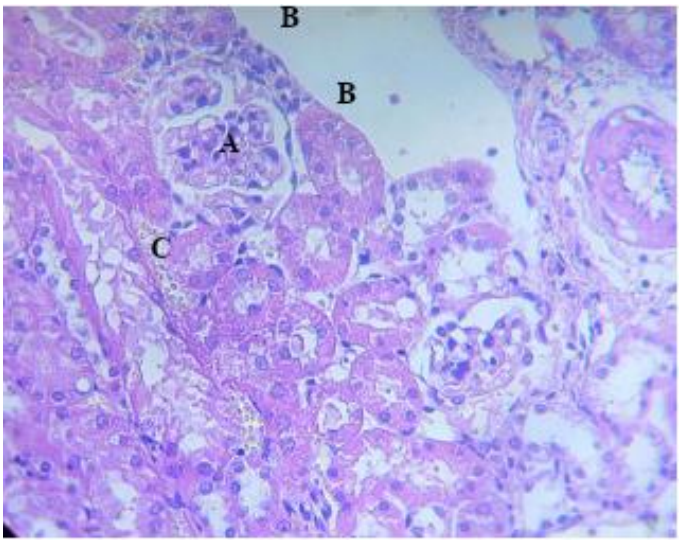

Figure 8: Section of Liver control 1: The hepatocytes are arranged in columns (A) and radial pattern around the central vein (B), and each hepatocyte is polygonal with spherical nuclei (C) (H &E x 40)

2. The liver:

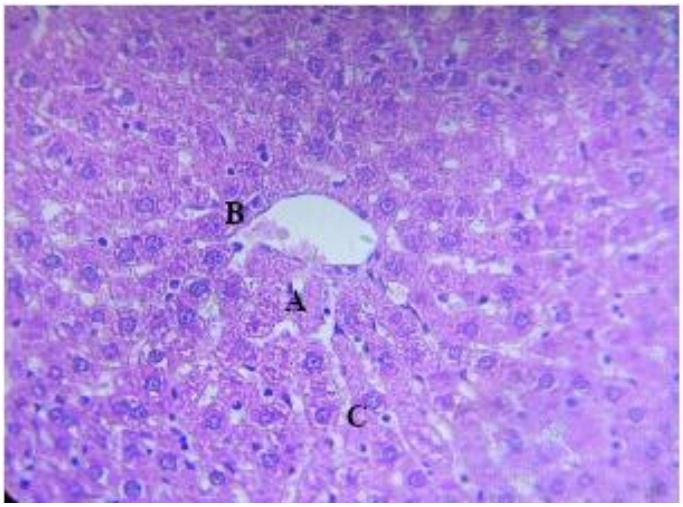

Figure 9: Section of liver group2- : The central vein of liver was wide lumen (A), surrounded by nodules aggregation of lymphocytes with macrophages (B), surrounded by columns of liver cells and in between blood sinusoids with Kupffer cells H&E (40X)

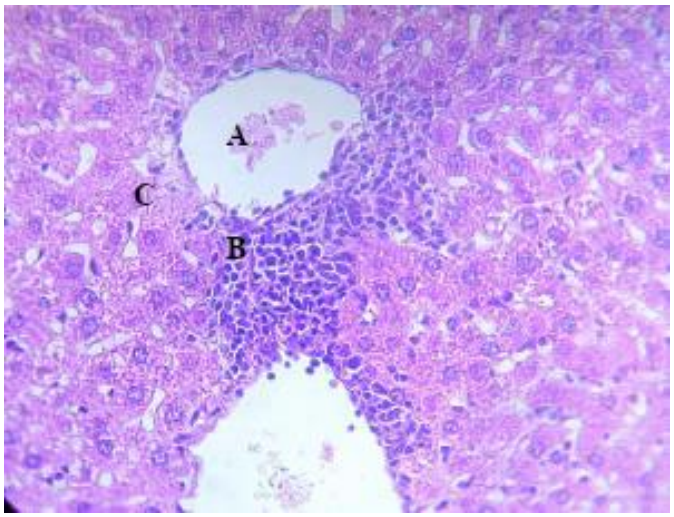

Figure 10: Section of Liver group 3-: The central vein had hemolysis blood (A) surrounded with WBCs (B) and hypertrophied liver cells H & amp; E40X)

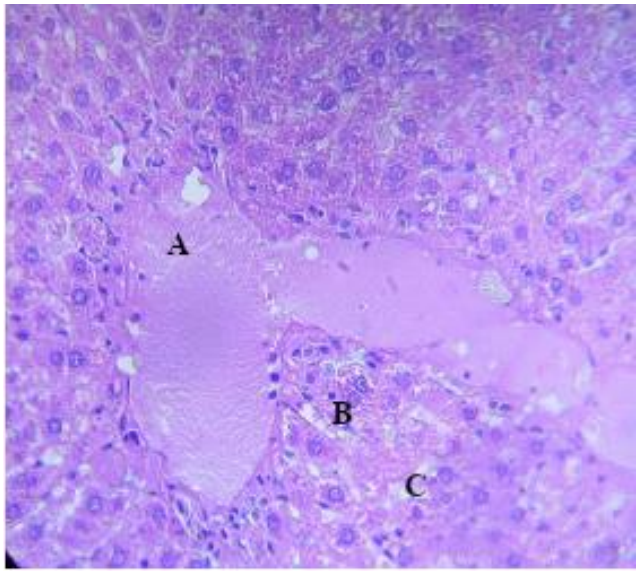

Figure 11: Section of Liver group 44-A: The central vein was wide lumen containing hemolyzed blood (A), surrounded by hypertrophied liver cells with grate nuclei (B), the blood sinusoids had Kupffer cells H & amp; E40X)

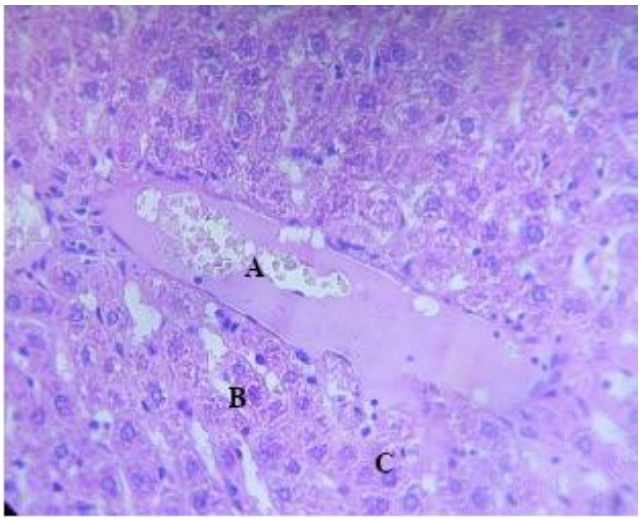

Figure 12

The Results and Discussions

The results revealed various structural changes in the kidneys, including glomerular hyperplasia, tubular hypertrophy, and atrophied glomeruli. These results are consistently with result of Smith *et al.,* (2009) who reported similarity histologically changes at the kidneys of animal exposure to higher doses of vitamin D3. The present study reporting the functionally weaknesses in the investigate kidney because the present of degeneration of the tubular epithelial cells with a clear renal filtration at the tubular lumen.

According to our results, the structure of the liver is affected by excess vitamin D3. This is consistent with other previous studies. For example, Zhang *et al.,* (2017) proposed that excessive vitamin D3 led to changes in liver structure, resulting in liver hypertrophy, vascular congestion, and fat deposition. In addition, multiple lymph nodes and cell infiltration were found in liver tissue, indicating the presence of an inflammatory response. Another study (Gupta *et al.,* 2014) found that excessive vitamin D3 may affect the inflammatory stimulation of liver tissue, leading to the occurrence of liver disease. In addition, excessive vitamin D3 can enhance liver function, as pointed out by Smith *et al.,* (2011) who noticed various changes in rat livers, such as cell infiltration and promotion of inflammation.

CONCLUSION

This study demonstrated various changes in rat liver structure, including tubular hypertrophy, glomerular hyperplasia, and glomerular atrophy. Inflammatory responses were detected by the accumulation of leukocytes and the presence of inflammatory exudates in liver tissue. Evidence of renal dysfunction was seen by degeneration of tubular epithelial cells and the presence of renal filtrate in the tubular lumen. Long-term vitamin D intake can lead to a variety of

histological changes in the liver and kidneys. This also can lead to congestion of blood, and increasing in the number of white blood cells and macrophages due to processes of inflammation that result from the overdose toxicity of vitamin D.

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