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Potential Effect on Aldosterone and Electrolyte Balance in Rats Caused by Hypothyroidism

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Abstract:

Hypothyroidism, also known as an underactive thyroid, is a condition in which the thyroid gland does not produce adequate thyroid hormones. So far, there is no evidence clarify that hypothyroidism affects the aldosterone hormone and electrolytes in female rats. The study aims to recognize the effect of hypothyroidism on the aldosterone hormone, Na, and K. Twenty female rats were divided equally into two groups (10 rats per group); the first group was intraperitoneally injected with saline for 28 days, and the second group was orally given 50 mg/kg propylthiouracil to induce hypothyroidism. At the end of the experiment, blood samples were used to assess hormones such as TSH and aldosterone. The levels of K+ and Na+ were also measured. In addition, the adrenal glands were obtained from the rats for histological examination using hematoxylin and eosin staining. The study revealed a significant increase in TSH concentration and a significant decrease in aldosterone and Na concentration. Histopathological examination of a part of the adrenal gland showed separation of the capsule from the cortex in multiple areas, along with a reduction in the thickness of the zona glomerulus, cell and fiber destruction, and the disintegration of plasma membranes, which led to fusion of cells, with nuclei appearing darker in color and nucleoli disintegrating in some cells, indicating reduced glandular activity. The study concluded that aldosterone and sodium were influenced by hypothyroidism, which led to histopathological changes in the adrenal gland, indicating a reduction in its activity.

Keywords: Aldosterone, Hypothyroidism, Na, Propylthiouracil

1- Introduction

Hypothyroidism, the second most widespread endocrine disease after diabetes [1], is characterized by thyroid gland inefficiency, resulting in a lack of thyroid hormone. Hypothyroidism can be caused by autoimmune diseases (e.g., Hashimoto's) [2], thyroid surgery, radiation therapy, certain medications, iodine deficiency, congenital defects, pituitary disorders, thyroiditis, pregnancy, and genetic predisposition [3,4] propylthiouracil is a medication used to treat hyperthyroidism by inhibiting thyroid hormone production, which was first described by Edwin W Astwood in 1943 [5]. Aldosterone is a key

mineralocorticoid steroid hormone secreted by the zona glomerulosa cells located in the adrenal cortex [6]. This hormone plays a crucial role in regulating various physiological processes, such as responses to oxidative stress, inflammation, fluid imbalance, and abnormal blood pressure, by exerting effects on tissues including the kidneys, heart, and central nervous system. The synthesis of aldosterone is primarily controlled by angiotensin II, potassium levels, and adrenocorticotropic hormone [7,8]. The existing study aimed to evaluate the effects of hypothyroidism on aldosterone levels and mineral salts, and focused on histological architecture components of adrenal tissues.

Research Gap

Although several studies have explored the effects of hypothyroidism on hormonal and metabolic balance, its specific impact on aldosterone levels and mineral homeostasis remains under investigated, particularly in animal models like rats. The relationship between hypothyroidism and disturbances in sodium and potassium regulation has not been thoroughly examined. This gap in the current literature limits the development of a clear concept of how hypothyroidism influences electrolyte balance and kidney function, necessitating further research to clarify these effects.

Methods

Animals Husbandry: All protocols for experimentation were applied according to the authorised guidelines for the care and use of laboratory animals in the education faculty for pure science / Thi-Qar University. The Thi-Qar ethical committee for animal research approved this research (Issue 7/ 54/ 1727). Twenty female rats aged 3-4 months, weighing 170-230 grams on average, were used. They were housed in a plastic cage in the animal facility in the College of Education Pure Sciences, Thi-Qar University, under standard conditions of temperature (22 ± 25 °C and lighting (12:12-hour light-dark cycle) for two weeks before and during the study period. Throughout the study, the rats had free access to feed and water. Rats were randomly and equally divided into 2 groups as follows: the first group (control) was intraperitoneally injected with normal saline; the second group (Hypothyroidism) was orally given 50 mg/kg of propylthiouracil to induce hypothyroidism [9.[

Biochemical analysis: Serum Thyroid-stimulating hormone (TSH), Aldosterone (Ald), potassium

(K) and Sodium (Na) were determined using commercial kits (Elisa, BT LAB, China).

Histopathological study: The adrenal glands were sectioned transversely and entirely submitted in a labeled histology cassette. Each specimen was cut to a thickness of 5 mm, immediately fixed in 10% formalin solution for forty-eight hours, treated with water wash, a graded ethanol series, and then embedded in paraffin wax at 70°C. The paraffin-embedded blocks were sectioned to prepare slides, which were then stained with Hematoxylin and Eosin. All sections were examined for histopathological changes under a light microscope.[10]

Statistical analysis:

Statistical computations were performed using SPSS V. 21 (SPSS Inc.) Data presentation included mean values ± standard deviation (Mean ± SD).

Result

The results of the present study showed a significant increase in TSH hormone (p-value=0.015; Figure 1) and a significant decrease in aldosterone and sodium (p-value=0.001 and p-value=0.001, respectively;

Figures 2 and 3) in hypothyroid rats compared to the control group. However, no significant difference in potassium levels between the two groups (p-value = 0.283), as shown in Figure 4.

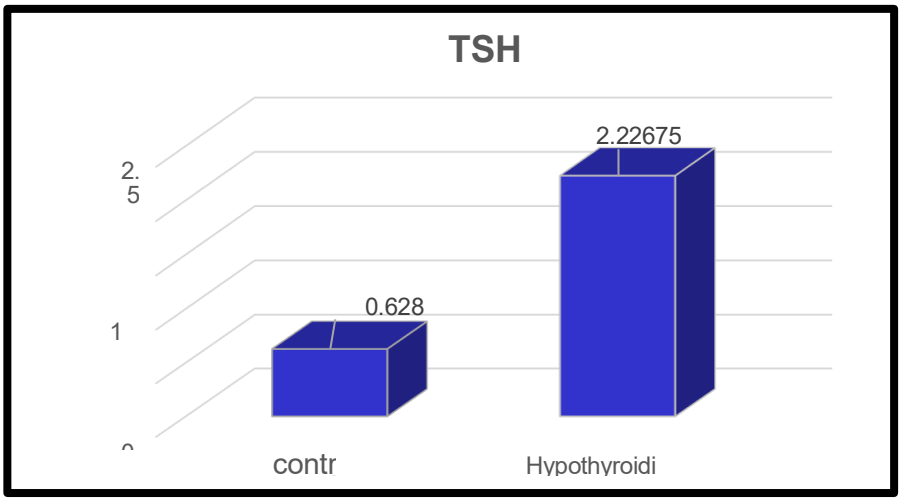

Figure (1) Thyroid-stimulating hormone l levels in study gpoups

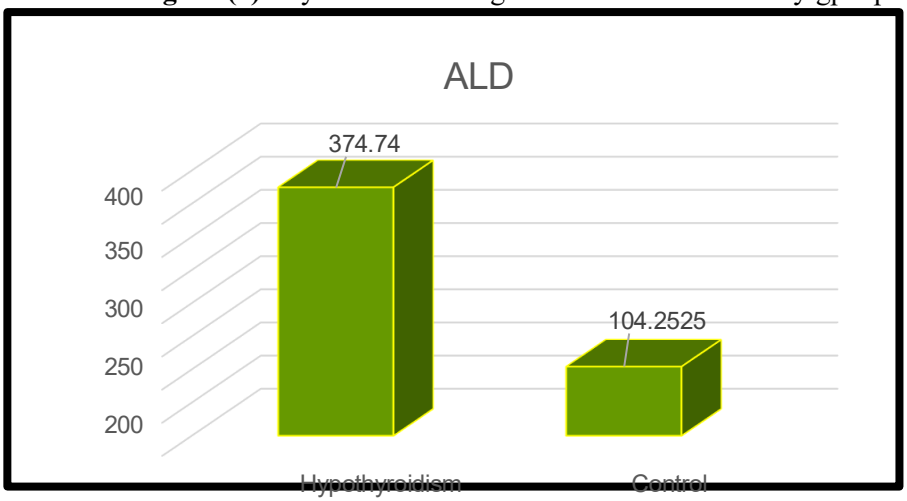

Figure (2) Aldosterone levels in study gpoups

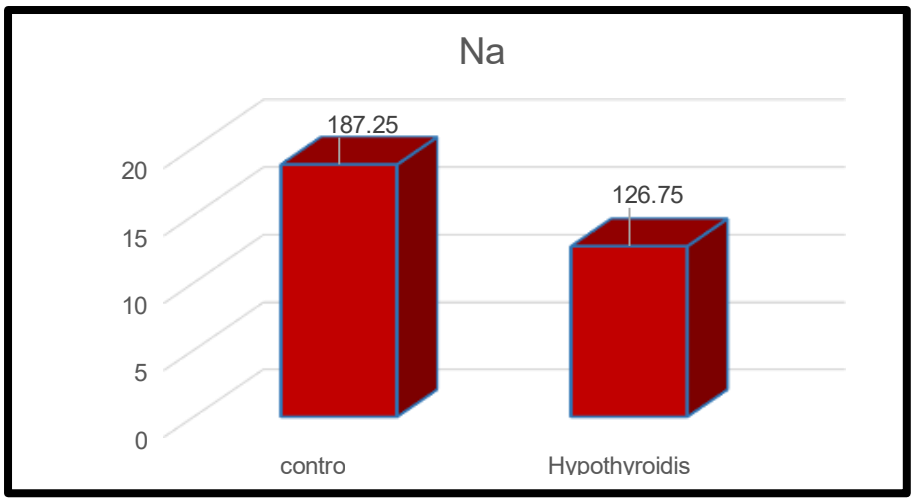

Figure 3: Sodium levels in study groups.

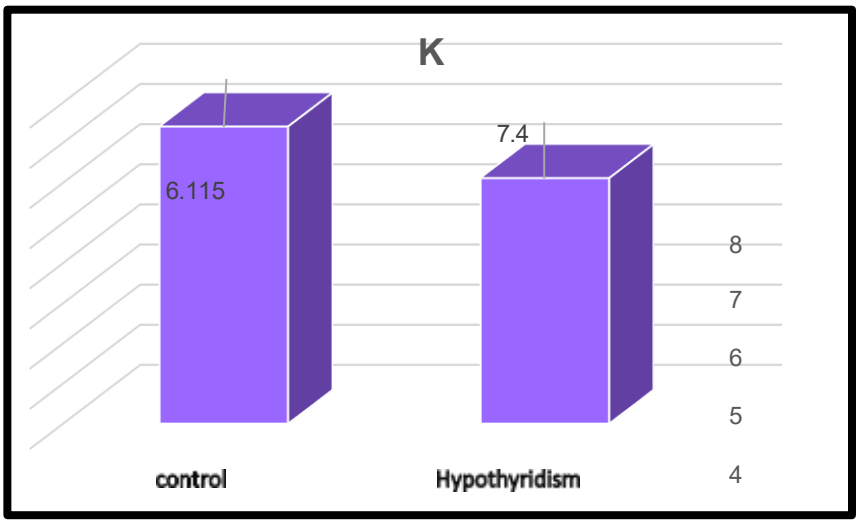

Figure 4: Potassium levels in study groups

HISTOLOGICAL STUDY:

The negative control group revealed that the tissue structure of the adrenal gland appears normal, active, and surrounded by a normal capsule, containing secretory materials. The zona glomerulosa appeared as flat or circular-shaped cells with clear, light-colored nuclei. The zona fasciculate was characterized by columnar cells arranged in cords, with cells organized in one or two rows, and the sinusoids contain lipids and blood capillaries. The zona reticularis had polygonal cells interwoven with each other, close to the yellow medulla, which is composed of chromaffin cells and nerve cells.

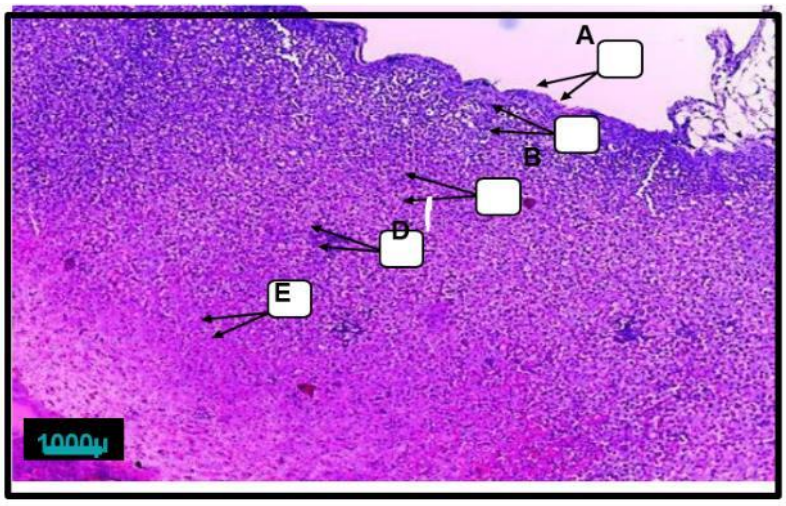

Figure 5: Normal histostructure of adrenal gland tissue in the control group show normal capsule (A) with normal zona glomerulosa (B), normal zona fasiculata (C), normal zona reticularis (D), normal medulla (E) (100X)

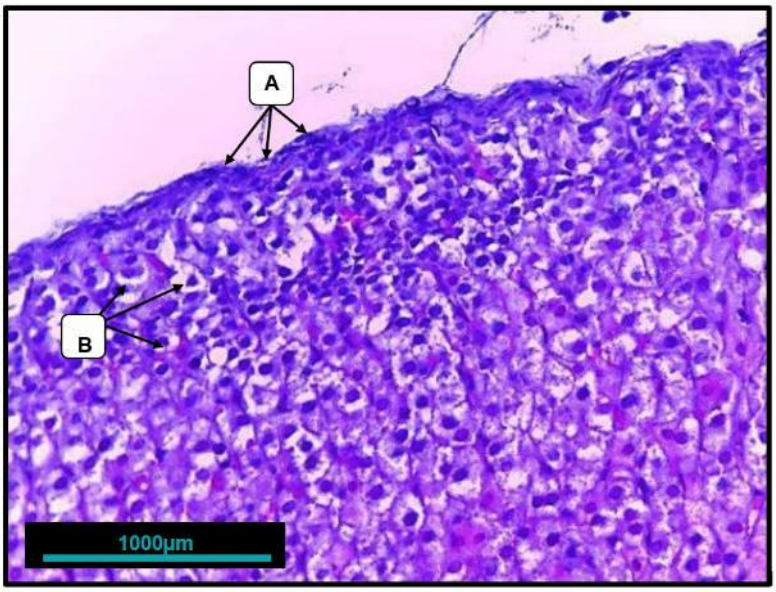

Figure 6: This microphotograph of the adrenal gland in the control group showing normal capsule (A) and normal zona glomerulosa cells with their normal nuclei (B) (400 X).

This study showed histological changes in the adrenal gland in the hypothyroid rats. There was atrophy of the Zona glomerulosa, and a reduction in the number of their cells. Necrosis and degeneration were noticed in a few cells near the capsule, where the cells were devoid of cytoplasm, and an increase in thickness in some nuclei was noted, as well as changes in the connective tissue surrounding the cells, which also showed dilatation and congestion of sinusoids compared tto the negative control.

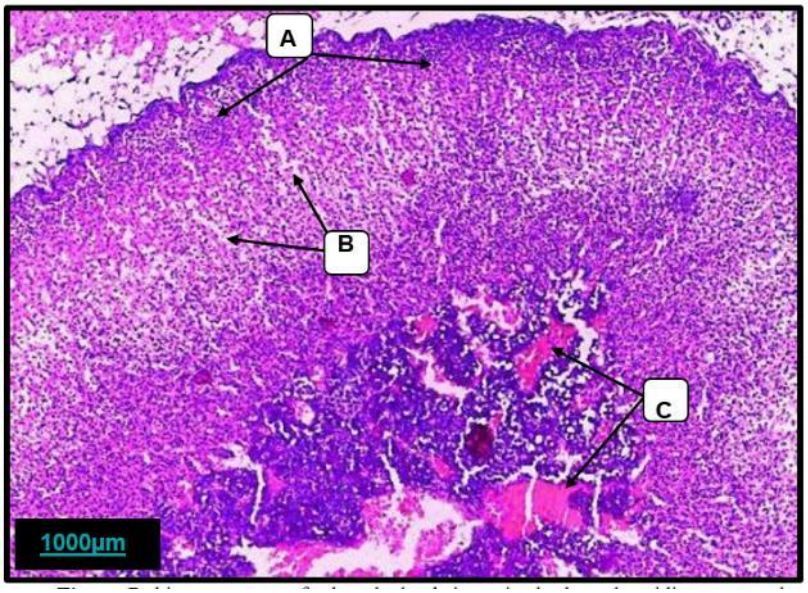

Figure 7: histo-structure of adrenal gland tissue in the hypothyroidism group showing a degenerated cell near the capsule (A) with vacuolation (B) and vascular hypertrophy (C) (100 X).

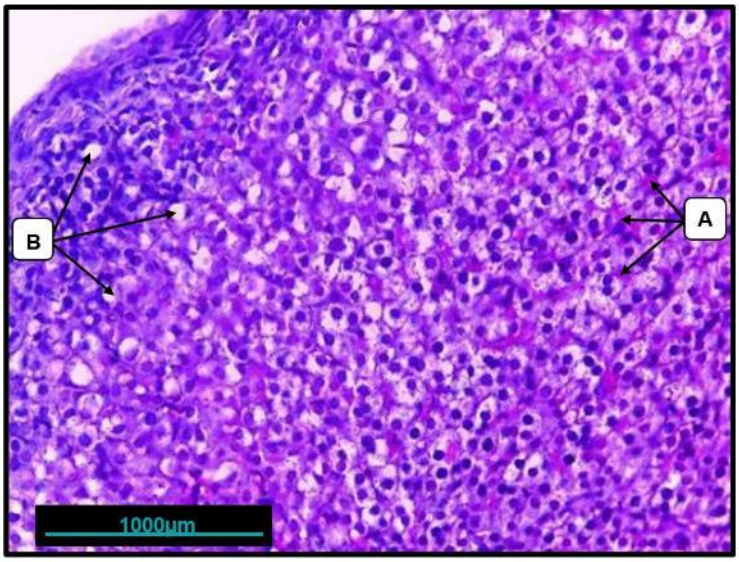

Figure (8) Histostructure of adrenal gland tissue in the hypothyroidism group showing congestion (**A**) of sinusoids and necrosis cells (**B**) (**400 X**)

DISCUSSION

Our study aimed to recognize the effect of hypothyroidism on the aldosterone hormone, Na, K, and its impact on the function and tissue architecture of the adrenal gland. The results of our study displayed an increase in thyroid stimulating hormone(TSH) as a result of primary hypothyroidism, which led to reduce the secretion of aldosterone hormone agree with [11], [12] and this may be due to damage in glomerulosa cells and reduced plasma renin activity (PRA) and concentration as a result of damage in juxtaglomerular cells [12].In the current study hyponatremia is noticed probably due to decrease in renal plasma flow lead to decline glomerular filtration rate(GFR) and restricted urinary concentrating ability and defect in renal conservation of sodium so lead to elevated urinary excretion of sodium agree with[13][14], and [15] who reported by them the thyroid hormones modulate the activity sodium – potassium pump in - most of the tissue [16]. The present study showed no significant variation in potassium levels agree with [17] but is contradictory to [18], who report a decrease in potassium levels in hypothyroidism, and in contrast to [19], where significant elevation in potassium levels is reported in hypothyroidism. There are many factors that collectively maintain potassium levels unaffected in the hypothyroid group, such as natural compensatory mechanisms and limited impact of thyroid hormones in potassium regulation, small sample size, and environmental conditions. The result of our study demonstrated the presence of histopathological changes in adrenal tissues in the hypothyroid rats. These changes include separation of the capsule from the cortex in several areas, cell and fiber destruction, and breakdown of plasma membranes. This leads to the fusion of cells with each other, and the nuclei

appear dark, while nucleoli disintegration is observed in some cells, indicating weakened gland activity compared to the control group, as noted by [20].

Conclusion

The study concluded that the disturbance in adrenal hormones and mineral salts, as well as the tissue destruction, is a result of the hypothyroid effect.

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