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Physiological Malfunctions for Hormones Exciting Histological Alterations of the Thyroid Glands in Cretinous Arabi Sheep

الإعطال الفسيولوجي الهرموني المؤثر على التركيبة النسجية للغدة الدرقية في الاغنام العرابية القميئة

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Abstract:

The present study showed that cretinous Arabi rams and ewes explained an obvious elevation in TSH values accompanied with a declined values of both T3 and T4 from the same samples. Each of these results revealed a significant difference in probability values under 0.05 ($p< 0.05$) when compared with samples from normal sheep of the same species. Histologically, the affected thyroid glands appeared to have big follicular radiuses accompanied with fibrosis and big sizes of surrounding epithelial cells.

The conclusion of our study proved that cretinous sheep had a disturbance in thyroid hormone secretion physiology opened the hypothesis that it is primary hypothyroidism type which affect negatively on the tissues of this gland.

Keywords: cretinism, Arrabi sheep, T3, T4, TSH, hypothyroidism.

الخلاصة:

بينت هذه الدراسة أن الكباش والنعاج القميئة أظهرت ارتفاعا واضحا في قيم TSH مصحوبة بقيم منخفضة لكل من هرموني T3 و T4 من نفس العينات. كل من هذه النتائج كشفت عن اختلاف كبير في القيم الاحتمالية تحت 0.05 ($0.05 > p$) عند مقارنتها مع عينات من الأغنام العادية من نفس الأنواع. أما الفحوصات المجهريّة النسيجيّة فأبدت تليّفاً مقروناً بوجود زيادة في أقطار الحويصلات الدرقانيّة مع علامات لزيادة في أعداد الخلايا الطلائيّة المبطّنة لتلك الجريبات.

ان الإستنتاج الواقعي لدراستنا يبين أن الأغنام القميئة عانت اضطرابات وظيفية في إفراز هرمون الغدة الدرقية مما يسند فرضيّة ان هذا النوع من العلّة هو قصور الأفراز الدرقاني من النوع الإبتدائي والذي أثّر سلباً في التركيبة النسجيّة للغدّة الدرقيّة.

كلمات مفتاحيّة: القماءة، الأغنام العرّابيّة، ثالث يود الثيرونين، رباعي يود الثايرونين، الهرمون المحرض للدرقيّة، قصور الغدّة الدرقيّة الأولي.

Introduction:

Histopathology term refers to the microscopic examination of tissue in order to study the manifestations of disease.in clinical medicine,histopathology refers to the examination of a biopsy or surgical specimen by a pathologist, after the specimen has been processed and histological sections have been placed on glass slides [(1)]. This branch of medical-life science help many researchers and doctors to investigate and solve a lot of thyroid problems in human as well as animals[(2.)].

Cretinism is a sickness arising from congenital deficiency of thyroid hormones (congenital hypothyroidism) usually due to maternal hypothyroidism.Congenital hypothyroidism can be endemic, genetic, or sporadic. If untreated, it results in mild to severe impairment of both physical and mental growth and development [(3)]. Signs of cretinous animals may include shortness of stature, swelling of the skin, loss of water and hair, delayed of bone maturation, thickened skin,

enlarged tongue, or a protruding abdomen, neurological impairment[4]. On the same line, sporadic and genetic cretinism results from abnormal development or function of the fetal thyroid gland. Thyroxine must be dosed to combat this case as it's done in many countries [5].

Around the world, the most common cause of congenital hypothyroidism is iodine deficiency [6]. Cretinism is therefore most probably due to a diet deficient in iodine. It has affected many people worldwide and continues to be a major public health problem in many countries. Iodine is an essential trace element, necessary primarily for the synthesis of thyroid hormones. Iodine deficiency is the most common preventable cause of brain damage worldwide. Although iodine is found in many foods, it is not universally present in all soils in adequate amounts. Most iodine, in iodide form, is in the oceans where the iodide ions oxidize to elemental iodine, which then enters the atmosphere and falls to earth as rain, introducing iodine to soils [7]. Earth deficient in iodine is most common inland and in mountainous areas and areas of frequent flooding, but can also occur in coastal regions owing to past glaciation, and leaching by snow, water and heavy rainfall, which removes iodine from the soil. Plants and animals grown in iodine deficient soils are correspondingly deficient. Populations living in those areas without outside food sources are most at risk of iodine deficiency diseases. Iodine deficiency results in the impairments in varying degrees of physical and mental development. It also causes gradual enlargement of the thyroid gland, referred to as a goitre. It is being combated in many countries by public health campaigns of iodine administration [8,9].

The thyronines act on nearly every cell in the body. They act to increase the basal metabolic rate, affect protein synthesis, help regulate long bone growth (synergy withgrowth hormone) and neural maturation, and increase the body's sensitivity to catecholamines (such as adrenaline) by permissiveness [10,11]. The thyroid hormones are essential to proper development and differentiation of all cells of the human body. These hormones also regulate protein, fat, and carbohydrate metabolism, affecting how body cells use energetic compounds. They also stimulate vitamin metabolism. Numerous physiological and pathological stimuli influence thyroid hormone synthesis. Thyroid hormone leads to heat generation in humans [12]. However, the thyronamines function via some unknown mechanism to inhibit neuronal activity; this plays an important role in the hibernation cycles of mammals and the moulting behaviour of birds. One effect of administering the thyronamines is a severe drop in body temperature [13].

The aim of this study was focused on determining the harmony between T3, T4, and TSH in cretinous Arrabi sheep in addition to record the type of hypothyroidism beating those animals and affecting its histology.

Materials and methods:

The numbers of cretinous animals used in this research reached to 20 ram and 15 ewe versus the same number of normal Arabi sheep, all of those were examined to detect and compare the values of thyrionines.

Blood samples had been collected by syringes from the jugular veins, later blood serum separated by electric centrifuge (Lab line stock center- India), then kept inside the jug supplemented with ice pieces before sending it to the clinical chemistry laboratory where they assayed about triiodothyrionine and thyroxin by radioimmunoassay Gamma instrument (HIDEX Co., Ltd- Finland), while thyrotropin releasing hormone assayed by immunoradiometric assay Gamma instrument (HIDEX Co., Ltd- Finland) Gamma instrument (HIDEX Co., Ltd- Finland). It's worth mentioning that the tools used in our experiment were manufactured by Yancheng huida medical instruments Co., Ltd- China, and the kits of immune analyses supplemented by Perkin-Elmer Co.- USA.

Histological samples obtained, kept, fixed, crossed, processed, and stained before they are examined under light microscope according to the text of practical histology techniques by Suvarna et.al.[14].(samples from thyroid gland tissue by process surgical).

Statistical analysis used in our research is T-student's test that it is a statistical hypothesis test follows a Student's *t* distribution where the null hypothesis is supported [15].

Results:

Histological sections explain signs of disorders includes obvious expansion in the radiuses of thyroid follicles accompanied with an incidence of hemorrhage and fibrosis familiar in several sections. Other slides explain what it's like non-symmetrical projections in some follicles. (image 1 & 2).

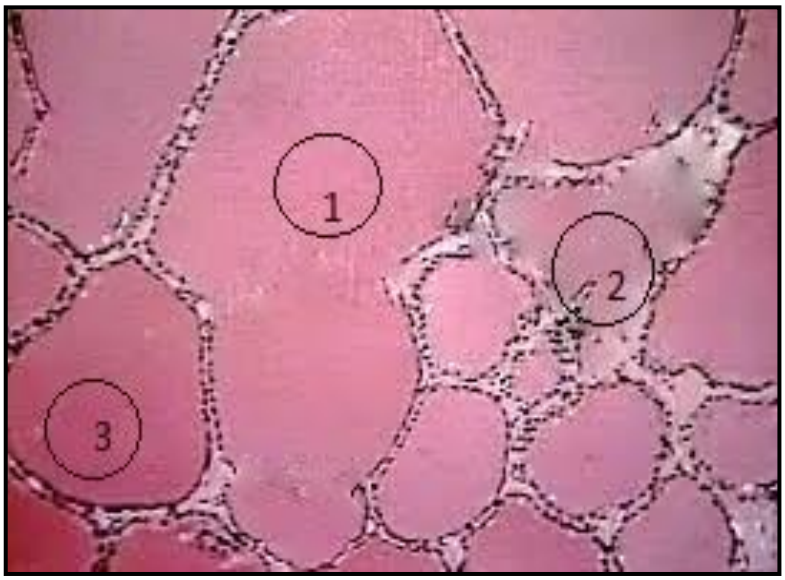

Image no. 1: showing large abnormal follicle① signs of fibrosis② and normal one③ H&E stain, 250 X.

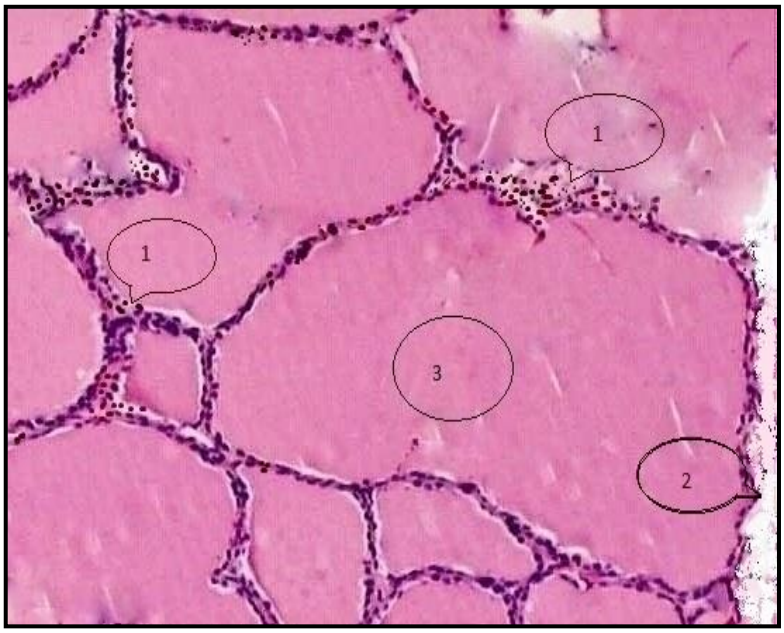

Image no. 2: declares abnormal number and reactions of epithelial cells① fibrotic and abnormal follicles②③ H&E stain, 250 X.

The collected data shows that each of triiodothyrionine and thyroxine declined in their values for the cretinous sheep in comparison with normal ones (controls). This elevation appeared to be as a significant difference where the P value < 0.05.

On the other hand, the values of thyrotropins releasing hormone in cretinous sheep elevated to record a significant difference at P value < 0.05 when compared with control normal sheep. (table 1).

Table (1): the T3, T4 and TSH values in cretinous and normal Arrabi sheep

Sheep casing	Sex	T3 values (Nmol/L)	T4 values (Nmol/L)	TSH values (MIU/L)
Cretinous= 35	Ram=20	1.01±0.81 ↓	55.11±1.21 ↓	0.19±0.11 ↑
	Ewe=15	1.09±0.6 ↓	58.09±1.54 ↓	0.2±0.019 ↑
Control=35	Ram=20	1.45±0.29	79.35±19.19	0.125±0.015
	Ewe=15	1.5±0.22	81.44±2.02	0.13±0.019

Discussion:

Histological data and investigations proved that there is hyperplasia case leading to abnormal malformations correlated directly or indirectly with the deficiency of iodide engulfed in the daily food due to several factors concentrated mostly about the pregnant female excessed food rich iodine intake which may cause an overload on the thyroid gland physiology in embedding this member [16], or what it'll be expected to being a deficiency in iodine supply in the foodstuff [17]. At this condition, Fibrosis are involving stimulated cells laying down connective tissue, including collagen and glycosaminoglycans. Immune cells called macrophages, and damaged tissue between surfaces called interstitium release TGF beta. This can be because of numerous reasons, including inflammation of the nearby tissue, or a generalized inflammatory state, with increased circulating mediators. TGF beta stimulates the proliferation and activation of fibroblasts, which deposit connective tissue [18].

According to the results we can interpret that all of the events recorded in this experiment and research precisely can be expressed as primary hypothyroidism that is considered a problem arose in the thyroid gland itself. Hypothyroidism is thyroid hormone deficiency. It is diagnosed by clinical features such as a typical facial appearance, hoarse slow speech, and dry skin and by low levels of thyroid hormones. Management includes treatment of the cause and administration of thyroxine [19,20].

Primary hypothyroidism is due to disease in the thyroid; thyroid-stimulating hormone (TSH) is increased. The most common cause is autoimmune [21]. It usually results from Hashimoto thyroiditis and is often associated with a firm goiter or, later in the disease process, with a shrunken fibrotic thyroid with little or no function. The 2nd most common cause is post-therapeutic hypothyroidism, especially after radioactive iodine therapy or surgery for hyperthyroidism or goiter. Hypothyroidism during overtreatment with propylthiouracil, methimazole, and iodide abates after therapy is stopped [22,23].

Several scientists and researchers shows that most patients with non-Hashimoto goiters are euthyroid or have hyperthyroidism, but goitrous hypothyroidism may occur in endemic goiter. Iodine deficiency decreases thyroid hormonogenesis. In response, TSH is released, which causes the thyroid to enlarge and trap iodine avidly; thus, goiter results. If iodine deficiency is severe, the patient becomes hypothyroid, a rare occurrence in the US since the advent of iodized salt [24,25].

Some research papers explained that iodine deficiency can cause congenital hypothyroidism. In severely iodine-deficient regions worldwide, congenital hypothyroidism (previously termed endemic cretinism) is a major cause of intellectual disability[26,27]. Rare inherited enzymatic defects can alter the synthesis of thyroid hormone and cause goitrous hypothyroidism [28].

Hypothyroidism according to several researches may occur in patients taking lithium perhaps because lithium inhibits the hormone release by the thyroid. Hypothyroidism may also occur in patients taking amiodarone or other iodine-containing drugs, and in patients taking interferon-alfa.

Hypothyroidism can result from radiation therapy for cancer of the larynx or Hodgkin lymphoma (Hodgkin disease) [29]. The incidence of permanent hypothyroidism after radiation therapy is high, and thyroid function (through measurement of serum TSH) should be evaluated at 6- to 12-mo intervals [30].

It proved that the majority of cases of hypothyroidism occurs due to the destruction of the thyroid glands by a type IV autoimmune response, a process known as lymphocytic thyroiditis because this type of response is mediated by T cells [31]. This autoimmune response develops spontaneously in most affected animals and usually progresses through a sequence of thyroiditis to necrosis and atrophy. In some cases, the administration of sulphonamide antibiotics may induce a reversible form of lymphocytic thyroiditis. Lymphocytic thyroiditis may occur concurrently with other immune-mediated endocrine diseases such as lymphocytic parathyroiditis or Addison's disease producing autoimmune polyglandular syndromes [32,33].

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