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Sex Differences in Thyroid Gland Structure of Rabbits

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Abstract**—**The aim of the present investigation was to compare sex differences in thyroid gland structure of rabbits. Five adult male and five adult female (3.1-3.5 kg body weight) New Zealand white rabbits were used in the experiment. Results showed that at light microscopic level, there was no sex difference in microscopic appearance of the thyroid glands. At electron microscopic level, however, the mitochondria and the microvilli of the follicular cells are more numerous and the Golgi complex is also more extensive in male rabbits in comparison to females. Results obtained from micrometric measurements showed that the volume density of the follicles is higher in males than in females, but the differences are not statistically significant .The volume density of epithelium and the height of follicular cells are significantly greater in males than in females and reverse is true about the volume density of interstitium ($p<0.05$). The volume density of colloid is also greater in females (66±6) than in males (60±7) but the differences are not statistically significant .It was concluded that sex has limited effects on histomorphometric properties of thyroid gland in rabbits.

Keywords**—**Rabbit, Thyroid Gland, Sex difference, Electron microscope

I. INTRODUCTION

THE thyroid gland is possibly the most highly vascularized endocrine gland in mammals and appears to be one of the oldest vertebrate endocrine glands phylogenetically. Thyroid hormones influence many aspects of reproduction, growth, differentiation, and metabolism. Many of these actions occur cooperatively with other hormones, and the thyroid hormones enhance their effectiveness [19]. The thyroid parenchyma is composed of two cell types: the follicular cell, which lines each follicle, and the parafollicular cell, which exists between adjacent follicles [20]. In both birds and mammals, thyroid and gonadal functions have often been linked through positive or negative thyroid-gonadal interrelationships and, in most species studied, thyroid activity follows an annual cycle closely correlated with the sexual cycle [1]. Presence of androgen receptors has been reported in thyroid tissue of rat, primate and human [2, 21]. Estrogen receptors are also observed in pituitary thyrotrophs and thyroid follicular cells [6, 24]. However, in available literature there is little information characterizing differences in thyroid gland structure between the sexes in animals. The aim of the present study was therefore to evaluate the effects of sex on thyroid histological and stereological parameters in rabbit.

II. MATERIALS AND METHODS

Five adult male (3.3-3.7 kg body weight) and five adult female (3.1-3.5 kg body weight) New Zealand white rabbits bred in our colony were used in the experiment. Animals were maintained on normal rabbit pellets and water ad libitum.

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After two weeks, the animals were deeply anesthetized with ketamin and fixed by intravascular perfusion via the left ventricle with buffered d pieces of tissue were immersed immediately in 10% buffered formalin for light microscopy or 2.5% glutaraldehyde in 0.1 neutral buffer for electron microscopy. Paraffin-embedded sections were cut at 5 µm and stained with haematoxylin-eosin. Small pieces (cubes of approximately 1 mm) of the previously removed segments of the glands were fixed by immersion in 2.5% glutaraldehyde in 0.1 M sodium cacodylate buffer for two hours. The pieces were washed with buffer, postfixed in 1% osmium tetroxide in buffer, dehydrated with ethanol and embedded in resin. Ultrathin (70-90 nm thick) sections of the thyroid glands were cut and mounted on 200 mesh copper grids and stained with uranyle acetate and lead citrate. Stereological measurements were performed using a point-counting method and relative volumes (Vv) of follicles, epithelium, colloid and interstitium were measured using method described by Šošić-Jurjević et al. [8]. All stereological results were statistically evaluated by Student t-test. Results are reported as mean ± SEM with a significance level of 0.05.

III. RESULTS

At light microscopic level, there was no sex difference in microscopic appearance of the thyroid glands. In both sexes the thyroid follicles vary greatly in shape as well as in size, but they are usually irregularly oval to spheroid in shape. Each follicle consists of a layer of simple epithelium enclosing a cavity, which usually is filled with a gel-like material, colloid. The nuclei of the follicular cells are rounded in shape, and their cytoplasm is highly basophilic.

At electron microscopic level, the mitochondria of the follicular cells which are typically rod-shaped are more numerous in males than in females. The Golgi complex which is located on the apical side of the nucleus is also more extensive in male rabbits in comparison to females. In both sexes, the cytoplasm contains numerous lipid droplets with different sizes. The apical end of the follicular cell has short, irregularly distributed microvilli which are more numerous in males than in females (Figure 1 and 2).

The important findings of morphometric measurements are as follows:

i. The volume density of the follicles is higher in males (88±5) than in females (82±6), but the differences are not statistically significant.

ii. The volume density of epithelium is significantly greater in males (28±4) than in females (16±4) ($p<0.05$).

iii. The volume density of interstitium is significantly greater in females (18±3) than in males (12±2) ($p<0.05$).

iv. The volume density of colloid is greater in females (66±6) than in males (60±7) but the differences are not statistically significant.

v. The height of follicular cells is significantly greater in males (12.2±0.2) than in females (10.9±0.4).

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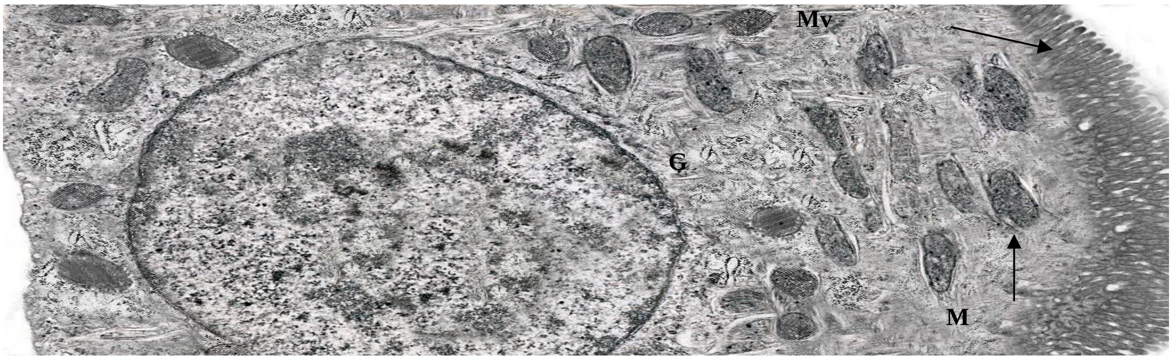

Fig. 1 Transmission electron micrograph showing a follicular cell of thyroid gland in male rabbit. Note the presence of numerous mitochondria (M), extensive Golgi complex (G) and many crowded apical microvilli (Mv) (× 15200)

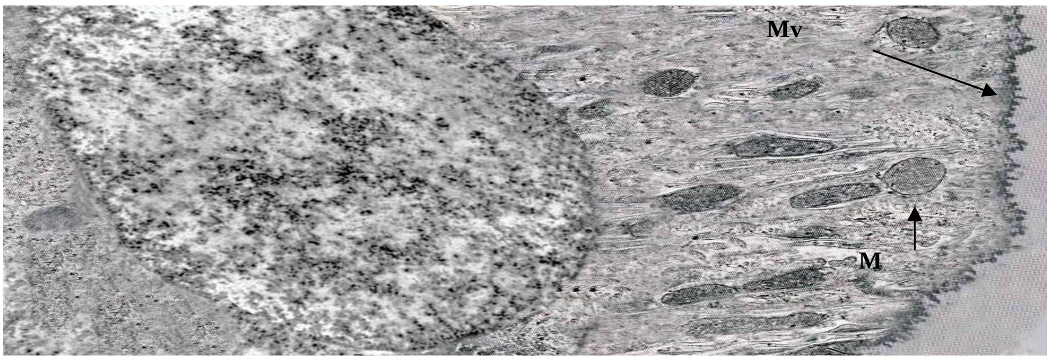

Fig. 2 Transmission electron micrograph showing a follicular cell of thyroid gland female rabbit. Note that the mitochondria (M) and microvilli (Mv) are less abundant in comparison to those in male rabbit. (× 15200)

IV. Discussion

The present study has highlighted some of the histomorphometric differences in the male and female thyroid gland. Results obtained from the present study showed that at light microscopic level, there was no sex difference in microscopic appearance of the thyroid glands. At electron microscopic level, however, the mitochondria and the microvilli of the follicular cells are more numerous and the golgi complex is also more extensive in male rabbits in comparison to females. These structural differences reveal an apparent structural dimorphism and show that the metabolic activity of the thyroid gland is probably higher in male in comparison to the female rabbits. The thyroid gland operates in a complex hormonal environment that involves the interplay of hormones of the pituitary and gonads, as well as other hormones and neurotransmitters. Thyroid hormones act on the gonadal axis, at peripheral or central levels. Estrogen receptors were observed in pituitary thyrotrophs and thyroid follicular cells [6, 7] and presence of androgen receptors has been reported in thyroid tissue of rat, primate and human [2, 16, 21]. Testosterone and estradiol modulate TSH-binding in the thyrocytes of Wistar rats, which is influenced by age and sex of the animals [3]. Sex hormones are important factors for development of thyroid neoplasms [22] and clinical and epidemiological studies suggest that diseases of the thyroid, including the incidence of tumours are predominant in females, while the rate of malignancy is higher in males [13, 25, 26]. In humans, the concentration of antigen receptors is higher in the thyroid gland of males, while estrogen receptors are higher in females [16]. Banu et al. (2002b) [4] stated that gonadectomy significantly decreases serum and thyroidal testosterone and estradiol and concentrations of androgen receptor and estrogen receptor in the thyroid and replacement of sex steroids to gonadectomised rats restores the normal level of sex steroids, androgen and estrogen receptors in rat. Fatahian and Parchami [9] stated that orchidectomy suppresses the function of the thyroid gland in male dogs. Doris [8] stated that gonadectomy depresses the function and, therefore, may affect the metabolic processes controlled by the thyroid gland in male rabbits. Mori et al. [18] stated that female rats are more susceptible to occurrence of thyroid carcinoma. They also stated that Ovariectomy lowers the incidence of thyroid carcinoma in female rats, but castration did not influence it.

Results obtained from the present study showed that parallel to the morphological appearance, the morphometric parameters in the rabbit thyroid gland show also a clear sexual dimorphism which depends primarily upon the densities of the epithelium and interstitium in the gland, so that the volume density and the height of follicular cells are significantly greater in males than in females and the reverse is true about the volume density of interstitium which is significantly greater in female rabbits in comparison to males. These findings may be due to the different effects of the sex steroids on the gland. Malendowicz and Bednarek [14] stated that volume fractions of epithelium and stroma are higher and that of colloid lower in male than in female rats and the epithelium/colloid ratio is higher in the males. They also stated that the average volume of a thyroid follicular cell is higher in males than in females, although the thyroid gland contained similar numbers of follicular cells in both sexes.

They concluded that the sex dimorphism in the rat thyroid depends upon a difference in the mean volume of thyroid follicular cells, with males having larger cells than females. However, in both sexes the thyroid gland contains a similar quantity of these cells. Malendowicz and Majchrzak [14] stated that after reaching puberty in the female thyroid gland a gradual lowering of the volume fraction of epithelium and an increase in volume fraction of colloid are observed. Due to these changes epithelium/colloid ratio in female rats markedly declines between 42 and 84 days of postnatal ontogenesis while in the male rats this ratio is higher and does not show such a distinct decline. Since sex steroids can affect thyroid activity at various points in the thyroid axis (thyroid gland, plasma thyroxine levels, thyroxine secretion rate, pituitary TSH values) [5, 7, 12, 15], the differences in volume densities of the epithelium and interstitium seen in the present study between males and females may also be due to the indirect effects of the sex steroids on the thyroid gland. Banu et al. [3] stated that thyrocytes of immature male rats challenged with linearly increasing doses of TSH or testosterone showed a dose-dependent increase in TSH-binding. However, thyrocytes of immature female rats challenged with testosterone showed a gender-specific response. While, there was a linear increase in TSH-binding in thyrocytes of males, a biphasic response was evident in thyrocytes of females. In the case of thyrocytes from adult rats, testosterone induced a dose-dependent change in TSH-binding in males, which reached the peak in response to 12.5 ng testosterone, and diminished thereafter. In contrast, estradiol was inhibitory to TSH-binding to thyrocytes of adult male rats. Estradiol showed a clear gender-specific stimulation of TSH-binding in thyrocytes of females and an inhibition of the same in males. They concluded that sex steroids modulate TSH-binding in rat thyrocytes, which may vary according to the age and sex of the animal. Lower plasma T4 and TSH concentrations associated with a higher plasma T3 level have been reported in the female in comparison with the male rats [24-26]. Santini et al. [17] stated that serum TSH is lower in female than in male adult rats. It was concluded that sex has limited effects on histomorphometric properties of thyroid gland in rabbits.

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