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EFFECT OF THYROID FUNCTION ON REPRODUCTIVE PERFORMANCE OF BALADI GOATS WITH EMPHASIS ON SUPEROVULATION RESPONSE AND EMBRYOS RECOVERY

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SUMMARY

This study aimed to investigate the effect of thyroid function on reproductive performance in female goats (does). Two experiments were carried out on 11 mature cyclic Baladi does. In the first experiment, does were either kept as a control group (N=3) or drenched thiourea (50 mg/ kg body weight/30 days) on day 7 of the synchronized estrus to induce hypothyroidism (N=8). Estrous activity was observed and blood samples were collected on days 0,15 and 30 after drenching thiourea as well as on day 7 after PGF2 injection. A trial was made for treatment of hypothyroidism group with thyroxine supplementation for 30 days. In the second experiment, the above-mentioned does were divided into 3 groups. A control (N=3), hypothyroidism (N =4) and thyroxine treated hypothyroidism (N=4) groups. All groups were synchronized using progesterone impregnated intravaginal sponge for 18 days. Does were given PMSG at sponge removal and LH at heat and allowed to be mated . Blood samples were collected on days 0,15 and 30 as well as on the days of heat and of slaughtering (day 5 after heat). Thyroids, pituitary glands and genital organs were collected. Numbers of CL and Graafian follicles were counted for evaluation of the superovulation response. Uterine horns were flushed with phosphate buffered saline and embryos were recovered. Tissue samples were processed for histopathological examination. All blood samples were analyzed for thyroid hormones and progesterone (RIA) as well as for total lipids, cholesterol, triglycerides and glucose (Colorimetrically).

Results indicated that thiourea is a strong goitrogenic agent in goats as indicated by marked reduction in T4 and T3 levels. Estrous activity was

completely ceased in hypothyroidism group with marked decreases in progesterone values and increases in total lipid and cholesterol values. Moreover, superovulation response, ovulation rate and embryos recovery as well as progesterone, T4 and T3 values were obviously decreased in hypothyroidism group compared with the control group. Hypothyroidism caused obvious pathological changes in the studied endocrine glands as well as the genital organs.

Following thyroxine therapy, estrous activity was not restored despite the improvement in thyroid function, lipid and glucose values. Also, the superovulation response, ovulation rate and embryos recovery as well as progesterone, T4 and T3 were low in the treated group compared with the control group. On the other hand, thyroid size became within normal, ovary revealed increased number of growing follicles and somewhat healthy lutein cells and uterine glansd showed moderate secretory activity after the therapy.

It was concluded that the normal function of the thyroid gland is important for the reproductive function of goats. Hypothyroidism impaired ovarian function even after stimulation with superovulation treatment and it induced pathological lesions in endocrine glands and genital organs. Thyroxine therapy should be applied for long period to give satisfactory results in hypothyroidism.

INTRODUCTION

The thyroid gland is important for maintaining growth, metabolism and function of all body tissues in living organisms (Villar et al., 1998). Reproductive and associated events involving gonadal activity, such as estrus, pregnancy and lactation are known to be under the control of the hypothalamo-hypophyseal-thyroid axis (Reddy et al., 1996). A tight positive relationship between thyroid hormone levels and ovarian function had been reported in bovine (Megahed et al., 1995; Hegazy et al., 1996; Mabrouk, 1997; Ahmed and Ezzo, 1998), ovine (Mostafa, 1998) and caprine (Reddy et al., 1996; Villar et al., 1998).

Hypothyroidism impaired fertility of many animal species and the condition could be improved by thyroid hormone therapy (Maruo et al., 1992). The number of ovulating follicles was reduced in animals suffering from hypothyroidism (Mattheij et al., 1995). There were evidences that thyroxine administration in the presence of gonadotrophic hormones (PMSG) increased the number of healthy follicles in mature rats (Jiang et al., 1999). On the other hand, it was found that the number of corpora lutea in superovulated cows markedly increased following hypothyroidism (Bernal et al., 1999).

The present study was planed to investigate : 1- The effect of experimental hypothyroidism on estrous activity, plasma progesterone values and

some metabolic functions of goats. 2-The superovulatory response and embryos recovery with special reference to possible changes in some blood metabolites and pathological alterations in genital organs and some endocrine glands and 3- The effect of supplementation therapy with thyroxine on the above-mentioned parameters.

MATERIALS AND METHODS

The present study was carried out during May-November, 1999 in the experimental farm of the National Research Center, Abou Rawash, Giza, Egypt.

Experimental animals:

Eleven healthy mature cyclic female Baladi goats (Does) were used. Body weight ranged between 28 and 30 kg and age ranged between 1-1.5 years. Does were raised in open shelter barn under the natural prevailing environmental conditions; at least 12-hrs light and 28-35C° temperature. Each animal was fed on 0.75kg commercial concentrate mixture (Protein not less than 16%). Rice straw and barseem (*Trifolium alexandrinum*) were provided *ad libitum*. Two proven mature males (Bucks) were used for teasing and mating. Does were used for performing two experiments.

Experiment I:

Does were daily observed and teased for detecting estrus for at least 3 cycles. All does were injected (i.m) with 2.50 mg prostaglandin $F_2\alpha$ (0.5 ml Lutalyse,Upjon, the Netherlands) two times 11 days apart for estrous synchronization. Seven days after estrus (Day 0), does were divided into 2 groups:

A-Control group: included 3 does kept without treatment.

B- Experimental group: included 8 does, drenched 50 mg /kg live body weight extra pure thiourea(Riedel-deHaen,Germany)for 30 days to induce hypothyroidism (Ramakrishna and Prasad, 1992).

All does were injected with $PGF_2\alpha$ again at the end of the experiment (in the previously mentioned manner) and were observed for estrous activity. Blood samples were collected in heparinized tubes at the start of treatment (day 0), every 15 days and 7 days after injection of the prostaglandin. Plasma was harvested, by centrifugation (4C°; X1500g) and kept at 20C° until analysis of some hormonal and metabolic constituents.

Experiment II:

Directly after the end of the first experiment, the previously mentioned does were divided into 3 groups:

A-Control group; the same control does of the first experiment.

B-Non -supplemented group; included 4 does kept without treatment following the induction of hypothyroidism.

C- Thyroxine-supplemented group; included 4 does given an oral dose of 100-µg·synthetic thyroxine sodium /doe for 30 days (Eltroxin, Glaxo Wellcome, UK).

All does were observed and blood samples were collected as in the first experiment (days 0,15 and 30 after supplementation and day7 after the second dose of PG $F_2\alpha$).

At the end of the experiment, all does were subjected for superovulatory regimen. Intravaginal progesterone impregnated sponges (Chronogest, Intervet, the Netherlands) were applied to all does for 18 days. At the time of sponge withdrawal, each animal was injected (i.m) with 750 i.u. PMSG (Folligon, Intervet, the Netherlands). Estrus was detected using marked bucks. At the time of heat, 1000 i.u.HCG (Pregnil, Nile Co,Egypt) was injected (i.m) and does were allowed to be mated. On day 5 post estrus, all does were sacrificed, genital organs were inspected and number of corpora lutea and/or Graafian follicles were counted. Uterine horns were flushed with 40 ml of Dulbeccos phosphate buffered saline (d-PBS) enriched with 2% superovulate ewe serum through a silicone 2 ways Foley catheter (8FR-3cc, Nippro, Japan) and embryos were examined for early development and cleavage rate under Stereo microscope(Pintado et al.,1998) . Blood samples were collected on the day of estrus and day of slaughtering. Plasma samples were separated and kept frozen (-20C°) until analysis of the selected parameters.

Plasma analysis:

Plasma samples were assayed for progesterone level (Abraham, 1981) as well as for thyroxine (T4) and triiodothyronine (T3) values (Albertini and Ekins, 1982) by RIA using kits from Diagnostic Product Corporation (Los Angles, USA). Assays had sensitivities of 0.02 ng/ml, 0.25µg/dl and 0.09 ng/ml with intra assays CVs of 4.65, 5.15 and 4.87 %, respectively. Total lipids, total cholesterol, triglycerides and glucose concentrations were colorimetrically determined using available commercial chemical kits (Stanbio, Texas,USA).

Tissue samples

Tissue samples were taken from thyroids, pituitary glands, ovaries and uteri . Samples were prepared for histopathological examination using H&E stain. Alcian blue PAS technique (Sheehan and Hrapchak,1980) was used as a special stain for examination of the pituitary gland.

Statistical analysis:

Data were computed and statistically analyzed using one way analysis of variance, Student t test and Chi square test as outlined by Snedecor and Cochran (1980).

RESULTS

Experiment 1 :

A. Effect of thyroid function on ovarian activity and some blood metabolites in Baladi does:

Oral administration of thiourea in Baladi does successfully induced hypothyroidism as indicated by the significant ($P<0.01$) reduction in

T4 and T3 levels in the blood plasma 15 days later (Table 1). Behavioral signs of estrus were not shown by the experimental goats, in contrast to control does which had cycles length between 19-21 days. Complete cessation of the estrous cycle following treatment with thiourea was confirmed by progesterone value. Just before treatment , progesterone value (ng/ml) on day 7 after the second dose of $PGF_2\alpha$ was not significantly differed between control (1.65 ± 0.18) and hypothyroidism (1.42 ± 0.02) groups. However, at the end of thiourea treatment, progesterone value on day 7 after the second dose of PGF2.was significantly (P<0.01) decreased in hypothyroidism group compared to the control one (<0.02 Vs.1.73 ± 0.20).

The effect of induction of hypothyroidism on some metabolic parameters in the blood of the experimental does was recorded in table (1). Total lipids (P<0.05) and cholesterol (P<0.01) concentrations markedly increased 30 days later while, triglycerides and glucose values did not change significantly (Table, 1).

B-Effect of thyroxine supplementation:

Supplementation of Baladi does following induction of hypothyroidism with thyroxine (100µg /head/30 days) did not lead to the regaining of estrous activity in animals suffering from hypothyroidism. Progesterone value was significantly (P<0.01) decreased on day 7 after $PGF_2\alpha$ injection in treated hypothyroidism group (0.05 ±0.01ng/ml) compared to the value before drenching thiourea (1.43 ± 0.38ng/ml). T4 value raised (P<0.05) 15 days following supplementation and reached the normal value 30 days later. However, T3 value raised (P<0.05) 30 days later. Total lipids, cholesterol, triglycerides and glucose values improved following supplementation as shown in table (2).

Experiment II:

A. Effect of thyroid function on superovulation response and embryos recovery:

Table (3) presents data showing high ovulation response in control does (Fig.1) compared with does suffering from hypothyroidism either before (Fig.2) or after (Fig.3) treatment. In the same time, ovulation rate as indicated by number of corpora lutea, was obviously lower in thyroxine treated group than either control or hypothyroidism groups .

Table(4) revealed that embryos recovery was low and the incidence of unfertilized ova was significantly (P<0.01) high in the hypothyroidism group when compared with either control or treated hypothyroidism groups. Morula and blastocyst were observed in the control group only. Moreover, the cleavage rate was high (P<0.01) in the control group when compared with the other two groups.

Table(1): Effect of thiourea administration on thyroid hormones, lipids and glucose values in blood of Baladi does (Mean ± SE).

Days after Hypothyroidism	Group	T4 (µg/dl)	T3 (ng/d)	Total.Lipids (mg/dl)	Cholesterol (mg/dl)	Triglycerides (mg/dl)	Glucose (mg/dl)
0	Control	3.42±0.12	91.06±1.52	464.00±34.08	105.91±9.16	200.20±25.04	59.02±8.32
	Experim.	3.49±0.10	89.08±0.26	454.13±6.59	107.10±4.23	188.26±7.95	56.12±2.91
15	Control	3.51±0.23	91.99±3.52	461.01±23.67	109.68±13.28	197.80±14.98	54.57±4.03
	Ecperim.	0.71±0.06**	42.64±0.94**	490.50±14.08	116.22±3.78	202.61±17.73	57.70±4.25
30	Control	3.52±0.16	89.16±0.52	460.07±19.09	126.83±1.81	191.89±22.39	54.89±1.97
	Experim.	0.87±0.04**	45.67±1.60**	522.25±2121*	163.10±16.75**	214.06±15.44	53.92±1.118

**P<0.01 * P<0.05 0 time =just after induction of hypothy roidism

Table (2): Effect of supplementation with thyroxine on thyroid hormones , lipids and glucose values in blood of Baladi does following induced hypothyroidism (Mean ±SE).

Days after Supplementation	Group	T4 (µg/dl)	T3 (ng/d)	Total.Lipids m(g/dl)	Cholesterol (mg/dl)	Triglycerides (mg/dl)	Glucose (mg/dl)
0	Non suppl	0.85±002	48.28±1.22	507.50±30.54	160.83±9.49	200.65±26.80	54.97±0.78
	Suppl	0.89±0.08	43.07±2.44	537.00±31.98	169.70±10.04	227.49±16.57	52.86±2.27
15	Non suppl	1.17±0.27	57.51±0.90	448.75±41.20	145.18±5.42	215.87±5.67	50.67±0.23
	Suppl	0.86±0.03*	62.99±6.49	430.25±37.44	127.78±3.99*	202.94±19.08	57.39±1.37**
30	Non suppl	1.48±0.22	60.31±2.79	431.50±16.40	126.90±3.27	219.67±12.32	53.02±1.72
	Suppl	3.30±0.47**	66.64±0.69*	427.25±51.32	123.05±5.43	187.80±18.37	57.34±2.32

**P<0.01 * P<0.05 0 time =just before thyroxin supplementation

Table (3): effect of thyroid function on superovulation response in Baladi does.

Group	No Anim.	Superovulation Response		Corpora lutea		Unovulated follicles	
		No of animals	%	No.	Mean ± SE	No.	Mean ± SE
Normal control	3	3	100.00	46	15.33±4.48[a]	15	5.00 ± 2.08
Hypothyroidism	4	2	50.00	51	12.75 ± 7.97	27	6.75 ± 3.94
Treated hypothyroid.	4	3	75.00	26	6.50 ± 2.70[b]	13	3.25 ±1.25

Groups with different alphabetical superscripts in the same column significantly differ at P< 0.05.

Progesterone values (ng/ml) were significantly (P<0.05) increased in does suffering from hypothyroidism (0.43 ± 0.03) on the day of estrus (day 0) compared with the control group(0.30 ±0.06). On the other hand, values were increased (P<0.05) in the control group (12.34 ± 2.21) during the luteal phase (day 5) if compared with hypothyroidism does either treated with thyroxine (5.14 ± 1.86) or not (4.18± 2.20). Moreover, The effect of thyroid function on some metabolic values in the blood of superovulated Baladi does was recorded in table(5). T4 and T3 values were significantly (P<0.01) decreased in the hypothyroidism group when compared with either thyroxine treated or control groups .

Table(4): Effect of thyroid function on embryo recovery in superovulated Baladi does(Mean± S.E animal).

Group	Unfertilized Ova	Number of cells			Morula	Blastocyst	Cleavage Rate(%)
		2	4	8-16			
Control	1.67±0.27[c]	0.33±0.27	1.33±0.27	4.00±0.47	2.00±0.47	1.33±0.27	86.70[a]
Hypothyroidism.	8.50±0.35[a]	2.50±0.35	2.00±0.00	00.00	00.00	00.00	34.60[c]
Treated hypothyroidism	2.33±0.27[c]	2.00±0.47	1.00±0.47	0.33±0.27	00.00	00.00	55.60[c]

Groups with different alphabetical superscripts in the same column significantly differ at P< 0.01

Table(5): Effect of thyroid function on thyroid hormones, lipids and glucose values in blood of superovulated Baladi does (Mean ±SE).@

Group	T4 (µg/dl)	T3 (ng/d)	Total.Lipids (mg/dl)	Cholesterol (mg/dl)	Triglycerides (mg/dl)	Glucose (mg/dl)
Normal control	3.58± 0.11^{a}	91.76 ±3.33^{a}	464.33 ± 16.18	116.74 ±13.71	190.23 ± 15.04	51.67 ±1. 19
Hypothyroidism	1.75± 0.34^{c}	57.92 ±1.45^{c}	451.50 ± 20.43	127.55 ±4.47	205.86 ± 4.98	53.12 ± 2.57
Treated hypothyroid.	3.22± 0.51^{b}	68.96 ± .98^{d}	429.50 ±21.52	118.50 ± 2.78	209.69 ± 5.54	56.32 ± 2.12

Groups with different alphabetical superscripts in the same column significantly differ at P< 0.01 for a&c, a&d and d&c and P<0.05 for b&c. @ at slaughtering on day 5 after estrus

B -Pathological studies:

Thyroid:

In the hypothyroidism group,the glands become diffusely enlarged in size, dark red to brown in color and firm in texture (Fig 5). Microscopical examination revealed that the thyroid follicles were in different shapes and sizes. Follicles were lined with a single to multiple layers of epithelium that revealed hyperplasia and hypertophy . Proliferation of epithelium cells that completely occupied the lumina with depletion of the colloid was observed in some cases (Fig 6). The proliferation was sometimes regular or mostly aberrant, filling the lumina either partially or completely (Fig 7). The follicular colloid appeared lightly eosinophilic and occasionally showed small vacuolation at the periphery. Blood capillaries were dilated and congested. Proliferation of interfollicular connective tissue was seen.

Following thyroxine therapy, the gland approximately returned to the normal size. Most of the follicles revealed signs of activity,whereas they were lined by high cuboidal epithelium, containing lightly eosinophilic colloid and showed foamy serration at the periphery (Fig 8). Abnormal large follicles distended with deeply eosinophilic colloid and lined by flattened epithelium were sometimes observed. The interface between colloid and follicular cells was smooth and lacked vacuoles (Fig 9).

Pituitary gland:

The most characteristic histopathological changes in the anterior pituitary in thiourea -treated does were hyperplasia, hypertrophy and vacuolation of the basophils (Fig 10). Following thyroxine treatment , basophils appeared more or less similar to those of the control does (Fig 11)and gave strong positive reaction with Alcian blue-PAS stain (Figs 12 & 13).

Ovaries:

The most important histopathological changes in

thiourea- treated does were thickening of tunica albuginea and proliferation of connective tissue stroma. In most of the cases, the number of growing ovarian follicles was reduced and associated with different stages of atresia. A higher incidence of cystic atresia was also observed in the mature follicles. Partial luteinization of theca interna and granulosa cells was noticed. Most of the developing corpora lutea showed necrobiotic changes in the lutein cells which appeared swollen with vacuolization and deeply eosinophilic cytoplasm and pyknotic nuclei (Fig 14). Proliferation of interstitial connective tissue was obvious. Blood vessels were few in numbers and had relatively thick walls. A single case revealed small sized ovaries with complete absence of growing follicles and corpora lutea (Fig.4) . The ovarian tissue consisted merely of proliferative connective tissue stroma with a fair number of primordial follicles.

Following thyroxine treatment, a fair number of growing follicles at different developmental stages associated with decreased number of atresia was observed. Corpora lutea consisted of normal , intact lutein cells with numerous blood capillaries.

Uterus:

In hypothyroidism group, the endometrium revealed focal hyperplasia, vacuolization and desquamation of the lining epithelium (Fig 15). Diffused stromal edema and mononuclear cell infiltration were seen. Blood capillaries were dilated and congested while, blood vessels showed thickening of their walls and hyalinization of tunica media with narrowing of lumina. Fibroblastic proliferation was predominantly observed in most of the cases. In some cases, endometrial glands showed moderate secretory activity. In other cases, degenerative and necrcotizing changes of the glandular epithelium associated with lymphocytic infiltration and periglandular fibrosis were observed (Fig 16).

Following treatment with thyroxine, the most observed picture was in the uterine glands. In most of the cases, they revealed proliferative changes with hypersecretory activity. The glands appeared coiled, branched and their lining epithelium showed hyperplastic changes leading to narrowing and /or occlusion of their lumina(Fig 17).Moreover,mitotic figures were frequently seen in the glandular epithelium (Fig 18).

DISCUSSION

The thyroid gland is the most important endocrine gland for metabolic regulation especially at the cellular level (Cunningham, 1997) . Inability to secrete adequate amount of thyroid hormones often causes metabolic and gonadal disturbances (Tohei et al., 1998).

In this study, administration of thiourea in Baladi does induced hypothyroidism as confirmed by the

reduction in T4 and 3 levels in the plasma (approximately 5 and 2 folds, respectively) 15 days later. Similar results were reported by Reddy et al. (1996) who added that thiourea is the most effective goitrogenic agent in goats. This antithyroidal drug inhibits the secretion of both T4 and T3 as well as the conversion of T4 to T3 in peripheral tissues through depressing the enzymatic activity responsible for their biosynthesis and cleavage (Villar et al., 1998). In the same time, Ramakrishina and Prasad, 1992) recorded that goats are comparatively more susceptible for hypothyroidism than other ruminant.

The present cessation of behavioral signs of estrus following the induction of hypothyroidism was confirmed later by a plasma progesterone value of <1ng /ml. This criterion was previously recorded in bovines (El Sharawy et al., 1987; Megahed et al., 1995; Ahmed and Ezzo, 1998). Hypothyroidism causes disorder in steroid synthesis, folliculogenesis and ovulation . T4 is known to increase the synthesis of adenyl cyclase which stimulates C~AMP formation and in turn steroid secretion from ovarian cells (Cunningham,1997).··The low T4 stimulates the basophils of the anterior pituitary to secrete higher level of TSH . The lower level of T4 and the higher level of TSH suppress the synthesis , release , ratio and the feedback mechanism of both FSH and LH and consequently result in decreased estrogen and progesterone levels and lower the ovarian sensitivity to gonadotrophins which in turn disturb ovarian function (Stewart et al., 1994; Reddy et al.,1996 ;Tohei et al., 1998).

The current blood analysis of hypothyroid does indicated significant increases in total lipids and cholesterol with little changes in triglycerides and glucose concentrations as compared with control goats 30 days following the induction of hypothyroidism. It has been reported that thyroid hormones affect all aspect of lipid metabolism .Low thyroid levels were reported to lower the basal metabolic rate and reduce lipolysis (Mostafa,1998) and to increase plasma cholesterol and lipid concentrations (Cunnigham, 1997). This appears to involve both decreased cell uptake of low density lipoprotein with associated cholesterol molecules and a tendency for decreased degradation of both cholesterol and low density lipoprotein. Therefore, hyperchloesterolemia becomes the hallmark of thyroid hormone deficiency (Cunnigham, 1997 ; Mostafa,1998). However, Simpson et al .(1991) added that hypothyroidism is usually associated with high level of serum triglycerides due to the impairment of its clearance, while Gottlieb and Braverman(1994) reported decreased glucose absorption from the gut with decreased insulin secretion .

Supplementation of Baladi does suffering from hypothyroidism with thyroxine relatively improved blood constituents of T4, T3, lipids and glucose values in a time dependant manner. However, this improvement was not associated with

the occurrence of estrous signs as confirmed later on by progesterone. It was reported that thyroxine supplementation regulates carbohydrate, protein and lipid metabolism via increasing intestinal glucose absorption and facilitating the movement of glucose into both fat and muscle (Gottlieb and Braverman,1994). Furthermore, thyroid hormones facilitate insulin-mediated glucose uptake by cells. Glycogen formation is facilitated by small amount of thyroid hormone, but, glycogenolysis occurs after large doses with emphasis on lipolysis (Cunnigham, 1997).

The high superovulation response (100%) and ovulation rate in control Baladi does in this study was in complete agreement with the findings of Saharrea et al.(1998) in goats superovulated with PMSG +HCG. Induction of hypothyroidism markedly decreased the superovulation response (50%) in experimental does. In rats subjected to hypothyroidism, it was reported that the number of ovulations decreased due to reduction of ovulating follicles (Mattheij et al.,1995) , increased incidence of atresia and interference with the differentiation of granulosa cells with consequent fewer number of antral follicles(Dijkstra et al.,1996) compared with control groups. On the other hand, induction of superovulation in Brahman cows suffered from hypothyroidism led to improvement of body condition status with high ovulation rate and over response to FSH (Bernal et al.,1999).

Following thyroxine therapy, the superovulation response was improved (75%) despite the significant decrease in the ovulation rate compared to control does. It was found that reproductive abnormalities in rats suffering from hypothyroidism were improved following treatment with thyroxine (Maruo et al.,1992). A synergistic effect between thyroxine and FSH was found to play a vital role in granulosa cell differentiation in both pigs (Mochizuki and Maruo,1988) and immature rats (Jiang et al.,1999). Moreover, normal ovulation rate was reported in thyroidectomized rats following thyroxine administration(Hagino,1971).

The marked decreases of embryo recovery and increases of unfertilized ova following induction of hypothyroidism in Baladi does as compared to control were in line with the results of Bernal et al.(1999) who reported low embryo recovery rate, fertilization rate and percent of blastocysts in superovulated Brahman cows following induction of hypothyroidism compared to control.

Mean progesterone values were markedly higher in superovulated normal does when compared with those suffering from hypothyroidism and even after treatment. It was demonstrated that progesterone value on day 6 after superovulation in goats is highly correlated with the number of normal looking CL (Saharrea et al.,1998). However, hypothyroidism induced subnormal general metabolic condition with low LH and FSH and

abnormal lutein cells (Reddy et al.,1996).

Following superovulation ,T4 and T3 values were obviously decreased in both hypothyroidism groups (non-treated and treated) when compared with control does. Similar findings were observed in multifetal pregnancies in women (Oguch et al., 2000)who added that the maternal thyroid function is also controlled by a fetal factor in addition to HCG level. In the same time , controlled ovarian hyperstimulation in women was found to affect the thyroid function, whereas , free T4 decreased while TSH, total T4 and total T3 increased with decreased LH level (Muller et al., 2000) .The later authors added that the low maternal freeT4 and elevated TSH levels during gestation have been associated with impaired psychomotor development in the offspring.

The most prominent pathological findings in the thyroid gland following thiourea treatment in this study were enlargement, hypertrophy and hyperplasia of the follicular epithelium and colloid depletion in some cases. These results were in agreement with those obtained by Nasseri and Prasad (1989; 1990) and Ramakrishna and Prasad (1991; 1992), who attributed the condition (Parenchymatous goiter) to deficiency of thyroid hormones as well as the release of TSH. In the same time, follicular cells can respond to the high level of TSH through the formation of numerous cytoplasmic pseudopodia resulting in increased endocytosis of colloid and release of preformed hormones from follicular lumina. The continued secretion of TSH stimulates the follicular epithelium to become more tall and increased in number (Jubb et al., 1993).

Histopathological examination of the pituitary gland of does suffering from hypothyroidism revealed hypertrophy, hyperplasia and vacuolation of basophils of the pars distalis. Nasseri and Prasad (1989) ,and Ramakrishna and Prasad (1992) reported similar results. These changes could be explained on the light of the over production of TSH as a result of low level of thyroid hormones (Cunningham,1997). Vacuolation of basophils may be related to the extensive distension of the rough endoplasmic reticulum with finely granular electron dense materials (Jubb et al., 1993).

The most obvious changes in ovaries of thiourea treated does were low number of growing follicles, high incidence of atresia and necrobiotic changes in lutein cells of the developing CL. Desquamation of the surface epithelium, necrosis of uterine glands and fibrosis were also evident in uteri. Similar findings were reported by Nasseri and Prasad (1990) The condition was attributed to low general metabolic status following hypothyroidism with consequent low levels of FSH, LH and steroids (Reddy et al., 1996).

Following thyroxine therapy, most of thyroid follicles showed signs of activity with the presence of some colloid distended macrofollicles (Colloid

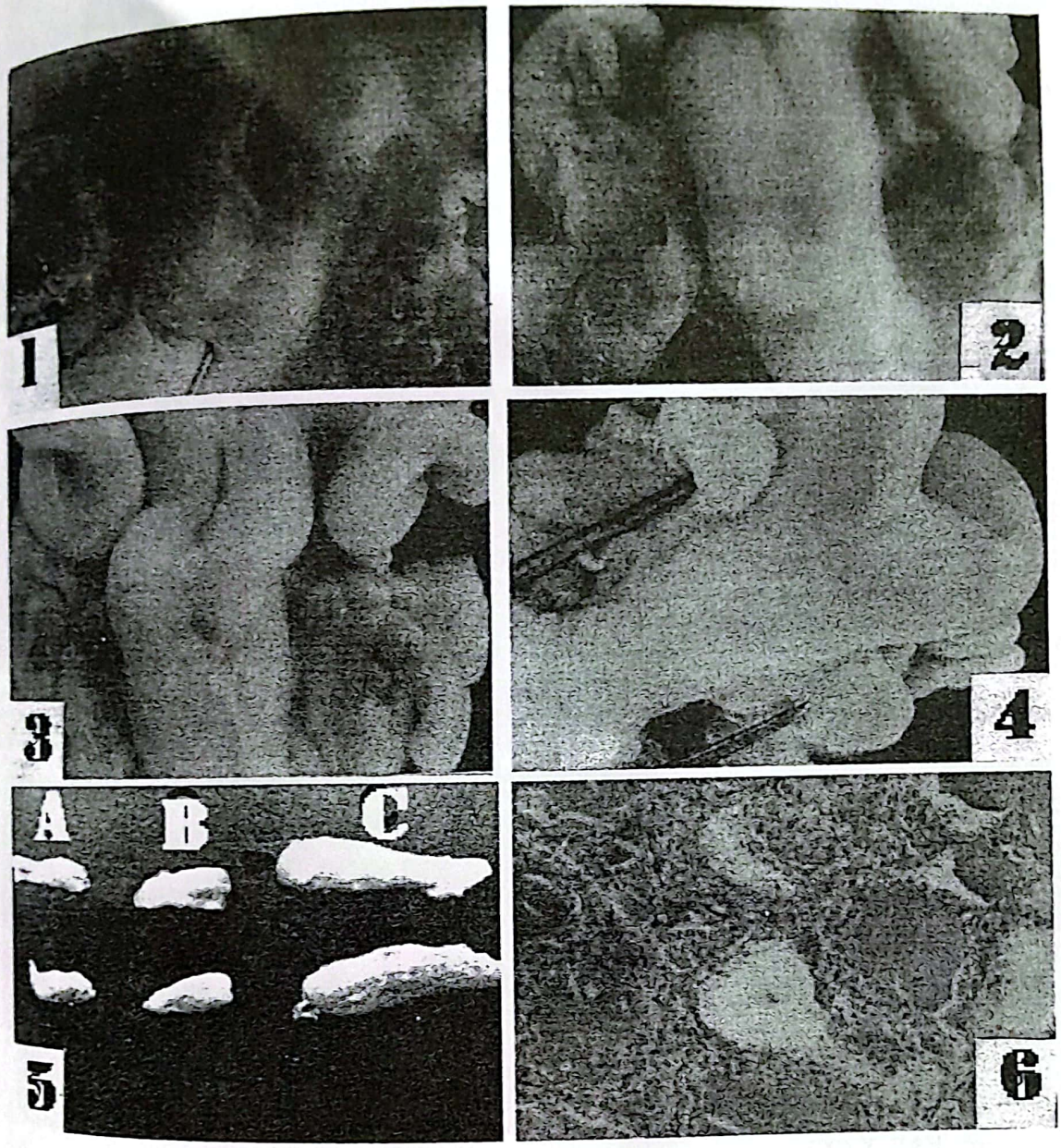

Fig. (1): High ovulation rate in a control doe after superovulation.
Fig. (2): Non ovulatory follicles in a superovulated doe following induction of hypothyroidism.
Fig. (3) : Weak superovulatory response in a doe suffering from hypothyroidism and treated with thyroxine.
Fig. (4): No response in a superovulated doe following hypothyroidism and treatment with thyroxine .
Fig. (5): Diffused enlarged thyroid following treatment with thiourea(C) in comparison with control (A) and thyroxine therapy(B) in does.
Fig. (6): Thyroid , showing follicles lined by multiple epithelial layers, collapsed follicles and depletion of colloid in a doe treated with thiourea (H&E, X 100).

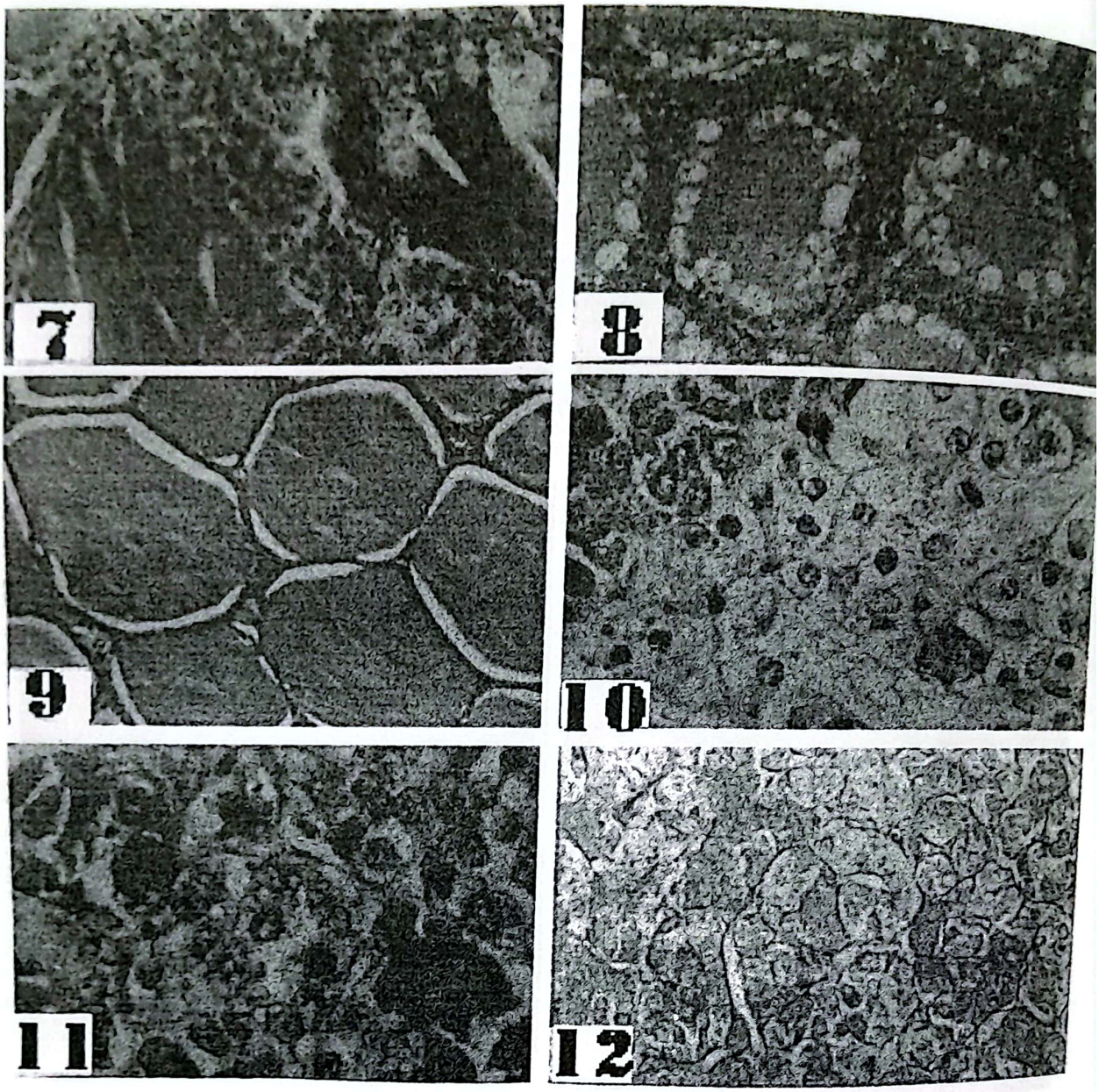

Fig. (7) :Thyroid gland showing proliferation of the follicular epithelium in a doe suffering from hypothyroidism (H&E, X 400).

Fig. (8) :Thyroid, showing active follicles lined by cuboidal cells, contained lightly eosinophilic colloid with vacuolated periphery following thyroxine therapy in a doe (H&E, X 200).

Fig. (9) :Thyroid, showing macrofollicles lined by flattened epithelium and distended with colloid following thyroxine therapy in a doe (H&E, X 100).

Fig. (10) :Pituitary, showing hypertrophy and vacuolation of basophils following hypothyroidism in a doe (H&E, X 400).

Fig. (11) :Pituitary from a normal control doe (H&E, X 400).

Fig. (12) :Positive Alcian blue-PAS reaction in the pituitary of a doe suffering from hypothyroidism, note the bluish coloration of the basophils(X 200).

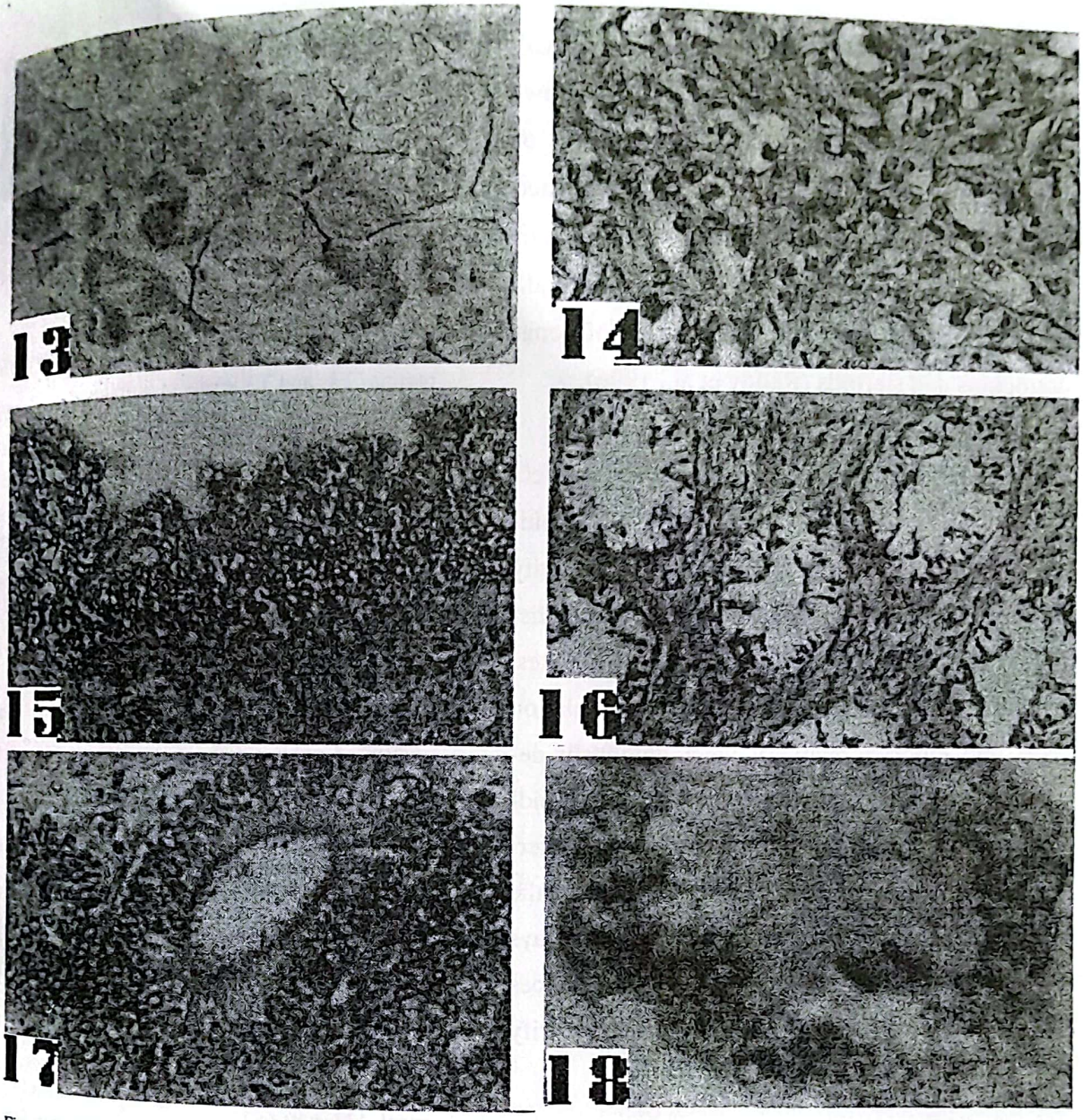

Fig. (13) :Pituitary of a control doe, stained by Alcian blue-PAS technique, note the normal acidophils (magenta) / basophils (bluish) ratio (H&E, X 200).

Fig. (14) :Developing CL. in an ovary of a doe suffering from hypothyroidism, note the necrobiotic changes in lutein cells and the proliferation of interstitial C.T. (H&E,X 100).

Fig. (15) :Endometrium of a doe following thiourea treatment, showing focal hyperplasia, vacuolation and desquamation of the lining epithelium (H&E, X 200).

Fig. (16) :Uterine glands showing necrotizing changes, lymphocytic infiltration and periglandular fibrosis in a doe suffering from hypothyroidism (H&E, X 200).

Fig. (17) :Hyperplasia of epithelium lining the uterine glands with occlusion of lumen after Thyroxine therapy in a doe (H&E, X 400).

Fig. (18): Mitotic division (arrow) of epithelium lining of uterine glands following thyroxine Treatment (H&E, X 1000).

goiter). Pituitary glands restored acidophils / basophils ratio. Ovaries showed fair number of growing follicles and uterine glands revealed signs of activity. Thyroxine supplementation diminished TSH-induced endocytosis following the return of thyroid hormones to the normal level (Jubb et al., 1993) with consequent normal secretion of gonadotrophins and steroids (Reddy et al., 1996).

In conclusion, thyroid function markedly affect reproductive performance of goats. Hypothyroidism interferes with the normal ovarian activity leading to cessation of estrous activity and disturbed the values of some blood metabolites, mainly lipids. Superovulatory response, ovulation rates and embryo recovery were obviously decreased in animals suffering from hypothyroidism. Moreover it also, induced pathological alterations in the endocrine glands as well as in the genital organs. Thyroxine therapy for 30 days provided unsatisfactory results in affected does and further investigations still needed to clarify this aspect.

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