**Evaluation of thyroid and ovarian hormones in rabbits at high altitude**

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Abstract

This study was done on 25 female rabbits (does) . The female rabbits (does) were collected from the Taif governorates. The serum was collected for evaluation of thyroid and ovarian hormones at high altitude.

The serum level of (T3 and FSH) of the rabbit doe showed gradual decrease from young up to senile age while the serum level of (T4) showed gradual decrease from young up to mature pregnant age then it showed increase in the adult lactating age and significant decrease in senile age.

The serum level of estradiol showed gradual decrease from young up to senile age while The serum level of progestone showed increase from young age to immature age then the hormone showed evoke at mature pregnant age then it showed decrease at adult lactating age and another evoke at senile age.

**Introduction**

The productions of domestic rabbits are used for many purpose, meat, fur, laboratory diagnosis and research. Rabbit's meat of all ages shows high values for human consumption, it has a higher percentage of protein than other meats and the meat itself is highly digestible, for this reason it is often recommended for sick people **(Sandford** and **Woodgate , 1974** and **Zotte, 2002).**

The thyroid gland is the largest endocrine gland in the body. It located at the third tracheal ring below the thyroid cartilage, consists of two lobes connected by narrow isthmus. (**Parchami** and **Dehkordi, 2012)**.

Thyroid function is manufacturing of thyroid hormones which are; T3 (triiodothyronine) & T4 (thyroxine) via follicular cells which represented the bulk cells of the thyroid follicles. Thyroid hormones are important in stimulating enzymes essential for glucose oxidation, thereby controlling cellular temperature and body metabolism. **(Moura et al.,1987).**

The ovaries are two in each side. It located on the lateral wall of the pelvis. It supported by the broad ligament. The ovary composed of cortex externally and medulla internally. The ovary functions as an organ of reproduction and also as a gland of internal secretion.. It secrete the mature graffian follicles (Exocrine function) and non-steroidal hormones that act locally **(**Endocrine function**) (Hodges et al.,1985).**

High altitude induces various physiological changes in sea level natives, both on acute and more prolonged exposure, including control of hormonal secretion. A substantial amount of work has been done on hormones regulating water and electrolytes handling or stress hormones at high altitude. Other hormones dealing with metabolic regulations have been scarcely examined in hypoxic conditions. Most studies showed increase in the (T3 and T4) although TSH secretion did not showed any changes at high altitude **(Barnholt et al., 2006),** while other papers showed decrease in thyroid hormones (**Sawhney** and **Malhotra,1990)**.

Certain biochemical, physiological and microanatomical responses occur during acclimatization and adaptation to chronic hypoxia of high altitude, so the aim of the present work is to evaluate the thyroid and ovarian hormonal changes (T3, T4, TSH, estrogen and progesterone ).

**Materials and Methods**

This study was done on 5 groups of female rabbits (5 does in each group) representing the different physiological pattern of the female life. The female rabbits (does) were collected from the Taif Governorates ( at 2512 meter high altitude at temperature ( 24-19 °C) , atmospheric pressure( 365-367 atm ) and RH ( 31-30 %). The collected rabbits belong to order [Lagomorpha](http://en.wikipedia.org/wiki/Lagomorpha) and family [Leporidae](http://en.wikipedia.org/wiki/Leporidae). They collected and raised at Al-shafa rabbits farm.

**Experimental design**

Five Groups of Female rabbits were classified according to age and physiological status young age-immature- mature pregnant – adult lactating - senile).

Blood samples were collected from jugular vein of the rabbits under ether anesthesia **(Boussarie, 1999).** Then, the blood was centrifuged at 4000 rpm for 15 min and serum was collected for hormonal assay.

**Results**

The thyroid hormone (T3) was 121.6333± 0.338428 in young age, 120.4667±0.351188 in immature age, 119.4±0.4 in mature pregnant age, 119.6±0.4 in adult lactating age and 117.9667±0.378594 in senile age. The serum level of (T3) showed gradual decrease from young up to senile age but not significant (Table.1 and Fig.1).

Fig.1: chart showing the serum level of ( T3) at high altitude during different age.

The thyroid hormone (T4) was 4.456667± 1.069268 in young age, 4.3±0.608276 in immature age, 4.086667±0.080829 in mature pregnant age, 4.13±0.417971 in adult lactating age and 3.823333±0.254231in senile age. The serum level of (T4) showed gradual decrease from young up to mature pregnant age then it showed increase in the adult lactating age and decrease in senile age. These changes were significant (Table.1 and Fig.2).

Fig.2: chart showing the serum level of ( T4) at high altitude during different age.

The thyroid hormone (TSH) was 2.436667±0.60302 in young age, 1.89±0.363868 in immature age , 1.77±0.331512 in mature pregnant age, 1.46±0.130767 in adult lactating age and 1.306667±0.106927 in senile age. The serum level of (TSH) showed gradual decrease in TSH from young up to senile age. These changes were significant (Table.1 and Fig.3).

Fig.3: chart showing the serum level of (TSH) at high altitude during different age.

The estradiol hormone was 628.6667±23.07235 in young age, 555.6667±32.1455 in immature age, 535.3333±21.73323 in mature pregnant age, 509.3333±9.609024 in adult lactating age and 493.6667±13.6504 in senile age. The serum level of estradiol showed gradual decrease from young up to senile age. These changes were significant (Table.1 and Fig.4).

Fig.4: chart showing the serum level of estradiol at high altitude during different age

The progesterone hormone was 22.85667±0.176163 in young age, 22.93333±0.723418 in immature age, 23.62333±0.831284 in mature pregnant age, 23.14±1.160517 in adult lactating age and 23.83333±0.321455 in senile age. The serum level of progestone showed increase from young age to immature age then the hormone showed evoke at mature pregnant age then it showed decrease at adult lactating age . The hormone level showed another evoke at senile age. Significant changes in immature and senile age (Table.1 and Fig.5).

Fig.5: chart showing the serum level of progesterone at high altitude during different age.

Table.(1): Serum evaluation of hormones at high altitude

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **young** | **immature** | **Mature Pregnant** | **Adult Lactating** | **Senile** |
| **T3****dl/ng** | 121.6333± 0.338428 | 120.4667±0.351188 | 119.4±0.4 | 119.4±0.6 | 117.9667±0.378594 |
| **P<0.05** |  | $$0.2689531660027543$$ | $$0.7412073089088149$$ | $$0.7582277154580801$$ | $$0.06364666379597277$$ |
| **T4****dl/ng** | 4.456667± 1.069268 | 4.3±0.608276 | 4.086667±0.080829 | 4.13±0.417971 | 3.823333±0.254231 |
| **P<0.05** |  | $$0.02034000189867454$$ | $$0.0405940100662662$$ | $$0.016815395560309088$$ | $$0.02241388580728107$$ |
| **TSH****ml/ng** | 2.436667±0.60302 | 1.89±0.363868 | 1.77±0.331512 | 1.46±0.130767 | 1.306667±0.106927 |
| **P<0.05** |  | $$0.007152120255869413$$ | $$0.00819134142305691$$ | $$0.008129271858356255$$ | $$0.013203020191325573$$ |
| **Estradiol ml/pg** | 628.6667±23.07235 | 555.6667±32.1455 | 535.3333±21.73323 | 509.3333±9.609024 | 493.6667±13.6504 |
| **P<0.05** |  | $$0.035944330094193365$$ | $$0.00753884265804583$$ | $$0.0012443738519240517$$ | $$0.0010076978752588$$ |
| **Progesterone- ml/ng** | 22.85667±0.176163 | 22.93333±0.723418 | 23.62333±0.831284 | 23.14±1.160517 | 23.83333±0.321455 |
| **P<0.05** |  | $$0.030499152762722397$$ | 1.0 | $$0.4883100186274485$$ | $$0.008428195031397107$$ |

**Discussion**

The reduced availability of oxygen owing to low barometric pressure is the basic problem associated with high altitude (HA). The acute exposure to reduced partial pressure of oxygen at (HA) decreases arterial oxygen saturation, stimulates the sympathoadrenal system, and provokes shifts in substrate metabolism **(Mazzeo** and **Reeves,2003).**

Our results indicated gradual decrease in the level of plasma T3 and T4, and it reached the maximum decrease at senile age. These observations in rabbits are in agreement with those of **Martin et al., (1971)** in rats who observed a 54% reduction in plasma protein bound iodine (PBI) and of **Connors and Martin (1982)** who recorded a marked decline in plasma T3 and T4 in rats exposed to chronic hypoxia for 5 weeks. These results indicate that repeated short-term hypoxic exposure is able to diminish the effect of chronic hypoxia on thyroid function. However, our findings of decreased thyroid activity in rabbits exposed to hypoxia are contradictory to that of **Nelson and Anthony (1966)** who observed unaltered thyroid activity in rats exposed to simulated altitude of 5486 m. Lowering serum level of T4 and T3 lead to hypofunction and failure of the thyroid activity **(Ingbar** and **Woeber 1981).**

Our results also reported decrease in the serum level of TSH. This hormone is secreted from the anterior pituitary as stimulating hormones for thyroid function through negative feedback mechanism **(Hershman** and **Pekary 1985)**. More recently, evidence for thyroid hormone inhibition of thyrotrophic releasing hormone (TRH) release has become available **(Rondeel et al., 1988).** On the other hand (**Benso et al., 2007)** showedan increase in free thyroxine and decrease in free tri-iodothyronine (T3) but the level of TSH not changed.

The serum level of female hormone showed fluctuation in rabbits does serum at high altitude due to cyclic changes. So the estimation of the hormones affected by the cyclic phase of the rabbit estrous cycle. These results were supported by the findings of (**Escudero et al.,1996)** reported that during early follicular phase serum estradiol levels were significantly higher at high altitude than at sea level (P < 0.05). During the late follicular phase the production of estradiol was higher at sea level than at high altitude (P < 0.05). The peak of serum estradiol was at day -1 in Lima and in day 0 at high altitude. At ovulation, the serum estradiol levels in women at sea level were 55.1% of the peak, but remained at high levels (80% of the peak) in women at high altitude (P < 0.05). The second increase of serum estradiol occurred earlier at sea level than at high altitude. From days +12 to +15, there was a significant decline in serum estradiol levels in women at sea level (P < 0.05) but not in those from high altitude (P > 0.05). Serum progesterone levels at days +5, and +8 to +12 were significantly higher at sea level than at high altitude.

Our results showed increase in the level of progesterone during the life time of the rabbits at high altitude. This increase is due to progesterone is known to increase hypoxic ventilatory responses with an improvement in oxygen saturation and a reduction in hematocrit for persons residing at 3100 m **(Kryger et al.,1978)** and to benefit patients with hypoventilation syndromes and sleep apnea **( Milerad et al.,1985).**

 In animals, progesterone reduces brain edema, **(Roof et al.,1992)** possibly by tightening the blood brain barrier through the inhibition of Na1/K1-adenosine triphosphatase (ATPase). Progesterone stimulates an estrogen-dependent receptor at hypothalamic sites and influences the respiratory center via a neural pathway **( Bayliss et al.,1992).** Progestrone made improvement in peripheral oxygen saturation (**Wright et al., 2004** )and (**Benso et al., 2007**). On the other hand high altitude induced increase in progesterone levels but no change in pituitary, gonadal, and adrenal hormones in subjects who had a prolonged stay at high altitude but were not performing any physical activity **(Basu et al.,1997).** In contrary to our findings **(Escudero et al., 1996)** showed decrease in the level of progesterone at high altitude.

 The level of estrogen showed fluctuation in serum level. It always decreased in high altitude in rabbits. These results were augmented by the findings of **(Escudero et al. 1996).** While (**Benso et al., 2007**) showed no significant changes in the serum level of estradiol at high altitude.

**References**

**Barnholt KE, Hoffman AR, Rock PB, Muza SR, Fulco CS, Braun B, Holloway L, Mazzeo RS, Cymerman A** and **Friedlander AL.** (2006). Endocrine responses to acute and chronic high-altitude exposure (4,300 meters): modulating effects of caloric restriction. Am J Physiol Endocrinol Metab 290: E1078–E1088.

**Basu M, Pal K, Prasad R, Malhotra AS, Rao KS and Sawhney R.C.** (1997) .Pituitary, gonadal and adrenal hormones after prolonged residence at extreme altitude in man. International Journal of Andrology, 20 153–158.

**Bayliss D.A and Millhorn DE.** (1992).Central neural mechanisms of progesterone action: application to the respiratory system. J Appl Physiol 73: 393–404.

**Benso A, Broglio F, Aimaretti G, Lucatello B, Lanfranco F** and **Ghigo E et al.**(2007). Endocrine and metabolic responses to extreme altitude and physical exercise in climbers. Eur J Endocrinol; 157(6):733–40.

**Boussarie, D.** (1999). Hématologie des Rongeurs et Lagomorphes de Compagnie, Bull. Acad. Vét. 72: 209-216.

**Connors J.M and Martin L.H.** (1982). Altitude induced changes in plasma thyroxine, 3, 5, 3'. Triiodothyronine, and thyrotropin in rats. J Appl Physiol 53:313-315.

**Escudero F, Gonzales GF, and Gonez C.** (1996). Hormone profile during menstrual cycle at high altitude. Int J Gynaecol Obstet 55:49–58.

**Hershman J.M and Pekary A.E** (1985). Regulation of thyrotropin secretion. In: The pituitary gland, pp 148-188. Ed. H. Imura. New York: Raven Press.

**Hodges JK, Harlow CR, and Hillier SG** (1985). Follicular function in the marmoset ovary. Ann Conf Soc for the Study of Fertility, Aberdeen. (Abstract46).

**Ingbar S.H and Woeber K.A** (1981). The thyroid gland. In: Text Book of Endocrinology. Ed. RH Williams, Igaku-Shoin, W.B. Saunders Co. Tokyo

**Kryger M, McCullough RE, and Collins D, et al.** (1978). Treatment of excessive polycythemia of high altitude with respiratory stimulant drugs. Am Rev Respir Dis;117:455–464.

**Martin L.H, Wertenberger G.E, Bullard R.W.** (1971). Thyroidal changes in the rat during acclimatisation to simulated high altitude. AJH J Physiol 221 : 1057-1063.

**Mazzeo, R.S and Reeves, J.T.** (2003). Adrenergic contribution during acclimatization to high altitude: perspectives from Pikes Peak. Exercise and Sport Sciences Reviews, 31 13–18.

**Moura E.G, Ramos C.F, Nascimento C.C.A, Rosenthal D and Breiten bach M.M.D.**( 1987). Thyroid function in rats variations in uptake & transient decrease in peroxidase activity. Braz. J. of Med. Biolo Res.:20, 407-410.

**Nelson B.D and Anthony A.** (1966). Thyroxine biosynthesis and thyroidal uptake of 131 in rats at the onset of hypoxia exposure. Proc Soc Exp Biol Med 121 : 1256-1261.

**Parchami A., and Fatahian Dehkordi R.F.** (2012). Sex Differences in Thyroid Gland Structure of Rabbits. International Journal of Medical and Biological Sciences.

**Roof, R.L, Duvdevani R, and Stein D.G.** (1992). Progesterone treatment attenuates brain oedema following contusion injury in male and female rats. Restorative Neurol Neurosci.; 4:425–427.

**Sanford, J. C., and Woodgate, F. G.** (1974). The domestic rabbit grenade Publishing Ltd. New York.

**Sawhney R.C. and A.S. Malhotra,** (1990). Thyroid function during intermittent exposure to hypobaric hypoxia. Int J Biometeorol 34:161-163.

**Zotte, D.A.** (2002) .Perception of rabbit meat quality and major factors influencingnthe rabbit carcass and meat quality. Livestock Production Science 75 ,11 –32.

**Wright Alex D., MB; Margaret F. Beazley, MB; Arthur R. Bradwell, MB; Ian M. Chesner, MB;Richard N. Clayton, MD; Peter J. G. Forster, MB; Peter Hillenbrand, MB; Christopher H. E. and Imray, M.B** (2004) .Medroxyprogesterone at High Altitude. The Effects on Blood Gases, Cerebral Regional Oxygenation, and Acute Mountain Sickness. Wilderness and Environmental Medicine, 15, 25 31.