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Research Article
Levels of Follicle Stimulating Hormone (FSH), Luteinizing Hormone (LH), Testosterone and Prolactin at Moderate Altitude Inhabitant Male

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Abstract

Background and Objective: Male fertility depends on the availability of the potent androgen called testosterone. Testosterone production is regulated by the hypothalamic anterior pituitary axis. Two anterior pituitary hormones Follicle Stimulating Hormone (FSH) and Luteinizing Hormone (LH) are involved in spermatogenesis and testosterone production, respectively. Hypoxia, resulting from high altitude, may induce a change in these four hormones and may affect male fertility. This study was done to evaluate and compare the changes that occur in FSH, LH, testosterone and prolactin in males lived in moderate versus low altitude. **Materials and Methods:** This study was conducted on 300 individuals who were categorized based on the altitude of their habitat into two equal groups, namely: Inhabitants at moderate altitudes and inhabitants at low altitudes. A venous blood sample was collected from each individual to measure the levels of FSH, LH and prolactin. **Results:** Both LH and testosterone levels were significantly lower in high altitude inhabitants compared with low altitude inhabitants ($p<0.01$). The FSH level showed a significant statistical difference between two groups with a lower level in individuals living at high altitudes compared with low altitude inhabitants but on a value ($p<0.05$). **Conclusion:** Moderate altitude hypoxia suppresses LH, FSH and testosterone levels as much as high altitude hypoxia does and these changes may depend on prolactin level.

Key words: Luteinizing hormone, follicle-stimulating hormone, testosterone, prolactin, low altitude, moderate-altitude, spermatogenesis

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Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Testosterone is a predominant type of androgen responsible for the development of sexual characteristics. It is produced by Leydig cells in male testes. In addition to male sexual characteristics, testosterone is also responsible for spermatogenesis[1]. Testosterone production is under the hypothalamic-anterior pituitary axis control. Gonadotropin-Releasing Hormone (GnRH) produced by the hypothalamus stimulates the anterior pituitary to secrete Follicle Stimulating Hormone (FSH) and Luteinizing Hormone (LH). Testosterone production occurs under the influence of LH secreted by anterior pituitary[2]. In addition to testosterone, FSH is responsible for spermatogenesis in males. Prolactin is another anterior pituitary hormone responsible for mammillary gland maturation and lactation in female[3]. Prolactin is a major cause of infertility in both males and females[4-6]. Several studies were carried out to evaluate the effect of high-altitude hypoxia on male sex hormones levels. These studies showed a variance in male sex hormones levels between males living at high altitude and others living at low altitude areas[7-9]. A previous study conducted on the Indian population showed that prolactin and testosterone levels differed according to the level of altitude and ethnicity[10]. Another study showed that elevated prolactin levels at high altitudes are the cause of depression of FSH, LH and testosterone[11]. Recently, newcomers exposed to high-altitude-hypoxia had a decrease in their fertility[12]. Taif city in Saudi Arabia is classified as a moderate-altitude area as it is located at an elevation of 1,879 m on the slopes of Sarawat Mountains[13]. This study aimed to determine whether moderate altitude hypoxia has the same effect as high altitude hypoxia on FSH, LH, testosterone and prolactin hormone levels.

MATERIALS AND METHODS

Study area: The study was carried out at the Faculty of Applied Medical Sciences Research lab, Taif University from January-September, 2019. It consisted of 300 healthy individuals who did not suffer from any chronic diseases such as diabetes mellitus, hypertension, chronic liver and kidney diseases.

Subjects: These individuals were classified into two equal groups. The first group consisted of 150 low altitude inhabitants who lived in Makkah city; while the other group consisted of 150 moderate altitude inhabitants who lived in Taif city.

Biochemical analysis: All chemicals were purchased from Dade Behring Company (Illinois, United States). Total of 5 mL of venous blood was collected into the plain tube under the standardized condition from each individual, left for about 3 min for clottings to occur, then centrifuged, after that serum was collected and incubated at -20°C until analysis. For each individual, serum prolactin, testosterone, LH and FSH were estimated by using ELISA sandwich immunoassay (BIO-RAD automated system, country). Normally, FSH and LH ranges in adult males are 1-14 and 1-9 mIU mL^{-1}, respectively[14]. The normal range of testosterone in adult males is 86.98-780.10 ng dL^{-1} [15]. Finally, the range for prolactin is 1.8-17 ng mL^{-1} in adult males[16].

Statistical analysis: All data were presented using the mean±standard deviation (SD). Comparisons of parameters between all groups were evaluated by t-test using SPSS software version 16 (SPSS Inc., Chicago, IL, USA). The level of significance was set at $p<0.05$.

RESULTS

This study was carried out on males that lived in Taif city to evaluate the effect of moderate altitude on the levels of FSH, LH, testosterone and prolactin. The results of this study were represented by Table 1 and presented as mean±standard deviation. Serum testosterone levels showed a significant statistical difference between the two groups. Subjects living at a moderate altitude area had a lower level (471±43.863) compared with subjects living at a low altitude area (659±56.321) ($p = 0.009$). Also, FSH showed a significant statistical difference with a lower level in subjects living at a moderate altitude area (3.524±1.290) compared to subjects living at a low altitude area (8.445±2.210) ($p = 0.028$). Eventually, the LH level showed a significant statistical difference between both groups ($p = 0.004$). A higher level was found in subjects living at a low altitude area (7.670±2.75), while a lower level was found in subjects living at a moderate altitude area (4.853±1.078). Age, BMI and prolactin levels did not show any statistical difference between both groups.

Table 1: Comparison of age, BMI, serum testosterone, Follicle Stimulating Hormone (FSH), Luteinizing Hormone (LH) and prolactin in low and moderate altitude groups by using t-test

Parameters	Low altitude area	Moderate altitude area	p-value
Age	39.000±4.00	35.000±5.00	0.186
BMI	31.220±5.222	29.760±4.027	0.071
Testosterone (ng dL^{-1})	659.000±56.321	471.000±43.863	0.009**
FSH (mIU mL^{-1})	8.445±2.210	3.524±1.290	0.028*
LH (mIU mL^{-1})	7.670±2.75	4.853±1.078	0.004**
Prolactin (ng mL^{-1})	11.840±2.666	11.020±3.206	0.118

**p<0.01, *p<0.05, BMI: Body mass index

DISCUSSION

The results of this study showed that the levels of testosterone, FSH and LH in males that lived in moderate altitude were lower than those levels in males that lived in low altitude. Levels of prolactin did not change in either one of the two groups. Hypoxia is a condition in which there is a deprivation of oxygen supply to a part of tissue or organ. This condition may be associated with symptomatic or asymptomatic disorders[17].

A recent study concluded that the critical highest altitude level is around 2400-5000 m, while moderate altitude level ranges from 1500-2400 m[15]. Saudi Arabia has many moderate altitude areas distributed along the Sarawat Mountains. Taif city is considered one of the moderate altitude areas present on SarawatMountain[18]. People living in high-altitude areas usually suffer from hypoxia which may be associated with insomnia and bad mood. In addition to insomnia and bad mood, people who lived in this area may suffer from metabolic and cardiorespiratory changes[19]. Metabolism is regulated by a variety of hormones that are produced by different endocrine glands[18]. Male fertility depends on a combination of some factors. One of which is the hormonal level changes which are when hormone levels fluctuate on either side of the spectrum. Several studies were conducted to evaluate the effect of high-altitude hypoxia on male and female sex hormones which helped obtain equivocal results[20]. The present study was conducted only on male subjects because female FSH, LH levels were unstable during the menstrual cycle. Earlier, a study conducted on Swiss males living at high altitude areas showed a reduction of both FSH and LH levels in these individuals compared with those living at low altitude[21]. Moreover, a study conducted on 52 soldiers who stayed at high altitudes for about 6 months showed that FSH, LH and testosterone were reduced. Also, sperm count and motility were reduced in these soldiers. It was concluded that the reduction of testosterone level was a result of LH suppression, while sperm count and motility reduction were caused by the reduction of FSH[22]. Collectively, the researchers have instructed that the decrease in LH, FSH and testosterone levels was a result of suppression of the hypothalamus-anterior pituitary axis[22]. This conclusion was developed in a study conducted on acute hypoxic patients after the administration of gonadotropin-Releasing Hormone (GnRH). Administration of GnRH failed to induce LH, FSH and testosterone levels[23]. A previous study conducted in 2010 found that a high altitude area suppresses the level of both LH and testosterone significantly; however, it was insignificant in FSH. The researchers conclude that prolonged exposure to high-altitude hypoxia induces hormonal levels changes that depend on the hypothalamic-anterior pituitary axis[23]. The results of this study are in line with the mentioned study that found a reduction in gonadotropic hormones (LH and FSH) levels at high altitude areas. Moreover, LH suppression is more significant than FSH suppression. Testosterone levels also changed at high altitude areas in both LH and FSH. A previous study showed that testosterone levels were reduced as a result of high altitude hypoxia[23]. A study conducted on eight male mountain climbers on the Himalayan Mountains revealed a reduction of testosterone levels[24]. Another study was done on 52 soldiers who lived for six months at a high altitude area resulted in suppressed levels of testosterone along with LH and FSH. Testosterone in the present study was much lower in males living at high altitude areas compared with others who lived at low altitude areas. This reduction was highly significant and may be a result of LH level suppression[23]. Prolactin is a peptide hormone produced by the anterior pituitary. High prolactin level is the most common cause of infertility in males and females[3]. A previous study showed a significant elevation in prolactin levels in men exposed to Hypoxia at high altitude (5380 m) for one year[22]. The result of the study did not show any significant difference in prolactin level between males lived at moderate and low altitude areas. Consequently, the critical level of effective high-altitude hypoxia may be lower than 5000 m as suggested by Wolff *et al.*[17]. Majumdar *et al.*[25] concluded that a reduction in LH, FSH and testosterone may be caused by hyperprolactinemia. This study contradicts the mentioned

study because the prolactin level is normal and did not show any significant difference between males living at moderate and low altitudes. A wide study on a large number of males and in interval altitude areas is recommended to give a critical altitude in which the hormonal changes occur.

CONCLUSION

This study concludes that moderate altitude hypoxia suppresses LH, FSH and testosterone levels as much as high-altitude hypoxia does and these changes may depend on prolactin level.

SIGNIFICANCE STATEMENT

This study discovers the difference in sex hormones that can be beneficial for determining the cause of infertility in a few cases lived in high or moderate altitude diagnosed as the idiopathic cause. This study will help the researcher to uncover the critical areas of infertility that many researchers were not able to explore. Thus, a new theory on infertility may be arrived at.

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REFERENCES

1. Oh, S., 2014. Disturbance in testosterone production in leydig cells by polycyclic aromatic hydrocarbons. Dev. Reprod., 18: 187-195.
2. Charlton, H., 2008. Hypothalamic control of anterior pituitary function: A history. J. Neuroendocrinol., 20: 641-646.
3. Bole-Feysot, C., V. Goffin, M. Edery, N. Binart and P.A. Kelly, 1998. Prolactin (PRL) and its receptor: Actions, signal transduction pathways and phenotypes observed in PRL receptor knockout mice. Endocr. Rev., 19: 225-268.
4. Donato, J.J. and R. Frazão, 2016. Interactions between prolactin and kisspeptin to control reproduction. Arch. Endocrinol. Metab., 60: 587-595.
5. Bernichtein, S., P. Touraine and V. Goffin, 2010. New concepts in prolactin biology. J. Endocrinol., 206: 1-11.
6. Saleem, M., H. Martin and P. Coates, 2018. Prolactin biology and laboratory measurement: An update on physiology and current analytical issues. Clin. Biochem. Rev., 39: 3-16.
7. Okumura, A., H. Fuse, Y. Kawauchi, I. Mizuno and T. Akashi, 2003. Changes in male reproductive function after high altitude mountaineering. High Alt. Med. Biol., 4: 349-353.
8. Pelliccione, F., V. Verratti, A. D'Angeli, A. Micillo and C. Doria *et al*., 2011. Physical exercise at high altitude is associated with a testicular dysfunction leading to reduced sperm concentration but healthy sperm quality. Fertil. Sterility, 96: 28-33.
9. Verratti, V., F. Berardinelli, C.D. Giulio, G. Bosco, M. Cacchio, M. Pellicciotta, M. Nicolai, S. Martinotti and R. Tenaglia, 2008. Evidence that chronic hypoxia causes reversible impairment on male fertility. Asian J. Androl., 10: 602-606.
10. Sachidhanandam, M., S.N. Singh, U.S. Ray and A.K. Salhan, 2009. Impact of prolonged high altitude exposure on plasma prolactin in men: Effect of age and ethnicity. High Altitude Med. Biol., 10: 343-348.
11. Strüder, H.K., W. Hollmann and P. Platen, 2007. Increased prolactin response to hyperoxia at rest and during endurance exercise. Int. J. Sports Med., 17: 390-392.
12. Hu, H., Y. Gao, H. Fang, J. Sun and L. Wei *et al*., 2016. Effect of high altitude exposure on spermatogenesis in male military personel. Int. J. Clin. Exp. Med., 9: 6783-6788.
13. El-Mouzan, M.I., A.S. Al-Herbish, A.A. Al-Salloum, M.M. Qurachi and A.A. Al-Omar, 2007. Growth charts for Saudi children and adolescents. Saudi Med. J., 28: 1555-1568.
14. Robertson, D.M., L.M. Foulds, R.C. Fry, J.T. Cummins and I. Clarke, 1991. Circulating half-lives of follicle-stimulating hormone and luteinizing hormone in pituitary extracts and isoform fractions of ovariectomized and intact ewes. Endocrinology, 129: 1805-1813.
15. Taieb, J., B. Mathian, F. Millot, M.C. Patricot and E. Mathieu *et al*., 2004. Testosterone measured by 10 immunoassays and by Isotope-Dilution gas chromatography–mass spectrometry in sera from 116 men, women, and children. Clin. Chem., 49: 1381-1395.
16. Kiehlbauch, J.A., G.E. Hannett, M. Salfinger, W. Archinal, C. Monserrat and C. Carlyn, 2000. Use of the National Committee for Clinical Laboratory Standards guidelines for disk diffusion susceptibility testing in New York state laboratories. J. Clin. Microbiol., 38: 3341-3348.
17. Wolff, M.V., C.T. Nakas, M. Tobler, T.M. Merz and M.P. Hilty *et al*., 2018. Adrenal, thyroid and gonadal axes are affected at high altitude. Endocr. Connections, 7: 1081-1089.
18. Parati, G., P. Agostoni, B. Basnyat, G. Bilo and H. Brugger *et al*., 2018. Clinical recommendations for high altitude exposure of individuals with pre-existing cardiovascular conditions. Eur. Heart J., 39: 1546-1554.
19. San, T., S. Polat, C. Cingi, G. Eskiizmir, F. Oghan and B. Cakir, 2013. Effects of high altitude on sleep and respiratory system and theirs adaptations. Sci. World J., 7: 1-7. 10.1155/2013/241569.

20. Sawhney, R.C., P.C. Chhabra, A.S. Malhotra, T. Singh, S.S. Riar and R.M. Rai, 1985. Hormone profiles at high altitude in man. Andrologia, 17: 178-184.
21. Keenan, D.M., J.P. Hefti, J.D. Veldhuis and M.V. Wolff, 2019. Regulation and adaptation of endocrine axes at high altitude. Am. J. Physiol. Endocrinol. Metab., 318: E297-E309.
22. He, J., J. Cui, R. Wang, L. Gao and X. Gao *et al*., 2015. Exposure to hypoxia at high altitude (5380 m) for 1 year induces reversible effects on semen quality and serum reproductive hormone levels in young male adults. High Alt. Med. Biol., 16: 216-222.
23. Richalet, J.P., M. Letournel and J.C. Souberbielle, 2010. Effects of high-altitude hypoxia on the hormonal response to hypothalamic factors. Am. J. Physiol. Integr. Comp. Physiol., 299: 1685-1692.
24. Benso, A., F. Broglio, G. Aimaretti, B. Lucatello, F. Lanfranco, E. Ghigo and S. Grottoli, 2007. Endocrine and metabolic responses to extreme altitude and physical exercise in climbers. Eur. J. Endocrinol., 157: 733-740.
25. Majumder, A. and N.S. Mangal, 2013. Hyperprolactinemia. J. Hum. Reproduct. Sci., 6: 168-175.