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ORIGINAL ARTICLE **OPEN ACCESS**

FSH, LH, testosterone and Prolactin levels in infertile males of Khyber Pakhtunkhwa

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ABSTRACT
Infertility is a worldwide problem and present in about 1/3 couples. Both male and female factors are involved with almost the same ratio. Different hormones especially the gonadotrophins (LH and FSH) and testosterone are the fundamental regulators of germs cell development. Abnormalities in these hormones may disturb the natural process of spermatogenesis. To assess the hormonal levels (FSH, LH, Testosterone, Prolactin) in infertile patients. A descriptive study conducted at the Institute of Paramedical Sciences, Khyber Medical University Peshawar from December 2016 to December 2017 on 229 patients (infertile). Fifty samples of proven fathers (fertile) were taken as control. Out of total 229, 72 were infertile. FSH and LH were elevated significantly with a p-value <0.05 in infertile patients, while the testosterone insignificantly decreased and prolactin insignificantly increased. The gonadotrophic hormones (LH and FSH), testosterone and prolactin (PRL) levels were abnormal which may be involved in infertility.
Key Words: *Infertility, LH, FSH, Azoospermia, Oligospermia*

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INTRODUCTION

Infertility is a worldwide common social, psychological, economic and medical problem which is defined as the inability of a man or women to reproduce, while fertility denotes ability to reproduce [21]. According to WHO definition, infertility is defined as trying to conceive for 12 Months after unprotected intercourse [15]. No reliable data related to prevalence is available but the estimated prevalence of infertility is about 8-12% in different countries [22]. Presently, male infertility in UK, USA and Nigeria is 6%, 10% and 30% respectively [1]. The prevalence of male infertility is 10-17% in Finland while 18-21% in Switzerland while in Pakistan it is 21.9%; primary being 3.5% and secondary, 18.4% [21].

Global, statistics revealed that about 72.4 million couples are facing infertility problem. While WHO estimates 8-12% (60-80 millions) couples are presently suffering from infertility. Infertility rate is high in men below the age of 30 years worldwide [15] and is not well documented as compared to female infertility [11, 2]. It is noticed that either male (40%) or female (40%) contribute in infertility while in the rest of 20% both sexes contribute [15], thus nearly one out of 6-8 couples are suffering from infertility problem [13, 14].

There are numerous factors which are responsible for male infertility ranging from lifestyle: smoking, malnutrition, physical and mental stress, drug abuse to infections and chronic disease: diabetes, sexually transmitted diseases. Trauma, be it iatrogenic, involving urogenital tract, direct injury to the supporting Sertoli (somatic) cells or the germs cells or Leydig cells (steroidogenic),or chemical, radiations, thermal trauma. These also include steroids, chromosomal and genetic mutation, germ cells malignancy, testicular cell calcification, , cryptorchidism and endocrine disorders [18, 12].

Complete and successful development of male germ cells is dependent on the balanced endocrine function of hypothalamus, testis and pituitary gland [5]. The most important, and essential hormones which are involved in male infertility are FSH, LH, testosterone and gonadotropin. These hormones regulate spermatogenesis and reduction of these hormones can lead toinfertility [13]. Hypothalamic Gonadotrophin Releasing Hormone (GnRH) stimulates the anterior pituitary glands which secretes

gonadotropin hormones (LH and FSH) [16]. LH predominately stimulates Leydig cells to promote secretion of steroidogenesis (testosterone) which further act on the peritubular and Sertoli cells of the seminiferous tubules and stimulates spermatogenesis [13, 16].

FSH is necessary for normal reproductive function [9] it mainly binds with FSH receptors (FSHR) and stimulates Sertoli cells which help in conversion of spermatids to spermatozoa [16, 13]. Additionally, FSH is required for initiation of pubertal spermatogenesis and maintaining normal quantity of sperm formation in adults [9]. Testosterone acting as an androgen plays main role in the formation of spermatozoa and its growth to the germinal cells [13]. The role of Prolactin (PRL) in male infertility is not clearly understood but it is suggested that it regulates intra-testicular testosterone by regulating LH receptors present on the Leydig cells. Whereas in female infertility hyperprolactinemia suppress the synthesis of testosterone, LH and FSH.Prolactin effects fertility of males by triggering over-secretion of adrenal corticoids or blocking the secretion of GnRH through prolactin receptors located on the hypothalamic dopaminergic neurons [10, 11]. Estradiol, inhibin and testosterone not only regulate secretion of gonadotropins, andincreasing level of these hormones disturb mechanism of negative feedback, resulting in higher level of FSH [5]. A range of values is used for each of these hormones to identify any deviation from normal but these have been identified for other populations and the extent of the normal is such that it introduces difficulty in interpretation of cause of infertility. Thus these hormones have to be considered together to understand each individual case.

Main objective of the present study was to investigate levels of FSH, LH, prolactin and testosterone in infertile male in our population and frequency of oligospermia, azoospermia and normospermia in these patientsand compared to normal controls.

MATERIALS AND METHODS

This descriptive cross sectional study was conducted at the Institute of Paramedical Sciences Khyber Medical University, Peshawar and Rehman Medical Institute, Peshawar on 229 infertile male patients along with 50 controls who had proved to be fathers (fertile). This study was carried out in one year from December 2016 to December 2017. All the married male patients attending the fertility clinic of Rehman Medical Institute, Peshawar, declared on the basis of semen analysis infertile by the concerned physician, were included in the present study irrespective of their duration of marriage, type of fertility problem and age. Patients were excluded from present study if they were suffering from thyroid disorder, underwent pelvic surgery, hernia repair or had STDs.History of all patients were recorded including duration of infertility, treatment, period after marriage, partner age, number of children, infertility history of family and physicalexamination. From each male patient, semen samples were collected through masturbation and ejaculated in dry, clean disposable bottle after three to five days of abstinence from sex and analyzed through conventional slide technique after incubation for 30 minutes at 37^{o}C.Blood samples (3-5milliliter) were collected under aseptic technique in clean plain labeled tubes, allowed to clot and centrifuged at 6000 rpm for analysis of hormones. Samples of subjects were analyzed according to WHO criteria using fully automatic Elecsys 2010 analyzer (MiniVIDAS apparatus, Biomerieux, France) through an Enzyme Linked Fluorescent Assay (ELFA) technique. Assessment of hormones (serum FSH, LH and Testosterone) was carried out at clinical laboratory of Rehman Medical Institute, Peshawar. Collected data were analyzed through SPSS software 21.0. Student *t* test was used for data analysis. p-value<0.05 was accepted as a statistically significant.

RESULTS

Results of hormones analysis and other parameters of patients are shown in Table 1, 2 and 3. Out of a total of 229 male patients studied, 72 were found infertile on the basis of semen analysis by the concerned physician. Mean age of all patients (fertile and infertile) was 30.72±7.11 years (range 20-56 years).Highest percentage of infertile patients was observed in age range of 20-30 years, followed by 31-40 years and 41-50 years, whereas lowest rate was found in age range of 50 years (Table 1).

All semen samples were Gray/white in color. Out of a total of 72 infertile patients, maximum number of samples were thin 71(98.61%) in consistency while 1(1.39%) sample was thick in viscosity.

The commonest feature identified for the infertile patients was primary hypogonadism (29) and spermatogenesis dysfunction (27 patients) followed by,pituitary adenoma in 7patients(Figure 1).

Out of 72 male patients investigated: 61(84.72%) were azoospermic and 11(17.28%) were oligozoospermic (Figure 1). As a control, 50 samples were taken from proven fathers,which showed normal morphology along with normal count, consistency and pH. Sperm count and motility of proven fathers was significantly higher (p<0.001) than patients (Figure 2).

FSH and LH levels are increased significantly in infertile patients as compared to control group, whereas testosterone increased insignificantly while insignificant decreased also observed in infertile patients (Table 3).

DISCUSSION

Results obtained in the present study show some accordance to the data published in the previous studies. Higher levels of LH and FSH have been recorded in infertile patients in the current study. Current report showed that statistically significant increase in the levels was observed for LH and FSH, which are similar to the reported data from Abbottabad and other researchers [5, 12, 27, 26, 8,]. Sulthan *et al*., [25] revealed similar reports that LH and FSH are increased significantly. Kuku *et al*., [11] reported that LH levels increased in 26.5% in the tested subjects which is similar to data presented in the current study (30.05%) of infertile patients. It has been shown that over production of LH and FSH hormones could be due to the mutation of LH and FSH receptor respectively [14]. De Kretser *et al*., [7] reported that disruption of seminiferous epithelium may lead to increasing level of FSH. Abnormally high levels of FSH and LH might be due to abnormal feedback mechanism of steroids, gonadal peptides or disruption in the gonadal axis [24].

In the present study, insignificant decrease was observed in testosterone levels as compared to testosterone level in proven fathers. Similar results were also reported byother investigators in their studies as well [24, 13], [5, 23]. High levels of LH and FSH induce the Leydig and Sertoli cells to produce testosterone, thereby increasing spermatogenesis process [8]. This process continues to increase the production of testosterone at certain level, after a threshold, high gonadotropin levels exercise a negative feedback effect on hypothalamo-pituitary-testicular axis thereby decreasing plasma testosterone levels [8]. Low level of testosterone might be due to congenital abnormality *i.e.* Klinefelter syndrome or acquired disorder [28]. Recently, it is reported that FSH and LH deficiency may prevent the production of sperms or sufficient amount of testosterone from the gonads [28]. Testosterone levels could be decreased due to the negative feedback of gonadotropins as well (high level of LH and FSH) [14].

Present study also supports the results of Babu *et al*., from India who revealed that LH and FSH levels increased significantly in infertile patients while insignificant decreased in testosterone levels was observed [5].

Insignificant elevation of prolactin level was also observed in the present study. Alici *et al*., [4] also revealed similar report that insignificant increased was noted in infertile male patients.. Moreover, significant increase of prolactin level was also reported by Younes [29] and [19].

Abnormal level of FSH and LH may be due to impairment of spermatogenesis, primary (testicular) hypogonadism (Klinefelter Syndrome), pituitary adenoma (acromegaly), and drug induced. These factors may lead to reduced sperm count and affect male fertility [6, 20]. Nanik Ram *et al*., [20] reported hypogonadism in 86% patients, whereas in the present study, it was recorded in only 4.17%, which is too low compared to that study. In addition, distribution of pituitary adenoma 9.72% reported in the current study, is similar to results of Nanik Ram *et al*., who found it as 9.6%..

The prevalence of azoospermia recorded in Spain is 24% and oligospermia is 6.7% which is different compared to that observed in the present study, azoospermia - 77.78% and Oligospermia - 15.28%, is much high in the instant report [3]. Mahboubi *et al*., [17] also reported azoospermia (30.6%)in the range to that reported from Spain, whereas oligospermia reported by Mahboubi *et al.* [17] ,(52.7%) which was much high compared to the results of the present study (15.28%). Eniola *et al*.,[8] revealed that prevalence of normosperia was 5.9 %, azoospermia 20.6% and oligospermia 73.5%, which are different from the findings of the present study.

Limitations of present study worth mentioning are that chromosomal analysis which was not done for the patients of Klinefelter syndrome, number of infertile patients were less (n=72) and no follow up of the etiological and risks factors of infertile patients was carried out.

Table 1: Different parameters of semen determined during semen analysis (n=72)

Parameters	Range	Mean±SD
Volume	0.5-4.8ml	2.05±0.97
Liquefaction Time	15-60 mints	22.04±2.51
pH	7.5-8.5	8.00±0.8

Table 2: Hormonal levels in infertile patients (n=72)

Hormones	High level	Low level	Normal
FSH	56 (77.78%)	05 (06.94%)	11 (15.28%)
LH	31 (43.05%)	03 (04.17%)	38 (52.78%)
Prolactin	08 (11.11%)	00 (00.00%)	66 (91.67%)
Testosterone	06 (08.33%)	02 (02.78%)	66 (91.67%)

Table 3: Comparison of hormones levels (FSH, LH, Testosterone and Prolactin) in patients and controls (n=72)

Hormone	(Reference range)	Control (N=50)	Infertile (N=72)	T-value	*p*-value
FSH	(0.95-11.95mlU/ml)	6.61±0.23	24.47±19.74	0.000	0.000
LH	(0.7-12.07mlU/ml)	7.08±2.58	13.46±10.69	0.000	0.000
Prolactin	(34-398mlU/ml)	264±61.08	322.01±209.95	0.034	0.077
Testosterone	(143-923ng/dl)	525±53	512.18±388.25	0.033	0.835

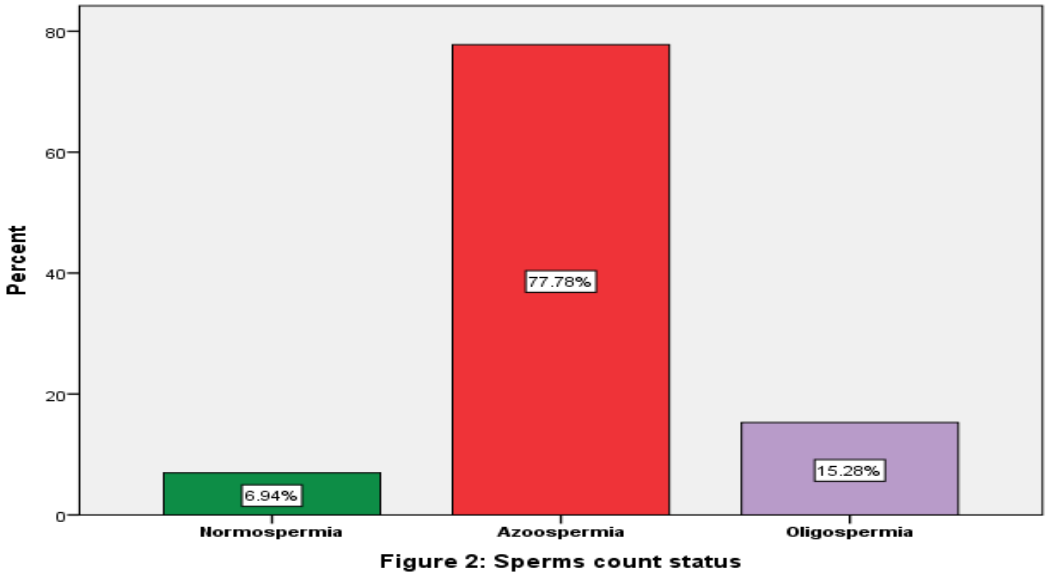

Figure 2: Sperms count status

CONCLUSION

Infertile patients have an abnormal level of hormones (FSH, LH, Testosterone and Prolactin) while fundamental risk factors are hypogonadism and abnormal spermatogenesis.

REFERENCES

1. Abarikwu, S. O. (2013). Causes and risk factors for male-factor infertility in Nigeria: a review. *African Journal of Reproductive Health, 17*(4).
2. Agarwal, A., Mulgund, A., Hamada, A., & Chyatte, M. R. (2015). A unique view on male infertility around the globe. *Reproductive biology and endocrinology, 13*(1), 37.
3. Al-Haija, R. W. (2011). *Main Causes of Infertility Among Men Treated At razan Centers in West Bank: Retrospective Study.* Tesis, An-Najah National University Faculty Graduate Studies.
4. ALICI, B., ÇITCI, A., OZKARA, H., AKKUS, E., & HATTAT, H. The Effect Of Hyperprolactinemia On Semen Parameters In Male Infertility. Cerrahpasa Medical Journal, 29 (2), 95-98.
5. Babu, S. R., Sadhnani, M., Swarna, M., Padmavathi, P., & Reddy, P. (2004). Evaluation of FSH, LH and testosterone levels in different subgroups of infertile males. *Indian Journal of Clinical Biochemistry, 19*(1), 45-49.
6. Cook, J. D. (2004). Reproductive Endocrinology in Infertility. *Laboratory Medicine, 35*(9), 558-569.
7. De Kretser, D. (1979). Endocrinology of male infertility. *British Medical Bulletin, 35*(2), 187.
8. Eniola, O. W., Adetola, A. A., Olufemi, A. A., & Oladipupo, M. A. (2012). Evaluation of hormonal and physical factors responsible for male infertility in Sagamu South Western Nigeria. *Der Pharmacia Lettre, 4*, 1475-1479.
9. Gharesi-Fard, B., Ghasemi, Z., Shakeri, S., Behdin, S., Aghaei, F., & Malek-Hosseini, Z. (2015). The frequency of follicle stimulating hormone receptor gene polymorphisms in Iranian infertile men with azoospermia. *Iranian journal of reproductive medicine, 13*(11), 673.

10. Keskin, M. Z., Budak, S., Aksoy, E. E., Yücel, C., Karamazak, S., Ilbey, Y. O., & Kozacıoğlu, Z. (2017). Investigation of the effect of body mass index (BMI) on semen parameters and male reproductive system hormones. *Archivio Italiano di Urologia e Andrologia, 89*(3), 219-221.
11. Khadim, A. H. A., Al-Wayelli, D. A. O. J., & Al-Rekabe, B. K. K. (2010). Evaluation of serum FSH, LH and Testosterone levels in infertile patients affected with different male infertility factors after IUI technique. *Thi-Qar Medical Journal, 4*(3), 112-122.
12. Khan, M. A., Shah, S., Akhtar, N., Sajid, M. A., Naeem, M., & Anwar, K. (2012). Spectrum Of Patients Presented In Male Infertility Clinic. *Khyber Medical University Journal, 4*(1).
13. Khan, M. S., Ali, I., Hussain, M., Nawaz, K., Zeb, M., Anwar, W., . . . Javaid, A. (2011). Determination of serum gonadotropin and testosterone levels in male infertility. *Journal of Postgraduate Medical Institute (Peshawar-Pakistan), 21*(2).
14. Kuku, S., Akinyanju, P., & Ojeifo, J. (1988). Serum levels of gonadotropins, prolactin, and testosterone in oligo/azoospermic Nigerian males. *International journal of fertility, 33*(1), 40-44.
15. Kumar, N., Choudhari, A. R., & Singh, A. K. (2015). Prevalence of male factor infertility in last ten years at a rural tertiary care centre of central India: a retrospective analysis. *Indian Journal of Obstetrics and Gynaecology Research, 2*(3), 132-136.
16. Liu, P. Y., & Handelsman, D. J. (2003). The present and future state of hormonal treatment for male infertility. *Human reproduction update, 9*(1), 9-23.
17. Mahboubi, M., Foroughi, F., Ghahramani, F., Shahandeh, H., Moradi, S., & Shirzadian, T. (2014). A case--ontrol study of the factors affecting male infertility. *Turkish journal of medical sciences, 44*(5), 862-865.
18. McClure, R. D. (2005). Endocrinology of male infertility *Office andrology* (pp. 11-37): Springer.
19. Ozden, C., Ozdal, O. L., Bulut, S., Guzel, O., Koyuncu, H. H., & Memis, A. (2008). Effect of varicocelectomy on serum inhibin B levels in infertile patients with varicocele. *Scandinavian journal of urology and nephrology, 42*(5), 441-443.
20. Ram, N., Asghar, A., Hashmi, F., & Islam, N. (2012). Male hypogonadism at a tertiary care hospital in Karachi, Pakistan. *Journal of Ayub Medical College Abbottabad, 24*(2), 65-67.
21. Shaheen, R., Subhan, F., Sultan, S., Subhan, K., & Tahir, F. (2010). Prevalence of infertility in a cross section of Pakistani population. *Pakistan Journal of Zoology, 42*(4).
22. Sohrabvand, F., Jafari, M., Shariat, M., Haghollahi, F., & Lotfi, M. (2015). Frequency and epidemiologic aspects of male infertility. *Acta Medica Iranica, 53*(4), 231-235.
23. Stanwell-Smith, R., Thompson, S., Haines, A., Jeffcoate, S., & Hendry, W. (1985). Plasma concentrations of pituitary and testicular hormones of fertile and infertile men. *Clinical reproduction and fertility, 3*(1), 37-48.
24. Subhan, F., Tahir, F., Ahmad, R., & Khan, Z. (1995). Oligospermia and its relation with hormonal profile. *JOURNAL-Pakistan Medical Association, 45*, 246-247.
25. Sultan, C., de Paulet Craste, B., Audran, F., Iqbal, Y., & Ville, C. (1985). *Hormonal evaluation in male infertility.* Paper presented at the Annales de biologie clinique.
26. Weghofer, A., Margreiter, M., Bassim, S., Sevelda, U., Beilhack, E., & Feichtinger, W. (2004). Minimal stimulation using recombinant follicle-stimulating hormone and a gonadotropin-releasing hormone antagonist in women of advanced age. *Fertility and sterility, 81*(4), 1002-1006.
27. Weinbauer, G. F., & Nieschlag, E. (1995). Gonadotrophin control of testicular germ cell development *Tissue Renin-Angiotensin Systems* (pp. 55-65): Springer.
28. Wosnitzer, M., Goldstein, M., & Hardy, M. P. (2014). Review of azoospermia. *Spermatogenesis, 4*(1), e28218.
29. Younes, A. K. H. (2000). Low plasma testosterone in varicocele patients with impotence and male infertility. *Archives of andrology, 45*(3), 187-195.

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