CORRELATION OF LH AND FSH WITH SPERM ANALYSIS IN INFERTILE MALES

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ABSTRACT

BACKGROUND

Infertility has been defined as the inability of sexually active couple to achieve pregnancy despite of unprotected intercourse for a period of greater than 12 months. The failure of pituitary to secrete FSH and LH will result in disruption of testicular function resulting infertility. Analysis of semen and hormone evaluation are essential parameters in giving a definitive diagnosis in infertile males. The aim of the present study was to evaluate FSH and LH levels and correlate with sperm count, smoking, and alcohol intake in infertile men.

MATERIALS AND METHOD

All the necessary formalities were taken in maintaining the confidentiality of the patient's samples and ethical clearance from the Ethical Committee of Seven Hills Hospital, Visakhapatnam and NRIIMS, Sangivalasa, was taken. The present study was a prospective cross-sectional one carried out in Seven Hills Hospital and NRI Institute of Medical Sciences, Sangivalasa, Visakhapatnam. FSH, LH, Sperm analysis were done in 50 infertile males (38 were azoospermic and 12 were oligospermic).

RESULTS

The association of smoking and alcohol with infertility showed statistical insignificance. There was significant increase in serum concentrations of Follicle Stimulating Hormone (FSH) Levels ($P=0.001$) and serum concentrations of Luteinizing Hormone (LH) Levels ($P=0.004$).

CONCLUSION

The present study showed that the high level of gonadotropins is an indication of testicular problems as the cause of infertility.

KEYWORDS

LH and FSH, Infertile Males, Sperm Analysis.

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INTRODUCTION

Infertility has been defined as the inability of sexually active couple to achieve pregnancy despite unprotected intercourse for a period of greater than 12 months.^[1] Among the various known pathologies that torment humans, infertility has special place. Though, it does hamper the daily life and usually does not result in physical morbidity, pain, limitation of activity, or longevity, its impact on the psychological and social wellbeing of not only the index patient, but also his or her partner makes it a major issue for health professionals. In the US, more than four in five practicing urologists admit to treating infertility. Accounting for its high prevalence and outspread impact, India has been included it as a part of the national program for reproductive and child health.^[2]

Anterior pituitary secretes FSH and LH. The name FSH and LH is based on the action of hormones in females whereas in males FSH stimulates the Sertoli cells of testis and thereby promotes spermatogenesis and LH stimulates the Leydig cells to secrete testosterone. That is why LH is also called interstitial cell stimulating hormone.^[3] Hypothalamic GnRH controls the production of the pituitary gonadotropins LH and FSH. GnRH is released in discrete pulses for every 2 hours approximately resulting in corresponding pulses of LH and FSH. These dynamic hormone pulses to a certain degree report for the wide variations in LH and testosterone even within same individual LH.^[4]

Serum FSH elevations are indicative of disturbances in spermatogenesis such as primary testicular failure (hypergonadotropic hypogonadism), although normal FSH levels do not dismiss spermatogenic failure.^[5] Smoking is associated with decline in basic semen parameters such as sperm concentration, viability, forward motility, and morphology^[6,7] as well as declines in sperm penetration ability and hence fertilisation rates.^[8] Although, long-term abuse of alcohol is associated with global suppression of the hypothalamic-pituitary gonadal axis and spermatogenesis, moderate intake is not associated with significant diminution in fertility.^[9] Semen analysis and hormone evaluation are of paramount importance in giving a definitive diagnosis in infertile males.^[10] Therefore, hormones measurement can help to determine whether the patient has deficiency of

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gonadotropin, primary testicular failure, spermatogenic failure, or androgen resistance. So, the present study aims to evaluate the levels of LH and FSH and correlate with sperm count, smoking, and alcohol intake in infertile men.

MATERIALS AND METHODS

The study was a prospective cross-sectional one carried out in the Seven Hills Hospital, Ram Nagar and NRI Institute of Medical Sciences, Sanghivalasa, Visakhapatnam. 50 infertile males (age group 25-40 years) with least 3 years' duration of infertility coming for evaluation to Seven Hills Hospitals during July 2014 to July 2015 were selected as subjects and were consented to complete a comprehensive questionnaire relating to their medical and personal history, lifestyle habits, and exposure to gonadotoxins (such as radiation therapy and drugs used for cancer chemotherapy). 25 age-matched controls with proven fertility were selected as control group. Semen was collected from the infertile subjects by masturbation after having abstained from sexual intercourse for a minimum of two days and a maximum of seven days in a private room near the laboratory in order to limit the exposure of the semen to fluctuations in temperature and also to control the time between collection and analysis. The collection was done into a clean, dry, wide-mouthed container made of glass that is non-toxic for spermatozoa. The specimen container was kept in an incubator at 30°C temperature.

The estimation of sperm counting was done using the Neubauer haemocytometer chamber. Sperm analysis was carried out according to the World Health Organisation guidelines.⁽¹¹⁾ Based on the sperm count, the subject were classified as normospermia (>20 million sperm/mL), oligospermia (<20 million sperm/mL), and azoospermia (no spermatozoa). In proven fertile controls, the sperm count ranged from 20-120 million sperm/mL. 10 mL fresh blood sample was aseptically collected from antecubital vein of each subject transferred into a clean plain labelled tube allowed to clot and then centrifuged at 6000 rpm for 5 minutes at room temperature. The clear serum was separated and kept at 20°C till assayed. Serum concentrations of Follicle-Stimulating Hormone (FSH), Luteinizing Hormone (LH) were measured by IMMULITE 1000 using the kits supplied by Siemens. The association of smoking and alcohol habits were analysed using chi-square test with statistical package for Social Sciences Software and the means of FSH and LH were compared and p-value is obtained by GraphPad.

RESULTS

Out of 50 infertile men, 38 (76%) were azoospermic, 12 (24%) were oligozoospermic. Frequency of alcoholics and smokers in infertile males were 41 (82%) and 28 (56%) whereas in proven fertile males, 28 (56%) and 19 (76%), respectively.

Table 1 demonstrates the distribution and association of smokers in infertility cases and controls. The chi-square statistic is 2.8495. The p-value is 0.0914. This result is not significant at $p < 0.05$.

Table 2 shows the distribution and association of alcoholics in infertility cases and controls. The chi-square statistic is 0.0465. The p-value is 0.829222. This result is not significant at $p < 0.05$.

Table 3 explains serum concentrations of FSH and LH levels in infertile and fertile men groups. The mean FSH and LH levels in azoospermic infertile men were 21.741 ± 4.17 and 20.888 ± 4.38 respectively whereas in oligospermic infertile males the mean FSH and LH levels were 17.387 ± 2.19 and 13.523 ± 5.46 respectively as against 5.245 ± 1.62 and 4.379 ± 1.66 in controls respectively.

The mean and std. dev. of serum FSH and LH levels in infertile and control groups are presented in tables 4. FSH and LH levels showed significant increased ($p > 0.05$) in infertile men when compared with the controls.

	Smokers	Non-Smokers	P-Value
Cases	28 (31.33) [0.35]	22 (18.67) [0.6]	0.0914
Controls	19 (15.67) [0.71]	6 (9.33) [1.19]	

Table 1: Association of Smokers with Infertility Cases and Controls

* $p < 0.01$ -Significant; ** $p < 0.02$ -Moderately significant; *** $p < 0.005$ -Highly Significant, NS-Not significant.

	Alcoholics	Non-Alcoholics	P-Value
Cases	41 (41.33) [0]	9 (8.67) [0.01]	0.8292
Controls	21 (20.67) [0.01]	4 (4.33) [0.03]	

Table 2: Association of Alcoholics with Infertility Cases and Controls

* $p < 0.01$ -Significant; ** $p < 0.02$ -Moderately Significant; *** $p < 0.005$ -Highly Significant, NS-Not significant.

Fig. 1: Frequency Distribution of Smokers and Alcoholics in Infertile Cases and Controls

Infertile and Fertile Men Groups	Numbers	Hormone Levels Mean+SD	
		FSH	LH
Azoospermia	38	21.741 ± 4.17	20.888 ± 4.38
Oligospermia	12	17.387 ± 2.19	13.523 ± 5.46
Fertile Men	25	5.245 ± 1.62	4.379 ± 1.66

Table 3: Serum Concentrations of FSH and LH Levels in Infertile and Fertile Men Groups

Parameters	Infertile Group (n=50)	Fertile Group (n=25)	95% CI	P-Value
FSH	20.722 ± 4.18	5.245 ± 1.625	17.2096 to -13.7444	<0.0001
LH	19.146 ± 0.92	4.379 ± 1.668	15.3615 to -14.1725	<0.0001

Table 4: Mean±SD of FSH and LH Parameters in the Infertile Cases and Controls

* $p < 0.01$ -Significant; ** $p < 0.02$ -Moderately Significant;

*** $p < 0.005$ -Highly Significant; NS-Not Significant

Fig. 2: Distribution of FSH Mean Levels in Infertile Cases and Controls

Fig. 3: Distribution of LH Mean Levels in Infertile Cases and Controls

DISCUSSION

Infertility remains a global health problem with an increasing incidence. It is generally defined as one year of unprotected intercourse without conception. Approximately, 85-90% of healthy young couples conceive within one year. Infertility affects 10-15% of couples is an important part of investigation and helps the couple to have children (Mosher L et al 1991).

Ascertaining the reproductive hormone levels is utmost important in the evaluation of male infertility. Emokpae MA et al 2007 reported that these hormones have an important role in male spermatogenesis.^[12] LH, FSH evaluation is useful in the management of male infertility.^[13] FSH is necessary for initiation of spermatogenesis and maturation of spermatozoa. In the infertile men, higher concentration of FSH is regarded to be a reliable indicator of germinal epithelial damage and was proven to be associated with azoospermia and severe oligozoospermia.^[14] De Kretser et al^[15] reported inflated levels of serum FSH with increasing severity of seminiferous epithelial destruction. In the present study, gonadotropin (FSH and LH) levels were elevated significantly in infertile males when compared with the levels in proven fertile controls, which are in accordance with the studies of Sulthan et al,^[16] Zabul et al,^[13] Weinbauer and Nieschlag,^[17] A Subhan et al,^[18] Ramesh Babu et al,^[19] and Dhananjay et al^[20] studies, which stated similar results of elevated levels of both follicle-stimulating hormone and luteinizing hormones in infertile males. Elevated levels of LH in oligospermic and azoospermic males when compared to normal fertile men were also reported.^[21] In germ cell development, FSH, LH, and testosterone are prime regulators and the quantitative production of spermatozoa generally needs the presence of FSH, LH, and testosterone in which FSH acts directly on the

seminiferous tubules whereas luteinizing hormone stimulates spermatogenesis indirectly via testosterone. FSH plays a major role in stimulating mitotic and meiotic DNA synthesis in spermatogonia.^[22] The overall results clearly indicate significant increase in gonadotropins (FSH and LH) in all the subgroups (azoospermia, oligozoospermia). The observed increase in the FSH and LH levels are to stimulate the Sertoli and Leydig cells for proportionate synthesis and secretion of testosterone thereby enhancing spermatogenesis. With advancement of age, decline in testosterone, and inflation in gonadotrophins are associated with a decrease in sperm production and number of normal sperm.^[23]

Among many factors which lowers reproductive functions, excessive intake of alcohol has been considered seriously in males. Jensen et al (1988), S. Samal et al (2012) stated that the complete cessation of alcohol consumption is associated with improved fertility. Durphy et al (1991) suggested that chronic alcoholism can cause testicular atrophy leading to oligospermia or azoospermia and also cause ejaculatory dysfunction. In the present study, the relationship between alcohol consumption and abnormalities of semen was not evident and are in contrast with the findings of the above authors.^[24-27] Ejaculatory dysfunction can also result from chronic alcoholism.⁽²⁸⁻²⁹⁾

In India, cigarette smoking is highly prevalent among men in the age group of 25-35. The effect of smoking on male reproduction has also been studied where semen quality was investigated in different cross-sectional studies including infertile patients with conflicting results. In males, it has been reported that cigarette smoking have negative effects on every system involved in the reproductive process. Spermatozoa from smokers have less fertilising capacity and embryos display lower implantation rates.^{30,31} Most of the studies reported that the effect of cigarette smoking on levels of male reproductive hormones; however, the findings still remain disputed. Though, the current study not shown a reduction in male fertility associated with smoking, smokers should quit smoking for the sense of responsibility for their future generation as tobacco smoke contains numerous mutagenic substances.

It is established that membrane damage and the formation of Leydig cell autoantibodies are due to excessive alcohol intake, which effects Leydig cell function by reducing testosterone synthesis and its metabolite, acetaldehyde. Also, it disturbs hypothalamopituitary function, further worsening testicular and sexual function. Impotence is a well-known effect of alcoholism as are the signs of hyperoestrogenism, which is probably secondary to disturbances of the metabolism of testosterone and oestrogens in the cirrhotic liver.⁽²⁸⁻²⁹⁾

CONCLUSION

From this study, it may be concluded that high plasma levels of gonadotropins, low sperm count are pathognomonic of male infertility. The high level of gonadotropins is an indication of testicular problems as the cause of infertility in studied subjects. However, further studies are recommended in large sample to evaluate the levels of gonadotropins and confirm the indication in infertile males.

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