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Association of Thyroid Hormones with Prolactin, Follicle Stimulating Hormone and Luteinizing Hormone in Female Infertility.

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ABSTRACT

Background: Human infertility is a major health problem worldwide having its impact on the social, psychological, economical and sexual life of a couple. **Methods:** Total of 80 subjects (Out of which 50 infertile female and 30 normal fertile female) were selected on gynecology infertility outpatient department between age group of 20 to 44 years. Out of 50 infertile women, 34 were of primary infertility and 16 of secondary infertility. **Results:** Statistically significant higher serum TSH levels were noted in the infertile subject with euthyroid ($p=0.03$) and hypothyroidism ($p<0.001$) when their distributions were compared to their respective fertile subjects. The rise in serum FT3 and FT4 in the infertile subjects with hyperthyroidism was found to be not significant as compared to the fertile subjects with hyperthyroidism. The mean serum prolactin concentration in the infertile female with euthyroid was significantly higher ($p<0.01$) than the fertile subjects with euthyroid. The infertile women with hypothyroidism had statistically significant higher prolactin levels than the other three categories (the fertile female and the infertile subjects with euthyroid and hyperthyroidism) ($p<0.01$). **Conclusion:** High prevalence of hypothyroidism was seen in infertile female. These disorders may lead to menstrual irregularities resulting in infertility.

Keywords: TSH, FT3, FT4, FSH, LH, Prolactin & Infertility.

INTRODUCTION

Human infertility is a major health problem worldwide having its impact on the social, psychological, economical and sexual life of a couple.[1] Infertility is an important condition in reproductive medicine and defined as the inability of a couple to access of pregnancy after 12 months of regular, unprotected intercourse.[2,3] The economic burden of infertility is also considerable as female infertility treatments impose a substantial financial burden.[4] In developed countries, 80-90% of couples attempting to conceive are successful after 1 year and 95% after 2 years.[5] There are no reliable estimates for global prevalence of infertility.[6] The incidence of female infertility is rising and varies from 10 to 20%.[7] Infertilities, either primary or secondary will occur for almost 15% of all women worldwide.[8] Female infertility occurs in about 37% of all infertile couples.[9] Infertility is divided in two groups of primary and secondary. Its rate has reported to be ranged from 0.6% to 3.4% for the primary infertility and 8.7% to 32.6% for the one infertility.[6] Hormonal disorders of female reproductive system are comprised of a number of problems resulting from dysfunction of hypo-thalamic-pituitary ovarian axis. These relatively common disorders often lead to infertility.[10] Thyroid dysfunction which is quite prevalent in the population affects many organs including male and female gonads, interferes with human reproductive physiology, which reduces the likelihood of pregnancy and adversely affects pregnancy outcome, thus becoming relevant in the algorithm of reproductive dysfunction.[11] However, many infertile women present with normal menses despite a raised serum prolactin level. Pituitary hormones such as TSH, prolactin or growth hormone may act synergistically with FSH and LH to enhance the entry of non-growing follicles into the growth phase.[12] Morphological changes observed in the follicles in hypothyroidism can be a consequence of higher prolactin production that may block both secretion and action of gonadotropins.[13,14] The prevalence of infertility is estimated to be between 10 and 18%. It thus represents a common condition, with important medical, economic and psychological implications.[12] Proper evaluation of these disorders involves a multidimensional diagnostic approach.

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Aim of this present study was to be the association of thyroid hormones level with prolactin, Follicle Stimulating Hormone and Luteinizing Hormone in female infertility.

MATERIALS AND METHODS

This present study was conducted in the Department of Biochemistry in collaboration with Obstetrics and Gynecology department at Hi-Tech Medical College and Hospital, Rourkela during the period July, 2015 to November, 2016. The study was conducted after getting ethical committee clearance from the institute. Informed, written and understood consent of the participants were taken. A total of 80 subjects (Out of which 50 infertile female and 30 normal fertile female) were selected on gynecology infertility outpatient. Out of 50 infertile female, 34 were of primary infertility and 16 of secondary infertility. Infertile women age between 20 to 44 years and Normal fertile female age between 20 to 40 years were included in the study. Infertile female having tubular blockage, pelvic inflammatory disease, endometriosis and with genital tuberculosis, those already on treatment for thyroid disorders or hyperprolactinemia were excluded from the study. Five (5) ml of fasting venous sample obtained in the morning of day were collected from all participants in their early follicular phase of menstrual cycle i.e. between days 3rd to 5th of menstrual cycle for serum biochemical analysis, Serum was separated after 1 hour by centrifugation at 3000 rpm for 10 minutes, and was tested for following parameters by "E cobas 411".

Serum FT3 (pg/ml)
Serum FT4 (ng/ml)
Serum TSH (µIU/L)
Serum FSH (IU/L)
Serum LH (IU/L)
Serum Prolactin (ng/ml)

Statistical analysis was done using by using online student t-test calculator and Pearson correlation of coefficient was used to see the association between thyroid hormones level with prolactin, Follicle Stimulating Hormone and Luteinizing Hormone in female infertility. P-value less than 0.05 was considered as significant.

RESULTS

The infertile female patients were compared with the fertile females as controls for association of thyroid hormones level with prolactin, Follicle Stimulating Hormone and Luteinizing Hormone. The subjects were categorized in fertility female as controls and Infertile female as cases. Infertile females are further sub categorized as Primary infertile female and secondary infertile female. The Reference Ranges of Prolactin, FSH, LH, FT3, FT4 and TSH hormones levels was given in table–1. Thyroid hormonal function status of study population was given in Fig.(1,2,3,4,5&6). Infertile female and fertile female were further categories in Euthyroid, Hyperthyroid and hypothyroid according to their thyroid hormones function status. Most of the fertile female 22 (73.3%) and infertile female 36 (72.0%) were euthyroid. The prevalence of hyperthyroidism in fertile and infertile female were 04 (13.3%) and 05 (10.0%), respectively.

Table 1: Reference Ranges of Prolactin, FSH, LH, FT3, FT4 and TSH hormones levels.

Sr. no.	Parameters	Reference Range	Units
1.	Prolactin	2 - 29	ng/ml
2.	FSH	3.84 - 8.78	IU/L
3.	LH	2.1 - 10.89	IU/L
4.	FT3	0.8 - 2	pg/ml
5.	FT4	6 - 12.23	ng/ml
6.	TSH	0.5 - 5	µIU/L

Table 2: Thyroid hormone status among the fertile and infertile female

Variables	Fertile female N=30	Infertile female N=50	Total N=80
Hypothyroid	04 (13.3%)	09 (18.0%)	13 (16.25%)
Euthyroid	22 (73.3%)	36 (72.0%)	58 (72.5%)
Hyperthyroid	04 (13.3%)	05 (10.0%)	09 (11.25%)

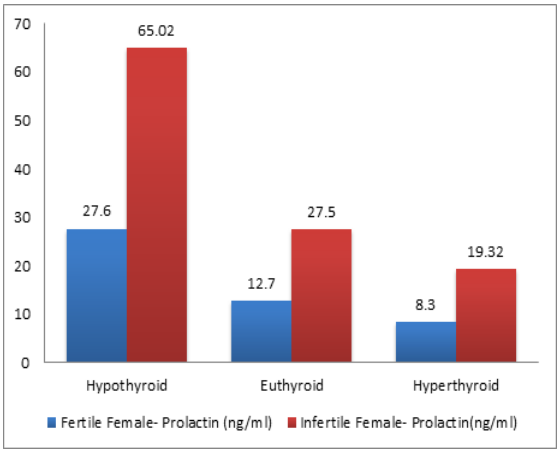

Figure 1: Mean of protactin level in between fertile and infertile female.

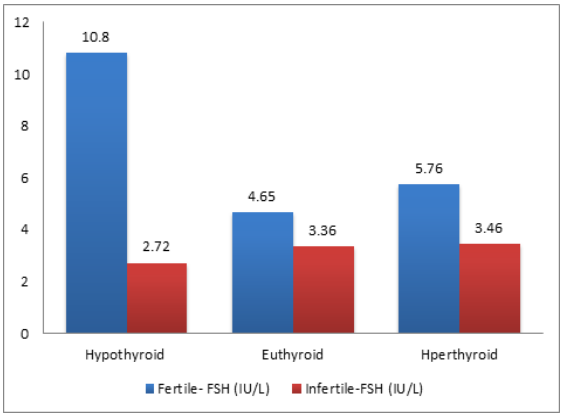

Figure 2: Mean of FSH level in between fertile and infertile female.

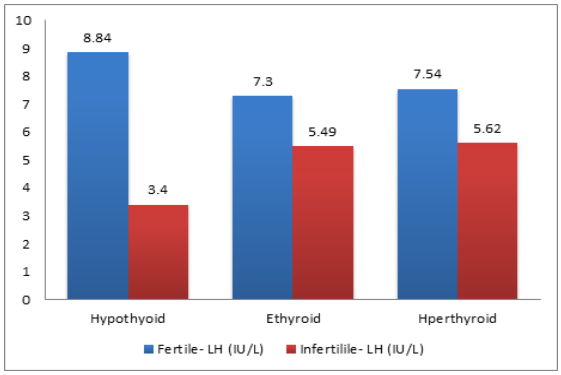

Figure 3: Mean of LH level in between fertile and infertile female.

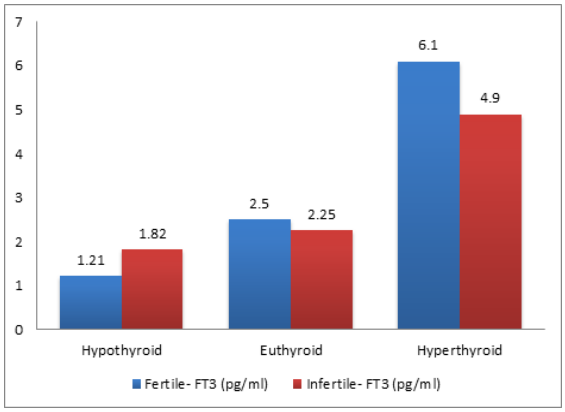

Figure 4: Mean of FT3 level in between fertile and infertile female.

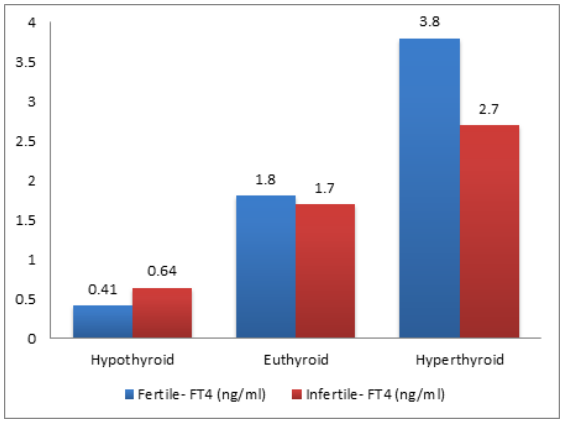

Figure 5: Mean of FT4 level in between fertile and infertile female.

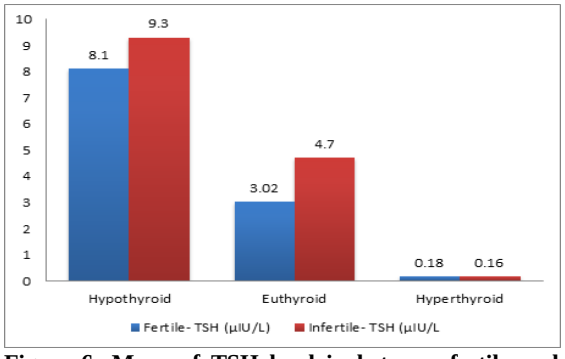

Figure 6: Mean of TSH level in between fertile and infertile female.

Hypothyroidism was seen in 09 (18.0%) of the infertile female whereas in the fertile female it was found to be 04 (13.3%). The crude prevalence of hypothyroidism was higher when compared to hyperthyroidism in the infertile female. Statistically significant higher serum TSH levels were noted in the infertile subject with euthyroid ($p=0.03$) and hypothyroidism ($p<0.001$) when their distributions were compared to their respective fertile subjects. The rise in serum FT3 and FT4 in the infertile subjects with hyperthyroidism was found to be not significant as compared to the fertile subjects with hyperthyroidism. The mean serum prolactin concentration in the infertile female with euthyroid was significantly higher ($p<0.01$) than the fertile subjects with euthyroid. The infertile women with hypothyroidism had statistically significant higher prolactin levels than the other three categories (the fertile female and the infertile subjects with euthyroid and hyperthyroidism) ($p<0.01$). There was also higher level of prolactin in hypothyroid fertile subjects as compared to euthyroid and hyperthyroid control. Thus, there were not any statitically significant difference in the concentration of FSH, LH and prolactin among groups of the studied i.e; infertile female. Positive correlation was found between Prolactin and TSH while LH, LSH, FT3 and FT4 shows negative correlation with Prolactin.

DISCUSSION

This present study has revealed that hypothyroidism is more prevalent than hyperthyroidism. Thyroid dysfunction is a condition known to reduce the likelihood of pregnancy and to adversely affect pregnancy outcome. Data on the relationship between thyroid disorders and infertility remain scarce and the association with a particular cause of infertility has not been thoroughly analyzed.[15] The increase in prolactin secretion can be physiological e.g. during pregnancy and lactation or pathological due to hypothalamic and pituitary diseases, or it can be iatrogenic. Hyperprolactinemia induces suppression of the hypothalamic-pituitary-gonadal axis and resistance of the ovary to gonadotropin action, which results in amenorrhea and lack of ovulation.[16] Serum levels of Prolactin and TSH increased in infertile female as compared to fertile subjects, the differences among three categories being highly significant. Serum Prolactin levels were found to be strongly correlated with TSH levels in primary infertile female and Secondary infertile female and this correlation was statistically significant. As per the study, we observed a greater percentage of infertile female with hypothyroidism exhibiting hyperprolactinemia (18.0%). These findings in our study strongly correlate with the findings of study by Goswami Binita, et al. (2009), they found 46.1% infertile women with hypothyroidism had hyperprolactinemia.[17]

Kumkum, et al. (2006), in their study incidence of hypothyroidism in hyperprolactinemic women was 25.50% (13/51). So, a positive correlation of 1:4 was found between hypothyroidism and hyperprolactinemia.[18] In our study serum LH and FSH was decreased in infertile female as compared to fertile subjects, the differences among three categories being highly significant. Follicle Stimulating Hormone and Luteinizing Hormone both are negatively correlated with prolactin. Azima Kalsum, Samina Jalali (2002), in their study shows a significant decrease in serum Luteinizing Hormone in follicular, ovulatory and luteal phase in hyperprolactinemic women having primary and secondary infertility. Significantly low serum follicle stimulating hormone levels were observed in ovulatory phase in women reported with primary infertility. Similarly significant decrease in serum follicle stimulating hormone in luteal phase in hyperprolactinemic women reported with secondary infertility was observed.[19] Yamaguchi, et al. (1991), found decreased luteinizing hormone secretion in nocturnal hyperprolactinemic women.[20] The correlation between thyroid stimulating hormone and prolactin was studied in 2006. It was observed that incidence of hypothyroidism in hyperprolactinemia was 25.5%. The ratio of proportions between hyperprolactinemia and hypothyroidism was 5:1 i.e. in every four hyperprolactinemic patients one had hypothyroidism.[21] Our study revealed a significant association between abnormal menstrual patterns, with hyperprolactinemia and hypothyroidism in the infertile female. It would be interesting to find out the incidence of hypothyroidism in infertile female with normal prolactin levels and compare it with the incidence in hyperprolactinemic infertile female.

CONCLUSION

These findings suggest that the high prevalence of hypothyroidism was seen in infertile female. These disorders may lead to menstrual irregularities resulting in infertility. This is also associated with hyper prolactinemia and these patients are commonly associated with ovulatory failure. The high prevalence of hyperprolactinemia and thyroid disorders in cases of primary infertility stresses the fact that all the female coming for infertility checkup should be recommended to undergo thyroid function tests and serum prolactin estimation.

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