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Research Article

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Correlation of Serum TSH with Ovarian Reserve in Patient of Infertility. A Retrospective Study

Nilam Subedi[1*], Padam Raj Pant[1] and Nirajan Subedi[2]

[1]*Department of Obstetrics and Gynaecology Grande International Hospital, Kathmandu, Nepal*

[2]*Department of Surgical Gastroenterology at National Academy of Medical Sciences Bir Hospital, Kathmandu, Nepal*

[*]**Corresponding author**

Nilam Subedi, Department of Obstetrics and Gynaecology, Grande International Hospital, Kathmandu, Nepal.

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ABSTRACT

Background: Various hormones have different impact in fertility either to predict, to investigate or to treat infertility. Due to hindrance in follicular growth, embryo development, implantation and placental formation thyroid dysfunction affects fertility. Studies suggest that thyroid disorder affecting follicular process is associated with ovarian reserve. Similarly serum FSH is directly related to AMH depicting strong correlation of age with each other. This study was conducted to see the association between thyroid dysfunction and serum Anti Mullerian Hormone (AMH) level.

Methods: All the female having infertility between age of 20 to 45 were included in the study. Those who did not undergo hormonal assay were excluded from study. All the data were taken from Opd record and their serum Thyroid Stimulating Hormone, AMH and Day2 Follicle Stimulating Hormone, Luteinizing Hormone, Prolactin, Estradiol and Progesterone were evaluated.

Result: A total of 292 patients visited infertility clinic at our institution over a period of 1.5 yrs and of them only 80 had undergone all hormonal assay. Majority of women enrolled for the study were in the age group 21-30 and the mean age was 29.98±5.4 yrs. Hypothyroidism was seen in 27.5% (n=22) females while we found no cases of hyperthyroidism in our study. Though 35% of females had TSH <2.5. Low serum AMH levels (<1.6 ng/ml) were noted in 25% (n=20). Among women of age less than 35 yrs and low AMH (<1.6) mean TSH was 7.27±6.93 and with normal AMH (>1.6) mean TSH was 3.61±1.73 which was statistically significant (p-value <0.001). Similarly mean FSH in women with low AMH (<1.6) was 8.66±2.89 and with normal AMH (>1.6) was 5.81±1.36 which was statistically significant (p-value <0.001).

Conclusion: TSH and FSH level is inversely related to ovarian reserve infertile women.

Keywords: Infertility, Anti Mullerian Hormone, Thyroid Dysfunction

Introduction

Infertility is defined as the failure to achieve clinical pregnancy after 12 months or more despite regular coitus without contraception. It can be primary and secondary [1]. Approx 8-12 % of couples are affected by infertility worldwide. It is important to determine ovarian reserve for better assessment and treatment of subfertility [2]. Various tests are done to assess ovarian reserve like estimation of basal serum follicle stimulating hormone (FSH), Anti Mullerian Hormone (AMH) and Antral Follicular Count (AFC) by sonography [3]. AMH is a dimeric glycoprotein produced by granulosa cells of preantral and small antral follicles and it is considered as a suitable biomarker of ovarian reserve [4]. Reduction in the quantity and quality of oocytes along with subsequent decrease in ovarian reserve is a age dependent process [5]. Presence of thyroid hormone receptors on oocytes suggests that thyroid hormones may influence ovarian functions [6]. Thyroid hormone is also found in follicular fluid so it plays an important role. Studies suggest higher level of serum TSH in infertile women than those in normal fertile women [7]. FSH along with TSH has synergistic effect in promoting the proliferation of granulosa cells. Similarly thyroid hormone regulates FSH stimulation in follicles and prevents their apoptosis [8]. Relationship between thyroid hormone and ovarian reserve is conflicting. Whereas when basal serum FSH is increased random serum AMH level is reduced which may be due to decline in ovarian reserve which tend to occur with increasing age [9]. May be with increasing age, both ovarian reserve decreases and thyroid disorder increases so this may be the cause of association between these two.

The aim of ovarian reserve assessment is to predict reproductive age, to detect early ovarian ageing or failure, to predict chances of conception and to counsel women who wants to delay childbirth despite increasing age. The present study aimed to determine the relationship of various hormones and ovarian reserve among women presenting with infertility at our centre.

Methods

The present study aimed to study the association between thyroid dysfunction and ovarian reserve in women presenting with

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infertility. All the cases of primary and secondary infertility were included in the study while those with known thyroid dysfunction, PCOD, past ovarian surgery and known Ovarian insufficiency were excluded from study. So total of 80 females were enrolled in the study. The study was conducted at Grande International Hospital, Kathmandu, Nepal over a period of past 1.5 yrs (2021.1.1 to 2022.6.1). It is a retrospective study. All the required data (Age, AMH, TSH, day 2 FSH, Estradiol, LH and Progesterone) were retrieved from OPD records and our electronic system. Lab cut off values were TSH (0.46-4.5 µIU/ml), AMH (<1.6 ng/ml=low, >1.6 ng/ml=normal), FSH (2.5-10.2mIU/ml) and estradiol (18.9-246.7 pg/ml). Participants were divided in two groups of age <35 yrs and age >35 yrs. According to TSH they were divided into three groups of <2.5, 2.5-4.5 and 4.5 mIU/L. In terms of AMH <1.6 and AMH >1.6.

Statistical Analysis

Data analysis was conducted with Statistical Package for the Social Sciences for Windows software, version 22 (SPSS). Descriptive statistics with a normal distribution were presented as mean ± standard deviation; those with a non-normal distribution were presented as median (min-max); and nominal variables were presented as number of cases and percentage (%). The significance of the difference between the two groups was evaluated with Student's t-test for means and the Mann-Whitney U test for medians. The significance of the mean difference between more than two groups was evaluated with the ANOVA test.

Results

Table No 1

AGE	FREQUENCY	PERCENTAGE
21-30	50	62.5%
31-40	24	30.0%
41-45	06	7.5%

Majority of women enrolled for the study were in the age group 21-30 and the mean age was 29.98±5.4 yrs.

Table No 2

TSH LEVEL	FREQUENCY	PERCENTAGE
<2.5	28	35%
>4.5	22	27.5%
2.5-4.5	30	37.5%

Hypothyroidism was seen in 27.5% (n=22) females while we found no cases of hyperthyroidism in our study. Though 35% of females had TSH <2.5.

Table No 3

AMH	FREQUENCY	PERCENTAGE
<1.6	20	25%
>1.6	60	75%
2.5-4.5	30	37.5%

Low serum AMH levels (<1.6 ng/ml) were noted in 25% (n=20).

Table No 4

	AGE <35 YRS			AGE >35 YRS		
	AMH<1.6 N=10	AMH>1.6 N=58	P-VALUE	AMH<1.6 N=10	AMH>1.6 N=2	P-VALUE
TSH	7.27±6.93	3.61±1.73	<0.001	1.53±0.72	3.6±00	0.003
FSH	8.66±2.89	5.81±1.36	<0.001	9.06±2.35	8.5±00	0.75
ESTRADIOL	41.34±4.41	51.01±24.87	0.228	43.7±7.92	41.9±00	0.76

Of the 80 females in the study 68 were of age less than 35 yrs and 12 of age more than 35 yrs. Among women of age less than 35 yrs and low AMH (<1.6) mean TSH was 7.27±6.93 and with normal AMH (>1.6) mean TSH was 3.61±1.73 which was statistically significant (p-value <0.001). Similarly mean FSH in women with low AMH (<1.6) was 8.66±2.89 and with normal AMH (>1.6) was 5.81±1.36 which was statistically significant (p-value <0.001). Among women of age more than 35 yrs mean TSH among the women with low AMH and normal AMH was 1.53±0.72 and 3.6±00 with p value 0.003. Similarly mean FSH among women with low AMH and normal AMH was 9.06±2.35 and 8.5±00 which was not statistically significant (p-value 0.75)

Mean age of patient with TSH <2.5 was 32.86±6.01 while those with TSH 2.5-4.5 and TSH >4.5 were 29.13±5.171 and 27.45±3.09 simultaneously which was satistically significant (p-value <0.001). Mean AMH in group with TSH <2.5, TSH 2.5-4.5 and TSH >4.5 was 3.55±3.69, 4.09±3.36 and 5.36±4.97. Similarly mean FSH in group with TSH <2.5, TSH 2.5-4.5 and TSH >4.5 was 7.17±2.64, 6.79±1.90 and 5.76±1.66 simultaneously. Mean estradiol in TSH <2.5, TSH 2.5-4.5 and TSH >4.5 was 41.76±10.16, 50.97±24.083 and 54.26±24.08 simultaneously.

Table No 5

TSH	<2.5(N=28)	2.5-4.5 (N=30)	>4.5(N=22)	P- Value
Age	32.86±6.01	29.13±5.171	27.45±3.09	0.001
AMH	3.55±3.69	4.09±3.36	5.36±4.97	0.273
FSH	7.17±2.64	6.79±1.90	5.76±1.66	0.97
Estradiol	41.76±10.16	50.97±24.083	54.26±24.08	0.069

Discussion

Thyroid dysfunction most often affects fertility and hypothyroidism is the common on. Some studies show association between thyroid dysfunction and decreased ovarian reserve while others show no significant correlation. But it is well known that both thyroid disorders and decreased ovarian reserve increase with age.

Hypothyroidism was the most common thyroid dysfunction in our study 27.5%. The study conducted by Unnikrishnan et al reported similar result [10]. Serum AMH which was chosen as biomarker of ovarian reserve was observed to be low <1.6 in 25% (n=20) lowest being 0.08ng/ml. The mean AMH in our study was 4.25 while study done by Vedantam et al. reported

mean AMH of 2.44 ng/ml which was lower than our study [2]. There was no significant association between age of women and thyroid dysfunction but there was significant association between age, TSH and AMH. Women of age less than 35 yrs and low AMH had mean TSH of 7.27±6.93 and with normal AMH it was 3.61±1.73. Similar result were observed by Kabodmehri et al where TSH was higher in participants with AMH <1.1 ng/ml [5]. In another study conducted by Al-Azzawi et al negative correlation was observed between serum TSH and serum AMH levels [11]. Michalakis et al have shown association between TSH and ovarian reserve, and in 18% of patients with low ovarian reserve, TSH levels were higher than 4μIU/ml [12]. In 2015, a cross sectional analytical study was conducted including patients with normal, low and high ovarian response. They found no relationship between thyroid hormone level and AMH level and similar result was obtained by Kucukler and colleagues [13]. Kambodmehri et al reported higher FSH levels in participants with AMH <1.1 ng/ml in women of all age group [5]. Present study also showed similar results. This suggests that reduced ovarian function causes changes in both quantity and quality of ovarian factors and FSH is increased through the feedback system.

To summarize, most women enrolled for the study were having primary infertility. Women with low AMH had higher TSH level in comparison to those with normal AMH. Association between hyperthyroidism and AMH could not be determined.

Limitations of the present study were small sample size, it being a single centre study and also a retrospective study.

Conclusion

Hypothyroidism was the most common thyroid disorder in this present study. There seemed no influence of age over thyroid disease but with increasing age FSH was increased and AMH was decreased. Ovarian reserve level in infertile patient were inversely correlated with TSH and FSH levels.

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