

ROLE OF THYROID DYSFUNCTION IN INFERTILE WOMEN WITH MENSTRUAL DISTURBANCES

Sabeen Nasir, Muhammad Mumtaz Khan, Sajjad Ahmed, Sadaf Alam, Sara Ziaullah

Department of Pathology, Peshawar Medical College, Peshawar, Pakistan

ABSTRACT

Background: Normal thyroid function is necessary to maintain reproductive physiology. An abnormality in its function may be the cause of infertility manifesting as abnormal menstrual cycle. The objective of this study was to find the role of thyroid dysfunction in primary and secondary infertile women with menstrual disturbances.

Material & Methods: A total of 168 subjects comprising of 106 primary and 62 secondary infertile women were evaluated. Their detailed clinical and menstrual histories were obtained and their blood samples were taken for thyroid profile.

Results: Out of 168 infertile patients 134(79.76%) had euthyroid, 31(18.45%) hyperthyroid and only 3(1.78%) patients had hypothyroid profile. Irregular menstrual cycles were found in 10 out of 31 (32.25%) hyperthyroid, 2 out of 3 (66.66%) hypothyroid and 21 out of 134 (15.67%) euthyroid infertile women. A significant p-value was obtained on comparison of thyroid profile with irregularities in menstrual cycle.

Conclusion: It was found that an abnormal thyroid profile may be the cause of infertility in women presenting with menstrual disturbances.

KEY WORDS: Female Infertility; Thyroid Hormones; Menstruation Disturbances; Menstrual Cycle; Hypothyroidism; Hyperthyroidism.

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INTRODUCTION

World Health Organization defines infertility as “failure of a couple to conceive after 12 months in spite of normal cohabitation”.¹ Around 60 to 80 million people suffer from infertility worldwide.^{2,3} Primary infertility is the complete inability to conceive and ranges from 2% to 5% and secondary infertility stands for cessation of further fertility and has a prevalence rate of 20% globally.²

For successful implantation and maintenance of pregnancy normal endocrine activity and hormone levels are essential. Thyroid hormones and reproductive functions interact with each other although their precise mechanism is poorly understood. Thyroid disease often causes menstrual disturbances and problems related to infertility. Thyroid hormones (TH) act through its receptors and transcription factors present in most cell types in the body. Thyroid stimulating hormone (TSH) stimulates TH synthesis in

the thyroid gland, but seems to have other functions as well in the female reproductive tract. The receptors of both TH and TSH increase in the receptive endometrium, suggesting that they are important for implantation, possibly by influencing inflammatory mediators such as leukemia inhibitory factor which is one of the most important cytokines in female reproduction. The association between thyroid disease and infertility indicates that TH and TSH affect the endometrium and ovary at the paracrine level.⁴

Thyroid hormone is important for growth and metabolism and it regulates cellular functions, therefore along with gonadotropins, e.g. follicular stimulating hormone (FSH), leutinizing hormone (LH) and prolactin also play an important role in female reproductive system and fertility. Thyroid disorders (hypo and hyperthyroidism) have known association with menstrual irregularities which may lead to infertility.⁵⁻⁷

An important cause of menstrual disturbance including oligomenorrhea, amenorrhea, polymenorrhea and menorrhagia is due to abnormal thyroid profile which can lead to irregularities in estrogen, prolactin and gonadotropin releasing hormone as well as pulsatile release of LH.⁸

Corresponding Author:

Prof. Muhammad Mumtaz Khan
Department of Pathology
Peshawar Medical College
Peshawar, Pakistan
E-mail: mmumtazkhan@gmail.com

Thyroid hormones have also a special effect on oocyte physiology and their normal thyroid levels helps in achieving maximum fertilization rates. This is also proven by the fact that treatment of hypothyroid infertile women normalized prolactin levels and LH response to leutinizing hormone releasing hormone (LHRH) resulting in a decrease of menstrual irregularities and thus increasing the chances of spontaneous fertility. Even in women undergoing in-vitro fertilization (IVF), serum TSH level can help in determining failure or success of fertilization.^{9,10}

In thyrotoxicosis oligomenorrhea or amenorrhea is common and fertility hormone levels are increased but normal ovulatory cycles can also occur. The increase in LH, FSH and estrogen metabolism is due to increase in activity of gonadotropin releasing hormone¹¹ but the mid-cycle LH peak may be reduced or absent.¹² There are also reports of a significant increase in release LH but not FSH after administration of thyrotropin releasing hormone (TRH).¹³

An elevated sex hormone binding globulins concentration and decrease in metabolic clearance rate of testosterone and estradiol are found in thyrotoxic females. In some of the patients there is increased peripheral conversion of androgen to estrogen.¹⁴⁻¹⁷

The prevalence of thyroid disorders in infertile women is variable globally. Hyperthyroidism ranges from 2.1% to 5.8% and hypothyroidism ranges from 2.3% to 6% in different studies in infertile women.¹⁸⁻²⁰ Therefore, in female infertility workup, the evaluation of thyroid hormone profile should be given its due importance. The objective of this study was to find the role of thyroid dysfunction in primary and secondary infertile women with menstrual disturbances.

MATERIAL AND METHODS

This cross-sectional study consisted of 168 infertile women (both primary and secondary) referred to Department of Pathology, Peshawar Medical College, Peshawar from Health Care Centre, University Town Peshawar from 21st April 2013 to 10th August 2013.

In this study all infertile women were included who attended the infertility clinic OPD for work up and their spouse had normal values on semen analysis. Those patients who had history of thyroid disease or thyroidectomy were excluded from the study. Their clinical details along with menstrual history was recorded on a predesigned proforma. Estimation of serum levels of thyroid hormones (TSH, T3 and T4) were performed on Chemiluminescence Immunoassay Analyzer CLIA-IIS manufactured by Biomed Engineering, China using Chemiluminescence Immu-

noassay Kits manufactured by Autobio Diagnostics Co. Ltd manufactured by Zhengzhou, China and the manufacturer's instructions were followed. The reference values for thyroid status were taken as TSH (0.35 to 5.3 μ IU/mL), T4 (5.0 to 13.0 μ g/dL), T3 (0.8 to 1.9 ng/mL) Values below/above were considered abnormal.

The study was approved by Institutional Ethical Committee of Peshawar Medical College. Statistical analysis was performed using the statistical package for social sciences (SPSS) version 19. Statistical results were given as mean and standard deviation for continuous variables. Difference between the primary and secondary infertility were analyzed for statistical significance using Chi square test and $p < 0.05$ was considered statistically significant.

RESULTS

Among 168 infertile women 106 (63.09%) were cases of primary infertility and 62 (36.91%) of secondary infertility. The mean age of primary infertile women was 26.74 ± 4.82 years and secondary infertile women 30.52 ± 4.74 years. The details of their thyroid status with age and type of infertility are provided below. (Table 1 & 2)

Out of 10 hyperthyroid patients having menstrual irregularities 6 (60%) had oligomenorrhea whereas 4 (40%) had polymenorrhea. As compared to this the two hypothyroid patients had oligomenorrhea. (Table 3) A significant p-value was obtained on comparison of thyroid profile with irregularities in menstrual cycle. (Table 4) It was concluded that menstrual irregularities due to abnormal thyroid profile can play a role in infertility. Mean values of TSH, T4 and T3, were found to be slightly higher in secondary infertile lightly higher than primary infertile women. (Fig. 1)

DISCUSSION

The study consisted of 168 infertile women of reproductive age group. It included 106 cases of primary infertility and 62 cases of secondary infertility. Their age groups ranged from 21-41 years and 22-42

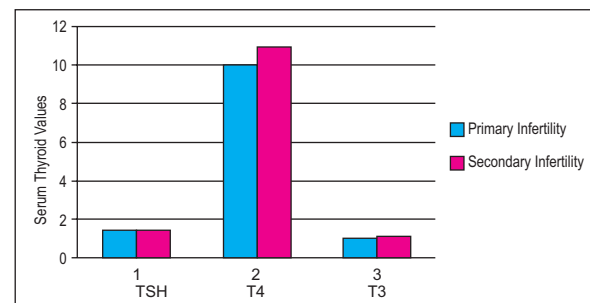


Figure 1: Mean values of TSH, T4 and T3 in primary and secondary infertile women.

Table 1: Age distribution and thyroid profile of infertile women.

Age group (years)	Primary (n=106)			Secondary (n=62)			Total	Percentage
	Hypo thyroid (n=1)	Hyper thyroid (n=15)	Eu thyroid (n=90)	Hypo thyroid (n=2)	Hyper thyroid (n=16)	Eu thyroid (n=44)		
> 20	0	1(0.94%)	10(9.43%)	0	0	(n= 44)	11	6.5
21--30	1(0.94%)	14(13.20%)	64(60.38%)	1(0.94%)	11(17.74%)	0	112	Total
31--40	0	0	15(14.15%)	1(0.94%)	5(8.06%)	21(33.87%)	43	25.6
41--50	0	0	1(0.94%)	0	0	22(35.48%)	2	11
						1(1.64%)		

Most of the patients with abnormal thyroid profile fell into 21–30 age group.

Table 2: Thyroid profile of primary and secondary infertile women.

Thyroid Status	Primary	Secondary	Total
Hypothyroid	1(0.94%)	2(3.22%)	3(1.78%)
Hyperthyroid	15(14.15%)	16(25.80%)	31(18.45%)
Euthyroid	90(84.90%)	44(70.96%)	134(79.76%)
Total	106(63.09%)	62(36.90%)	168

In our cases hyperthyroidism is more common than hypothyroidism.

Table 3: Comparison of thyroid profile with menstrual irregularities in primary and secondary infertile women.

	Primary infertility (106)			Secondary Infertility (62)			Total
	Eu thyroid (n=90)	Hyper thyroidism (n=15)	Hypo thyroidism (n=1)	Eu thyroid (n=44)	Hyper thyroidism (n=16)	Hypo thyroidism (n=2)	
Regular Menstrual Cycle	74(82.2%)	8(53.3%)	0	39(88.6%)	13(81.3%)	1	135(80.4%)
Irregular Menstrual Cycle	16(17.8%)	7(46.7%)	1	5(11.4%)	3(18.8%)	1	33(19.6%)

The percentage of menstrual irregularities is more common in hyperthyroid as compared to euthyroid infertile women.

Table 4: Comparison of thyroid profile with menstrual cycle.

Menstrual Cycle	Abnormal thyroid	Euthyroid	p-value
Irregular	12	21	0.01
Regular	22	113	

The significant p value indicates an association of menstrual irregularities with abnormal thyroid profile in infertile women.

years respectively. Their thyroid profile was evaluated in the light of menstrual history.

The prevalence of primary infertility in this study population was 63.09% and secondary infertility 36.90% which is close to another study conducted at Peshawar i.e. 73.31% and 26.68% respectively.²¹ The study conducted by Ghazi et al²² shows 54.5% for primary infertility and 45.6% secondary infertility.

Other studies conducted by Mosher²³ and Kasius et al²⁴ also have identical values. In contrast the study conducted by Girish & Manjunath²⁵ showed a higher incidence for primary infertility i.e. 80% and much lower for secondary infertility i.e., 17.8% as compared to this study.

In this study the prevalence of hyperthyroidism was 18.45%, which is almost similar to a study done

at a local tertiary care hospital which was 16%.²⁶ Other studies report prevalence of hyperthyroidism as 26% by Biradar et al²⁷ and 23% by Singh et al²⁸. Many studies have found prevalence of hyperthyroidism as 2.1%,²⁹ 2.2%,³⁰ 3.1%³¹ and 4.2%³² respectively. These percentages are much lower than my study which may reflect regional differences.

Hyperthyroidism was observed to be more common in age group 21-30 years in our study. The Prevalence of hypothyroidism in our study was 1.78% but several studies showed prevalence of hypothyroidism in infertile women as 8%,³³ 7.6%,³⁴ 6.4%³⁵ and 8.7%³⁶ respectively which are higher than our study. While in a study carried out by Sharma et al³¹ the prevalence of hypothyroidism was 35.4%.

In the present study menstrual irregularity was seen in 33 out of 168 cases i.e., 19.64%. (Table 2) Corresponding values (18.94%) have been reported by Shanti & Priyadarshini³⁵ but there is conflict with this study conducted by Goswami³³ which showed 60% cases had menstrual irregularities. The reason claimed by the author was due to special referral pattern of patients to the hospital based on suspicion of thyroid disease.

In our study we observed that menstrual irregularities due to both hypo and hyperthyroidism may play a significant role in infertility as compared to euthyroid status.

Petta et al³⁶ and Rahman et al³⁷ have described hyperthyroidism in infertile women of reproductive age group as 3.2% and 3.3% respectively. In the latter study out of 30 infertile women 53.3% had menstrual irregularities which he did not correlate with their thyroid profile. Joshi¹⁹ studied 53 hyperthyroid women among them 5.8% were infertile. He found menstrual irregularities in 65% hyperthyroid women. Both studies show a higher value than ours for hyperthyroidism but corresponding values for hypothyroidism were not available.

In another study Sharma & Baliarsingh³⁸ showed that hyperthyroidism was significantly correlated with menstrual disorders in infertile women. In our study 33 patients had menstrual irregularities out of which 10 had hyperthyroidism, 2 had hypothyroidism and 21 had normal thyroid profile. Among primary infertile women 46.7% had hyperthyroidism compared to 17.8% having euthyroid profile. In secondary infertile group 18.3% had hyperthyroidism as compared to 11.4% with euthyroid profile. It was observed that patients with abnormal thyroid profile with menstrual irregularities were at higher risk of infertility as compared to euthyroid patients.

CONCLUSION

Our study concludes that thyroid dysfunction plays a significant role in female infertility which may

manifest as menstrual disturbances especially in primary infertile women. Thyroid profile can help us in prompt diagnosis and timely initiation of therapy. Therefore thyroid hormone profile must be included in the routine workup of infertile women in our setup.

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CONFLICT OF INTEREST
Authors declare no conflict of interest.
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None declared.

AUTHORS' CONTRIBUTION

Conception and Design:	SN, MMK, SA
Data collection, analysis and interpretation:	SN, MMK
Manuscript writing and Revision:	SN, MMK, SA, SA