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Screening for thyroid disorders in infertile women

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Abstract
Infertility is defined as the inability of a couple to achieve conception after one year of unprotected coitus. In an era of advanced assisted reproduction technology (ART), we must not overlook screening for a condition like hypothyroidism. The present study was therefore undertaken to find out the incidence of hypothyroidism in infertility so as to ascertain the cost effectiveness of thyroid function test in routine infertility workup.
Materials and Methods: The present study was a prospective observational study done at infertility clinic and outpatient department (OPD) of Obstetrics and Gynecology, Government College and Hospital, Nagpur, Maharashtra, India.
Results: Out of total 150 cases, duration of infertility was maximum in the group 4 to 6 years comprising of 83 (55%) cases, followed by 59 (33%) cases in 1 to 3 years group and 4 each in 7 to 10 and >11 years groups. Primary in fertility was encountered in 127 (85%) of the cases, while secondary infertility was seen in 23 cases. Primary infertility was seen in 2 cases of clinical hypothyroidism, 8 cases of subclinical hypothyroidism and 2 cases of hyperthyroidism, while secondary infertility was detected in 1 case each in clinical hypothyroidism, subclinical hypothyroidism and hyperthyroidism.
Conclusion: In all cases of persistent anovulation following failure of ovulation induction drugs, thyroid dysfunction should be evaluated to rule out subclinical hypothyroidism as a major cause of infertility even though overt signs and symptoms of hypothyroidism are absent.

Keywords: Infertility, hypothyroidism, primary, secondary, hyperthyroidism, subclinical hypothyroidism

Introduction
Infertility is defined as the inability of a couple to achieve conception after one year of unprotected coitus. Infertility can be primary or secondary, the latter developing after an initial phase of infertility. 10-15% of the marriages prove to be childless. In any series of infertile marriages, the main etiological factor is found in the females in about 40% cases, while 35% of the husbands have some degree of infertility [1].
The factors responsible for infertility in females can be categorized as cervico-vaginal, uterine, tubo-peritoneal, ovarian, endocrinological and metabolic, immunological and psychological. In 10-20% of the cases, combination of factors operate and rest have unexplained infertility where no cause is found and it amounts to 10-20% in spite of increased sophistication of tests now available [2]. This group is the most versatile group and its percentage depends on meticulous examination, depth of probing for the causes and facilities available. It has been long been recognized that thyroid dysfunction may have profound effects on the female reproductive system and was described as early as 1840 by Von Basedow [3].
From the coincidence of thyrotoxicosis and pregnancy, it is clear that pregnancy occurs with considerable frequency in women with definite thyrotoxicosis. However, hypothyroidism is known to cause infertility of the anovulatory type [4]. Various factors implicated for anovulation are absence of mid cycle gonadotropin surge, low progesterone levels throughout the cycle, relatively low estrogen levels due to increase in estradiol metabolic clearance and increased production of estrol at the expense of estrone, constant reduction in sex hormone binding globulin leading to increase in free testosterone, enhancement of conversion of androstenedione to testosterone contributing to a disturbance of estrogen/ testosterone balance [3].
The treatment of infertility has come a long way as the disease itself. The list of investigations to ascertain the cause of infertility can be exhaustive, hence the specificity and cost effectiveness of these test if determined may reduce the burden of an already emotionally and economically drained infertile couple.

In an era of advanced assisted reproduction technology (ART), we must not overlook screening for a condition like hypothyroidism. The present study was therefore undertaken to find out the incidence of hypothyroidism in infertility so as to ascertain the cost effectiveness of thyroid function test in routine infertility workup.

Material and Methods: The present study was a prospective observational study done at infertility clinic and outpatient department (OPD) of Obstetrics and Gynecology, Government College and Hospital, Nagpur, Maharashtra, India. Study duration was of one year from October 2017 to October 2018.

Inclusion criteria

- All cases attending infertility clinic above 20 years of age
- All cases of primary and secondary infertility of more than 1 year duration
- Females staying with husband and not using contraception
- Cases willing to give informed consent.

Exclusion criteria

- Cases with gross Mullerian duct anomalies like uterine and vaginal agenesis
- Cases not willing to give informed consent.

Data collected

- Detailed history of both partners: duration of infertility, menstrual history, history of tuberculosis, pelvic inflammatory disease, diabetes, etc.
- Clinical examination: including general examination, systemic examination, per vaginal examination, etc.
- Routine investigations: including hemogram, blood sugar, VRDL, post coital test to rule out cervical factor, husband's semen analysis, etc.
- Thyroid profile: Serum T3, T4, TSH estimation by computerized radio immunoassay. [Table 1] [5]
- Hormonal assay: Serum FSH, LH, estrogen, progesterone, testosterone, prolactin. [Table 1] [5]

Table 1: Showing normal ranges of serum parameters

Normal values	Follicular phase	Ovulatory phase	Luteal phase
Serum FSH	5 to 20 mIU/ml	12-30 mIU/ml	1.5 to 9.1 mIU/ml
Sr. LH	5 to 25 mIU/ml	25 to 100 mIU/ml	0.5 to 16.9 mIU/ml
Sr. estrogen(estradiol)	20 to 60 pg/ml	>200 pg/ml	27 to 246 pg/ml
Sr. progesterone	0.98 to 3 ng/ml		2 to 20 ng/ml
Sr. testosterone	20 to 80 ng/dl		
Sr. prolactin	1 to 20 ng/dl		
Sr. T3	0.6 to 5 µ IU/ml		
Sr. T4	75 to 220 ng/dl		
Sr. TSH	4 to 11 µg/dl		

Ethical approval was taken prior to start of the study from Institutional Ethics Committee. Data was expressed as percentage value.

Results

Out of total 150 cases, maximum cases were in the age group25 to 30 years, which comprised of 83 cases (55%) followed by 60 (40%) cases in 20 to 24 age group and least in age group >31 years. Duration of infertility was maximum in the group 4 to 6 years comprising of 83 (55%) cases, followed by 59 (33%) cases in 1 to 3 years group and 4 each in 7 to 10 and >11 years groups. Primary in fertility was encountered in 127 (85%) of the cases, while secondary infertility was seen in 23 cases (15%). [Table 2]

Table 2: Showing age, duration and type of infertility in the study cases.

Sr. No.	Category	Sub-category	n (%)
1	Age	20 to 24 yrs	60(40%)
		25 to 30 yrs	83 (55%)
		>31 yrs	7(5%)
2	Duration of infertility	1 to 3 yrs	59(33)
		4 to 6 yrs	83(55)
		7 to 10 yrs	4(6)
		≥11 yrs	4(6)
3	Type of infertility	Primary	127(85)
		Secondary	23 (15)

On investigating the causes of infertility, it was found that major cause of infertility was ovulatory comprising of 40 cases (28%), followed by tubal factor in 32 cases (24%), thyroid dysfunction in 15 cases (10%), uterine factor in 11 cases (8%), and 29 cases (21%) were labelled as idiopathic as no cause was found. [Table 3]

Table 3: Showing causes of infertility in the cases

Causes of infertility		
Category	**Sub-category**	**n (%)**
Ovulatory		40 (28%)
Tubal		32 (24)
Uterine		11 (8)
Cervical		5 (5)
Thyroid dysfunction	hyperthyroidism	3 (2)
	hypothyroidism	12 (8)
Hyperprolactinemia		7 (5)
Male infertility		32 (27)
Cause not found		29 (21)

On analyzing the menstrual pattern in euthyroid cases, it was found that majority of the cases had regular menses, which comprised of 90 cases (67%), followed by oligomenorrhea in 41 cases (30%), and least in amenorrhea group comprising of 1 case (0.74%).

Table 4: showing menstrual pattern in euthyroid cases

Menstrual pattern in euthyroid cases		
Sr. No.	**Menstrual pattern**	**n (%)**
1	Regular	90(67%)
2	Menorrhagia	2(1)
3	Oligomenorrhea	41(30)
4	Polymenorrhea	2(1)
5	Amenorrhea	1 (0.74)

On analyzing age and thyroid dysfunction, it was found that 2 cases of clinical hypothyroidism were detected in age group 25 to 30 years and 1 case in 20 to 24 years; subclinical hypothyroidism was detected in 6 cases in the age group 25 to

30 years and 3 cases in the age group 20 to 24 years, while 3 cases of hyperthyroidism were detected in age group 25 to 30 years. Primary infertility was seen in 2 cases of clinical hypothyroidism, 8 cases of subclinical hypothyroidism and 2 cases of hyperthyroidism, while secondary infertility was detected in 1 case each in clinical hypothyroidism, subclinical hypothyroidism and hyperthyroidism. Regular menstrual pattern was seen in 1, 3 and 1 cases of clinical, subclinical hypothyroidism, and hyperthyroidism respectively. Oligomenorrhea was seen in 1, 6 and 1 case of clinical, subclinical hypothyroidism and hyperthyroidism, respectively. [Table 5]

Table 5: Showing age, duration of infertility and menstrual pattern in cases of thyroid dysfunction.

Thyroid dysfunction	Age in years		Duration in years				Type of infertility		Menstrual pattern			
	20-24	25-30	1 to 3	4 to 6	7 to 10	>10	primary	secondary	Regular	Oligomenorrhea	Menorrhagia	Amenorrhea
Clinical hypothyroidism	1	2	2	0	1	0	2	1	1	1	1	0
Subclinical hypothyroidism	3	6	6	2	1	0	8	1	3	6	0	0
Hyperthyroidism	0	3	0	1	2	0	2	1	1	1	0	1

Serum FSH was raised in 2 cases of hyperthyroidism and hypothyroidism, each. Serum LH was raised only in 2 cases of hypothyroidism. Serum estrogen was raised in 4 cases of hypothyroidism and reduced in 5 cases of hypo and 2 cases of hyperthyroidism. Serum progesterone was reduced in all the 12 cases of hypothyroidism and 2 cases of hyperthyroidism. Serum prolactin was raised in 3 cases of hypothyroidism and 1 case of hyperthyroidism. [Table 6]

Table 6: Showing serum hormone levels in cases with thyroid dysfunction.

Sr. No.	Serum hormones	Hypothyroid (n=12)			Hyperthyroid (n=3)		
		Normal	High	Low	Normal	High	Low
1	FSH	10(83%)	2(17)	0	1(33)	2(67)	0
2	LH	10(83%)	2(17)	0	3(100)	0	0
3	Estrogen	3(25)	4(33)	5(42)	1(33)	0	2(67)
4	Progesterone	0	0	12 (100)	0	1(33)	2(67)
5	Testosterone	3(25)	6(50)	3(25)	3(100)	0	0
6	Prolactin	9(75)	3(25)	0	2(67)	1(33)	0

Discussion

The present study was focused on analyzing various etiologies of infertility. Maximum cases in the present study were in the age group 25-30 years. Same finding was corroborated by a similar study [6]. However, other studies reported maximum cases in the age group 25 to 35 years age group [7]. This might be attributed to the fact that early marriages are common in India and the concerns for fertility are immense, hence subjects report earlier to infertility clinics.

The duration of infertility in the present study was maximum in the group of 4-6 years. Also, majority of the cases belonged to primary infertility group, as compared to secondary infertility. This was corroborated by the findings of other such study [6]. The incidence of hypothyroidism in the present study was around 8%, while other studies reported it in the range of 2.3% to 13.3% [8]. The discrepancy in findings can be attributed to either genetic factors, endemicity, or to delayed diagnosis in India.[5]

Out of the 12 cases of hypothyroidism, maximum cases i.e. 66% were found in the age group of 25-30 years and 33% belonged to the age group of 20-24 years. However in one study, it was found that 39% of the cases were in age group 26-30 years and 18% in the age group 21-25 years [9]. In the present study, maximum cases had infertility since 1-3 years, while hyperthyroid subset of these cases had infertility in the duration range of 7-10 years and majority of hypothyroid cases had infertility since 1-3 years. In a clinical study done by Lahri *et al*, it was found that majority of hypothyroid cases had total duration of infertility in the range of > 5 years [9]. Duration of infertility is comparatively less in our study, which may be because cases seeking infertility treatment are reporting earlier in our area. Also. Same study found that majority of the cases suffered from primary infertility as compared to secondary infertility, and that it is also the commonest type in both, hypo and hyperthyroidism [9].

Oligomenorrhea was the commonest menstrual aberration in the present study, which is almost twice as common in hypothyroid cases as compared to euthyroid cases. This finding was corroborated by other such study, which reported oligomenorrhea in >60% of the hypothyroid cases [7]. Other studies reported less incidence of oligomenorrhea in hypothyroidism, ranging from 30% to 44% [9].

In the present study, one third of the cases had proliferative endometrium suggestive of anovulation, while one quarter of the cases showed out of phase secretory endometrium suggestive of inadequate luteal phase, amounting to total of 58% of the cases with ovulatory dysfunction in the hypothyroid group. In similar such study, it was found that ovulatory dysfunction was present in one third of all hypothyroid cases, of which luteal phase was common as compared to anovulation [10]. High incidence of ovulatory dysfunction was reported in a study, accounting to 93% cases of hypothyroid infertile cases, comprising of proliferative phase in 73% cases and luteal phase defect in 20% of the cases. However, other studies reported high incidence of anovulation in hypothyroid cases i.e. >80% of the cases [7].

In the present study, all the cases had low progesterone values which is presumptive evidence of anovulation. Also, estrogen was low and testosterone was raised in most cases. In other clinical study, it was found that high gonadotropin levels was present in more than 50% of the cases, while serum estradiol was normal in all cases and testosterone was raised in more than 50% of the cases of hypothyroidism [7].

Conclusion

From the findings of the present study, it is evident that thyroid dysfunction is high in infertile women, and subclinical hypothyroidism is the commonest thyroid abnormality associated with infertility. Hence, in all cases of persistent anovulation following failure of ovulation induction drugs, thyroid dysfunction should be evaluated to rule out subclinical

hypothyroidism as a major cause of infertility even though overt signs and symptoms of hypothyroidism are absent.

References

1. Patra S, Unisa S. Female infertility in India: Causes, treatment and impairment of fertility in selected districts with high prevalence. Global Journal of Medicine and Public Health. 2017; 6(4):1-11.
2. Adamson P, Krupp K, Freeman A *et al*. Prevalence & correlates of primary infertility among young women in Mysore, India. Indian J Med Res. 2011; 134: 440-6.
3. Hamilton-Fairley D, Taylor A. ABC of subfertility: anovulation. BMJ 2003; 327:546-9.
4. Karaca N, Akpak Y. Thyroid disorders and fertility. Int J Res Med Sci 2015; 3:1299-304.
5. Veeresh T, Moulali D, Sharma D. A Study on Serum FSH, LH and Prolactin Levels in Women with Thyroid Disorders. International Journal of Scientific and Research Publications 2015; 5(3):1-4.
6. Shridevi N, Sandhyarani M. Study of Thyroid Profile in Infertile Women. IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS). 2015; 10(3):57-61.
7. Verma I, Sood R, Juneja S *et al*. Prevalence of hypothyroidism in infertile women and evaluation of response of treatment for hypothyroidism on infertility. Int J Appl Basic Med Res. 2012; 2(1):17-19.
8. Lincoln S, Ke R, Kutteh W. Screening for hypothyroidism in infertile women. J Reprod Med. 1999; 44(5):455-7.
9. Lahiri D, Dasgupta A, Kundu S. Menstrual pattern and fertility status of hypothyroid women. Journal of Obstetrics and Gynecology of India. 1996; 46(5):663-71.
10. Fupare S, Jambhulkar R, Tale A. Correlation of thyroid hormones with infertility in reproductive age group women. Indian Journal of Basic and Applied Medical Research. 2015; 4(4):488-495.