Original Research Paper Medical Science

Impact of Hypothyroidism on Infertility and Conception Following Oral Levothyroxine

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ABSTRACT

CONTEXT: Prevalence of hypothyroidism in reproductive age group is 2-4%. Hypothyroidism as a cause of infertility remains undiagnosed and untreated. Normal thyroid function is essential for conception as well as for healthy pregnancy. Hypothyroidism affects fertility by causing luteal phase defects, hyperprolactinemia, anovulatory cycles, sex hormone imbalance.

AIMS AND OBJECTIVES:

To study the prevalence of hypothyroidism in infertile women and evaluate the response to treatment with oral levothyroxine.

MATERIALS AND METHODS: 150 infertile women visiting the infertility clinic for the first time were investigated for thyroid function and serum prolactin. Women with clinical and subclinical hypothyroidism were treated with 25-150 micrograms of levothyroxine.

RESULTS: Of 150 infertile women, 31% were hypothyroid. Following treatment 30% conceived, 17% within three months and 83% conceived within 1 year of treatment.

CONCLUSION: Serum TSH and prolactin levels should be included in basic infertility work up. Oral levothyroxine increased the chances of conception in otherwise asymptomatic infertile women.

KEYWORDS HYPOTHYROIDISM, SUBCLINICAL, INFERTILITY

INTRODUCTION:

Hypothyroidism as a cause of infertility remains undiagnosed and untreated in many couples coming for infertility work up. Hypothyroidism can cause luteal phase defects, anovulatory cycles, hyperprolactinemia, sex hormone imbalances. Thyroid evaluation should be done in infertile couple as conception rate improves with oral thyroxine. Hypothyroidism can be assessed by detecting serum TSH levels. Subclinical hypothyroidism denotes increase in serumTSH with normal T3 andT4. Clinical hypothyroidism refers to increased serum TSH with low T3 and T4 levels. Hypothyroidism is associated with hyperprolactinemia due to increased TRH and ovulatory dysfunction. Subclinical hypothyroidism should be detetected and treated for spontaneous conception and maintenance of pregnancy.

MATERIALS AND METHODS:

150 primary infertile females aged 20-40 years consulting at Government RSRM Hospital over a period of one year were considered for the study obtaining consent from the institutional ethical committee. Complete medical, surgical, gynaecological history were obtained from the female. Male infertility and reproductive function of either partner was evaluated. Physical examination of female including height, weight, BMI, hair distribution, thyroid gland and pelvic examination were done. Semen analysis, tests for ovulation, tubal patency were done. All females were systematically screened on day3 of menstrual cycle for serumTSH and T4 using third generation electrochemiluminescence immunoassay.

Reference values:

Serum TSH-<2.5Miu/L
Free T4- 0.8-2ng/dl
Serum prolactin- 1.9-25ng/ml
Anti TPO antibodies-<35mIU/L

INCLUSION CRITERIA:

20-40 year old females, first visit to infertility clinic

EXCLUSION CRITERIA:

Women with tubal block, women with PID, women with endometriosis, women with genital tuberculosis, women with liver/ renal/ cardiac disease, women whose husbands have abnormal semen analysis

Prospective evaluation of patients meeting inclusion and exclusion criteria was done.

Infertile women with hypothyroidism alone or with associated hyperprolactinemia were given treatment for hypothyroidism with thyroxine 25-150 micrograms, regulating the dose by serial serumTSH monitoring at 6-8 weeks interval. The effectiveness and outcome of treatment was studied by assessing the fertility rate over three months to one year.

OBSERVATION AND RESULTS:

Of 150 infertile women 49 were found to be hypothyroid accounting for 30% of the study group[Table 1: prevalence of hypothyroidism]. 4 were excluded from the study due to other associated causes of infertility. 40 had subclinical hypothyroidism and 5 had clinical hypothyroidism.

TABLE 1: PREVALENCE OF HYPOTHYROIDISM IN INFRTILILE WOMEN

HYPOTHYROIDISM	49	30%
MALE FACTOR	24	16%
TUBAL FACTOR	20	14%
PCOD	32	22%
ENDOMETRIOSIS	6	4%
UTERINE ANAMOLIES	3	2%
UNEXPLAINED	16	12%

45 hypothyroid females were treated with oral levothyroxine 25-150 micrograms per day and serum TSH was monitored serially at 6weeks intervals. Conception rate among treated females was found to be affected by certain confounding factors.

TABLE 2: AGE Vs HYPOTHYROIDISM

AGE IN YEARS	HYPOTHYROID	CONCEPTION
20-30	28	8
30-40	17	4

P value 0.956, suggests that age factor does not significantly affect the rate of conception in hypothyroidism.

TABLE 3: BMI VsHYPOTHYROIDISM

BMI	HYPOTHYROID	CONCEPTION
18.5- 24.9	13	5
25- 29.9	19	7
30- 34.9	12	0
>35	1	0

P value 0.049 – BMI affects conception significantly.

TABLE 4: HYPOTHYRODISM Vs SERUM PROLACTIN:

SERUM PROLACTIN	HYPOTHYROID	CONCEPTION
<19.9	15	9
20- 24.9	22	3
>25	8	0

P value 0.026 suggests that serum prolactin <25ng/ml responds better to treatment.

TABLE 5: HYPOTHYROIDISM Vs ANTI TPO ANTIBODIES:

SERUM ANTI TPO AB LEVEL	HYPOTHYROID	CONCEPTION
<= 34	27	11
>34	18	1

P value 0.045. Greater the anti TPO titre lesser is the chance of conception due to coexisting autoimmune thyroid disorder.

TABLE 6: HYPOTHYROIDISM AND MENSTRUAL IRREGULARITY:

MENSTRUAL PATTERN	HYPOTHYROID	CONCEPTION
OLIGOMENORRHOEA	27	3
AMENORRHOEA	2	0
NORMAL	16	9

P value 0.047 women with regular menstrual cycles have high chance of conception.

TABLE 7: HYPOTHYROIDISM AND ENDOMETRIAL SAMPLING:

HISTOPATHOLOGY	HYPOTHYROID	CONCEPTION
SECRETORY ENDOMETRIUM	17	9
NON SECRETORY ENDOMETRIUM	28	3

P value 0.048. secretory phase endometrium indicates ovulatory cycles and thus has high conception rate.

TABLE 8: HYPOTHYROIDISM AND ALTERED LH /FSH :

FSH> 10	2	0
REVERSED LH/FSH	9	1
NORMAL	34	11

P value 0.454. conception is not altered by LH/FSH ratio.

TABLE 9: HYPOTHYROIDISM AND PERIOD OF INFERTILITY:

PERIOD OF INFERTILITY	HYPOTHYROID	CONCEPTION
<3	9	2
3-5	12	6
5-10	9	1
>10	5	3

P value 0.107. period of infertility does not affect the rate of conception.

TABLE 10: INITIAL TSH LEVEL AND CONCEPTION:

INITIAL TSH LEVEL	HYPOTHYROID	CONCEPTION
2.5-6.5	25	11
6.6-10	15	1
>10	5	0

P value 0.040. lower the level of serum TSH better is the chance of conception.

TABLE 11: CLINICAL Vs SUBCLINICAL HYPOTHYROIDISM:

	HYPOTHYROID	CONCEPTION
SUBCLINICAL	40	12
CLINICAL	5	0

TABLE 12: DURATION OF TREATMENT AND CONCEPTION RATE:

6 WEEKS TO 3 MONTHS	2
3MONTHS TO 1 YEAR	10

DISCUSSION:

Thyroid dysfunction manifests as a broad spectrum of reproductive disorders ranging from abnormal sexual development to menstrual irregularities and infertility.

Prevalence of subclinical hypothyroidism(23.3%) was more common than overt hypothyroidism(3.3%)., results were found to be consistent with Verma et al, Birader et al and Rijal et al(2011). Conception rate was significantly influenced by BMI in patients with hypothyroidisim, the result was similar to Rahman et al. Higher TSH levels were associated with lower conception rate, which was similar to that of Raber et al and Gerhard et al.

64% of hypothyroid were found to have irregular menstrual cycles in par with the study conducted by Joshi et al. 68% patients with regular menstrual cycles had better chance of conception. Secretory phase endometrium in pre menstrual endometrial sampling suggestive of ovulatory cycle favours conception in hypothyroid women.

Hyperprolactinemia and associated auto immune thyroid disease affects conception. Period of infertility ,LH/FSH ratio and age doesn't affect conception significantly in hypothyroid women.

Study by Verma et al in 2012:

394 infertile women were investigated for serum TSH and prolactin. 94 were found to be hypothyroid of which 72(76.6%) females conceived following levo thyroxine treatment. 45(62.5%) conceived after 6 weeks to three months of treatment and 27(37.5%) conceived following 3 months to 1 year of treatment.

Study by Nishat Akhtar and D. Mohanapriya at Jawaharlal Nehru medical college, A.M.U,Aligarh:

Of 98 infertile females three were excluded due to associated causes. Of the 95, 51(53.7%) were hypothyroid and 44(46.3%) were euthyroid. Of 51, 48(50.5%) were sub clinical hypothyroid and 3(3.2%) were overt hypothyroid. Of 48, 16(33.3%) conceived,1(6.3%) within 6 months of treatment and 4(25%) within 6 months to 1 year and 11(68.7%) within 1 to 2 years of treatment. None among overt hypothyroid conceived.

In our study:

Of the 150 infertile women 4 were excluded due to associated ovarian factors, male factors and tubal factors. Of the remaining 146, 45(31%) were hypothyroid and 101(69%) were euthyroid. Of the 45 hypothyroid, 40(89%) had subclinical hypothyroidisim and 5(11%) had clinical hypothyroidisim. Among 40 sub clinical hypothyroid patients 12 (30%) conceived after thyroxine treatment. Of the 12, 2(17%) conceived within three months and the remaining 10(83%) within 1 year of thyroxine treatment.

Thyroid dysfunction is a common cause of infertility which can be corrected by levo thyroxine supplementation and bringing TSH to appropriate levels. In case of elevated serum TSH and prolactin, the treatment is first targeted to normalise thyroid hormone levels even before evaluating the cause of hyperprolactinemia. Levo thyroxine treatment regularises menstrual cycle, normalises prolactin levels and improves the fertility rate. Hence with simple oral treatment hypothyroid infertile patients have high chance of successful pregnancy. TSH levels are maintained by adequate drug dosage and serial monitoring at 6 to8 weeks interval.

Therefore as normal TSH levels <2.5mIU/L are pre requisite for fertility, screening for serum TSH and serum prolactin become essential before adopting a battery of hormone assays and costly invasive procedures. Thus oral thyroid replacement therapy in sub clinical hypothyroidisim at early stage is justified in infertile women.

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