Journal of Medical and Scientific Research

JMSR
www.jmsronline.com

Borgaonkar K et al. J Med Sci Res. 2024; 12(1):68-71
http://dx.doi.org/10.17727/JMSR.2024/12-12

ORIGINAL RESEARCH OPEN ACCESS

Biochemical evaluation of thyroid hormone level in infertile women: A case control study

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Abstract

Introduction: Infertility in women is an important health problem which imposes psychological stress and affects the wellbeing of couples. Thyroid disorders is the most frequently encountered endocrine problem among the women in the age reproductive and it can lead to infertility and miscarriage. The objective of the study was to evaluate the thyroid hormone level in infertile women and compared to the healthy controls.

Materials and methods: The study was conducted on 50 infertile women (cases) and 50 fertile healthy women (controls). Thyroid stimulating hormones (TSH), free triiodothyronine (fT3), free thyroxine (fT4) and Anti-thyroid peroxidase (Anti-TPO) levels were estimated and compared between the cases and controls.

Results: The mean TSH level was significantly higher in infertile women (cases) as compared controls (6.76±0.87 vs 2.54±0.12mIU/L; p=0.002).The prevalence of hypothyroidism among the infertile women in the present study was 28%. The anti-TPO antibody level was significantly higher was in infertile women as compared to controls (4.87±0.8 vs 2.32±0.05 IU/ml; p=0.000). In addition the number of positive Anti-TPO antibody cases was higher in infertile women as compared to controls (24% vs 4%; p=0.02).

Conclusion: Therefore, women planning for pregnancy and infertile women must be evaluated for thyroid profile and if there are any abnormalities they should undergo proper treatment for better pregnancy outcome.

Keywords: infertility; women; thyroid profiles; thyroid stimulating hormone; hypothyroidism

Introduction

The term infertility is referred as a complete inability to conceive even after one year of routine intercourse without any precautionary measures [1]. Based on the demographers point of view infertility in women is defined as the lack of pregnancy after exposure to pregnancy for >5years among the women in their reproductive age (15–49) [2]. The CDC, USA stated infertility as health problem related to quality of life and provokes psychological distress, prevents from social gatherings, economic burden, and marital discord [3]. The global data for the prevalence of infertility is estimated to be 8–12% in women between the 20–44 years and 1 in 6 couples had some infertility problems [4]. Infertility due to females accounts for 35% among the couples and the important risk factors are poly cystic ovarian disease, endometriosis, ovulatory dysfunction and tubal occlusion [5]. Thyroid dysfunction is the predominant cause of infertility in women and it is mediated by alteration in anovulatory cycles, defective luteal phase, increased prolactin levels and alteration in the sex hormone levels [6]. Thus normal thyroid function is vital for the state of fertility and also for a healthy pregnancy. The predominant endocrine

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Received 15 September 2023; *Revised* 25 November 2023; *Accepted* 4 December 2023; *Published* 14 December 2023

Citation: Borgaonkar K, Patil R. Biochemical evaluation of thyroid hormone level in infertile women: A case control study. J Med Sci Res. 2024; 12(1):68-71. DOI: http://dx.doi.org/10.17727/JMSR.2024/12-12

disorder reported in the reproductive age women is thyroid disease [7].

Various clinical reports highlights that there is a significant physiological association between hypothalamic–pituitary–thyroid axis and hypothalamic–pituitary–ovarian axis [8]. Pituitary related hormones, thyroid stimulating hormone (TSH) , prolactin, and growth hormone displays significant association with follicle stimulating hormone (FSH) and luteinizing hormone (LH) and increases the nongrowing follicles entry to the growth phase [9]. Thyroid hormones orchestrates an important role precisely in all the phase of the reproduction stating from folliculogenesis to early weeks post conception [10]. Localization of thyroid hormone receptors is detected in human granulosa cells and oocytes and it aids the binding of thyroid hormone to perform the ovarian related function [11]. In addition, thyroid hormone receptors are also localized in placenta and it is important for the placental development [12]. Credible clinical evidences indicate that TSH is important for the embryo implantation and enhances the olliculogenesis by activating the metabolism of estrogen and androgen metabolism, regular menstrual cycle as well as endometrial receptivity [13]. So evaluation of thyroid dysfunction is an important part in the routine infertility work-up among the susceptible women [14]. In this backdrop, the present study was carried to evaluate the thyroid hormone levels in infertile women and compared with healthy fertile women.

Materials and methods

This prospective case control study was conducted at the Department of Biochemistry, Government Medical College, Latur, and Maharashtra, India who were referred from Department of Obstetrics & Gynecology at the same institution. The study was approved by institutional ethical committee and patient consent was obtained before conducting the study. The study included 50 infertile women who were referred as cases and 50 normal fertile women as control aged between 20-40 years. The study was conducted for a period of one year between May 2022 and April 2023. Based on the clinical and laboratory investigation the patients were selected. The study participants demographics details, menstrual and obstetric history and history of prior medications were recorded.

Inclusion criteria: Infertile women and healthy controls aged between 20 to 40 years were included in the study.

Exclusion criteria: Women having infertility due to tubular defects, pelvic disorders, PCOD, tuberculosis of genital parts, prior thyroid disease who were on thyroid medications and abnormalities in husbands semen were excluded from the study. Patients who were taking drugs which could alter thyroid hormones levels were also excluded from the study.

Biochemical analysis

About 5ml of the blood samples was withdrawn from the cases and controls and collected in the sterile contained and the serum was collected after centrifuging at 5000rpm. The collected serum was stored at -200c until further use for thyroid estimation. The serum levels of TSH, FT3 and FT4 was estimated by Chemiluminiscence assay using Acculite CLIA micro wells. The reliability of the assay was compared using commercially available sera. The patients were hyperthyroidism, if TSH < 0.3 mIU/L and hypothyroidism if TSH >4.0 mIU/ L

Statistical analysis

The data were represented as mean±SD. Comparison was doing using unpaired student t-test. A p value < 0.05 was considered statistically significant. A P value <0.05 was considered as statistically significant.

Results

The demographics details of the study participants were shown in Table 1. In infertile group majority of the patients were in the age group between 26-30 years, 27 (54%) and in fertile group majority of the women were in the age group between 26-30 years, 24 (48%). The mean age of the patients in infertile group was 26.75±3.65 years in fertile groups the mean age was 25.87±4.12 years. The incidence of irregular menstrual cycle was higher in infertility group as compared to fertility and it was significant (23 (46%) vs 12 (24%); p=0.03). In our study most the participants in infertile and fertile groups had marriage duration of 1-5 years.

The distribution of thyroid stimulating hormones (TSH) levels was shown in Table 2. The TSH levels was significantly higher in infertile group as compared to fertile group (6.76±0.87 vs 2.54±0.12; p=0.002). The incidence of hypothyroidism was higher in infertile groups as compared to fertile group and it was significant (28% vs 12%; p=0.001).

The distribution of free triiodothyronine (fT3) levels among the study groups were shown in Table 3. The mean fT3 level was significantly lower in infertile group as compared to fertile group and it was significant (1.18±0.001 vs 2.76±0.009pg/ml; p=0.02). The incidence of deceased fT3 level was higher in infertile group as compared to fertile group and it was significant (24% vs 2%;p=0.006).

Table 1: Demographics parameters among the study groups.

Parameters	*Infertile women (n=50)*	*Fertile women (n=50)*	*p value*
Age groups (in years)			
20-25	14 (28%)	20 (40%)	0.34[NS]
26-30	27 (54%)	24 (48%)	
31-35	6 (12%)	4 (8%)	
36-40	3 (6%)	2 (%)	
Menstrual history			
Irregular	23 (46%)	12 (24%)	0.03*
Regular	27 (54%)	38 (7650	
Married life (years)			
1-5	32 (64%)	40 (80%)	0.07[NS]
6-10	15 (30%)	7 (14%)	
11-15	3 (6%)	3 (6%)	

Table 2: Distribution of TSH level among the study groups.

TSH levels	*Infertile women (n=50)*	*Fertile women (n=50)*	*p value*
< 0.30 mU/L	4 (8%)	1 (2%)	0.001*
0.30 - 4 mU/L	32 (64%)	43 (86%)	
> 4 mU/L	14 (28%)	6 (12%)	

Table 3: Distribution of free triiodothyronine (fT3) level among the study groups.

Free triiodothyronine (fT3) levels	*Infertile women (n=50)*	*Fertile women (n=50)*	*p value*
< 2 pg/ml	12 (24%)	1 (2%)	0.006*
2.0 - 4.40 pg/ml	35 (70%)	47 (94%)	
> 4.40 pg/m	3 (6%)	2 (4%)	

The distribution of free thyroxine (fT4) levels among the study groups were shown in Table 4. The mean fT4 levels was significantly lower in infertile group as compared to the fertile group and it was significant (1.28±0.005 vs 3.42±0.08 ; p=0.001). The incidence of deceased fT3 level was higher in infertile group as compared to fertile group and it was significant (20% vs 6%; p=0.002).

The distribution of Anti-thyroid peroxidase (Anti-TPO) levels was shown in Table 5. The frequency of positive Anti TPO antibody titre level was significantly higher in infertile group as compared to the fertile group and it was significant (24% vs 4%;p=0.02). The mean Anti-TPO level was significantly higher in infertility group as compared to the fertility group and it was significant (4.87±0.8 vs 2.32±0.05 IU/ml; p=0.000).

Table 4: Distribution of free thyroxine (fT4) level among the study groups.

Free thyroxine (fT4) levels	*Infertile women (n=50)*	*Fertile women (n=50)*	*p value*
<0.90 ng/ml	10 (20%)	3 (6%)	0.002*
0.90 - 1.70 ng/ml	36 (72%)	45 (90%)	
> 1.70 ng/ml	4 (6%)	2 (4%)	

Table 5: Distribution of anti-thyroid peroxidase (anti-TPO) level among the study groups.

Anti TPO antibody titre	*Infertile women (n=50)*	*Fertile women (n=50)*	*p value*
Normal	38 (76%)	48 (96%)	0.02
Positive	12 (24%)	2 (4%)	

Discussion

Thyroid hormones have significant association with reproduction and pregnancy. Altered thyroid hormone levels are implicated in the wide range of reproductive diseases. Hypothyroidism condition leads to dysregulation in ovarian functions, irregular menstrual cycle, increased miscarriage rates and subfertility [15]. In addition hyperthyroidism in woman also causes irregular menstrual cycles and it is often associated with amenorrhea, oligomenorrhea and hypomenorrhea [16]. In our study the incidence of irregular menstrual cycle is higher in infertile women as compared to fertile women. Likewise in a study done by Koyyada [17] about 30.62% of hypothyroid patients and 7.5% of hyperthyroid patients had irregular menstrual cycles. In the present study the mean TSH level was significantly (p=0.002) higher in infertile women as compared to fertile women. Likewise in a study done by Kameswaramma et al [18]. TSH level is significantly elevated in infertile woman as compared to the fertile women, 5.43 ±6.88 vs 2.12 ±1.03 μIU/ml, p<0.001. Mounting research explored the association between TSH and conception rates and time with conflicting results, in Plowden et al [19] study TSH ≥2.5 mIU/L is not related with increased pregnancy time in women diagnosed with proven fecundity. Meanwhile, in a study done by Feldthusen et al [20] on large population cohorts in women with thyroid abnormalities displayed low pregnancy rate in women with increased TSH levels. In our study, incidence of hypothyroidism in infertile women is 28% which is comparatively higher when compared to fertile women. Similar to our report, in Verma et al [21] study

the prevalence of hypothyroidism in infertile women is 23.86%.

In the present study, the free triiodothyronine (fT3) levels were significantly lower in infertile women as compared to fertile women (p=0.02). Similarly in a study done by Orazulike and Odum,[22] there was a significant decrease in fT3 levels in infertile groups as compared to the control group and it was significant (2.19 vs 2.79pg/ml; p<0.01). Further, free thyroxine (fT4) level was decreased in infertile women as compared to the fertile group and it was found to be significant (p=0.001). Likewise in a study by done by Sharma et al. [23] the fT4 level was decreased in infertile cases as compared to the controls and it was significant (83.5 vs 939; p<0.001).

Thyroid autoimmunity is one of the predominant causes of hypothyroidism and it has significant relationship with adverse pregnancy outcomes. Previous reports shows that in euthyroid women with TSH range of < 2.5 mIU/l and the presence of antithyroid antibodies leads to preterm delivery and increased miscarriage rates [24, 25]. In our study the mean anti-TPO antibody level was increased among the infertile women as compared to the control women. Similarly, in a study done by Gupta et al [26] the mean anti-TPO antibody level was significantly higher in infertile group as compared to the controls 50.86±19.01IU/ml vs 43.04±16.09IU/ml, p=0.02. In our study the incidence of positive anti-TPO was higher in infertile as compared to the control group (24 vs 4%; p=0.02). In a study done by Gupta et al [26] positive TPO-Abs was higher in infertile cases as compared to the controls (20% vs 10%).

Conclusion

The present study concludes that there is a significant alteration in thyroid hormone levels in infertile women along with the presence of serum anti-TPO antibody levels. Thyroid disease elicits negative effects on pregnancy and early screening with appropriate management can improve the pregnancy rate in this patient population.

Conflicts of interest

Authors declare no conflicts of interest.

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