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Comparison of Lipid profile, oxidative stress and thyroid hormones levels in infertile women

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ABSTRACT

Introduction: Infertility is a major problem worldwide today. It is a global problem affecting about 15% of all couples and about 33% of infertility cases are mainly attributed to women. Several multifactorial causes of female infertility, such as thyroid and sex hormone hormonal imbalances. In recent years, thyroid hormone deficiency and increased oxidative stress have been studied as one of the predisposing factors considered to be very important in the knowledge of causes and diagnosis as well as treatment. **AIM**: The aim and objective of this study was to compare the lipid profile, oxidative stress and thyroid hormones levels in infertile women with healthy volunteers. **Method:** A total of 200 subjects were included in this study. Of these, 100 were healthy subjects and 100 cases were infertile women. They were analyzed by measuring of several physiological and biochemical parameters such as age, body mass index, blood parameters such as lipid profile (total cholesterol, triglycerides, low-density lipoprotein, very low-density lipoprotein, high-density lipoprotein), oxidative biomarkers (MDA, catalase, glutathione peroxidase), thyroid hormone levels (T3, T4, TSH), and Prolactin. **Result:** This study showed that T3, T4 are usually greatly decreased while TSH levels increased in the infertile women group compared to the control group. The results of the present study also showed a significantly increased level of MDA, a significant decrease in the activity of catalase (CAT) and glutathione peroxidase (GPx) in the group of infertile women compared to the control group. Serum total cholesterol, triglycerides, VLDL and LDL levels were greatly increased, while HDL levels were significantly lower in the infertile women group. **Conclusion:** Thyroid hormone imbalances and increased oxidative stress have been strongly associated with causative and predisposing factors in female infertility.

KEYWORDS: Infertile women, Oxidative stress, thyroid hormone, lipid profile

INTRODUCTION

Infertility, defined as the inability to conceive after one or two years of unprotected intercourse or the inability of a woman to carry a pregnancy to full term, is a global health issue that affects

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approximately 15% of all couples. About 33% of infertility cases are attributed to female factors [1].

Various factors contribute to female infertility, including hormonal imbalances such as thyroid and sex hormones. Recent research has focused on the potential role of thyroid hormone deficiencies and increased oxidative stress levels as predisposing factors for female infertility [2].

Oxidative stress, which results from an imbalance between reactive oxygen species (ROS) and antioxidant defense mechanisms, has been implicated in female infertility. Malondialdehyde (MDA), a marker of oxidative stress, is formed in all cells as a natural byproduct of lipid peroxidation. Catalase (CAT) is an antioxidant enzyme that catalyzes the breakdown of hydrogen peroxide (H2O2) into water and oxygen. Glutathione peroxidase, an enzymatic antioxidant compound found in living cells, also plays a critical role in reducing oxidative stress [3].

Prior studies have established a link between thyroid hormones and reproductive functions, with hormonal changes in women potentially contributing to the relationship between hyper- or hypothyroidism and reproductive dysfunctions or menstrual disturbances [4].

Hypothyroidism, characterized by decreased levels of thyroid hormones, stimulates the increased secretion of Thyrotrophic Releasing Hormone, which in turn stimulates thyrotrophs and lactotrophs, causing an increase in the levels of both Thyroid Stimulating Hormone and prolactin [5].

The researchers hypothesized that patients with hypothyroidism may have low antioxidant capacity in infertile women. The objective of the study was to explore the relationship between thyroid hormone levels and oxidative stress in infertile women. The findings of this study contribute to our understanding of the complex interplay between hormonal imbalances and oxidative stress in the context of female infertility, potentially opening new avenues for diagnosis and treatment.

MATERIAL AND METHODS:

Study design: Comparative analytical study

Study duration: From February 2022 to March 2023

Ethical consideration: A written consent was obtained from the patients and the study procedure monitored the guidelines of the ethics committee at our organization.

Sampling method: Consecutive sampling method was used for the study, and included a total number of 200 subjects.

Study population: Study subjects were selected from obstetrics and gynaecology out-patient of a tertiary care teaching hospital from central India.

Inclusion criteria: Female with primary and secondary infertility.

Exclusion criteria: Female with any other reproductive disorder(s), male factor infertility or any reproductive disability and age ranges varies to 20-40-years.

Health volunteers were selected from the same locality and age matched group.

Grouping: The subjects were divided into two groups as follows

Group 1: 100 healthy control

Group 2: 100 infertile women

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Methodology:

A detailed history was taken to gather demographic data, including age, sex, height, body weight, and BMI, from each patient. Additionally, blood pressure, hypertension, smoking habits, and dietary patterns (vegetarian and non-vegetarian) were documented for each patient.

The body mass index (BMI) was calculated by the formula (kg/m^2), weight (Kg) divided by height (m) squared. Healthy reference range of BMI is between 18.4–24.8kg/m^2

Peripheral venous blood samples were collected from patients within 24 hours after admission, following a period of physical and mental rest. These samples were subjected to biochemical examinations to determine lipid profiles, including total cholesterol, triglycerides, LDL, HDL, VLDL, lipid peroxidation marker such as MDA levels, and antioxidant enzymes (GPx and Catalase).

Lipid profile estimation: The serum total cholesterol and serum triglycerides were estimated using the COD –POD and Tinder's GPO-POD method, respectively, according to the manufacturer's protocol. Serum HDL-cholesterol was estimated using the phosphotungstate method, while serum VLDL and serum LDL-cholesterol values were determined by calculation using Friedewald's formula.

Antioxidants and Oxidative stress levels estimation: The serum concentration of Malondialdehyde (MDA) was estimated by the calorimetric reaction with thiobarbituric acid (TBA) to form a pink-colored product, which was measured by spectrophotometer [3]. The activities of antioxidant enzymes such as Catalase were determined by measuring the decrease in the absorbance due to hydrogen peroxide (H2O2) consumption, as described by Aebi [6]. Glutathione Peroxidase (GPx) activity was estimated using the UV method [7].

Hormonal estimation: The levels of hormones, including Thyroid Profile T3, T4, TSH, and Prolactin, were estimated using immunoassay methods based on enzyme-linked immunosorbent assay (ELISA) kits.

All the parameters were measured using a fully automated analyzer XL-1000 Erba Mannheim and ELISA reader Hydro flux (TECAN).

Data collection and analysis: Data was tabulated and compared with control group.

RESULTS:

The present study was carried in 200 subjects out of them100 were healthy subjects and 100 subjects of infertile women cases.

Table 1: Anthropometric parameters of controls Healthy and Infertile women case groups.

Parameters	**Group 1 (control)**	**Group 2 Infertile women**	**P value**
Age	31.1±5.2	31.3±4.6	>0.05
Weight (Kg)	55.7±6.5	59.12±7.45	<0.05
BMI	22.9±3.3	28.5±4.19	<0.05
Waist/hip ratio	0.8±0.1	0.9±0.08	>0.05

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Table 2: Biochemical levels of controls Healthy and Infertile women case groups.

Parameters	Group 1 (control)	Group 2 Infertile women	P value
Total Cholesterol (mg/dl)	184.06±38.76	260.3±42.09	P<0.001
TG (mg/dl)	114.09±19.49	182.78±48.13	NS
HDL (mg/dl)	42.46±8.19	32.31±6.05	P<0.001
LDL (mg/dl)	86.2±18.23	128.8±26.4	NS
VLDL (mg/dl)	25.61±5.02	45.90±10.5	NS
Malondialdehyde (nmol/ml)	2.78±0.18	5.49±0.18	P<0.001
Catalase (nmol/ml)	34.3±10.7	20.24±8.35	P<0.001
Glutathione Peroxidase (mg/dl)	68.24±2.26	42.56±1.20	P<0.001

Significant at p-value (P<0.001), NS- Not Significant

Table- 3 Hormone levels in controls Healthy and Infertile women case groups.

Parameters	Group 1 (control)	Group 2 Infertile women	P value
T3 (ng/ml)	2.99±0.96	1.41±0.43	<0.05*
T4 (µg/dl)	18.97±5.37	8.46±3.18	<0.05*
TSH (mIU/ml)	5.18±1.99	12.27±3.44	<0.05*
Prolactin (nmol/ml)	12.68±9.46	17.37±5.87	<0.05*

*Significant

DISCUSSION

The World Health Organization reports that infertility affects 8-12% of couples worldwide, making it a global public health concern. The complexity of infertility's underlying causes and the challenges associated with preventing, diagnosing, prognosing, and treating it contribute to its significance [8].

Our study analyzed anthropometric parameters of control and case groups, revealing that the mean age of the infertile women case group (31.3±4.6 years) did not significantly differ from that of the control group (31.1±5.2 years). However, the infertile women had a significantly higher mean BMI (28.5±4.19) than the control group (22.9±3.3), indicating that the former group was overweight according to standard criteria. Although waist and hip circumferences were higher in infertile women (0.9±0.08) than in healthy subjects (0.8±0.1), the difference was not significant.

Furthermore, infertile women had significantly increased levels of Total Cholesterol, Triglycerides, Low Density Lipoprotein, and Very Low-density Lipoprotein and decreased levels of High-Density Lipoprotein compared to healthy women. These lipid parameters were positively correlated with Malondialdehyde (MDA) levels in infertile women. Additionally, the infertile women group had significantly higher MDA levels and significantly lower Catalase (CAT) and Glutathione Peroxidase (GPx) levels than the fertile control group.

The present study also showed a high significant increase in the level of Malondialdehyde (MDA) (control 2.78±0.18 and infertile women 5.49±0.18) in infertile women, a significant decrease in the activity of Catalase (CAT) (control 34.3±10.7 and infertile women 20.24±8.35), and also a highly significant decrease in the level of Glutathione Peroxidase (GPx) (control 68.24±2.26 and infertile women 42.56±1.20) in the infertile women group as compared to fertile (control) group. [9-11]

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Recent research has indicated that oxidative stress caused by reactive oxygen species (ROS) overproduction from increased macrophage activity, rather than antioxidant deficiency, may independently cause female infertility. Furthermore, Tullanithi et al. have found that selenium deficiency, an essential component of the antioxidant system, leads to a significant decrease in GPx antioxidant activity in hypothyroid patients [12,13].

The mean serum levels of T3and T4 in infertile women was found to be lower (1.41±0.43and 8.46±3.18) in compare to fertile women (2.99±0.96 and 18.97±5.37) and there was a statistical significance found between two study group ($p < 0.5$).The mean serum level of TSH in infertile women was found to be higher (12.27±3.44) in compare to fertile women (5.18±1.99).The mean value of serum Prolactin was 17.37±5.87 ng/ml in infertile women was higher in fertile women 12.68±9.46 ng/ml which was highly significant ($p<0.5$).

Our study also found that infertile women had significantly lower serum levels of T3 and T4 and higher serum levels of TSH and Prolactin compared to fertile women. The positive correlation between Prolactin and TSH and the negative correlation between Prolactin and T4 and T3 in infertile women suggest primary hypothyroidism. Hypothyroidism itself may contribute to infertility since thyroid hormones are necessary for maximum estradiol and progesterone production [14-16].

Infertile women with high Prolactin and disturbance of thyroid profile due to there are other factors effect infertility in women may be caused by an underlying medical condition that may damage the fallopian tubes, interferes with ovulation; these medical conditions include pelvic inflammatory disease, endometriosis, polycystic ovarian syndrome, premature ovarian failure, uterine fibroids and environmental factors. Other causes of infertility in females include ovulation problems, tubal blockage, age-related factors, uterine problems [17-19]

CONCLUSION

In conclusion, the study showed that lipid profile, oxidative stress markers, thyroid hormones, and prolactin levels were significantly different between infertile and fertile women. These findings suggest that oxidative stress and hypothyroidism may be involved in female infertility, and high prolactin levels may also be a contributing factor. Early diagnosis for these parameters can help prevention of female infertility and therapy may be beneficial for some women. Further research is needed to better understand the complex etiology of female infertility and to develop effective prevention and treatment strategies.

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