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Assessment of Total and Free Testosterone, Prolactin Level among Infertile Women Attending Gynecology Clinic in Ondo State.

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Abstract
Infertility is a significant concern affecting many women, and hormonal imbalances can often contribute to this issue. The aim of this study was to assess the levels of total and free testosterone as well as prolactin levels in infertile women attending a Gynecology Clinic in Ondo State. The study involved a sample of infertile women who were assessed for total and free testosterone, as well as prolactin levels through blood tests. The data collected was analyzed to determine the prevalence of abnormal hormone levels in this population. Understanding the hormonal status of infertile women can provide valuable insights into potential underlying causes of infertility, thereby guiding appropriate treatment strategies. There was significantly lower free testosterone in primary infertile women when compared with control ($p<0.05$). The free testosterone was significantly lower in secondary infertile women when compared with control $p<0.05$ but not significant when compared primary and secondary infertile women ($p>0.05$). The total testosterone was significantly lower in secondary infertile women ($p<0.05$) when compared with control and higher in primary infertile women when compared with control ($p<0.05$) but no significant when compared primary with secondary infertile women. The findings from this study may contribute to the development of more targeted and effective interventions for infertility in women. This research is crucial for healthcare providers and policymakers in Ondo State to improve the management and care of infertile women attending gynecology clinics.

Keywords: Total and free testosterone, prolactin, Infertile women, gynecology clinic.

Introduction

Infertility impacts millions of people worldwide. The World Health Organization reports approximately one in six people of reproductive age around the world experience infertility in their lifetime (WHO, 2024). Around 11% of women of reproductive age in the United States are estimated to experience fertility issues. (Kennedy, 2024). The causes associated with female infertility can be challenging to diagnose and sometimes unknown. If the cause of the infertility is known, treatment options could be available. However, many times, infertile couples may go on to conceive a child without treatment. The definition of infertility is an unsuccessful pregnancy with frequent, unprotected sex for at least a year (Walker M.H, 2022).

Infertility in women is a challenging condition that affects many individuals and couples worldwide. It is defined as the inability to conceive after regular, unprotected intercourse for at least a year. Various factors can contribute to female infertility, including age-related issues, hormonal imbalances, medical conditions like polycystic ovary syndrome (PCOS), endometriosis, and lifestyle choices (Boerma, 2012). Understanding the causes of infertility in women is crucial for proper diagnosis and treatment. Women experiencing infertility may face emotional distress, societal stigma, and challenges related to societal expectations linking womanhood with motherhood. Seeking medical advice and exploring treatment options, such as medications,

surgery, or assisted reproductive technologies, can help address the underlying causes of infertility and improve the chances of conception. It's essential to provide support and care to individuals dealing with infertility to navigate the emotional and physical aspects of this condition effectively (Gore, 2015).

Infertility can be either primary or secondary. Primary infertility means a woman have never been pregnant and can't get pregnant after six months (older than 35) or one year (younger than 35) of trying. Secondary occurs when a woman can't get pregnant again after having at least one successful pregnancy and birth.

Infertility is a common disease. At least 10% of women and people assigned female at birth deal with infertility of some kind. The chances of infertility increase with age. The most common sign of infertility is being unable to get pregnant despite having regular, unprotected sex. Other signs may include absent or irregular periods.

When assessing infertile women attending a gynecology clinic, it is crucial to evaluate total and free testosterone levels, as well as prolactin levels. Research indicates that prolactin plays a significant role in fertility and infertility. Elevated prolactin levels can impact fertility by inhibiting gonadotropin production, leading to infertility. However, it's essential to consider the complex relationship between prolactin and fertility, as prolactin may also have beneficial effects on other aspects of reproduction. Additionally, assessing testosterone levels both total and free, is important as testosterone imbalance can affect fertility, especially in conditions like polycystic ovary syndrome (PCOS). Women with PCOS may have higher testosterone levels, potentially impacting aggression levels but not necessarily directly linked to outward aggression. Therefore, when evaluating infertility in women, understanding the interplay of prolactin and testosterone levels is crucial for comprehensive fertility assessments (Segal, 2019).

Aim and Objectives

The aim of this study was to assess total and free testosterone, as well as prolactin levels, among infertile women attending Obstetrics and Gynecology clinics in Ondo State.

Specific Objectives

The specific objectives of the study are.

1. To assess the levels of total and free testosterone among infertile women attending Obstetrics and Gynecology clinics in Ondo State.
2. To assess the levels of total prolactin among infertile women attending Obstetrics and Gynecology clinics in Ondo State.
3. To determine the relationship between total and free testosterone levels and infertility among study participants.
4. To assess the association between prolactin levels and infertility among study participants.

Materials and Methods

Study Design

A cross-sectional design was employed to assess total and free testosterone, as well as prolactin levels, among infertile women attending Obstetrics and Gynecology clinics in the study location. Ondo North, Ondo Central, Ondo south.

Study Duration

This study was carried out within a period of Six (6) months (September, 2023-February, 2024).

Study Population

The study population consisted of infertile women attending Obstetrics and Gynecology clinics at different randomly selected private and public hospitals including University of Medical Sciences, Ondo, State Specialist Hospital, Okitipupa and General Hospital, Igbokoda.

Selection Criteria

Inclusion Criteria

1. Women aged 25-49 years.
2. Women diagnosed with infertility, defined as the inability to conceive after 12 months regular unprotected sexual intercourse.
3. Women attending Obstetrics and Gynecology clinics for evaluation of infertility.
4. Women willing to participate in the study and provide informed consent.

Exclusion Criteria

1. Women outside the age range of 25-49years.
2. Women with a history of hysterectomy or bilateral oophorectomy.
3. Women who are pregnant or currently breastfeeding

4. Women with known endocrine disorders affecting testosterone or prolactin levels (e.g., Cushing's syndrome, congenital adrenal hyperplasia).
5. Women taking medications known to affect testosterone or prolactin levels (e.g. oral contraceptives, antipsychotics).
6. Women with a history of pituitary disorders or tumors affecting prolactin levels.
7. Women with a history of untreated thyroid disorders, as these can affect prolactin levels.
8. Women with a history of significant systemic illness or major surgery within the past six months.
9. Women with a history of substance abuse or significant psychiatric disorders.
10. Women unwilling or unable to provide informed consent.

Ethical Considerations

This study was conducted in accordance with the principles and procedure of ethical considerations. Also, formal permission was sought from the health facilities visited. While Informed consent was obtained from all study participants before enrollment. UNIMEDTH/ERC/24/115.

Sample Size

The sample size was calculated based on cross-sectional study formula which takes the prevalence of infertility in Ondo state (found to be 80%) into consideration.

At Confidence level of 95%,

Where:

$N= P(1-P)Z2/e^2$

N-sample size

P = Documented prevalence (80%) e–0.05 at 95% confidence interval Z= 1.96 (Adepeju *et al*., 2021) Therefore,

$N= 0.8(1-0.8)1.962 / 0.05^2$

$N=0.8(0.2)3.8416/0.0025$

$N=3.07328 (0.2)/0.0025$

$N=0.614656 \div 0.0025$

N=246 samples

Materials and Method

Laboratory Supplies: Blood collection tubes (Lithium heparin tubes for total testosterone and prolactin), needles and syringes for blood collection, centrifuge for separating serum/plasma, and laboratory reagents for hormonal assays etc.

Questionnaire: Structured questionnaire was used to collect demographic and clinical data from study participants, including age, duration of infertility, menstrual history, and medical history.

Laboratory Equipment: Automated analyzer for measuring total and free testosterone, as well as prolactin levels, in blood samples.

Consent Forms: Informed consent forms for study participants, outlining the purpose of the study, procedures involved, and risks/benefits of participation.

Data Collection Sheets: Sheets for recording data from hormonal assays, including participant identification numbers, hormone levels, and any relevant clinical information.

Statistical Software: Statistical software (e.g., SPSS, Graph Pad prism) for data analysis, including descriptive statistics, t-tests, ANOVA, and correlation analysis.

Personal Protective Equipment (PPE): PPE including gloves, lab coats, and eye protection was used by researchers involved in blood collection and laboratory work. Standard Operating Procedures (SOP) for blood collection, sample processing, and laboratory assays were followed to ensure consistency and accuracy in procedures. Refrigerators and freezers were used for storing blood samples and reagents at appropriate temperatures.

Result

Table 1 showed the basic characteristics of study population of infertile women (subjects) attending obstetrics and gynecology clinic in Ondo State and normal control individuals. Table 1 shows the number and percentage of primary infertility was 18(22%) while secondary status was 64(78%). The 50 control women based of age groups indicated that 13 (26%) were in the 20-30 years age group; 26 (52%) were in the 31-40 and 11(22%) were greater than 40 years. Among the subjects, 23(28%) were in the 20-30 years age group, 34 (42%) were in the 31-40 years age group while 25(30%) were greater than 40 years.

Table 1: Basic Characteristics of Study Population

Index		Control	Subject Group
Total		50 (100%)	82 (100%)
Status	Primary	-	18 (22%)
	Secondary	-	64 (78%)
Age	20-30	13 (26%)	23 (28%)
	31-40	26 (52%)	34 (42%)
	>40	11 (22%)	25 (30%)

Table 2 shows the mean and standard deviation in control and subject. The mean and standard deviation of prolactin was very high in both primary infertile women (9.21± 2.14 and in secondary infertile women (9.40±0.1) when compared with control (3.88±1.2). The mean and standard deviation of free testosterone both in primary (1.03±0.1) and secondary (1.04±0.1) was low when compared with control (1.99±0.26) and also total testosterone in primary (0.23±0.1) and in secondary (0.26±0.1) were also low compared with control (0.35±0.09).

Table 2: Mean and Standard Deviation in Control and subject

Parameter	Control	Primary Infertility	Secondary Infertility	Subject (Total)
Prolactin	3.88±1.39	9.21±2.14	9.40±0.1	9.31±2.54
Free Testosterone	1.99±0.26	1.03±0.1	1.04±0.1	1.06±0.1
Total Testosterone	0.35±0.09	0.23±0.1	0.26±0.1	0.25±0.07

Table 3 shows the comparative analysis of prolactin, free testosterone and total testosterone in control, primary and secondary infertile women subjects. There was significantly lower prolactin level when compared between control and primary ($p<0.05$), and also significantly higher in secondary infertile women ($p<0.05$) when compared with control subject but no significant when compare prolactin level between primary and secondary infertile women. Figure 1 shows the comparative Description of Analysis of Prolactin levels between subjects and controls.

There was a significantly lower free testosterone in primary infertile women when compared with control ($p<0.5$) and significantly higher in secondary infertile women when compared with control ($p<0.05$). There was no significant difference when the levels were compared between primary and secondary infertile women. The total testosterone was significantly lower in secondary infertile women ($p<0.05$) when compared with control and higher in primary infertile women when compared with control ($p<0.05$) but not significant when levels were compared between primary with secondary infertile women. Figure 2 shows the comparative Description of Analysis of Free and Total Testosterone levels between subjects and controls.

Table 3: Comparative Analysis of Prolactin, free Testosterone and total Testosterone in Control, Primary and Secondary Infertile Women Subjects.

Parameters		Control vs Subject (Total)	Control vs Primary Infertility	Control Vs Secondary Infertility	Primary Vs Secondary Infertility
Prolactin	"t"	29.75	20.80	30.00	5.85
	"p"	0.00001**	0.00001**	0.00001**	1.86
Free Testosterone	"t"	16.09	15.79	16.81	2.69
	"p"	0.00001**	0.00001**	0.00001**	1.67
Total Testosterone	"t"	5.81	6.21	4.89	1.65
	"p"	0.00001**	0.00001**	0.00001**	2.30

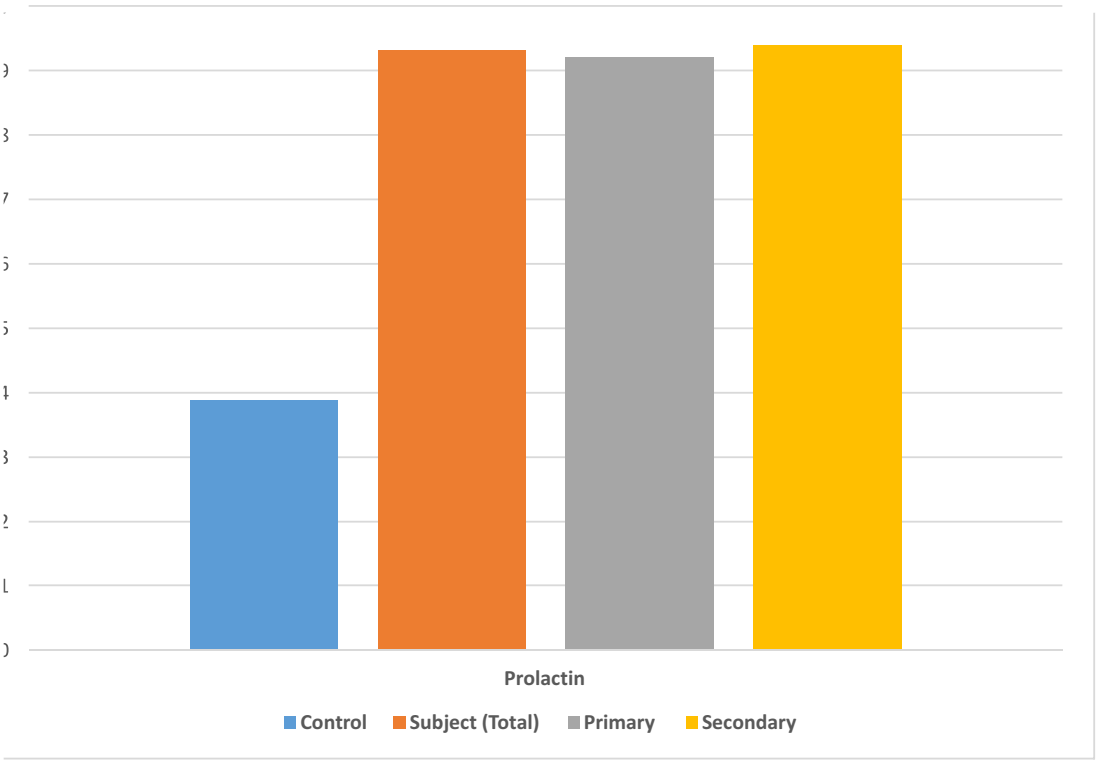

Figure 1: Comparative Description of Analysis of Prolactin levels between subjects and controls

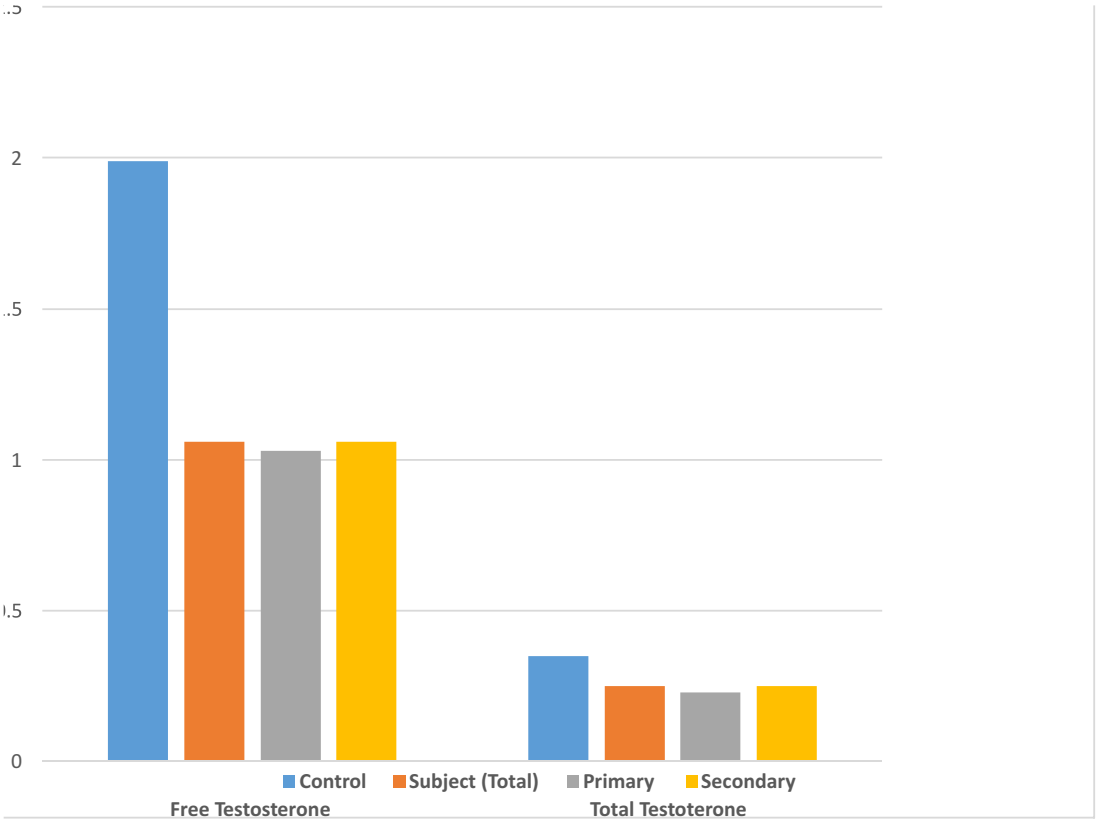

Figure 2: Comparative Description of Analysis of Free and Total Testosterone levels between subjects and controls

Discussion

Hyperprolactinemia plays a significant role in infertility among women by disrupting the delicate hormonal balance necessary for ovulation and reproductive health. Elevated levels of prolactin can lead to irregular menstrual cycles, anovulation, and decreased fertility potential. In women, high prolactin levels can interfere with the release of eggs from the ovaries, causing ovulation problems and irregular periods. This disruption in the menstrual cycle can directly impact fertility by hindering the chances of conceiving naturally. The impact of hyperprolactinemia on infertility is multifaceted. It affects the levels of reproductive hormones, such as follicle-stimulating hormone (FSH) and luteinizing hormone (LH), which are essential for egg growth and ovulation. Anovulation, a direct consequence of hyperprolactinemia, can lead to infertility or inconsistent ovulation, reducing the chances of conception. Additionally, high prolactin levels can cause irregular periods, disrupt the menstrual cycle, and affect the overall reproductive function in women.

The present study investigated the prolactin level, total and free testosterone among the infertile women in Ondo State both primary and secondary. The result showed an increased prolactin levels among women both primary (9.21±2.14) and secondary (9.40±0.1) infertility when compared with control (3.88±1.39). According to Bernerd (2015), hyperprolactinemia is a known cause of amenorrhoea and infertility. However, there is an increasing body of evidence suggesting that prolactin is involved in multiple physiological aspects of normal reproduction.

Low total testosterone levels in women can lead to hormonal imbalances that affect ovulation, menstrual regularity, and fertility. Testosterone is involved in the regulation of the menstrual cycle and plays a role in follicle development and maturation. Imbalances in testosterone levels can disrupt these processes, potentially leading to ovulatory dysfunction and reduced fertility. Previous research by Pugeat (2018) indicates that high testosterone levels in females can prolong the follicular phase of the menstrual cycle, increase the incidence of anovulation, and affect the overall pregnancy rate. In this present study, there is significant increase in total testosterone among primary infertile women. Levels of total testosterone higher in women are most often associated with hyperandrogenic signs, menstrual irregularities, and a rapid virilization onset (Haddad, 2019).

However, in this present study there was a significant decrease in the level of total testosterone both in the primary (0.23±0.1) and secondary (0.26±0.1) when compared with the control (0.35±0.09). According to world health organization 2024, one of the most common causes of infertility is low level of total testosterone in women or issues with conceiving. Therefore, high or low total testosterone levels in the blood could lead to women's infertility.

Low free testosterone levels in women can have implications for fertility and reproductive health. Testosterone, although present in smaller amounts in women compared to men, plays a crucial role in female reproductive function. Free testosterone is the unbound form of testosterone that is readily available for use by the body's tissues and cells. In women, low free testosterone levels can impact libido, energy levels, and overall well-being, potentially affecting fertility. Research suggests that testosterone levels, including free testosterone, are important for regulating follicle development, supporting the structure of follicles that hold and release eggs, and stimulating the synthesis of hormones like Follicle-Stimulating Hormone (FSH) in the ovaries. Additionally, testosterone contributes to increasing blood flow to the reproductive organs and can influence libido, which is essential for reproductive success.

In this study, it was observed that there was significant decrease in the level of free testosterone both in primary (1.03±0.1) and in secondary (1.04±0.1) when compared with the control (1.99±0.26). This study agrees with a previous report by Brighten (2022) that low testosterone, is an important but often overlooked issue with fertility and female hormones.

Conclusion and Recommendation

In conclusion, hyperprolactinemia is a significant factor contributing to low, free and total testosterone level among infertile women. The hormonal imbalance resulting from elevated prolactin level can disrupt the reproductive process leading to infertility, addressing hyperprolactinemia is essential in restoring testosterone levels and improving fertility outcomes in affected women. It is recommended that infertile women presenting with either low,

total or free testosterone should undergo thorough medical evaluation including serum prolactin testing to identify and address hyperprolactinemia. Follow up and monitoring of prolactin and testosterone levels is necessary to assess treatment efficacy with a goal of achieving successful conception and pregnancy.

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