

Research Article

Assessment of Sex Hormones (FSH, LH, Prolactin, Estrogen, Progesterone and Testosterone) of Pulmonary Tuberculosis Patients

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Abstract

Background: Tuberculosis (TB) is a one of the major global health problems ranking as the eighth leading cause of death in low- and middle-income countries. This study was carried out to evaluate the Follicle Stimulating Hormone (FSH), Luteinizing Hormone (LH), Prolactin, Estrogen, Progesterone and Testosterone of pulmonary tuberculosis patients in Edo State. **Objectives:** The objectives of the study are to assess the FSH, LH, Prolactin, Estrogen, Progesterone and Testosterone levels of Pulmonary Tuberculosis (PTB) patients compared with control, hormonal levels of PTB patients of new case, 2 months and 6 months therapy compared with control, hormonal levels of PTB patients in relation to gender and hormonal levels of PTB patients in relation to age.

Material and methods: A total of 120 samples were used in this study comprising PTB new cases (30), PTB 2 months therapy (30), PTB 6 months therapy (30) and Control (30) respectively. FSH, LH, Prolactin, Estrogen, Progesterone and Testosterone were measured by Enzyme-Linked Immunoassay Test (ELISA). The results were presented using tables as mean $\pm$ standard deviation. Statistical analysis was done using one-way Analysis of Variance (ANOVA) and the student's t-test. Significant difference was accepted at $p < 0.05$.

Results: The results obtained showed that the FSH (mIU/ml) of new case subjects, 2 months on therapy, 6 months on therapy and control were 13.42 ± 3.58 , 11.38 ± 3.04 , 6.52 ± 2.57 and 8.71 ± 3.15 ; LH (mIU/ml) was 10.43 ± 2.95 , 8.32 ± 2.44 , 5.21 ± 2.23 and 6.05 ± 2.44 ; prolactin (μ g/L) was 10.17 ± 4.04 , 9.47 ± 2.56 , 10.11 ± 6.74 and 12.96 ± 7.09 ; estrogen (pg/ml) was 35.97 ± 9.27 , 41.50 ± 12.65 , 57.60 ± 17.46 and 64.97 ± 29.24 , progesterone (ng/ml) was 0.18 ± 0.05 , 0.25 ± 0.06 , 0.40 ± 0.10 and 0.37 ± 0.08 ; and testosterone (ng/ml) was 2.49 ± 0.95 , 2.48 ± 1.46 , 4.00 ± 2.92 and 4.32 ± 3.84 respectively.

Conclusion: In conclusion, there was significant difference ($p < 0.05$) in the FSH, LH, Prolactin, Estrogen, Progesterone and Testosterone of the subjects in the different groups compared with control. FSH, LH, Prolactin, Estrogen and Progesterone were significantly higher ($p < 0.05$) in female subjects compared with male subjects, while Testosterone was non-significantly ($p > 0.05$) higher in male subjects compared with female subjects.

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Keywords: Tuberculosis; Sex Hormones; FSH; LH; Prolactin; Estrogen; Progesterone; Testosterone

Introduction

Tuberculosis (TB) is an infectious disease caused by the bacillus of *Mycobacterium* species. It typically affects the lungs (pulmonary TB [PTB]) but can affect other sites as well (extrapulmonary TB [EPTB]). TB is one of the major global health problems ranking as the eighth leading cause of death in low- and middle-income countries (seventh for men and ninth for women); among adults aged 15-59 years, it ranks as the third cause of death, after HIV/AIDS and ischemic heart disease [1,2]. Studies have shown that the major risk factors especially in poor income countries for infections and death due to TB are less health care access, higher exposure to unhealthy and crowded living, unhealthy working conditions, malnutrition, HIV-infection, diabetes mellitus, smoking, alcoholism, and drug abuse. *Mycobacterium* species causes TB in the lungs and other tissues of the human body. The other species causing TB includes *hominis*, *bovis*, *avium*, *murine*, and non-pathogenic *smegmatis* [3,4]. *Mycobacterium tuberculosis* is transmitted from a patient with infectious PTB to other persons by droplet nuclei, which are aerosolized by coughing, sneezing, or speaking. Other routes of transmission of tubercle bacilli, such as through the skin or the placenta, are uncommon and of no epidemiologic significance. The organism also spread to other organs, such as the lymphatics, pleura, bones/joints, or meninges, and cause EPTB [5]. Tuberculin skin testing is the most common method used to screen for latent *M. tuberculosis*. Acid Fast Bacilli (AFB) microscopy is based on the finding of AFB on microscopic examination of smear of expectorated sputum or of tissue (a lymph node biopsy) [6].

Hormones are chemical substances having a specific regulatory effect on the activity of a certain organ or organs. Hormones travel through the blood to distant tissues and organs, where they can bind to specific cell sites called receptors. By binding to receptors, hormones trigger various responses in the tissues/cells containing cognate receptors. On the basis of their chemical nature, hormones are classified as peptides, steroids, and amino acid derivatives [7]. Mechanism of action of hormones comprises two components. Protein hormones interact with a receptor on the outer surface of cell membrane and they signal via second messengers generated by interacting with receptors at the cell surface. Steroid hormones pass through cell membrane and interact with intracellular receptors and the hormone receptor complex eventually binds to a segment of chromatin, which induces formation of messenger RNA that in turn enters the cytoplasm and initiates the synthesis of protein or peptides that carry out the action attributed to the hormone [8]. Their functions can be broadly grouped into several categories: reproduction and sexual differentiation; development and growth; maintenance of the internal environment; and regulation of metabolism and nutrient supply. A single hormone may affect more than one of these functions and each function may be controlled by several hormones. For example, Glucocorticoids (GCs), such as cortisol, are important both in growth and nutrient supply and are also modulators of immune function [9].

Hormones often act as immunomodulators, altering the sensitivity of the immune system, either as immunostimulators, immunosuppressors or immunoregulators. Several cytokines produced during TB not only exert a direct effect on immunocompetent cells, but may also influence immune cells indirectly, due to their ability to affect several neuro-endocrine mechanisms, among them the stimulation of the hypothalamus-pituitary-adrenal axis [10]. Recent studies have shown that specific hormone profiles particularly, steroid hormones, correlate with TB treatment outcomes and increased levels of cortisol and growth hormones and reduced levels of Dehydroepiandrosterone (DHEA) was observed in TB patients compared to healthy controls [10-12].

Interactions between immune and endocrine system during infectious diseases may determine the failure or success of the immune response. This is particularly true for an infection like TB, in which pathogen and immune system coexist in a continuous interaction [13]. TB is associated with different type of altered endocrine hormones. Hormonal changes are likely to occur since some of the cytokines produced during this disease could affect endocrine mechanisms that, in turn, influence the course of infectious/inflammatory processes [14]. This communication pattern exists due to the fact that cytokine-producing cells as well as hormone-producing cells share common receptors and ligands [15]. Hormones could play a role in the spectrum of this disease, in which their interactions with immune system during infectious diseases may determine the failure or success of the immune response, therefore understanding hormone levels in the TB disease spectrum could provide important insight in the understanding of the disease that ultimately contribute to the development of biomarker pools [16]. More so, endocrine hormone profiles are not fully characterized in TB disease [17]. This study was therefore carried out to evaluate the Follicle Stimulating Hormone (FSH), Luteinizing Hormone (LH), Prolactin, Estrogen, Progesterone and Testosterone of pulmonary tuberculosis

patients in Edo State.

Material and Methods

Area of Study

This study was carried out in Central Hospital, Benin City, Edo State. Edo State is an inland state in western Nigeria. It is bounded in the north and east by Kogi State, in the south by Delta State and in the west by Ondo State. English is the official language of the state. The major tribal languages spoken in the state are Igarra, Edo, Esan and Okpamheri. Edo State is the home to several ethnicities; among them are Edo, Okpe, Esan, Afemai, Ora, Akoko-Edo, Igbanke, Emai and Ijaw. The 2014 population of Edo State was estimated to be 6 million. Benin City is the capital of Edo State with a population of 2,147,188. It is a city approximately 25 miles (40 km) north of the Benin River. It is situated 200 miles (320 km) by road east of Lagos. Benin is the centre of Nigeria's rubber industry, processing palm nuts for oil is also an important traditional industry.

Ethical Approval and Informed Consent

Ethical approval for the collection of samples was obtained from the Ministry of Health, Benin City, and from Ambrose Alli University, Ekpoma, both in Edo State. Informed consent was also obtained from each subject who participated in the study before the collection of blood sample.

Sample Size

The sample size shall be calculated using the Cochran formula for sample size determination:

$$n = \frac{z^2 pq}{d^2} \quad n = \frac{z^2 pq}{d^2} \dots\dots\dots$$

n= minimum sample size

z=standard normal deviation (1.96)

p=8% =0.08

q=1-p = 0.92

d=degree of precision at the confidence level of 95%=0.05

Substituting into the formula above

$$n = \frac{1.96^2 \times 0.08 \times 0.92}{0.05^2}$$

$$n = \frac{0.28274176}{0.0025}$$

$$n = 113.09$$

To make up for the sampling error one hundred and twenty (120) samples comprising of thirty (30) patients with pulmonary tuberculosis (new cases), thirty (30) on 2 months therapy, thirty on (30) 6 months therapy and thirty (30) apparently healthy individuals (control) was collected and used for the research.

Study Criteria

Inclusion Criteria: Selection of these subjects was based on the following criteria: age 20-65 years, sputum specimens positive for acid-fast bacilli by microscopy and clinical and radiographic abnormalities consistent with pulmonary tuberculosis.

Exclusion Criteria: Individuals infected with TB on antiretroviral therapy were excluded. Patients diagnosed with pulmonary tuberculosis but having diabetes mellitus were excluded from the study. Tobacco smokers, alcohol drinkers, pregnant and lactating women, those using immunosuppressive drugs and participants who had other clinical problems such as diabetics and cardiovascular diseases were excluded from the study.

Sample Collection

Five (5.0) mls of blood sample was collected from fasting subjects via venipuncture. It was dispensed into a plain container without any additive for the determination of hormonal profile. It was allowed to stand for one hour to clot. It was then centrifuged at 3000g for 10 min in order to separate blood cells and suspended particles from serum. The serum was aliquoted and stored at 4°C until required for analysis.

Sample Analysis

Follicle Stimulating Hormone (FSH), Luteinizing Hormone (LH), Prolactin, Estrogen, Progesterone and Testosterone were measured by enzyme-linked immunoassay test (ELISA) kits (Bio Check Inc., Vintage Park Dr, California, USA) using stat fax. All analysis was carried out in the Clinical Chemistry Laboratory at University College Hospital, Ibadan, Oyo State, Nigeria.

Estrogen [18]

Principle

The principle of Estrogen ELISA is based on competitive immunoassay. Competition occurs between total estrogens (estrone, estradiol, and estriol) present in standards, controls and patient samples and an enzyme-labelled antigen (conjugate) for a limiting number of anti-estrogen antibody binding sites on the micro-plate wells. After a washing step that removes unbound materials the enzyme substrate is added and approximately 15-20 minutes later the enzymatic reaction is terminated by addition of stopping solution. The resulting Optical Density (OD), measured with a microplate reader, is inversely proportional to the concentration of total estrogens in the sample. A standard curve is plotted with a provided set of standards to calculate directly the concentration of total estrogens in patient samples and controls.

Luteinizing Hormone (LH)

Principle: The LH ELISA is based on the principle of a solid phase Enzyme-Linked Immunosorbent Assay (ELISA) [18]. The assay system utilizes mouse monoclonal anti- α -LH for solid phase (microtiter wells) immobilization, and a mouse monoclonal anti- β -LH antibody in the antibody-enzyme (horseradish peroxidase) conjugate solution. The test sample is allowed to react simultaneously with the antibodies, resulting in the LH molecules being sandwiched between the solid phase and enzyme-linked antibodies. After 45-minutes incubation at room temperature, the wells are washed with water to remove unbound-labeled antibodies. A solution of TMB Reagent is added and incubated for 20 minutes, resulting in the development of a blue color. The color development is stopped with the addition of stop solution, and the color is changed to yellow and measured spectrophotometrically at 450 nm. The concentration of LH is directly proportional to the color intensity of the test sample.

Follicle Stimulating Hormone (FSH)

Principle: The Abnova FSH EIA Test is based on a solid phase Enzyme-Linked Immunosorbent Assay (ELISA) [19]. The assay system utilizes a mouse monoclonal anti- α -FSH for solid phase (microtiter wells) immobilization, and mouse monoclonal anti- β -FSH antibody in the antibody-enzyme (horseradish peroxidase) conjugate solution. The test sample is allowed to react simultaneously with the antibodies, resulting in the FSH molecules being sandwiched between the solid phase and enzyme-linked antibodies. After 45-minute incubation at room temperature, the wells are washed with water to remove unbound-labeled antibodies. A solution of TMB Reagent is added and incubated at room temperature for 20 minutes, resulting in the development of a blue color. The color development is stopped with the addition of Stop solution, and the color is changed to yellow and measured spectrophotometrically at 450 nm. The concentration of FSH is directly proportional to the color intensity of the test sample.

Testosterone

Principle: The DIA source Testosterone ELISA Kit is a solid phase Enzyme-Linked Immunosorbent Assay (ELISA), based on the principle of competitive binding [17]. The microtiter wells are coated with a monoclonal [mouse] antibody directed towards a unique antigenic site on the Testosterone molecule. Endogenous Testosterone of a patient sample competes with a Testosterone horseradish peroxidase conjugate for binding to the coated antibody. After incubation the unbound conjugate is washed off. The amount of bound peroxidase conjugate is reverse proportional to the concentration of Testosterone in the sample. After addition of the substrate solution, the intensity of colour developed is reverse proportional to the concentration of Testosterone in the patient sample.

Progesterone

Principle: The Progesterone ELISA Kit is a solid phase Enzyme-Linked Immunosorbent Assay (ELISA), based on the principle of competitive binding [17]. The microtiter wells are coated with a polyclonal antibody directed towards an antigenic site on the Progesterone molecule. Endogenous Progesterone of a patient sample competes with a Progesterone horseradish peroxidase conjugate for binding to the coated antibody. After incubation the unbound conjugate is washed off. The amount of bound peroxidase conjugate is reverse proportional to the concentration of Progesterone in the sample. After addition of the substrate

solution, the intensity of colour developed is reverse proportional to the concentration of Progesterone in the patient sample.

Prolactin

Principle: The GenWay Prolactin ELISA Kit is a solid phase Enzyme-Linked Immunosorbent Assay (ELISA) based on the sandwich principle [17]. The microtiter wells are coated with a monoclonal antibody directed towards a unique antigenic site on a Prolactin molecule. An aliquot of patient sample containing endogenous Prolactin is incubated in the coated well with enzyme conjugate, which is an anti- Prolactin antibody conjugated with horseradish peroxidase. After incubation the unbound conjugate is washed off. The amount of bound peroxidase is proportional to the concentration of Prolactin in the sample. Having added the substrate solution, the intensity of colour developed is proportional to the concentration of Prolactin in the patient sample.

Statistical Analysis

The results were presented using tables. Data was presented as mean $\pm$ S.D (Standard Deviation). Comparison was made between subjects and control groups using one-way Analysis of Variance (ANOVA) and the student's t-test. Significant difference was accepted at $p < 0.05$.

Results

Table 1 showed the Follicle Stimulating Hormone, Luteinizing Hormone, Prolactin, Estrogen, Progesterone and Testosterone in Pulmonary tuberculosis subjects and control. The results presented in mean $\pm$ standard deviation showed that the FSH (mIU/ml) of new case subjects, 2 months on therapy, 6 months on therapy and control were 13.42 ± 3.58 , 11.38 ± 3.04 , 6.52 ± 2.57 and 8.71 ± 3.15 respectively. The LH (mIU/ml) of new case subjects, 2 months on therapy, 6 months on therapy and control was 10.43 ± 2.95 , 8.32 ± 2.44 , 5.21 ± 2.23 and 6.05 ± 2.44 respectively. Similarly, prolactin ($\mu\text{g/L}$) of new case subjects, 2 months on therapy, 6 months on therapy and control was 10.17 ± 4.04 , 9.47 ± 2.56 , 10.11 ± 6.74 and 12.96 ± 7.09 respectively. The estrogen (pg/ml) of new case subjects, 2 months on therapy, 6 months on therapy and control was 35.97 ± 9.27 , 41.50 ± 12.65 , 57.60 ± 17.46 and 64.97 ± 29.24 respectively. Furthermore, the progesterone (ng/ml) of new case subjects, 2 months on therapy, 6 months on therapy and control was 0.18 ± 0.05 , 0.25 ± 0.06 , 0.40 ± 0.10 and 0.37 ± 0.08 respectively. Finally, the testosterone (ng/ml) of new case subjects, 2 months on therapy, 6 months on therapy and control was 2.49 ± 0.95 , 2.48 ± 1.46 , 4.00 ± 2.92 and 4.32 ± 3.84 respectively. There was significant difference ($p < 0.05$) in the FSH, LH, Prolactin, Estrogen, Progesterone and Testosterone of the subjects in the different groups compared with control.

Parameter	New case N = 30 Mean $\pm$ SD	2 months N = 30 Mean $\pm$ SD	6 months N = 30 Mean $\pm$ SD	Control N = 30 Mean $\pm$ SD	F-value	p-value
FSH (mIU/ml)	13.42 ± 3.58^a	11.38 ± 3.04^b	6.52 ± 2.57^c	8.71 ± 3.15^d	15.654	0.000
LH (mIU/ml)	10.43 ± 2.95^a	8.32 ± 2.44^b	5.21 ± 2.23^c	6.05 ± 2.44^d	14.251	0.000
PROL ($\mu\text{g/L}$)	10.17 ± 4.04^a	9.47 ± 2.56^b	10.11 ± 6.74^a	12.96 ± 7.09^c	12.404	0.000
ESTRO (pg/mL)	35.97 ± 9.27^a	41.50 ± 12.65^a	57.60 ± 17.46^c	64.97 ± 29.24^c	19.360	0.000
PROG (ng/ml)	0.18 ± 0.05^a	0.25 ± 0.06^b	0.40 ± 0.10^c	0.37 ± 0.08^c	11.241	0.000
TESTO (ng/ml)	2.49 ± 0.95^a	2.48 ± 1.46^a	4.00 ± 2.92^b	4.32 ± 3.84^b	6.365	0.003
*Values in a row with different superscript are significant at $p < 0.05$ Key: N - Sample size; FSH - Follicle Stimulating Hormone, LH - Luteinizing Hormone, PROL - Prolactin, ESTRO - Estrogen, PROG - Progesterone; TESTO - Testosterone						

Table 1: Follicle Stimulating Hormone, Luteinizing Hormone, Prolactin, Estrogen, Progesterone and Testosterone in Pulmonary tuberculosis subjects and control.

Post-Hoc analysis for table 1 showing ANOVA statistics for various levels of Follicle Stimulating Hormone (FSH), Luteinizing Hormone (LH), Prolactin, Estrogen, Progesterone and Testosterone in pulmonary tuberculosis patients. The Post-Hoc analysis in table 2 showed that there was significant difference ($p < 0.05$) in FSH of control compared with new case subjects, control compared with 2 months therapy group, control compared to 6 months therapy group, new case compared to 2 months, new case compared to 6 months and 2 months compared to 6 months respectively. There was significant difference ($p < 0.05$) in LH, Estrogen and Progesterone in all compared groups, except in control compared with 6 months group which was not significantly

different ($p>0.05$). There was significant difference ($p<0.05$) in prolactin of control compared with new case subjects, control compared with 2 months therapy group and control compared to 6 months therapy group, but there was no significant difference in ($p>0.05$) of new case compared to 2 months, new case compared to 6 months and 2 months compared to 6 months respectively. Finally, there was significant difference ($p<0.05$) in Testosterone of control compared with new case subjects, control compared with 2 months therapy group and new case compared with 6 months, but there was no significant difference ($p>0.05$) in control compared with 6 months therapy group, new case compared with 2 months and 2 months compared with 6 months respectively.

Parameters	Control vs new case	Control vs 2 months	Control vs 6 months	New case vs 2 months	New case vs 6 months	2 months vs 6 months
FSH	0.000(S)	0.000(S)	0.001(S)	0.010(S)	0.000(S)	0.000(S)
LH	0.000(S)	0.000(S)	0.068(NS)	0.001(S)	0.000(S)	0.000(S)
PROL	0.156(NS)	0.012(S)	0.009(S)	0.400(NS)	0.973(NS)	0.602(NS)
ESTRO	0.000(S)	0.000(S)	0.144(NS)	0.016(S)	0.000(S)	0.000(S)
PROG	0.000(S)	0.000(S)	0.160(NS)	0.000(S)	0.000(S)	0.000(S)
TESTO	0.009(S)	0.003(S)	0.417(NS)	0.969(NS)	0.006(S)	0.000(S)

Keys: NS - Not significant at $p<0.05$; S - Significant at $p<0.05$; FSH - Follicle Stimulating Hormone, LH - Luteinizing Hormone, PROL - Prolactin, ESTRO - Estrogen, PROG - Progesterone; TESTO - Testosterone

Table 2: Post-Hoc analysis for table 1 showing ANOVA statistics for various levels of FSH, LH, Prolactin, Estrogen, Progesterone and Testosterone in pulmonary tuberculosis patients.

Relationship between FSH, LH, Prolactin, Estrogen, Progesterone and Testosterone in pulmonary tuberculosis subjects using Pearson Correlation. Table 3 showed the relationship between FSH, LH, Prolactin, Estrogen, Progesterone and Testosterone in Pulmonary tuberculosis subjects using Pearson correlation. The results obtained showed that FSH had a positive correlation with LH ($p=0.000$) and Estrogen ($p=0.558$), but had a negative correlation with Progesterone ($p=0.000$), Prolactin ($p=0.554$) and Testosterone ($p=0.027$) respectively. LH had a negative correlation with Prolactin ($p=0.804$), Progesterone ($p=0.000$) and Testosterone ($p=0.035$), but had a positive correlation with Estrogen ($p=0.220$) respectively. Prolactin had negative correlation with Estrogen ($p=0.049$) and Testosterone ($p=0.369$), but had positive correlation with Progesterone ($p=0.266$). Furthermore, Estrogen had negative correlation with Progesterone ($p=0.500$) and Testosterone ($p=0.332$), while Progesterone had positive correlation with Testosterone ($p=0.026$) respectively.

		FSH	LH	PROL	ESTRO	PROG	TESTO
FSH	Pearson Correlation		.798**	-.113	.111	-.628**	-.404*
	Sig. (2-tailed)		.000	.554	.558	.000	.027
	N		30	30	30	30	30
LH	Pearson Correlation	.798**		-.047	.231	-.669**	-.387*
	Sig. (2-tailed)	.000		.804	.220	.000	.035
	N	30		30	30	30	30
PROL	Pearson Correlation	-.113	-.047		-.363*	.210	-.170
	Sig. (2-tailed)	.554	.804		.049	.266	.369
	N	30	30		30	30	30
ESTRO	Pearson Correlation	.111	.231	-.363*		-.128	-.184
	Sig. (2-tailed)	.558	.220	.049		.500	.332
	N	30	30	30		30	30
PROG	Pearson Correlation	-.628**	-.669**	.210	-.128		.405*
	Sig. (2-tailed)	.000	.000	.266	.500		.026
	N	30	30	30	30		30
TESTO	Pearson Correlation	-.404*	-.387*	-.170	-.184	.405*	
	Sig. (2-tailed)	.027	.035	.369	.332	.026	

	N	30	30	30	30	30	
**. Correlation is significant at the 0.01 level (2-tailed).							
*. Correlation is significant at the 0.05 level (2-tailed).							

Table 3: Relationship between FSH, LH, Prolactin, Estrogen, Progesterone and Testosterone in pulmonary tuberculosis subjects using Pearson Correlation.

FSH, LH, Prolactin, Estrogen, Progesterone and Testosterone in pulmonary tuberculosis male and female subjects. Table 4 showed the Follicle Stimulating Hormone, Luteinizing Hormone, Prolactin, Estrogen, Progesterone and Testosterone in pulmonary tuberculosis male and female subjects. The results obtained showed that the FSH (mIU/ml) of male subjects and female subjects was 11.81 ± 2.97 and 15.11 ± 3.24 , LH (mIU/ml) was 8.78 ± 1.86 and 11.92 ± 2.75 , Prolactin ($\mu\text{g/L}$) was 6.92 ± 2.90 and 12.46 ± 3.02 , Estrogen (pg/ml) was 31.61 ± 6.98 and 41.86 ± 9.19 , Progesterone was 0.14 ± 0.04 and 0.19 ± 0.03 , and Testosterone (ng/ml) was 2.77 ± 0.99 and 2.14 ± 0.74 respectively. FSH, LH, Prolactin, Estrogen and Progesterone were significantly higher ($p < 0.05$) in female subjects compared with male subjects, while Testosterone was non-significantly ($p > 0.05$) higher in male subjects compared with female subjects.

Parameter	Male Mean $\pm$ SD	Female Mean $\pm$ SD	t-value	p-value
FSH (mIU/ml)	11.81 ± 2.97	15.11 ± 3.24	3.516	0.004
LH (mIU/ml)	8.78 ± 1.86	11.92 ± 2.75	3.803	0.003
PROL ($\mu\text{g/L}$)	6.92 ± 2.90	12.46 ± 3.02	-3.501	0.004
ESTRO (pg/mL)	31.61 ± 6.98	41.86 ± 9.19	5.408	0.000
PROG (ng/ml)	0.14 ± 0.04	0.19 ± 0.03	-3.600	0.004
TESTO (ng/ml)	2.77 ± 0.99	2.14 ± 0.74	-1.408	0.184
*Values are significant at $p < 0.05$				
Key: N - Sample size; FSH - Follicle Stimulating Hormone, LH - Luteinizing Hormone, PROL - Prolactin, ESTRO - Estrogen, PROG - Progesterone; TESTO - Testosterone				

Table 4: FSH, LH, Prolactin, Estrogen, Progesterone and Testosterone in pulmonary tuberculosis male and female subjects.

FSH, LH, Prolactin, Estrogen, Progesterone and Testosterone in pulmonary tuberculosis subjects with respect to age. Fig. 1 showed the FSH, LH, Prolactin and Testosterone in pulmonary tuberculosis subjects with respect to age. The FSH (mIU/ml) of the subjects in age group 18-25 years, 26-40 years and 41-55 years was 10.66 ± 2.27 , 13.77 ± 2.72 and 17.64 ± 2.13 , LH (mIU/ml) was 9.25 ± 3.44 , 10.31 ± 1.74 and 12.73 ± 2.79 , Prolactin ($\mu\text{g/L}$) was 8.52 ± 3.05 , 11.50 ± 3.78 and 10.14 ± 5.38 , and Testosterone (ng/ml) was 2.65 ± 1.27 , 2.58 ± 0.64 and 2.21 ± 0.89 respectively. Fig. 2 showed that the estrogen (pg/ml) of the subjects in age group 18-25 years, 26-40 years and 41-55 years was 39.82 ± 11.25 , 33.00 ± 4.67 and 36.29 ± 10.05 respectively. Fig. 3 showed that the Progesterone (ng/ml) of the subjects in age group 18-25 years, 26-40 years and 41-55 years was 0.19 ± 0.06 , 0.18 ± 0.04 and 0.20 ± 0.07 respectively. There was no significant difference ($p > 0.05$) in LH, Prolactin, Testosterone, Estrogen and Progesterone of the subjects with respect to age, but there was significant difference ($p < 0.05$) in FSH of the subjects with respect to age.

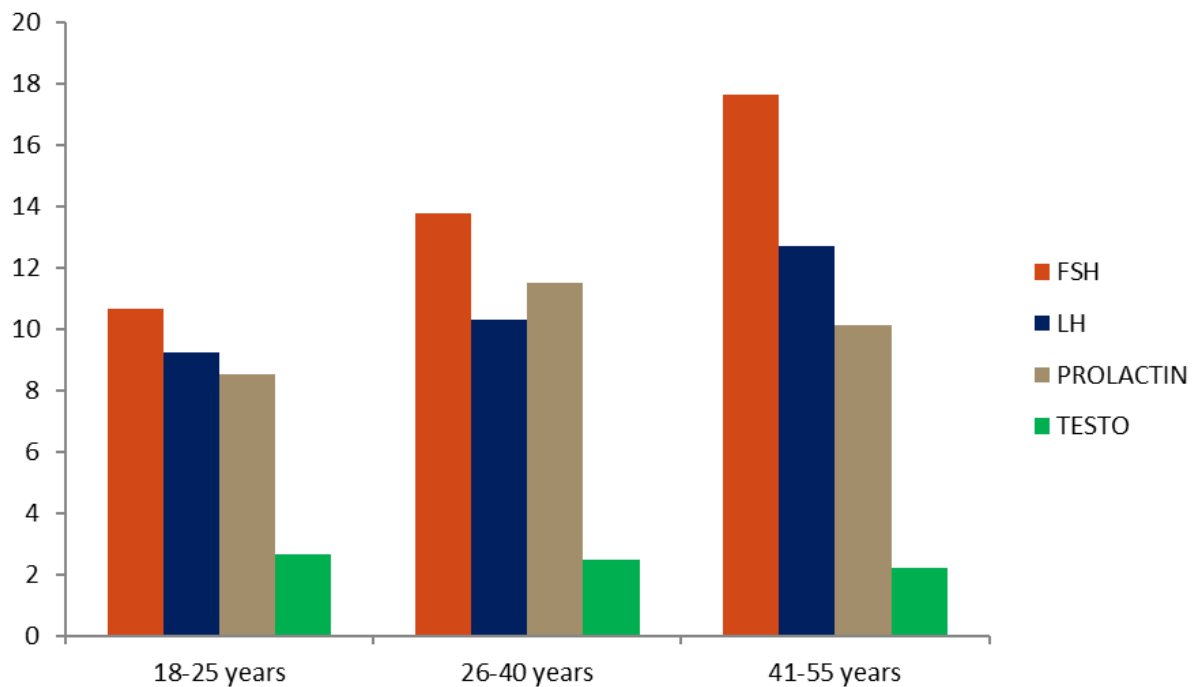


Figure 1: FSH, LH, Prolactin and Testosterone levels in Pulmonary tuberculosis patients with respect to age.

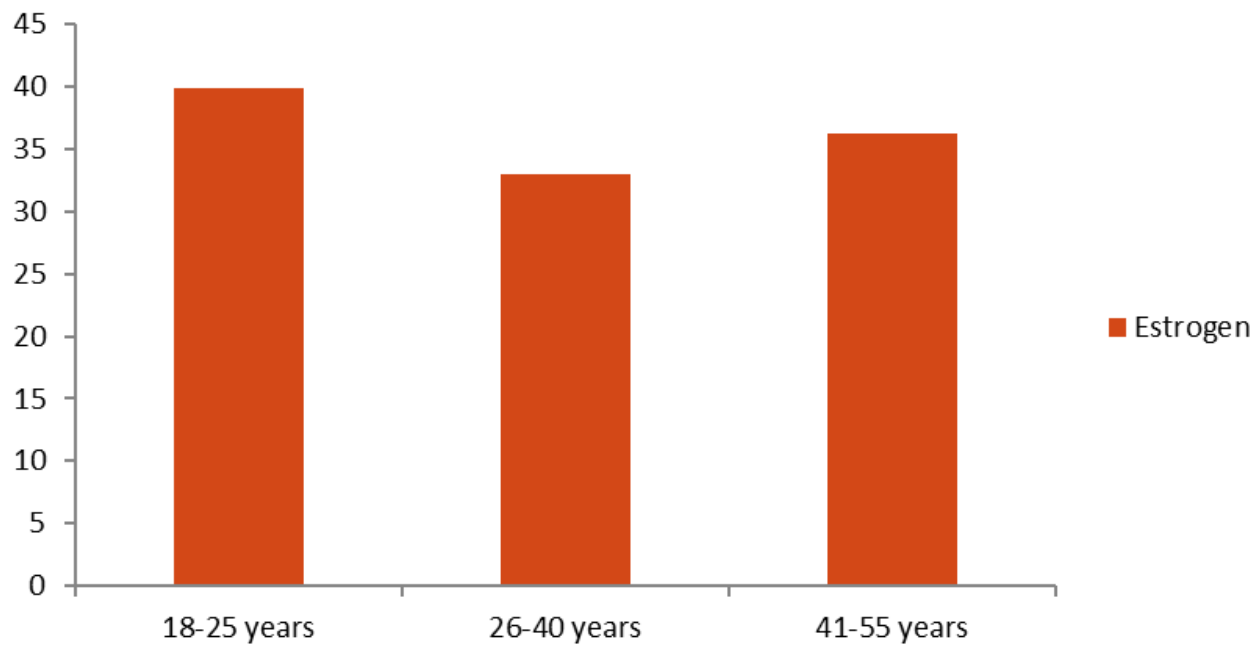


Figure 2: Estrogen level is Pulmonary tuberculosis patients with respect to age.

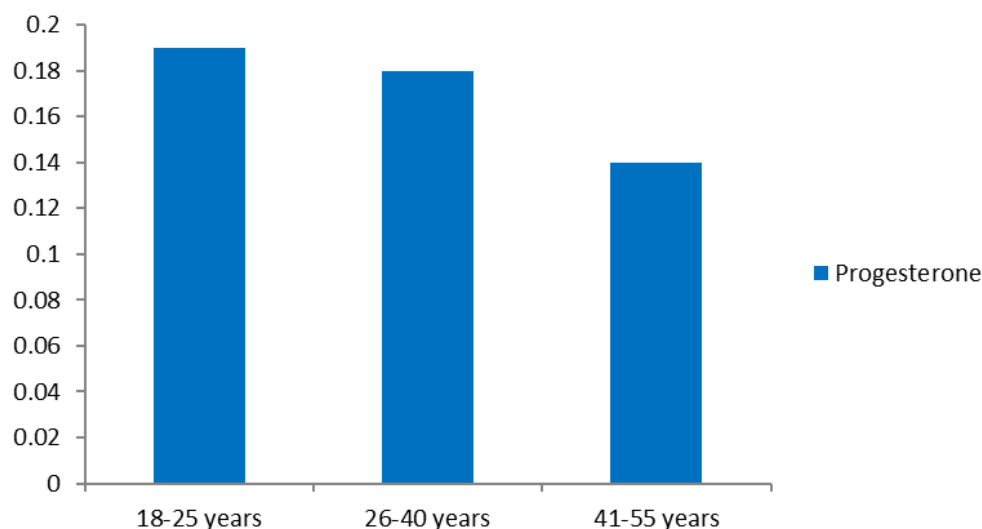


Figure 3: Progesterone level in Pulmonary tuberculosis patients with respect to age.

Discussion

TB is one of the major global health problems ranking as the eighth leading cause of death in low- and middle-income countries (seventh for men and ninth for women); among adults aged 15-59 years, it ranks as the third cause of death, after HIV/AIDS and ischemic heart disease [20,21]. This study was carried out to evaluate the Follicle Stimulating Hormone (FSH), Luteinizing Hormone (LH), Prolactin, Estrogen, Progesterone and Testosterone of pulmonary tuberculosis patients in Edo State.

In this study, serum FSH and LH levels were statistically significantly higher ($p < 0.05$) in the TB group as compared to controls, while the serum progesterone and estrogen levels were significantly ($p < 0.05$) low in TB cases. This finding is in agreement with previous study by Ansari, who reported that Serum FSH and LH levels were statistically significantly higher in the TB group as compared to controls, while the serum progesterone and estradiol levels were significantly low in TB cases ($p < 0.05$). Malhotra et al. (2012) in a study on the effects of TB on ovarian reserve in females undergoing IVF treatment observed FSH levels to be statistically significantly high in TB cases ($p < 0.05$). Our findings were also consistent with those published by Gurgan et al, (1996) and Doaa et al, (2019) who reported that the mean values of FSH and LH were higher in TB positive.

In this study, the mean serum progesterone and estrogen levels were statistically significantly low in the TB group than in the controls. While mean serum FSH and LH levels were statistically significantly high in healthy individuals, FSH and LH levels are high in the follicular phase and peak at the mid-cycle to facilitate ovulation, whereas progesterone and E2 levels are increased in the luteal phase. Disturbance in the hormonal level balance causes irregularities and can affect the reproductive capabilities of the females. A reduction in serum levels of progesterone in the luteal phase can result in spontaneous abortion [22]. Amenorrhoea or other menstrual cycle abnormalities are caused due to hypogonadism and may significantly affect the fertility of TB sufferers [19]. Ukibe, et al., assessed the hormonal changes in the menstrual cycle in 67 women suffering from TB and observed serum levels of FSH and LH to be at high levels while progesterone and E2 to be significantly low in females diagnosed with pulmonary TB [22,23]. Doaa, et al., and Ansari also reported similar findings [14,24].

The appreciation in the level of progesterone in TB subjects on therapy suggests stimulatory effects of the treatment on the gonads with intact negative feedback mechanism thereby resulting in the restoration of the gonadal functions showing some beneficial effects and a tendency to return to normal. This may reduce the incidence of menstrual abnormality and infertility. Unfortunately however, studies have reported that prolonged use of TB therapy especially protease inhibitors have been associated with other problems such as hyperprolactinaemia [25]. Hyperprolactinaemia has been associated with increased incidence of anovulation and hence infertility [26].

In this study, Prolactin and Testosterone were statistically significantly lower ($p < 0.05$) in the TB group as compared to controls. This is consistent with previous study by Kranti, et al., who reported that serum Prolactin and Testosterone were statistically

significantly lower ($p < 0.05$) in the TB group as compared to controls [27]. Menstrual disturbances in patients with PTB without involvement of ovary or genital system are poorly understood which may be related to disease severity. The other additional factor may be changes in hormonal profile and antigonadotrophic effects of *Mycobacterium tuberculosis*, which have been observed in these patients; all increase incidence of menstrual abnormality [24,25].

The significantly lower level of testosterone observed in TB female subjects on drugs when compared to Control females are also due to the reduced ovarian function. In normal physiology, testosterone is produced by the ovaries in the females in very small quantities which serve to maintain muscle mass and hence prevents weight loss. In diseased individuals, this quantity becomes much smaller because of reduced ovarian function and is not able to achieve its physiological function anymore hence the excess weight loss that is associated with these diseases (TB inclusive) [25].

FSH, LH, Prolactin, Estrogen and Progesterone were significantly higher ($p < 0.05$) in female subjects compared with male subjects, while Testosterone was non-significantly ($p > 0.05$) higher in male subjects compared with female subjects. More than 70% of individuals who develop active TB are males and wide epidemiological studies in endemic areas from developing countries have shown that males suffer more severe disease, higher rates of recent transmission, more reactivation of latent infection and poorer treatment outcomes [26]. These differences have been attributed to socioeconomic and cultural factors leading to barriers in accessing health care systems, which might cause under notification in women [27,28]. The differences in TB rates between females and males have also been attributed to biological factors [29]. In this regard, polymorphisms or mutations in genes located in chromosome X can confer more TB susceptibility in males, as well as specific features of metabolism and nutrition related to gender, or anatomical and functional differences in the respiratory tract between males and females [30,31]. Nevertheless, perhaps the most important biological factor associated to different TB susceptibility between males and females is the immune regulatory activities of the sexual hormones [32].

Conclusion

In conclusion, there was significant difference ($p < 0.05$) in the FSH, LH, Prolactin, Estrogen, Progesterone and Testosterone of the subjects in the different groups compared with control. FSH, LH, Prolactin, Estrogen and Progesterone were significantly higher ($p < 0.05$) in female subjects compared with male subjects, while Testosterone was non-significantly ($p > 0.05$) higher in male subjects compared with female subjects. There was no significant difference ($p > 0.05$) in LH, Prolactin, Testosterone, Estrogen and Progesterone of the subjects with respect to age, but there was significant difference ($p < 0.05$) in FSH of the subjects with respect to age. Age also affect TB patients testosterone, progesterone tends to decrease as age increase while FSH and LH increases as the age of PTB increases with age. Based on the findings of this work, it is recommended that female patients suffering from any form of TB be comprehensively managed. Because of highly sensitive issues related to infertility and reproductive health in today's era, it is imperative that any future complications of the same are kept into consideration in female patients with TB.

Conflict of Interest

The authors declare that they have no conflict of interest.

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Patient Consent

Informed consent for examination and for publishing anonymized data were obtained from the patients.

Data Availability

Data is available for the journal. Informed consents were not necessary for this paper.

Author's Contribution

The authors contributed equally.

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