

## EFFECT OF PULMONARY TUBERCULOSIS DISEASE ON FEMALE SEX HORMONES AND REPRODUCTORY HEALTH – A PROSPECTIVE CLINICAL STUDY

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### ABSTRACT

**Background:** Recent medical literature shows the negative effects of pulmonary tuberculosis disease on female reproductive health with disturbance in levels of female sex hormones affecting the menstrual cycle and resulting in infertility. Thus the present prospective clinical trial was conducted to evaluate the levels of female sex hormones in females suffering from pulmonary tuberculosis and its association with reproductive health. **Materials and the methods-**This the prospective clinical study included 100 female participants (18yrs to 55yrs) out of which 70 patients diagnosed with pulmonary TB were taken in the test group and 30 females with no history of TB were included in the control group. All patients were evaluated for complete medical, menstrual history, clinical signs and symptoms, serum levels of FSH, LH (follicular phase), progesterone and estradiol (luteal phase). **Results-** Sociodemographic variable did not show any statistically significant difference between the two groups( $p>0.05$ ). Menstrual irregularities were observed in 65.8% of cases in the TB group and 10% of the controls. In the pulmonary TB group, 70 % had menstrual irregularity, 40% had secondary amenorrhea, 14.2% had hypomenorrhea, 2.8% had Hypermenorrhea, 2.8% had Metrorrhagia, and 5.71% Dysmenorrhea was noted. 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 ( $p<0.05$ ). **Conclusion:** Pulmonary Tuberculosis negatively affects female reproductive health and can be a cause of infertility. It disturbs the hormonal balance with subsequent menstrual cycle abnormalities. Successful treatment by antitubercular drugs could reverse these changes and restore the hormonal balance and the reproductive health.

**Keywords:** Pulmonary Tuberculosis, Female sex hormone, Reproductive health, Menstrual irregularities

### INTRODUCTION

Tuberculosis (TB) is a chronic infectious and wasting disease and adversely affects different organ systems. The causative agent is *Mycobacterium tuberculosis*. Around 24 lakh people were infected with TB in 2019 in India. The average prevalence is estimated to be 5.05 /1000 and average annual incidence of smear-positive cases at 84 /one lakh yearly in India. Risk factors for TB are malnutrition, alcoholism, silicosis, smoking, diabetes, poverty, overcrowding, and male predilection. (1)

Women suffering from TB have to face many challenges in accessing health care services.

Tuberculosis is one of the major causes of infertility in women. Tuberculosis involving genital organs and its corresponding negative health outcomes such as menstrual irregularity, hypomenorrhea, amenorrhea, and infertility is well documented in the literature.(2) Hassan and Darwish 2010 showed TB to have a remarkable effect on the menstrual cycle which was reversible but minimally associated with genital TB and infertility. If symptoms persist after treatment completion then involvement of the genital tract should be investigated. (3)

Moreover, studies by Tripathy et al and Hamadeh et al stated no effect on the course of pregnancy in females suffering from pulmonary TB.(4,5)

The medicines used in the treatment of the disease can also have a negative impact on contraception and female reproductive health. Females co-infected with HIV and having multidrug-resistant tuberculosis may suffer from detrimental effects on their reproductive health. The clinicians should be trained in a manner to address these issues and manage them accordingly.

Recently, the implications of pulmonary TB on female hormonal changes and menstrual cycle are being quoted. In India due to the social stigma attached to TB disease, females are not able to discuss their problems and suffer in silence.(6)

Thus, the present prospective clinical study was designed to assess the effect of pulmonary TB on female sex hormones and reproductive health.

## MATERIAL and METHODS

This prospective clinical study included 100 female participants in the age range of 18yrs to 55 yrs who came to the outpatient department of our hospital from March 2019 to December 2019.70 patients diagnosed with pulmonary TB were taken as a test group and 30 females with no history of TB were taken as the control group. A prior ethical clearance was taken from the institutional ethical board. Written consent was taken from all the participants and nature of the study was explained.

Complete medical history with details of the reproductive cycle was recorded and subsequently classified as Secondary amenorrhea (absence of menstrual periods for 3 months), Hypomenorrhea (slight bleeding), and hypermenorrhea (heavy and prolonged bleeding), Metrorrhagia: bleeding at irregular intervals), Dysmenorrhea (painful menstruation). Venous blood samples were collected and sent to the laboratory for estimation of serum FSH and LH at follicular phase (day 3-7 of the menstrual cycle), Progesterone and estradiol levels at luteal phase (day 20-22 menstrual cycle) in both the groups.

A confirmed diagnosis for pulmonary TB was made with the sputum smear test for acid-fast bacilli (AFB) after staining with Ziehl-Neelson. Patients on hormonal therapy, pregnant and lactating were excluded.

## Statistical analysis

Statistical software SPSS version 22 was utilized to conduct the analysis. Data were expressed as mean  $\pm$  standard deviation, and proportions were presented as percentages. Independent Student *t*-tests and chi-square analysis were done to assess the comparison between groups. P value is considered significant if less than 0.05.

## RESULTS

The socio-demographic variable did not show any statistically significant difference between the two groups ( $p > 0.05$ ) (Table 1). Menstrual irregularities were observed in 65.8% of cases in the TB group and 10% of the controls (Table 2). 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 the TB group ( $p < 0.05$ ) (Table 3).

**Table 1 shows Sociodemographic patterns**

Variables	Pulmonary TB Group	Control Group	P-value
<b>Age (mean <math>\pm</math>SD) yr</b>	35.5 $\pm$ 5.8	37.3 $\pm$ 4.3	>0.05
<b>BMI</b>	27.3 $\pm$ 3.4	25.7 $\pm$ 3.65	>0.05
<b>Parity(%)</b>	80%	92%	>0.05
<b>Menarche Age (yr)</b>	13.3 $\pm$ 1.4	13.5 $\pm$ 2.1	>0.05
<b>Menstrual irregularity (n, %)</b>	49(70%)	5(16.6%)	<0.05
<b>Marital Status</b>	60(85.71%)	26(86.6%)	>0.05
<b>Hypertension</b>	8(11.4%)	4(13.3%)	>0.05
<b>Diabetes</b>	7(10%)	2(6.66%)	>0.05

**Table 2 Shows Menstrual patterns in both the groups**

	Pulmonary TB Group	Control Group	P-value
Normal menstrual pattern	24(34.2%)	27	<0.05
Secondary amenorrhea	28(40%)	0	
Hypomenorrhea	10(14.2%)	1	
Hypermenorrhea	2(2.8%)	0	
Metrorrhagia	2(2.8%)	0	
Dysmenorrhea	4(5.71%)	2	

**Table 3 Hormonal profile among women with pulmonary tuberculosis and control**

Hormones	Normal Range	Pulmonary TB group	Control Group	P-value
LH (mIU/ml)	2.4-12.6	6.78±2.24	5.02±1.52	<0.05
FSH (mIU/ml)	3.5-12.5	8.78±2.98	5.5±0.76	<0.05
E2 (pg/ml)	21- 75	37.5±9.5	50.32±6.4	<0.05
Progesterone (nmol/l)	10-60	27.7±9.6	41.21±3.6	<0.05

## DISCUSSION

TB is one of the most common chronic infectious diseases with India sharing a heavy burden of TB patients. It can affect almost all parts of the body, also affecting genital organs. TB affecting the reproductive health in females is literature proven but due to the social stigma attached to it is not well assessed. (7)

Irregularities in the menstrual cycle are more commonly observed in TB affecting genital organs than the lungs. Substantial number of infertility cases in India with menstrual irregularities is due to genital TB. (8) Areas with a high burden of TB care should be taken to diagnose TB in infertile females as they could be asymptomatic TB cases.

Early diagnosis and treatment could prevent further major damage to reproductive organs and permanent infertility. (9) Also abnormalities in hormonal levels have been observed in various researches. TB clinically presents with appreciated weight loss, and high systemic inflammatory reactions resulting in abnormal menstrual cycle patterns. (10)

In the present study, in the pulmonary TB group, 70 % had menstrual irregularity, 40% had secondary amenorrhea, 14.2% had hypomenorrhea, 2.8% had Hypermenorrhea, and 2.8% had Metrorrhagia and 5.71% had Dysmenorrhea was noted. Similar results were reported by Magdy et al who noted around 68% of menstrual irregularities in women. (11) 42% of female patients with advanced disease have amenorrhea. Fallahian and Tikhani et al

<sup>12</sup> noted amenorrhea and hypomenorrhea to be common menstrual patterns in female TB patients.(12) Hassan and Darwish reported that these irregularities were reversed after the completion of anti-tubercular treatment. In 66% of females, a menstrual irregularity was noted 66% women. (12)

TB affects the hypothalamus, pituitary gland, and ovaries resulting in amenorrhea.(3)Also endometrial involvement was noted in 13% of women with pulmonary TB patients by Tripathy and Tripathy.(4) Similar findings were noted by Sharma et al 2002.(6)Research are been carried out to study the mechanism of Mycobacterium tuberculosis causing antigonadotrophic effects and menstrual disturbances without the involvement of the reproductory organs. (13)

In the present, study, 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. Malhotra et al 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. (14)Similar findings were noted by Gurgan et al.(15)

In the present study, the mean serum progesterone and E2 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 cause 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 (14).Amenorrhoea or other menstrual cycle abnormalities are caused due to hypogonadism and may significantly affect the fertility of TB sufferers.

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 E2to be significantly low in females diagnosed with pulmonary TB.(16)

## CONCLUSION

This prospective clinical study evaluated the effects of pulmonary TB on female sex hormones. In TB, decreased ovarian function (hypogonadism) occurs with significantly high levels of FSH and LH

resulting in menstrual irregularities. This can have effects on reproductive health and fertility among females.

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