

## Original Research Article

# Evaluation of genital tuberculosis as a cause of female infertility in a tertiary care hospital in North India

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## ABSTRACT

**Background:** Female genital tuberculosis (FGTB) poses a great diagnostic challenge in women of reproductive age. It causes significant morbidity or short and long term sequelae, especially infertility. The disease often remains silent or may present with non-specific symptomatology. As a result, the prevalence of genital tuberculosis is largely underestimated. A high degree of suspicion aided by intensive investigations is important in the diagnosis of the disease, especially in its early stage, so that treatment may improve the prospects of cure before the tubes are damaged beyond recovery. Objectives were to find out the prevalence of genital tuberculosis in females presenting with infertility in a tertiary care hospital over a given period of time, and diagnostic comparison of endometrial tuberculosis by histopathological examination (HPE) and GeneXpert.

**Methods:** The prospective observational study was conducted over one year duration. A total of 96 endometrial samples were collected from the women, satisfying the inclusion and exclusion criteria.

**Results:** On HPE, out of 96 patients, proliferative endometrium (anovulatory) was found in 38 cases (39.6%), non-specific endometritis in 2 cases (2.08%) and 2 cases (2.08%) were found positive for tubercular endometritis. GeneXpert scored negative in our study.

**Conclusions:** Endometrial biopsy shows not only the tuberculous endometritis, but also gives additional information about local factors of endometrium concerning non-specific and specific infections and anovulatory cycles. GeneXpert if positive on endometrial biopsy is a reliable test for FGTB and treatment can be started on its basis.

**Keywords:** Infertility, Female genital tuberculosis, Histopathological examination, GeneXpert test

## INTRODUCTION

WHO has defined infertility as “failure to conceive despite over 12 months of regular and unprotected intercourse”. Tuberculosis, a chronic infectious disease, is one of the major etiological factors of female infertility. According to Global TB Report 2016, there were estimated 10.4 million new tuberculosis (TB) cases worldwide (3.5 million in women), with 2 million deaths.<sup>1</sup> At present, female genital tuberculosis is considered the cause of 10-27.8% of female infertility cases and seen as a serious medical and social problem in women of

reproductive age (24-35 years).<sup>2</sup> India has one of the highest incidences of TB in the world. It is therefore, suggested that every patient consulting for infertility in developing countries should be investigated for female genital tract tuberculosis (FGTB).

Unlike pulmonary tuberculosis, the clinical diagnosis of genital tuberculosis is difficult because in majority of cases, the disease is either asymptomatic or has varied clinical presentation. Routine laboratory investigations like microscopy and culture are of little value in the diagnosis. PCR (polymerase chain reaction) has highest

sensitivity as compared to other methods for diagnosis of tuberculosis but due to false positive results, specificity is low.<sup>3</sup> Only histo-pathological evidence in premenstrual endometrial tissue biopsy can provide diagnosis with certainty. GeneXpert MTB/RIF (mycobacterium tuberculosis/ resistance to Rifampicin) has potentially led to revolution in diagnosis of active tuberculosis disease and MDR-TB (multidrug resistance tuberculosis). WHO recommended use of GeneXpert assay by 'December 2010'.<sup>4</sup> It is an important breakthrough in fight against tuberculosis.

The present study evaluates the prevalence of FGTB among infertile patients. Study aimed at evaluating the histological patterns of endometrium in infertile women in an attempt to establish the cause of infertility. It has also been designed to evaluate the efficacy of GeneXpert test for diagnosing endometrial tuberculosis.

## **METHODS**

### ***Study setting***

Tertiary health care setting of the Department of Obstetrics and Gynaecology, Santosh Medical College and Hospital, Ghaziabad, U.P., India

### ***Study design***

Prospective observational study

### ***Duration of study***

One year study from July 2017 to June 2018

### ***Study participants***

Infertile women attending the out-patient Department of Obstetrics and Gynaecology, Santosh Medical College Hospital.

### ***Sample size***

Since it was a time bound study, all the samples received during the study period and satisfying the inclusion and exclusion criteria were considered. On the basis of the clinical presentation, 96 women of infertility were included.

### ***Eligibility***

#### ***Inclusion criteria***

Inclusion criteria were primary infertility; secondary infertility.

#### ***Exclusion criteria***

Exclusion criteria were endometriosis; fibroid; cervical polyp; sexually transmitted diseases.

## ***Methodology***

After getting approval from the ethical committee and after taking informed consent from the patients, they were called for endometrial aspiration or biopsy one week before start of menstrual cycle or within 12 hours of onset of menses.

Patients were advised abstinence in menstrual cycle before the month of procedure.

Two samples were taken by Karmann's cannula number 4 or endometrial biopsy curette.

One sample was sent for Histopathological Examination in formalin and second sample in normal saline for GeneXpert test.

The results of the two were analysed and compared.

## ***Outcome measures***

### ***Primary outcome measure***

- To find out the prevalence of genital tuberculosis in all females presenting with infertility in a tertiary care hospital over a given period of time.
- Diagnostic comparison of endometrial tuberculosis by histopathological examination (HPE) and GeneXpert test.

### ***Secondary outcome measure***

- To find out other causes of infertility.

## ***Data analysis***

In the statistical analysis, percentages (frequencies) of various parameters were calculated and subjected to statistical test using chi-square test. The computation was done using Microsoft Excel 2007.

## **RESULTS**

Ninety six patients with primary or secondary infertility were recruited for the study.

Table 1 describes the baseline characteristic of the study participants.

The patients were in the range of 20 to 40 years of age. Maximum patients were from age group 26-30 years (41.7%) (Table 1).

Out of 96 women from the study population, 45.8% were primary infertility patients and 54.2% were secondary infertility patients (Table 2).

**Table 1: Socio-demographic factors of the patients.**

Characteristic	n=96	%
Age (in years)	≤20	5.2
	21-25	27.1
	26-30	41.7
	31-34	17.7
	≥35	8.3
Religion	Muslim	16.7
	Hindu	83.3
Family history of tuberculosis	Yes	12.5
	No	87.5
Past history of tuberculosis	Yes	22.9
	No	77.1

**Table 2: Distribution according to type of infertility.**

Type of infertility	n=96	%
Primary	44	45.8
Secondary	52	54.2

On histopathological examination of endometrium, 2 cases (2.08%) were found positive for tubercular endometritis; proliferative endometrium (anovulatory) was found in 38 cases (39.6%), non-specific endometritis in 2 cases (2.08%) and secretory endometrium was found

in 54 cases (56.3%). GeneXpert test scored negative for tuberculosis in our study (Table 3)

**Table 3: Results of GeneXpert and histopathology.**

Investigation	n=96	%
GeneXpert test	Positive	0
	Negative	96
Histology of endometrium	Secretory phase	56.3
	Proliferative phase	39.6
	Non-specific endometritis	2.08
	Tubercular endometritis	2.08

As a secondary outcome, other causes of infertility were also evaluated and compared between primary and secondary infertility patients. No significant difference was found between two groups in regards to any particular investigation like ESR, Serum TSH, Serum Prolactin, Ultrasound etc. Proliferative endometrium (anovulatory) was found in 14 cases (31.8%) of primary infertility whereas 24 cases (46.2%) of secondary infertility, which was more in the second group. The 'p' value was 0.209 which was not statistically significant. (Table 4).

**Table 4: Other investigations of infertility.**

Investigation	Primary infertility		Secondary infertility	
	n=44	%	n=52	%
ESR (n=0-29)	8	18	10	19.2
S.TSH (n=0.5-6)	6	13.6	11	21.1
S.Prolactin (n=2.8-29.2 NG/ml)	0	0	1	1.9
Mantoux test positive	7	15.9	8	15.4
Chest x-ray (S/o TB)	1	2.3	0	0
Husband semen analysis (abnormal)	10	22.7	12	23.1
Ultrasound	Fibroid	6.8	1	1.9
	PCOD	25	10	19.2
Proliferative endometrium in premenstrual phase	14	31.8	24	46.2
Conceived	6	13.6	8	15.4

**DISCUSSION**

Due to the lack of specific test and diagnostic modalities, it is difficult to diagnose and conclude the presence of genital tuberculosis. On the basis of clinical presentation alone, a woman cannot be diagnosed with FGTB. Multiple imaging techniques are not specific for tuberculosis confirmation. Endometrial biopsy should be taken in premenstrual phase for good results on AFB smear, culture, GeneXpert, PCR and other tests.<sup>5</sup> Early diagnosis and treatment will improve fertility outcome.

Very few studies have been done on GeneXpert as a diagnostic modality for endometrial tuberculosis and hence not much data could be made available to compare

our results. GeneXpert scored negative in present study, whereas one study showed 1.6% positive results.<sup>5</sup> The sensitivity of Xpert MTB/RIF in detecting TB is quite high (88%).<sup>4</sup> GeneXpert if positive on endometrial biopsy is a reliable test for FGTB and treatment can be started on its basis.<sup>6</sup> The negative predictive value (NPV) is greater than 98% both in settings with a low prevalence of TB and in those with a high prevalence of TB; that is, a negative result accurately excludes TB in most situations. When XPERT MTB/RIF does not detect *M. tuberculosis*, the disease can be ruled out in most cases unless there is still a strong suspicion of TB.<sup>4</sup>

Histo-pathological evidence of tuberculous granulomas in tissue samples leads to definitive diagnosis of genital

tuberculosis. The technique is easy, quick and cheap and provides characteristic features of MTB. The reported incidence from various studies ranges from 0% to 4.92%. Prasad et al and Kafeel showed 0.6% and 0.8% positive cases respectively.<sup>7,8</sup> In the study by Rao, 1.5% cases were positive for FGTB, and 2.6% in study by Goel G.<sup>9,10</sup> Murmu et al reported 2.5% positive cases on HPE. In the present study, we diagnosed 2.08% of GTB cases on endometrial HPE. Our results were comparable with other studies. A study by Shende documented 10% women of GTB having positive histopathological reports.<sup>12</sup> The detection rate by HPE was also low in study by Thangappah, as only 4% samples were positive for tuberculosis.<sup>13</sup> The low prevalence of M. tuberculosis in endometrial biopsy may be due to various reasons. Due to secondary nature of the genital tuberculosis, the infecting organisms are sparse in number, and the sampled site may not represent the infected area; or in 50% of cases, the infection may be limited to the fallopian tube.<sup>14</sup> Moreover, due to the cyclical shedding of the endometrium, granulomas do not have enough time to form; so, the endometrium may not show evidence of tuberculosis in all the cycles.<sup>15</sup> The incidence may also be lower because of improved health care facilities over the years.

## CONCLUSION

Tuberculous endometritis as a cause of infertility is still a major problem in the developing countries; any woman having infertility with no definite cause found should be investigated for tuberculosis. Therefore, in countries where tuberculosis is endemic, early and aggressive strategies should be pursued to diagnose and treat it. A multi-pronged approach to diagnosis increases the chances of successfully diagnosing this destructive disease.

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