

Prevalence of Genital Tuberculosis in Infertile Women; a Study from a Tertiary Care Center in North India

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ABSTRACT

Introduction: Female genitourinary tuberculosis (FGTB) is an important cause of infertility in women of reproductive age group. The disease remains undetected due to its asymptomatic nature and lack of sensitive tests. This study was conducted with the aim of detecting the prevalence of genital tuberculosis in infertile women.

Material and methods: Endometrial curetting of 193 infertile women suspected of genital tuberculosis were taken laparoscopically and sent for histopathological examination, ZN staining, culture on LJ media and GeneXpert testing.

Results: Out of 193 women, 13 were positive for *Mycobacterium tuberculosis* making the overall prevalence of FGTB in infertile women to the extent of 6.73%. Of these 11 presented with primary infertility while 2 patients presented with secondary infertility. The histopathological examination of all the samples was non-specific. No case of positive acid fast bacilli on ZN staining was observed. Comparison of culture and GeneXpert revealed that Xpert assay was more sensitive in detecting the positive cases.

Conclusion: Our study concluded that FGTB is common in our population and women presenting with infertility should be evaluated for genital tuberculosis. A high degree of suspicion and combination of histopathological and microbiological tests are important methods for the detection of genital tuberculosis

Keywords: Female Genital Tuberculosis, Infertility, Prevalence, Culture, GeneXpert

INTRODUCTION

Despite the availability of effective anti-tubercular drugs, tuberculosis still remains an important cause of morbidity and mortality across the globe. Female genital tuberculosis is a form of extra pulmonary TB which is found particularly in areas where pulmonary or other forms of extrapulmonary TB are common. The global prevalence of GTB is estimated to be 8-10 million cases with a rising incidence, particularly as a result of HIV pandemic and the emergence of multidrug resistant strains.^{1,2}

Genital tuberculosis in females affects fallopian tubes, uterine endometrium, ovaries, cervix, uterine myometrium and vagina/vulva. Genital TB causes infertility, menstrual irregularity and pregnancy loss in women. It is thus well recognized as an important etiological cause for infertility in areas with high prevalence of tuberculosis. This disease not only causes tubal obstruction and dysfunction but also impairs implantation due to endometrial involvement and ovulatory failure from ovarian involvement.³

The burden of tuberculosis is largely underestimated as most

of the patients are asymptomatic and usually diagnosed during evaluation for infertility. A study on female genital TB among patients with infertility from India shows an incidence of 3-16%. Despite the availability of various techniques, diagnostic dilemma for genital TB still exists. A high degree of suspicion and elaborate history and clinical examination are essential for diagnosis. Laparoscopic findings cannot help in absolute diagnosis in early stages, however it is a valuable procedure for obtaining tissue specimen for culture and other tests.^{4,5,6}

Keeping in view the endemicity of tuberculosis in the state of Jammu and Kashmir and the lack of information about the prevalence of FGTB, the study was undertaken with the aim of determining the prevalence of genital tuberculosis in females of infertility and determine the utility of the existing standard diagnostic tests in the diagnosis of female genital TB.

MATERIAL AND METHODS

This descriptive, cross sectional study was carried in the Department of Microbiology, Government Medical College, Srinagar from June 2014 to May 2018 for a period of 4 years. The ethical clearance for the study was obtained from the institutes' ethical clearance committee. Infertile women suspected of having genital tuberculosis were included in this study. A detailed history such as age, duration of infertility, menstrual and gynecological history, past history of tuberculosis and systemic examination was undertaken. All women underwent detailed laproscopic examination. Premenstrual endometrial biopsy for histopathology, AFB microscopy and culture were taken as a part of diagnostic workup. Whenever possible, fluids from pouch of douglas was also aspirated at the time of laparoscopy. For

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histopathological studies, samples were sent in 10% formalin solution while for microbiological studies, samples were sent in normal saline. Prior to 2016, the samples were processed for ZN staining and culture whereas after 2016, samples were processed for ZN staining, culture and GeneXpert testing.

On receipt of the samples in the laboratory, the samples were grinded in 1ml of normal saline in mortar and pestle and decontaminated with H₂SO₄ method. Homogenised decontaminated sediment was used for AFB microscopy, culture, and Xpert testing. AFB staining was done by Ziehl Neelson staining method and observed under oil immersion microscope. Culture was put on LJ medium. Samples were observed on 3rd day to check the growth of contaminants and weekly thereafter for the growth of colonies typical of mycobacteria. *Mycobacterium tuberculosis* was identified by colony morphology and biochemical characteristics. Cultures were incubated for 8 weeks before being declared as negative.

For Xpert testing, the manufacturers' recommendations were followed. A sample diluent was added to the samples in the ratio of 2:1 to kill mycobacteria and liquefy the samples. After intermittent shaking and incubation for 20 minutes, 2ml of the mixture was added to the cartridge and loaded in to the instrument. Tests were rerun if the results were invalid or error was reported.

STATISTICAL ANALYSIS

Data was entered in a Microsoft excel sheet. Categorical variables were summarized as frequency and percentage. Continuous variables were summarized as mean and standard deviation. Data analysis was done using EpiInfo 7.0.

RESULTS

A total of 193 patients suspected of female genital tuberculosis were included in the study. Of these, 117 (60.6%) patients were suffering from primary infertility while 76 (39.4%) patients were suffering from secondary fertility. Most women were in the age group of 25-35 years followed by followed by 35-45 years. Mean age of patients included in the study was 30 years.

Of the 193 samples, 124 samples were put for smear microscopy and culture (prior to year 2016) and 69 samples were put for smear microscopy, culture and GeneXpert (in the year 2016 and thereafter). However, the histopathological examination was performed in all the 193 patients.

Of the 193 samples, 5 samples were positive for non tubercular mycobacteria. A total of 13 patients were found to be positive for *Mycobacterium tuberculosis* by either of the three methods. Out of these 13 women, 11 (84.6%) presented with primary infertility while 2 (15.4%) women had secondary infertility. Therefore the total prevalence of genital tuberculosis found in our study was 6.73%.

None of the patients came positive on smear microscopy. Culture was positive in 10 samples while as gene xpert was positive in 5 samples. Prior to 2016, 8 of the 124 samples were positive by culture while 2 of the 69 samples after 2016 grew mycobacteria on culture. 2 samples found positive on

Tests	No. of samples	Positive result (%)
Histopathological examination (HPE)	193	nil (0)
AFB smear	193	nil (0)
Culture	193	10 (5.18)
GeneXpert	69	5 (7.25%)

Table-1: Results of specific diagnostic tests on endometrial samples

gene xpert were also found positive on culture while the other 2 samples that were gene xpert positive were culture negative. The 5th sample that was positive by gene xpert was contaminated on culture. The histopathological examination of these specimen revealed non specific findings. None of the specimen showed findings consistent with TB endometritis. (Table-1)

DISCUSSION

Infertility is defined as the inability of a sexually active, non contracepting couple to achieve pregnancy in one year. It can be primary or secondary. Infertility is classified as primary when women has never been able to bear a child ever either due to inability to become pregnant or ability to carry a pregnancy to a live birth. When a women is unable to bear a child following either a previous pregnancy or a previous ability to do so, it is refered as secondary infertility.^{7,8}

Genital tuberculosis which affects the fallopian tubes and endometrium significantly contributes to infertility in developing countries. *Mycobaterium tuberculosis* may cause irreversible damage to fallopian tube which may not get corrected by medical and surgical methods. Therefore early diagnosis and treatment of genital tuberculosis is important as it may improve fertility outcome. This study was undertaken to determine the prevalence of infertility as evaluated by microbiological and histopathological techniques.^{2,4,9}

In our study the prevalence of genital tuberculosis was found to be 6.73%. The prevalence of genital tuberculosis has been reported from less than 1% to 20% in various studies. Overall prevalence of genital tuberculosis in infertile women has been found to be 24.2%. It is possible that the actual prevalence of genital tuberculosis in our setting may be higher due to the fact that most of the cases are asymptomatic or present with non specific symptoms and therefore may go undetected . Also a larger proportion of cases go unreported due to lack of sensitive and specific investigations.^{10,11} Non tubercular mycobacteria were isolated in 5 samples. However the association of non tubercular mycobacteria with infertility has not been established.

As there is no gold standard for the diagnosis of female genital tuberculosis, various methods were employed for detecting tubercle bacilli in the specimen. Laparoscopy may detects macroscopic changes such as peritubal adhesions, tubercles and tubo-ovarian masses; however such changes are seen in chronic cases. Subtle changes produced by the tubercle bacilli during early stages may be overlooked on laparoscopy. However in our study, laparoscopic finding were not available for all the patients and therefore the test

could not be compared with other methods employed. None of the specimen had histopathological findings specific for tuberculosis. The reasons could be the cyclic shedding of the endometrium which leads to inadequate granuloma formation and the sampling site may not contain the tubercle bacilli.^{3,12}

None of the samples submitted to the lab was positive on AFB microscopy. This could be explained by the paucibacillary nature of the specimen. Culture for *M. tuberculosis* was positive in 10 of the 13 patients. Studies have demonstrated the low detection rates of tubercle bacilli in cultures. The reason could be the paucibacillary nature of the mycobacteria in endometrial samples and also the fact that the sampled site may not be the infected site.¹³

Various studies have demonstrated the increased sensitivity of polymerase chain reaction (PCR) for the diagnosis of FGTB. However, PCR is associated with high false positive rates and therefore it is not recommended to start the treatment for FGTB on the basis of PCR results only.^{14,15}

The use of geneXpert has been advocated by world health organization for the detection of *Mycobacterium tuberculosis* and rifampicin susceptibility. Gene Xpert was done in 69 patients. Of these, 5 came positive. 2 of the samples that came positive on GeneXpert were positive on culture as well while as 2 Xpert positive samples were geneXpert negative while one grew contamination on culture. A comparison of culture and Xpert demonstrated that geneXpert was useful in confirming diagnosis of female genital tuberculosis in clinically suspected cases.^{16,17,18}

CONCLUSION

To conclude, female genital tuberculosis is an underestimated disease mainly due to its asymptomatic nature and lack of sensitive tests. It is detected most frequently when a women presents to with unexplained infertility. Therefore screening for genital TB should be routinely done for the evaluation of infertility.

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