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Evaluation of endometrial tuberculosis among subjects undergoing endometrial biopsy at our teritiary care centre

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***Abstract*---**Background: Female genital tuberculosis (FGTB) is known to cause severe tubal disease leading to infertility and its incidence closely parallels with the overall prevalence of tuberculosis (TB) in a community. Objectives of the study: To study the prevalence of endometrial tuberculosis among the infertility subjects undergoing endometrial biopsy. Materials and Methods: Demographic data regarding age, Socioeconomic status based on the Modified Kuppuswamy scale, menstrual pattern, type of infertility, past-history of TB in any part of the body or history of TB contact (living in the same household or in frequent contact with a sputum smear positive TB patient in last 2 years). Body Mass Index/ BMI was calculated. All the subjects were evaluated for GTB by CXR, CBNAAT, USG, Culture AFB, Biopsy, and histopathological examination. Results and Discussion: We performed various investigations which include CXR, USG, CBNAAT and CS for AFB, we found that all the subjects had normal CXR, 132 had tubo-ovarian mass on USG, 36 had CBNAAT positive and culture for AFB was positive in 23 subjects. We further evaluated endometrial involvement in 78 infertility subjects we found that tubercular endometritis was found in 14 subjects accounting for 17.9% prevalence, 2 women had endometrial hyperplasia, 8 had nonspecific endometritis, 26 had proliferative epithelium, and 28 had secretary epithelium. Conclusion: In our study, we fund the prevalence of 17.9% endometrial tuberculosis in subjects suffering from infertility, and CBNAAT was superior to histopathology in the detection of GTB and had strong correlation with Culture for AFB.

***Keywords*---**genital tuberculosis, acid fast bacilli, endometrial tuberculosis, chest X-ray, ultrasonography, infertility.

Introduction

Female genital tuberculosis (FGTB) is known to cause severe tubal disease leading to infertility and its incidence closely parallels with the overall prevalence of tuberculosis (TB) in a community. Its magnitude is underreported because diagnosis is difficult and requires invasive techniques. In developing countries like India Genital tract tuberculosis is identified as an important cause of infertility. Most often, hysterosalpingograms (HSG) remain the primary method of diagnosis for understanding various tubal and peritoneal factors that might lead to cases of infertility. This method has been identified as a unique procedure for ascertaining the internal architecture of female genital tract which is essential for ascertaining the changes associated with tuberculosis infection. It has been found that around 0.75% to 1% of total gynecological complaints are associated with genital tuberculosis in India although this number varies from place to place. Around 5% of all pelvic infections are cases of genital tuberculosis and further it accounts for 10% of all cases of pulmonary tuberculosis. Although most of the cases are from females of reproductive ages only, it has also bene reported in post-menopausal individuals also.[1-3]

Female genital tuberculosis (FGTB) is still a major cause of infertility in India in spite of the availability of specific therapy. The prevalence of FGTB in infertility clinics shows marked variations in different countries ranging between 15 and 25%. In 80-90% of cases, FGTB affects young women between 18 and 38 years of age and is an important cause of infertility. Genital tuberculosis (TB) predominantly affects individuals below 40 years of age and peak age frequency ranges between 21 to 30 year of age. Infertility is defined as the inability to conceive by at least one year of unprotected intercourse. Treatment may be started earlier in case of an obvious cause or advanced age of the couple. Genital tuberculosis is an important cause of sub fertility, more so in endemic zones such as South India. Still, the true epidemiology of this disease remains unknown due to lack of highly sensitive and specific tests. Genital tuberculosis not only causes tubal obstruction and dysfunction but also impairs implantation due to endometrial involvement and ovulatory failure from ovarian involvement.

The prevalence of infertility is about 10-20% among couples (with somewhat equal prevalence among men and women). There are many factors that can affect female fertility. Some, such as tubal or age factor, are completely known and some are in debate (e.g. endometriosis, cervical or immunologic factors. The prevalence of FGTB increases in countries with a high burden of high Pulmonary Tuberculosis (PTB). Five to 13% of all PTB patients develop GTB. In addition to the subtle presentation of the disease, the low sensitivity and specificity of routine diagnostic methods and the paucity of the organism in clinical samples are the main factors for the lower detection of genital TB (GTB). Most cases of GTB are secondary to gastrointestinal TB spreading to the fallopian tubes causing TB salpingitis. Further spread of the organism involves the uterine endometrium (50%), ovaries (10–30%), cervix (3%), and vagina and vulva (< 1%).[3-6]

The most frequent symptom of FGTB is infertility, as a result of irreversible damage to the fallopian tube. TB salpingitis and endometritis are responsible for 5 to 20% of all causes of infertility, and up to 39–41%in women with tubal factor

infertility. Peritubal adhesions and pelvic masses were detected in most patients with GTB. Women with GTB have a low fertility rate varying from 16 to 38.2%. Although most cases of GTB are asymptomatic, chronic pelvic inflammatory disease, menstrual irregularities, low grade fever, loss of weight and appetite, and tuboovarian masses are manifestations of GTB. Depending upon the damage to the uterine cavity and the endometrium, uterine tuberculosis can be described as mild, moderate, or severe.[7-10] Hence we have taken up this study to evaluate the prevalence of endometrial tuberculosis in infertility subjects.

Aim and Objectives

Aim

To study the prevalence of endometrial tuberculosis among the infertility subjects undergoing endometrial biopsy

Objectives

- To calculate the prevalence of endometrial tuberculosis.
- To compare CBNAAT and the histology of genital tissue in suspected cases of endometrial tuberculosis.

Materials and Methods

Study area

The study will be conducted in the Department of Obstetrics and Gynaecology at Prasad Institute of Medical Sciences in collaboration with Dept. of Respiratory Medicine.

Study Design

This was the cross-sectional study conducted in conducted in the Department of Obstetrics and Gynecology at Prasad Institute of Medical Sciences in collaboration with Dept. of Respiratory Medicine

Study population

We included a total of 150 cases aged between 24-40 years visiting OPD of OBG with complaints as per the inclusion criteria.

Inclusion Criteria

- A woman presenting with infertility (defined as the inability to conceive despite regular unprotected intercourse for 1 year).
- A woman with provisional diagnosis of Pelvic inflammatory disease (triad of Pelvic pain, cervical motion and adnexal tenderness and presence of fever (>38° c) with or without other features like Pelvic organ tenderness, white discharge, and/ or mucopurulent endocervicitis).

Exclusion criteria

- Women not willing to participate in the study.
- Women with already diagnosed gynaecological problems or chronic discharge due to Fibroid, PCOS, CIN, Dysplasia.
- Infertility due to male infertility factor

Study Period

The study was conducted from Sept 2020 to August 2021.

Sample Size

Sample size will be calculated using the formula
$n = Z^2_{1-\alpha}P(1-P)/d^2$
Where n = Required sample size
P = Prevalence of the cause
d = Precision

Data collection

Demographic data regarding age, Socioeconomic status based on the Modified Kuppuswamy scale, menstrual pattern, type of infertility, past-history of TB in any part of the body or history of TB contact (living in the same household or in frequent contact with a sputum smear positive TB patient in last 2 years). Body Mass Index/ BMI was calculated. In PID patients, common causes of PID other than M. Tuberculosis- Chlamydia, N. Gonorrhea was ruled out by Nucleic acid amplification test. Mantoux test using PPD 23 (5 TU), Erythrocyte sedimentation rate (ESR), Histopathology (HPE) examination of endometrial aspirate(EA)/ endometrial tissue (ET) and CBNAAT of EA/ ET/ pouch of douglas fluid was performed in all the subjects. According to clinical situation, cases were subjected to one or more of the following examination with aseptic precaution-Endometrial biopsy (EB), Hysterosalpingography (HSG), Hysteroscopy and laparoscopy. CBNAAT Samples of EB collected in normal saline containing falcon tubes (container) and EAs & fluid from the POD transported in sterile Falcon tubes. Patient with clinical features of genital TB, supported with TB suggestive test like mantoux/ ESR / Hysterosalpingography/ laparoscopy/ hysteroscopy were diagnosed as high suspicious genital TB (GTB+) and remaining were diagnosed as Low suspicious GTB (GTB-) cases. Sputum for AFB examination and Chest X- ray was done in all GTB+ cases to rule out pulmonary Koch.

Statistical Analysis

Statistical analysis of the data will be performed using the statistical package for social sciences for window SPSS Inc. Microsoft word and Excel have been used to generate graphs and tables. Sensitivity and specificity was calculated.

Results

We included a total 150 subjects suspected of Genital Tuberculosis in the age group of 21-40 years, out of which 78 women were suffering from infertility and 72 women had PID.

Table 1
Shows Distribution of subjects according to demographic profile

Demographic Characteristics	Number of patients	Percentage
Age group (in years)		
21-25	46	30.66
26-30	39	26
31-35	35	23.3
36-40	30	20
Parity		
Nullipara	78	52
Primipara	40	26.6
Multipara	32	21.33
History of TB		
Past history	7	4.66
Family history	9	6
No history	134	89.33

Table 2
Shows Distribution of subjects according to presenting symptoms

Presenting symptoms	Number of patients	Percentage
Amenorrhea	6	4
Menorrhagia	34	26.6
Oligomenorrhea	32	21.33
Primary infertility	44	29.33
Secondary infertility	34	22.66

Table 3
Shows Distribution of subjects according to results of investigation

Investigations		Number of patients	Percentage
Chest radiograph PA view	Normal	150	100%
Ultrasonography	Normal	28	18.66%
	Tubo-ovarian mass	132	88%
CBNAAT for TB	Positive	36	24%
	Negative	124	82.66%
Culture for AFB	Positive	23	15.33%
	Negative	127	84.66%

Table 4
Shows histopathology findings of the endometrium among infertility subjects

Histopathology findings of the endometrium	Number of patients	Percentage
Endometrial hyperplasia	2	2.56%
Nonspecific endometritis	8	10.25%
Proliferative epithelium	26	33.33%
Secretary epithelium	28	35.89%
Tubercular endometritis	14	17.9%

All the subjects with positive culture for AFB and CBAAT were referred to Dept. of Respiratory medicine and were subjected to treatment regimen that involves the WHO recommended treatment scheme (PZA= 1500 mg/day + INH (300 mg/day) + Rifampicin (450 mg/day) + Ethambutol (800 mg/day) for 4 months and Rifampicin + INH = 450:300 for 5 months respectively. Post treatment all the subjects were referred for IVF treatment to Dept. of OBG.

Discussion

In our study, we included a total of 150 subjects in the age group of 21-40 years as per the inclusion and exclusion criteria after taking voluntary consent from the subjects for their participation in the study, the mean age was found to be 29.4 years. Out of the 150 subjects participated in the study, 78 were suffering from infertility and 72 had PID (pelvic inflammatory disease). Out of 150, 46, 39, 35 and 30 subjects were in the age group of 21-25, 25-30, 31-35 and 36-40 respectively. 78 were nulliapara, 40 were primi and 32 were multi para. 7 women had history of tuberculosis in the past, 9 had family history of TB and 134 had no history of TB. 6 women had amenorrhea, 34 had menorrhagia, 32 had oligomenorrhea, 44 had primary infertility and 34 had secondary infertility.

We performed various investigations which include CXR, USG, CBNAAT and CS for AFB, we found that all the subjects had normal CXR, 132 had tubo-ovarian mass on USG, 36 had CBNAAT positive and culture for AFB was positive in 23 subjects. We further evaluated endometrial involvement in 78 infertility subjects we found that tubercular endometritis was found in 14 subjects accounting for 17.9% prevalence, 2 women had endometrial hyperplasia, 8 had nonspecific endometritis, 26 had proliferative epithelium, and 28 had secretary epithelium. India is a highly prevalent zone for TB; therefore, it is highly suspected when considering the diagnosis. To date, none of the available tests can detect all cases of genital TB. The CBNAAT/Xpert MTB/RIF assay can be used for the early detection of FGTB and provides the added advantage of early results, minimal technical expertise, and the detection of drug-resistant TB. This is because it has a higher detection rate as compared to conventional methods. Moreover, larger multicenter studies are required to suggest the most appropriate and cost-effective test for the diagnosis of genital TB.[11-16]

Clinically the diagnosis of female genital tuberculosis is challenging as it does not have any specific symptoms. Elaborate examination and diagnostic methods like ultrasound, chest x-rays, histopathological examination, culture, Ziehl-Neelson

(ZN) stain and PCR analysis should be carried out for accurate diagnosis. Recently, PCR has emerged as a rapid, sensitive and specific molecular method to diagnose female genital TB with a turnaround time of 1-2 days. The fallopian tubes are affected in 94% of women with genital TB. There is almost always bilateral involvement. Salpingitis results from haematogeneous infection. Spread from TB salpingitis can cause peritonitis, endometriosis, or rarely, cervicitis and vaginitis.

Conclusion

In our study, we fund the prevalence of 17.9% endometrial tuberculosis in subjects suffering from infertility, and CBNAAT was superior to histopathology in the detection of GTB and had strong correlation with Culture for AFB.

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