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A STUDY ON ROLE OF CARTRIDGE BASED NUCLEIC ACID AMPLIFICATION TEST (CBNAAT) AND HISTOPATHOLOGY IN DIAGNOSIS OF GENITAL TUBERCULOSIS AMONG PATIENTS OF INFERTILITY.

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ABSTRACT

BACKGROUND: the diagnosis of genital tuberculosis if difficult as majority of the patients are asymptomatic and routine investigations have little value. The cartridge based nucleic amplification (CBNAAT)/Xpert RIF test is quick and may diagnose FGTB from any tissue type.

OBJECTIVE: To study the role of Cartridge based nucleic acid amplification test (CBNAAT) and Endometrial Histopathology in diagnosis of genital tuberculosis among patients of infertility.

MATERIAL AND METHODS: The study was a hospital based prospective study, from December 2019- June 2021. 100 patients of infertility were enrolled for our study. All cases were enrolled for Laparoscopy and hysteroscopy for workup of infertility and Mantoux, Histopathology, CBNAAT was performed in all 100 cases and results were compared.

RESULT: Primary infertility was the most common complaint and oligomenorrhoea was the most common menstrual irregularity (23%) Mantoux test was positive in 77% cases and 42% cases of infertility were diagnosed of genital TB on the basis of findings of laparoscopy and Hysteroscopy. In our study, endometrial histopathology was positive in only 5 cases (12.8%) with finding suggestive of TB. CBNAAT could detect tubercular bacilli only in 21.4% TB cases and all were rifampicin sensitive.

CONCLUSION: the role of CBNAAT in the diagnosis of female genital TB is limited but can diagnose more cases as compared to histopathology. PPV of CBNAAT for diagnosis of GTB is almost 100%.

KEYWORDS : Cartridge based nucleic acid amplification test, Female genital tuberculosis, Infertility, menstrual irregularity, Laparoscopy, Hysteroscopy

INTRODUCTION

Female genital tuberculosis is an insidious disease, and is the leading cause of infertility[1]. incidence of FGTB in Infertility varies from 3%-16% in India[2]. As per the WHO Global TB report 2019, the estimated incidence of tuberculosis (TB) in India is approximately 27% of the world's TB cases[3]. Female genital TB is paucibacillary disease and is mostly secondary infection acquired by hematogenous spread from an extra-genital source such as pulmonary or abdominal tuberculosis[4]. The Fallopian tube More along with the endometrium are the prime areas of involvement in genital tuberculosis. These patients may present with infertility or some may have menstrual disturbances, pelvic pain or discharge per vaginum[5]. Given the high prevalence of diseases in patients with infertility and menstrual disorders, a high degree of clinical suspicion for FGTB should be considered. Therefore, detailed history, systemic examination, and series of investigations are needed[4]. Histopathology of genital/ endometrial tissue may detect tuberculosis (TB) by granulomatous lesions; however, it is not diagnostic because granulomas may also be found in other infectious diseases[6]. CBNAAT is fully automated and based on polymerase chain reaction (PCR) that detects deoxyribonucleic acid (DNA) directly from the clinical specimens and also detects rifampicin resistance. Though in 2012, W.H.O. has recommended the CBNAAT for routine use under programmatic conditions but its role in the diagnosis of extrapulmonary TB seems to have limited role[8]. Therefore, the present study was conducted to establish a correlation between the histopathology of endometrial tissue with CBNAAT.

MATERIAL AND METHODS

The study was conducted in the department of obstetrics and gynaecology, Muzaffarnagar Medical College and Hospital, Muzaffarnagar, Uttar Pradesh, in collaboration with the department of pathology and microbiology from February 2020 to June 2022, after obtaining ethical clearance. After a detailed history, thorough clinical examination, and investigations, such as complete blood count, chest radiography, human immunodeficiency virus (HIV) I and II, Mantoux test. Detailed Contact history was taken. Patients of infertility with suspicion of tuberculosis were randomly selected and after obtaining informed consent, Diagnostic Laparoscopy and Hysteroscopy was performed.

female genital tuberculosis has been described as a disease of young women, with 80-90% patients diagnosed between 20-40 years therefore Married women of reproductive age group with primary/secondary infertility willing for infertility workup and Menstrual irregularities- oligomenorrhoea, hypomenorrhea, amenorrhoea, menorrhagia, dysmenorrhoea were included after ruling out of other causes by routine investigations, USG and various serum hormonal assays such as S.TSH/ Prolactin/ FSH/ LH/ DHEA, Normal semen analysis of husband.

All Patients undergoing Laparoscopy and Hysteroscopy were evaluated and Endometrial sampling was done by Dilation and curettage. HPE and CBNAAT was send in all cases as a routine investigation. Specimens was collected in the in premenstrual phase. Tissue collected was divided into two containers: one for histopathological analysis in a 10% formalin vial and one for CBNAAT in sterile containers with normal saline.

Findings of Laparoscopy such as Tubal beading, Perihepatic adhesions, Tubercles, Delayed spill, Fimbrial block, Hydrosalpinx, Bowel and omental adhesions, Frozen pelvis and Hysteroscopy- Fibrosed ostia, Intrauterine adhesions, Small uterine cavity, Cervical stenosis, Poor endometrium, Distorted Ostia, Tubercles was noted.

Positivity of anyone of the following is considered gold standard for the diagnosis of female genital tuberculosis Data was entered in MS EXCEL spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0.

RESULT:

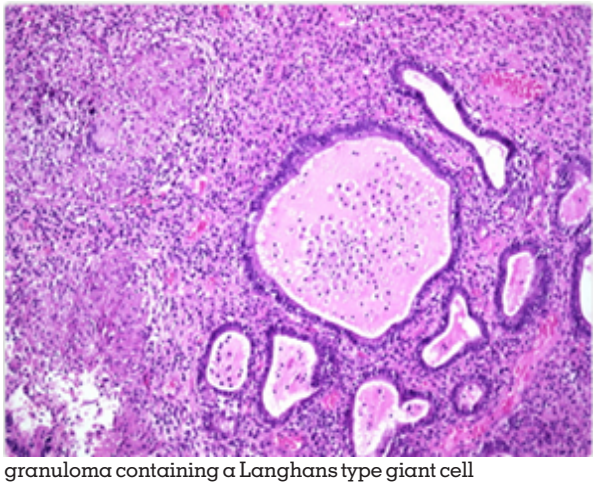
The present study included female patients presenting with Infertility, with majority belonging to 26-30 years age group (40.0%) with the mean age of 30.81 ± 4.12 years. Their infertility period ranged from 1.5-17 years, with the mean duration 5.21 ± 3.13 years. 54% of patients presented with primary infertility while 46% with secondary infertility. Majority of the

patients were asymptomatic and the clinical complaint reported were Infrequent menses (20.0%), Dysmenorrhoea (19.0%), Chronic pelvic pain (16.0%), Decreased flow during menses (7.0%), Abnormal discharge per vaginum (6.0%), Amenorrhoea (5.0%). The commonest menstrual abnormality reported was Oligomenorrhoea among 23.0%, Hypomenorrhea among 8.0%, Menorrhagia among 6.0%, and Secondary amenorrhoea among 3.0%.

Table 1: Distribution of patients diagnosed of genital tuberculosis based on various methods.

Method	Positive	Percentage
Mantoux test	19	45.2%
Hysteroscopy	31	73.8%
Laparoscopy	41	97.6%
Histopathology	8	19.04%
CBNAAT	9	21.4%

A positive Mantoux test was reported in 30 cases. 42 patients were diagnosed of genital tuberculosis on laparoscopy and hysteroscopy. 19 cases of Mantoux test positive were confirmed of genital tuberculosis by laparoscopy and hysteroscopy. CBNAAT could confirm 9 cases of genital tuberculosis and Endometrial Biopsy (EB) could confirm diagnosis of genital TB in 5 cases Histopathology showed granuloma in 3 cases and tubercular endometritis in 2 cases. All cases confirmed on CBNAAT were rifampicin sensitive.



granuloma containing a Langhans type giant cell

Table 2: Correlation of CBNAAT, clinical complaints and histopathology findings

Investigation	Positive	Percentage
CBNAAT	3	60%
Menstrual complaints	4	80%

Primary infertility with genital tuberculosis was diagnosed in 23% patients and secondary infertility with genital tuberculosis in 19% cases. All the cases that showed evidence of genital tuberculosis were started on ATT under RNTCP using DOTS Strategy.

CONCLUSION

High significant association was found between the histopathology of endometrial tissue and their CBNAAT ($p<0.001$). Clinical diagnosis is still the most important way of diagnosing FGTB. The CBNAAT/Xpert MTB/RIF assay can be used for the early detection and the detection of drug-resistant TB.

DISCUSSION

FGTB remains a cause of concern in developing countries such as India, owing to its potential to cause infertility. Early diagnosis remains a challenge because of the absence of symptoms, whereas some patients seek treatment at a stage when the infection has caused irreparable damage to the fallopian tubes and endometrium[9].

In current study, majority women belonging to 26-30 years age group followed by 31-35 years, > 35 years and 20-25 years with those of other similar studies.[10,11] The mean duration of infertility was 5.21 ± 3.13 years.

In this study of 100 infertile women who underwent endometrial biopsy procedures as part of their diagnostic evaluation for infertility, only 5 cases (5%) were confirmed to have FGTB. Of these three cases had CB-NAAT positive. 6 cases were CBNAAT positive and histopathology did not show signs of tuberculosis. Most previous studies detected TB on endometrial slides, but only a few have diagnosed FGTB on CBNAAT/Xpert. Thangappah found that 6.9% of the endometrial samples were positive.[15] Goel et.al. found that 2.6% of patients had histopathological slides of the endometrium suggestive of TB.[16] Farhan et al. reported an improvement in the detection rate of TB using the CBNAAT/Xpert method and found 8.05% positive cases.[4] Sensitivity of CBNAAT was 21.4% and positive predictive value was 100%. In studies of Keshari V et al [13] Sensitivity of CBNAAT for FGTB was 25%. PPV was 100% and NPV was 74.4%. Jai Bhagwan Sharma et al stating that CBNAAT has 35% sensitivity and 100% specificity in the detection of FGTB.

Therefore, CBNAAT if also included in investigational workup for Female Genital TB adds additional value but surely cannot replace any of the other gold standard investigations in surgically obtained samples neither is fully dependable.

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