



COMPARISON OF ENDOSCOPY FINDINGS WITH HISTOPATHOLOGY EXAMINATION AND TUBERCULOSIS POLYMERASE CHAIN REACTION IN THE DIAGNOSIS OF FEMALE GENITAL TUBERCULOSIS IN INFERTILE WOMEN

Obstetrics & Gynaecology

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ABSTRACT

Background: Female genital tuberculosis is an important cause of infertility. Diagnosis of GTB is challenging as sensitivity of most of the tests is low and cases of early disease can be missed. **Methods:** This was a cross sectional, prospective, observational study on 100 infertile women. All patients underwent history taking, clinical examination followed by hysteroscopy with endometrial sampling for TB-PCR, HPR, AFB culture. Laparoscopy findings were divided into definite and probable findings. **Results:** The mean age was 31 years with primary infertility found in 58% and secondary infertility in 42% cases. Positive AFB culture (endometrium) was seen in 6%, HPR with epitheloid granuloma in 9%, TB-PCR (endometrial/peritoneal sample) in 32% cases. Definite findings of FGTV on laparoscopy was seen in 47% and probable findings seen in 53% cases. **Conclusion:** Since GTB is paucibacillary, diagnosis may be missed by traditional diagnostic modalities, therefore, laparoscopy should be done where clinical suspicion is high.

KEYWORDS

Laparoscopy, paucibacillary, diagnosis, composite reference standard

INTRODUCTION

Female genital tuberculosis is a type of extra pulmonary tuberculosis (EPTB) which causes infertility by affecting the fallopian tubes and endometrium.

Most common spread is through haematogenous or lymphatic route and less commonly by contiguous spread from abdominal organs or lymph nodes.⁽¹⁾

It may be asymptomatic or present with abnormal uterine bleeding, pelvic pain or mass.⁽²⁾

The prevalence of FGTV is around 5-30% cases of infertility.

Traditionally, diagnosis of FGTV is done by detection of mycobacterium tuberculi on microscopic examination of AFB smear or BACTEC culture or mycobacteria growth indicator culture or presence of epitheloid granuloma on endometrial or peritoneal biopsy.⁽³⁾

Polymerase chain reaction (PCR) is a sensitive test but has high false positive rates, hence is not recommended as a basis to initiate treatment. Gene Xpert has low sensitivity to detect FGTV.⁽⁴⁾

Laparoscopy can detect most cases of FGTV by direct visualization of the abdomen and pelvis which are otherwise missed by traditional tests.⁽⁵⁾

AIMS And OBJECTIVES

This study is aimed to compare laparoscopic findings with HPR and TB-PCR to diagnose FGTV and to start ATT, even if the confirmatory tests are negative.

MATERIALS And METHODS

This study was carried out at the department of Reproductive Medicine and Surgery, Mahatma Gandhi Medical College and hospital, Jaipur, after seeking approval from the Institute Ethical Committee.

Study Design: This was a cross sectional, prospective, observational study on 100 infertile women, for two years, from August 2021-August 2023.

Informed written consent was taken prior to the procedure. Complete medical/ obstetric / family history of TB was taken. General physical examination and gynaecological examination were performed.

Women were subjected to video hysteroscopy (VHL) according to inclusion criteria. The laparoscopy findings were categorised into definite and probable findings and were compared with HPE (endometrium, tissue) and PCR.

Laparoscopic criteria of GTB was taken as evidence to start ATT even in the absence of microbiological and histopathological evidence.

DEFINITE FINDINGS⁽⁶⁾

- Presence of tubercles on the uterus, adnexa, peritoneum, intestine, mesentery, omentum and other abdominal organs
- Beaded tubes
- Caseous nodules

PROBABLE FINDINGS⁽³⁾

- Adhesions (Perihepatic / pelvic / abdominal)
- Tubal block
- Hydrosalpinx/ pyosalpinx
- Tubo-ovarian masses
- Thickened, rigid appearance of tubes
- Shaggy white areas
- Straw coloured fluid in the Pouch of Douglas (POD)
- Frozen pelvis

Inclusion Criteria

- Women of reproductive age >21 years to ≤40 years
- Unexplained infertility
- H/o Ectopic pregnancies in past
- Imaging suggestive of GTB (TVS, HSG findings suspicious of GTB)
- Symptoms suspicious of TB like prolonged fever, anorexia, weight loss, h/o exposure
- Dysmenorrhea, Abnormal uterine bleeding (hypomenorrhoea, oligomenorrhoea),

Exclusion Criteria

- Women >40 years of age
- Acute PID
- Women who have completed ATT within a year
- H/O dense adhesions, frozen pelvis in previous laparoscopy
- Women not giving consent for the study

Follow up

Monthly for first two months with CBC and LFT and at 5th month.

Primary outcome in respect to clinical pregnancy rate (CPR) for natural spontaneous conception or ART was noted. ART was done after minimum of three months of ATT. Secondary outcome in term of improvement in menstrual symptoms was noted.

Statistical Analysis:

Descriptive statistics (mean, standard deviation and range) were carried out for normally distributed data. The Statistical software namely SAS9.2, SPSS15.0, Stata10.1, MedCalc9.0.1, were used for the analysis of the data.

RESULTS

A total of 460 patients were screened over a period of two years and 100 cases were suspected to have FGTB. Out of these 100 women in whom laparoscopy was done, findings were seen in 72 cases, making the prevalence of FGTB in infertility to be 15.6%.

Table 1: Age Distribution (n=100)

Age in years	Number of patients (%)
21-25	23
26-30	32
31-35	28
36-40	17

The mean age observed was 30.23 ± 2.36 years.

Table 2: Nature Of Infertility (n=100)

Nature of infertility	Number of patients (%)
Primary	58
Secondary	42

In our study 58% patients had primary infertility while 42% had secondary infertility.

Table 3: Clinical Features Of Suspected FGTB Patients (n=100)

Clinical features	PERCENTAGE (%)
A) GENERAL SYMPTOMS	
1) No symptom	16
2) Anorexia	4
3) Weight loss	3
B) MENSTRUAL SYMPTOMS	
1) Normal menstrual cycle	32
2) Hypomenorrhoea	45
3) Oligomenorrhoea	22
4) Secondary amenorrhoea	2
C) Chronic pelvic pain	14
D) SIGNS	
1) Normal appearing cervix	73
2) Erosion	10
3) Vaginal discharge	17
E) TVS with Colour Doppler	
1) Internal os calcification	66
2) Subendometrial calcification	12
3) Thin endometrium	56
4) Reduced vascularity	36
5) TO masses/ cogwheel appearance	7

Most common menstrual complaint was hypomenorrhoea (45%), On per speculum examination, 73% of the patients had normal looking cervix.

On detailed TVS with colour by an experienced reproductive medicine and surgery specialist, internal os calcifications were seen in 66% cases, followed by thin endometrium, reduced vascularity in 56% and 36% cases respectively.

Table 5:- Laparoscopy Findings (n=100)

DEFINITE FINDINGS	PERCENTAGE (%)
Beaded tubes	
Bilateral	42
Unilateral	26
Tubercles	
Uterus	16
Fallopian tubes	40
Ovaries	3
POD	32
Pelvic peritoneum	21
Abdominal peritoneum	4

Caseous nodules	
Pelvis	8
Upper abdomen	3
PROBABLE FINDINGS	
Hydrosalpinx/ pyosalpinx	
Bilateral	12
Unilateral	8
Tubal block	
Bilateral	52
unilateral	28
Adhesions	
Pelvic	49
Peri hepatic	52
Abdomen	29
Tubo- ovarian masses	
Bilateral	11
Unilateral	4
Thickened rigid tubes	8
Shaggy white areas	
Uterus	11
Fallopian tubes	8
POD	6
Upper abdomen	2
Straw coloured fluid in POD	12
Frozen pelvis	2

In our study, 72% cases had either one or more definitive or probable findings of GTB on laparoscopy.

Bilateral and unilateral beaded tubes were seen in 42% and 26% cases respectively.

Fallopian tubes had maximum percentage of tubercles (40%) followed by in POD (32%)

Bilateral tubal block was seen in 52%, bilateral hydrosalpinx/ pyosalpinx in 12% and bilateral tubo-ovarian masses in 11% patients.

Peri hepatic adhesions were seen in 52% and pelvic adhesions in 49% cases.

Table 6: Hysteroscopy Findings (n=100)

HYSTEROSCOPY FINDINGS	PERCENTAGE (%)
Peri-ostial fibrosis	52
Peri-ostial tubercles	14
Cervical stenosis	10
Thin endometrium	28
Synechiae	3
Calcification	3

One or more positive hysteroscopy findings were seen in 63 % patients.

Table 7: Methods Of Diagnosis Of Female Genital Tuberculosis (n=100)

DIAGNOSTIC MODALITY	PERCENTAGE (%)
Positive AFB culture (endometrium)	6
HPR- epitheloid granuloma	9
Positive TB- PCR (endometrium, peritoneal sample)	32
Definite findings of FGTB on laparoscopy	47
Probable findings of FGTB on laparoscopy	53

Postive AFB culture (endometrium) was seen in 6% of cases.

On HPR, epitheloid granuloma was seen in 9% of cases.

Postive TB- PCR was seen in 32% of cases.

Diagnosis of FGTB, on definite findings of laparoscopy was 47% and on probable findings was 53%. Those patients who had positive AFB culture, HPR or TB-PCR also had positive visual findings.

There were 9 patients in whom TB-PCR was positive but other tests were negative.

Table 8:- Comparison Of All Tests With Laparoscopy

TEST	SENSITIVITY(%)	SPECIFICITY(%)
AFB culture	8.1	100

HPR	11.7	100
TB-PCR	53.1	90
LAPAROSCOPY	90	96

ATT was started on positive AFB culture or HPR or definite laparoscopy findings of GTB.

ATT was also started on probable laparoscopy findings along with other clinical features suspicious of GTB after consultation with the Chest and TB department.

ATT was not started solely on the basis of positive TB-PCR (9 patients), if other diagnostic modalities were negative, i.e., AFB culture, HPR, definite laparoscopy findings.

72% of the patients received ATT based on one or more diagnostic criteria according to composite reference standard.

Table 9: Outcomes (n=72)

OUTCOME	PERCENTAGE (%)
1) Improvement in menstrual symptom	69
2) Increase in endometrial thickness	40
3) Increase in subendometrial vascularity	54
4) Clinical pregnancy rate	24

Primary outcome in terms of clinical pregnancy rate was seen in 24% patients, which were followed up for 6 weeks post conception. Out of these patients, 35 % had spontaneous conception while 65% had ART.

Secondary outcome in terms of improvement in menstrual symptoms was seen in 69% cases.

DISCUSSION :

FGTB has been described as a disease of young women, with 80-90% of patients diagnosed between 20-40 years of age. ⁽¹⁾ In our study the mean age of women with genital tuberculosis was 31 years.

The menstrual cycle may be normal in majority of the cases. Abnormal uterine bleeding in GTB has been reported in 10%-40% of patients. ⁽⁷⁾ In our study hypomenorrhoea (45%) was the most common menstrual abnormality while 32% had normal menstrual pattern. Similar pattern has been seen in one study was where the most common menstrual abnormality was hypomenorrhoea (30.1%) followed by oligomenorrhoea (3.5%). ⁽⁸⁾

In studies performing mycobacterial cultures, positivity rates of 10% to 15% were seen in GTB patients diagnosed on clinical and morphological criteria and a positive TB-PCR. ⁽⁹⁾

In our study, 6% cases had positive AFB culture (endometrium), HPR in 9% with epithelioid granuloma and PCR was seen in 32% cases.

In our study, laparoscopy demonstrated bilateral beaded tubes in 42% cases, tubercles on fallopian tubes and in POD in 40% and 32% respectively. Bilateral tubal block was seen in 52% cases with peri hepatic and pelvic adhesions in 52% and 49% respectively. Similar findings were seen in one study by Dr.J.B. Sharma. ⁽³⁾

In our study, one or more positive hysteroscopy findings were seen in 63% of cases with peri-ostial fibrosis seen in 52% cases, thin endometrium in 28% cases and synechiae in 3% cases.

TB is a well known cause of intrauterine synechiae.

In another study, abnormal hysteroscopy findings were seen in 20.3% cases, thin endometrium in 11.6% cases, synechiae in 1.4% cases. ⁽¹¹⁾

An Indian study has reported cervical involvement in around 5-10% of the cases. ⁽¹⁰⁾ Our study reported cervical stenosis in 10% cases.

Being paucibacillary in nature, its diagnosis remains a dilemma and can be missed even on AFB microscopy/ culture or Gene Xpert or epithelioid granuloma on endometrial / peritoneal biopsy. ⁽¹¹⁾

A high index of suspicion is required as HPR, AFB culture have very low sensitivity. PCR has a high false positive rate. Typical endometrial caseation is rare due to it's cyclical shedding. ⁽¹²⁾

All patients are treated with six months of ATT as recommended by the

WHO. ⁽¹³⁾ National TB Elimination Program of India states that six-months therapy is equally effective to nine month therapy. ⁽⁶⁾



Fig 1:- Composite Reference Standard (CRS) employed to diagnose FGTB ⁽⁶⁾

CONCLUSION

Laparoscopy appears to be a useful diagnostic modality in the diagnosis of FGTB along with the screening tests and clinical history and should be considered where clinical suspicion is high.

Weakness Of The Study-

Limited sample size. Chlamydial infection was not ruled out. For diagnosis of FGTB, the specimen was not sent for CBNAAT.

REFERENCES

- Arpitha, V. J., Savitha, C., & Nagarathnamma, R. (2016). Diagnosis of genital tuberculosis: correlation between polymerase chain reaction positivity and laparoscopic findings. *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*, 5(10), 3425-3433.
- Sharma, J. B., Khurana, A., Hari, S., Singh, U., & Dharmendra, S. (2021). Evaluation of role of transabdominal and transvaginal ultrasound in diagnosis of female genital tuberculosis. *Journal of Human Reproductive Sciences*, 14(3), 250-259.
- Sharma, J. B., Sharma, S. K., Dharmendra, S., Singh, U. B., Kumar, S., & Roy, K. K. (2023). Laparoscopic evaluation of female genital tuberculosis in infertility: An observational study. *Indian Journal of Medical Research*, 157(2&3), 183-191.
- Kohli, M., Schiller, I., Dendukuri, N., Dheda, K., Denkiner, C. M., Schumacher, S. G., & Steingart, K. R. (2018). Xpert® MTB/RIF assay for extrapulmonary tuberculosis and rifampicin resistance. *Cochrane Database of Systematic Reviews*, (8).
- Malhotra, N., Singh, U. B., Iyer, V., Gupta, P., & Chandhiok, N. (2020). Role of laparoscopy in the diagnosis of genital TB in infertile females in the era of molecular tests. *Journal of Minimally Invasive Gynecology*, 27(7), 1538-1544.
- India, T. B. C. (2014). Directorate General of Health Services. *Ministry of Health and Family* [3].
- Simon, H. B., Weinstein, A. J., Pasternak, M. S., Swartz, M. N., & Kunz, L. J. (1977). Genitourinary tuberculosis: clinical features in a general hospital population. *The American journal of medicine*, 63(3), 410-420.
- Sharma, J. B., Roy, K. K., Pushparaj, M., Kumar, S., Malhotra, N., & Mittal, S. (2008). Laparoscopic findings in female genital tuberculosis. *Archives of gynecology and obstetrics*, 278, 359-364.
- Abebe, M., Lakew, M., Kidane, D., Lakew, Z., Kiros, K., & Harboe, M. (2004). Female genital tuberculosis in Ethiopia. *International Journal of Gynecology & Obstetrics*, 84(3), 241-246.
- Bhanu, N. V., Singh, U. B., Chakraborty, M., Suresh, N., Arora, J., Rana, T., ... & Seth, P. (2005). Improved diagnostic value of PCR in the diagnosis of female genital tuberculosis leading to infertility. *Journal of medical microbiology*, 54(10), 927-931.
- Sharma, J. B., Sharma, E., Sharma, S., & Dharmendra, S. (2018). Female genital tuberculosis: Revisited. *Indian Journal of Medical Research*, 148(Suppl 1), S71-S83.
- Sharma, J. B., Sharma, E., Sharma, S., & Dharmendra, S. (2021). Recent advances in diagnosis and management of female genital tuberculosis. *The Journal of Obstetrics and Gynecology of India*, 71(5), 476-487.
- World Health Organization. (2021). Global tuberculosis report 2020. Geneva: WHO; 2020.