International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Eeram et al. Int J Reprod Contracept Obstet Gynecol. 2024 Nov;13(11):3089-3093
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20243156

Original Research Article

A comparative study of various diagnostic modalities for female genital tuberculosis in infertility in a tertiary hospital

Eeram*, Yati Tiwary, Tripti Gupta

Department of Obstetrics and Gynaecology, Rohilkhand Medical College and Hospital, Bareilly, Uttar Pradesh, India

Received: 25 September 2024
Revised: 16 October 2024
Accepted: 17 October 2024

***Correspondence:**
Dr. Eeram,
E-mail: eeramsiddique@gmail.com

ABSTRACT

Background: Infertility is a complex and emotionally challenging issue that affects millions of people worldwide. Infertility has a detrimental effect on women's social standing and psychological health. The aim of this study is to compare the effectiveness of several diagnostic techniques for female genital tuberculosis (TB) in infertility. Objectives to study various diagnostic techniques in patients with infertility attending Obstetrics and Gynaecology outpatient department (OPD) of Rohilkhand Medical College and Hospital (RMCH), Bareilly.
Methods: This was a one-year hospital based cross-sectional comparative study carried out in Department of Obstetrics and Gynaecology, RMCH, Bareilly, from 01 November 2019 to 31 October 2020 in women with age group 18-45 years presented with indications of primary and secondary infertility and the estimated sample size was 50.
Results: Highest percentage of cases (48%) have been reported for 21-30 age group, least below 20 age group (2%). The detection rates for acid-fast bacilli (AFB) smear, Lowenstein-Jensen (L-J) culture, *Mycobacteria* growth indicator tube (MGIT) culture and histopathological examination (HPE), were 4%, 4%, 16% and 12%, respectively. Accuracy of MGIT-960 culture correlating with HPE was found to be 92%. The overall comparative analysis between different methods of diagnosis showed that sensitivity was highest for MGIT-960 (62.5%), however, specificity was found to be 100% for both AFB and LJ culture, while 97.6% for MGIT-960 culture.
Conclusions: Our results indicate that MGIT-960 is an efficacious detection strategy for GTB, in cases of female infertility.

Keywords: Diagnostic modalities, GTB, Infertility

INTRODUCTION

Genital tuberculosis (TB) in female is an extrapulmonary tuberculosis, and accounts for 9% of total cases. It is characterised by wide range of symptoms and a high rate of morbidity.[1] According to World Health Organization (WHO) estimate from 2005, the annual incidence of tuberculosis was 2.2 million, the annual rate death rate was 29 per 100000 people, and the estimated prevalence of tuberculosis was 168 per 1 lakh people annually. Infertility is the most common clinical presentation with a prevalence rate of 43 to 74%, particularly in developing countries.[2] The precise incidence of the condition is still unknown, as majority of the patient go undiagnosed because of their asymptomatic presentation. There is dearth of research on GTB and its connection to infertility, despite the condition being very common in the community.

The inability to conceive after at least one year of unprotected sexual activity is known as infertility. If the couple is older or there is obvious cause, treatment may begin earlier. Sub fertility is largely caused by GTB, especially in the endemic areas like South India. In addition to causing tubal blockage and dysfunction, genital TB also effects implantation because it affects the endometrium and can lead to ovarian involvement and ovulatory failure.[3] About 10-20% of couples have infertility, the rate is roughly equal for men and women.

Nevertheless, due to lack of extremely sensitive and precise diagnostic means, the exact epidemiology of the disease is still unknown.

The diverse clinical presentations of GTB in females continue to pose a diagnostic conundrum, even with the availability of many methods. Therefore, in order to make a diagnosis, a thorough clinical examination and a detailed history are necessary. Routine laboratory results are of little value. Investigations may be necessary if there is a positive tuberculin test, increased erythrocyte sedimentation rate (ESR), contact history, or positive chest X-ray showing healed or active pulmonary tuberculosis. Although laparoscopic findings are not always absolutely diagnostic in the early stages, they are a useful method for acquiring tissue specimens for further tests and culture. The evidence from imaging investigations, laparoscopic and hysteroscopic findings, histology of genital tract material, culture, and serology is therefore combined to determine the diagnosis of female GTB. Gold standard for diagnosis of GTB is culture of clinical specimen.[4]

Conventional method of microscopic examination with Ziehl-Neelsen (ZN) staining and/or culture of sample Lowenstein-Jensen (LJ) culture medium, were time consuming and often yield false negative results which is now replaced by automated liquid culture, *Mycobacteria* growth indicator tube 960 (MGIT) which produce result within 2 weeks, however there is no data to support its diagnostic value in evaluating GTB in clinical practice.

The detection rate of female GTB using diagnostic methods such as AFB staining, LJ culture media, histopathology, and MGIT 960 varies widely. The current study was conducted with the intention of evaluating the effectiveness of various diagnostic modalities in females presenting with infertility owing to GTB, taking into consideration the paucity of information regarding routine diagnostic procedures. Furthermore, the efficacy of MGIT 960 in the diagnosis of genital tuberculosis was evaluated in order to effectively adopt it into routine clinical practice.

METHODS

This was a one-year hospital based cross-sectional comparative study carried out in Department of Obstetrics and Gynaecology, Rohilkhand Medical College and Hospital (RMCH), Bareilly, a tertiary care and teaching hospital in Western Uttar Pradesh after getting approval by Institutional Ethical Committee, from 01 November 2019 to 31 October 2020 in women with age group 18-45 years presented with indications of primary and secondary infertility and the estimated sample size was 50.

Inclusion criteria

The study included females in the age group of 18-45 years, presented with complaints of primary infertility, secondary infertility.

Exclusion criteria

Women who have taken or on the regimen of anti-TB drug were excluded from the study. Also, HIV positive women were non-included in the study.

After obtaining initial demographic details, medical history and clinical examination, as per the inclusion and exclusion criteria, the patients suggestive of genital tuberculosis were enrolled in the study at the OPD.

The patients were then subjected to basic laboratory investigations and routine blood examinations such as haemoglobin estimation, total leucocyte count, differential count, Mantoux test, chest X-ray, sputum AFB (in patients with cough with expectoration), ultrasound abdomen and pelvis, urine routine, HIV screening (after obtaining informed consent from both the patient and her spouse-according to standard guidelines), PAP smear, followed by an endometrial curettage. Endometrial tissue was taken in pre-menstrual phase using pipelle endometrial curette under aseptic condition. To confirm that every participant had endometrial thickness of at least 10 mm, it was cross-checked using an ultrasonogram. The material was divided into two parts, with one sent for histopathological investigation in 10% formalin solution and the other in normal saline to the Microbiology Department.

The endometrial tissue sample was crushed using a tissue homogenizer, and then modified Petroff's procedure (with 4% NaOH-NALC modification) was used for digestion and decontamination. The processed sample was divided into 3 parts for staining acid-fast bacilli (AFB) and culture (convention and rapid): AFB staining, LJ medium culture, and MGIT 960.

Statistical analysis

Normality of data was tested by Kolmogorov–Smirnov test. If the normality was rejected, then non parametric test was used. Quantitative variable was tested using paired t–test/Wilcoxon test. A p value of <0.05 was considered statistically significant. Data was entered and analyzed using statistical package for social sciences (SPSS) version 21.0.

RESULTS

Table 1 represents distribution of patients correlating percentage of cases with respective age groups. Highest percentage of cases (48%) have been reported for 21-30 age group, followed by 31-40 (38%), above 40 (12%) and below 20 age group (2%). The mean±SD value has been calculated as 31.96±7.77.

Table 2 show distribution of patient according to the stages of infertility, while 55% cases are in the primary stage 44% are in the secondary stage.

Table 1: Distribution of patients according to age groups.

Age group (years)	No. of cases	Percentage
Below 20	1	2
21-30	24	48
31-40	19	38
Above 40	6	12
Total	50	100
Mean±SD	31.96±7.77	

Table 2: Distribution of patient according to infertility type.

Infertility	No. of cases	Percentage
Primary	28	56
Secondary	22	44
Total	50	100

Distribution of patients with/without GTB with respect to stages of infertility. While 73.2% cases of primary infertility showed no incidence of GTB, 55.6% cases showed presence of genital tuberculosis. However, 26.8% cases of secondary infertility did not show GTB but 44.4% cases showed presence of genital TB. A non-significant value p value (0.423) was observed, correlating GTB incidence and infertility (Table 3).

Table 3: Correlation between infertility and GTB.

Infertility	No GTB		GTB		P value
	n	%	n	%	
1°	30	73.2	5	55.6	0.423
2°	11	26.8	4	44.4	
Total	41	100	9	100	

Table 4 represents distribution of patients' positivity according to different method of testing. Incidence of positivity found through HPE is highest 16%, followed by MGIT 960 i.e. 12%, AFB and culture represents the least percentage 4% each.

Table 4: Distribution of positive patients using different methods for detection of genital TB.

Test	No. of cases	Percentage
AFB	2	4
Culture	2	4
HPE	8	16
MGIT-960	6	12

Table 5 shows distribution of patient according to positivity among patient using different methods. It was observed that 10% of the patient had HPE + MGIT-960 positivity, 4% of the patients each had AFB + HPE positivity, only HPE positivity, AFB + MGIT-960 positivity and LJ + HPE positivity. 2% of the patient each had only MGIT-960 positivity, AFB + LJ positivity, LJ + MGIT-960 and AFB + CULTURE + HPE + MGIT-960 positivity, respectively.

Table 5: Distribution of patient's positivity for genital tuberculosis using different methods and combination.

Tests	No. of cases	Percentage
AFB + LJ	1	2
AFB + HPE	2	4
AFB + MGIT-960	2	4
LJ + HPE	2	4
LJ + MGIT-960	1	2
HPE + MGIT-960	5	10
AFB + culture + HPE +MGIT-960	5	10

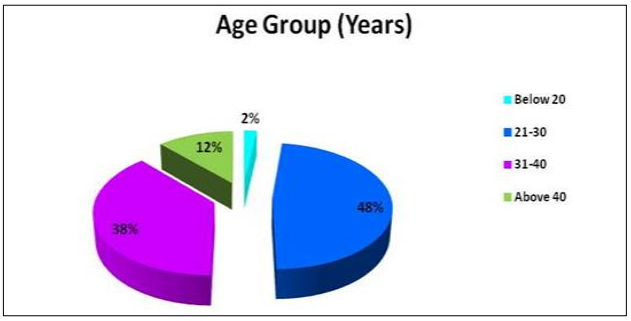

Figure 1: Distribution of patients according to age groups.

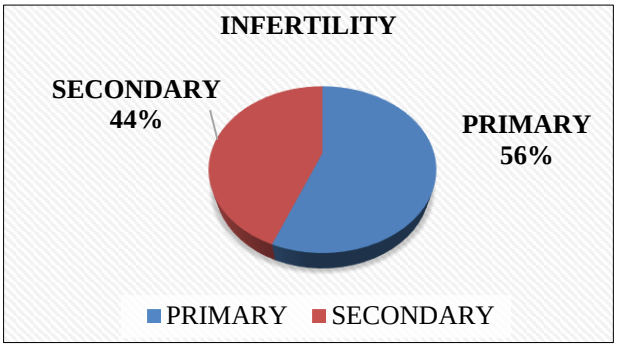

Figure 2: Distribution of patient according to infertility type.

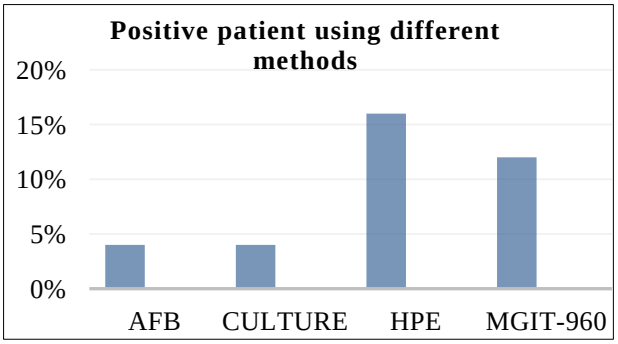

Figure 3: Distribution of positive patients using different methods for genital TB.

DISCUSSION

Female GTB is an important under diagnosed factor responsible for infertility in women. Early detection of GTB can assist in identifying asymptomatic patients and facilitate in making a plan of treatment that are appropriate for these women, thereby minimizing damage and averting eventual infertility. The current diagnosis is based on a combination of data from imaging tests, histology of genital tract material, bacterial cultures, serological testing, and direct observation using laparoscopy and hysteroscopy. However, there is diagnostic dilemma due to varied clinical presentations and diverse result on various tests available. This study was conducted in the Department of Obstetrics and Gynaecology, Rohilkhand Medical College and Hospital, Bareilly, after obtaining clearance from institutional ethical committee. Fifty women in the age group 18-45 years presented with indications infertility were enrolled, among which maximum (48%) were in the age group of 21-30 years. The mean age of study population was 31.96±7.77 years. Patients were investigated for GTB using a battery of diagnostic test like AFB, LJ culture, HPE, and MGIT-960.

In study by Sharma et al, the mean age of subjects was 27.91±5.88 years. Among the total 200 patients, 72% of women were in the age group of 20-30 years, while remaining in 30-40 years group.[5] Further, our results are in concordance with Jindal et al, where in they found maximum cases (45.7%) belonging to lower-middle socioeconomic strata of the society.[6]

Table 6: Distribution of patients according to age.

S. no.	Study	Age category (years)	
		20-30	30-40
1	Sharma et al (2015)[5]	72	28
2	Jindal et al (2017)[6]	45.7	54.3
3	Present study	50	50

Table 7: Comparison of different diagnostic tests.

S. no.	Study	Tests			
		AFB	LJ culture	HPE	MGIT-960
1	Jindal et al (2017)[6]	50	46.7	33.3	46.7
2	Mittal et al (2016)[10]	12.5	12.5	-	12.5
3	Present study	4	4	16	12

The endometrial biopsy sample was positive for GTB in 18 cases by either of the four tests employed in the diagnostic battery. The detection rates for AFB smear, LJ culture, MGIT culture and HPE, were 4%, 4%, 16% and 12%, respectively. The number of AFB positive patients were less as compared to the study conducted by Jindal et al.[6] Furthermore the present study showed 12% positivity by MGIT 960 which was similar to study conducted by Mittal et al.[10]

Histopathological examination is important for diagnosing GTB. On comparison with different culture methods, we found that out of 16% positive HPE cases, 75% were false negative by AFB smear, Thus, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of AFB smear was 25%, 100%, 100%, 87.5% respectively, while accuracy of AFB correlating with HP was found to be 88%. Similar co-relation was found between L.J culture and HPE. Thus, no difference in HPE positivity was detected in culture. Although isolation of *Mycobacteria* and its bacterial culture is considered as gold standard test, however it was found to be most unreliable in our study, with very low sensitivity. Similar results were reported by Al Eryani et al, Shrivastava et al, and Mittal et al.[7,10,11] Along with low sensitivity, another major disadvantage of AFB culture is the prolonged time required for its growth, this limits its practical utility.

Further, usefulness of more advanced MGIT 960 culture was co-related with HPE. Out of the total MGIT confirmed cases, 83.3% cases report positive MGIT-960 and HPE, however, only 2.4% cases were false positive.[12] Similarly, among the 97.6% negative cases with both MGIT-960 and HPE, 16.7% cases were false negative by MGIT-960. The sensitivity of MGIT was comparatively higher than AFB culture (62.5% versus 25%), specificity of 97.6%, PPV and NPV of 83.3% and 97.6% respectively. Accuracy of MGIT-960 culture correlating with HPE was found to be 92%.

The overall comparative analysis between different methods of diagnosis showed that sensitivity was highest for MGIT-960 (62.5%), followed by AFB (25%) and LJ-culture (25%, however, specificity was found to be 100% for both AFB and LJ culture, while 97.6% for MGIT-960 culture. For AFB smear, LJ-culture and MGIT-960, comparable PPV and NPV values were found, (100% versus 87.5%), (83.3% versus 97.6%) respectively. These results corroborated with previous studies by Sorlozano et al, and Rodrigues et al.[13,14]

Sorlozano et al found out the sensitivity of MGIT-960 to be the best (86.5%) among a comparison of MGIT 960, MB/BaCT ALERT 3D and LJ medium. However, they, found that LJ medium was best to detect non-tuberculous *Mycobacteria* with a senstivity of 76.2% Rodrigues et al determined that MGIT culture was able to detect 97.9% of isolate containing *Mycobacterium tuberculosis*, while LJ medium was able to detect 57.4% of isolates.[14]

In clinically suspected subjects, a statistically significant co-relation was found between incidence of GTB and in patients diagnosed positive by AFB smear (p value=0.029), culture (p value=0.029), by HPE (p value <0.001) and MGIT-960 (p value <0.001).

In a review by Sharma et al, the incidence of GTB in infertility patients was reported to be between 3 and 16%.[4] A meta-analysis conducted by Chaman-Ara et al showed that the overall prevalence of GTB in infertile women is 24.2%.[15] The differences in the findings of various studies stem from the differences in study populations since the prevalence of TB in general depends on several factors like the socioeconomic levels and the degree of congestion.

CONCLUSION

Genital TB is a major cause of infertility in women and prevalence is generally underestimated because of the asymptomatic nature of the infection and diagnostic challenges. A combination of histopathological and microbiological studies is required to detect GTB, as a single test is insufficient to diagnose all cases. Judicious utilization of investigations and various modalities, particularly endometrial collection for AFB, solid culture, MGIT-960, and HPE, demonstrates that the combination of HPE and MGIT-960 is crucial in the diagnosis of GTB in females presenting with infertility. The study demonstrates that negative endometrial biopsy results do not rule out GTB because it can occur at another sites.

This study also provides insight into the MGIT-960 system as a potential diagnosis tool for infertile patients. Conclusively screening for genital tuberculosis should be a crucial part for early diagnosis and treatment of infertility, ultimately restoring fertility.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Aliyu MH, Aliyu SH, Salihu HIM. Female genital tuberculosis: a global review. Int J Fertil Womens Med. 2004;49(3):123-36.
2. Bose M. Female genital tract tuberculosis: how long will it elude diagnosis? Indian J Med Res. 2011;134:13-4.
3. Xiang W, Liao, ACR and Chan, C. A new molecular variant of Luteinizing Hormone associated with female infertility. Fertil Steril. 1998;69:102.
4. Sharma JB. Current Diagnosis and Management of Female Genital Tuberculosis. J Obstet Gynaecol India. 2015;65(6):362-71.
5. Sharma D, Depan A, Yadav K, Narayan S, Sharma A. Prevalence of female genital tract tuberculosis in suspected cases attending Gynecology OPD at tertiary centre by various diagnostic methods and comparative analysis. Int J Reprod Contracept Obstet Gynecol. 2019;8:2286-92.
6. Jindal N, Gainder S, Dhaliwal LK, Sethi S. The Role of MGIT 960 Culture Medium in Resolving the Diagnostic Dilemma for Genital Tuberculosis Patients Presenting with Infertility. J Obstet Gynaecol India. 2018;68(2):123.
7. Ali AA, Abdallah TM. Clinical presentation and epidemiology of female genital tuberculosis in eastern Sudan. Int J Gynaecol Obstet. 2012;118(3):236-8.
8. Goel G, Khatuja R, Radhakrishnan G, Agarwal R, Agarwal S, Kaur I. Role of newer methods of diagnosing genital tuberculosis in infertile women. Indian J Pathol Microbiol. 2013;56:155.
9. Potter J, Leddy S, Kunst H, White V. P184 Female Genital Tuberculosis: The Long Road To Diagnosis. Thorax. 2014;69:A156-7.
10. Mittal P, Gupta S. A comparative study for detection of mycobacteria by direct AFB smear examination, culture by Lowenstein Jensen media, fluorescent sensor technology based BACTEC, micro MGIT system & PCR. Int J Med Sci Educ. 2016;3(3):257-63.
11. Shrivastava G, Bajpai T, Bhatambare GS, Patel KB. Genital tuberculosis: Comparative study of the diagnostic modalities. J Hum Reprod Sci. 2014;7(1):30-3.
12. Alan JW, Louis RK, Andrew CN, Partin AW, Peters CA. Campbell-Walsh Urology. 9th Edition. New York: Saunders, Elsevier. 2006.
13. Sorlozano A, Soria I, Roman J, Huertas P, Soto MJ, Piedrola G, et al. Comparative evaluation of three culture methods for the isolation of mycobacteria from clinical samples. J Microbiol Biotechnol. 2009;19(10):1259-64.
14. Rodrigues C, Shenai S, Sadani M, Sukhadia N, Jani M, Ajbani K, et al. Evaluation of the bactec MGIT 960 TB system for recovery and identification of Mycobacterium tuberculosis complex in a high through put tertiary care centre. Indian J Med Microbiol. 2009;27(3):217-21.
15. Chaman-Ara K, Bahrami MA, Bahrami E, Bahrami S, Bahrami MN, Moosazadeh M, et al. Prevalence of genital tuberculosis among infertile women: a systematic review and meta-analysis. Int J Med Res Health Sci. 2016;5(4):208-15.

Cite this article as: Eeram, Tiwary Y, Gupta T. A comparative study of various diagnostic modalities for female genital tuberculosis in infertility in a tertiary hospital. Int J Reprod Contracept Obstet Gynecol 2024;13:3089-93.