ISSN NO. 2320–7418 DOI: 10.22270/jmpas.V10I4.1223

International open access journal

Journal of Medical Pharmaceutical and Allied Sciences

Journal homepage: www.jmpas.com

Research article

Rural hospital correlation of clinical presentation, histopathology, and polymerase chain reaction for genital tuberculosis diagnosis

Dr. Swati Garg[1*], Dr. Sahitya Vodithala[1], Dr. Sunita Vagha[2], Dr. Neha Bhatt[2]

1. Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences, Sawangi,, Wardha, Maharashtra, India
2. Datta Meghe Medical College, Nagpur, Maharashtra, India

ABSTRACT

In India, vaginal tuberculosis (FGTB) is a common cause of infertility, but diagnosis is difficult because of the form of the disease of people in need. Traditional diagnostic methods include the detection of rapid bacilli acid in endometrial or peritoneal biopsy, epithelioid granuloma biopsy, or a positive Expert type in biopsy, although this is only available in a small percentage of cases, leaving patients many are not available. Diagnosis of GTB by PCR along with histopathological findings leads to high sensitivity and specificity. So, both diagnostic and operative laparoscopy and hysteroscopy are the modalities essential for management of genital TB in infertile women. This review discusses various diagnostic modalities including endometrial or peritoneal biopsy to detect epithelioid granuloma on microscopy, role of PCR for GTB and correlation of two for early diagnosis of genital tuberculosis so that management will be started at early stage which can prevent patient from getting permanent damage to organs. Tuberculosis being endemic in counties likes India; it is often a leading cause of infertility. Early diagnosis is crucial because, by the time patient reports with infertility, already the damage has started and reverting tubal patency is almost impossible. Early diagnosis typically fails in developing countries, primarily because there are no pathognomonic signs of the disease and either poor sensitivity or procedurally invasive diagnostic methods are in use.

Keywords: TB, vaginal tuberculosis, Histopathology, And Polymerase Chain Reaction

Received - 05-06-2021, Reviewed - 04/07/2021, Revised/ Accepted- 07/08/2021

Correspondence: Dr. Swati Garg* ✉ swatigdagr8@gmail.com

Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences, Sawangi (Meghe), Wardha, Maharashtra, India

INTRODUCTION

Tuberculosis (TB), once assumed to be a disease of poor countries and nearly eradicated in the Western world, has reemerged worldwide and has become a global concern. (1) It is a key cause of death affecting about a third of the global population. The Mycobacterium Tuberculosis (MTB), a bacterial pathogen is the cause of tuberculosis.

TB was considered a unique clinical business before 1000BC. Morgagni first wrote about genital tuberculosis in 1744, following the murder of a 20-year-old woman who died of tuberculosis and her uterus and uterus were found to be covered with material (GTB). (2)

GTB is a rare form of extra-pulmonary tuberculosis (EPTB) that in young women can lead to infertility. (3) In any population, the true prevalence of GTB cannot be reliably determined, since at least 11% of patients are estimated to be asymptomatic and the disease is accidentally detected. (4) Depending on socio-economic and public health conditions, the prevalence varies greatly; it typically coincides with the incidence of pulmonary and abdominal tuberculosis.

According to reports, 18-19 percent of infertile women in India have GTB. According to a recent report, GTB accounts for 1% of all gynecological admissions in India and 17.4% of infertility clinic admissions.(5)

GTB is often caused secondary to pulmonary or extra pulmonary TB foci in the kidney, meninges, skeletal system, gastrointestinal tract, and military TB. (6) Bacilli from tuberculosis can infect the genital tract in four ways being hematogenous transmission (with the lungs as the main focus), lymphatic transmission, descending direct dissemination, and, in extreme cases, sexual transmission as a primary infection of the genitalia. (7)

Fallopian tubes (95-100 percent), uterine endometrium (50-60 percent), ovaries (20-30 percent), cervix (05-15 percent), uterine myometrium (2-5 percent), and vagina/vulva (1 percent) are the genital organs affected by MTB.[8]

Pathogenesis

Genital TB almost always follows TB elsewhere in the body - it usually denies and sometimes kidneys, intestines, bone, or joint; sometimes it is part of the normal radiation process. If bacilli are not extracted, there is a risk of lifelong recovery, especially in combination with diseases or drugs that cause a decrease in the T-cell response (e.g. Hodgkin's lymphoma, AIDS, steroids, stress or malnutrition). The mode of transmission is usually Hematogenous or lymphatic and sometimes occurs in a manner directly related to abdominal or peritoneal concentration. The focus on the lungs is usually healed, and the wound may remain in the genital area for years, only to be regenerated over time.

Hematogenous Spread

After the tubercle bacilli have invaded the lungs, in most cases the bacilli are still distributed in the blood within a few hours and are injected into various parts of the body. This bacillemia can last for six weeks or more, if the disease is not detected and treated immediately with anti-TB drugs. No organ or tissue in the human body is immune to the bacillus of TB, although there is a significant difference in the level of infection. This variation is due to the degree to which various organs are exposed directly to the bacilli, to mechanical substances that affect the level of bacilli delivered by blood flow to each body, and in part the ability of different tissues to support the bacilli in them.

The tubercle bacilli can also reach the bloodstream and thus the genital tract extends from the lung lesions above the lungs. The fallopian tube forms a nidus that responds positively to tubercle bacilli, with the first wound found in the mucosa. The tendency of the tubercle bacillus to affect both organs of the body leads to both tubes being involved in the tuberculosis process. There is probably an early involvement of the thighs, with subsequent circulation to other organs and peritoneum. Tuberculosis peritonitis is most commonly seen in the involvement of the genital tract and may be associated with rupture of the abdominal lymph node or, more often, by spreading from intestinal obstruction.

Lymphatic Spread

When the original lesion is in the abdominal cavity, lymphatic spread is a less prevalent mechanism of infection.

Direct Spread from a Neighboring Viscus

Certain definitions of genital organs from the abdominal viscera, such as the other, rectum, appendix and intestines. Some researchers believe that prevalence is very important. However, peritoneal involvement can also be the result of the destruction of infected material from the fallopian tubes; therefore, the main process is not always clear. It can also occur when adhesions bind to the bladder or intestines in the fallopian tubes and soften the toxic ulcer leading to direct spread of the genitals.

Once the genital tract is connected, granulomata contain a type of tubercle bacilli that works inside different organs. After the development of tubercular hypersensitivity, this is usually clinical, and can last for 1 to 10 years or more before infection in the area is reactivated or seen clinically, if symptoms appear at all. Most foci are not clinically relevant. In most cases, there is little or no evidence of infection in the genital area. There is some evidence that when serious infections occur during menstruation, there is a high risk of sexual involvement.

Most pathologists claim that primary infection of the vagina does not occur. It is known that infected foci can be present in the body and remain undetected for a long time. These sores can precede genital sores and treat them without leaving traces shown in clinical trials.

Ulcers of the cervix and the vagina are rare and are often seen as independent, permanent, ulcer sores. Infectious diseases in TB usually become TB. Mycobacterium bovis can sometimes cause human infections, including vaginal infections, especially in highly developed countries without milk supply and an effective TB control program for cattle. Mycobacteria target aerobes in a cycle of 17-24 hours and are characterized by rapid acid spots.

PATHOLOGY

A polymorph nuclear inflammatory exudate is produced when a susceptible host is infected by tubercle bacilli. Within 48 hours, mononuclear cells take their place, becoming the primary site for intracellular tubercle replication. Tubercle bacilli degradation and caseation necrosis occur as cellular immunity grows. A proliferative granulomatous lesion with core caseation necrosis surrounded by concentric layers of epithelial cells and giant cells with peripheral lymphocytes, monocytes, and fibroblasts causes the reactivation of an infection centre.[9]

CLINICAL PRESENTATION

It can affect women of any age group, but the reproductive age group (15-45 years) is the most affected.(10) The clinical diagnosis of GTB involves a high index of suspicion. About 20% of genital tuberculosis patients have a family history of tuberculosis.(11) In most cases, the condition is asymptomatic or has just a few symptoms, the most common of which is infertility. Menstrual irregularities such as oligomenorrhoea, amenorrhea, hypomenorrhoea, menorrhagia, dysmenorrhoea, metrorrhoea, pelvic pain, and excessive vaginal discharge have also been recorded. [7]

Diagnosis

The discovery of tubercle bacilli in 1882 and the isolation of the bacilli in urine and sputum samples in 1883 greatly contributed

to the diagnosis and treatment of TB [12]. There is still a diagnostic dilemma, particularly for genital TB, despite the availability of different diagnostic techniques. FGTB therefore requires a detailed systematic clinical review with a high degree of skepticism and the use of intensive investigations. [13]

Women with prolonged menstrual cycles, postmenopausal bleeding and frequent vaginal discharge (where genital neoplasia has been ruled out) should be aware of the risk of FGTB [14]. Contact with a smear-positive pulmonary TB patient, a previous history of TB infection, residence in endemic areas or recent travel, low socioeconomic status, people living with HIV, and drug abuse too are risk factors for FGTB [15]. There is no single diagnostic test that can confirm the diagnosis of FGTB. For the diagnosis of characteristic structural changes, a high level of clinical skepticism, thorough history taking, system wise analysis, various microbiological and pathological tests, as well as imaging methodologies, are needed. [16]

INVESTIGATIONS IN GENITAL TUBERCULOSIS

Blood tests

- Anemia, leukocytosis with lymphocytosis, and an elevated ESR; nonspecific
- Serological tests such as ELISA are not very sensitive or specific.
- In genital TB, there is a moderate increase in CA 125 levels.

2. Interferon gamma release tests and the Mantoux (tuberculin) test have low sensitivity and specificity.
3. Chest X-ray

Imaging methods

- Ultrasonography
- Axial tomography on a computer (CT scan)
- Magnetic resonance imaging (MRI).
- PET scan for tubercular tubo-ovarian masses tubercular tubo-ovarian masses
- HSG stands for hysteron salpingography. Synechiae development, a distorted, erased, or T-shaped hollow, and venous and lymphatic intra vasation is all symptoms of endometrial TB.

Endometrial biopsy, curettage or aspirate

- Histopathology Demonstration of epithelioid granuloma
- Mycobacterial smear and culture Using Lowenstein–Jensen (LJ) medium or BACTEC 460 or mycobacteria growth inhibitor tube (MGIT) and specific gene probes can help in rapid identification and diagnosis
- Polymerase chain reaction (PCR)

Histopathological examination

In histologic examination, the image is one of the most rare, often isolated, small lesions that are abnormally dispersed through the endometrium.

Endometrial tuberculosis is similar to tuberculosis in other tissues, but advanced stages namely caseation, fibrosis and calcification are rarely seen during the birth of a normal rupture of the endometrium.

The oldest ulcer in endometritis is an infectious granuloma, consisting of epithelial cells, large langerhans cells, and lymphocytes. These granulomata are found throughout the endometrium but occur in large numbers in just the upper layers. Occasionally they replenish the lumina gland, trigger a strong inflammatory response and provide the appearance of a micro abscess. Endometrial glands adjacent to granulomata do not produce a secretory response or can be suppressed, resulting in a pseudo adenomatous appearance.

In most cases, the endometrial lesion consists of circular lesions of endothelioid cells surrounded by lymphocyte sites and plasma cells. Inflammatory cells can be present in the stroma without focused lesions. However, larger cells do not always show strong infection. Endometrial tuberculosis lesions are usually concentrated and may not grow because they usually erupt every month except in women or women with amenorrhea after menstruation. Granulomatous lesions are usually best seen on the 24-26th day of the cycle or within 12 hours of menopause.

Application of PCR in genital tuberculosis

One of the most important medical applications of the old PCR method is the discovery of viruses and is currently widely used by nurses and researchers to diagnose, synthesize and sequence genetics, and to perform complex quantitative and genomic studies in a very fast and critical manner.

The PCR procedure was first proposed to obtain M. TB. The experimental ability to make double billions of copies from each copy of the target DNA meant that less than 10 input molecules of the targeted DNA could lead to a positive signal. Therefore, a diagnosis using a raw specimen can be completed in just a few days or perhaps a few hours after the arrival of the sample.

Utility of histopathological examination for diagnosis of GTB

A histopathological analysis of the specimen reveals granulomatous caseous lesions, which IS characteristic of tuberculosis infection. While the presence of typical caseous granulomas with giant epithelioid cells suggests tuberculosis, these lesions can also be found in fungal infections, syphilis, leprosy, rheumatoid arthritis, systemic lupus erythematosus, pneumoconiosis, and sarcoidosis.[17]

In a study done by Geetika Goel et al., 546 samples of endometrial biopsy suspected of GTB were studied. Out of total 546 samples, 13 (2.63%) cases had evidence of TB on histopathological examination. [18]

Utility of Polymerase chain reaction (PCR) for diagnosis of GTB

PCR is a rapid molecular tool for detecting MTB and other mycobacteria nucleic acid sequences in tissue samples from patients

with GTB. The PCR assay can detect less than 10 bacilli/ml, including dead bacilli, and takes 8-12 hours to complete. [19] PCR has a higher sensitivity than culture and histopathological analysis, and its specificity in detecting GTB can be as high as 100 percent. [20, 21, 22, 23]

In a study done by Gunjan Shrivastava et al., out of 227 patients suspected of suffering from GTB, a total of 126 (55.50%) were found to be positive by PCR. [22]

Another study done by Bharti Malhotra et al. found that out of total 555 female genital samples, GTB was diagnosed in 132 (23.78%) cases by PCR. [24]

Therefore we want to glorify the fact that most studies want to frame a better approach for diagnosis of GTB in cases of infertility.

Correlation of histopathological examination and PCR for diagnosis of GTB

In a study done by Srivastava G et al. on evaluating microscopy, culture, histopathology and PCR for diagnosis of GTB, a total of 218 endometrial samples were studied of which histopathology was evident of TB in 1.37% while PCR gave positive results in 38.50% samples.[25]

In another study done by RBP Thangappah on evaluating PCR, culture and histopathology in diagnosis of GTB, out of total 72 samples studied 6.9% samples were positive on histopathology whereas 36.7% samples were positive on PCR. [26]

The present study was undertaken to analyse and assess the correlation between histopathology and PCR for diagnosis of GTB in cases of infertility and to find a better diagnostic approach.

CONCLUSION

TB being endemic in counties like India, it is often a leading cause of infertility. Early diagnosis is crucial because, by the time patient reports with infertility, already the damage has started and reverting tubal patency is almost impossible. Early diagnosis typically fails in developing countries, primarily because there are no pathognomonic signs of the disease and either poor sensitivity or procedurally invasive diagnostic methods are in use. A high index of scepticism is also absent on the doctors' side, thereby delaying diagnosis. Since diagnosis based on clinical symptoms alone is not accurate, there is a bad need to find or establish a better means of diagnosis. PCR may be the tool of choice for its higher sensitivity and precision in symptomatic clinically suspected subjects.

REFERENCES

1. Shaheen R, Subhan F, Tahir F, 2003. Epidemiology of Genital tuberculosis in infertile population, J Pak Med Assoc 56:306–9.
2. Morgagni JB, De Sedibuset Causismeorboram, Epistola 38:34, 1744.
3. Arpitha VJ, Savitha C, Nagarathnamma R, 2016. Diagnosis of genital tuberculosis: correlation between polymerase chain reaction positivity and laparoscopic findings, Int J Reprod Contracept Obstet Gynecol 5:3425-32.
4. Goldin AG, Baker WT, 1985. Tuberculosis of the female genital tract, J Ky Med Assoc 83:75.
5. Arora R, Sharma JB, 2014. Female genital tuberculosis - A diagnostic and therapeutic challenge, Indian J Tuberc 61:98-102.
6. Rozati R, Agiri SR, Rajeshwari CN, 2006. Evaluation of women with infertility and genital tuberculosis, J Obstet Gynecol India 56:423-6.
7. Sharma JB, 2015. Current diagnosis and management of female genital tuberculosis, J Obstet Gynaecol India 65:362–71.
8. WHO, 2017. WHO global tuberculosis report 2016, accessed on April 27.
9. Daly JW, Monif GRG, 1982. Mycobacteria, In Monif GRG (ed): Infectious Diseases in Obstetrics and Gynaecology, p 301, 2nd ed, Philadelphia, Harper & Row.
10. Qureshi RN, Samad S, Hamid R, Lakha SF, 2001. Female genital tuberculosis revisited, J Pak Med Assoc. 51:16–8.
11. Schaefer G, 1976. Female genital tuberculosis, Clin Obstet Gynecol 19:223.
12. Zajaczkowski T, 2012. Genitourinary tuberculosis: Historical and basic science review: Past and present, Cent European J Urol 65:182–7.
13. Bhanothu V, Theophilus JP, Rozati R, 2014. Use of endo-ovarian tissue biopsy and pelvic aspirated fluid forthe diagnosis of female genital tuberculosis by conventional versus molecular methods, PLoS One 9:e98005.
14. Varma TR, 2008. Tuberculosis of the female genital tract, Glob Libr Women's Med.
15. Chowdhury NN, 1996. Overview of tuberculosis of the female genital tract, J Indian Med Assoc 94:345–6 361.
16. Bose M, 2011. Female genital tract tuberculosis: How long will it elude diagnosis? Indian J Med Res 134:13–4.
17. Baxi A, Neema H, Kaushal M, Sahu P, Baxi D, 2011. Genital tuberculosis in infertile women: Assessment ofendometrial TB PCR results with laparoscopic and hysteroscopic features, J Obstet Gynecol India 61:301–6.
18. Goel G, Khatuja R, Radhakrishnan G, Agarwal R, Agarwal S, Kaur I, 2013. Role of newer methods of diagnosing genital tuberculosis in infertile women, Indian J Pathol Microbiol.
19. Arora S, Merchant R, Allahbadia GN, 2014. Reproductive medicine: Challenges, solutions andbreakthroughs, New Delhi: JP Medical Ltd.
20. Bhanothu V, Theophilus JP, Rozati R, 2014. Use of endo-ovarian tissue biopsy and pelvic aspirated fluid forthe diagnosis of female genital tuberculosis by conventional versus molecular methods, PLoS One 9:e98005.
21. Bhanu NV, Singh UB, Chakraborty M, Suresh N, Arora J, Rana T, et al, 2005. Improved diagnostic value of PCR in the diagnosis of female genital tuberculosis leading to infertility, J Med Microbiol 54(Pt10):927–31.
22. Shrivastava G, Bajpai T, Bhatambare GS, Patel KB, 2014. Genital tuberculosis: Comparative study of thediagnostic modalities, J Hum Reprod Sci 7:30–3.
23. Rana T, Singh UB, Kulshrestha V, Kaushik A, Porwal C, Agarwal N, et al, 2011. Utility of reversetranscriptase PCR and DNA-PCR in the diagnosis of female genital tuberculosis, J Med Microbiol 60(Pt 4):486–91.
24. Malhotra B, Sinha P, Hooja S, Vyas L, 2012. Rapid Diagnosis of Genital Tuberculosis by Real-Time Polymerase Chain Reaction, J South Asian Feder Obst Gynae 4(1):00-00.

25. Shrivastava G, Patel K, 2014. Genital tuberculosis: evaluating microscopy, culture, histopathology and PCR for diagnosis all play their role, Int J CurrMicrobiol App Sci 3:439-45.
26. Thangappah RB, Paramasivan CN, Narayanan S, 2011. Evaluating PCR, culture & histopathology in the diagnosis of female genital tuberculosis, Indian J Med Res 134(1):40-46.

How to cite this article

Dr. Swati Garg, Dr. Sahitya Vodithala, Dr. Sunita Vagha, Dr. Neha Bhatt, 2021. "Rural hospital correlation of clinical presentation, histopathology, and polymerase chain reaction for genital tuberculosis diagnosis". Jour. of Med. P'ceutical & Allied. Sci. V 10 - I 4, 1223, P- 3474-3478. doi: 10.22270/ jmpas.V10I4.1223.