Review Article

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COMPARISON OF VARIOUS DIAGNOSTIC MODALITIES FOR GENITAL TUBERCULOSIS IN SUB-FERTILE WOMEN IN RURAL HOSPITAL

Abstract:

In India, tuberculosis of the genital tract, particularly of the Fallopian tubes and endometrium, is a leading cause of persistent infertility in women. The identification of FGTB so that therapy can begin as soon as possible is still a clinical problem. The paucibacillary character of the illness, as well as the few diagnostic assays available, make laboratory diagnosis problematic. Because of the lengthy and tough treatment, a confirmed diagnosis of tuberculosis (TB) is required to assist and urge the patient to comply. In a rural hospital, the review compares multiple diagnostic methods for genital TB in infertile women. This review includes descriptions of the condition as well as reports that are now accessible and focus on the tests and procedures required for early identification and treatment of female genital tuberculosis [FGTB].

Introduction:

Mycobacterial infections have become a serious health concern in both industrialised and developing countries during the previous two decades, prompting the World Health Organization to declare tuberculosis (TB) a global crisis in 1994.[1] ~~1~~ In 2008, an estimated 9.4 million (range 8.9–9.9) TB incident cases were reported globally (equal to 139 cases per 100,000 people). The majority of these incidents occurred in Asia (55 percent; mostly in India, China, and Indonesia) and Africa (30 percent; primarily in South Africa and Nigeria), with small proportions in the Eastern Mediterranean Region (7 percent), Europe (5 percent), and the Americas (3 percent). [2]

Although tuberculosis primarily manifests as pulmonary disease, extrapulmonary tuberculosis (EPTB) is becoming more common. Because of its non-specific clinical and laboratory findings, EPTB is notoriously difficult to diagnose. Ggenital tuberculosis (FGTB) is a rare form of EPTB that can lead to infertility in females. The current FGTB review summarises recent achievements in the field and highlights doctors' concerns about the condition. In some circumstances, early detection and treatment of FGTB might prevent infertility and avoid the patient from having to undergo unnecessarily invasive operations.[3]

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Methods:

The following goals are being pursued with this review: l) To gain a general understanding of the diagnostic tests used to detect FGTB. 2) To comprehend the diagnostic tests' limitations as well as their benefits. 3) To offer clinical advice on detecting FGTB in women who have a suspected infection.

The electronic databases PubMed, Medline, Embase, and Google were used to conduct a literature search in English. In the search, we used the phrases extrapulmonary tuberculosis OR genital tuberculosis OR tuberculosis in India OR female genital tuberculosis OR infertility. The authors' personal expertise and experience with the subject aided in the collection and analysis articles. The present review includes studies that meet the following criteria:

1. Studies in English are included.
2. It also includes studies published in the recent 10 years, from 2009 to 2019.
3. There are studies that are primarily focused on FGTB.

Discussion:

Due to the wide range of clinical symptoms, t~~T~~he battery of bacteriological tests and histopathological examinations that are frequently required for FGTB diagnosis, as well as examiner bias on imaging and laparoscopy, paucibacillary yield of microorganisms in samples, exact diagnosis of FGTB has always been difficult for clinicians.[4,5] Infertile women have been the subject of a large number of research, with endometrial biopsy being the most common specimen utilised for diagnosis. When compared to traditional endometrial biopsy/curettage, menstrual blood has been observed to have the lowest sensitivity.

Traditional microbiological tests such ~~as Ziehle Neelsen (ZN) s such~~ as Ziehle Neelsen (ZN) staining, Lowenstein Jenson (LJ) medium culture, epithelioid granuloma histological diagnosis, and polymerase chain reaction [PCR] all aid in the diagnosis FGTB, in addition to the commonly used hysterosalpingography and hysterolaproscopy.[6]

Acid-fast bacilli (AFB) staining:

Although Ziehle Neelsen (ZN) Staining is a low-cost and quick method for identifying tubercular bacilli, it is insensitive. To allow for improved readability at lower magnifications, fluorescent dyes (auramine, rhodamine) are employed instead of standard staining, and ~~L~~light microscopy is around 10% more sensitive than fluorescence microscopy (FM). Traditional fluorescent microscopes are expensive, and they need the use of dark rooms to perform tests. To address these challenges, light emitting diode (LED) microscopes have been created. Kashyap et al[7] in 2013 looked at a variety of different staining techniques for bacteriological diagnosis, including Gabbett staining, fluorescent staining, and haemotoxylin and eosin[HE] staining, in addition to ZN staining. ~~Gabbet cold staining n Staining with Ziehl Neelsen~~. When compared to ZN staining, fluorescent and HE staining had better sensitivity and comparable specificity. Gabbett staining and modified cold staining are variations of cold staining techniques. Cold staining procedures such as Gabbett staining and modified cold

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Comment [KRISH4]: Mention the sensitivity and specificity of each test.

staining are easier from a technical perspective, quicker, as well as efficient for detecting pulmonary tuberculosis, according to 7Abdelaziz et al.[8], but its value in diagnosing FGTB is questionable. Inspite of better staining techniques, the problems of sensitivity persist, also staining technology will never be a trailblazer in the diagnosing FGTB.

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Culture methods:

The gold standard for TB diagnosis is still mycobacteria isolation from clinical specimens by culture, and its value is widely documented. Mycobacteria can be cultured using traditional egg-based solid media like Lowenstein Jenson (LJ) medium and agar-based 7H10 or 7H11 broth, as well as liquid media like Krischner or Middlebrook 7H9 broth. Due to the slow development of Mycobacterium tuberculosis, culture on ordinary media can take up to 6 weeks. Various fast procedures that can identify mycobacterial development in as little as two weeks are now available. However, these culture systems are not widely available in rural regions.[9]

Identification of mycobacteria from culture:

Because the treatment of non-tuberculous mycobacterial (NTM) infections differs from that of Mycobacterium tuberculosis complex infections, mycobacterial clinical isolates must be identified by species. Traditional Lateral Flow Immunochromatography, biochemical tests, antibody-based assays such as HPLC, matrix assisted laser desorption/ionization time of flight mass spectrometry (MALDI-TOF MS), and matrix assisted laser desorption/ionization time of flight mass spectrometry (MALDI-TOF MS), and matrix assisted laser desorption/ionization time of flight mass spectrometry (MALDI-TOF MS) are some of the species identification methods available (Rapid strip test). PCR restriction enzyme analysis, AccuProbe test All of these molecular tests, such as DNA chips (DNA microarrays), are exciting prospectives.

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Mycobacteria have often been cultured in a variety of solid or liquid culture medium for phenotypic drug susceptibility testing (DST). DST requires less time when using commercial liquid culture methods like BACTEC MGIT than DST using solid medium, about 9-10 days. As a result, using the rapid culture approach for medication susceptibility testing can help in better patient management.[10]

Non culture based methods

Lipoarabinomannan assay is a test that measures the amount of lipoarabinomannan in the The Mycobacterium tuberculosis lipoarabinomannan (LAM) antigen is detected in the urine of individuals with pulmonary and extrapulmonary tuberculosis by the TB LAM test. The detection of mycobacterial lipoarabinomannan (LAM) antigen in urine has become an essential point-of-care tuberculosis diagnostic tool (TB). However, because it appears to be present mostly in those with active TB, its application in genital tuberculosis is restricted.[11]

WHO has barred the use of serological assays in patients suspected of any kind of active TB, independent of HIV status, due to the uneven quality of available on the market serological tests and a considerable variation in sensitivity and specificity. [12]

Molecular diagnostic tests

Polymerase chain reaction (PCR) test (PCR) PCR is a more sensitive, specific, and quicker way of detecting genital tuberculosis than culture and histology. The inability of PCR to discriminate between viable and nonviable organisms is one of its most serious flaws.[13] As a result, in people who are receiving anti-TB drugs or who have completed TB treatment, the test can stay positive for a long time. When Extraction of DNA is ineffective owing to low mycobacterial counts or the existence of PCR inhibitors, false-negative results might arise. Sankar et al.[14] did a study in 2012 to investigate the utility of for the diagnosis using multiplex PCR TB since uniplex PCR detects just one target gene.

A notable benefits of multiplex PCR was the ability to discriminate amongst Mycobacterium TB, Mycobacterium kansasii, Mycobacterium avium complex, and other nontuberculous mycobacteria (NTM) in a single tube and gel electrophoresis run. In a study by Bhanothu V et al.[15] 2014, it was discovered that the multi-gene/multi-primer PCR method has ~~With~~ a sensitivity of 99.01 percent and a specificity of 100 percent, T~~,~~ the 19 kDa antigen (131bp) gene has a positive predictive value of 100 percent and a negative predictive value of 98.03 percent. Before any conclusions can be formed, multiplex PCR or multigene PCR must be used for genital TB diagnosis.

Immunological tests:

The diagnostic value of immunological testing in female genital TB is controversial. The TB d~~D~~ue to its low sensitivity, the ma~~e~~ntoux (TST) has restricted use in the detection of genital TB. The sensitivity of interferon gamma release assays (IGRAs) is great (99.4%), and it is unaffected by BCG vaccination. Cell - mediated immune responses to MTB-specific antigens are what they're searching for. T-SPOT. In TB testing, the enzyme-linked immunospot (Elispot) assay is employed. T-SPOT was recommended by Liu X et al., 2016,16. TB might be used as a prospective FGTB triage test since it is quick, easy to use, and looks to have a good sensitivity of 94 percent and specificity of 76 percent.

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After M. tuberculosis antigens excite sensitised T cells, the QuantiFERON-TB test detects the production of IFN-gamma in serum. QuantiFERON-TB Gold (QFN Gold) is a more accurate variant of the QuantiFERON-TB test. It makes use of antigens that are very specific to MTB. The US FDA approved QuantiFERON-TB Gold Plus, an enhanced variant of QFT, in June 2017. ~~(QFT-Plus).~~ The QFT-Plus is distinguished from the A fourth tube was added to QFT to measure interferon gamma produced from CD8 cytotoxic cells. IGRA and DNA-PCR

show a low correlation when it comes to detecting subclinical Patients suffering from unexplained infertility should consider FGTB.[17]

Comparison of various diagnostic modalities for genital TB

According to the literature, traditional procedures such as ZN staining and HPE culture have low sensitivity in identifying FGTB when ~~if you~~ comparing ~~e it~~ to molecular assays. Because the study sample was infertile women suspected of having FGTB on laparoscopic inspection, the sensitivity in a study by Bhanothu V et al.[15] was greater than in earlier investigations.

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~~When compared to molecular tests, conventional techniques like as ZN staining and HPE culture have limited sensitivity in detecting FGTB, according to the literature. The sensitivity of all tests in a research by Bhanothu V et al.[15] was higher than in previous studies since the study group comprised On laparoscopic inspection, infertile women suspected of having FGTB.~~

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Despite the fact that molecular techniques have been available for decades, diagnosing FGTB remains a difficulty. Any test for genital TB ought to –be sensitive enough to detect the disease early enough to start treatment. Laparoscopy, hysteroscopy, and hysterosalpingography have all been employed as adjuvants in studies in impoverished countries to detect FGTB using various microbiological tests. Attempts were made by Arpitha et al.[18] and Mala et al.[19] to compare the utility of laparoscopy with commonly performed microbiological testing.

While culture and molecular tests are critical in the diagnosis of FGTB, these studies show that laparoscopy enhances the chances of detecting the illness in suspected women. According to Sharma et al.[20], nucleic acid amplification tests like LAMP and Xpert MTB/RIF are now being studied for early detection of FGTB, however cost and infrastructure availability remain key barriers in resource-poor settings. Due to the vast variety of

gynaecological presenting symptoms, FGTB diagnosis is based on a strong clinical suspicion. ~~Ddifferent microbiological testing suggested by Arpitha et al.[18] and Mala et al.[19] compared the usefulness of laparoscopy to routine microbiological tests.~~

Clinical testing for FGTB, on the other hand, should not be limited to infertile women, but should include ~~W~~women with various reproductive morbidities like ,,,,,,,. ~~are also included..~~ These numerous clinical symptoms, as well as current breakthroughs in FGTB diagnostic testing that will help in early identification and treatment, should be known to all levels of health care practitioners that interact with women. Because of the increased frequency of MDR TB in developing countries, FGTB patients with a range of clinical symptoms, such as tubo-ovarian abscess that does not respond to anti-tubercular therapy, should undergo molecular testing for multidrug resistance.[21]

Though newer methods for molecular detection of pulmonary tuberculosis, such as t~~T~~he potential of whole genome sequencing, specimen transportation mediated technology, mycobacterium load detection test, and molecular diagnosis of multidrug resistant TB to identify genital tuberculosis has yet to be examined. The~~se~~ protocols for early diagnosis of FGTB, which can prevent long-term reproductive morbidity, should be developed using a significant threshold of clinical suspicion and a mix of screening procedures that complement each other.

Conclusion:

Finally, FGTB is a rare kind of tuberculosis that usually develops as a result of pulmonary tuberculosis. It usually goes unnoticed or causes only minor symptoms such as pelvic pain, menstruation irregularities, or vaginal bleeding. Tubal injury is the major cause of infertility in premenopausal women. Early diagnosis entails the High-risk patients should be identified,

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Comment [KRISH15]: who are these high risk patients.

sample sizes for cultures and histology should be collected, and molecular approaches should be used.

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