



Assessment of female genital tuberculosis and Infertility

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Abstract: Background: To assess female genital tuberculosis and infertility. **Materials and Methods:** One hundred six females with infertility were enrolled in this prospective observational study. All were selected for endometrial aspiration or biopsy one week before start of menstrual cycle or within 12 hours of onset of menses. All the clinical samples were screened with conventional microbiological tests such as Ziehl-Neelsen acid fast staining for recording smear-positivity, identification by cultural isolation and biochemical tests. **Results:** Age group <20 years had 6, 21-25 years had 35, 26-35 years had 42 and >30 years had 23 patients. Family history of tuberculosis was seen in 15 and past history of tuberculosis in 24. Primary type of tuberculosis was seen among 48 (45.2%) and secondary type in 58 (54.8%). Histology of endometrium showed secretory phase in 52, proliferative phase in 38, non-specific endometritis in 5 and tubercular endometritis in 11 cases. **Conclusion:** There was a strong relationship between genital TB and infertility. Tuberculous endometritis as a cause of infertility is still a major problem in the developing countries.

INTRODUCTION

Infertility is defined as “failure to conceive despite over 12 months of regular and unprotected intercourse”. Primary infertility is the term used to describe a couple that has never been able to conceive a pregnancy, after a minimum of one year of attempting to do so through unprotected intercourse¹. Tuberculosis, a chronic infectious disease, is one of the major etiological factors of female infertility. According to global TB report 2016, there were estimated 10.4 million new tuberculosis (TB) cases worldwide (3.5 million in women), with 2 millions death².

Female genital tract tuberculosis (FGT) as a cause of infertility is one of the commonest causes of infertility in developing countries³. The prevalence of genital tuberculosis is higher than one might imagine, based on the lack of reports in the literature, and may account for a significant amount of female infertility. It is therefore, suggested that every patient consulting for infertility in developing countries should be investigated for female genital tract tuberculosis (FGT)⁴. India has one of the highest incidences of TB in the world. It is therefore, suggested that every patient consulting for infertility in developing countries should be investigated for female genital tract tuberculosis (FGTB)⁵. Unlike pulmonary tuberculosis, the clinical diagnosis of genital tuberculosis is difficult because in majority of cases, the disease is either asymptomatic or has varied clinical presentation^{6,7}. We attempted present study to assess female genital tuberculosis and infertility.

MATERIAL and METHODS

A total of one hundred six females with infertility were enrolled in this prospective observational study after they agreed to participate and the ethical approval was sorted before commencing the study.

All underwent per vaginal examination. All were selected for endometrial aspiration or biopsy one week before start of menstrual cycle or within 12 hours of onset of menses. Patients were advised abstinence in menstrual cycle before the month of procedure. Two samples were taken by Karmann’s cannula number 4 or endometrial biopsy curette. Ziehl-Neelsen staining and culture of Acid fast bacilli on conventional methods and automated liquid cultures was done. All the clinical samples were screened with conventional microbiological tests such as Ziehl-Neelsen acid fast staining for recording smear-positivity, identification by cultural isolation and biochemical tests. For culture, each specimen was de-contaminated by N-acetyl-L-cysteinesodium hydroxide as per Kubica. Result were compiled and analysed using chi- square test with level of significance set significant below 0.05.

RESULTS

Age group <20 years had 6, 21-25 years had 35, 26-35 years had 42 and >30 years had 23 patients. A significant difference between age groups was seen ($P < 0.05$) (Table 1, Figure 1).

Family history of tuberculosis was seen in 15 and past history of tuberculosis in 24. A significant difference was seen ($P < 0.05$) (Table 2, Figure 2).

Received : 09/03/2022
Received in revised form : 22/05/2022
Accepted : 06/06/2022
Available online : 21/06/2022

Keywords:

Genital Tuberculosis,
Infertility,
Women

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<http://dx.doi.org/10.47009/jamp.2022.4.2.21>

Int J Acad Med Pharm,
2022; 4 (2); 100-102



Primary type of tuberculosis was seen among 48 (45.2%) and secondary type in 58 (54.8%). A non-significant difference was seen ($P > 0.05$) (Table 3, Figure 3).

Histology of endometrium showed secretory phase in 52, proliferative phase in 38, non-specific endometritis in 5 and tubercular endometritis in 11 cases. A significant difference was seen ($P < 0.05$)

Table 1: Age wise distribution of cases

Age group (years)	Number	P value
<20	6	<0.05
21-25	35	
26-30	42	
>30	23	

Table 2: Socio-demographic factors

Parameters	variables	Number	P value
Family history of tuberculosis	Yes	15	<0.05
	No	91	
Past history of tuberculosis	Yes	24	<0.05
	No	82	

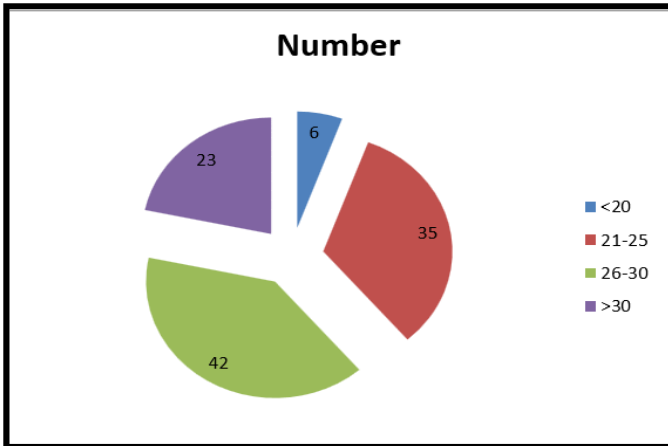


Fig 1: Age wise distribution of cases.

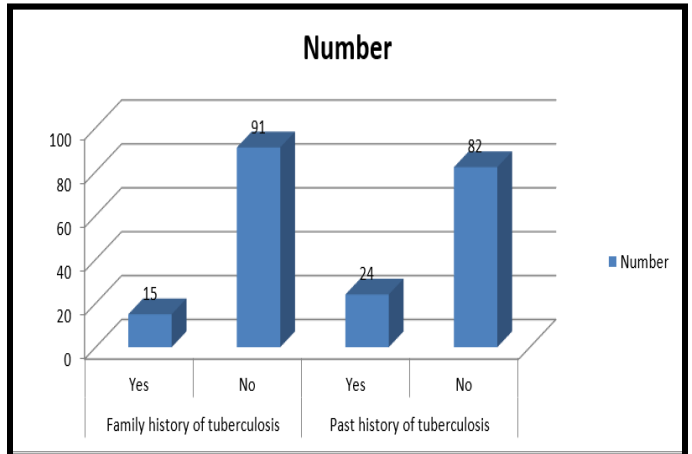


Fig 2: Socio-demographic factors.

Table 3: Type of infertility

Type	Number	P value
Primary	48 (45.2%)	>0.05
Secondary	58 (54.8%)	

Table 4: Histology of endometrium

Histology	Number	P value
Secretory phase	52	<0.05
Proliferative phase	38	
Non-specific endometritis	5	
Tubercular endometritis	11	

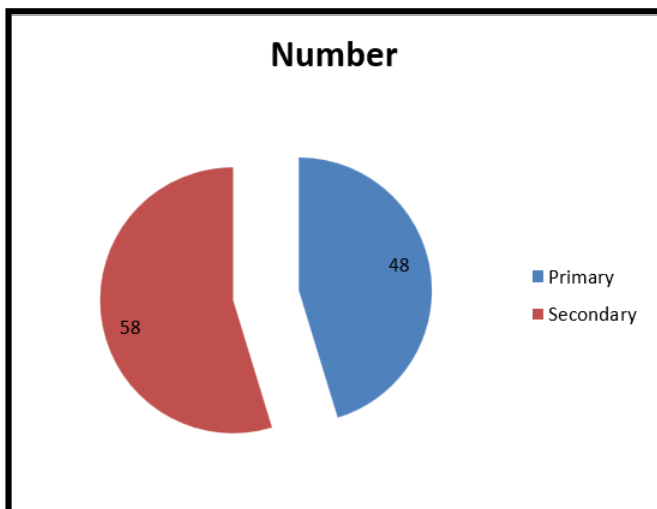


Fig 3: Type of infertility

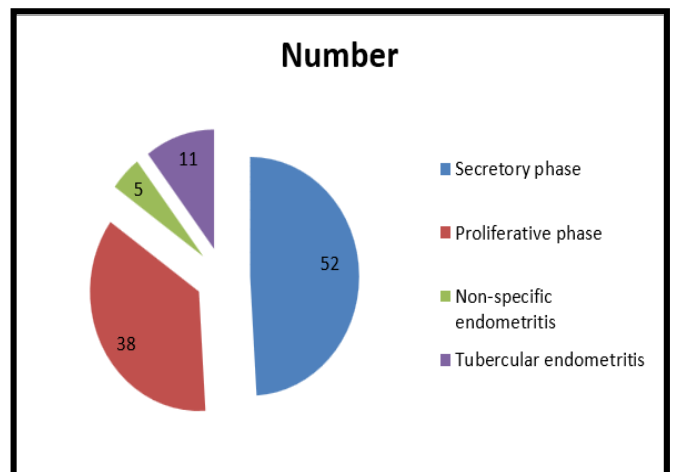


Fig 4: Histology of endometrium

DISCUSSION

Genital TB may be asymptomatic and diagnosis requires a high index of suspicion. Moreover, the disease may masquerade as other gynaecological conditions and can go unrecognized.⁸ The most common form of extra pulmonary TB is genitourinary disease, accounting for 27% (range, 14 to 41%) worldwide.⁹ Tuberculosis is one of the major etiological factors of female tubal infertility. Due to the lack of specific test and diagnostic modalities, it is difficult to diagnose and conclude the presence of genital tuberculosis^{10,11}. On the basis of clinical presentation alone, a woman cannot be diagnosed with FGTB. Multiple imaging techniques are not specific for tuberculosis confirmation. Endometrial biopsy should be taken in premenstrual phase for good results on AFB smear, culture, GeneXpert, PCR and other tests. Early diagnosis and treatment will improve fertility outcome^{12,13}. We assessed female genital tuberculosis and infertility.

Age group <20 years had 6, 21-25 years had 35, 26-35 years had 42 and >30 years had 23 patients. Srinivas Rao et al¹⁴, evaluated the prevalence of female genital tuberculosis in 1102 cases. 23 women were diagnosed as having genital TB based on the standard pathological and microbiological criteria of tissue specimens. Out of 23 cases diagnosed as having genital tuberculosis, 3 patients (13.04 %) presented with abdominal or pelvic pain. In 17cases (73.91%) tuberculosis was diagnosed during studies performed to evaluate the cause of their infertility, and the most common diagnostic procedure was endometrial curettage. Remaining 3 cases (13.05 %) have past, present or contact history of tuberculosis. Female genital TB accounted for 2.08 % of all tuberculosis patients in this study

Our results showed that family history of tuberculosis was seen in 15 and past history of tuberculosis in 24. Agarwal N et al¹⁵, found out the prevalence of genital tuberculosis in females presenting with infertility in a tertiary care hospital over a given period of time, and diagnostic comparison of endometrial tuberculosis by histopathological examination (HPE) and GeneXpert. A total of 96 endometrial samples were collected from the women, satisfying the inclusion and exclusion criteria. Results: On HPE, out of 96 patients, proliferative endometrium (anovulatory) was found in 38 cases (39.6%), nonspecific endometritis in 2 cases (2.08%) and 2 cases (2.08%) were found positive for tubercular endometritis. GeneXpert scored negative.

Our results revealed that Primary type of tuberculosis was seen among 48 (45.2%) and secondary type in 58 (54.8%). Djuwantono T¹⁶, reported three patients; two patients were admitted with irregular menstrual cycle as their chief complaint, while one patient came due to infertility. The results from laparoscopy were suggestive of FGTB; including the presence of caseating granulomas surrounded by epithelioid cells, lymphocytes, plasma cells, and Langhans giant cells. Additionally, PCR testing confirmed presence of MTB. Subsequent to diagnosis, continuous TB medications was administered with excellent clinical outcome in two patients (pregnant in 18 months after under gone laparoscopy). The infertile patient remain in one of the treated patient above. In infertile patients who live in countries where Tuberculosis is an endemic disease, such as Indonesia, a comprehensive history taking, along with ultrasonography results can be used to diagnose FGTB. Confirmation of this diagnosis can be achieved through polymerase chain reactions result. Timely diagnosis and treatment are imperative to prevent any permanent injury to patient's reproductive organs.

We found that histology of endometrium showed secretory phase in 52, proliferative phase in 38, non-specific endometritis in 5 and tubercular endometritis in 11 cases. TB can be classified into two forms: pulmonary and extrapulmonary. GTB is a form of extrapulmonary TB that affects 12.1% of patients with pulmonary TB and represents 15–20% of extra pulmonary TB. It has been estimated that 5–13% of patient in fertility clinics have GTB. Majority of these patients are predicted to be in the age group of 20–40 years old. In most cases, GTB is secondarily acquired by hematogenous spread from an extragenital source, such as pulmonary or abdominal TB.

Anatomically, GTB is mainly infested in the fallopian tubes and endometrium, causing infertility as the most likely result. If infection is not recognized early, fulminating destruction of these organs could result in permanent inability to conceive. GTB is almost always secondary to other TB infections in the body with most common infected sites is lung. Other organs, including bone, joint, gastrointestinal and renal¹⁷. If patients are not treated well to eradicate the bacteria, there is chance that the bacteria will be reactivated especially when the immune response of the patients is decreased. Getting diseases or drugs that cause attenuation of T cell response (e.g. Hodgkin's lymphoma, AIDS, steroids, stress or malnutrition) will also increase the risk of bacteria reactivation¹⁸. The mode of spread is usually hematogenous or lymphatic and occasionally occurs by way of direct contiguity with an intra-abdominal or peritoneal focus.

CONCLUSION

There was a strong relationship between genital TB and infertility. Tuberculous endometritis as a cause of infertility is still a major problem in the developing countries.

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