DOES THIN ENDOMETRIUM IN INFERTILE WOMEN INDICATE GENITAL TUBERCULOSIS?

Meghna M. Pai¹, Muralidhar V. Pai², Roopa P. S³, Pratap Kumar⁴

¹Post Graduate Student, Department of Obstetrics and Gynaecology, Kasturba Medical College, Manipal.

²Professor and Unit II Head, Department of Obstetrics and Gynaecology, Kasturba Medical College, Manipal.

³Associate Professor, Department of Obstetrics and Gynaecology, Kasturba Medical College, Manipal.

⁴Professor and Unit I Head, Department of Obstetrics and Gynaecology, Kasturba Medical College, Manipal.

ABSTRACT

BACKGROUND

Female genital tuberculosis (FGTB) primarily an asymptomatic disease, is one of the most important causes of female infertility in developing countries. The diagnosis of GTB has been a challenge. In recent years, polymerase chain reaction (PCR) technique has evolved as a useful and rapid technique for the diagnosis of GTB, but this method has some limitations. Ultrasound of the endometrium is easy to perform and therefore the imaging modality of choice in a clinical setting, however its role in diagnosing genital tuberculosis has not been explored to a large extent.

The aim of the study was to determine whether thin (<8mm) endometrium in infertile women indicates genital tuberculosis (GTB) and to ascertain the validity of thin (<8mm) endometrium in the diagnosis of genital tuberculosis.

METHODS

This prospective study was carried out from August 2014 to June 2015 in the Department of Obstetrics and Gynaecology, Kasturba Medical College, Manipal. Sixty infertile women with endometrial thickness (ET) <8mm and/or those with normal ET in whom GTB was suspected as a cause of infertility were recruited for the study. PCR test results were correlated with the ET.

RESULTS

ET was <8mm in 52 patients and ≥8mm in 8 patients; PCR was positive in 11 patients and negative in 49 patients; Sensitivity was 81.81%, Specificity was 12.24%, PPV was 17.30% and NPV was 75%.

CONCLUSIONS

Thin ET may not be a good indicator of the presence of genital tuberculosis and normal endometrial thickness does not rule out genital tuberculosis.

KEYWORDS

Genital Tuberculosis, Infertility, Endometrium, Endometrial, Polymerase Chain Reaction, Ultrasound.

HOW TO CITE THIS ARTICLE: Pai MM, Pai MV, Roopa PS, et al. Does thin endometrium in infertile women indicate genital tuberculosis? J. Evolution Med. Dent. Sci. 2016;5(18):905-907, DOI: 10.14260/jemds/2016/209

INTRODUCTION

Infertility is a problem of immense magnitude and out of the many causes of infertility in India, female genital tuberculosis (GTB) plays a major role. The incidence of GTB in infertility clinics in India varies from 3-16% while the incidence of infertility in GTB is about 58%.^{1,2}

The organ most commonly affected in GTB is the fallopian tube (92-100%), followed by the endometrium (50%) while the less-frequently affected ones are the: ovaries (10-30%), cervix (5%), and rarely the vagina or the vulva (<1%).³ However some reports have found endometrium to be the most commonly involved site.⁴ Tubercular endometritis causes thinning of the endometrium, which disfavours implantation.⁵ Unlike pulmonary tuberculosis (TB), the clinical diagnosis of GTB is difficult because in the majority of cases the disease is either asymptomatic or may even masquerade as other gynaecological conditions, infertility being the most frequent clinical presentation.⁶

A definite diagnosis can be made by positive mycobacterial culture and by demonstrating specific histopathological lesion in the specimen. In recent years, polymerase chain reaction (PCR) technique has evolved as a useful and rapid technique for the diagnosis of pulmonary and extra-pulmonary tuberculosis and it requires <10 bacilli/mL for diagnosis.⁷ However, these methods have limitations due to their invasive nature, secondary nature of the GTB, low detection rates of infecting organisms or the sampled site not being representative of the infected area.⁸

The two-dimensional ultrasound analysis of endometrial thickness was one of the first clinically relevant techniques to assess endometrial function. However, even though ultrasound of the endometrium is easy to perform and therefore the imaging modality of choice in a clinical setting, its role in diagnosing genital tuberculosis not been explored. Hence, this study aimed to determine whether thin (<8mm) endometrium in infertile women indicates genital tuberculosis (GTB) and to ascertain the validity of thin (<8mm) endometrium in the diagnosis of genital tuberculosis.

MATERIALS AND METHOD

This prospective, observational study was conducted in the Department of Obstetrics and Gynaecology, KMC, Manipal between Aug 2014 and Jun 2015. Ethical committee approval was obtained to conduct the study and informed consent was obtained from each patient.

Financial or Other, Competing Interest: None.

Submission 17-01-2016, Peer Review 12-02-2016,

Acceptance 18-02-2016, Published 03-03-2016.

Corresponding Author:

Dr. Muralidhar V. Pai,

Professor and Unit Head,

Department of Obstetrics and Gynaecology,

Kasturba Medical College,

Manipal-576104, Karnataka.

E-mail: mvpai@manipal.edu, drmvpai@yahoo.com

DOI: 10.14260/jemds/2016/209

A Total of 60 Women were Included in the Study based on

- High suspicion of genital tuberculosis as cause of infertility, irrespective of their endometrial thickness, OR
- Thin endometrium (ET <8mm) found during follicular imaging by transvaginal sonography (TVS) between day 11 and 14 of IUI treatment.

Infertile women with known current tuberculosis were excluded from the study.

Endometrial sampling was done on Day 23 of the same cycle or the next cycle (For those recruited from the IUI cohort) and the samples were sent for PCR.

The thickness of endometrium was correlated with the results of PCR. Sensitivity, Specificity, Positive and Negative predictive values of thin endometrium (<8mm) in the diagnosis of genital tuberculosis were calculated.

RESULTS

The age of the women recruited for the study ranged from 20 to 45 years with a mean age of 30.72 ± 1.79 years. 42 (70%) had primary infertility, while 18 (30%) had secondary infertility with mean duration of infertility being 5.7 ± 0.84 years; 42 women (70%) had no previous history of tuberculosis, while 18 (30%) had previous history of tuberculosis; 40 women (66.7%) had regular menstrual cycles, while 16 women (26.7%) had hypomenorrhea/oligomenorrhea, 2 (3.3%) had menorrhagia and 2 (3.3%) had amenorrhea.

The mean day of the cycle of ET measurement was the 13th day and the mean endometrial thickness was 5.9 ± 0.74 mm. The endometrial thickness (ET) was <8mm in 52 women (86.66%) and ET ≥ 8 mm in 8 women (13.33%). PCR was positive in 11 women (18.33%) and negative in 49 women (81.66%).

Mean Age	30.72±1.79 Years
Type of infertility	Number
Primary infertility	42 (70%)
Secondary infertility	18 (30%)
Previous h/o tuberculosis	Number
Positive	18 (30%)
Negative	42 (70%)
Type of menstrual cycle	Number
Regular menstrual cycle	40 (66.7%)
Hypomenorrhea/oligomenorrhea	16 (26.7%)
Menorrhagia	2 (3.3%)
Amenorrhea	2 (3.3%)
Endometrial thickness	Number
<8mm	52 (86.66%)
≥ 8 mm	8 (13.33%)
PCR result	Number
Positive	11 (18.33%)
Negative	49 (81.66%)
Table 1: Patient Characteristics (n=60)	

TVS (n=60)	PCR Positive (n=11)	PCR Negative (n=49)
ET <8mm (n=52)	9 (True positive)	43 (False positive)
ET ≥ 8 mm (n=8)	2 (False Negative)	6 (True negative)
Table 2: Comparison of Endometrial thickness (ET) and PCR results		

The sensitivity of thin endometrium in predicting tuberculosis was 81.81%, while its specificity was 12.24%.

Positive predictive value of thin endometrium was 17.30% and negative predictive value was 75%.

DISCUSSION

Female genital tuberculosis poses a diagnostic challenge, because of its varied presentations and lack of sensitive and specific methods of diagnosis. Although culture remains the gold standard of diagnosis, PCR method of DNA amplification gives rapid results and it requires <10 bacilli/mL for diagnosis. PCR was used in this study because a number of studies have shown it to be the best method of diagnosing genital tuberculosis in women.^{4,6,7}

11 (18.33%) of the 60 infertile women in this study had PCR positivity indicating genital tuberculosis, which correlated well with the incidence of female genital tuberculosis in India.^{1,2}

However, as compared to the PCR results in studies by Thangappah et al.⁷ (36.7%), Goel et al.⁹ (22.2%) and Khanna and Aggarwal.¹⁰ (26%), the positive results were lower in this study. The study by Kohli et al.¹¹ (13%) and Prasad et al.¹² (14.6%) showed low positivity as compared with the present study.

Endometrium was considered to be thin if it was >8mm as per the studies by Miwa I, et al.¹³ and Takasaki et al.¹⁴ Endometrial thickness was >8mm in 52 women (86.66%), while it was ≥ 8 mm in 8 (13.33%). The incidence of thin endometrium in natural cycles has been reported to be 5% in women <40 years of age. The present study showed a much higher incidence.

The thickness of endometrium was correlated with the PCR results. The sensitivity of thin endometrium in predicting tuberculosis was 81.81%, while its specificity was 12.24%. Positive predictive value of thin endometrium was 17.30% implying that 17.30% of women with ET <8mm have GTB and negative predictive value was 75% implying that 75% of women with ET ≥ 8 mm truly do not have GTB. Since, no similar study had been conducted in the past, the observations of the present study could not be compared.

The limitation of this study was that endometrial thickness was evaluated during follicular imaging by Transvaginal sonography between Day 11 and 14 of IUI treatment. Evaluation on the 21st day of the cycle would have been more appropriate.

CONCLUSION

Thin endometrium may not be a good indicator of the presence of genital tuberculosis and normal endometrial thickness does not rule out genital tuberculosis.

REFERENCES

1. Tripathy SN. Infertility and pregnancy outcome in female genital tuberculosis. International Journal of Gynaecology and Obstetrics 76(2002);159-163.
2. Shanti Sri, Nazia Khannum, Padmaja P. Prevalence of endometrial tuberculosis in infertility cases; International Journal of Science and Research. June 2015; Volume 4, Issue 6:278-9.
3. Dawn CS. Pelvic infections; In: Dawn CS; ed Textbook of Gynaecology and Contraception: 9th ed; Calcutta: Arati Dawn; 1998, 321.

4. Rozati R, Roopa S, Rajeshwari CN. Evaluation of women with infertility and genital tuberculosis. *J Obstet Gynaecol India* 2006;56:423-6.
5. Khurana G Sahi. Ultrasound in female genital tuberculosis: a retrospective series. *Ultrasound in Obstetrics and Gynaecology* 2013;42 (Suppl 1):28.
6. Shrivastava G, Bajpai T, Bhatambare GS, et al. Genital tuberculosis: comparative study of the diagnostic modalities. *J Hum Reprod Sci* 2014 Jan;7(1):30-3.
7. Thangappah RB, Paramasivan CN, Narayanan S. Evaluating PCR, culture and histopathology in the diagnosis of female genital tuberculosis. *Indian J Med Res* 2011 Jul;134:40-6.
8. Bhanothu V, Theophilus JP, Rozati R. Use of endo-ovarian tissue biopsy and pelvic aspirated fluid for the diagnosis of female genital tuberculosis by conventional versus molecular methods. *PLoS One* 2014;9(5):e98005.
9. Goel G, Khatuja R, Radhakrishnan G, et al. Role of newer methods of diagnosing genital tuberculosis in infertile women. *Indian J Pathol Microbiol* 2013;56:155-7.
10. Khanna A, Agrawal A. Markers of genital tuberculosis in infertility. *Singapore Med J* 2011;52:864-7.
11. Kohli MD, Nambam B, Trivedi SS, et al. PCR based evaluation of tubercular endometritis in infertile women of North India. *J Reprod Infertil* 2011;12:9-14.
12. Prasad S, Singhal M, Negi SS, et al. Targeted detection of 65 kDa heat shock protein gene in endometrial biopsies for reliable diagnosis of genital tuberculosis. *Eur J Obstet Gynaecol Reprod Biol* 2012;160:215-8.
13. Miwa I, Tamura H, Takasaki A, et al. Pathophysiologic features of "thin" endometrium. *Fertil Steril* 2009 Apr;91(4):998-1004.
14. Takasaki A, Tamura H, Miwa I, et al. Endometrial growth and uterine blood flow: a pilot study for improving endometrial thickness in the patients with a thin endometrium. *Fertil Steril* 2010 Apr;93(6):1851-8.
15. Sher G, Herbert C, Maassarani G, et al. Assessment of the late proliferative phase endometrium by ultrasonography in patients undergoing in-vitro fertilization and embryo transfer (IVF/ET). *Hum Reprod* 1991;6:232-7.