

Assessment of Conception Rate in Infertile Couples with Genital Tuberculosis Diagnosed with Multiplex Polymerase Chain Reaction

Anjali Patil^{1*}, R. P. Patange²

{¹Assistant Professor, ²Professor and HOD} Department of OBGY, KIMSDU, Malkapur Maharashtra INDIA.

*Corresponding Address:

dr.anjalipatil21@gmail.com

Research Article

Abstract: Objective: Mycobacterium infections of genital tract of couple have an impact on fertility. Both suspected male or female were subjected to investigation of genital TB and treating the affected or the couple and rise in pregnancy rate was studied. **Methods:** After detailed history and investigations to rule out other causes of infertility in couple both husband and wife who were strongly suspected of genital tuberculosis were tested by multiplex Polymerase chain reaction(PCR) technique for confirming evidence of genital tuberculosis. The affected individual or both husband and wife were treated effectively by antitubercular therapy and results were correlated in terms of pregnancy outcome. **Results:** Out of 229 couples studied 208 females and 99 males were diagnosed of having latent genital tuberculosis with multiplex DNA TB PCR test. After ATT pregnancy outcome was studied. Overall pregnancy rate was 135 (59%). The spontaneous conception rate was 91 (67.4 %) within 6 months of ATT. This rate is much higher compared to other studies in which only the female partner was diagnosed and treated for genital tuberculosis. **Conclusion:** The diagnosis of genital tuberculosis is very difficult. It is considered as severe form of extrapulmonary tuberculosis. This silent invader creates diagnostics dilemmas. But accurate diagnosis of early genital tract tuberculosis in one or both partners and treatment accordingly has given infertile couple an excellent chance for spontaneous conception.

Keywords: infertility, genital tuberculosis, PCR, anti tubercular therapy.

Introduction

Tuberculosis is an ancient disease that remains elusive in the 21st century and is on the rise. The reasons of increasing incidence are

- Poverty and widening of gap between poor and rich ,
- Neglect of disease (inadequate care e.g. Developing countries, detection, diagnosis and cure.)
- Collapse of health infrastructure in countries with severe economic crisis
- Impact of HIV pandemic [1]

Tuberculosis continues to be leading Killer disease for Indian adults among all infectious diseases. It is estimated that 5-13% of pulmonary tuberculosis develops genital involvement. [2,3,4] Genital tuberculosis should always

be considered as a probable cause of infertility. 1/5th of World's tuberculosis cases are in India. In developing countries more than 75% of TB patients are in economically productive age group of 15-45 years, [5] Average worldwide incidence of female genital tuberculosis in infertile population has been reported as 5-10% with range between < 1% in USA and about 10% in India.[6] Infertility is the commonest symptoms associated with genital tuberculosis [2,7]and it seems to be an important under diagnosed factor in Infertility[8] The exact incidence of genital TB in female and male is not known because partly the disease remains silent and there is lack of reliable confirmatory investigations. Genital Tuberculosis is secondary to tuberculosis elsewhere in body and in most cases sexual transmission is least likely. Haematogenous or lymphatic spread is most common method of spread. Infection can spread in females from intra abdominal sites through fallopian tubes. When an individual acquires the infection 90% do not get infected but develops latent infection. 3% to 5% latent TB can become active in first year and 5% to 15% can acquire the disease later. Thus incidence of active tuberculosis in infected individual is only 10%.[9] Depending on virulence of organism, immune response of host the disease remain either active or becomes asymptomatic with latent infection persisting for many years up to 20 years.[10] The disease can reactivate when host response becomes low. During the process of reactivation, the bacilli induce immunomodulation within local tissues which mimics process seen during infection. The final effect depends on tissue resistance. [11] The adverse impact impairs the delicate function of reproductive organs continuing the consequences or infection may remain dormant or cured. It is realized that fertility can be impaired in tubercular disease even when there is no anatomical damage. This is brought about by intense immunomodulation and probable physical changes that organism brings about when it lies dormant in the body(12). So with any measure to treat infertility

tuberculosis must be excluded. In males tuberculosis can result in infertility but is an uncommon first sign of male genital TB. Infection can involve any part of reproductive tract including prostate, seminal vesicles, epididymis, testis in that order. Oligospermia is common and may lead to infertility. Infertility in males results from inflammation and scarring that follow infection resulting in distortion of normal anatomy and causing obstruction. Sometimes infertility may be first presentation and may have no other symptoms. [13] Testis is a rare site for tuberculosis involvement. Shah et al in his study concluded that epididymal infection due to TB could resolve using ATT. [14] Dr. Shah in his series found appearance of sperms in the ejaculate following medical therapy who prior to therapy were azoospermic.[15]

The semen analysis may be useful in evaluation of male infertility associated with prostatic TB. The reported semen analysis revealed low volume in 89% of patients and azoospermia or oligospermia in 53% of patients. Significant leukocytospermia was identified. Prostate Specific Antigen (PSA) levels may be elevated. [16] Patient may be asymptomatic but can present with testicular mass, nodules over epididymis or vas, frequency and burning micturition, ulceration of glans and erectile dysfunction. Thus in males minimally invasive diagnostic approach should be preferred while managing the active infection. Severe male factor cases will require assisted reproduction which provides results comparable to those in men without this disease(17)

Materials and Methods

Mostly females are investigated and treated for genital tuberculosis. But need to screen the male partner was felt when pregnancy was not achieved in spite of treating the female partner after ATT. In total 229 infertile couples in whom either male or female or both who were suspected and confirmed to have genital tuberculosis were enrolled in the study from June 2009 to June 2011 and follow up assessment was done for two years.

Assessment criteria

Detailed history of the infertile couple was taken. In females previous records of investigations, treatment, Coital history, history of recurrent vaginitis, menstrual pattern, (oligomenorhea, menorrhagia, scanty, altered colour, foul smell) and history of dysmenorrhea and dysparunia was noted. Per vaginal examination was done to see for tenderness and palpable masses if any and per speculum examination was done to see for cervical lesions suggestive of genital TB. All patients with altered menstrual pattern were assessed for ovulation and hormone profile was done. Patients were called on day one of menses within 12 hours of onset and menstrual blood was collected with aseptic precautions in sterile test tubes after informed consent and sent for multiplex PCR

for mycobacterium test. Those who had scanty bleeding were called for endometrial biopsy under GA and sent for multiplex TBPCR test and results were noted. In males – history was taken about occupation, coital history, any urinary complaints, recurrent balanitis, addiction of tobacco was noted. Any h/o antibiotics taken, any systemic complaints of malaise, evening rise of fever was noted. Routine investigations like haemogram, blood group, AuAg, blood sugar, HIV status of both were done. Previous semen analysis reports were assessed and any records of previous treatment were noted. Semen analysis was done according to WHO criteria and TB PCR test was done on semen under aseptic precautions after informed consent.

All couples with either one or both partner who had positive TBPCR test were taken for the present study. Prior to this a long course of antibiotics was given. Males were given antioxidant, Vitamin E, C and arginitric powder as adjuvants. All those with positive PCR were counselled and treated with antitubercular treatment. They were subjected to four drug regime (HRZE) INH 300 mg, Rifampicin 450-600mg, Pyrizinamide 1200-1500 mg, Ethambutol 800-1200 mg for 2 months followed by same doses of INH and Rifampicin for 4 months. Only one case had hepatotoxicity. Another had visual disturbance for which ethambutol was stopped. Patient's previous reports of hysterosalpingography or laparoscopy were reviewed. Females with positive TB PCR test were started ATT without undergoing HSG or Laparoscopy for fear of flare of the disease. LFT was done prior to ATT and repeated after 1-2 months of treatment to rule out hepatotoxicity. The patients were asked to report any time if they had any complaints or side effects of drugs. Barrier contraception was advised for first two months. They were called if missed menses or symptom s/o pregnancy were seen. Any improvements in menstrual pattern, symptomatic relief of dysmenorrhea or dysparunia were noted. In males improvements regarding symptomatic relief if any were noted and repeat semen analysis was done. We in our study did not do HSG or Laparoscopy prior to completion of ATT for fear of flare up of disease due to trauma to pelvic organs. All the patients were followed for spontaneous conception till ATT was complete. Only those with azoospermic husbands were started with I.U.I treatment after completion of 3 months of ATT. Laparoscopy & Hysteroscopy was planned for patients who failed to conceive after full course of ATT. The outcome in terms of pregnancies achieved was documented.

Results

In the present study 229 infertile couples were enrolled during the period of two years from June 2009 to June 2011. In these 229 couples studied minimum age of

wife was 18 years and maximum 45 years with mean age 27.67 years and SD 21.18 years. Maximum females were below 40 years. The minimum age husband was 21 years and maximum 50 years with mean age 31.5 years and SD 26.21 years. Minimum infertility period in these couples was of 1 year in 2 (1.1%) cases and maximum 25 years in one (0.5%) case with mean 6.66 year with SD 16.96 years. There was a very high proportion of cases 220 (96%) with h/o of infertility period up to 15 years, amongst these 118 (51.5%) were with 2-5 years of infertility. While very few, 9 (3.9%), were with h/o of infertility period between 16 to 25 years. (Table 1).

Table 1: Years of Infertility

Years of Infertility	No of Couples	Percentage
1-5 yrs	120	52.4%
6-10 yrs	71	31.0%
11-15 yrs	29	12.7%
16-20 yrs	8	3.5%
21-25 yrs	1	0.4%
Total	229	100.0%

Amongst 229 couples very less proportion of cases, 46 (20.08%), were of secondary infertile type. Significantly high proportion 36(78.26%) of them conceived (Chi-

Square = 8.869, p = 0.0029). However, 99(54.1%) of primary infertile cases conceived.

Table 2: Type of Infertility & Pregnancy Rate

Type	No of Couples	Total pregnancy	Percentage
Primary	183	99	54.1%
Secondary	46	36	78.3%
Total	229	135	59.0%

In case of 99 husbands who had positive semen TB PCR, normal semen parameters were seen in 25 cases, while 74 cases had abnormal semen parameters in terms of increased viscosity (39), oligozoospermia (36), aggregation, significant puscells (13), azoospermia (3) asthenozoospermia (63). 50(50.5%) wives of these 99 men conceived. In these 99 males there was significant proportion of spontaneous pregnancy in women with normal husband semen parameters as compared to abnormal semen parameters(chi square-7.733,p=0.0054). However there was no significant difference in pregnancy rate when ART were used (chi square-1.206,p=0.2721) Out of 130 TBPCR negative males spontaneous pregnancy rate in their wives was significantly high when semen report was normal (chi square-16.817, p<0.001)

Table 3: Semen TBPCR status and pregnancy rate

Semen TBPCR	Normal or abnormal Semen report	No. of cases	Pregnancy achieved				Total pregnancy
			Spontaneous pregnancy	IUI	D-IUI	IVF	
Positive PCR	Normal	25	14	1	0	0	15(60%)
	Abnormal	74	19	9	4	3	35(47.3%)
Total		99	23	10	4	3	50(50.5%)
Negative PCR	Normal	80	47	4	1	3	56(56%)
	Abnormal	50	11	6	11	1	29(58%)
Total		130	58	10	12	5	85(65.3%)

It has been observed that abnormal pelvic findings such as tender uterine movements and tenderness in fornices, nodularity over cervix and cervical erosion, recurrent vaginitis were noted in 147 (70.7%) TB PCR positive females. Out of them 90(61.2%) achieved pregnancy after treatment. The pregnancy rate was higher in abnormal per

vaginal findings. However the difference in pregnancy rate in normal and abnormal per vaginal findings cases was not significant (Chi-Square = 0.08802, p = 0.7667). Similarly there was no difference in pregnancy rate in normal and abnormal pv findings in women with negative TBPCR (Fisher's exact test p=1.000)

Table 4: Per Vaginal Findings

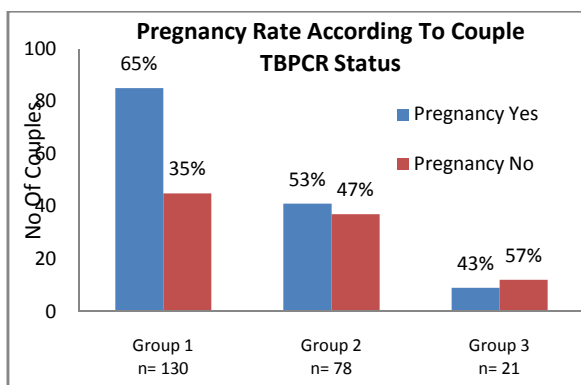
Test	TB PCR positive	Pregnancy Yes	Pregnancy No	TB PCR negative	Pregnancy Yes	Pregnancy No
Normal	61	36	25	10	4	6
Abnormal	147	90	57	11	5	6
Total	208	126 (60.6%)	82(39.4%)	21(9.2%)	9(42.8%)	12(57.2%)

As per inclusion criteria, at least one of the partners of these 229 couples had positive PCR. Among 130 (56.7%) couples in which wife had Positive PCR and Husband Negative PCR, 85 couples (65.4%) achieved pregnancy. In group of 78 (34.0%) couples where both

husband and wife had positive PCR, 41 (52.6%) had experienced pregnancies. However, in 21(9.17%) couples where only male partner was positive PCR 9(42.9%) pregnancies were achieved. Thus the total pregnancies achieved were 135 (59.0%) out of 229 couples.

Table 5: Total Pregnancy Rate

No. of Couples	Conceptions	No conception
229	135	94
Percentage	59.0%	41.0%



Group 1- Wife TB PCR Positive Husband semen TB PCR Negative

Group 2- Both wife and husband TBPCR positive

Group 3- Wife TBPCR negative & Husband TBPCR positive

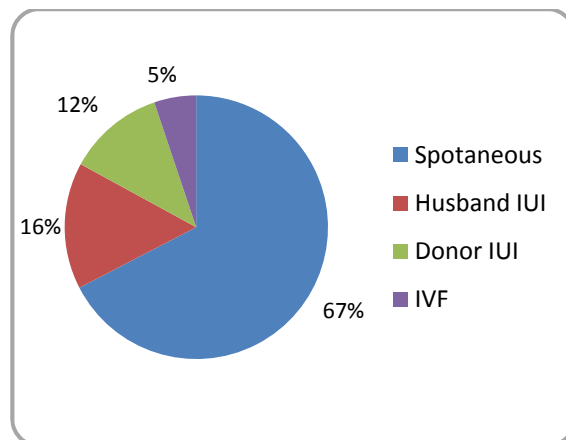
Table 6: TB PCR positive cases and pregnancy status

Pregnancy	Only wife TB PCR positive	Both TB PCR Positive	Only husband TBPCR positive	Total no. Of cases
Conception	85 (65.4%)	41 (52.6%)	9 (42.9%)	135 (59%)
No pregnancy	45 (34.6%)	37 (47.4%)	12 (57.1%)	94 (41%)
Total cases	130 (100%)	78 (100%)	21 (100%)	229 (100%)

High proportion of women with positive TBPCR and who had their husbands semen TBPCR test positive conceived which was significant (Chi square-5.786, p value-0.055 significant). Of 135 women conceived, very high number of women 91 (67.4%) conceived spontaneously. Women those conceived with Donor IUI had under gone many failed Donor IUI cycles in past. (Table 7)

Table 7: Method of conception

Method of conception	No	Percentage
Spontaneous	91	67.4%
Husband IUI	21	15.5%
Donor IUI	16	11.9%
IVF	7	5.2%
Total	135	100.0%



Out of 208 women with positive TBPCR 81 cases had irregular menstrual cycles while 97 women had regular cycles, 30 cases had menorrhagia. While out of 21 women with negative TBPCR only 5 cases had irregular cycles and 2 cases had menorrhagia. It was observed that, 113 (83.7%) women had full term deliveries. The babies had 8-10 Apgar score at birth with weight 2.4kg – 3.5kg. Only two babies were stillborn, 14 women aborted. Only one case is still undergoing antenatal care.

Table 8: Pregnancy Outcome

Outcome	No.	Percentage
Full term Delivery	113	83.7%
Preterm	5	3.7%
Abortion	14	10.4%
Stillbirth	2	1.5%
Ongoing	1	0.7%
Total	135	100.0%

Discussion

Extra pulmonary TB is difficult in making conclusive diagnosis as it is paucibacillary disease. In India Genital TB causes 10% of all infertility in women and 58% of all genital TB present with infertility [18]. The disease is responsible for 5% of all female pelvic infection. The disease is frequently asymptomatic and the diagnosis requires high index of suspicion [19]. The typical presentation of TB includes infertility (58-60%). So genital TB should therefore always be considered as a probable cause in diagnostic work up of infertile couple especially in population with high prevalence of tuberculosis as in India. Other than infertility the clinical symptoms are pelvic pain, menstrual irregularity (10-40%) like menometrorrhagia, oligomenorrhea and amenorrhea. [20]. Pelvic tuberculosis should be suspected in chronic PID refractory to standard antibiotic therapy. [21]. Diagnosis of early TB is difficult and early diagnosis may be associated with a more favorable result before extreme genital damage occurs. [22]. When clinical suspicion is high and smear, culture, histopathology reports are negative and yet signs and symptoms

suggestive of TB are apparent then PCR technique is the method of choice for identifying the disease.[23] It is said that due to test like PCR genital tuberculosis can be seen even in presence of normal HSG findings and treatment of these cases gives rewarding results as far as fertility is concerned [24]. In present study 106 cases (55.6%) had normal HSG findings. The coordinated ovarian endocrine activity are disrupted either directly through toxins produced by mycobacterium TB or indirectly by adverse immune modulatory change in intra follicular environment. The consequences may be gonadotropin deficiency, anovulation, endometrial hyperplasia, LPD etc[25] which prevents nidation. In proved genital tuberculosis endometrial and glandular hyperplasia has been demonstrated associated with chronic anovulation [26]. In females irregular menses, ovulation disorders, decreased endometrial receptivity, fallopian tubal disorders can occur. So detailed history of menstrual complaints is must. Pelvic inflammatory disorders are one of the most prevalent causes of infertility. In this regard it has been mentioned that about 11% of tuberculous pelvic inflammation can occur with no clinical symptoms. [27] In the present study 147 cases (70.7%) had chronic pelvic inflammatory disease diagnosed on per vaginal exam. In males though uncommon, infertility may be the first presentation of genitourinary tuberculosis and patients may have no other symptoms. Involvement of genital tract occurs usually in reproductive age group. Epididymis is one of the favoured sites for tuberculous infections.

Semen analysis may be useful in evaluation of male infertility. In their study on TB of genitourinary system by Klaus revealed low value in 89% of patients & azoospermia or oligospermia in 53% of patients.[16] In the present study 99(43.2%) males had semen TB PCR test positive which can be compared to study by K CHAWALA in April 2012 who had 36.4% TBPCR positive in males[28] while N SHARMA had 42.3% males detected positive with semen TB PCR [29] In present study abnormal semen parameters like highly viscous semen, oligozoospermia, asthenozoospermia, aggregation, azoospermia were found in 74 (74.7%) out of 99 cases with positive TB PCR . These patients were previously given lot of antibiotics and adjuvant to increase sperm count & semen quality. Wives with azoospermic husbands had undergone repeated donor I.U.I failed cycles. All the TBPCR positive patients (male and female) were given ATT after explaining all probabilities of side effects and followed for 6 months. All the patients in this study were HIV negative. We have found genital tuberculosis though less common in male partners in 99 cases (43.2%) and treatment to both or only males has given us a rise in terms of pregnancy outcome

up to 135 cases i.e. 59% with 113 live births. The pregnancy rates reported in some other studies in female genital tuberculosis cases with positive PCR ranged from 19.35% to 59.8%. Suman Puri and Bhavana Bansal in march 2009 investigated 60 patients for genital tuberculosis by PCR technique 28 patients were positive (46.6%) and the pregnancy rate was 19.35% [30] In a study by Vidushi, Alka kriplani and others in 2011 on genital tuberculosis in 196 cases and fertility outcome after ATT 31% pregnancies were achieved.[31] In a study of Infestation of endometrium by mycobacterium tuberculous bacilli- cause of reproductive failure by RAJIB GON CHOUDHARY and others at Kolkata had positive DNA PCR in 230 cases and their pregnancy rate was 37.3% after ATT for 6 months[32] V.N JINDAL S VERMA AND Y BALA in their study of 443 cases in 2011 on fertility outcomes following ATT on sole basis of positive PCR test for endometrial tuberculosis 52 patients conceived spontaneously out of 169 patients. The overall pregnancy rate was 59.8%[33] In our study we have diagnosed genital tuberculosis in 99 male partners (43.2%) out of 229 couples. Treatment to affected individual or both has given us pregnancy rate of 59%. Spontaneous pregnancies were achieved in 91(67.4%) women, all within 6 months after initiation of ATT. Those who did not conceive spontaneously were subjected to additional treatment with assisted artificial reproductive techniques like intrauterine insemination and IVF. In highly prevalent country for tuberculosis as in India, the fact that males may be infected too with mycobacterium Tuberculosis should be considered while treating infertile couples. Screening, diagnosing and then treating male partners too will improve fertility outcome in shorter duration.

Conclusion

We all are aware that Infertility is a couple disorder. In this first-of -its-kind study in Indian infertile couples, one or both partners were diagnosed to have genital tuberculosis by multiplex TB PCR test. The spontaneous conception rate was much higher in this study than other studies as both partners were considered to have genital tuberculosis as a cause of infertility. Treatment with DOTS to one or both gave a good take home baby rate. This is an economically feasible option before switching to expensive methods of assisted reproductive techniques which have definitive role in cases with severe tubal disease and severe male factor. New researchers should be encouraged for conducting studies to find genital tuberculosis in one or both partners as a cause of repeated IVF failures in tuberculosis prevalent country as in INDIA.

Acknowledgements

1. Dr S V Kakade (Associate Professor) PSM Department, KIMSDU Malkapur Maharashtra INDIA.
2. Utkarsha Patil for compiling data.

References

1. Treatment of Tuberculosis guideline for National programmers W.H.O 3rd Edition 2003.
2. Punnonen R, Kiilholma P, Meurmen L; Female Genital Tuberculosis and consequent infertility. *Int J Fertil* 1983;28:235-38.
3. KK Deshmukh, JA Lopez, TAK Naidu, MD Gaurkhede, MV Place of laparoscopy in pelvic tuberculosis in infertile women – *Arch Gynecol*, 1985;237(suppl)197-200.
4. Chhabra S, Genital tuberculosis – a baffling disease: *Journal of obstetrics and Gynecology India*, 1990;40:569-73.
5. R.N.T.C.P India Central T.B. Division New Delhi. March-2006.
6. Jindal U N Genital tuberculosis: An important cause of Asherman's syndrome in India; *International journal of tuberculosis and lung disease* 2006.
7. Nogales-Ortiz F, Ildefonso T., Nogales FF: The pathology of genital tuberculosis -. *Obstetric Gynecol* 1979;53:422-428.
8. Oosthuizen AP., Wessels PH., Hefer JN: Tuberculosis of the female genital tract in patients attending an infertility clinic . *S Afr Med J* 1990;77(11);562-564.
9. Stead WW-. Pathogenesis of a first episode of chronic pulmonary tuberculosis in man: recrudescence of residuals of the primary infection or exogenous reinfection; *Am Rev Resp Dis* 1967;95:729-74.
10. Stead WW, Kerby GR, et. al-. The clinical spectrum of primary tuberculosis in adults: confusion with reinfection in the pathogenesis of chronic tuberculosis. *Ann Intern med* 1968;68:731-45.
11. Raghupathy R, Makhseed M, Azizieh F; Th1 & Th2 cytokine profiles in successful pregnancy and unexplained recurrent abortions ; In: Gupta SK, Editor. *Reprod Immunol* 1994;14:149-57.
12. Malik s- Genital tuberculosis and implantation in assisted reproduction. *Reviews in Gynaecological Practice* Vol 3; issue 3, September 2003;160-64.
13. Lubbe J, Ruef C, Spiig W, Dubs M, Sigg C. Infertility as the first symptom of male genitourinary tuberculosis. *Urol Int* 1996;56:204-6.
14. Gueye SM, Ba M, Syll C, Ndoeye Ak, Fall PA, Daiw JJ, et. al., epididymal manifestations of urogenital tuberculosis. *Prog Urol*. 1998;8:240-3 [PubMed].
15. Shah RS-. Obstructive azoospermia following genital tuberculosis may be reversible with medical therapy . *AUA2004 Abstract* 1600.
16. Klaus- Dieter Lessnau MD, FCCP. Tuberculosis of the Genitourinary System-- *Medscape Reference* Updated March 29, 2011.
17. Rajeev Kumar- Reproductive tract tuberculosis and male infertility, *Indian Journal of Urology* 2008 July September 24(3) 392-395(18).
18. Tripathi SN-, Infertility and pregnancy outcome in female Genital TB, *Int .J of Obst Gynec* 2002, vol 70, Page 159-63.
19. Baxi Asha , Neema Hansali, Kushal Manila , - Genital Tuberculosis in infertile women; assessment of endometrial TB PCR results with laparoscopy and hysteroscopy features; *The Journal of obstetric and gynecology of India* volume 61 number 3 may , june 2011 pages 301-306.
20. Tripathy and Tripathy.- Epidemiology and clinical features of genital tuberculosis-current concepts. *Frontiers in Obstetric Gynaecology* 2nd edition. Jaypee book 1999.
21. VARMA T, Tuberculosis of the female genital tract *Global Library of Women's Medicine* Oct 2008 DOI 10;3843/Glown 10034.
22. Gatongi DK, Gitah G, Kay V et al. Tuberculosis. *Obstet Gynecol* 2005;7:75-96.
23. Clarridges JE, Shawar RM, Shinnick TM, and Plikaytis B B: Improved diagnostic value of PCR in the diagnosis of microbiological tuberculosis in a routine microbiological laboratory . *J Clin Microbiol* 1993;31:2049-58.
24. Roy H, Roy S, Roy S. Use of PCR for the diagnosis of endometrial tuberculosis in high risk subfertile women in an endemic zone , *J obstet Gyneacol India* 2003;53:260-3.
25. Ravindranath N, Little-Ihrig L, Phillips HS, Ferrara n, Zelezinik AJ. Vascular endometrial growth factor messenger ribonucleic acid expression in the primate ovary . *Endocrinology*, 1992;131:254-60.
26. MGM pelvic inflammatory disease. In Rock JATJ editors *Editor-elind's operative Gynecology*. New York : Lippincot-Raven 1997:678-685.
27. VARMA TR-. Genital Tuberculosis and Subsequent fertility *Int.J. Gynecol .Obst* 1991;35:1-11.
28. K Chawla ; Role of PCR for diagnosing male genital tuberculosis - 22nd European congress of clinical microbiology and infectious disease April 2012 13:30-14:30.
29. Narotam Sharma, Zoab Ahmed et al- Incidence of genital tuberculosis in reproductive age group – *Journal of microbiology and biotechnology Research* 2013 (3):15-19.
30. Suman Puri, Bhavana Bansal - Diagnostic value of polymerase Chain Reaction in Female Tuberculosis Leading to infertility and Conception Rate After ATT, -. *JK Sciences* Vol 11 No 1, March 2009.
31. Vidushi Kulshrestha, Alka kriplani, Nootan Agrawal, Urvashi B. Singh, Tanu Rana - Genital Tuberculosis among infertile women and fertility outcome after antitubercular therapy, *International Journal of Gynecology Obstetrics* Volume 113, issue 3 – p 229-234. June 2011.
32. Rajib Gon Choudhary, Suman Kalyan Paine, Basudev Bhattacharjee - Infestation of Endometrium By Mycobacterium Tuberculosis Bacilli - Cause of Reproductive Failure, *AJMS* (2010)3(4):322-331.
33. U.N. Jindal, S. Verma, Y. Bala- Favourable infertility outcomes following antitubercular treatment prescribed on sole basis of a positive polymerase chain reaction test for endometrial tuberculosis.- *human Reproduction* Vol 0 No 0 pp 1-7 March 2012.