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## Female Infertility Due to Genital Tuberculosis: Bangladesh Perspective

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Infertility is defined as the inability of a couple to achieve conception after one year of unprotected coitus. Globally, about 8.0% to 12.0% of all couples are infertile<sup>1</sup>. In developing countries like ours, this problem is sidelined due to population explosion. The situation cannot be neglected as failure to bear children often leads to psychological distress, social disgrace and divorce. According to a report, 15.0% couples of Bangladesh are unable to conceive and bear a child<sup>2</sup>. Genital tuberculosis is a chronic inflammatory disease process. The resulting inflammatory cells create tubal damage and adhesion constraining ovum transport<sup>3</sup>. Tubal obstruction may result in pyosalpinx or hydrosalpinx or a low degree of interstitial salpingitis thus interfering with ciliary activity and muscle peristalsis<sup>4</sup>. Minimal damage to the tube may lead to ectopic pregnancy<sup>5</sup>. Extensive damage may lead to complete tubal occlusion<sup>6-7</sup>. Peri-tubal adhesions and tubo-ovarian mass have been found in 47.2% of cases<sup>8</sup>. Various grades of intrauterine adhesion (Asherman's syndrome) or non-receptive endometrium have been reported in association with genital tuberculosis9. The infected uterine cavity is deformed due to adhesions and synechiae. Endometrial involvement may result in an endometrial ulcer or accumulation of caseous material to form pyometra. Intrauterine adhesions and partial obliteration of the uterine cavity may also occur10.

A healthy intrauterine pregnancy requires a healthy endometrium. The endometrial part of implantation involves the secretion of several molecules or markers

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generated by hormonal, biochemical, genetic and immunomodulatory changes within the endometrium. Cytokines and growth factors bring immuno-modulatory changes. Some of these cytokines and growth factors help in implantation, while others antagonize the procedure. If an immuno-modulatory response is favorable, helpful cytokines and growth factors will appear, and successful implantation will take place, known as the T helper 2 (Th2) response. On the other hand, if harmful immuno-modulators develop, the response is said to be a T helper 1 (Th1) response, resulting in implantation failure. The mere presence of MTB in the endometrium creates an inflammatory environment and excites inflammatory process. Thus, there is production of adverse cytokines and antibodies, inhibiting the down-regulation of Th111.

Depending on the virulence of the organism and the immune response of the host, the disease remains either active or becomes asymptomatic with latent infection persisting for many years. Individuals with latent infection contain dormant, yet viable bacilli, which may re-activate when the host response becomes low. During the process of reactivation, the bacilli induce immune modulation within the local tissues, which mimics the process seen during infection. There is release of harmful cytokines like IL2, TNFα and INFγ. The final effect will depend upon how strongly the host tissue (endometrium/ ovary) can resist this trauma. If unable to resist, the endometrial receptivity will be affected adversely. Once this adverse impact has been established on the delicate function of these reproductive organs, the consequences may continue to persist<sup>10-11</sup>. In one study, it was found that the level of IFN  $\gamma$  and TNF $\alpha$  were significantly higher (p-value = 0.01) in diagnosed genital tuberculosis patients and had higher sensitivity and specificity than the TB-negative patients<sup>12</sup>.

Detection of infertility due to GTB becomes difficult

with the available TB diagnostic tools owing to paucibacillary nature of the bacteria and varied presentations. In Bangladesh, few sporadic works on FGTB have been conducted at different times. The actual rate of infertility in Bangladesh (BD) in still unknown but World Infertility Survey revealed that in South Asian Country stated 4.0% in Bangladesh and 15.0% of woman9 FGTB with infertility (40.7%) as the only symptom, commonly seen among young women in their reproductive years belonging to the age group 22 to 40 years<sup>1,12</sup>. Majority of the cases resided in urban areas and completed their graduation<sup>1</sup>. In one study, endometrial tissues from 91 infertile women tested TB positive (64.8%) by different laboratory tests such as AFB Microscopy, Culture, PCR. Among them, PCR detected highest positive cases with 51.1% sensitivity and 72.7% specificity in comparison to AFB smear microscopy and culture with a very high significant association. A recent study from Bangladesh detected 12.5% infertility cases among 78 suspected FGTB with 11.5% positive for TB by both AFB Microscopy and Culture<sup>12</sup>. Large scale studies on FGTB needs to be conducted in Bangladesh to ascertain the precise incidence of FGTB in the general population, as the majority of cases remain undiagnosed<sup>7</sup>.

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