



Genital tuberculosis and its consequences on subsequent fertility

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OBJECTIVE(S) : To study the effect of tuberculosis, still a common infectious disease in the third world countries on female fertility, and the outcome of IVF-ET in these patients.

METHOD(S) : Routine hysteroscopy was done with or without laparoscopy in all patients before admitting them in our in vitro fertilization and embryo transfer (IVF-ET) program. Results of IVF-ET were analyzed.

RESULTS : The incidence of genital tuberculosis in patients presenting with infertility was 16.4%. History of extra-genital tuberculosis was present in 28.04% and tubercular abdomen in 50% of patients. Laparoscopy findings in 55 patients showed tubal involvement in 72.4% cases and frozen pelvis in 17.2%. 24.4% patients had synechias of varying degrees at hysteroscopy and 40% of them had endometrial biopsy positive for tuberculosis. The pregnancy rate after IVF-ET was 19.1% per transfer.

CONCLUSION(S) : Tuberculosis is one of the major etiological factors for female infertility. IVF-ET offers the only realistic treatment to these unfortunate women. Preliminary assessment of endometrium by hysteroscopy is helpful in assessing prognosis in these cases.

Key words : genital tuberculosis, IVF-ET, pregnancy rate

Introduction

Tuberculosis remains a major health problem in many developing countries including India and in these countries genital tuberculosis is responsible for a significant proportion of women presenting with infertility¹. The actual incidence of genital tuberculosis cannot be assessed accurately in any population, since the disease is discovered incidentally in many patients, and in a large number of symptomless patients, this disease remains undiscovered². It is estimated that 5-10% of infertile women the world over have genital tuberculosis although this varies from less than 1% in the United States to nearly 18% in India².

The infertility due to female genital tract tuberculosis is

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considered an almost absolute one, and the medical therapy, surgical tuboplastic intervention, and combined treatments are all associated with a relatively poor fertility outcome^{2,3}. The recent availability of hysteroscopy, and in vitro fertilization and embryo transfer technic (IVF-ET) has however given promising results in these patients.

Methods

A retrospective analysis of 82 women suffering from infertility due to genital tuberculosis during the two year period from January 2001 to December 2002 was done at our center. A detailed history, including demographic particulars, was taken and a thorough clinical examination done. Apart from routine hematological investigations, specialized investigations consisting of transvaginal sonography of uterus and adnexa, hormone profiles, immunological assays, and endoscopy were performed as and when needed. Currently advocated method of polymerase chain reaction for mycobacterial tuberculosis was not available to us. Although it is not absolutely diagnostic, it is desirable to employ it.

Past history of antitubercular treatment was noted in detail,

including the duration of treatment, organs / systems involved and the diagnostic criteria by which tuberculosis was confirmed. Previous operative interventions and operative findings were recorded in detail. Details of laparoscopy findings like unilateral or bilateral tubal block, adhesions, hydrosalpinx, tubo-ovarian masses and tubercles were noted. Postmenstrual hysteroscopy was performed in all patients.

Results

Tubal factor was responsible in 186 out of the 500 (37.2%) women who presented with infertility during the study period. 44.1% (82/186) patients were found to have genital tuberculosis. The median age of these patients was 31 years (range 22 to 40 years). The duration of infertility ranged from 1 to 23 years (median 7 years). Fifty-one women suffered from primary infertility while 31 had secondary infertility.

Laparotomy had been done in nine patients for ectopic pregnancy, in four for intestinal pathology, in one for tubo-ovarian mass, in eight for history of tuboplasty, and in two for ovarian cyst. In one patient, laparoscopic adhesiolysis and fimbrioplasty were done.

Thirty-three patients had already undergone laparoscopy and received full course of antitubercular treatment for genital or extragenital tuberculosis. Twelve patients had tubal block, with or without adhesions, five had frozen pelvis, five had hydrosalpinx and 10 had tubercular salpingitis. One patient had normal findings at laparoscopy. During our study, we performed laparoscopy in 25 women. Tubal blockage was detected in 21 of them while four had patent tubes with mild hydrosalpinx and flimsy adhesions. Five patients had frozen pelvis while 13 had varying degree of adhesions. Nine patients had hydrosalpinx, six had tubercles on the uterus and adnexa, and six had tubercular salpingitis (Table 1).

Table 1. Laparoscopy findings.

Findings	Previous laparoscopy (n=23)	Laparoscopy during study (n=25)
Tubal block	12	21
Adhesions	8	13
Frozen pelvis	5	5
Hydrosalpinx	5	9
Tubercular salpingitis	10	12

Some patients had more than one abnormal finding

Table 2. Results of IVF- ET in patients with genital tuberculosis.

	Frydman et al ⁶	Parikh et al ⁷	Soussis et al ¹¹	Marcus et al ¹²	Gurgan et al ¹³	Present study
Number of patients	20	30	13	10	24	49
Number of transfers	32	NM	21	31	44	89
Pregnancy rate per transfer	8/32 (25%)	6/3 (16%)	6/21 (28.6%)	6/31 (19.35%)	4/44 (9.1%)	17/89 (19.1%)
Delivery/Number of patients	6/20 (30%)	5/30 (16.7%)	4/13 (30.7%)	4/10 (40%)	1/24 (4.2%)	12/49 (24.5%)
Abortion/Number of patients	1/20 (5%)	- -	2/13 (15.4%)	1/10 (10%)	3/24 (12.5%)	5/49 (10.2%)
Ectopic pregnancy/Number of patients	1/20 (5%)	1/30 (3.3%)	- -	1/30 (10%)	- -	- -

NM - Not Mentioned

In 24 patients, even though laparoscopy was not done previously, we did not perform laparoscopy for various reasons. These included biopsy proven tubercular endometritis in three patients, advanced age (>38 years) with positive serology in three, history of abdominal tuberculosis in 14 including six who had tuboplasty and three who had tubercular salpingitis on hysterosalpingography, and tuboplasty and history of ectopic pregnancy in four.

Hysteroscopy was attempted in all patients. However in two patients it could not be performed because of cervical stenosis. On hysteroscopy, 57 patients had normal uterine cavities, two had a submucous fibroid and one had polyps, while synechias of varying degrees were present in 20 patients. Eight patients with synechias had biopsy proven tubercular endometritis. Synechiotomy followed by intrauterine device insertion and estrogen supplementation was the treatment given to six patients who had dense synechias and reduced uterine capacity. In the remaining 14 patients, flimsy synechias were broken by the scope and as the uterine capacity was adequate estrogen supplementation was not given. Of these 20 patients with synechias, one had primary amenorrhea, four had secondary amenorrhea, three had only spotting at menstruation, five had scanty flow and seven had normal menstrual flow. Of these 20 patients, 16 underwent 26 cycles of IVF-ET resulting in four pregnancies (15.38%; 4/26 pregnancies per transfer). All had singleton pregnancy, three delivered at term and one at 32 weeks.

Tubercular endometritis was present in 10 patients on biopsy. Forty-one patients had tubercular abdomen of whom 16 had positive biopsy for tuberculosis. Family history of tuberculosis was present in eight patients. Twenty-three patients had received antitubercular treatment for extragenital tuberculosis.

Two of our patients conceived spontaneously while on antitubercular treatment and delivered at term. All women were counseled for IVF-ET procedure. However, only 49 opted for it and underwent 89 cycles of IVF-ET. Seventeen women conceived of whom five aborted. Nine women had singleton pregnancy while three had twin pregnancy. One woman with singleton pregnancy delivered prematurely at 32 weeks but went home with a healthy baby. Of the remaining 11 women, two delivered vaginally and nine by cesarean section. All of them had healthy babies. The total pregnancy rate per transfer was 19.1% (17/89) in women with genital tuberculosis (Table 2). One patient conceived spontaneously after down regulation for frozen embryo transfer and one conceived spontaneously after two failed attempts at IVF-ET.

Discussion

Although the frequency of tuberculosis has been reported to have decreased significantly during the last many years as a result of widespread vaccination, antibiotic treatment, and improved socioeconomic conditions, the female genital tuberculosis and the infertility related to it are much more frequent in third world countries ⁴.

The average incidence of genital tuberculosis in infertility clinics throughout the world is 5-10% and it varies from 0.69% in Australia to 17.4% in India ². Out of the 500 patients who came to us for infertility because of various reasons, 82 had genital tuberculosis, giving an incidence of 16.4%. Classically, female genital tuberculosis has been described as a disease of young women, with 80-90% of patients diagnosed between 20 and 40 years of age ². The median age of women with genital tuberculosis in our study was 31 years (range 22-40 years). About 20% of patients with genital tuberculosis give a history of tuberculosis in their immediate family ². In our study, family history was present in 10% of cases.

Genital tuberculosis is almost always secondary to tuberculosis elsewhere – usually lungs and sometimes kidneys, gastrointestinal tract, bones, and joints. Occasionally it is part of a generalized miliary disease process. The mode of spread is usually hematogenous or lymphatic and occasionally via direct contiguity with an intraabdominal or peritoneal focus ². Primary genital tuberculosis is extremely rare. In most series, a history of previous diagnosis of or treatment for extra-genital tuberculosis is present in 25-50% of patients ^{2,3}. Inactive pulmonary lesions are demonstrable in about one third of the patients who have genital tuberculosis ². History of extra-genital tuberculosis was present in 28.05%(23/82) of the patients in our study. (Table 1).

Tubercular peritonitis is seen in combination with female genital tract tuberculosis in approximately 45% of patients and is responsible for extensive adhesions ³. History of tubercular abdomen was present in 50% of the patients in our study.

Fallopian tubes constitute the initial focus of genital tuberculosis in a majority of the cases and tuberculosis has accounted for approximately 5% of all cases of salpingitis in many parts of the world ^{3,4}. The tubes are involved in at least 90% cases and the disease probably starts there ³. The finding of endometrial tuberculosis almost always means that the tubes are infected, although not necessarily closed. But tubercular salpingitis is sometimes found without associated endometritis. The gross appearance varies and is often consistent with chronic salpingitis. Rarely, the peritoneal

surface of the tubes is studded with tubercles and filled with caseous material³. Dense adhesions are also seen in some cases. In our study, laparoscopy findings in 58 patients showed tubal involvement in 72.4% and a frozen pelvis in 17.2%.

The endometrium is involved in approximately 50-60% of women with genital tuberculosis^{2,3}. In our study, however, only 12.5% of patients showed positive histopathological diagnosis on endometrial biopsy, probably because postmenstrual biopsy was taken at the time of hysteroscopy in many patients, whereas premenstrual biopsy is desirable.

A preliminary hysteroscopy was performed in all patients with genital tuberculosis because of the possibility of endometrial and cervical damage due to the tubercular process. It gave us valuable direct information about endometrial trophicity. Genital tuberculosis is one of the main etiological factors causing synechia of uteri⁵. On hysteroscopy, synechias were present in 25% of patients of whom 40% had positive endometrial biopsy. Therefore a hysteroscopic examination should be performed routinely, before admitting patients with genital tuberculosis into an IVF program. The preliminary evaluation reduces the failure rate and increases the cancellation rate⁶. A history of tubercular endometritis represents a special indication for a preliminary hysteroscopy before IVF⁶. Preferred treatment for synechias is lysis of adhesions at hysteroscopy, followed by immediate insertion of an intrauterine device to prevent further adhesions⁶. Use of estrogens or a combination of estrogen and progestogen for rapid endometrial growth has been controversial⁵. The success of treatment regarding term deliveries and rate of abortions depend on the severity of adhesions⁵. Twenty-five percent of the patients with intrauterine synechia presented with amenorrhea while 40% had mild to severe hypomenorrhea. In a study by Parikh et al⁷, 59% patients with genital tuberculosis developed oligomenorrhea.

The treatment consists of initial multidrug medical therapy for a period of 6 months to 1 year. Pregnancy after a diagnosis of genital tuberculosis is rare and when it does occur, it is more likely to be an ectopic one or result in spontaneous abortion.

In 1976, Schaefer² reviewed 7000 cases of genital tuberculosis from the literature and stated that 155 patients had full term pregnancies (2.2%), 67 had abortions (0.9%), and 125 (1.8%) had ectopic pregnancies. When the histologic or bacteriologic examinations were used as proof of genital tuberculosis, the number of full term pregnancies was reduced to 31. The conception rate was 19.2% while the live birth rate was only 7.2% in a study

by Tripathy SN⁸. The risk factors not conducive to pregnancy are secondary amenorrhea, no endometrium on curettage and negative chromopertubation⁸. Tuboplastic macro- or micro-surgical operations in these cases very rarely or almost never lead to term pregnancies. They even increase the chances of tubal pregnancy and may reactivate silent pelvic tuberculosis. Therefore, they are contraindicated^{9,10}. None of the eight patients who underwent microsurgical tubal operations previously conceived spontaneously in our study.

IVF represents a useful treatment and improves the chances of fertility in what was earlier considered a desperate situation. The total pregnancy rate per transfer was 19.1% in our study while 24.4% (12/49) had live births. Soussis et al¹¹ reported 28.6% success rate with IVF in 13 patients with histologically proven genital tuberculosis. Frydman et al⁶ reported 25% pregnancy rate per transfer in tuberculous infertility (Table 2). Thus, IVF represents the only treatment for tubal and possibly endometrial tubercular infertility.

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