Comparison of Clinical and Laparascopic Features of Infertile Women suffering from Genital Tuberculosis (TB) or Pelvic Inflammatory Disease (PID) or End ometriosis

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Abstract

Objective: The objective of the study was to analyze the clinical and laparascopic features, which may help to differentiate between infertility in females due to Genital Tuberculosis from Pelvic Inflammatory Disease (PID) and Endometriosis.
Methods: This case control study was carried out in a teaching tertiary care hospital. Medical records were searched from 1St January 1987 to 31St December 2000 and 43 infertile women with biopsy proven genital tract tuberculosis were found. Equal number of infertile females with diagnosed PID and Endometriosis were randomly selected. Comparisons were done between features of Genital Tuberculosis with PID and Endometriosis separately and also genital tuberculosis with combined controls of PID and Endometriosis.
Results: Patients with genital tuberculosis commonly had primary infertility. PID and Endometriosis patients had early menarche and 'increased duration of menstruation. On physical examination, patients with Genital Tuberculosis were found to have short heights. No significant findings were observes in the pelvic examination and menstruation history between the comparison groups. Laparascopic examination revealed that fallopian tubes were abnormal, tortuous, bilaterally blocked and thickly adherent more commonly in Genital Tuberculosis when compared to other groups.
Conclusion: The primary infertility patients with chronic malnutrition and massive adhesive fallopian tubes on laproscopic examination should be evaluated for genital tuberculosis (JPMA 51 :393,2001).

Introduction

The global burden of Tuberculosis infection still holds enormous significance in this day and age. It has been estimated that eight million new cases and three million deaths occur due to Tuberculosis annually. In the developing countries, 3/4th of these deaths are between 15-59 years age group[1]. Lungs are the most common sites of infection, however weak immune mechanism may lead to hematogenous spread of Tuberculosis Bacilli and involve other sites in the body, especially the genital tract in females[2].
The prevalence of female Genital Tuberculosis varies from region to region. It has been reported to range as high as 10-19% amongst Indian women to less than 1% in the developed countries[3-5]. Current situation of AIDS and its emerging epidemic in the developing countries has. raised serious concerns for public health[6]. The linkage between AIDS and Tuberculosis heralds the development of the subsequent epidemics of pulmonary and genital TB.
The incidence of TB in Pakistan is 181 per 100,000 individuals and is ranked 5th in the world[7]. Genital Tuberculosis is commonly implicated as a cause of infertility where Tuberculosis infection is prevalent and it is the leading cause of infertility in some developing countries[8]. However data about prevalence of infertility especially due to Genital Tuberculosis is scarce in Pakistan[9]. A study conducted in North Western Frontier Province of Pakistan reported the frequency of female genital tract tuberculosis to be

23%[10] and in another study infertility was the commonest mode of presentation of Genital Tuberculosis[11]. The fallopian tubes are the initial site of involvement being affected in 100% cases of Genital Tuberculosis, followed by Endometrium (79%), cervix (24%), ovaries (11%), vulva and vagina (0.07%)[2].

Overburdened clinics in the developing countries often take a haphazard approach to evaluate infertility. Hence health care providers may offer advice or treatment without conducting a complete evaluation. A complete work-up includes repeated consultations comprising of exhaustive histories, physical examinations and procedures. This evaluation of infertility may drain limited resources from health care systems, apart from the psychological stress suffered on the part of patients[12].

Alongside Genital Tuberculosis, PID and Endometriosis are other common causes of infertility in women in the developing countries. The leading preventable cause of infertility is PID which is a common sequel to chlamydia, gonorrhea, and other reproductive tract infections. It may also follow postpartum and post-abortion infections. Prompt treatment of PID reduces, but does not eliminate the risk of infertility[13]. Endometriosis is usually associated with infertility and presents a difficult diagnostic problem and the symptoms are often similar to PID[14]. Despite the high prevalence of predisposing factors for Genital Tuberculosis, such as pulmonary TB, poor socioeconomical condition and associated weak immune response, obstetricians rarely evaluate Genital Tuberculosis, as a main cause of infertility in the developing countries. Part of the problem lies in the fact, that there is very little information available regarding Genital Tuberculosis.

Infertility due to Genital Tuberculosis is difficult to differentiate from other similar causes of female infertility, especially PID and Endometriosis. The lack of clear evidence and clinical criteria in this regard often create a dilemma for the clinicians. There are no guidelines or diagnostic criteria for Genital Tuberculosis except biopsy and culture.

The objective of this study is to evaluate the clinical and Laproscopic features, which would help to differentiate infertility in females due to Genital Tuberculosis from PID and Endometriosis. These fmdings would be beneficial in guiding the obstetrician in a similar set-up to suspect Genital Tuberculosis earlier in the workout plan for female infertility and to make appropriate decisions for defmite diagnosis and treatment.

Material and Methods

This is a case-control study based on the chart review of the medical records. The study was conducted at the Aga Khan University Hospital (AKUH) Karachi, which is an academic tertiary care hospital. All infertile women• who attended the Outpatient Consulting Clinics of the Gynecology and Obstetric Department of AKUH from 1st January 1987 to 31st December 2000 were included as the study subjects. They were considered as infertile if they had not conceived after 12 months or more of unprotected intercourse[15]. Cases were defined as infertile patient with biopsy proven Genital Tuberculosis, being positive at least on histology, culture or cytology.

Tvvo types of controls were taken in the study i.e. PID and Endometriosis. The diagnosis of genital Endometriosis was made on the basis of direct Laproscopic visualization of Endometriotic spots or cyst, while PID was confirmed on the basis of Laproscopy. All other relevant concurrent etiological conditions of infertility were ruled out for both cases and controls. All those subjects that had either significantly missing records or in which cases Laproscopic examination was not performed were also excluded from the selection.

Sampling

After extensive review of the medical records, 43 cases were identified who fulfilled the selection criteria during that period. An equal number of both type of controls (PID and Endometriosis) were

taken in order to avoid any influence by the imbalance in proportions in combined controls comparison. Among all the Endometriosis and PD patients' records, 43 study subjects were selected randomly from records in each category that fulfilled the criteria.
The information was collected about the clinical presentation including menstrual history, physical examination, laboratory fmdings and Laparascopic features. The data was entered twice into the computer for verification. The data entry and analysis was done on Statistical Package of Social Sciences (SPSS) version 10.0. For analysis amongst comparative groups T-test for equality of mean, Pearson Chi- square test and Fisher Exact test were used accordingly to estimate the significance.

Results

A. Comparison of Genital Tuberculosis with PID or Endometriosis alone

Table 1. Comparison of clinical profile of infertile women between genital tuberculosis and controls (endometriosis and PID) at AKUH.

Variable	TB n=43	PID n=43	Endometriosis n=43	Combined Control n=86
Clinical History				
Age (years)~	28.5 (5.5)	30.5 (5.4)	30.6 (5.4)	30.6 (5.4)
Infertility (years)~	7.7 (5.1)	6.5 (6.0)	5.1 (4.5)*	5.8 (5.33)
Infertility type				
Primary	31 (72.1)	17 (39.5)**	27 (62.8)	44 (51.2) *
Secondary	12 (27.9)	26 (60.5)	16 (37.2)	42 (48.8)
History of D&C				
Yes	17 (39.5)	21 (48.8)	22 (51.2)	43 (50.0)
No	26 (60.5)	22 (51.2)	21 (48.8)	43 (50.0)
Menstruation				
Menarche age (yrs)~	13.7 (1.4)	12.8 (1.1) *	13.1 (1.0)	12.8 (1.1) *
Menstrual cycle (days)~	26.0 (13.3)	36.1 (35.6)	29.4 (7.0)	32.6 (25.3)
Duration of menses (days)~	3.7 (2.4)	4.5 (2.6)	5.2 (2.6) *	4.9 (2.6) *
Regularity of menses				
Irregular/abnormal	11 (25.6)	8 (18.6)	7 (16.3)	15 (17.4)
Regular/normal	32 (74.4)	35 (81.4)	36 (83.7)	71 (82.6)
Menstrual flow				
Moderate	25 (58.1)	31 (67.4)	27 (62.8)	58 (67.4)
Heavy	6 (14.0)	6 (16.3)	8 (18.6)	14 (16.3)
Other (scanty/nil)	12 (27.9)	6 (16.3)	8 (18.6)	14 (16.3)
Dysmenorrhea				
Yes	24 (55.8)	25 (58.1)	30 (69.8)	55 (64.0)
No	19 (44.2)	18 (41.9)	13 (30.2)	31 (36.0)

*= $p<0.05$ **= $p<0.001$ ~= Mean (SD)

Table 1 presents the profile of study subject based on clinical history. The age of the subjects studied, ranged from 16-42 years. Mean age of infertile women with Genital Tuberculosis (cases) was 28.5 ± 5.5 years, and statistically it was not different from infertile women with PB) or Endometriosis (controls). Mean duration of infertility for Genital Tuberculosis patients was significantly more

compared to Endometriosis (p=0.01), but no such difference was present between Genital Tuberculosis and PID infertility patients.
Primary infertility was significantly more common in Genital Tuberculosis patients as compared to PID patients (p<0.001), but no significant difference was observed in proportion of primary infertility between Genital Tuberculosis and Endometriosis patients. There was no significant difference of previous history of dilatation and curettage (D&C) amongst the cases and PID or Endometriosis controls.
The mean age of onset of menstruation was 13.66 ±1.4 years in Genital Tuberculosis patients, which was significantly more compared to PID patients (p =0.02). The duration of menstrual cycle in Genital Tuberculosis patients was 26 days with no meaningful statistical difference with the comparison groups. The similarity in symptoms between genital TB, PID and Endometriosis observed were the regularity of menstruation, amount of menstrual flow and dysmenorrhea, except for the duration of menstrual bleeding which was significantly high in the Endometriosis patients (p =0.0 1).
On physical examination (Table 2), mean weight of study subjects was 59.44 ± 10.26 kg. with mean height of 155.59 ± 6.47 cm. No difference was observed on these physical health parameters between Genital Tuberculosis patients as compared to both control groups, with the exception of Endometriosis patients,. who were found significantly taller as compared to women with Genital Tuberculosis (p = 0.03).
On vaginal examination, no statistically significant fmdings were observed when Genital Tuberculosis patients were compared with either Endometriosis or PID patients. However, the proportion of patients having pelvic pain was more evident in PID patients (48.8%) and the proportion of patients having immobile uterus and palpable adenexal mass was more evident in Genital Tuberculosis (27.9% and 20.9%).
Amongst the study subjects, basic laboratory workout showed no significant difference in values of Genital Tuberculosis patients as compared to Endometriosis and PB) patients. In our study, sample mean haemoglobin levels were 12.29 ± 1.35 gm/dl, hematocrit 36.92 ± 4.48% and erythrocyte sedimentation rates (ESR) 23.31 ± 18.95 mm/hr.
Laparascopic examinations of the patients revealed that there was no difference in gross appearance of uterus between the comparison groups (Table 3). Ovarian visibility on Laparoscope was more than 80% in all three groups. Among them, ovaries were enlarged in almost 56% of Endometriosis patients and it was significantly more compared to Genital Tuberculosis patients (p = 0.03). There was no significant difference found in ovarian adhesions between patients of Genital Tuberculosis and Endometriosis orPID.
There was no significant difference in visibility of fallopian tubes in the Genital Tuberculosis patients as compared to patients with Endometriosis and PD. Among visible fallopian tubes, the gross appearance of the fallopian tubes was abnormal in significantly greater number of patients with Genital Tuberculosis as compared to Endometriosis (p=0.01), but this difference was not significant in comparison between Genital Tuberculosis and PID (p =0.70).
The proportion of tortuous fallopian tubes was also significantly more common in the in the Genital Tuberculosis patients as compared to patients with Endometriosis.
Among those subjects upon which dye test was performed, fallopian tubes were blocked in Genital Tuberculosis twice as often as compared to either Endometriosis or PID (p<0.001). In addition, bilateral blockade of fallopian tubes was significantly more common in Genital Tuberculosis group as compared to the other groups.

B. Comparison of Genital Tuberculosis with combined Controls (PID and Endometriosis)

The significant finding in presenting complaints was primary infertility, which was 72% in the Genital Tuberculosis patients as compared to 51.2 % in combined controls (p=0.02). The age of patients, duration of infertility and history of D&C was unable to meaningfully differentiate between Genital Tuberculosis and combined controls.

The onset of menstruation was significantly late in. Genital Tuberculosis patients as compared to combined controls (p=0.02). Duration of menses was significantly more for combined controls as compared to Genital Tuberculosis patients, while other variables in the menstruation history were statistically not different in their presentation among the cases and the combined controls.

Table 2. Comparison of Physical examination and laboratory profile of infertile women between genital tuberculosis and controls (endometriosis and PID) at AKUH.

Variable	TB n=43	PID n=43	Endometriosis n=43	Common Control n=86
Physical Exam				
Weight (kg)~	57.5 (10.7)	61.4 (9.9)	59.5 (10.1)	60.41 (9.9)
Height (cm)~	153.5 (7.8)	155.4 (5.8)	158.1 (4.5) •	156.8 (5.3) •
Pelvic pain				
Yes	15 (34.9)	21 (48.8)	10 (23.3)	31 (36.0)
No	28 (65.1)	22 (51.2)	33 (76.7)	55 (64.0)
Uterine position				
Retroverted	8 (18.6)	8 (18.6)	11(25.6)	19 (22.1)
Normal	35 (81.4)	35 (81.4)	32 (74.4)	67 (77.9)
Uterine mobility				
Immobile	12 (27.9)	8 (18.6)	8 (18.6)	16 (18.6)
Mobile	31 (72.1)	35 (81.4)	35 (81.4)	70 (81.4)
Adenexal mass				
Yes	9 (20.9)	7 (16.3)	5 (11.6)	12 (14.0)
No	34 (79.1)	36 (83.7)	38 (88.4)	74 (86.0)
Laboratory				
Hemoglobin (mean)~	12.6 (1.4)	12.1 (1.5)	12.2 (1.2)	12.1 (1.3)
Hematocrit (mean)~	37.5 (6.1)	36.3 (3.9)	36.7 (3.0)	36.5 (3.40)
ESR (mean)~	22.6 (16.3)	29.7 (24.4)	12.2 (10.0)	24.2 (24.4)

• = p<0. 05 •• = p<0.001 ~ = Mean (SD)

In Table 2, physical examination and laboratory findings were not statistically different between Genital Tuberculosis and combined controls, except for height of the women (p0.03).
Laparascopic examinations of the patients in revealed that no statistically meaningful differences exist in uterus and ovarian features between Genital Tuberculosis and combined controls. There was also no significant difference in the proportion of patients with visible fallopian tubes in Genital Tuberculosis and combined controls. Among the visible fallopian tqbes on Laparascopy, the proportion of genital tuberculosis patients having adhered and tortuous fallopian tubes were more as compared to combine

controls (p=0.03).
Blockade of fallopian tubes was highly significant in genital TB as compared to combined controls (p<0.001) and it was bilaterally blocked more in the Genital Tuberculosis patients than in combined controls, when dye test was performed

Table 3 Comparison of Laparascopic features of infertile women between genital tuberculosis and controls (endometriosis and PID) at AKUH.

Variable	TB n=43	PID n=43	Endometriosis n=43	Common Control N=86
Uterus (grossly)				
Abnormal	18 (41.9)	18 (41.9)	25 (58.1)	43 (50.0)
Normal	25 (58.1)	25 (58.9)	18 (41.9)	43 (50.0)
Ovary				
Visible	38 (88.4)	36 (83.7)	43 (100.0)	79 (91.9)
Not visible	5 (11.6)	7 (16.3)	0 (0.0)	7 (8.1)
Ovary size				
Enlarged	12 (31.6)	8 (22.2)	24 (55.8)	32 (45.3)
Normal	26 (68.4)	28 (77.8)	19 (44.2) *	47 (54.7)
Ovarian adhesions				
Present	24 (55.8)	27 (62.8)	20 (46.5)	47 (54.7)
Absent	19 (44.2)	16 (37.2)	23 (53.5)	39 (45.3)
Ovarian adhesion type				
Thick	17 (39.5)	17 (39.5)	15 (34.9)	32 (37.2)
Flimsy	7 (16.3)	10 (23.3)	5 (11.6)	15 (17.4)
Nil	19 (44.2)	16 (37.2)	23 (53.5)	39 (45.4)
Fallopian Tubes				
Visible	42 (97.7)	40 (93.0)	42 (97.7)	82 (95.3)
Not visible	1 (2.3)	3 (7.0)	1 (2.3)	4 (4.7)
FT gross appearance				
Abnormal	34 (81.0)	31 (77.5)	22 (52.4) *	53 (64.6)
Normal	8 (19.0)	9 (22.5)	20 (47.6)	29 (35.4)
FT tortuous				
Yes	31 (73.8)	25 (62.5)	19 (45.2) *	44 (53.7)*
No	11 (26.2)	15 (37.5)	23 (54.8)	38 (46.3)
FT adhesions				
Present	30 (69.8)	26 (60.5)	17 (39.5) *	43 (50.0) *
Absent	13 (30.2)	17 (39.5)	26 (60.5)	43 (50.0)
FT adhered				
Nil	13 (30.2)	17 (39.5)	13(30.2) *	43 (50.0) *
Flimsy	5 (11.6)	11 (25.6)	4 (9.3)	15 (17.4)
Thick	25 (58.2)	15 (34.9)	26 (60.5)	28 (32.6)
Dye test done	39 (90.7)	39 (90.7)	42 (97.7)	81 (97.7)
FT blocked				
Present	32 (82.1)	14 (35.9) **	14 (33.3)	28 (34.6) **
Absent	7 (17.9)	25 (64.1)	28 (66.7) **	53 (65.4)
FT block				
Bilateral	24 (61.5)	6 (15.4) **	2 (4.8)	8 (9.9) **
Unilateral	8 (20.5)	8 (20.5)	12 (28.5) *	20 (24.7)
Nil	7 (17.9)	25 (64.1)	28 (66.7)	53 (65.4)

*= p<0. 05 **= P<0.001

(Table 3).

Discussion

The literature on developing guidelines to evaluate an etiological diagnosis in infertile women is deficient, due to lack of appropriate controls to elucidate any differentiating features[16]. The use of healthy controls in research studies has also not been helpful in elucidating differentiating etiologies among common conditions such as infertility. Therefore, we directed this study to make comparison among the common etiologies of infertility by selecting genital tuberculosis as cases and comparing it with two other common categories (PID and Endometriosis) as controls. Besides comparing each control separately, the study also combined both the control groups and compared it with genital tuberculosis.

This comparison showed that some of the symptoms overlap in these groups of infertile women, however there are some useful differences among the patients as well that could help differentiate among these patients. Tuberculosis is a disease of compromised nutritional and immune status[17]. Relatively lesser height and late onset of menarche among the genital tuberculosis could also be due to chronic poor nutritional status, and consequently to their susceptibility to infection.

Infertility is the commonest presenting symptom in the genital tuberculosis patients[18] and the study confirms this finding. Primary infertility is more common in these patients as compared to Endometriosis and PID. Except for the excessive duration of menstrual bleeding, no other feature of menstrual history can reasonably differentiate between these infertility-related conditions and it is more common in Endometriosis patients[19].

Among the laboratory tests, raised ESR is always significantly associated with the genital tuberculosis[20], but this fmding is valid only when comparison is made against healthy controls in some studies. No other single baseline blood profile or physical examination gives distinguishing information for diagnosis among different causes of infertility studies.

In laproscopic examination, three main female genital tract organs involved in infertility were considered, uterus, ovaries and fallopian tubes. No uterine characteristic in our study sample differentiated studied pathologies. However, ovarian size was significantly enlarged in Endometriosis compared to the Genital Tuberculosis. Fallopian tubes are the initial site of involvement in genital tuberculosis and it is invariably affected in 100 percent of cases. It initially affects the mucosa and finally spreads beyond the wall of the fallopian tubes resulting in extensive scarring and adhesion formation. This could either block the fallopian tubes completely or it damages the mucosa and cilia and impairs its function[4,21]. We observed the same fmding in this study. Extensive adhesion and tortuousity due to scar formation were observed in Genital Tuberculosis compared to the other two conditions. The most striking feature was significantly greater proportion of bilateral blockade of fallopian tubes due to tuberculosis compared to Endometriosis and PID.

Therefore, to summarize, the presentation of a patient who is chronically malnourished with primary infertility complaints, massive adhesions and fibrosis in the pelvic region on Laproscopic examination, should be provisionally considered as Genital Tuberculosis and should also be further evaluated accordingly.

Financial burdens of tuberculosis are enormous, as it requires exhaustive diagnostic plan and prolonged treatment regimen. Indirect cost of inability to work, simultaneous stigmatization of tuberculosis and infertility gives another dimension to the burden of disease[22]. Timely identification of such patients is required in a cost-effective manner.

Early diagnosis of genital tuberculosis is difficult[23]. The spectrum of clinical features, physical examination and laboratory investigations elucidated, will help in differentiating it from the similar

conditions that cause infertility among females such as PID and Endometriosis. It is often not clear to investigators as to what particular features are attributed to patients with infertility with different diseases and general deficiency regarding it in medical literature.
Although, the three conditions (genital tuberculosis, PID and Endometriosis) studied, often present with infertility in women, they have different treatment modalities. These findings could also help in selection of appropriate treatments based on their probable results and costs to conserve resources. These could help improve the diagnostic ability of general practitioners and gynecologists involved in establishing the etiology of infertile women in Pakistan. In addition they are also useful, especially for underdeveloped countries, where tuberculosis is widespread and genital tuberculosis is a common etiology for infertility[24].

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