Tuberculosis and Pregnancy : A Ten Year Overview

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OBJECTIVES - To study the pattern of tubercular desease (TB) over a span of 10 years with a special reference to the pregnancy outcome in women with tuberculosis and also to make an attempt to understand whether pregnancy alters the course of tuberculosis. **METHODS** - This is a prospective observational study analyzing 10 years experience of pregnancies complicated by tuberculosis. The patients were studied over two phases : phase I: Jan 1991 to Dec. 1995, [n=76] and phase II: Jan 1996 to Dec. 2000, [n=77]. Pregnancy outcome and course of the disease in these 153 pregnant women with tuberculosis were studied. **RESULTS** - Fifteen percent of women had reactivation of tuberculosis. Pulmonary tuberculosis was by far the most common in both the phases. Cough and low grade fever were commonest symptoms. Severity of the disease reduced over the years and was found mainly in seropositive patients in phase II. Pregnancy outcome was not adversely affected except for a very high incidence of low birth weight babies. There were two maternal mortalities in phase I and one mortality in phase II. **CONCLUSION** - The incidence of TB has remained steady in spite of improved treatment strategies. Perinatal mortality decreased with time but the incidence of low birth weight babies remained quite high. The differences in the observations in phase I and II were not significant by Z test. Since high index of suspicion helps early diagnosis and treatment there is a strong need for health education, antenatal counseling and combined TB and AIDS awarness campaign.

Key words : tuberculosis, pregnancy outcome

Introduction

Tuberculosis (TB) continues to be a major health hazard in India even today, despite excellent chemotherapeutic agents available to us. Timely use of drugs can actually cure the disease completely and can prevent the morbidity and mortality of pregnancy complicated by tuberculosis. In India, national tuberculosis program was started in 1962. Epidemiological curve of any infectious disease has an ascending limb, the summit and a descending limb. After the national tuberculosis program we have reached the descending limb on the epidemiological curve of this disease but the curve has plateaued far above the acceptable level. The highest incidence of pulmonary TB is usually between 17 to 35 years of age and this also corresponds to the childbearing years of women. Hence, every effort should be made to control the disease before, during and after pregnancy to prevent the adverse effects of the disease on the reproductive health of the mother. We conducted prospective observational study of pregnancies with tuberculosis aimed at studying the pattern of the disease over a span of 10 years, the pregnancy outcome in patients with TB and whether pregnancy alters the course of TB.

Paper received on 9.4.02 ; accepted on 27.9.02

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Material and Methods

The patients were studied over two phases : phase I: January 1991 to December 1995 and phase II : January 1996 to December 2000. Total of 153 pregnant women with TB were selected for the study. In phase I there were 76 women whereas in phase II 77 women. Interestingly a similar study was carried out in the same hospital in 1960[1] which reported a very high 18% incidence of the disease which this has gradually fallen after the national tuberculosis control program. High degree of clinical suspicion helped to clinch the diagnosis that was further confirmed by supportive diagnostic tests. However, in three patients diagnosis was not suspected but it came as surprise at the time of tubal sterilization. Women were clinically suspected to have TB when they complained of cough with expectoration for more than 15 days, had fever for more than one week not responding to routine line of treatment or had symptoms specific to less common sites of TB. All these patients were subjected to sputum for AFB, X-ray chest with abdominal shielding, CBC, ESR, Mantoux test or other specific tests. In phase II even though rapid culture, PCR and anti-TB antibody tests were available more freely we could not use them being unaffordable to our women. After diagnosis they were given three drugs anti-tubercular treatment (INH, rifanpicin and ethambutol) for the period of 6-9 months. Pyrazinamide was used as a fourth drug in a few women in phase II. The course of the disease and pregnancy outcome were studied in both the

phases and results were compared. All women were encouraged to breast-feed givine INH prophylaxis to the neonates of sputum positive mothers. Tubal sterilization was done in multiparous women.

Results

Out of 153 pregnant women diagnosed to have TB, 76 belonged to phase I and 77 to phase II of the study. Total number of deliveries gradually declined over the study period and there is a slight rise in overall incidence in phase II (0.38% phase I; 0.5% phase II) but this is statistically not significant. As seen in Table I majority of women were below25 years of age. This is the most vulnerable age group. Only 4.2% were above 30 years of age. There were more multiparas than primyparas in both the phases (Table II). Multiparity adds the problems of anemia, undernutriton and overcrowding. Women from both the phases match fairly well in age and parity (Tables I and II). Table III shows that majority were diagnosed in third trimester, more so in phase II (Table III). In 18.5% of patients in phase I and 24.7% in phase II diagnosis was made and full treatment completed preconceptionally. Amongst those diagnosed during pregnancy 15% revealed a past history of tuberculosis. Hence they had reactivation of old tuberculosis suggesting that in a small number pregnancy perhaps worsens the course of the disease. In phase II, two women were diagnosed to have genital TB in post-partum period at the time of puerperal sterilizarion. One of them had such badly damaged tubes that pregnancy seemed an impossible event with those findings. So it was postulated that preexisting genital tuberculosis must have flared up during pregnancy and condition of the tubes worsened after conception and implantation. Another woman who desired termination of pregnancy with tubal ligation was also found to have active genital tuberculosis. The only significant finding was an ESR of 55mm at the end of 1 hour. Sterilization was abandoned in all the three patients after the abdomen was opened as there were densle adhesions, anatomy was distorted and identification of tubes was impossible. Majority of our patients had high ESR but this is often seen in pregnancy. Generally speaking an ESR of more than 45mm / 1hr should raise the suspicion of TB.

Pulmonary TB was by far the most common in both the phases (Table IV). We had six women with genital TB in phase II as against one in phase I. Out of these, three had infertility and conception after a course of anti-TB drugs. This perhaps is related to increasing awareness and early treatment in infertile women preventing the advanced stage of the disease making pregnancy more likely.

In phase I there were four interesting clinical presentations –

Case 1. Tubercular meningitis : Fever, headache, vomiting and convulsions leading to fatal outcome.

Case 2. Tubercular mastitis: Pain and swelling in the breast leading to abscess formation needing incision and drainage followed by anti TB drugs.

Case 3. Abdominal TB leading to subacute intestinal obstruction responding to conservative treatment.

Case 4. Pott's spine: Pregnancy and labour were uneventful in spite of mechanical disadvantages due to deformity. Vaidya et al[2] have reported one interesting phenomenon in patients with Pott's spine and quadriplegia. These patients may get "automatic hyperreflexia syndrome" characterized by excessive sweating, headache severe hypertension, convulsions and coma.

Table V shows the analysis of various symptoms. Cough and low grade fever were most common presenting symptoms in both the phases. Haemoptysis has significantly reduced over the years indicating less severity of the disease in phase II. As many as 55% of the patients were found to be anemic i.e. Hb<10 gms%. This incidence is very high and is almost twice than in general antenatal women.

In phase II there were six HIV positive women. One of them had undergone emergency LSCS at term and required ventilator support but eventually died of septicemia on 19th postoperative day. Actual incidence of sero-positivity may be higher as we have not been able to do HIV test in all the women. Increasing number of HIV positive women could be the reason for persistence of high incidence in spite of improved treatment strategies and awareness over the last few years. In Phase I, HIV data was unavailable.

Majority of the women had mild to moderate changes on chest radiography. Less commonly the chest x-ray may appear normal but sputum may be positive for AFB[3]. Ideally three sputum samples are required before committing the diagnosis. Only one third of our women were sputum positive.

Pulmonary TB was quite extensive in 14.5% in phase I and in 7.6% in phase II. This suggests that extensive disease is not on the rise and is commonly seen amongst HIV positive women as observed in four of our sero-positive women.

Table I : Age Distribution

Age distribution	Phase I (n=76)		Phase II (n=77)	
	No.	Percentage	No.	Percentage
<20 years	16	21	12	15.5
20-25 years	39	51	44	57.1
26-30 years	16	21	18	23.2
>30 years	5	7	3	4.2

Table II : Distribution of Parity

Parity	Phase I (n=76)		Phase II (n=77)	
	No.	Percentage	Number	Percentage
Zero	27	35.5	24	31.2
One	23	30.2	21	27.3
Two	16	21.0	23	29.9
Three and above	10	13.1	9	11.6

Table III : Gestational Age at the Diagnosis of Tuberculosis

Gestational Age at Diagnosis	Phase I (n=76)		Phase II (n=77)	
	No.	Percentage	No.	Percentage
Preconceptional	14	18.5	19	24.7
1st Trimester	15	20.0	07	9.1
2nd Trimester	20	26.00	11	14.3
3rd Trimester	25	33.0	38	49.4
Post Partum	2	2.5	02	2.5

Table IV : Site of Active Tuberculosis

Site	Phase I (n=76)		Phase II (n=77)	
	No.	Percentage	No.	Percentage
Lungs	68	89.9	65	84.5
Lymph Nodes	2	2.6	4	5.3
Cervical spine	—	—	1	1.2
Thoracic spine [T10]	1	1.3	—	—
Genital	1	1.3	6	7.8
CNS	1	1.3	—	—
Abdominal	3	3.9	1	1.2
Breast and lungs	1	1.3	—	—

Table V : Analysis of Presenting Symptoms

Presenting Symptoms	Phase I (No.)	Phase II (No.)
Cough	48	45
Low grade pyrexia	39	32
Failure to gain weight	23	18
Dyspnoea	12	9
Haemoptysis	9	3
Abdominal pain	6	2
Asymptomatic	3	3
Chest pain	3	—
Swelling in the neck	2	4
Giddiness	1	5

Table VI : Pregnancy Outcome

Pregnancy Outcome	Phase I		Phase II	
Number	Number	Percentage	Number	Percentage
FTND	35	46.1	33	42.9
IUGR / Preterm normal delivery	27	35.5	32	41.6
LSCS	5	6.6	6	7.8
Abortion	2	2.6	3	3.8
Still birth	4	5.3	2	2.6
Voluntary termination of pregnancy	3	3.9	1	1.3
Neonatal death	3	3.9	—	—
Maternal mortality	2	2.6	1	1.3

Sometimes CT scan of the lungs may become necessary to have a precise knowledge of the extent of the disease. However it is to be avoided during pregnancy. Three of our women underwent CT scan in post-partum period giving us precise diagnosis. Two women had respiratory failure. One of them expired and the other recovered.

Table VI shows the comparison of pregnancy outcome in both the phases. LSCS rates are not significantly different in the two phases and are actually lower in study groups (6.6% in phase I and 7.8% in phase II) than the general incidence of LSCS at our institute, which ranged between 8-10% in phase I, and 15-20% in phase II. IUFD rate also has gone down but not significantly in phase II. IUGR babies were higher in phase II (41.6%) than in phase I, (35.5%) but the difference was not statistically significant. There were two maternal deaths in phase I one due to tubercular meningitis and one due to respiratory failure. A study of TB meningitis in pregnancy has reported a very high maternal mortality viz., 21 deaths in 32 patients[4]. Hence this diagnosis must be kept in mind in every woman having headache fever and convulsions during pregnancy. In phase II one HIV positive women expired as already mentioned above.

Most of the women tolerated antiTB drugs fairly well, but, we came across drug induced hepatitis in seven. Three women showed multi-drug resistance and needed second line drugs (eg. ethionamide, cifran). The current recommended treatment of drug susceptible active tuberculosis is INH (300mg/day), rifampicin (450mg/day) and ethambutol (800mg/day or 25 mg/kg/day) for two months. Pyridoxine (50mg/day) should always be given with INH to avoid deficiency of this vitamin. Later only INH and rifampicin should be continued for nine months and further in the postpartum period to prevent worsening of the disease. WHO recommended DOTS (direct observational treatment strategy) may be a useful tool to overcome non-compliance.

We had no congenital abnormalities related to drugs. All the drugs cross the placenta but none of these standard three drugs have proven teratogenicity. However, rifampicin has been blamed for hemorrhagic disease of newborn. It also has action on DNA dependent RNA polymerases and should be avoided during 1st trimester. INH is considered safe even during first trimester. Ethambutol is linked with eye abnormalities. It is universally accepted that streptomycin and other aminoglycosides must be avoided during pregnancy because of high incidence of ototoxicity reported in the fetuses. The CNS effects of cycloserine and gastrointestinal effects of PAS make their use in pregnancy undesirable.

Discussion

Hippocrates believed that pregnancy had a beneficial effect on TB. Midnineteenth century scientists started believing that pregnancy worsens the course of the disease and advised therapeutic abortion. In 1940s it was believed that course of TB remains unaffected by pregnancy. Later a view of flaring of TB in postpartum period came up. One study reported that 31 out of 101 pregnant women with quiescent tuberculosis experienced a relapse after delivery; 20 of the 31 relapses occurred in the first postpartum year[5]. Several theories were proposed to explain this phenomenon, including postpartum descent of the diaphragm, nutritional stress of pregnancy and lactation, insufficient sleep because of demands on a new mother, rapid hormonal changes and depression of cell mediated immunity in late pregnancy and puerperium. In United Kingdom. Edge[6] found no increased risk of tuberculosis in postpartum women compared with age matched women in the general population. From these and other studies, it became clear that the anatomic extent of the disease, its radiographic pattern and the susceptibility of the individual patient to tuberculosis are more important than pregnancy itself in determining the cause and prognosis of the pregnant woman with tuberculosis. Since the advent of effective chemotherapy pregnant women with tuberculosis have the same prognosis as non-pregnant women. Our study supports the same except that in a small proportion of women flare up of the disease was noted. Schaefer et al[7] reported that the infant mortality and maternal mortality from untreated advanced tuberculosis was between 30% and 40%. One study from Norway[10] revealed a higher incidence of toxaemia, postpartum haemorrhage and difficult labour in mothers with tuberculosis compared with control subjects[8]. In phase I we had five cases of PPH complicated by anemia but in phase II we had no case of PPH. We had associated pathologies like PIH (n=2), oligohydramnios (n=3) and polyhydramnios (n=1). None of these were significantly high compared to those in nontuberculous women. We had a high incidence of IUGR in both the phases but incidence of IUFD dropped in phase II though not significantly. Improved fetal monitoring prevented the IUFD and helped these IUGR babies to be born alive. Jana et al[9] reported 33% incidence of IUGR babies in patients with TB. This is comparable with our incidence. Vallejo and Starke[10] have reported dramatic increase in the incidence of TB in young child bearing age group in USA.

Recent epidemic of HIV infection has caused much concern about TB even in developed countries[11]. HIV seroprevalence in tuberculous patients was 26 to 35.3% in the Democratic Republic of Congo[12] we had only six seropositives in 77 women. In Zambia despite improved obstetric services, the maternal mortality at UTH, Lusaka, has increased eight-fold over the past two decades. This dramatic increase is mainly due to non-obstetric causes of death. Malaria and AIDS-associated TB and unspecified chronic respiratory illnesses are now major causese of maternal death there[13].

References

1. Deshmukh MD, Master TB. Pregnancy and Tuberculosis, *Ind J Tuberc 1961; 2:71-81.*
2. Vaidya MK, Shah GV, Bharucha KE: Pregnancy and its outcome in quadriplegia due to Pott's spine. *Int J Gynecol Obstet 1995; 49:319-21.*
3. Marciniuk DD, McNab BD, Martin WT et al. Detection of pulmonary tuberculosis in patients with a normal chest radiograph. *Chest 1999; 115: 445-52.*
4. D' Cruz IA, Dandekar A. Tuberculous Meningitis in pregnant and Puerperal women", *Obstet Gynecol, 1968; 31: 775-8.*
5. Crombi JB: Pregnancy and pulmonary tuberculosis, *Br J Tuberc 1954; 7: 47-97.*
6. Edge JI. Pulmonary tuberculosis and pregnancy, *BMJ 1952; 2:845-67.*
7. Schaefer G, Zevoudakis IA, Fuchs FF et al. Pregnancy and pulmonary tuberculosis. *Obstet Gynecol. 1975; 46: 706-15.*
8. Bjerkedal T, Bahna SL, Lehmann EH. Course and outcome of pregnancy in Women with pulmonary tuberculosis. *Scand J Respir Dis 1975; 56:245-50.*
9. Jana N, Vasishta K, Saha SC et al. Obstetrical outcomes among women with extrapulmonary tuberculosis. *N Engl J Med 1999 Aug; 341: 649-9.*
10. Vallejo JG, Starke JR. Tuberculosis and pregnancy. *Clin Chest Med. 1992; 13 : 693-707.*
11. Henderson CE: Management of tuberculosis in pregnancy. *J Assoc Acad Minor Phys 1995; 6:38-42.*
12. Mulanga KC, Nzilambi N et al. Evidence of stable HIV seroprevalences in selected populations in the Democractic Republic of the Congo. *AIDS 1998; 12 :905-10.*
13. Casper GR, Garland SM: AIDS associated tuberculosis as a major non-obstetric cause of maternal death. *Int J Tuberc Lung Dis 1999; 3:675-80.*