OBSTETRICAL OUTCOMES AMONG WOMEN WITH EXTRAPULMONARY TUBERCULOSIS

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ABSTRACT

Background The prevalence of tuberculosis, especially extrapulmonary tuberculosis, is increasing worldwide. Because information on the outcome of pregnancy among women with extrapulmonary tuberculosis is limited, we studied the course of pregnancy and labor and the perinatal outcome in these women and their infants.

Methods From 1983 to 1993, we followed 33 pregnant women who had extrapulmonary tuberculosis (12 with tuberculous lymphadenitis and 9 with intestinal, 7 with skeletal, 2 with renal, 2 with meningeal, and 1 with endometrial tuberculosis) through their deliveries. Of the 33, 29 received antituberculosis treatment during pregnancy. The antenatal complications, intrapartum events, and perinatal outcomes were compared with those among 132 healthy pregnant women without tuberculosis who were matched for age, parity, and socioeconomic status.

Results Tuberculous lymphadenitis did not affect the course of pregnancy or labor or the perinatal outcome. However, as compared with the control women, the 21 women with tubercular involvement of other extrapulmonary sites had higher rates of antenatal hospitalization (24 percent vs. 2 percent, $P<0.001$), infants with low Apgar scores (≤ 6) soon after birth (19 percent vs. 3 percent, $P=0.01$), and low-birth-weight (<2500 g) infants (33 percent vs. 11 percent, $P=0.01$).

Conclusions Extrapulmonary tuberculosis that is confined to the lymph nodes has no effect on obstetrical outcomes, but tuberculosis at other extrapulmonary sites does adversely affect the outcome of pregnancy. (N Engl J Med 1999;341:645-9.)

TUBERCULOSIS is a major public health concern worldwide.[1-4] Although the lung remains the commonest site of infection, extrapulmonary disease is becoming more prevalent,[2-6] and the increase is more pronounced among young women[6] and immigrants from countries with a high prevalence of tuberculosis.[2,3,6] Among 16 pregnant women with tuberculosis in New York City, 6 had extrapulmonary disease.[7]

Active pulmonary tuberculosis in pregnant women has been associated with increased risks to their infants, including prematurity, fetal-growth retardation, low birth weight, and perinatal mortality, as compared with the infants of healthy pregnant women who do not have tuberculosis.[8] However, information on the obstetrical outcome among women with extrapulmonary tuberculosis is scanty and is usually in the form of case reports[9-12] or case series.[13] Therefore, we compared the course of pregnancy and labor and the perinatal outcome among women with extrapulmonary tuberculosis and matched control women without tuberculosis.

METHODS

We studied 33 pregnant women with extrapulmonary tuberculosis (Table 1). These women were identified from among 178 pregnant women with tuberculosis who attended the Obstetric Medical Disorder Clinic at the Postgraduate Institute of Medical Education and Research, Chandigarh, India, from 1983 to 1993. Three other women (two with intestinal and one with skeletal tuberculosis) were excluded from the study because of inadequate information. The diagnosis of extrapulmonary tuberculosis was established by clinical findings combined with bacteriologic, histologic, and radiologic studies, and all patients fulfilled the diagnostic criteria of the World Health Organization.[14] Twenty-nine women had active disease requiring antituberculosis treatment during pregnancy, and four women (three with intestinal and one with spinal [skeletal] tuberculosis) had completed such treatment before conception. Two women with tuberculous lymphadenitis also had pulmonary tuberculosis, but the remaining 31 women had no evidence of pulmonary tuberculosis.

We recorded the women's age, parity, weight, timing of the diagnosis in relation to the index pregnancy, and antituberculosis drugs and monitored the women for complications and hospitalization during pregnancy and for antituberculosis-drug toxicity. We recorded intrapartum maternal and fetal events, the progress of labor, the mode of delivery, the type of anesthetic drugs administered, the perinatal outcome, and the course in the puerperium. The mean birth weight of the women's infants and the frequency of low birth weight (defined as a weight of less than 2500 g), prematurity (birth before 37 weeks' gestation), neonatal depression (Apgar score of 6 or less one minute after birth), and death in the perinatal period were used as indexes of perinatal outcome. Perinatal deaths included stillbirths after 28 weeks' gestation and deaths within 7 days after birth. The autopsy results were reviewed to ascertain the cause of death.

For each woman, we selected 4 healthy pregnant women without tuberculosis (total, 132) as controls. Each control was matched for age and parity with a woman with tuberculosis and had given birth in the hospital within 48 hours before or after the matching woman had given birth. The institute is a referral center for neighboring states of northern India; therefore, both the study and control groups were from the same area and had similar socioeconomic backgrounds. The results in the two groups were compared with the use of Student's t-tests and chi-square tests with Yates' correction.

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TABLE 1. SITES OF EXTRAPULMONARY TUBERCULOSIS, CLINICAL PRESENTATIONS, AND METHODS OF DIAGNOSIS IN 33 WOMEN.*

EXTRAPULMONARY SITE	NO. OF PATIENTS (%)	CLINICAL PRESENTATION	METHODS OF DIAGNOSIS
Lymph nodes	12 (36)	Persistent cervical lymphadenopathy, cold abscess, and sinus discharge	Fine-needle or surgical biopsy
Intestines	9 (27)	Subacute intestinal obstruction, abdominal mass, and ascites	Laparotomy or fine-needle or endoscopic biopsy
Skeleton	7 (21)	Chronic progressive backache, paraplegia, and dorsolumbar kyphoscoliosis	Radiography of bones and joints
Kidney	2 (6)	Pyrexia of unknown origin and perinephric abscess	Urinalysis and intravenous pyelography
Meninges	2 (6)	Fever and altered sensorium	Cerebrospinal fluid analysis
Endometrium	1 (3)	Primary infertility	Endometrial biopsy

*All 33 women with extrapulmonary tuberculosis fulfilled the diagnostic criteria of the World Health Organization.[14]

RESULTS

During the study period, for every 1043 women who delivered infants at our hospital, 1 had extrapulmonary tuberculosis, and the 36 women identified for the study (including the 3 who were excluded) accounted for 20 percent of all cases of tuberculosis among pregnant women. A preliminary analysis revealed no significant differences in the overall perinatal outcome between the women with tuberculosis and the control women. However, the 21 women who had extrapulmonary tuberculosis at sites other than lymph nodes had an increased incidence of perinatal complications and were therefore analyzed as a separate subgroup.

Clinical Presentation

The clinical presentations and the methods of diagnosis of extrapulmonary tuberculosis in the 33 women are summarized in Table 1. Age, parity, literacy rate, weight, and hemoglobin concentrations were similar among the two groups of women with tuberculosis and the control group (Table 2). Twenty-two women (67 percent) had started treatment with antituberculosis drugs before the index pregnancy. Among the remaining 11 women, all of whom were given a diagnosis during the index pregnancy, 4 (12 percent) started treatment in the first trimester, 4 (12 percent) in the second trimester, and 3 (9 percent) in the third trimester.

Treatment with Antituberculosis Drugs

Of the 29 women who had active tuberculosis during the index pregnancy, 18 (62 percent) received isoniazid, rifampin, and ethambutol for nine months. Five women (17 percent) received isoniazid and ethambutol for 12 to 18 months (four had also received streptomycin before conception). All of the remaining six women (21 percent), four of whom were in an advanced stage of pregnancy and two of whom had tuberculous meningitis, received isoniazid, rifampin, and pyrazinamide. Treatment with pyrazinamide was stopped after two months, and all therapy was stopped after nine months. No adverse effects were observed.

TABLE 2. CHARACTERISTICS OF THE WOMEN WITH TUBERCULOSIS AND THE CONTROL WOMEN.*

CHARACTERISTIC	WOMEN WITH LYMPH-NODE TUBERCULOSIS (N=12)	WOMEN WITH TUBERCULOSIS AT OTHER EXTRAPULMONARY SITES (N=21)	CONTROL WOMEN (N=132)
Age (yr)	24±5	25±4	25±4
Primiparity (%)	58	62	59
Able to read and write (%)	75	71	74
Weight (kg)	52±4	50±7	52±6
Hemoglobin (g/dl)	11.4±1.2	10.9±1.0	11.2±1.6

*Plus–minus values are means ±SD. There were no significant differences between the groups (with comparisons by Student's t-test or the chi-square test as appropriate).

Antenatal Events

Six women were hospitalized in the antenatal period; the reason for hospitalization was effusion of the left ankle in one woman with skeletal tuberculosis, deep venous thrombosis in one woman with spinal tuberculosis without paraplegia, severe pregnancy-

TABLE 3. ANTENATAL AND INTRAPARTUM EVENTS AMONG THE WOMEN WITH TUBERCULOSIS AND THE CONTROL WOMEN AND THEIR INFANTS.

EVENT	WOMEN WITH LYMPH-NODE TUBERCULOSIS (N=12)	WOMEN WITH TUBERCULOSIS AT OTHER EXTRAPULMONARY SITES (N=21)	CONTROL WOMEN (N=132)
		number (percent)	
Pregnancy-associated complications	3 (25)	7 (33)	24 (18)
Antenatal hospitalization	1 (8)	5 (24)	3 (2)*
Preterm labor	1 (8)	2 (10)	14 (11)
Acute fetal distress†	0	4 (19)	10 (8)
Mode of delivery			
Cesarean section	3 (25)	3 (14)	25 (19)
Forceps delivery	0	3 (14)	8 (6)
Spontaneous vaginal delivery	9 (75)	15 (71)	99 (75)

*P<0.001 for the comparison with women with tuberculosis at other extrapulmonary sites.

†Acute fetal distress was defined as the presence of any or all of the following: prolonged fetal bradycardia, repeated decelerations, and thick, meconium-stained amniotic fluid in association with cephalic presentation of the infant during labor.

TABLE 4. PERINATAL OUTCOME AMONG THE WOMEN WITH TUBERCULOSIS AND THE CONTROL WOMEN AND THEIR INFANTS.*

OUTCOME	WOMEN WITH LYMPH-NODE TUBERCULOSIS (N=12)	WOMEN WITH TUBERCULOSIS AT OTHER EXTRAPULMONARY SITES (N=21)	CONTROL WOMEN (N=132)
Maternal			
Mean duration of gestation — wk	38.9±1.5	38.6±2.1	38.8±1.7
Infant			
Mean birth weight — g	2894±430	2617±540	2868±498†
Prematurity — no. (%)	1 (8)	2 (10)	10 (8)
Low birth weight — no. (%)	1 (8)	7 (33)	14 (11)‡
Apgar score ≤6 at 1 min — no. (%)	1 (8)	4 (19)	4 (3)‡
Congenital anomaly — no. (%)	0	0	2 (2)
Perinatal death — no. (%)	0	2 (10)	2 (2)

*Plus–minus values are means ±SD. P values are for the comparison with the women with tuberculosis at other extrapulmonary sites.

†P=0.04.

‡P=0.01.

induced hypertension in one woman with tuberculous lymphadenitis, prolonged fever in one woman with renal tuberculosis, and tuberculous meningitis in two women. The rate of admission among the women with extranodal tuberculosis was 24 percent (5 of 21), as compared with a rate of 2 percent in the control group (P<0.001) (Table 3). However, none had progression of tuberculosis or a relapse during the pregnancy or puerperium. The frequency of complications of pregnancy was similar among the two groups of women with tuberculosis and the control group (Table 3).

Labor and Delivery

Labor was induced in eight of the women with tuberculosis (24 percent). Two women with spinal tuberculosis and paraplegia had spontaneous vaginal deliveries. Cesarean sections were performed only for obstetrical indications. One woman with tuberculous kyphoscoliosis required cesarean section for pelvic contraction, and in another woman, cesarean section was complicated by the presence of extensive intraabdominal adhesions resulting from intestinal tuberculosis.

Perinatal Outcome

The mean (±SD) birth weight (2894±430 g) of the infants of the 12 women with tuberculous lymphadenitis was appropriate given the mean gestation of 38.9±1.5 weeks and was similar to the institute's reference values and to the value in the infants of the women in the control group (Table 4). However, the mean birth weight of the infants of the 21 women with tuberculosis at other extrapulmonary sites was 251 g lower than that of the infants of the women in the control group (2617 g vs. 2868 g, P=0.04); these infants also had a significantly higher incidence of low birth weight (33 percent vs. 11 percent, P=0.01) and an Apgar score of 6 or less one minute after birth (19 percent vs. 3 percent, P=0.01).

Two infants of women with tuberculosis died perinatally, one from antepartum placental abruption and one from aspiration of gastric contents. There were no cases of congenital tuberculosis or fetal malformation, and no maternal deaths.

DISCUSSION

Extrapulmonary tuberculosis, which is present in 10 to 27 percent of all patients with tuberculosis,[5,6,15,16] is rare among pregnant women.[10-13] The diagnosis of this condition is often delayed because of its protean manifestations,[5,15,16] and this type is less easy than pulmonary tuberculosis to identify with the use of radiologic evaluation and bacteriologic confirmation.[16] Biopsy and surgical intervention during pregnancy may not be possible because of the risk of preterm labor, poor accessibility of the lesions, and anesthetic risk to the fetus.[12] Since our institute is a referral center, the prevalence of extrapulmonary tuberculosis among pregnant women — 1 in 1043 deliveries — does not reflect the prevalence among pregnant women in the community.

In this study, we assessed the obstetrical implications of extrapulmonary tuberculosis by matching two groups of pregnant women — one group with extrapulmonary tuberculosis and one without tuberculosis — with similar demographic characteristics. Tuberculous lymphadenitis, the most common form of extrapulmonary tuberculosis,[5,15,17] had no adverse effect on maternal and fetal outcome. Because lymphadenitis is often diagnosed early, it rarely causes debility or systemic toxicity.[17] However, women with extranodal tuberculosis had infants who weighed a mean of 251 g less at birth than the infants of the control women, although there was no significant difference between the groups in the mean gestational age at delivery or the rate of prematurity. These results suggest that like pulmonary tuberculosis,[8] maternal extranodal tuberculosis increases the risk of fetal-growth retardation. There were also significant increases in the frequency of low-birth-weight infants and infants with low Apgar scores soon after birth in this subgroup. Furthermore, in our previous study, which did not include any of the women who were in the current study, we found that the infants of women with pulmonary tuberculosis were approximately twice as likely as the infants of healthy women without tuberculosis to be premature, to be small for gestational age, and to have a low birth weight. In both studies diagnosis late in pregnancy and advanced disease probably contributed to the perinatal problems, as did physical disability in the present study.

Intestinal tuberculosis is difficult to diagnose without the use of laparotomy.[9,16] However, we found endoscopic or fine-needle aspiration biopsy to be useful in selected patients. In one woman with intestinal tuberculosis in our study, cesarean section was complicated by the presence of extensive abdominal and pelvic adhesions.

Spinal tuberculosis, although rare in pregnancy, is associated with serious morbidity.[18,19] The absence of systemic symptoms and reluctance to perform spinal radiography in pregnant women often delayed the diagnosis in our study, resulting in early-onset paraplegia in two women. In women with paraplegia, pregnancy is associated with an increased risk of urinary tract infection, decubitus ulcers, preterm labor, and autonomic hyperreflexia — a potentially life-threatening complication.[10] In our study, the condition of both women with paraplegia improved with antituberculosis-drug therapy, and both had vaginal deliveries, although one woman had a preterm delivery. In other reports, five women with tuberculous paraplegia who required spinal surgery during pregnancy or the puerperium had successful vaginal deliveries and normal infants.[10,12] However, spinal deformity and reduced cardiopulmonary reserve associated with kyphoscoliosis can complicate the use of regional and general anesthesia during delivery.[20]

Tuberculous meningitis in pregnant women is associated with neurologic morbidity and an increased risk of death to both the women and their infants.[11] Endometrial tuberculosis often leads to infertility, miscarriage, or ectopic pregnancy.[21] In contrast, the patients who had tuberculous meningitis and endometritis in our study had good outcomes, probably as a result of early diagnosis and treatment.

Treatment with antituberculosis drugs poses special problems during pregnancy because of concern about potential teratogenic effects. Most of the women in our study received isoniazid, ethambutol, and rifampin, all of which are relatively safe to use during pregnancy,[22] and none of their infants had any congenital anomalies. Little is known about the fetal effects of pyrazinamide. The six women who received pyrazinamide because of its bactericidal effects and penetration of cerebrospinal fluid had no adverse effects.[11]

In summary, the effects of extrapulmonary tuberculosis on pregnancy depend on the sites involved, the severity and duration of the disease, and the occurrence of pregnancy-associated complications. Tuberculous lymphadenitis had no significant effect on perinatal outcome. However, extrapulmonary tuberculosis at other sites was associated with an increased frequency of maternal disability, hospitalization during pregnancy, fetal-growth retardation, and infants with low Apgar scores soon after birth.

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