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ORIGINAL ARTICLE

Pregnancy and tuberculosis: to assess tuberculosis cases in pregnancy in a developing region retrospectively and two case reports

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Abstract
Pregnancy and tuberculosis (TB) To assess TB cases during pregnancy in a developing region retrospectively and to present two case reports.
Objectives Since TB cases activated by HIV infection during pregnancy are well reported in the literature, we aimed to investigate the aggressiveness of pulmonary TB among pregnant women and to assess the effects of TB on the fetus in Kutahya, an area where HIV positive cases are not seen.
Materials and methods The medical records between 2000 and 2005 of the Provincial Health Directorate and Dispensary Against Tuberculosis in Kutahya were reviewed and analyzed retrospectively.
Results Between 2000 and 2005, 667 pulmonary TB cases were examined in the Kutahya region. Of these, 106 occurred in women at reproductive ages between 20 and 44. All were HIV negative cases. In this area, five TB cases were found during pregnancy. There were three cases seen in the first trimester, but pregnancy was ended by curettage. Two women had pulmonary TB and gave birth. Five cases were evaluated as class 1 TB. During and after pregnancy, isoniazid, rifampin, ethambutol, and pyrazinamide (INH + RFP + ETB + PRZ) were used for the treatment. Resistance to anti-TB drugs was not seen during the treatment. Neither congenial nor neonatal TB was seen.
Conclusion Generally, TB is expected to be more aggressive during pregnancy. Since our cases were HIV negative, it can be thought that TB did not progress aggressively. Less aggressiveness and non-resistance to TB treatment in HIV-negative pregnant women compared with HIV-positive women were observed. Therefore, HIV infection results in greater mortality than the triple combination of human immunodeficiency virus, mycobacterium TB, and pregnancy. Besides, the advance of TB in pregnant women was not different from that in non-pregnant women in Kutahya. The fetus and the newborn were not affected. INH, RFP, ETB, and PRZ were used for therapy.

Keywords Pregnancy · Tuberculosis · Pulmonary

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Introduction

Tuberculosis (TB), one of the oldest diseases in history, is again a major public health problem as human immunodeficiency virus (HIV) infection has recently increased. People in both western societies and the developing countries are much more affected. The World Health Organization (WHO) and the International Union Against Tuberculosis and Lung Disease (IUATLD) stated that, in 1990, 1.7 billion people were infected by mycobacterium TB and this number reached 1.9 billion in 1994. Approximately 2 billion people have died of TB and mortality has increased twice to this day [1–3]. Data from the Turkey Ministry of Health and Dispensaries Against Tuberculosis showed that the number of infected persons who had no BCG vaccine was 12–15 million in the country. Every year, 30,000–40,000 new cases are estimated. Incidence studies

revealed that most of the patients were young (64% of TB victims were between 15 and 44 years old) [4]. When diminished cellular immunity is taken into account, it is obvious that fertile women are especially under high risk of contracting TB. Kothari et al. [5] reported that the incidence of TB during pregnancy was 250–100,000. The ratio of extrapulmonary TB and late admission to the clinics was found to be high (52%). Pregnancy does not alter the course of active TB; however, the evaluation of the degree of activity of the pulmonary disease radiographically may be diffucult at times [6]. It is important to diagnose and treat infected patients aggressively because congenital infection and bacteremia develop in a pregnant patient [7].

Human immunodeficiency virus infection leads to a progressive debilitation of the immune system, rendering infected individuals susceptible to opportunistic infections such as pulmonary TB and recurrent pneumonia that rarely afflict patients with intact immunosystem [7].

In our study, we aimed to evaluate the aggresiveness of TB cases seen in Kutahya and their fetal effects in the last 5 years. Since TB cases activated by HIV infection in pregnancy are presented mainly in the literature, we aimed to investigate the aggressiveness of pulmonary TB among pregnant women and the effects of the disease on the fetus in Kutahya where HIV positive cases are not seen.

Materials and methods

Pregnant women, aged between 20 and 44 years old, were investigated retrospectively in Kutahya region from 2000 to 2005. The status and prevalence of the disease, medical therapy, results of treatment, and its effect on the fetus were analyzed by reviewing the files and interviewing patients face to face. Respondents were asked whether they have prenatal care, have sexually transmitted infections, and have undergone any laboratory tests. The Kutahya medical records of the Provincial Health Directorate were used (Table 1; Fig. 1). The definitive diagnosis of TB remains to be based on tuberculin skin test, direct microscopic sputum examination, sputum culture for mycobacterium TB, and chest radiography. Rapid diagnosis of infectious TB by simple sputum smear for acid-fast bacilli remains an important tool, as more rapid molecular techniques are being developed [8]. Also, HIV infection tests [HIV antibody test, antigen test, and polymerase chain reaction (PCR) test] were done. The cases where tuberculin skin tests were positive (greater than 15 mm) were examined systematically and a chest radiography was taken. Also, they were investigated in terms of HIV infection. Two pregnant women at 30 and 34 weeks gestational age were diagnosed to have TB at the last trimester. These cases clinically had less weight and poor nutrition. Treatment was started at 30 and 34 gestational weeks as soon as TB was diagnosed. Isoniazid at 300 mg, rifampin at 600 mg, pyridoxine (vitamin B6) at 50 mg daily for 6 months to prevent peripheric neuropathy, pyrazinamid at 25 mg per kilogram for 2 months and ethambutol at 25 mg per kilogram for 2 months were given during their pregnancy. Resistance of anti-TB drugs was assessed with drug resistance tests at 2, 4, and 8 weeks of treatment. The effectiveness of the treatment and the progression of the disease were assessed with physical examination, laboratory tests, and chest radiograph. The cases of TB in the pregnant women were evaluated in terms of contagion of TB 1 week before delivery and sputum smear was done for acid-fast bacilli. Congenital TB was not

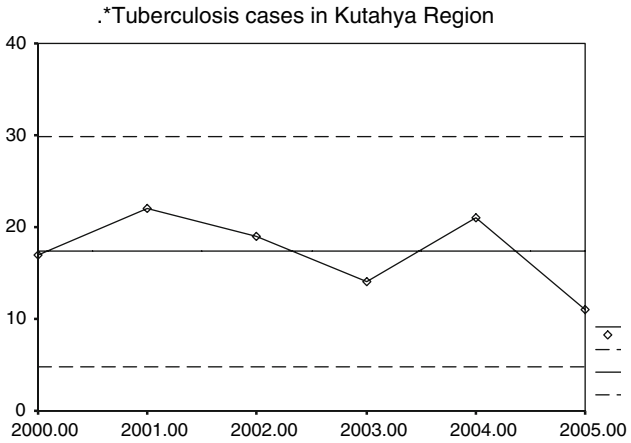

Fig. 1 Tuberculosis cases in Kutahya region

Table 1 Tuberculosis cases and tuberculosis cases during pregnancy in Kutahya region from 2000 to 2005[a]

Years	20–29 (age)	30–45 (age)	Total number of patients	Number of pregnancy
2000	7	10	17	2
2001	7	15	22	1
2002	10	9	19	1
2003	6	8	14	0
2004	9	12	21	1
2005	5	6	11	0
2000–2005	45	61	106	5

[a] Kutahya medical records of the Provincial Health Directorate were used

determined and their babies were evaluated by a pediatrician postnatal. Labor was induced in a sterile delivery room. Both mothers and babies were examined for TB infection postnatal and again 1 month later. While the mothers were receiving anti-TB drugs during puerperium, they continued to breast-feed at the same time.

Results

There were 667 registered TB cases in Kutahya region between 2000 and 2005 (Fig. 1). Of these, 264 (39.58%) were women and 106 (40.15%) of them were between 20 and 44 years old. All of the cases had pulmonary TB. Tuberculosis was determined in five pregnant women—2 (2000), 1 (2001), 1 (2002), and 1 (2004) (Table 1). None of the TB cases had HIV infection. These cases were evaluated as class 1 TB. Three pregnancies excluded from the study were terminated electively below 10 weeks. Two women gave birth at 38 weeks gestation. One baby was born through vaginal delivery and the other was born with SCA as a consequence of unsuccessful induction. Anti-TB drugs were begun as soon as the three pregnancies were ended and after the delivery of the two women. Resistance to anti-TBdrugs was analyzed with drug resistance tests at 2, 4, and 8 weeks of treatment. No resistance was determined. Both babies underwent physical examinations and laboratory tests; the results were normal. Neither congenital nor postnatal TB was determined 1 year after delivery. Babies were given INH at 5 mg per kilogram for 3 months prophylactically. Tuberculin skin test was performed after 3 months. Under 5-mm endurations were assessed as negative.

Discussion

Among the communicable diseases, TB is the second leading cause of death worldwide, killing nearly 2 million people each year. It is estimated that about one-third of the world population is infected with TB (2 billion people) and about 10% of this figure will progress to a disease state. Most cases occur in less developed countries [8]. Approximately 2 billion people have died of TB [1, 2]; 98% of them live in developing countries. In the late 1980s and in early 1990s, TB incidence increased with emigration of people from different countries, owing to many factors such as HIV prevalence, poverty, highly resistant strains of TB, and drug abuse [3].

A review of the literature pointed to a few studies which emphasize that TB continues more aggressively during pregnancy and has been associated with HIV in recent years. Mofenson et al. [9] had described the HIV, mycobacterium TB, and pregnancy as a deadly combination [10–12]. However, our study showed that HIV infection proved fatal in this deadly combination. In a study done by Ramogale et al. [13] pregnancy related with HIV is evaluated as having a great impact on maternal mortality. Other studies emphasized that TB is the main fatal factor in HIV-positive women [14, 15]. It is neccesseary to clarify that the quartet combination of INH + RFP + ETB + PRZ for treatment can be life saving in HIV negative cases, although there is immunosuppression in pregnancy.

TB courses are more aggressive and fatal in pregnancy [16]. Goel et al. [11] reported paraplegy in a pregnant woman who had Pott's disease. The fetal outcome of this pregnancy was good. Kingdom et al. [12] stated that delayed diagnosis and therapy for TB was responsible for mortality and neurological morbidity during pregnancy. McInytre et al. [17] presented two pregnant women with TB in 1985–1987. One of them died; the other was reported to be an asymptomatic case with pleural effusion. Despite these few case declarations, TB in pregnancy was cured successfully with the quartet treatment.

Pillay et al. [18] reported that HIV infection rate in 146 TB cases was 71.9%. Mortality rate was 10.3% in these cases. They pointed out the importance of correct diagnosis of TB during pregnancy for maternal and perinatal health in regions where TB and HIV prevalence is high. In addition, TB with HIV positive cases are not cured easily and result in early mortality [16]. Conversely, our HIV negative TB cases in pregnancy did not progress aggressively.

In a study done by Figueroa et al. [19] TB was presented as a risk factor for pregnancy. Early treatment of the disease during gestation brings about a good perinatal outcome. To support this idea, three cases were cured by ending their pregnancies with curretage. It can be thought that improving immunosuppression by ending the pregnancies is a main factor to consider in increasing the effectiveness of the therapy. Schaefer et al. [20] emphasized the importance of treatment and reported that chemotherapy is the most important cornerstone in pregnancy with pulmonary TB. The isoniazid and ethambutol regimen was pointed out as the best choice. In the same study, it was shown that the course of TB was not clinically good and drug resistance could be seen frequently. The quartet therapy with INH + RFP + ETB + PRZ was used for the treatment in our study. Contrary to what the literature said, drug resistance was not seen in our research. Steichen et al. [21] reported that INH augmented the necessity of pyridoxine because of peripheric neuropathy in both HIV positive and pregnant TB cases. We did not determine peripheric neuropathy in our cases.

The diagnostic approach for the evaluation of TB or latent mycobacterium TB infection was unchanged by pregnancy. It included clinical suspicion of disease, tuberculin skin

testing or interferon-gamma-based assay, chest radiography with appropriate shielding when indicated, and acid-fast bacillus stain and culture of clinical material. For patients with active TB, therapy should be initiated as soon as the diagnosis is established. Initiation of treatment for latent infection during pregnancy should be considered based on the risk for progression to active disease [22]. In our cases, the diagnostic tests were done according to the literature as soon as TB was diagnosed. The results of early diagnosis and quartet treatment showed good outcome in HIV negative TB cases.

Bello et al. [8] reported that 95% of TB cases can be cured with anti-TB drugs. However, these patients were not pregnant. Despite pregnancy, treatment of TB was done successfully as long as it involved HIV negative cases, as in our study. Tripathy et al. [23] studied a total of 111 pregnant women diagnosed as having pulmonary and glandular TB between 1986 and 2001. If appropriate chemotherapy is given to pregnant women with TB, they are not at a higher risk than non-pregnant women with TB. But HIV with TB and pregnancy are currently a big challenge. When we compare our study to Tripathy's, TB was less seen among pregnant women in Kutahya due to two reasons: first, Only a few case records were found; and second, the HIV positive cases were not seen. In our two cases, the progression of disease and drug resistance were the same as those found in Tripathy's study. Besides, resistance to anti-TB drugs during pregnancy was noted in the literature [24–26].

TB is a major problem among women in the reproductive age, but congenital TB is rare. The greatest threat to the neonate is the acquisition of TB infection shortly after birth, which tends to progress rapidly to a serious TB disease in a large proportion of untreated infants. The clinician caring for pregnant women should be aware of the risk factors for TB infection and disease and should test women and families accordingly [27].

Because of good control and preventive programs, TB incidence has decreased gradually since 1993. The proportion of TB cases estimated was 6.8 per 100,000 population in 1998 in the USA. The US Center for Disease Control and Prevention (CDC) reported that TB diminished in proportion to 31% in 1992. Therefore, the TB threat to mothers and infants remains [3].

However, in our case, there is no difference in terms of aggressiveness of TB between pregnant and non-pregnant women. Also, considerable increase in the incidence of TB and multidrug resistance was not seen. In contrast to HIV positive with TB cases in developed countries, the prognosis of our cases was quite well in terms of both mother and newborn. Whether prenatal or natal contamination with TB happened was not determined. Contrary to what was previously reported in the literature, two cases of TB were diagnosed during the advanced period of pregnancy. But the results of the treatment were good. It is thought that the combined isoniazid, rifampin, ethambutol, and pyrazinamide regimen is a good choice for antimycobacterial therapy.

Conclusion

In conclusion, TB resurgence is recently increasing in comparison with former cases in less developed countries. The rise of HIV infections seems to be the cause of increased TB incidence. However, in Kutahya region, TB cases during pregnancy were markedly fewer than those in developed countries. It is expected that TB progresses aggressively during pregnancy. Moreover, HIV, mycobacterium TB, and pregnancy are described as a deadly combination [9]. However, TB did not progress aggressively in our cases because HIV infection was not seen. HIV negative pregnant cases are less aggressive and nonresistant to treatment compared with HIV positive pregnant cases. It is attributed to the absence of HIV infection in the area and the improved socioeconomic status of Kutahya recently. Isoniazid, rifampin, ethambutol, and pyrazinamide are the preferred drugs for therapy.

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