

Infectious respiratory diseases in pregnancy - results of a 15-year study in Seoul

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Summary

Purpose: To determine the incidence, clinical course, and outcomes of infectious disease during pregnancy. **Methods:** A retrospective review was performed of pregnant woman with infectious lung diseases including pneumonia and active tuberculosis. Demographic, clinical data and radiologic findings were collected for all the cases identified. **Results:** During the study period, our hospital had 14,603 pregnancies. Among these, eight patients (55/100,000) had pneumonia and two (14/100,000) had active pulmonary tuberculosis. The median interval between onset of symptoms and diagnosis was 8.8 days for pneumonia and 41 days for tuberculosis. All the pneumonia patients recovered, and death during the study period occurred in one patient with active tuberculosis. **Conclusion:** The incidence of pneumonia during pregnancy was not higher than that of non-pregnant women and the patients evidenced complete recovery. The incidence of tuberculosis was a higher incidence than reported in developed countries and could cause diagnostic delays and progress to acute respiratory failure. Therefore, clinicians should be aware of the potential for nonspecific presentation of tuberculosis in pregnancy and should consider a diagnosis in women particularly in endemic areas.

Key words: Lung; Pregnancy; Infection.

Introduction

Pregnancy is a physiological change which renders a woman more susceptible to a variety of pulmonary disorders. Several manuscripts have reported on pulmonary diseases of pregnancy, including conditions specific to pregnancy and diseases of non-specific causes. Pulmonary complications owing to non-pregnancy-specific conditions are known to be the leading cause of death and poor prognosis; among these, infectious respiratory diseases are an essential cause of morbidity and mortality in pregnant women [1-3]. The majority of these respiratory diseases included pneumonia and tuberculosis, especially in endemic regions. Several reviews and studies concerning pneumonia and tuberculosis during pregnancy have already been conducted [4-7]. Pregnant patients with infectious disease have been found to be significantly more likely to evidence nonspecific symptoms and to experience delays in obtaining chest radiographs than non-pregnant women; even with regard to tuberculosis, up to 20% of pregnant women are asymptomatic. On the other hand, reported infant and maternal mortality from untreated active tuberculosis is generally reported as between 30%-40%, despite the fact that mortality due to pneumonia was in a range similar to that of community-acquired pneumonia (CAP) in non-pregnant patients [8, 9]. Therefore, clinicians and radiologists should attempt to gain a better understanding of the incidence of these diseases in large series and clinical courses, as well as image findings. In this article, we have assessed the incidence of infectious respiratory disease (pneumonia, tuberculosis) in pregnancy for 15 years at our institute, and describe the correlation of the clinical course with the initial and follow-up chest radiological images.

Materials and Methods

Setting

Our institute is an 850-bed district general hospital. The hospital serves a population of approximately 500,000 in the territory of Yangcheon-gu. The notification rate of tuberculosis in Korea in 2008 was 70.3/100,000. The hospital notifies approximately 2,600 pneumonia patients annually and 380 tuberculosis patients annually. The obstetric unit performed approximately 1,100 deliveries/year from 1995-2003 and 800 deliveries/year from 2004-2009 with a recent apparent decrease in the fertility rate in Korea.

Patients

Over a 15-year period spanning November 1994 to November 2009, pregnant women who were cared for at our institute were retrospectively investigated. In this study, patients with pneumonia and active tuberculosis (TB) during pregnancy were selected. The incidence, disease progression, and its effects on delivery were evaluated by reviewing the patient's medical records and radiologic studies. A total of 14,603 delivery cases and 13,015 pregnant women presented at our hospital for 15 years. Among these, ten women (10 cases) were identified who had pneumonia and active TB during pregnancy.

Results

During the 15-year period, our hospital had 14,603 pregnancies, and the total number of pregnant women was 13,015. Among these, ten women (68/100,000) had pregnancy-related infectious respiratory diseases, including pneumonia (n = 8) and active pulmonary tuberculosis (n = 2) in our hospital. The mean age was 32 years (range

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28-36 years). All cases were initially diagnosed during pregnancy without any exacerbation of pre-existing disease. They had no past or familial histories or chronic medical condition. Mean gestational age at the time of symptom onset was 26 weeks (range 3-37 weeks) and mean gestational age at the time of diagnosis was 28 weeks (range 4-39 weeks). Mean gestational age at the time of delivery was 36 weeks (range 15-40 weeks) and two women were still pregnant during the study period (32 weeks and 36 weeks) without significant medical and radiological problems. One woman with pneumonia delivered before 37 weeks of gestation by cesarean section due to high fever, and one woman with active pulmonary TB had a spontaneous abortion at a gestational age of 15 weeks; however, none of the patients in the pneumonia group delivered prior to 34 weeks of gestation. All women delivered by normal spontaneous vaginal deliveries except for the previously mentioned patient with pneumonia, who delivered by cesarean section. Death due to pregnancy-related infectious disease during the study period occurred in one patient with active TB. The details of each case and disease including incidence, symptoms, gestational age at symptom onset, and diagnosis are presented in Tables 1 and 2. Patient outcomes of pregnancy and infectious disease are provided in Table 3.

Pneumonia

Eight patients (55/100,000) had pneumonia during pregnancy. The median interval between onset of symptoms and diagnosis of pneumonia was 8.8 days. Among these patients, two women had *Mycoplasma pneumonia* infections confirmed by serum Ab test. A gram-negative bacillus was cultured from the patient's blood in one case. In the other cases, microorganisms were not confirmed from blood or sputum cultures, but could be diagnosed as pneumonia by clinical symptoms, laboratory findings, and chest radiography. All the pneumonia patients recovered without significant compliance with commonly used antibiotics in pregnancy (category A and B) and the mean recovery time was 9.7 days from the day of diagnosis.

Active pulmonary tuberculosis

Two women (14/100,000) had active pulmonary TB during pregnancy. They had a mild fever during the mean 41 days prior to admission (42 days and 40 days, respectively), but the diagnosis of TB was delayed without adequate treatment. One of these patients was diagnosed with miliary TB at a gestational age of 13 weeks by chest roentgenography and computed tomography (CT) scan, and had an abrupt spontaneous abortion at a gestational age of 15 weeks. Her condition worsened soon after abortion with combined pneumonia, acute renal failure, hepatic failure, DIC, ARDS, and she finally expired within 18 days of diagnosis from TB. The other woman had no significant symptoms except intermittent mild fever, and TB was identified at a gestational age of 39 weeks and three days due to abnormalities on chest roentgenography and CT scan. In the result of the sputum study, the growth of *Mycobacterium tuberculosis* was reported. She delivered

Table 1. — Incidence of pneumonia and pulmonary tuberculosis during pregnancy.

Disease	No. of patients (%)	No. of cases (%)
Pneumonia	8 (0.061)	8 (0.055)
Active pulmonary tuberculosis	2 (0.015)	2 (0.014)

Table 2. — Clinical symptoms, gestation at onset, and gestation at diagnosis of ten patients with infectious respiratory disease during pregnancy.

Disease	Case	Age	Clinical symptoms	Gestation at onset of symptoms	Gestation at diagnosis
Pneumonia	1	36	Cough	36 weeks	38 weeks
	2	34	Cough, dyspnea	3 weeks	4 weeks
	3	33	Cough, fever	35 weeks	36 weeks
	4	28	Cough, fever	21 weeks	21 weeks
	5	32	Fever	26 weeks	28 weeks
	6	30	Cough, fever	37 weeks	39 weeks
	7	28	Fever, dyspnea, chest pain	31 weeks	33 weeks
Active pulmonary tuberculosis	8	30	Cough	33 weeks	33 weeks
	9	36	Fever	33 weeks	39 weeks
	10	32	Fever	8 weeks	13 weeks

Table 3. — Outcome of pregnancy and infectious respiratory diseases during pregnancy.

Disease	Case	Type of delivery	Outcome of pregnancy (gestation at delivery, weeks)	Clinical outcome
Pneumonia	1	NVD	Full term (40)	Treated for 1 week
	2*	—	—	Treated for 2 weeks
	3	C/S	Full term (37)	Treated for 2 weeks
	4	unknown	unknown	unknown
	5	NVD	Full term (40)	Treated for 5 days
	6	NVD	Full term (39)	Treated for 1 week
	7	NVD (twin)	Full term (38)	Treated for 2 weeks
	8*	—	—	Treated for 1 week
Active pulmonary tuberculosis	9	35 weeks	Full term (40)	Treated for 6 months
	10	8 weeks	Spontaneous abortion (15)	Death due to ARDS, DIC, and renal failure

—*: women on pregnancy during study period, NVD = normal vaginal delivery, C/S = cesarean section, ARDS = acute respiratory distress syndrome, DIC = disseminated intravascular coagulation.

a baby on the next day with a spontaneous vaginal pattern without induction, and recovered after six months of treatment with Pyrazinamide, Rifampicin, Isoniazid, and Ethambutol.

Discussion

Our study involved a series of patients who developed infectious pulmonary complications including TB in pregnancy, reported in a tuberculosis-endemic area. An accurate estimate of the incidence of pneumonia during pregnancy is somewhat difficult to obtain. The few studies of pneumonia in pregnancy conducted thus far mostly include small numbers of cases, and evidence marked variations in incidence over the years, with values of 0.44-8.5 per 1,000 deliveries [10, 11]. In the 1970s and early 1980s, reduced incidence was reported with 0.44-

Fig. 1



Fig. 2

Figure 1. — On simple chest roentgenography diffuse ground glass opacities in both lungs can be seen. Right-sided aortic arch is also seen.

Figure 2. — Axial image of chest HRCT scan (1 mm in thickness) shows miliary nodules with diffuse bilateral ground glass attenuated lesions.

0.78 per 1,000 deliveries in comparison with the results noted in the years prior to 1965 (6.3–8.5 per 1000 deliveries), presumably due to advanced antibiotics and improvements in obstetric care [4, 6]. Recently, an incidence of 1.1–2.7 per 1,000 deliveries has been reported, and this increase in incidence may be reflective of the higher proportion of pregnant women with chronic medical conditions [12]. The results of our study demonstrated an incidence of pneumonia at 0.55 per 1,000 deliveries, which is lower than in many other contemporary reports. However, these results were obtained from pregnant women who did not use drugs and were HIV-negative; therefore, these results are not representative or applicable to the general population.

Some studies have compared pregnant women with pneumonia and pregnant women without pneumonia in order to establish risk factors associated with the development of pneumonia and the effects of pneumonia on pregnancy. However, there have been no studies in which pneumonia in pregnant and non-pregnant women has been directly compared. Hence, there is currently no information as to whether pneumonia is any different in pregnant women and non-pregnant adults. There is certainly no convincing evidence to suggest that the documented changes in the immune system result in clinically significant immunosuppression with increased susceptibility to respiratory tract infection. Therefore, pregnancy is generally not regarded as a risk factor for pneumonia, and its incidence in pregnancy has been reported in recent studies not to differ from that in non-pregnant adults [13, 14].

There have been no detailed studies specifically focusing on the microbial agents involved in pneumonia during pregnancy. In bacterial and atypical pathogens, *Streptococcus pneumoniae* is the most common organism identified, followed by *Hemophilus influenzae*. *Mycoplasma pneumoniae* might be expected to be an additional common pathogen, particularly in this age group.

Pneumonia has been cited as the third most frequent cause of indirect obstetric death in North America. However, recent studies have reported a maternal mortality of 1–4%, which approximates a mortality of 0–4% from pneumonia in hospitalized non-pregnant adults. In our series, only one patient permitted a cesarean section to be conducted due to aggravated fever with pneumonia – however, the patient recovered completely seven days after delivery. The others were well controlled with antibiotics for a mean 9.7 days after normal vaginal deliveries, without complications. This result corresponds well with their results showing very low mortality from pneumonia in pregnancy.

Recent publications have described series of cases of TB in pregnancy within various populations, but no large-series data have been published thus far in endemic areas, to the best of our knowledge. Approximately two million deaths occurred from TB worldwide in 1997, 98% of them in developing countries. In South Korea, the incidence of active TB was reported to be approximately 70.3/100,000 persons in 2008 [15]. This is still much higher than in the US, where the value was 6.8/100,000 population between 1993 and 1998. In our series, two cases of TB developed in 15 years, and this result was consistent with an incidence of 14 per 100,000 people, which is higher than reported in developed countries, but lower than the data from results including all ages and all regions in Korea. This discrepancy with a total incidence in Korea is most probably the result of differences in the study populations. All of our patients were < 40 years of age, had no history of corticosteroid use, HIV-infection, or other comorbidities, including diabetes mellitus and chronic renal disease. Another possible contributory factor might be that Yangcheon-gu in Seoul, which is served by our hospital, was deemed the nation's best "tuberculosis-controlled city" in 2008.

It is a matter of great interest to consider whether pregnancy is an independent risk factor for developing TB and progression to acute respiratory failure. The question of pregnancy as a risk factor for TB has been previously debated. The one deceased patient in the TB group was the only case in which the patient died as the result of infectious complications during the study period. The radiologic findings of this patient showed a miliary pattern. A true estimate of the incidence of non-miliary TB versus miliary TB during pregnancy is difficult to obtain. As a predictor of miliary TB, one recent study indicated that age < 30 years, HIV infection, and corticosteroid use were strong independent predictors of miliary TB [16]. Our patient had a family history of TB with her father; however, there were no other risk factors, including history of diabetes mellitus or immunodepressive conditions, including HIV infection. It is difficult to describe pregnancy as a risk factor or poor prognostic factor in TB because our results were obtained from only two cases; however, although pregnancy is not thought to change the course of TB, TB clearly poses a risk to the pregnant woman and her fetus. A larger series on studies of this topic are clearly warranted.

Two patients with TB who, because they were pregnant, were subjected to regular medical reviews. The fact that these patients had symptoms of TB for over 40 days before diagnosis is clearly a cause for concern. We identified a variety of reasons for this delay, including non-specific symptoms and tendency to defer radiological investigations during pregnancy. Up to 20% of pregnant women with TB have been shown to be asymptomatic [17]. In one study, a group of pregnant patients with pulmonary TB were significantly more likely to be asymptomatic at the time of diagnosis [18]. In another, pregnant patients with TB were significantly more likely to experience non-specific symptoms and also to experience delays in obtaining chest radiographs, as compared to non-pregnant women with TB [19].

Conclusion

The incidence of pneumonia in this study was 0.55 per 1,000 deliveries, which is not higher than that of non-pregnant women and the patients evidenced recovery without compliance within a mean of 9.7 days. Diagnosis and management strategies for non-pregnant adults can, therefore, also be applied to pregnant women, thus addressing possible toxicity to the fetus. The incidence of TB was 0.14 per 1,000 deliveries in this study, which was a higher incidence than reported in developed countries. Moreover, TB during pregnancy can cause diagnostic delays, and may progress to acute respiratory failure. Therefore, clinicians and radiologists should be aware of

the potential for nonspecific presentation of TB in pregnancy and should consider such a diagnosis in women, particularly in areas in which the prevalence of TB is high.

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