Upper Respiratory Tract Infection during Pregnancy: Is It Associated with Adverse Perinatal Outcome?

Liran Stiller-Timor, M.D.,[1] Amalia Levy, Ph.D.,[2] Gershon Holcberg, M.D.,[3] and Eyal Sheiner, M.D., Ph.D.[3]

ABSTRACT

We sought to determine whether there is an association between upper respiratory tract infection (URTI) requiring hospitalization during pregnancy and adverse perinatal complications. A retrospective population-based study comparing all singleton pregnancies of patients with and without URTI requiring hospitalization was performed. Multiple logistic regression models were performed to control for confounders. Data were collected from the computerized perinatal database. Out of 186,373 deliveries, 0.13% ($n = 246$) required hospitalization due to URTI during pregnancy. URTI was significantly associated with preterm deliveries (PTD; 15.9% versus 7.9%; $p < 0.001$), lower birth weight (3082 ± 624 versus 3183 ± 546 g; $p < 0.001$), and higher rate of cesarean deliveries (CD; 20.3% versus 13.2%; $p < 0.001$) as compared with the comparison group. Even after controlling for possible confounders using multivariable analyses, the significant association between URTI and PTD (weighted odds ratio [OR] = 2.2; 95% confidence interval [CI] 1.6 to 3.1; $p < 0.001$) and CD (weighted OR = 1.5; 95% CI 1.1 to 2.2; $p = 0.020$) persisted. In contrast, no significant association was documented between URTI and premature rapture of membranes (4.9% versus 6.9%; $p = 0.212$), low Apgar scores (< 7) at 5 minutes (0.4% versus 0.6%; $p = 0.761$), and perinatal mortality (0 to 4% versus 1.3%; $p = 0.223$). Maternal URTI requiring hospitalization is an independent risk factor for PTD and CD.

KEYWORDS: URTI, preterm delivery, low birth weight, cesarean delivery

The healthy adult will experience an average of two upper respiratory tract infections (URTIs) annually.[1] The disease is characterized by sore throat, cough, and nasal discharge and resolves within 3 weeks without medical treatment.[1] The most common infectious etiology is viral. More than 200 respiratory viral antigens are known. The most important are: coronavirus, rhinovirus, and adenovirus.[2] The most common bacterial agents are group A Streptococcus, which commonly causes pharyngeal infections, and *Streptococcus pneumonia*, *Haemophilus influenzae*, and *Moraxella catarrhalis*, which cause secondary infections in the middle ear and paranasal sinuses.[2]

[1]Otolaryngology Head & Neck Surgery Department, [2]Epidemiology and Health Services Evaluation and [3]Obstetrics and Gynecology, Faculty of Health Sciences, Soroka University Medical Center, Ben Gurion University of the Negev, Beer-Sheva, Israel.

Address for correspondence and reprint requests: Eyal Sheiner, M.D., Ph.D., Department of Obstetrics and Gynecology, Soroka University Medical Center, P.O. Box 151, Be'er-Sheva, Israel (e-mail: sheiner@bgu.ac.il).

Am J Perinatol 2010;27:619–624.

Received: October 22, 2009. Accepted after revision: January 4, 2010. Published online: March 3, 2010.
DOI: http://dx.doi.org/10.1055/s-0030-1249364.
ISSN 0735-1631.

During pregnancy, physiological changes in the upper and lower respiratory system take place, as well as in the general immunologic status. In the lower respiratory system, physiological changes are expressed as elevated pulmonary ventilation. In the upper respiratory system, sinonasal mucosal congestion occurs and is attributed to hormonal changes.[3,4] These changes are suggested as a reason for higher incidence of snoring.[4] Snoring may be associated with higher incidence of preeclampsia, gestational hypertension, intrauterine growth restriction (IUGR), and low Apgar scores.[4] Controversy exists in the literature regarding the relationship between respiratory tract infections and adverse perinatal outcomes, such as preeclampsia, premature rapture of membrane (PROM), preterm delivery (PTD), and low birth weight.[3,5–7] Microbial endotoxins and proinflammatory cytokines increase the production of prostaglandins and matrix-degrading enzymes, all factors implied in the mechanisms of term and preterm labor. Fever was recently noted as a risk factor for PTDy.[8] However, while searching the Medline, only a small number of studies regarding this issue was found.[3,5–7,9] Although correlation between asthma with acute respiratory tract infection and PROM was suggested by Getahun et al.[4] Hartret et al[5] did not find a correlation between respiratory hospitalization during influenza season and perinatal adverse outcomes like PTD, low birth weight, and cesarean delivery (CD). In 2006, Laibl and Sheffield[6] concluded after reviewing the literature that respiratory tract infections correlate with higher rate of both morbidity and mortality.

Mouth breathing can increase periodontal disease by drying oral mucosa and denture, causing caries. Periodontal disease as well as nasal congestion can cause sinusitis.[7] The special immunologic state in pregnancy is characterized by activation of the innate immunity and suppression of the acquired limb of the immune response. These changes make pregnant women more susceptible to infections and to the effects of toxins of microorganisms.[9,10]

This population-based cohort study was aimed to determine whether URTI requiring hospitalization during pregnancy is associated with adverse perinatal outcomes.

MATERIALS AND METHODS

A retrospective population-based study comparing all singleton pregnancies of women with and without URTI was conducted. Deliveries occurred between the years 1988 and 2008 at the Soroka University Medical Center. This is the sole hospital in the Negev, the southern part of Israel, serving the entire obstetric population in this region. The group of URTI requiring hospitalization was defined as pregnant women hospitalized with fever and with symptoms of URTI of unspecified site or acute tonsillitis.

National health services in Israel provide comprehensive perinatal care for all women. Data were collected from the computerized perinatal database that consists of information recorded directly after delivery by an obstetrician. Only four skilled medical secretaries routinely examine the information, including gestational morbidity and hospitalizations, before entering it into the database. Coding is done after assessing the medical prenatal care records as well as the routine hospital documents. These procedures ensure maximal completeness and accuracy of the database. The following clinical characteristics were evaluated: maternal age, parity, gestational age, and birth weight. The following obstetric risk factors were examined: previous CD, recurrent abortions (two or more consecutive spontaneous abortions), fertility treatments (either ovulation induction or in vitro fertilization), hypertensive disorders (preeclampsia, eclampsia, and chronic hypertension), gestational diabetes mellitus, smoking, PROM, and IUGR. The following labor characteristics and perinatal outcomes were assessed: malpresentation, placental abruption, placenta previa, nonprogressive labor one to two stages, labor induction, CD, Apgar score less than 7 at 1 and 5 minutes, birth weight (and specifically low birth weight, <2500 g), and perinatal mortality. The local ethics institutional review board approved the study.

Statistical analysis was performed with the SPSS package (SPSS 15 version, Chicago, IL). Statistical significance was calculated using the chi-square test for differences in qualitative variables and analysis of variance for differences in continuous variables. Stratified analysis was performed using multivariable logistic regression models and the Mantel-Haenszel technique. Odds ratios (ORs) and their 95% confidence intervals (CIs) were computed; $p < 0.05$ was considered statistically significant.

RESULTS

Out of 186,373 deliveries, 0.132% ($n = 246$) required hospitalization because of URTI. The clinical and obstetric characteristics of women with and without URTI are displayed in Table 1. Women with URTI had a higher rate of PTD than those without URTI (15.9% versus 7.9%; $p < 0.001$). In addition, the group of women with URTI delivered neonates with a significantly lower birth weight and had a higher rate of CD (20.3% versus 13.2%; $p < 0.001$) as compared with the comparison group. Even while controlling for labor induction, using the Mantel-Haenzel technique, the association between URTI and PTD remained significant (weighted OR = 2.2; 95% CI 1.6 to 3.1; $p < 0.001$; data not shown in the table).

Table 1 Clinical Characteristics of Women with or without Upper Respiratory Tract Infections (URTI) during Pregnancy and Delivery

Characteristics	Women with URTI ($n=246$)	Women without URTI ($n=186{,}373$)	p
Maternal age, y (%)			
<18	1.3	1.1	0.145
18–35	90.3	86.2	
36+	8.5	12.7	
Smoking (%)	2.0	1.3	0.340
Gestational age (wk)	38.6 ± 2.5	39.2 ± 2.2	<0.001
Gestational age at delivery, wk (%)			
<37	15.9	7.9	
37–42	80.5	87.5	
42+	3.7	4.7	<0.001
Birth weight, g (%)			
<2500	11.0	7.8	0.170
2500–4000	85.0	87.3	
>4000	4.1	4.8	
Gravid (%)			
1	20.7	20.0	0.308
2–4	52.0	48.2	
5+	27.2	31.7	
Parity (%)			
1	28.9	24.1	0.128
2–4	51.2	51.7	
5+	19.9	24.2	

Data are expressed as means $\pm$ standard deviation, or numbers and percentages.

Table 2 Maternal Risk Factors of Pregnancy Outcome of Women with and without Upper Respiratory Tract Infections (URTI)

Characteristics	Women with URTI ($n=246$), %	Women without URTI ($n=186{,}373$), %	OR	95% CI	p
Maternal history					
Previous cesarean delivery	14.2	11.7	1.2	0.9–1.8	0.214
Recurrent abortions	4.9	5.4	0.9	0.5–1.6	0.71
Fertility treatment	4.1	1.9	2.2	1.2–4.1	0.013
Hypertensive disorders	8.5	6.0	1.4	0.9–2.3	0.095
Mild preeclampsia	4.9	3.5	1.4	0.8–2.5	0.235
Severe preeclampsia	1.2	1.1	1.1	0.3–3.4	0.866
Chronic hypertension	2.8	1.8	1.6	0.7–3.4	0.201
Diabetes mellitus	8.9	6.7	1.4	0.8–2.1	0.169
Gestational diabetes	6.5	5.5	1.2	0.8–1.6	0.481
Pregestational diabetes	2.4	1.3	1.9	0.9–4.4	0.100
Premature rapture of membranes	4.9	6.9	0.7	0.4–1.2	0.212
Placental abruption	0.8	0.7	1.1	0.3–4.4	0.884
Placenta previa	0.1	0.4	1.0	0.9–1.1	0.310
Labor induction	35.4	28.1	1.4	1.0–1.8	0.012
Failure to progress stage I	4.1	1.9	2.1	1.1–4.1	0.014
Failure to progress stage II	1.6	1.6	1.0	0.3–2.7	0.99
Cesarean delivery	20.3	13.2	1.7	1.2–2.3	<0.001

Data are presented as percentages, odds ratios (OR), 95% confidence intervals (CI), and p values for statistical significance.

Table 3 Neonatal Outcome of Women with and without Upper Respiratory Tract Infections (URTI)

Characteristics	Women with URTI ($n = 246$), %	Women without URTI ($n = 186,373$), %	OR	95% CI	p
Apgar score <7 at 1 min	5.8	4.0	1.4	0.8–2.5	0.165
Apgar score <7 at 5 min	0.4	0.6	0.7	0.1–5.2	0.761
Perinatal mortality	0.4	1.3	0.3	0.0–2.2	0.223
Gender					
Male	53.7	51.3			0.456
Female	46.3	48.7			

Data are presented as percentages, odds ratios (OR), 95% confidence intervals (CI), and p values for statistical significance.

Maternal risk factors as well as pregnancy outcomes of women with and without URTI are shown in Table 2. Women with URTI had a significantly higher rate of labor induction, failure to progress in labor (first stage), and fertility treatment as compared with patients without URTI.

While controlling for labor dystocia, labor induction, maternal age, and gestational age using a multivariable logistic regression model with CD as the outcome variable, URTI was noted as an independent risk factor for CD (weighted OR = 1.5, 95% CI 1.1 to 2.2; $p = 0.020$; data not shown in the table).

Table 3 presents fetal and neonatal outcomes between the groups. No significant differences were noted between the groups regarding low Apgar scores or perinatal mortality.

DISCUSSION

There is a controversy in the literature concerning the relationship between URTI and the incidence of adverse perinatal outcomes.[3–7] Microbial endotoxins and proinflammatory cytokines increase the production of prostaglandins and matrix-degrading enzymes, all factors implied in the mechanisms of term and preterm labor. Indeed, fever was recently noted as a risk factor for PTD.[8] However, while searching Medline, only a small number of studies regarding this issue were found.[3,5–7,9] The most important finding of this study is that maternal URTI requiring hospitalization during pregnancy is an independent risk factor for PTD, low birth weight, and CD. On the contrary, our study did not establish a significant association between URTI and preeclampsia, gestational hypertension, IUGR, and PROM. The higher rates of CD in patients with URTI can partially be explained by the higher rate of complications observed in these women such as PTD (either before 34 weeks or 37 weeks of gestation), as well as the higher rate of labor induction. A solid body of evidence indicates that induction of labor during pregnancy is a risk factor for CD rather than spontaneous labor at term gestation.[11,12]

Van Putte-Katier showed lower lung compliance among neonates born to mothers suffering from respiratory infections during pregnancy, suggesting higher neonatal morbidity.[9] Surprisingly, the results of this study indicated that although there was a higher rate of complications during pregnancy, both perinatal mortality and Apgar score <7 at 5 minutes where not significantly different between women with URTI and those without URTI, even when adjusted for maternal age and parity.

The strength of this study is that this population-based study is one of the largest studies analyzing the relationship between pregnancy outcome and URTI requiring hospitalization. Still, this study has weaknesses mostly due to its retrospective nature. Unfortunately, most cases in our database were classified as unspecified URTI requiring hospitalization, rather than specifically mentioning the site of infection or inflammation. It is important to emphasize that these outcomes are only applicable to the hospitalized population.

In summary, URTI requiring hospitalization during pregnancy is an independent risk factor for PTD, lower birth weight, and CD. Further prospective studies should investigate the correlation between specific sites and symptoms to perinatal complication.

REFERENCES

1. Infectious causes of rhino sinusitis. In: Merchant SN, Nadol JB, eds. Cummings Otolaryngology. 2005;1182–1196
2. Ellegård EK. Pregnancy rhinitis. Immunol Allergy Clin North Am 2006;26:119–135, vii
3. Franklin KA, Holmgren PA, Jönsson F, Poromaa N, Stenlund H, Svanborg E. Snoring, pregnancy-induced hypertension, and growth retardation of the fetus. Chest 2000;117:137–141
4. Getahun D, Ananth CV, Oyelese Y, Peltier MR, Smulian JC, Vintzileos AM. Acute and chronic respiratory diseases in pregnancy: associations with spontaneous premature rupture of membranes. J Matern Fetal Neonatal Med 2007;20:669–675
5. Hartert TV, Neuzil KM, Shintani AK, et al. Maternal morbidity and perinatal outcomes among pregnant women with respiratory hospitalizations during influenza season. Am J Obstet Gynecol 2003;189:1705–1712
6. Laibl V, Sheffield J. The management of respiratory infections during pregnancy. Immunol Allergy Clin North Am 2006;26:155–172, viii

7. Sacks G, Sargent I, Redman E. An innate view of human pregnancy. Immunol Today 1999;20:114–118
8. Bensal A, Weintraub AY, Levy A, Holcberg G, Sheiner E. The significance of peripartum fever in women undergoing vaginal deliveries. Am J Perinatol 2008;25:567–572
9. Van Putte-Katier N, Uiterwaal CS, De Jong BM, Kimpen JL, Verheij TJ, Van Der Ent CK; Whistler Study Group. The influence of maternal respiratory infections during pregnancy on infant lung function. Pediatr Pulmonol 2007;42:945–951
10. Naccasha N, Gervasi MT, Chaiworapongsa T, et al. Phenotypic and metabolic characteristics of monocytes and granulocytes in normal pregnancy and maternal infection. Am J Obstet Gynecol 2001;185:1118–1123
11. Simhayoff N, Sheiner E, Levy A, Hammel RD, Mazor M, Hallak M. To induce or not to induce labor: a macrosomic dilemma. Gynecol Obstet Invest 2004;58:121–125
12. Newman DE, Paamoni-Keren O, Press F, Wiznitzer A, Mazor M, Sheiner E. Neonatal outcome in preterm deliveries between 23 and 27 weeks' gestation with and without preterm premature rupture of membranes. Arch Gynecol Obstet 2009; 280:7–11