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**OBJECTIVE:** Using 2 nationwide population-based datasets, this study aimed to assess the risk of adverse pregnancy outcomes, including low birthweight (LBW), preterm birth, small for gestational age (SGA), cesarean section (CS), lower Apgar score, and preeclampsia/eclampsia, between women with and without pneumonia.

**STUDY DESIGN:** This study included 1462 women who had been hospitalized with pneumonia during pregnancy and used 7310 matched women without pneumonia as a comparison group.

**RESULTS:** Compared to women without pneumonia, conditional logistic regression analyses showed that the adjusted odds ratios for LBW, preterm birth, SGA, CS, and preeclampsia/eclampsia in women with pneumonia were 1.73 (95% confidence interval [CI], 1.41–2.12), 1.71 (95% CI, 1.42–2.05), 1.35 (95% CI, 1.17–1.56), 1.77 (95% CI, 1.58–1.98), 3.86 (95% CI, 1.64–9.06), and 3.05 (95% CI, 2.01–4.63), respectively.

**CONCLUSION:** Women with pneumonia during pregnancy had significantly higher risk of LBW, preterm birth, SGA, low Apgar scores infants, CS, and preeclampsia/eclampsia, compared to unaffected women.

**Key words:** pneumonia, pregnancy, pregnancy outcome

Cite this article as: Chen Y-H, Keller J, Wang I-T, et al. Pneumonia and pregnancy outcomes: a nationwide population-based study. Am J Obstet Gynecol 2012;207:288.e1-7.

Pneumonia is a common infection of the pulmonary parenchyma that is a significant cause of hospitalization for respiratory disorders during pregnancy, complicating 0.5–1.5 per 1000 pregnancies in the United States. Pneumonia is the most frequent cause of fatal non-obstetric maternal death in the United States. It is widely held that several physiologic and immunologic changes experienced during pregnancy may predispose pregnant women toward a more severe course of pneumonia, which may result in greater maternal and fetal morbidity and mortality.

The relationship between pneumonia and pregnancy outcome has long been a topic of interest among researchers. A growing number of studies have found that women with pneumonia were more likely to have preterm deliveries as well as lower average birthweight and small for gestational age (SGA) infants compared to women without pneumonia. Moreover, Romanyuk et al also found that pneumonia was significantly associated with placental abruption, intrauterine growth restriction, cesarean section (CS), low Apgar scores, and severe preeclampsia.

Even though several studies have explored the risk of adverse pregnancy outcomes among women with pneumonia, their studies generated inconsistent findings that remain to be resolved. A number of studies failed to observe any increased risk of preterm and low birthweight (LBW) infants among women with pneumonia. In addition, Shariatzaheh and Marrie suggested that pneumonia may not have any negative effects related to fetal outcome at all, and speculated that pneumonia may be very well tolerated during pregnancy. Therefore, the relationship between pneumonia and pregnancy outcomes remains unclear to date. Since prior studies dealing with the present topic have tended to be hospital-based studies often characterized by low case numbers or population subgroups, their inconsistent finding may have been due to the use of selective data, limited sample sizes, and inadequate control of confounding factors.

To fill this gap in the literature this study aimed to examine the risk of adverse pregnancy outcomes (LBW, preterm birth, SGA, CS, congenital anomalies, Apgar scores at 5 minutes, and preeclampsia/eclampsia) in pregnant women with pneumonia using a nationwide population-based dataset in Taiwan. To the best of our knowledge, this is the largest and most complete nationwide population-based study to investigate the relationship between pneumonia and adverse pregnancy outcomes.

**Materials and Methods**

**Database**

Two nationwide population-based datasets were used in this study: The Taiwan National Health Insurance (NHI) Research Dataset (NHIRD) and the Taiwan national birth certificate registry. The NHIRD includes all the registration files as well as original claims data for reimbursements covered by the Taiwan NHI pro-
### TABLE 1
Sociodemographic characteristics of pregnant women with and without pneumonia in Taiwan, 2005 (n = 8772)

| Variable                                      | Women with pneumonia (n = 1462) | Comparison women (n = 7310) | P value |
|-----------------------------------------------|---------------------------------|-----------------------------|---------|
| **Infant characteristics**                    |                                 |                             |         |
| Sex                                           |                                 |                             | .068    |
| Male                                          | 788                             | 3749                        |         |
| Female                                        | 674                             | 3561                        |         |
| **Maternal characteristics**                  |                                 |                             | .616    |
| Parity                                        |                                 |                             |         |
| 1                                             | 744                             | 3625                        | 50.0    |
| 2                                             | 554                             | 2784                        | 38.1    |
| ≥3                                            | 164                             | 874                         | 11.9    |
| Age, y                                        |                                 |                             | 1.000   |
| <20                                           | 50                              | 250                         | 3.4     |
| 20-24                                         | 352                             | 1760                        | 24.1    |
| 25-29                                         | 454                             | 2270                        | 31.1    |
| 30-34                                         | 427                             | 2135                        | 29.2    |
| >34                                           | 179                             | 895                         | 12.2    |
| Education level                               |                                 |                             | .070    |
| ≤Junior high school                          | 160                             | 713                         | 9.7     |
| Senior high school                            | 1041                            | 5121                        | 70.1    |
| ≥College                                      | 261                             | 1476                        | 20.2    |
| Alcohol abuse/alcohol dependence syndrome    | 3                               | 7                           | 0.4     | .258    |
| Gestational diabetes                          | 48                              | 227                         | 3.1     | .722    |
| Gestational hypertension                      | 44                              | 192                         | 2.6     | .409    |
| Anemia                                        | 158                             | 723                         | 9.9     | .287    |
| Coronary heart disease                        | 20                              | 45                          | 0.6     | .002    |
| Hyperlipidemia                                | 31                              | 139                         | 1.9     | .579    |
| Obesity                                       | 9                               | 36                          | 0.5     | .548    |
| Geographic region                             |                                 |                             | .604    |
| North                                         | 614                             | 3105                        | 42.5    |
| Center                                        | 393                             | 1988                        | 27.2    |
| South                                         | 412                             | 2045                        | 27.9    |
| East                                          | 43                              | 172                         | 2.4     |
| Paternal age, y                               |                                 |                             | .892    |
| <30                                           | 518                             | 2602                        | 35.6    |
| 30-34                                         | 466                             | 2363                        | 32.3    |
| >34                                           | 478                             | 2345                        | 32.1    |

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in this study, which allowed us to calculate the period of pregnancy for each woman. In addition, we randomly retrieved 7310 comparison women (5 for every woman with pneumonia) to match the distribution of the study group in terms of age (<20, 20-24, 25-29, 30-34, and ≥35 years). As a result, 8772 women were included in this study.

**Variables of interest**

The selected variables for adverse pregnancy outcomes were LBW (<2500 g), preterm gestation (<37 completed weeks of gestation), SGA (birthweight <10th percentile for gestational age–specific birthweight distribution), major congenital anomalies (hydrocephaly, anencephaly, microcephaly, meningomyelecele, encephalocele, and spina bifida), Apgar scores at 5 minutes (<7), preeclampsia/eclampsia, and CS.

This study also took potential confounding factors into consideration in the regression models. These included factors consisting of maternal characteristics (highest educational level, gestational diabetes, gestational hypertension, coronary heart disease [CHD], anemia, hyperlipidemia, alcohol abuse/alcohol dependence syndrome, and obesity), infant sex and parity, and paternal age.

**Statistical analysis**

We performed all the analyses conducted in this study using a software package (SAS System for Windows, version 8.2; SAS Institute Inc, Cary, NC). We used $\chi^2$ tests to explore the differences in maternal, paternal, and infant characteristics between women with and without pneumonia. We further used conditional logistic regression analyses (conditioned on maternal age) to calculate the odds of adverse pregnancy outcomes between women with and without pneumonia after adjusting for maternal, paternal, and infant characteristics. A 2-sided $P$ value <.05 was considered statistically significant in this study.

**Results**

Of the 1462 women with pneumonia, 1363 (about 93%) were bacterial pneumonia. Table 1 presents the distributions of maternal, paternal, and infant characteristics between women with and without pneumonia. A higher prevalence of LBW infants (9.8% vs 5.9%, $P < .001$), preterm births (12.3% vs 7.1%, $P < .001$), SGA infants (20.7% vs 16.2%, $P < .001$), CS (55.5% vs 40.6%, $P < .001$), preeclampsia/eclampsia (2.7% vs 0.8%, $P < .001$), and Apgar scores <7 at 5 minutes (0.7% vs 0.2%, $P < .001$) than women without pneumonia. There were no significant differences in the prevalence of major congenital anomalies (0.9% vs 0.7%, $P = .396$) between women with and without pneumonia. Moreover, the distributions of adverse pregnancy outcomes did not differ significantly for women with viral and with bacterial pneumonia (data not shown in table).

Table 2 presents the crude and adjusted odds ratios (ORs) for adverse pregnancy outcomes between women with and without pneumonia. Conditional logistic regression analyses (conditioned on maternal age group) revealed that compared to women without pneumonia, the OR for LBW, preterm birth, SGA, CS, Apgar scores <7 at 5 minutes, and preeclampsia/eclampsia in women with pneumonia were 1.73 (95% confidence interval [CI], 1.41–2.12), 1.71 (95% CI, 1.42–2.05), 1.35 (95% CI, 1.17–1.56), 1.77 (95% CI, 1.58–1.98), 3.86 (95% CI, 1.64–9.06), and 3.05 (95% CI, 2.01–4.63) respectively, after adjusting for highest maternal educational level, marital status, geographic region, gestational diabetes, gestational hypertension, CHD, anemia, hyperlipidemia, obesity, and alcohol abuse/alcohol dependence syndrome, as well as infant sex and parity, and paternal age. There was no increased OR for congenital anomalies for women with pneumonia.

Furthermore, we analyzed the OR for adverse pregnancy outcomes according to pregnancy trimester. We found that the onset of pneumonia in about 93.6% of the women analyzed in this study occurred during the first trimester. Table 4 shows that when compared to comparison women, the adjusted OR for LBW, preterm birth, SGA, CS, Apgar scores <7 at 5 minutes, and preeclampsia/eclampsia in women with pneumonia during...
We found that the onset of pneumonia in women more likely than unaffected mothers to have LBW, preterm birth, SGA, CS, and low Apgar scores. The risks of adverse pregnancy outcomes associated with pneumonia are presented in Table 3.

| Variable                      | Women with pneumonia vs comparison women |
|-------------------------------|------------------------------------------|
| Low birthweight               | ORa (95% CI) 1.74c (1.43–2.12)            |
|                               | Adjusted ORb (95% CI) 1.73c (1.41–2.12)    |
| Preterm birth                 | ORa (95% CI) 1.84d (1.53–2.20)            |
|                               | Adjusted ORb (95% CI) 1.71d (1.42–2.05)    |
| Small for gestational age     | ORa (95% CI) 1.35c (1.17–1.56)            |
|                               | Adjusted ORb (95% CI) 1.35c (1.17–1.56)    |
| Cesarean section              | ORa (95% CI) 1.83c (1.63–2.06)            |
|                               | Adjusted ORb (95% CI) 1.77c (1.58–1.98)    |
| Congenital anomalies          | ORa (95% CI) 1.30 (0.71–2.41)             |
|                               | Adjusted ORb (95% CI) 1.15 (0.62–2.15)    |
| Low Apgar score at 5 min      | ORa (95% CI) 4.19d (1.81–9.72)            |
|                               | Adjusted ORb (95% CI) 3.86d (1.64–9.06)    |
| Preeclampsia/eclampsia        | ORa (95% CI) 3.31c (2.20–4.98)            |
|                               | Adjusted ORb (95% CI) 3.05c (2.01–4.63)    |

CI, confidence interval; OR, odds ratio.

* Calculated by conditional logistic regression (conditioned on maternal age group); b Adjustment made for mother’s education, gestational diabetes, gestational hypertension, anemia, coronary heart disease, hyperlipidemia, obesity, alcohol abuse/alcohol dependence syndrome, geographic region, paternal age, and infant’s sex, and parity; c P < .001; d P < .01.

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the first trimester of pregnancy were 1.73, 1.70, 1.35, 1.79, 3.74, and 3.17, respectively.

**COMMENT**

Our nationwide population-based study demonstrated that after adjusting for comorbidities and potential confounders, mothers with pneumonia were 1.73, 1.71, 1.35, 1.77, 3.86, and 3.05 times more likely than unaffected mothers to have LBW, preterm birth, SGA, CS, low Apgar scores, and preeclampsia/eclampsia, respectively. Furthermore, we analyzed the risk for adverse pregnancy outcomes according to pregnancy trimester. We found that the onset of pneumonia of about 93.6% of the women with pneumonia analyzed in this study occurred during the first trimester. These women were also found to be more likely than comparison women to have adverse pregnancy outcomes. However, we further investigated the effect of etiology on the occurrence of adverse pregnancy outcomes among women with a case of pneumonia during their pregnancies, and failed to detect a statistically significant difference in the occurrence of LBW, preterm birth, SGA, CS, and preeclampsia/eclampsia between women with viral and bacterial pneumonia.

Our findings are consistent with prior studies that found women with pneumonia were more likely to have preterm deliveries babies with lower average birthweights and SGA infants than women without pneumonia. In addition, our results are also in line with 1 study conducted by Romanuyk et al that found pneumonia to be significantly associated with CS, low Apgar scores, and preeclampsia. Although some previous studies failed to observe any increased risk of preterm or LBW infants among women with pneumonia, these inverse conclusions were mostly based on studies utilizing patient self-reports and characterized by relatively small sample sizes and an inadequate control of confounding. Therefore, their recall bias and other potential limitations may have resulted in an under-ascertainment of pneumonia during the study pregnancy, which would have clearly undermined the strength of their findings.

The mechanisms by which pneumonia produces adverse pregnancy outcomes are still unclear. Development of the fetus is largely determined by the morphology and functioning of the mother-placenta-fetus system. It is possible that pneumonia during pregnancy may infect the placenta. Infection may then be transmitted to the fetus from the placenta through the umbilical vein, or via the aspiration or ingestion of amniotic fluid contaminated by placental or genital infections. Intrauterine infection has emerged as a frequent and important mechanism of disease in preterm birth. The onset of preterm labor can be considered a mechanism of the host defense against intrauterine infection whereby the mother eliminates infected tissues (membranes, decidual, and/or fetus) to maintain reproductive fitness. Moreover, a higher risk of LBW and SGA was noted in the pneumonia group, probably due to the lower gestational age at delivery.

On the other hand, there is a widespread general belief that pregnant women with severe acute respiratory syndrome have frequent episodes of oxygen desaturation. Their gravid uterus has been shown to elevate the diaphragm by up to 4 cm in the third trimester, while oxygen consumption is increased by 20% during pregnancy and functional residual capacity is decreased, rendering the woman intolerant to hypoxia. Therefore, severe maternal respiratory
illness affecting the fetal oxygen supply may seriously endanger the fetus. Wong et al. found that these patients had frequent episodes of oxygen desaturation, often falling <90%. The situation resembles that of those living at high altitudes, causing a low arterial partial pressure of oxygen (PaO2) and consequent adverse pregnancy outcomes. In addition, since the stress of severe hypoxia usually necessitates delivery by CS, a higher risk of CS was also noted in our pneumonia mothers.

This study used a large, unselected national dataset to demonstrate that women with pneumonia were at an increased risk for having adverse pregnancy outcomes compared to unaffected mothers. Moreover, in this study the majority of pregnant women with a case of pneumonia experienced the onset of disease during their first trimester. This finding is supported by a study conducted by Lindsay et al. that reported a decline in the rate of influenza-like illness episodes as the stage of pregnancy progressed. One possible reason underlying this finding may involve behavioral changes that may be associated with a woman’s pregnancy status and knowledge of her pregnancy status. Women in the second and third trimesters of their pregnancies, who are more likely to be aware of their pregnancy status, may be more prudent in avoiding occasions where they may encounter people with colds, the flu, or other respiratory tract infections, and may adopt a stricter practice of other preventative behaviors such as an increased frequency of hand washing. On the other hand, women who are not yet pregnant or have become pregnant but are unaware of their pregnancy status may be less likely to engage in such preventative behaviors. It is further possible that some of the women experiencing pneumonia in this study had already encountered or had been infected with pneumonia at the time they became pregnant but were only at a subclinical or incubation stage of the disease. Nevertheless, the underlying factors contributing to the higher incidence of pneumonia during the first trimester remain obscure and deserve further investigation.

There are substantial implications of this study. We believe that the increased risk for adverse birth outcomes among women with pneumonia during their pregnancies warrants a higher level of surveillance among this population to ensure that medical intervention be exercised as soon as possible. This recommendation is supported by a recent review study which observed that concern for fetal outcome should not delay treatment, as improvement in maternal status and most particularly oxygenation is the best way to ensure that the fetus will be protected. In addition, the treatment in the gravid patient should generally follow standard guidelines for the treatment of pneumonia in adults. Therefore, early recognition of the disease process and prompt treatment are required to best ensure for an optimal outcome for both mother and fetus. Furthermore, primary prevention in the form of a pneumococcal vaccine is both available and recommended for pregnant women.

### Table 4

| Variable                        | Comparison women n = 7310 | Women with pneumonia  |
|--------------------------------|---------------------------|-----------------------|
|                                 |                           | First trimester n = 1368 | Second trimester n = 45 | Third trimester n = 49 |
| Low birthweight                 |                           |                       |                       |                       |
| Adjusted OR (95% CI)            | 1.00                      | 1.73 (1.40–2.13)      | 1.18 (0.36–3.88)      | 1.34 (1.01–1.80)      |
| Preterm birth                   |                           |                       |                       |                       |
| Adjusted OR (95% CI)            | 1.00                      | 1.70 (1.41–2.05)      | 0.85 (0.25–2.84)      | 1.43 (1.12–1.84)      |
| Small for gestational age       |                           |                       |                       |                       |
| Adjusted OR (95% CI)            | 1.00                      | 1.35 (1.17–1.57)      | 1.34 (0.64–2.80)      | 1.12 (0.89–1.42)      |
| Cesarean section                |                           |                       |                       |                       |
| Adjusted OR (95% CI)            | 1.00                      | 1.79 (1.59–1.99)      | N/A                   | N/A                   |
| Congenital anomalies            |                           |                       |                       |                       |
| Adjusted OR (95% CI)            | 1.00                      | 1.04 (0.54–2.03)      | 2.75 (0.36–21.19)     | 1.41 (0.72–2.75)      |
| Low Apgar score at 5 min        |                           |                       |                       |                       |
| Adjusted OR (95% CI)            | 1.00                      | 3.74 (1.55–9.01)      | N/A                   | 2.18 (1.09–4.38)      |
| Preeclampsia/eclampsia          |                           |                       |                       |                       |
| Adjusted OR (95% CI)            | 1.00                      | 3.17 (2.08–4.83)      | N/A                   | N/A                   |

CI: confidence interval; N/A: case number <5; OR: odds ratio.
*a Adjustments made for mother’s education, gestational diabetes, gestational hypertension, anemia, coronary heart disease, hyperlipidemia, obesity, alcohol abuse/alcohol dependence syndrome, geographic region, paternal age, and infant’s sex, and parity; b P < .001; c P < .01; d P < .05.

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with underlying diseases (e.g., immunocompromised states, diabetes, chronic cardiopulmonary diseases) to reduce their risks of pneumonia episodes. The results of this study further underscore the utility of this vaccine.

The clinical course of pneumonia in pregnancy was well described 20–30 years ago. However, to the best of our knowledge all the previous studies investigating pregnancy outcomes among women with pneumonia have been conducted in Western countries with this investigation being the first study regarding pregnancy outcomes among women with pneumonia in Asia. Unlike prior studies that included participants from diverse ethnic groups, >98% of Taiwan’s residents are of Chinese Han ethnicity, so the composition of the population is quite homogenous. While this may exempt our study from potential confounding by race, it also means that our results may not be generalizable to other ethnic groups. In addition, we used nationwide population-based datasets, linking the NHIRD with the national registry of births, which leaves little room for selection and nonresponse biases. Moreover, the very large sample size used in this study provides ample statistical power to detect differences between pregnant women with and without pneumonia in risk of adverse birth outcomes.

Despite the strengths of our study mentioned above, our findings still need to be interpreted with caution due to several important limitations. First, the NHIRD lacks clinical information, and therefore did not allow us to differentiate study participants according to the severity of their pneumonia. Secondly, the NHIRD uses discharge diagnoses provided by treating physicians, and no standardized criteria were used to define cases. This may have left room for bias due to case misclassification. Lastly, although we have adjusted for the influence of some potential maternal and pregnancy-specific confounders, information such as maternal smoking history, substance abuse, alcohol consumption, and body mass index (particularly prepregnancy maternal body mass index) was not available through our datasets.

Our study demonstrated that after adjusting for potential confounders, women with pneumonia during pregnancy had significantly higher risks of LBW, preterm birth, SGA, low Apgar scores, CS, and preeclampsia/eclampsia, compared to unaffected mothers. Since the exact mechanisms underlying these associations are not yet known, future studies are recommended, both to replicate the results of this study and to clarify the mechanisms behind them, enabling more specific interpretation of these findings.

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