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Oligohydramnios increases the risk of respiratory hospitalization in childhood: a population-based study

Li-Nien Chien[1], Hung-Yi Chiou[2], Chia-Woei Wang[3], Tsu-Fu Yeh[4] and Chung-Ming Chen[4,5,6]

BACKGROUND: Pulmonary hypoplasia is associated with reduced lung function in infancy. The aim of this study was to evaluate the hypothesis that children exposed to oligohydramnios display an increased risk of hospitalization for respiratory illness by using a population-based matched-cohort design.

METHODS: We used three nationwide population-based data sets to identify 5,228 women who gave birth during 2004 to 2007 and were diagnosed with oligohydramnios during the third trimester of pregnancy. A cohort of 20,912 unaffected pregnant women was matched with these cases, according to neonatal sex and gestational age, maternal age and education, and level of prenatal care. Respiratory hospitalization and respiratory failure were defined using discharge diagnostic codes.

RESULTS: Oligohydramnios-exposed children had an 8% higher incidence rate of respiratory hospitalization and an 80% higher incidence rate of respiratory failure, compared with children without oligohydramnios exposure. This risk remained after adjusting for all potential risk factors. Cox regression analyses indicated that the adjusted hazard ratios of respiratory hospitalization and respiratory failure were 1.07 (95% confidence interval (CI): 1.01–1.15; $P = 0.030$) and 2.20 (95% CI: 1.26–3.84; $P = 0.005$), respectively.

CONCLUSION: Children exposed to oligohydramnios during the third trimester of pregnancy display an increased risk of hospitalization for respiratory illness.

Pulmonary hypoplasia is uncommon in the perinatal period but is a critical cause of death in newborn infants. Oligohydramnios is one of the abnormalities most commonly associated with pulmonary hypoplasia (1). Lung growth is influenced by physical factors such as the intrauterine space, lung liquid volume and pressure, and breathing movements. For lungs to develop, the physical space in the fetal thorax must be adequate, and amniotic fluid must be drawn into the lungs through fetal breathing movements, leading to their distension. Physical forces play vital roles in regulating fetal lung growth and maturation (2,3). During lung development, the main physical force experienced by the lung is stretching induced by breathing movements and lung fluid in the air spaces (4). Oligohydramnios reduces the intrathoracic cavity size, disrupting fetal lung growth and leading to the development of pulmonary hypoplasia (5,6).

Oligohydramnios is a critical factor affecting short- and long-term clinical prognoses. In a study by Lindner *et al.* (7), neonates exposed to oligohydramnios experienced short-term respiratory morbidity (including high ventilator settings, increased incidence of hypoxemia and hypercapnia, and pulmonary hypertension) and tended to experience more air leaks than did healthy neonates. Pulmonary hypoplasia is also associated with reduced lung function in infancy (8). Previous studies have reported the short-term perinatal outcomes of pregnancies complicated by oligohydramnios (9–12). A small case–control study found that infants born following the preterm rupture of membranes are at a high risk of prolonged initial hospitalization and significant respiratory morbidity in their first 2 y of life (13). However, the long-term effects of oligohydramnios on the respiratory system remain unknown. We hypothesized that children exposed to oligohydramnios *in utero* are likely to develop respiratory diseases during the first few years of life, which is typically the period of rapid lung growth and development. We evaluated whether children with a history of oligohydramnios displayed an increased risk of hospitalization for respiratory illness by using a population-based matched-cohort design.

RESULTS

Table 1 displays the neonatal, maternal, and paternal characteristics of oligohydramnios-exposed children (cases, n = 5,228) and children without oligohydramnios exposure (controls, n = 20,912). Compared with the matched cohort, children with oligohydramnios exposure were more likely to have a low birth weight, to be born to mothers of low parity, to have young fathers, and to have mothers with gestational hypertension, diabetes, or atopic dermatitis during pregnancy.

Table 2 displays the incidence rates of respiratory hospitalization and respiratory failure. During the observational period, 1,165 cases and 4,372 controls were hospitalized because of a diagnosis of respiratory diseases. Among the children who were hospitalized during the observational period, 19.9% had

[1]School of Health Care Administration, College of Public Health and Nutrition, Taipei Medical University, Taipei, Taiwan; [2]School of Public Health, College of Public Health and Nutrition, Taipei Medical University, Taipei, Taiwan; [3]Department of Obstetrics and Gynecology, Taipei Medical University Hospital, Taipei, Taiwan; [4]Maternal and Child Health Research Center, College of Medicine, Taipei Medical University, Taipei, Taiwan; [5]Department of Pediatrics, Taipei Medical University Hospital, Taipei, Taiwan; [6]Department of Pediatrics, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan. Correspondence: Chung-Ming Chen (cmchen@tmu.edu.tw)

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Table 1. Neonatal, maternal, and paternal demographics, as well as the maternal risk factors of pregnant women diagnosed with oligohydramnios and pregnant women without oligohydramnios

Variables	Oligohydramnios *n* = 5,228 (%)	No oligohydramnios *n* = 20,912 (%)	*P* value
Neonatal characteristics			
Sex (female)	2,635 (50.4)	10,154 (50.4)	1.000
Gestational age (wk)			
37	464 (8.9)	1,856 (8.9)	1.000
38	1,140 (21.8)	4,560 (21.8)	
39	1,552 (29.7)	6,208 (29.7)	
40	1,644 (31.4)	6,576 (31.4)	
41	411 (7.9)	1,645 (7.9)	
42	17 (0.3)	67 (0.3)	
Birth weight (g), mean (SD)	3,145 (337)	3,195 (327)	<0.00
Parity			
1	4,372 (83.6)	16,532 (79.1)	<0.001
2	753 (14.4)	3,813 (18.2)	
3	103 (2.0)	567 (2.7)	
Mode of delivery (cesarean section)	1,496 (28.6)	6,098 (29.2)	0.437
Five-min Apgar score <7	58 (1.1)	253 (1.2)	0.549
Maternal characteristics			
Age (y)			1.000
15–24	914 ((17.5)	3,656 (17.5)	
24–29	2,052 (39.3)	8,208 (39.3)	
30–34	1,706 (32.6)	6,824 (32.6)	
35–49	556 (10.6)	2,224 (10.6)	
Education level (y)			1.000
<9	380 (7.3)	1,520 (7.3)	
9–12	2,132 (40.8)	8,528 (40.8)	
>12	2,716 (52.0)	10,864 (52.0)	
Unmarried	84 (1.6)	314 (1.5)	0.578
Level of prenatal care			1.000
10 visits	2,349 (44.9)	9,396 (44.9)	
7–9 visits	1,688 (32.3)	6,752 (32.3)	
4–6 visits	1,049 (20.1)	4,196 (20.1)	
0–3 visits	142 (2.7)	568 (2.7)	
Paternal characteristics			
Age (y)			0.001
15–24	309 (5.9)	1,098 (5.3)	
24–29	1,409 (27.0)	5,232 (25.0)	
30–34	1,997 (38.2)	8,004 (38.3)	
35–49	1,405 (26.9)	6,074 (29.0)	
50–80	108 (2.1)	504 (2.4)	
Education level (y)			0.184
<9	435 (8.3)	1,907 (9.1)	
9–12	2,156 (41.2)	8,601 (41.1)	
>12	2,637 (50.4)	10,404 (49.8)	
Insurance eligibility groups			
1 (highest)	1,016 (19.4)	4,117 (19.7)	0.084
2	1,703 (32.6)	6,651 (31.8)	
3	865 (16.5)	3,390 (16.2)	
4	723 (13.8)	2,875 (13.7)	
5	340 (6.5)	1,613 (7.7)	
6	581 (11.1)	2,266 (10.8)	
Urbanization of area of residence			<0.001
1 (most urbanized)	994 (19.0)	4,208 (20.1)	
2	1,706 (32.6)	6,242 (29.8)	
3	1,331 (25.5)	4,857 (23.2)	
4	1,197 (22.9)	5,605 (26.8)	
Maternal risk factors during pregnancy			
Gestational hypertension	106 (2.0)	178 (0.9)	<0.001
Hypertension	22 (0.4)	107 (0.5)	0.402
Gestational diabetes	439 (8.4)	1,827 (8.7)	0.435
Diabetes	62 (3.1)	386 (1.8)	<0.001
Asthma	63 (1.2)	256 (1.2)	0.910
Allergic rhinitis	257 (4.9)	1,061 (5.1)	0.641
Atopic dermatitis	112 (2.1)	312 (1.5)	0.001

two admissions, 7.5% had four admissions, and 5.9% had four or more admissions. Less than 0.5% had more than 10 admissions. Children with a history of oligohydramnios were more likely to be hospitalized for respiratory illness than were those without a history of oligohydramnios. The incidence rates were 6.51 (95% confidence interval (CI): 6.14–6.89) per 100 person-years in oligohydramnios-exposed children and 6.04 (95% CI: 5.86–6.22) per 100 person-years in children without oligohydramnios exposure. Respiratory failure occurred in 19 cases and 38 controls, with incidence rates of 0.09 (95% CI: 0.06–0.14) per 100 person-years in the oligohydramnios cases and 0.05 (95% CI: 0.03–0.06) per 100 person-years in the controls.

The cumulative risk of hospitalization with respiratory illness was similar between the cases and controls, but the risk differed as the duration of the observation period increased (log-rank test; $P = 0.026$; **Figure 1a**). The risk of hospitalization for respiratory failure was higher in the cases than in the controls and differed significantly with increasing duration of the observation period (log-rank test; $P = 0.012$; **Figure 1b**).

Table 2. Incidence of respiratory hospitalization and respiratory failure in children with and without oligohydramnios exposure during gestation, per 100 person-years

	Oligohydramnios			No oligohydramnios		
Outcomes	Per 100 person-years	Events	Incidence (95% CI)	Per 100 person-years	Events	Incidence (95% CI)
Respiratory hospitalization	17,901	1,165	6.51 (6.14, 6.89)	72,398	4,372	6.04 (5.86, 6.22)
Respiratory failure	20,756	19	0.09 (0.06, 0.14)	83,126	38	0.05 (0.03, 0.06)

CI, confidence interval.

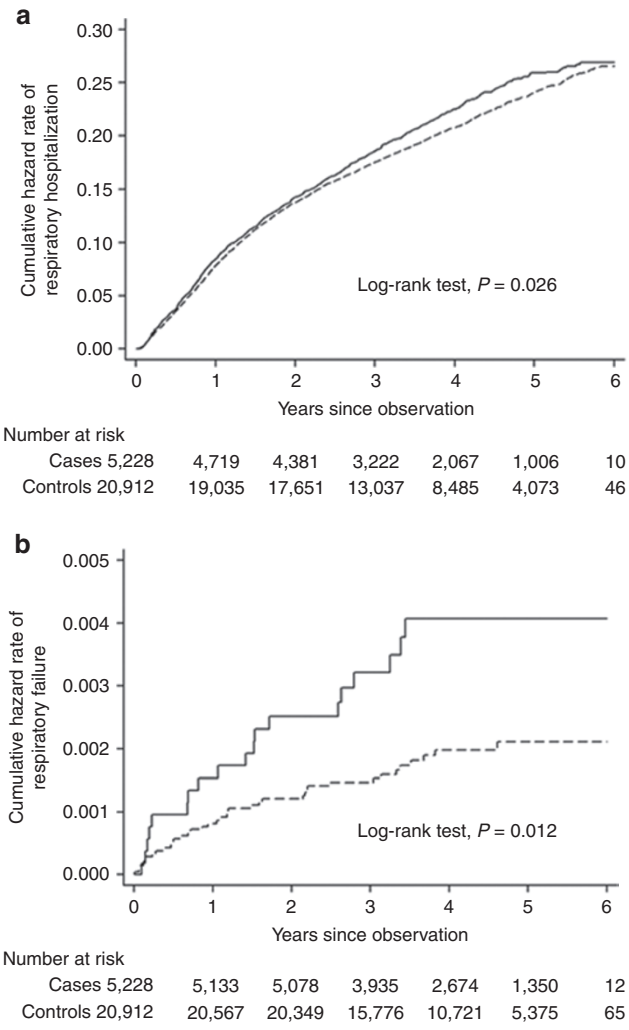

Figure 1. Kaplan–Meier failure curve for (**a**) respiratory hospitalization and (**b**) respiratory failure in oligohydramnios-exposed children (cases, solid line) and children without oligohydramnios exposure (controls, dashed line). The top panel shows that the risk of respiratory hospitalization was significantly higher in cases than in controls (log-rank test; $P = 0.026$). The bottom panel shows that the risk of respiratory failure was also significantly higher in cases than in controls (log-rank test; $P = 0.012$).

Table 3 displays the hazard ratios (HRs) of hospitalization for respiratory illness and respiratory failure. The results from Cox regression analysis indicated that oligohydramnios increased the risk of respiratory hospitalization; the adjusted HR was 1.07 (95% CI: 1.01–1.15; $P = 0.030$). Oligohydramnios also increased the risk of respiratory failure; the adjusted HR was 2.20 (95% CI: 1.26–3.84; $P = 0.005$).

Table 3. Unadjusted and adjusted HRs of respiratory hospitalization and respiratory failure in children with oligohydramnios exposure

	Respiratory hospitalization		Respiratory failure	
Model	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Unadjusted	1.08 (1.01, 1.15)	0.026	2.00 (1.15, 3.47)	0.013
Adjusted	1.07 (1.01, 1.15)	0.030	2.20 (1.26, 3.84)	0.005

Reference group: children without oligohydramnios exposure.
Adjusted for infant characteristics (sex, 5-min Apgar score <7, and cesarean section), parental demographics (age and education), marital status, insurance eligibility category, urbanization of area of residence, level of prenatal care, maternal risk factors (gestational hypertension, hypertension, gestational diabetes, diabetes mellitus, asthma, allergic rhinitis, and atopic dermatitis), and birth year.
CI, confidence interval; HR, hazard ratio.

DISCUSSION

In this 1:4 matched retrospective cohort study, we monitored a cohort of 5,228 children exposed to oligohydramnios and 20,912 children without oligohydramnios exposure, for hospitalization for respiratory illness and respiratory failure. Oligohydramnios-exposed children had an 8% higher incidence rate of respiratory hospitalization and an 80% higher incidence rate for respiratory failure compared with children without oligohydramnios exposure. This risk remained after adjusting for neonatal characteristics, parental demographics, insurance eligibility group, urbanization of insurance registration area, level of prenatal care, and maternal risk factors. The observation that children with oligohydramnios exposure were at greater risk of respiratory hospitalization in later life compared with the control group is biologically reasonable. Oligohydramnios can result in pulmonary hypoplasia in human fetuses, and pulmonary hypoplasia is associated with reduced lung function in infants. Although the number of events was low, children exposed to oligohydramnios displayed a higher risk of respiratory failure requiring hospitalization than did those without oligohydramnios exposure.

The reported incidence of oligohydramnios ranged from 1.2 to 11.2% (11,14–16). The incidence was influenced by the population studied and the gestational age at the time of the ultrasound examination. In this study, the incidence of oligohydramnios was 0.89% (5,228/584,653), which was similar to the incidence (0.88%) reported between 1990 and 1996 in Taiwan (17). Previous studies have reported the short-term outcomes of pregnancies complicated by oligohydramnios (9–12).

The perinatal effects of oligohydramnios on birth weight, cesarean section rate, and the Apgar score were inconsistent. Locatelli *et al.* (9) observed that oligohydramnios is associated with a high risk of low birth weight. However, Rainford *et al.* (10), Zhang *et al.* (11), and Ek *et al.* (12) reported that pregnancies with isolated oligohydramnios exhibited perinatal outcomes similar to pregnancies without oligohydramnios. One limitation of these studies was the small sample size. In our population-based matched-cohort study, we observed that the birth weight of infants exposed to oligohydramnios was lower than that of infants without oligohydramnios exposure.

We observed the effects of maternal oligohydramnios on the risk of respiratory illness in children. These findings were supported by Biard *et al.* (18), who found that half of the children with a history of oligohydramnios and lower urinary tract obstruction suffered from long-term respiratory symptoms, mainly asthma and recurrent respiratory tract infections. However, the underlying mechanisms remain unclear. Because it is usually impossible to obtain lung tissue from infants and children, we have no direct evidence of the effects of oligohydramnios on infant lung structure. Pulmonary hypoplasia is also associated with various degrees of vascular dysplasia. Previous studies have identified vascular hypoplasia, increased arteriole muscularization, and decreased radial alveolar count and generation of alveolar saccules in lung samples in rodent neonates with oligohydramnios-induced pulmonary hypoplasia (19,20). The direct consequences of these pathologies remain unknown; however, it is likely that infants with pulmonary hypoplasia in fetal life are prone to respiratory infections. Pulmonary arteries and airways develop concurrently (21). Brassard and Johnson reported that patients with an isolated unilaterally absent pulmonary artery experienced recurrent respiratory infections (22). *Mycoplasma pneumoniae* is a common cause of bacterial community-acquired pneumonia in pediatric patients and can lead to severe and long-term disease (23). Neonates with pulmonary hypoplasia often require extended periods of respiratory support, such as oxygen supplementation and mechanical ventilation. Mechanical ventilation use in infants is frequently associated with acute complications and long-term respiratory morbidity.

Exposure to oligohydramnios *in utero* can lead to a low birth weight. Low birth weight (less than 2,500 g) is a significant risk factor for hospitalization with respiratory illness (24). Magann *et al.* (25) observed that exposure to oligohydramnios at a low gestational age substantially increased the probability of neonatal intensive care unit admission. In our study, we selected women aged between 15 and 49 y, and then we matched delivered singleton newborn cases and controls according to neonatal sex and gestational age, maternal age and education, and level of prenatal care. However, the birth weights of oligohydramnios-exposed infants were slightly lower than those of infants without oligohydramnios exposure. According to these results, there was not a clear correlation between low birth weight and increased risk of respiratory hospitalization in oligohydramnios-exposed infants because the birth weights of the cases and controls were within the reference range (between 2,500 and 4,000 g).

The three nationwide population-based computerized data sets used in this study did not provide parental smoking information, except for maternal smoking. Therefore, parental smoking status was unknown. We excluded maternal smoking to prevent it from interfering with the effect of oligohydramnios on respiratory hospitalization. Parental smoking is associated with an increased risk of respiratory infections during childhood (26). Smoking habits are typically more common in parents with low education levels and household incomes than in those with high education levels and household incomes (27,28). In Taiwan, the prevalence rate of prenatal tobacco smoking varies inversely with socioeconomic status, educational level, and family income (29). Therefore, we used parental education level and insurance eligibility category as proxies to adjust for the effects of prenatal smoking, resulting in an increased incidence rate of hospitalization for respiratory illness in children with oligohydramnios exposure.

The major limitation of this study was using the *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) codes of medical claims to identify the occurrence of oligohydramnios and respiratory illness. The validity of the coding could have affected the study outcomes. However, we used prenatal ultrasonography, which is the examination recommended by the National Health Insurance Claims from the National Health Insurance Administration (NHIA) to confirm the diagnosis of oligohydramnios in Taiwan. Respiratory illness was defined according to discharge claims, which were coded by a certified coding assistant in the hospitals under NHIA regulations. Both processes can increase the validity of clinical diagnoses. In addition, in this study, we experienced the surveillance bias that occurs when one group is followed more closely than the other group. This could lead to an exposure being diagnosed more often in the more closely followed group. However, we matched cases and controls according to the level of prenatal care to reduce the bias of surveillance. Therefore, the result was robust. The third limitation was that the NHIA lists the medical claims of children in the medical records of their mothers during the first month of life. Therefore, we were unable to observe the effects of oligohydramnios on respiratory illness at birth. This might have led to the underestimation of the effects of oligohydramnios on the risk of respiratory hospitalization during childhood. The fourth limitation was the lack of information on parental smoking and ambient air pollution. The prevalence rate of parental smoking and percentage of air pollution exposure is associated with educational level and family income (29,30). Air pollution is related to urbanization and a higher population density has been shown to result in more severe air pollution in Taiwan (31). Therefore, we used parental education level and urbanization of area of residency to correct for the effects of parental smoking and ambient air pollution.

In conclusion, our findings suggested that these respiratory illnesses were clinically significant and were associated with increased health care use. Early respiratory tract infections can have critical long-term consequences. Children who have respiratory infections early in life are prone to developing

asthma during childhood (32). Goldin *et al.* (33) observed that hospitalization for a respiratory infection in infancy led to an increased risk of non-Hodgkin lymphoma during childhood and young adulthood. The effects of early respiratory tract infection on the etiology of later illness are complex. Developing effective strategies to prevent or treat oligohydramnios could potentially reduce the risk of this morbidity in the next generation of children.

METHODS

Data Sets

We used three Taiwanese nationwide population-based computerized data sets. The first was the National Birth Reporting Database from the Health Promotion Administration, which contains data on maternal risk during pregnancy (e.g., diabetes and gestational diabetes), as well as on the risk of delivery (e.g., induced labor and prolonged delivery). This data set also contains information on neonatal sex, gestational age, birth weight, and mode of delivery. These data are provided by obstetricians and pediatricians. Hospitals and clinics are obligated to report and provide detailed information of births to the local health department within 10 d of delivery. The second data set was that of the NHIA, which covers all inpatient and outpatient visit claims. Residents of Taiwan have universal health insurance provided by the NHIA, which is the single payer for all medical services for almost all residents, providers, and hospitals. Disease diagnoses and treatment procedures were acquired from health claims databases, and all diagnoses were coded according to the ICD-9-CM. The NHIA also contains the eligibility records of all enrollees. The third data set was the Birth Certification Registry from the Ministry of Interior, which contains data on the parity and residency of newborns, as well as parental age, education, and aboriginal status. Because it is mandatory to register all births, the data are considered highly accurate and complete.

Unique personal, encrypted identification numbers were provided to link the three nationwide population-based data sets. By combining the three data sets, we identified the effects of oligohydramnios on respiratory morbidities during childhood after adjusting for all potential confounders.

Ethics Statement

Confidentiality was ensured by abiding by the data regulations of the Collaboration Center of Health Information Application, Ministry of Health and Welfare, Executive Yuan, Taiwan. Because deidentified secondary data are released to the public for research purposes only, this study was exempt from full review by the Institutional Review Board.

Patient Selection

From the initial cohort of more than 800,000 women who gave birth between 1 January 2004, and 31 December 2007, we first selected those aged between 15 and 49 y who delivered a singleton infant with a weight greater than or equal to 2,500 g at a gestational age between 37 and 42 wk. We excluded macrosomic infants (birth weight > 4,000 g) because they may have specific complications related to their birth weight, distinct from those of normal-birth-weight infants. If a woman had more than one singleton birth during the study period, we selected the first birth for our study. A total of 584,653 women fulfilled our eligibility criteria. Cases were selected if women had a diagnosis of oligohydramnios (ICD-9-CM: 658.0) in the third trimester of pregnancy, according to inpatient or outpatient claims. Ultrasonography is widely used in Taiwan to diagnose oligohydramnios during prenatal care because the amniotic fluid index is less than 5 cm (17). During a normal pregnancy, the amount of amniotic fluid typically increases until the sixth month and then slightly decreases during the eighth and ninth months (34). Therefore, women with oligohydramnios in the third trimester of pregnancy were of interest in this study.

We excluded women diagnosed with premature rupture of membranes (ICD-9-CM: 658.1) or chorioamnionitis (ICD-9-CM: 658.4), in addition to excluding those who had been subjected to smoke during pregnancy. Infants reported to have any type of birth defect or a diagnosis of intrauterine hypoxia or birth asphyxia (ICD-9-CM: 768), respiratory distress syndrome (ICD-9-CM: 769), or other fetal or neonatal respiratory conditions (ICD-9-CM: 770), such as meconium aspiration syndrome, were also excluded. Birth defects were defined using data from the National Birth Reporting Database, which contains data on eight newborn congenital anomalies based on morphogenesis (related to central nervous system, eye, or ear, in addition to cardiovascular, orofacial, gastrointestinal, genitourinary, chromosomal, and other anomalies). These patients were excluded to eliminate respiratory hospitalizations attributed to risks other than oligohydramnios. Finally, those with missing variables of interest were also excluded, resulting in a sample of 5,228 cases. From the remaining women who were not diagnosed with oligohydramnios, we adhered to the previously described exclusion criteria and performed a 1:4 matched case–control analysis. A sample of 20,912 controls was selected at random and matched with cases according to neonatal sex and gestational age, maternal age and education, and level of prenatal care. Because we defined the oligohydramnios diagnosis based on medical claims, matching patients according to the level of prenatal care prevented a potential surveillance bias.

Variables

Main outcomes. The outcome of interest was hospitalization for respiratory diseases during childhood. Respiratory hospitalization was selected if children received a discharge diagnosis of acute and chronic respiratory diseases (ICD-9-CM: 493, 494, 496, 512, 518, 786.00, 786.05, 786.07, 786.09, 786.1–786.4, 799.02, or 799.1), respiratory infections (ICD-9-CM: 466, 480–487, 490, 491, 510, or 513), or respiratory symptoms (ICD-9-CM: 786). Respiratory failure was defined as having nonoperative mechanical ventilation (ICD-9-CM: 96.70, 96.71, or 96.72) in conjunction with any of these respiratory-related codes. All children were followed from their date of birth to their earliest hospitalization for the defined respiratory disorders, death (which was obtained from the death registry), withdrawal from the NHIA, or the end of the evaluation period (31 December 2009). This provided a follow-up period of 2–6 y.

Possible confounding factors. To control for confounding, we included neonatal characteristics (sex, gestational age, birth weight, parity, mode of delivery, 5-min Apgar score <7, and urbanization of area of residence), parental demographics (age, education, marital status, and insurance eligibility group), and maternal risk factors. Most of the demographic information was obtained from the National Birth Reporting Database and Birth Certification Registry. We classified the urbanization level into four categories according to population density, percentage of residents with college or higher education, percentage of residents older than 65 y of age, percentage of residents who were agricultural workers, and number of physicians per 100,000 people, which might reflect regional differences in air pollution (31,35). Data on six insurance eligibility groups were obtained from the insurance enrollment records of the NHIA, and the classification rule was predominantly based on monthly income (36,37). A few people paid no premium because they were eligible for public assistance according to the Public Assistance Act of Taiwan. Maternal risks during pregnancy included gestational hypertension (ICD-9-CM: 642), hypertension (ICD-9-CM: 401–405), gestational diabetes (ICD-9-CM; 648.0, 648.8), diabetes mellitus (ICD-9-CM: 250), asthma (ICD-9-CM: 493), allergic rhinitis (ICD-9-CM: 477), and atopic dermatitis (ICD-9-CM: 691), as identified from the medical claims of the NHIA. The National Birth Reporting Database also included some of the maternal risk factors considered in this study; however, the information was based on the discharge records and may not include diseases detected during pregnancy. Therefore, we used the disease information from the medical claims and found that we could identify women with hypertension during pregnancy.

Statistical Analysis

We used GMATCH Macro, which is maintained by the staff of the Division of Biomedical Statistics and Informatics, Mayo Clinic, to

match four controls for each case, using the GREEDY algorithm (38). A sample of 20,912 controls was collected at random and matched with cases according to neonatal sex and gestational age, maternal age and education, and level of prenatal care. Because we defined the diagnosis of oligohydramnios based on medical claims, matching patients according to the level of prenatal care prevented a potential surveillance bias. The basic characteristics of patients exposed to oligohydramnios and their matched controls were compared using the χ^2 test for categorical variables and the Student's *t*-test for continuous variables. The cumulative proportion of children developing respiratory illness during the follow-up period was estimated using life-table methods, and log-rank tests were performed according to the maternal risk of oligohydramnios. By using Cox proportional-hazard regressions, we estimated the unadjusted HR of hospitalization for outcomes in the oligohydramnios cases in comparison with the controls. The adjusted HR was then estimated by adjusting for all other covariates. All analyses were performed using SAS/STAT software version 9.2 (SAS Institute, Cary, NC) and STATA 12 (StataCorp LP, College Station, TX). A *P* value <0.05 was considered significant.

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