Association between Petrochemical Air Pollution and Adverse Pregnancy Outcomes in Taiwan

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ABSTRACT. The petrochemical industry is the main source of industrial air pollution in Taiwan. To date, little is known about the possible effects of such pollution on the human fetus. In this study, the authors investigated the relationship between term low birthweight and preterm delivery and residence in a petrochemical industrial municipality (PIM). The study areas included 16 PIMs (which were defined as municipalities in which the number of workers in the petroleum and petrochemical industry made up at least 2% of the municipality's total population) and 16 matched reference municipalities (RFMs). Among 39,750 1st-parity singleton live births, the prevalences of preterm delivery in the PIMs and RFMs were 4.72% and 4.58%, respectively, and the prevalences of term low birthweight were 2.51% and 2.35%, respectively. When PIMs were compared with RFMs, and after controlling for possible confounders (including maternal age, marital status, maternal education, and gender of the baby), the adjusted odds ratios were 1.07 (95% confidence interval [CI] = 0.95, 1.22) for term low birthweight and 1.03 (95% CI = 0.94, 1.13) for preterm delivery, respectively.

<Key words: air pollution, infant, low birthweight, petrochemical industry, preterm delivery>

SEVERAL ENVIRONMENTAL POLLUTANTS are associated with unfavorable pregnancy outcomes, such as spontaneous abortion, prematurity, and stillbirth.[1] During the past decade there has been growing concern about the reproductive health hazards of air pollution.[2] Axelsson and Molin[3] found that the rate of miscarriages was slightly elevated in areas exposed to emissions from petrochemical industries. However, in a British study in which the authors compared a population living around a point source of air pollution with a control population, no increase in the prevalence of low birthweight (LBW) was evident in the polluted area.[4] Landgren[5] conducted a study in southern Sweden and also found that air pollution did not affect the incidences of short gestation and LBW. However, in a study conducted in China the authors suggested that exposure to total suspended particulates (TSPs) and sulfur dioxide (SO_2) was associated with an excess risk of preterm delivery[6] and LBW.[7] Bobak and Leon[8] observed an association between TSPs and SO_2 and LBW in an ecologic study in the Czech Republic in 1986–1988. Most recently, Dejmek et al.[9] observed an increased risk of intrauterine growth retardation in a highly polluted region in the Czech Republic. Increases in growth retardation were associated with levels of particulate matter with a 50% cut-off aerodynamic diameter of 10 µm (PM_{10}) greater than 40 µg/m^3 and a $PM_{2.5}$ greater than 37 µg/m^3 during the 1st trimester of pregnancy.

Development of the petrochemical industry in Taiwan began in 1968. According to pollution reports compiled since 1983 by the Environmental Protection Administration of Taiwan, Republic of China, 9 serious air-pollution events have occurred in petrochemical municipalities between 1971 and 1990.[10] In addition, investigators have considered the petrochemical industry to be the main source of industrial air pollution in Taiwan. The pollutants emitted by the petrochemical industries include not only the vinyl chloride monomer and polycyclic aromatic hydrocarbons (PAHs)—which have been recognized as environmental carcinogens[11] —but also large quantities of criteria pollutants such as SO_2, PM_{10}, and nitrogen dioxide (NO_2). Subsequent to these events, public concern has been elevated regarding potential health hazards for residents in petrochemical municipalities.

In our recent studies, we found that exposure to petrochemical air pollution is associated with increased rates of acute irritative symptoms in adults,[12] and upper respiratory symptoms and asthma in school children.[13] In addition, we found that residential petrochemical air pollution may increase the risk for liver cancer in males[14] and the risk for lung cancer in females.[15]

In the present study, we explored the association between adverse birth outcomes and petrochemical air pollution. This is the first article in a series of studies evaluating the potential hazards posed by exposure to petrochemical air pollution.

Materials and Method

Study areas. Taiwan is divided into 361 administrative municipalities. According to the 1989 Census of Manufacturers, a total of 218 municipalities had plants engaged in petrochemical manufacturing, although there were fewer than 50 employees in about 30% of these municipalities.[16] A study design that contrasted high and low levels of petrochemical industrial pollution was chosen in which an individual municipality was classified as a *petrochemical industrial municipality* (PIM) if the number of workers in the petroleum and petrochemical industry comprised at least 2% of the municipality's total population. This proportion was used as an indicator of a resident's exposure to air emissions from petrochemical plants. In all, 19 municipalities satisfied these criteria. In contrast to a PIM, a *reference municipality* (RFM) had low petrochemical industrial pollution, and employed petrochemical workers made up less than 2% of the total population.

Also from the 1989 Census of Manufacturers[16] we gleaned the number of employees for 18 nonpetrochemical manufacturing industries for each municipality. We determined that the fraction of workers employed in nonpetrochemical manufacturing industries in a RFM should be comparable with that of its associated PIM; in other words, nonpetrochemical manufacturing industries were apportioned nearly equally between the PIMs and RFMs.

To account for the possible confounding effect of the urbanization discrepancy, the urbanization level of the PIM should be the same as its RFM. We defined the urbanization level with the urban-rural classification system of Tseng and Wu.[17] Each township in Taiwan (n = 361) was assigned a degree-of-urbanization category designation from 1 to 8. A district with the highest urbanization score, such as the Taipei metropolitan area, was classified in category 1, whereas mountainous areas with the lowest scores were assigned to category 8. This urbanization index has been applied in our previous studies.[18–21]

More specifically, each PIM was matched with 1 RFM, in accordance with the following criteria: (a) the PIM and RFM should have the same urbanization level; (b) the PIM and RFM should differ in the percentage of petrochemical workers employed; and (c) the fraction of workers employed in nonpetrochemical industries in the PIM vs. RFM should differ by no more than 10%.

Among the 19 PIMs, 3 were excluded because no appropriate municipality satisfied the criteria for matching. If a PIM had more than 1 municipality that met the criteria for a RFM, random sampling was used to select 1 municipality as the RFM. The final sample consisted of 16 PIMs and 16 RFMs. Their details have been described in a previous publication.[14] The sociodemographic characteristics of the PIMs and RFMs were similar (Table 1).

Data collection. Data on pregnancy outcomes were taken from routine birth registrations, which are required by law in Taiwan. It is the responsibility of the parents or the family concerned to register an infant's birth at a local household registration office within 15 days of birth. Computerized data on live births are collected from the Household Registration System, which is managed by the Department of Interior. The registration form asks for information on maternal age, education, parity, gestational age, date of delivery, infant sex, and birthweight. Given that most deliveries in Taiwan occur in either a hospital or a clinic,[22] and the birth certificates are completed by physicians attending the delivery, and inasmuch as it is mandatory that all live births be registered at local household registration offices, the birth registration data used in this study are considered complete and accurate. These data were also used in an earlier study.[23] Twins or multiple births were not included in the analysis. Data on gestational

Table 1.—Demographic Indices for the Petrochemical Industrial Municipalities (PIMs) and Reference Municipalities (RFMs)

Variable	16 PIMs	16 RFMs
Population density (per km^2)	1,203.2	1,251.6
White-collar (%)*	31.5	30.1
Blue-collar (%)†	45.4	41.4
Agriculture (%)‡	23.1	28.6
High school graduate (%)§	28.0	26.9
Employed in non-petrochemical industries (%)#	20.5	19.5

*Professional, technical, administrative, superintendents, clerical, sales and service workers as percentage of total employed population (age ≥ 15 yr).
†Producers, transportation operators, and laborers as percentage of total employed population.
‡Farmers, loggers, grazers, fisherman, hunters and related workers as percentage of total employed population.
§Educated above senior high school level as percentage of population (age ≥ 15 yr).
#The proportion of nonpetrochemical workers as percentage of municipality's total population.

age for live births outside the range of 20–50 wk were considered invalid.[24]

Statistics. Information on birth outcomes, from the birth registration forms, included birthweight and gestational age, but not information on stillbirths and congenital anomalies. The outcomes of interest in this study were term LBW (≥ 37 gestational wk and < 2,500 gm) and preterm delivery (< 37 gestational wk). We used multiple logistic-regression analysis to estimate the effects of petrochemical air pollution on the risk of term LBW and preterm delivery. All odds ratios (ORs) were adjusted for maternal age (< 25 yr, ≥ 25 yr), marital status (married, unmarried), maternal education (< 12 yr, ≥ 12 yr), and gender of the infant (male, female). Analyses were performed with the SAS package. All statistical tests were 2-sided. Values of $p < .05$ were considered statistically significant.

Results

There were 99,788 singleton deliveries in the study municipalities between 1993 and 1996. Of 99,694 live births with information on parity, 1st parity accounted for 41.82%. Of 41,688 1st-parity singleton live births, we excluded 372 subjects who had invalid or missing information on gestational age. Among the remaining 41,316 subjects, 992 were missing birthweight data or maternal age data. Of the 40,324 1st-parity births with complete information on the above variables, 574 births were excluded because data were missing on at least 1 of either maternal education, marital status, or birthplace. A total of 39,750 births were included in the final analysis.

Table 2 shows the number of delivered 1st-parity singleton live infants for our PIMs and RFMs. The prevalences of preterm deliveries in the PIMs and RFMs were 4.72% and 4.58%, respectively, whereas the prevalences of term LBW were 2.51% and 2.35%, respectively. Both prevalences were higher in the PIMs, but they were not statistically significant.

Table 2.—Maternal Characteristics, Mean Birthweight, and Term Low Birthweight (LBW) Prevalence in 1st-Parity Singleton Live Births in Petrochemical Industrial Municipalities (PIMs) and Reference Municipalities (RFMs)

	PIMs (n = 20,077)		RFMs (n = 19,673)		
Variable	No.	%	No.	%	*p*
Birthweight (gm)					
$\bar{x} \pm SD$	3,173.2	432.3	3,169	437.2	.346
Gestational age (wk)					.517
< 37	948	4.72	902	4.58	
≥ 37	19,129	95.28	18,771	95.42	
Term LBW	503	2.51	462	2.35	.309
Maternal age (yr)					.552
< 25	7,973	39.71	7,870	40.00	
≥ 25	12,104	60.29	11,803	60.00	
Marital status					.416
Married	19,479	97.02	19,114	97.16	
Unmarried	598	2.98	559	2.84	
Maternal education (yr)					.710
< 12	17,099	85.17	16,781	85.30	
≥ 12	2,978	14.83	2,892	14.70	
Gender of infant					.060
Male	10,524	52.42	10,127	51.48	
Female	9,553	47.58	9,546	48.52	
Birthplace					.339
Hospital/clinic	20,074	99.99	19,667	99.97	
Other	3	0.01	6	0.03	

Note: $\bar{x}$ = mean, and *SD* = standard deviation.

Table 3.—Estimated Odds Ratios (ORs) and 95% Confidence Intervals (CIs) Associated with Petrochemical Air Pollution for Term Low Birthweight (LBW) and Preterm Delivery in 1st-Parity Singleton Live Births, Based on Multiple Logistic-Regression Analysis

	Term LBW		Preterm delivery	
Variable*	OR	95% CI	OR	95% CI
PIMs†	1.07	0.95, 1.22	1.03	0.94, 1.13
Maternal age‡	1.32	1.15, 1.51	1.24	1.12, 1.38
Marital status§	1.37	0.99, 1.88	1.95	1.58, 2.41
Maternal education#	1.44	1.15, 1.79	0.91	0.79, 1.04
Sex of infant††	1.59	1.40, 1.81	0.86	0.78, 0.94

Note: PIM = petrochemical industrial municipality, and RFM = reference municipality.
*Logistic models include all 5 variables.
†Reference group: RFMs.
‡Reference group: > 25 yr.
§Reference group: Married women.
#Reference group: > 12 yr.
††Reference group: Males.

Table 3 contains the ORs for term LBW and preterm delivery, based on comparisons of PIMs and RFMs by logistic regression. After controlling for possible confounders (including maternal age, marital status, maternal education, and infant's gender), the adjusted ORs were 1.07 (95% confidence interval [CI] = 0.95, 1.22) for term LBW and 1.03 (95% CI = 0.94, 1.13) for preterm delivery, respectively, when PIMs were compared with RFMs. Analyses in which term birthweight was used as a continuous variable did not indicate an association between birthweight and petrochemical air pollution (data not shown).

Discussion

The present study indicates that residential exposure to air pollution—specifically the petrochemical industry pollution—resulted in a nonsignificant excess of term LBW and preterm delivery. The few studies that have examined the relationship between LBW[4,5,7–9] or preterm delivery[5,6] and air pollution have yielded mixed results. The absence of an association with LBW and preterm delivery in our study accords with the lack of association found in Sweden[5] and England.[4]

The major difficulty in studying health effects associated with air pollution lies in the assessment of exposure. In our study, we used "extreme points contrast" to study health effects of petrochemical air pollution on adverse birth outcomes to maximize the inherent power of the design.[25,26] (In essence, in the establishment of an extreme point contrast a specific petrochemical-exposed population is compared with what may reasonably be considered a corresponding "control" group [nonexposed population, which is used as an appropriate reference background for the determinant.]) This method was also applied in our previous studies.[14,20,21] Workers employed in the petrochemical industry made up 0.61% of the RFM's total population; the corresponding value for the PIMs was 4.86%.[14] In previous studies researchers have attempted to quantify the concentration of air pollutants (e.g., SO_2, PM_{10}, $PM_{2.5}$) and assign exposure values to individual women.[6–9] In our study, we made no attempt to quantify exposure to air pollutants; however, we assumed that women living in PIMs, on average, experienced a higher exposure to air pollutants than women living in RFMs. Information on the outcomes and covariates was collected from individual birth records. This study design is semi-individualized, which is considered a valid design, compared with traditional ecologic studies.[27]

Although we used the extreme-point-contrast method to assess exposure, the potential for misclassification remains. Mobility of subjects between PIMs and RFMs during pregnancy was most likely an obstacle in this study. In 2 U.S. studies, investigators reported that approximately 25%[28] and 37%[29] of women relocated during pregnancy; however, no data were available regarding subjects who moved between our PIMs and RFMs during pregnancy. Misclassification of exposure is likely to be nondifferential with respect to outcome, and effect estimates are likely to be biased toward the null.[26] Whatever the extent of exposure misclassification, it would likely bias the effect estimates in this study toward unity.

Other risk factors that were not considered in this study affect birthweight or preterm delivery. These factors include maternal nutrition, prepregnancy weight, and weight gain[30]; cigarette smoking[31]; and occupational exposures.[32–36] Unfortunately, no information was available on these variables for our individual study subjects, and the variables could not be adjusted for directly in the analysis. The prevalence of smoking among Taiwan's women is extremely low. According to a 1993 national smoking survey, only 3% to 4% of women aged 16 yr or older were smokers.[37] Thus, maternal smoking status should not be a significant confounder in this study. In addition, even if other factors varied among the study subjects, it was unlikely that these variables would have been correlated with petrochemical air pollution. Therefore, we believe that our inability to control for these factors had a negligible effect on our results. Furthermore, it is unlikely that even a high degree of public awareness regarding air pollution could have influenced the women to relocate during pregnancy, because the possible role of air pollution as a risk factor for LBW or short gestational age has not received public attention in Taiwan.

In summary, the present study provides no evidence of an increased risk of term LBW or preterm delivery related to petrochemical air pollution exposure. Given the inherent methodological limitations, future investigations of the relationship between air pollution and adverse pregnancy outcomes should include a more accurate means of exposure assessment, including quantifying total individual exposure to air pollutants from all sources.

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