Association between Chlorination of Drinking Water and Adverse Pregnancy Outcome in Taiwan

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Chlorination has been the major means of disinfecting drinking water in Taiwan. The use of chlorinated water has been hypothesized to lead to several adverse birth outcomes, including low birth weight and preterm delivery. We performed a study to examine the relationship between the use of chlorinated water and adverse birth outcomes in Taiwan. The study areas included 14 chlorinating municipalities (CHMs), which were defined as municipalities in which > 90% of the municipal population was served by chlorinated water, and 14 matched nonchlorinating municipalities (NCHMs), defined as municipalities in which < 5% of the municipal population is served by chlorinated water. The CHMs and NCHMs were similar to one another in terms of level of urbanization and sociodemographic characteristics. The study population comprised 18,025 women residing in the 28 municipalities who had a first parity singleton birth between 1 January 1994 and 31 December 1996 and for which complete information on maternal age, education, gestational age, birth weight, and sex of the baby were available. The results of our study suggest that there was no association between consumption of chlorinated drinking water and the risk of low birth weight. *Key words:* chlorination, disinfection by-products, drinking water, infants, low birth weight. *Environ Health Perspect* 108:765–768 (2000). [Online 30 June 2000]
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The economy and effectiveness of chlorine in killing waterborne organisms has made water chlorination a tremendous public health success worldwide. However, chlorination of water can produce trace amounts of by-products such as trihalomethanes (THMs), which are carcinogenic organic halogenated contaminants of water chlorination (*1–3*). A number of epidemiologic studies have focused on the possible associations between the consumption of chlorinated drinking water and cancer mortality or incidence (*4–15*). Most studies have shown positive associations between the use of chlorinated drinking water and colorectal and bladder cancer risk.

Recently, several epidemiologic studies have examined the associations between the consumption of chlorinated water and adverse pregnancy outcomes (*16–24*). These studies found associations between chlorination and risk of spontaneous abortion, infants being small for gestational age, having low birth weight, or displaying specific birth defects. These studies considered a wide range of populations and regions but have been mainly carried out in the United States. The present study was carried out because few epidemiologic studies have been conducted outside the United States (*21,23*). There was a need for additional studies using new independent data from other populations, so we undertook the present study in Taiwan to explore further the association between adverse birth outcomes and the use of chlorinated water. This paper is one in a series of studies to assess the hazard potential posed by exposure to chlorinated drinking water.

Materials and Methods

Selection of study municipalities. Taiwan is divided into 361 administrative districts, which are referred to here as municipalities. We excluded from the analysis 30 aboriginal townships and 9 islets that encompassed different lifestyles and living environments; we also excluded the 12 municipalities of the city of Taipei because of Taipei's distinctly more urban character and larger population than other municipalities in Taiwan. This elimination left 310 municipalities.

Chlorination has been the major means of disinfecting drinking water in Taiwan. Chlorine is currently added to approximately 75.8% of the nation's drinking water. The current Taiwan water system is rather simple. Residents obtain their drinking water either from the public drinking water supply systems served by the Taiwan Water Supply Corporation or from nonmunicipal sources. The major sources of municipal water supplies are almost all surface waters and are treated with chlorine. The nonmunicipal sources are mainly privately owned wells (groundwater) and are unchlorinated.

In this study, we classified an individual municipality as a chlorinating municipality (CHM) if > 90% of the municipal population was served by chlorinated water. In all, 156 of the 310 municipalities satisfied this criterion. A nonchlorinating municipality (NCHM) was defined as one in which < 5% of the municipality population was served by chlorinated water (i.e., > 95% of the residents obtained their drinking water from unchlorinated water sources). In all, 15 municipalities satisfied this criterion. These 15 NCHMs provided a unique opportunity to investigate the issue of chlorination. To take into account the possible confounding effect resulting from differing levels of urbanization, the urbanization level of the nonchlorinating municipalities should be the same as that of the chlorinating municipalities. The assignment of urbanization levels was based on the urban–rural classification of Tzeng and Wu (*25*). This urbanization index has been applied in our previous studies (*26–29*). Each municipality in Taiwan (n = 361) was assigned to an urbanization category from 1 to 8. Municipalities with the highest urbanization score, such as the Taipei metropolitan area, were classified in category 1, whereas mountainous areas with the lowest score were assigned to category 8.

Each NCHM was matched with a CHM with the same urbanization level. Among the 15 NCHMs, one was excluded because there was no appropriate municipality for matching. If an NCHM had more than one appropriate matching CHM, we used a random sampling method to select the CHM. Details of the procedure were described by Yang et al. (*15*). The sociodemographic characteristics of the CHMs and NCHMs were generally similar except for a higher population and a higher percentage of population using the chlorinated water among the CHMs (96.1 vs. 1.5%) (Table 1).

Data collection. Data on pregnancy outcomes were taken from the routine registration of births. Registration of births is required by law in Taiwan. It is the responsibility of the parents or the family to register infant births at a local household registration office within 15 days. Computerized data on live births were collected from the Household

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Registration System, which is managed by the Department of Interior in Taipei. The registration form, which asks for information on maternal age, education, parity, gestational age, date of delivery, infant sex, and birth weight, is completed by the physician attending the delivery. Because most deliveries in Taiwan take place in either a hospital or clinic (*30*) and the birth certificates are completed by physicians attending the delivery, and because it is mandatory to register all live births at local household registration offices, the birth registration data are considered complete and accurate. We did not include twins or multiple pregnancies in the analysis. Gestational ages for live births that were outside the range of 20–50 weeks were considered invalid (*31*).

There were 43,807 singleton deliveries in the study municipalities between 1 January 1994 and 31 December 1996. Of the 43,782 births with information on parity, first-parity births accounted for 43.76%. Of 19,159 first-parity singleton live births, we excluded 163 subjects who had invalid or missing information on gestational age. Among the remaining 18,996 subjects, 656 were missing birth weight data or maternal age data. Of the 18,340 first-parity births with complete information on these variables, we excluded 315 births because data were missing on at least one of three variables: maternal educational, maternal marital status, or infant birth place. These exclusions left 18,025 births for the final analysis.

Statistics. The outcomes of interest in this study included term low birth weight (LBW) (≥ 37 gestational weeks and < 2,500 g) and preterm delivery (< 37 gestational weeks). We used an unconditional logistic regression model to estimate the effects of chlorination practice on the risk of term LBW and preterm delivery. All odds ratios (ORs) were adjusted for maternal age (< 25 or ≥ 25 years), marital status (married or unmarried), maternal education (< 12 or ≥ 12 years), and sex of baby. The analyses were performed using SAS software (SAS Institute Inc., Cary, NC). All statistical tests were two-sided. Values of $p < 0.05$ were considered statistically significant.

Table 1. Some characteristics of two groups of Taiwan municipalities, grouped according to chlorination practice.

Characteristic	14 CHMs	14 NCHMs
Total population (1989)	463,657	397,588
Mean population	28,399	33,118
Population density (per km^2)	611.2	600.4
Population served by chlorinating water (%)	96.1	1.5
White collar (%)[a]	25.4	24.8
Blue collar (%)[b]	24.6	22.2
Agriculture (%)[c]	50.0	53.0

[a]Professional, technical, administrative, superintendents, clerical, sales, and service workers as a percentage of the total employed (≥ 15 years of age) population. [b]Producers, transportation operators, and laborers as a percentage of the total employed population. [c]Farmers, loggers, grazers, fisherman, hunters, and related workers as a percentage of the total employed population.

Results

Altogether, 18,025 (10,007 CHMs and 8,018 NCHMs) first-parity singleton live births with complete information were included in the analysis. Table 2 shows the distribution of birth outcomes and maternal characteristics by chlorination practice. The mean birth weights in the CHMs and NCHMs were 3,181.8 and 3,170.6 g, respectively. The prevalences of preterm delivery in the CHMs and NCHMs were 4.48 and 3.38%, respectively. The CHMs had a significantly higher rate of preterm delivery than the CHMs.

The CHMs had a lower rate of term LBW than the CHMs (2.49 vs. 2.81%) but the difference was not statistically significant. Table 3 shows the ORs for term LBW and preterm delivery based on comparisons between CHMs and NCHMs using logistic regression. After controlling for possible confounders (including maternal age, marital status, maternal education, and sex of the infant), the adjusted ORs were 1.34 [95% confidence interval (CI), 1.15–1.56)] for preterm delivery and 0.90 (CI, 0.75–1.09) for term LBW, respectively, when comparing CHMs with NCHMs. Analysis using term birth weight as a continuous variable did not indicate an association between birth weight and the use of chlorinated water (data not shown).

Discussion

The results of this study suggest that there is no association between the use of chlorinated drinking water and the risk of term low birth weight.

A few previous studies have looked at the relation between birth weight and preterm delivery and water chlorination (*17,19–22*). Kramer et al. (*17*) carried out a population-based case–control study in Iowa. Chloroform concentrations > 10 ppb in drinking water were associated with a small increase in risk of LBW (OR, 1.3; CI, 0.8–2.2) and preterm delivery (OR, 1.1; CI, 0.7–1.6). Bove et al. (*19*) carried out a large retrospective cohort study in New Jersey. Elevated ORs were found for term LBW at THM concentrations > 100 ppb (OR, 1.42; CI, 1.22–1.65) when compared with the reference level of ≤ 20 ppb. No association was found between concentrations of THMs and preterm birth (OR not shown). Savitz et al. (*20*) conducted a population-based case–control study in North Carolina. THM concentrations (82.2–168.8 vs. 40.8–63.3 ppb) were not associated with preterm delivery (OR, 0.9; CI, 0.6–1.5) and LBW (OR, 1.3; CI, 0.8–2.1). Dodds et al. (*21*) conducted a large retrospective cohort study in Canada. The authors did not find excess risk for LBW (OR, 1.04; CI, 0.92–1.18) or preterm delivery (OR, 0.97; CI, 0.87–1.09) for women whose water contained ≥ 100 ppb THM. Gallagher et al. (*22*) carried out a retrospective cohort study in Colorado. The authors found an excess risk for LBW (OR, 2.1; CI, 1.0–4.8) and term LBW (OR, 5.9; CI, 2.0–17.0) for those exposed to ≥ 60 ppb THM compared with those in the low-exposure group (≤ 20 ppb), but no association between preterm delivery (OR, 1.0; CI, 0.3–2.8) and THM concentrations. Various epidemiologic studies point toward an association between THMs and term LBW (> 37

Table 2. Maternal characteristics, mean birth weight, and prevalences of term LBW and preterm delivery in first-parity singleton live births in CHMs and NCHMs.

Variables	CHMs	NCHMs	*p*-Value
Singleton live births (*n*)	10,007	8,018	—
Mean birth weight	3,181.8 ± 440.6	3,170.6 ± 439.0	0.089
Gestational age	—	—	0.001
< 37 weeks	448 (4.48%)	271 (3.38%)	—
≥ 37 weeks	9,559 (95.52%)	7,747 (96.62%)	—
Term LBW (%)	238 (2.49%)	218 (2.81%)	0.148
Maternal age	—	—	0.001
< 25 years	4,156 (41.53%)	3,801 (47.41%)	—
≥ 25 years	5,851 (58.47%)	4,217 (52.59%)	—
Marital status	—	—	0.888
Married	9,773 (97.66%)	7,833 (97.69%)	—
Unmarried	234 (2.34%)	185 (2.31%)	—
Maternal education	—	—	0.001
< 12 years	8,544 (85.38%)	7,167 (89.39%)	—
≥ 12 years	1,463 (14.62%)	851 (10.61%)	—
Sex of infant	—	—	0.289
Male	5,209 (52.05%)	4,110 (51.26%)	—
Female	4,798 (47.95%)	3,908 (48.74%)	—
Birth place	—	—	0.999
Hospital/clinic	10,006 (99.99%)	8,018 (100.0%)	—
Other	1 (0.01%)	0 (0.00%)	—

gestational weeks and < 2,500 g) (*19,22*) but not LBW (≤ 2,500 g) (*17,20,21*). The absence of an association with term LBW in our study is not consistent with the association found in New Jersey (*19*) and Colorado (*22*). Furthermore, our finding appears to be the first investigation to report a significant association between the use of chlorinated drinking water and preterm delivery. Because there is no evidence to date for an association between THMs and preterm delivery (*17,19–22*), the possibility that this is a chance finding should be considered.

The major difficulty in studying health effects associated with chlorination lies in assessing exposure (*32*). In our study, we investigated the effects of drinking water chlorination on adverse birth outcomes using an extreme points contrast to maximize the inherent power of the design (*33,34*). We used this method in our previous studies (*15,28*). The percentage of the population served by chlorinated water in the CHMs and NCHMs was 96.1 and 1.5%, respectively. Also, the municipalities selected for this study were rural municipalities, and it is unlikely that the residents would be able to afford bottled water, thus reducing the likelihood that water came from a source other than the home. In line with this assumption, we expect that women living in the CHMs drink water from the public supply and that women living in NCHMs drink water from the private wells (nonchlorinated water).

THMs are common contaminants of chlorinated drinking water and are the most consistently measured contaminants in treated water. Previous studies attempted to quantify the concentration of THMs and assign exposure values to women (*17,19–22*). In our study we made no attempt to quantify exposure to THMs in chlorinated water. However, we assumed that women living in CHMs, on average, experience a higher exposure to THMs than women living in NCHMs (nonchlorinated water) (*23*). Fear of delivering an LBW baby should not have deterred women from drinking chlorinated water because the possible role of THMs in drinking water as a risk factor for LBW has not received public attention in Taiwan.

Table 3. Adjusted ORs for term LBW and preterm delivery in first-parity singleton live births by logistic regression.

Variables[a]	Term LBW (CI)	Preterm (CI)
CHMs[b]	0.90 (0.75–1.09)	1.34 (1.15–1.56)
Maternal age[c]	1.17 (0.96–1.42)	1.02 (0.87–1.21)
Marital status[d]	1.29 (0.75–2.23)	1.83 (1.24–2.70)
Maternal education[e]	1.32 (0.95–1.83)	0.98 (0.78–1.23)
Sex of infant[f]	1.34 (1.11–1.62)	0.81 (0.70–0.95)

[a]Logistic models include all five variables in the model. [b]The reference group was NCHMs. [c]The reference groups was ≥ 25 years of age. [d]The reference group was married women. [e]The reference group was ≥ 12 years of education. [f]The reference group was male.

Recently, Gallagher et al. (*22*) reported an association between LBW, in particular term LBW (OR, 5.9; CI, 2.0–17.0) and exposure to THMs. The authors have taken an important step in reducing misclassification of exposure by using the hydraulic model to identify census blocks for which individual THM exposure levels were all well represented by one or more sampling point measurement. Their ability to reduce misclassification may account for the stronger effect estimate, despite the relatively low levels of THMs observed in their study.

A number of factors are known or suspected to affect birth weight, including maternal nutrition and prepregnancy weight and weight gain (*35*), cigarette smoking (*36*), and occupational exposures (*37–41*). Unfortunately, there is no information available on these variables for individual study subjects and they could not be adjusted for directly in the analysis. However, none of these variables are likely to be associated with chlorination practice, and therefore the estimated effects of chlorination are likely to be free of confounding by these factors.

We used the extreme point contrast method to assess exposure. Nonetheless, the potential misclassification of exposure remains. Mobility between CHMs and NCHMs during pregnancy is likely to be a problem in this study. Two U.S. studies reported that approximately 25% (*42*) and 37% (*43*) of women changed residency during pregnancy. No data were available about women who moved between the CHMs and NCHMs during pregnancy. Because misclassification of exposure is likely to be nondifferential with respect to outcome and effect estimates are likely to be biased toward the null (*34*), whatever the level of such misclassification, its effect would likely bias the effect estimates reported here toward the null.

In summary, the present study provides no evidence of an increased risk of term LBW related to the consumption of chlorinated water. More accurate means of exposure assessment, including quantifying individual exposure to THMs or other disinfection by-products from tap water at home, work, and elsewhere, and other water uses or use of more sophisticated modeling techniques, may help clarify the effect of water chlorination on reproduction (*24*).

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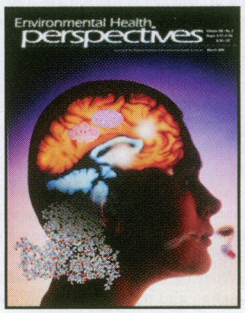

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