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Original Contribution

Passive Smoking and Preterm Birth in Urban China

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Studies investigating the relationship between maternal passive smoking and the risk of preterm birth have reached inconsistent conclusions. A birth cohort study that included 10,095 nonsmoking women who delivered a singleton live birth was carried out in Lanzhou, China, between 2010 and 2012. Exposure to passive smoking during pregnancy was associated with an increased risk of very preterm birth (<32 completed weeks of gestation; odds ratio = 1.98, 95% confidence interval: 1.41, 2.76) but not moderate preterm birth (32–36 completed weeks of gestation; odds ratio = 0.98, 95% confidence interval: 0.81, 1.19). Risk of very preterm birth increased with the duration of exposure (*P* for trend = 0.0014). There was no variability in exposures by trimester. The associations were consistent for both medically indicated and spontaneous preterm births. Overall, our findings support a positive association between passive smoking and the risk of very preterm birth.

birth cohort; China; passive smoking; preterm birth

Abbreviations: CI, confidence interval; OR, odds ratio; PPROM, preterm premature rupture of membranes.

Preterm birth is the leading cause of neonatal deaths and is associated with various infant morbidities, such as acute respiratory illness, gastrointestinal and immunologic deficits, lifelong neurologic handicaps, and chronic diseases, that can extend into adulthood (1–3). In addition to the intense physical and emotional tolls associated with these illnesses, economic costs to families and society due to neonatal intensive care, ongoing health care, and specialized educational needs can be devastating.

The estimated prevalence of preterm birth ranges from 5% to 18% worldwide, with the lowest rates occurring in more developed areas and the highest rates in less developed areas (4). During the past decade, a rising trend of preterm births has been observed in most countries for which reliable data were available (4). Finding a solution to this growing problem is a priority for Millennium Development Goal 4 by the World Health Organization (5), as preterm birth continues to emerge as a major public health concern.

Several factors are believed to predispose women to preterm delivery, including underlying infection, certain preexisting anatomical considerations, and active smoking during pregnancy. Unlike disease processes, tobacco smoke is an environmental exposure that is much easier to eliminate. Though maternal active smoking is a well-documented risk factor for preterm delivery (6), evidence for passive smoking has been mixed (7). Some studies suggested that maternal passive smoking was associated with an increased risk of preterm birth (8–14), whereas others found no association (15–21). A systematic review and meta-analysis showed no significant association between passive smoking and preterm birth (22), although the ranges of gestational ages in the different populations varied between these studies, complicating the comparability of the results. Decreasing gestational age at birth is associated with increasing rates of mortality and morbidity (4), and thus the relationship between passive smoking and the risk of preterm birth may vary with gestational age. In addition, preterm birth is a complex outcome that can be further categorized into medically indicated or spontaneous preterm birth based on cause. To our knowledge, our study is the first to comprehensively examine the association between passive smoking and preterm birth by clinical subtypes.

China contains one fifth of the world's population and has the second highest number of preterm births in the world (23). According to results from a national survey in China, very few women (3.2%) and a large number of men (48.9%) are active smokers (24). This fact provides a unique opportunity for us to study passive smoking and reproductive health in nonsmoking women. Given the previous inconclusive findings regarding maternal passive smoking and preterm birth risk, we conducted a large birth cohort study in Lanzhou, China, to examine the relationship by various clinical subtypes.

METHODS

A study of a birth cohort was conducted in 2010–2012 at the Gansu Provincial Maternity and Child Care Hospital, the largest maternity and child care hospital in Lanzhou, China. Pregnant women who came to the hospital for delivery at 20 weeks of gestation or more, who had no mental illness, and who were 18 years of age or older were eligible. A total of 14,535 pregnant women came to the hospital for delivery, of whom 176 were judged to be ineligible for the study (13 had mental illness, 39 were younger than 18 years of age, and 124 gave birth at less than 20 gestational weeks). Thus, a total of 14,359 eligible women were approached for participation. Of those, 3,712 refused to participate and 105 did not complete in-person interviews, which yielded 10,542 (73.4%) women who completed in-person interviews, 10,179 of whom had a singleton live birth.

All study procedures were approved by the human investigation committees at the Gansu Provincial Maternity and Child Care Hospital and Yale University. Eligible women were informed of study procedure upon their arrival at the hospital for delivery. After obtaining written consent, trained study interviewers conducted in-person interviews at the hospital using a standardized and structured questionnaire. The majority of women (84%) were interviewed within 1 to 3 days after delivery. The questionnaire collected information regarding demographic factors, reproductive and medical history, smoking behavior, alcohol and tea consumption, occupational and residential history, physical activity level, and diet. Information on birth outcomes and pregnancy complications were abstracted from the medical records.

Active smokers were defined as women who smoked 1 or more cigarettes per day for at least 1 month. Because so few women were active smokers ($n = 85$), we excluded active smokers from the study population, which yielded a final sample size of 10,094. Passive smokers were defined as women who were exposed to cigarette smoke at home, at work, during social and recreational activities, and/or while commuting to and from work for at least 30 minutes per week during pregnancy. Information on passive smoking exposure, duration (hours per day) of exposure, and location (home vs. other location) was collected separately for each trimester.

Preterm birth was defined as delivery before 37 completed weeks of gestation. The gestational age at delivery was calculated in completed weeks from the first day of the last menstrual period. According to the World Health Organization classification (5), preterm birth was divided into moderate preterm birth (32–36 weeks of gestation), very preterm birth (28–31 weeks of gestation), and extremely preterm birth (<28 completed weeks of gestation). To increase statistical power, we combined very preterm and extremely preterm births into a single group labeled very preterm birth. Preterm births were further classified as either medically indicated or spontaneous (25, 26). A medically indicated preterm birth occurs when a placental, uterine, fetal, or maternal condition exists that prompts the medical team to proceed with delivery after the risks and benefits of continuing pregnancy are weighed against the risks and benefits of early delivery. Examples include placenta or vasa previa, placenta accreta, placental abruption, prior classical cesarean delivery, uterine rupture or dehiscence, fetal growth restriction, select fetal anomalies, severe preeclampsia, uncontrolled gestational or chronic hypertension, complicated pregestational diabetes, and oligohydramnios. Medically indicated preterm birth does not include deliveries that result from spontaneous preterm labor or preterm premature rupture of membranes (PPROM).

Univariate analyses were used to compare selected characteristics between preterm and term births. *P* values were obtained using χ^2 test or Fisher's exact test for categorical variables and Student's *t* test for continuous variables. Unconditional logistic regression models were used to estimate odds ratios and 95% confidence intervals for the association of passive smoking with preterm birth and its clinical subtypes. In the final models, we adjusted for potential confounding variables, including maternal age (<25, 25–29, ≥30 years), years of education (<10, 10–15, >15), employment status during pregnancy (yes or no), preeclampsia/eclampsia (yes or no), gestational diabetes (yes or no), parity (nulliparous or parous), history of preterm birth (yes or no), and cesarean delivery of the current birth (yes or no). Additional adjustment for alcohol consumption, maternal prepregnancy body mass index (weight (kg)/height (m)^2), maternal weight gain, physical activity during pregnancy, and infant sex did not result in material changes in the observed associations and thus were not included in the final models. All analyses were performed using SAS software, version 9.2 (SAS Institute, Inc., Cary, North Carolina).

RESULTS

Of the 10,094 singleton live births, 10.0% were preterm with a gestational age less than 37 completed weeks. Of those 1,009 preterm births, 81.6% ($n = 823$) were moderate preterm births (32–36 weeks of gestation) and 18.4% ($n = 186$) were very preterm births (<32 weeks of gestation). One third of the preterm births were medically indicated ($n = 337$), with a mean gestational age of 33.6 (standard deviation, 2.5) weeks. Spontaneous preterm births accounted for approximately two thirds of the preterm births ($n = 672$), with a mean gestational age of 33.5 (standard deviation, 3.2) weeks.

Table 1 shows the distributions of selected characteristics in women with preterm and term deliveries. Women who had preterm deliveries were more likely to be either younger than 25 years of age or older than 30 years of age, have fewer years

Table 1. Distribution of Selected Characteristics of the Study Population ($n = 10{,}094$), Urban China, 2010–2012

Characteristic	Preterm Birth ($n = 1{,}009$)		Full-Term Birth ($n = 9{,}085$)		*P* Value[a]
	No.	%	No.	%	
Age, years					<0.0001
<25	239	23.7	1,383	15.2	
25–29	361	35.8	4,452	49.0	
≥30	409	40.5	3,250	35.8	
Education, years					<0.0001
≤9	392	39.7	1,835	20.6	
10–15	373	37.8	3,556	39.8	
≥16	222	22.5	3,532	39.6	
Missing	22		162		
Employment status					<0.0001
No	593	58.8	4,287	47.2	
Yes	416	41.2	4,798	52.8	
Parity					<0.0001
Nulliparous	623	61.7	6,751	74.3	
Parous	386	38.3	2,334	25.7	
History of preterm delivery					<0.0001
No	962	95.3	9,053	99.6	
Yes	47	4.7	32	0.4	
Preeclampsia					<0.0001
No	876	86.8	8,887	97.8	
Yes	133	13.2	198	2.2	
Diabetes					0.024
Yes	992	98.3	9,000	99.1	
No	17	1.7	85	0.9	
Prepregnancy body mass index[b]					0.025
≤18.5	192	20.2	1,863	21.2	
18.6–23.9	629	66.2	5,996	68.1	
≥24	129	13.6	941	10.7	
Missing	59		285		
Alcohol drinking during pregnancy					0.81
No	1,007	99.8	9,070	99.8	
Yes	2	0.2	15	0.2	
Cesarean delivery					<0.0001
No	482	49.8	5,680	63.0	
Yes	486	50.2	3,334	37.0	
Missing	41		71		
Sex of the child					0.15
Boy	551	54.9	4,761	52.6	
Girl	452	45.1	4,297	47.4	
Missing	6		27		

[a] The analysis did not account for missing data.
[b] Weight (kg)/height (m)^2.

of education, be unemployed during pregnancy, have a higher prepregnancy body mass index, be parous, and have a history of preterm delivery. Women who were diagnosed with preeclampsia or diabetes were also more likely to have a preterm birth. Distributions of alcohol consumption and infant sex were similar for preterm and term deliveries.

As shown in Table 2, passive smoking during pregnancy was slightly associated with an increased risk of preterm birth overall (odds ratio (OR) = 1.12, 95% confidence interval (CI): 0.95, 1.32). After stratification by gestational age, a 98% increased risk was observed for very preterm birth (OR = 1.98, 95% CI: 1.41, 2.76) but not moderate preterm birth. The risk of a very preterm birth increased with the duration of exposure (*P* for trend = 0.0014). When the association was examined by exposure location, a significantly increased risk of very preterm birth was associated with exposure to passive smoking at home (OR = 2.12, 95% CI: 1.48, 3.03) but not at work (OR = 1.58, 95% CI: 0.90, 2.79). Risk increased with increasing duration of exposure at home ($P < 0.0001$) and at other locations ($P = 0.032$; data not shown). Similar results were seen when using mutually exclusive categories for location of exposure (data not shown). These observations showed similar patterns across exposure during all pregnancy trimesters.

We then analyzed the data separately for medically indicated and spontaneous preterm births (Tables 3 and 4). The associations with passive smoking were similar for both. Significant associations were observed for medically indicated and spontaneous very preterm births but not for medically indicated or spontaneous moderate preterm births.

We further stratified the analysis for spontaneous very preterm births by the presence or absence of PPROM (Table 5). The significant associations between passive smoking and spontaneous very preterm birth were seen for women without PPROM (OR = 2.72, 95% CI: 1.70, 4.34) but not for those with PPROM (OR = 0.91, 95% CI: 0.39, 2.13).

DISCUSSION

To our knowledge, the present study is the first to comprehensively examine the association between passive smoking and the risk of preterm birth by various clinical subtypes among Chinese nonsmokers. It supports the hypothesis that exposure to passive smoking is associated with an increased risk of very preterm birth and that risk increases with increasing duration of exposure. Similar patterns were observed between medically indicated and spontaneous preterm births.

Previous studies investigating the association between passive smoking and preterm birth provided conflicting results (8–21). Comparison of results from these studies is a challenge because passive smoking was inconsistently defined and gestational age cut offs varied from study to study. The majority of these studies had limited statistical power because of small numbers ($n < 200$) of preterm births (9–12, 16, 18, 20, 21). Several larger studies (13–15, 17, 19) reported nonsignificant associations between passive smoking and preterm birth overall, which is consistent with the results of our study. However, none of these studies examined the associations by various clinical subtypes except for a study by Windham et al. (14), in which the authors reported a 2-fold increase in the risk

Table 2. Associations Between Passive Smoking and Preterm Birth ($n = 10{,}094$), Urban China, 2010–2012

Passive Smoking	No. of Term Births	Preterm Births (<37 Weeks of Gestation)			Moderate Preterm Births (32–36 Weeks of Gestation)			Very Preterm Births (<32 Weeks of Gestation)		
		No.	OR[a]	95% CI	No.	OR[a]	95% CI	No.	OR[a]	95% CI
No	7,405	783	1.00	Referent	657	1.00	Referent	126	1.00	Referent
During the entire pregnancy										
Yes	1,680	226	1.12	0.95, 1.32	166	0.98	0.81, 1.19	60	1.98	1.41, 2.76
Duration[b], hours/day										
<1	994	135	1.10	0.90, 1.36	100	0.98	0.78, 1.23	35	1.89	1.26, 2.84
≥1	458	67	1.27	0.96, 1.69	47	1.05	0.76, 1.46	20	2.61	1.56, 4.34
P for trend				0.19			0.67			0.0014
Exposure location										
Home	1,243	189	1.17	0.98, 1.41	137	1.02	0.83, 1.25	52	2.12	1.48, 3.03
Other	695	63	0.92	0.70, 1.22	48	0.82	0.60, 1.12	15	1.58	0.90, 2.77
During the first trimester										
Yes	1,574	212	1.11	0.94, 1.32	156	0.98	0.81, 1.18	56	1.98	1.41, 2.79
Duration, hours/day										
<1	822	115	1.09	0.88, 1.37	83	0.95	0.74, 1.22	32	2.00	1.30, 3.06
≥1	532	74	1.24	0.95, 1.62	53	1.04	0.76, 1.42	21	2.46	1.50, 4.03
P for trend				0.25			0.68			0.0023
Exposure location										
Home	1,155	176	1.16	0.96, 1.40	126	0.99	0.80, 1.22	50	2.22	1.55, 3.19
Other	610	54	0.91	0.68, 1.23	40	0.79	0.56, 1.12	14	1.66	0.93, 2.96
During the second trimester										
Yes	1,437	192	1.10	0.92, 1.31	139	0.94	0.77, 1.15	53	2.09	1.47, 2.96
Duration, hours/day										
<1	775	110	1.11	0.88, 1.39	80	0.96	0.74, 1.24	30	2.03	1.31, 3.14
≥1	492	69	1.22	0.92, 1.61	48	1.00	0.72, 1.38	21	2.55	1.55, 4.20
P for trend				0.15			0.73			0.0005
Exposure location										
Home	1,050	163	1.18	0.97, 1.43	118	1.01	0.81, 1.26	45	2.20	1.51, 3.20
Other	543	44	0.81	0.58, 1.13	33	0.70	0.48, 1.02	11	1.56	0.82, 2.94
During the third trimester										
Yes	1,271	177	1.13	0.94, 1.37	129	0.98	0.79, 1.21	48	2.06	1.43, 2.97
Duration, hours/day										
<1	716	103	1.12	0.88, 1.41	73	0.95	0.73, 1.24	30	2.08	1.34, 3.23
≥1	421	63	1.31	0.98, 1.75	47	1.13	0.81, 1.57	16	2.39	1.38, 4.16
P for trend				0.26			0.69			0.0029
Exposure location										
Home	948	153	1.22	1.00, 1.49	112	1.06	0.85, 1.32	41	2.14	1.45, 3.15
Other	452	39	0.88	0.62, 1.25	29	0.75	0.50, 1.12	10	1.69	0.86, 3.31

Abbreviations: CI, confidence interval; OR, odds ratio.

[a] Adjusted for maternal age, educational level, employment status, preeclampsia, diabetes, parity, history of preterm delivery, and cesarian delivery.

[b] We did not have this information for a total of 24 preterm births and 228 term births.

of a preterm birth with a gestational age less 35 completed weeks in women exposed to passive smoking.

Our study found that passive smoking was associated with a slight, though nonsignificant, increased risk of preterm birth overall. However, when data were stratified by gestational age, passive smoking was strongly associated with very preterm birth (<32 weeks of gestation) but not moderate preterm birth (32–36 weeks of gestation). Several studies of active

Table 3. Associations Between Passive Smoking and Preterm Birth by Clinical Subtype ($n = 10{,}094$), Urban China, 2010–2012

Passive Smoking	No. of Term Births	Subtype of Preterm Birth: Medically Indicated ($n = 337$)			Subtype of Preterm Birth: Spontaneous ($n = 672$)		
		No.	OR[a]	95% CI	No.	OR[a]	95% CI
No	7,405	252	1.00	Referent	531	1.00	Referent
During the entire pregnancy							
Yes	1,680	85	1.23	0.94, 1.61	141	1.07	0.88, 1.31
Duration, hours/day							
<1	994	51	1.18	0.85, 1.64	84	1.08	0.85, 1.39
≥1	458	26	1.54	0.98, 2.41	41	1.15	0.82, 1.62
P for trend			0.30			0.33	
Exposure location							
Home	1243	73	1.30	0.98, 1.74	116	1.12	0.90, 1.40
Other	695	22	0.96	0.60, 1.53	41	0.89	0.64, 1.24
During the first trimester							
Yes	1,574	81	1.22	0.93, 1.61	131	1.06	0.87, 1.31
Duration, hours/day							
<1	822	45	1.21	0.85, 1.71	70	1.06	0.81, 1.38
≥1	532	29	1.44	0.94, 2.20	45	1.15	0.83, 1.58
P for trend			0.33			0.45	
Exposure location							
Home	1,155	69	1.30	0.97, 1.74	107	1.11	0.89, 1.39
Other	610	19	0.97	0.59, 1.61	35	0.87	0.61, 1.25
During the second trimester							
Yes	1,437	71	1.18	0.88, 1.57	121	1.08	0.87, 1.33
Duration, hours/day							
<1	775	41	1.12	0.78, 1.61	69	1.12	0.86, 1.47
≥1	492	26	1.45	0.93, 2.27	43	1.13	0.81, 1.57
P for trend			0.49			0.28	
Exposure location							
Home	1,050	63	1.27	0.94, 1.73	100	1.15	0.91, 1.45
Other	543	14	0.79	0.44, 1.40	30	0.83	0.56, 1.22
During the third trimester							
Yes	1,271	64	1.20	0.89, 1.62	113	1.13	0.91, 1.41
Duration, hours/day							
<1	716	36	1.08	0.74, 1.58	67	1.16	0.88, 1.52
≥1	421	24	1.56	0.98, 2.48	39	1.21	0.85, 1.71
P for trend			0.38			0.40	
Exposure location							
Home	948	58	1.31	0.96, 1.80	95	1.21	0.95, 1.53
Other	452	12	0.85	0.45, 1.58	27	0.89	0.59, 1.34

Abbreviations: CI, confidence interval; OR, odds ratio.
[a] Adjusted for maternal age, educational level, employment status, parity, history of preterm delivery, and cesarian delivery.

maternal smoking also reported a stronger association with very preterm birth than with moderate preterm birth (6, 27–30). Very preterm births account for 1%–2% of all births but more than 50% of neonatal deaths (31), which suggests that very preterm birth is a severe and distinctive clinical subtype of preterm birth that may have a different etiological profile and be more susceptible to the effects of active and passive smoking exposure.

Table 4. Associations Between Passive Smoking and Very Preterm Birth[a] by Clinical Subtype ($n = 10,094$), Urban China, 2010–2012

Passive Smoking	Subtype of Preterm Birth					
	Medically Indicated ($n = 337$)			Spontaneous ($n = 128$)		
	No.	OR[b]	95% CI	No.	OR[b]	95% CI
No	38	1.00	Referent	88	1.00	Referent
During the entire pregnancy						
Yes	20	2.09	1.18, 3.69	40	1.98	1.33, 2.97
Duration, hours/day						
<1	11	1.83	0.90, 3.73	24	2.06	1.27, 3.33
≥1	8	3.57	1.60, 8.00	12	2.14	1.12, 4.11
P for trend		0.044			0.010	
Exposure location						
Home	17	2.11	1.15, 3.87	35	2.22	1.45, 3.41
Other	4	1.40	0.49, 4.03	11	1.64	0.85, 3.17
During the first trimester						
Yes	19	2.11	1.18, 3.78	37	1.97	1.30, 2.98
Duration, hours/day						
<1	10	1.91	0.91, 4.00	22	2.22	1.34, 3.67
≥1	9	3.53	1.64, 7.61	12	1.98	1.05, 3.75
P for trend		0.060			0.015	
Exposure location						
Home	16	2.16	1.16, 4.01	34	2.35	1.52, 3.62
Other	4	1.66	0.58, 4.77	10	1.66	0.84, 3.30
During the second trimester						
Yes	18	2.19	1.21, 3.97	35	2.14	1.40, 3.26
Duration, hours/day						
<1	10	1.96	0.93, 4.10	20	2.28	1.36, 3.83
≥1	8	3.33	1.49, 7.44	13	2.17	1.16, 4.08
P for trend		0.029			0.0059	
Exposure location						
Home	15	2.16	1.14, 4.07	30	2.34	1.49, 3.68
Other	3	1.33	0.40, 4.42	8	1.69	0.80, 3.56
During the third trimester						
Yes	16	2.16	1.16, 4.00	32	2.16	1.40, 3.35
Duration, hours/day						
<1	9	1.87	0.87, 4.04	21	2.38	1.42, 4.00
≥1	6	2.94	1.19, 7.24	10	2.14	1.08, 4.26
P for trend		0.11			0.013	
Exposure location						
Home	14	2.18	1.14, 4.19	27	2.31	1.45, 3.70
Other	2	1.15	0.27, 4.90	8	1.92	0.90, 4.08

Abbreviations: CI, confidence interval; OR, odds ratio.
[a] Less than 32 weeks of gestation.
[b] Adjusted for maternal age, educational level, employment status, parity, history of preterm delivery, and cesarian delivery.

There is no consensus about whether medically indicated and spontaneous preterm births should be grouped together or evaluated separately in studies of etiology (32). Conditions that motivate medically indicated preterm birth (e.g., pre-eclampsia, placental abruption, and restricted fetal growth) are also strong predictors of spontaneous preterm birth (33–35),

Table 5. Associations Between Passive Smoking and Spontaneous Very Preterm Birth[a] by PPROM Status ($n = 10{,}094$), Urban China, 2010–2012

Passive Smoking	No. of Term Births	Very Preterm Births					
		With PPROM ($n = 34$)			Without PPROM ($n = 94$)		
		No.	OR[b]	95% CI	No.	OR[b]	95% CI
No	7,406	27	1.00	Referent	61	1.00	Referent
During the entire pregnancy							
Yes	1,680	7	0.91	0.39, 2.13	33	2.72	1.70, 4.34
Duration, hours/day							
<1	994	5	1.03	0.39, 2.76	19	2.74	1.57, 4.79
≥1	458	2	0.96	0.22, 4.15	10	2.88	1.38, 6.01
P for trend			0.95			0.0057	
Exposure location							
Home	1,243	7	1.11	0.47, 2.62	28	3.03	1.84, 4.99
Other	695	0			11	2.61	1.32, 5.20

Abbreviations: CI, confidence interval; OR, odds ratio; PPROM, preterm premature rupture of membranes.
[a] Less than 32 weeks of gestation.
[b] Adjusted for maternal age, educational level, employment status, parity, history of preterm delivery, and cesarian delivery.

and these conditions share mechanisms such as inflammation and vascular compromise that can lead to spontaneous preterm birth (32, 36). On the other hand, spontaneous onset of labor and membrane rupture appears clinically distinctive from fetal distress or severe hypertension that must be managed by early delivery. In our study, we found similar associations for both medically indicated and spontaneous preterm births. The risks of both medically indicated and spontaneous very preterm births were associated with exposure to passive smoking. However, the risk of spontaneous very preterm delivery was limited to women without PPROM. Although chance findings cannot be ruled out because of the small numbers of very preterm births without PPROM, this result may suggest that the effects of passive smoking on very preterm delivery are not due to premature rupture of membrane. Early studies have provided controversial results linking smoking and PPROM (37–39).

Exposure to smoking later in pregnancy is generally considered to be more strongly associated with low birth weight than is exposure during early pregnancy (40). It is unclear whether exposures during different trimesters differentially impact the risk of preterm birth. Although our study showed that exposures to passive smoking anytime during pregnancy increased risk of very preterm birth, exposure to passive smoking in each trimester was not mutually exclusive. There were high correlations of exposures to passive smoking between the 3 trimesters. Nicotine was found to cause a substantial decrease in the mitotic potential of cytotrophoblasts in vitro testing. This effect was also observed in women who smoked (41), which suggests a mechanism for abnormal placental development during early pregnancy (42) because ischemic placental disease is known to lead to preterm birth (43).

Our study also found that exposure to passive smoking at home but not in other locations was associated with the risk of very preterm birth. Although the risk of very preterm birth without PPROM showed a significant association with exposure at both work and other locations, the association was much stronger for passive smoking at home. These findings may indicate that there is a greater exposure to smoke from smokers at home compared with at work or in other public areas. Because the mean duration of exposure to passive smoking was lower at home (0.65 hours/day) compared with that at other locations (1.46 hours/day) in our study, one possible explanation for the observed association could be that smoke concentrations are higher at home than at other locations. This may be because homes generally have a more confined spaces and less efficient ventilation mechanisms than do work places and/or public areas. One early study reported a positive association between children born small for gestational age and passive smoking at home but not at other locations (21). Because several comparisons have been made and the numbers were small for the stratified analyses, these findings could be due to chance.

Unlike another study (8) that reported an 80% increased risk of preterm birth associated with passive smoking among women who were 30 years of age or older and no association between passive smoking and preterm birth among those who were younger than 30 years of age, we did not find that age was an effect modifier. Because information on passive smoking was based on self-report and the majority of women were interviewed after delivery (83.4% among women with term deliveries and 89.4% among women with preterm deliveries), it is possible that women who had a preterm delivery were more likely to underreport the duration of exposure to passive smoking because of the negative connotations associated with smoking around pregnant women. Studies have also suggested that self-reported exposure to passive smoking tends to be underreported (44, 45), resulting in the misclassification of exposed women as unexposed. If any potential biases were present, the association was likely underestimated. Two earlier studies examined the relationship between preterm birth and passive smoking using maternal hair nicotine levels (9, 11), a valid biomarker for measuring chronic exposure to passive smoke (11, 46, 47). Both studies found that high hair nicotine levels were associated with an increased risk of preterm birth and also saw a strong correlation between self-reported passive smoking and hair nicotine levels (9, 11). Another study found no association between salivary nicotine levels and preterm birth, but the study had limited statistical power (20 miscarriage and preterm cases and 13 controls) (48). In addition, a significant association was observed for very preterm birth but not moderate preterm birth, which suggests that differential recall did not affect our findings. The study population was recruited from the largest maternity and child care hospital in Lanzhou, the capital city of Gansu Province. Although the study was a hospital-based study, which might impact generalizability, the rate of preterm births (10.0%) in our study population was within the range of the reported preterm birth rate (4.1%–18.9%) in other Chinese populations, as reviewed by Blencowe et al. (4).

The present study excluded both current and former smokers, minimizing potential differences in health effects of active versus passive smokers. All study participants were Chinese, minimizing differences in genetic susceptibility to passive smoking by ethnic group. We collected and controlled for detailed information on potential confounding factors in the analysis. Information on birth outcomes and maternal complications during pregnancy was obtained from medical records, which minimized misclassification.

In conclusion, our study found that passive smoking was significantly associated with an increased risk of very preterm birth. Because an increased risk was seen for both medically indicated and spontaneous very preterm births but not for medically indicated or spontaneous moderate preterm births, more studies are needed to understand the mechanism by which nicotine influences the in utero developmental processes. Our findings indicate a strong need for public health campaigns to increase awareness of the negative health effects of passive smoking, especially during pregnancy, to protect the health of women and infants.

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