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Air Pollution and Adverse Pregnancy Outcome

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1. Introduction

Air pollution is known to be associated with increased total mortality, including cardiovascular and respiratory mortality. People with chronic disease in adulthood, such as cardiovascular disease, metabolic syndrome and respiratory diseases, are very susceptible with air pollutants (Kwon HJ et al., 2003). However, air pollution adversely impacts not only adults and the elderly but also fetuses and children. In fact, fetuses are the most vulnerable group to air pollution because vulnerability and susceptibility to air pollution are formed at early ages. Low birth weight (LBW), pre-term delivery (PTB), intrauterine growth restriction, and post-neonatal infant mortality are such undesirable outcomes.

LBW affects 20 million infants worldwide (UNICEF, 2004). LBW is comprised of two overlapping etiologies: PTB and intrauterine growth retardation (IUGR). In particular, LBW is associated with a higher risk of infant and childhood mortality, coronary heart disease, and other health problems. LBW additionally has a well-established association with early-onset insulin resistance and a later risk of adulthood diseases, including all aspects of the metabolic syndrome.

PTB remains the leading cause of perinatal mortality and occurs in approximately 4-10% of pregnancies (Reagan and Salsberry 2005). Known risk factors for PTB include lower social class, less education, single marital status, low income, younger maternal age, low body weight, ethnicity, smoking, and poor housing, along with medical factors such as induction, premature rupture of membranes, infection, multiple pregnancy, intrauterine death, fetal and uterine abnormalities and chorioamnionitis (Bibby and Stewart 2004).

LBW and PTB are both significantly associated with infant mortality and an array of infant morbidities that range from pulmonary to neurologic outcomes. These associations form the basis for the “fetal origins” or the “Barker hypothesis” which postulates that “fetal growth retardation consequent to malnutrition has long-term structural and physiologic impacts that predispose an individual to chronic diseases in adulthood” (Barker, 2007).

Is there the association between air pollution and adverse pregnancy outcomes, such LBW, and PTB? In this chapter, we will review the association between air pollution and adverse pregnancy outcomes(APO), such as LBW and PTB. We also will estimate the disease burden of LBW and PTB caused by air pollution, and discuss how to decrease these APOs.

2. Air pollution and adverse pregnancy outcomes

2.1 Air pollution and low birth weight

Fifteen (Alderman et al., 1987; Bell et al., 2007; Bobak and Leon, 1999; Bobak, 2000; Dugandzic et al., 2006; Gouveia et al., 2004; Ha et al., 2001; Lee et al., 2003; Lin et al., 2004; Liu et al., 2003; Maisonet et al., 2001; Morello-Frosch et al., 2010; Ritz and Yu, 1999; Rogers et al., 2000; Salam et al., 2005) studies reported data on birth outcomes following SO₂ exposure (Table 1): ten reported increased odds of LBW births following SO₂ exposure, five reported no association with LBW, and one reported significant association with extreme LBW (Rogers et al., 2000).

Little is known about the association between nitrous oxide (NO) and APO. But in natural condition, NO is converted into nitrogen dioxide (NO₂), which is 5~10 times more toxic than NO. NO₂ is known to be associated with APO by several studies. The association between NO₂ exposure and LBW was explored in 11 studies (Bell et al., 2007; Bobak, 2000; Gouveia et al., 2004; Ha et al., 2001; Lee et al., 2003; Lin et al., 2004; Liu et al., 2003; Madsen et al., 2010; Marozienne and Grazuleviciene, 2002; Morello-Frosch et al., 2010; Salam et al., 2005) (Table 1). Increased LBW risk with increased NO₂ exposure was reported by Ha et al. (2001) (first trimester), Lee et al. (2003) (second trimester), Bell et al. (2007) (during the entire gestation) and Morello-Frosch et al. (2010). However, other reports did not identify significant increases in LBW births.

The association between carbon monoxide(CO) exposure and birth outcomes was explored in 13 studies (Alderman et al., 1987; Bell et al., 2007; Chen et al., 2002; Gouveia et al., 2004; Ha et al., 2000; Huynh et al., 2006; Lee et al., 2003; Lin et al., 2000; Liu et al., 2003; Maisonet et al., 2001; Morello-Frosch et al., 2010; Salam et al., 2000; Ritz and Yu, 1999) (Table 1). Of these, five studies (Ritz and Yu, 1999; Ha et al., 2000; Maisonet et al., 2001; Lee et al., 2003; Morello-Frosch et al., 2010) reported an increased risk of LBW births.

Seven studies (Chen et al., 2002; Dugandzic et al., 2006; Gouveia et al., 2004; Ha et al., 2001; Lin et al., 2004; Liu et al., 2003; Morello-Frosch et al., 2010) investigated the association between exposure to ozone and LBW (Table 1). None of these studies reported a statistically significant increase in LBW with higher exposure to ozone.

The effects of PM_{2.5} (Particulate matter less than 2.5 µm in aerodynamic diameter) on LBW were evaluated in four studies (Bell et al., 2007; Huynh et al., 2006; Madsen et al., 2010; Morello-Frosch et al., 2010) (Table 1). Huynh et al. (2006) reported an association between high levels of PM_{2.5} and LBW when the exposure was measured at any time during the gestation, and particularly in the last 2 weeks of pregnancy and the first month of gestation. Bell et al. (2007) and Morello-Frosch et al. (2010) also reported that high levels of PM_{2.5} were associated with LBW. But Madsen et al. (2010) did not report any association between exposure to high levels of PM_{2.5} and LBW.

Twelve studies (Bell et al., 2007; Chen et al., 2002; Dugandzic et al., 2006; Gouveia et al., 2004; Lee et al., 2003; Maisonet et al., 2001; Lin et al., 2004; Salam et al., 2005; Seo et al., 2010; Madsen et al., 2010; Morello-Frosch et al., 2010; Xu et al., 2011) assessed the effects of PM₁₀ (Particulate matter less than 10 µm in aerodynamic diameter) on LBW (Table 1). Lee et al. (2003) and Xu et al. (2011) reported on a possible association between LBW and an increase of more than an interquartile range in PM₁₀ exposure during the first and second trimesters, and Gouveia et al. (2004) reported higher odds of LBW among mothers in the highest quartile of exposure during the second trimester. Seo et al. (2010) reported that among seven Korean cities, two had higher odds of LBW births with incremental exposure to PM₁₀, whereas five had no association. Other studies have reported no association between PM₁₀ and LBW births.

Of five studies (Bobak, 2000; Bobak and Leon, 1999; Ha et al., 2001; Rogers et al., 2000; Wang et al., 1997) that reported on the association between total suspended particles and LBW (Table 1), three (Ha et al., 2001; Rogers et al., 2000; Wang et al., 1997) reported an increased risk of LBW births with higher concentrations. The other two (Bobak, 2000; Bobak and Leon, 1999) reported no association between TSP (total suspended particle) and LBW births.

Pollutants or exposure variable	Results	Reference
SO ₂	NE*	Alderman et al ,1987
	AOR**=1.22(95% CI, 1.03–1.44) for > 5.5 ppm during the last trimester	Ritz and Yu,1999
	AOR=1.10(95% CI, 1.02–1.17) for 50 µg/m ³ increase	Bobak and Leon, 1999
	NE	Bobak, 2000
	AOR=2.88(95% CI, 1.16–7.13) for > 56.75 µ/m ³ in annual exposure for very LBW infant outcome	Rogers et al.,2000
	ARR=1.06(95% CI, 1.02–1.10) for IQR increase in the first trimester	Ha et al.,2001
	Second trimester exposures falling within the 25 and < 50th (AOR 1.21; CI 1.07,1.37), the 50 to < 75th (AOR 1.20; CI 1.08,1.35), and the 75 to < 95th (AOR 1.21; CI 1.03,1.43) percentiles were also at increased risk for term LBW when compared to those in the reference category (< 25th percentile).	Maisonet et al. 2001
	OR=1.14(95% CI, 1.04–1.24) for IQR increase in all trimesters OR=1.06(95% CI, 1.02–1.11) for IQR increase in the second trimester.	Lee et al. 2003
	AOR=1.11(95% CI, 1.01–1.22) for 5 ppb increase in the first month	Liu et al. 2003
	NE	Gouveia et al. 2004
	AOR=1.16(95% CI, 1.02–1.33) for 7.1–11.4 ppb increase in entire pregnancy AOR=1.26(95% CI, 1.04–1.53) for >11.4 ppb increase in entire pregnancy AOR=1.20(95% CI, 1.01–1.41) for >12.4 ppb increase in third trimester	Lin et al. 2004
	NE	Salam et al., 2005
	ARR=1.15(95% CI, 1.00–1.31) increase in the first trimester	Dugandzic et al. 2006
	NE	Bell et al. 2007
	AOR=1.01(95% CI, 1.00– 1.02) for ppb increase at 10 km monitor distance	Morello-Frosch et al. 2010
NO ₂	NE	Bobak. 2000
	ARR=1.07(95% CI, 1.03–1.11) for IQR increase in the	Ha et al. 2001

	first trimester	
	NE	Maroziene and Grazuleviciene. 2002
	OR=1.04(95% CI, 1.00-1.08) for IQR increase in all trimester OR=1.03(95% CI, 1.01-1.06) for IQR increase in the second trimester	Lee et al. 2003
	NE	Liu et al. 2003
	NE	Gouveia et al. 2004
	NE	Lin et al. 2004
	NE	Salam et al. 2005
	AOR=1.03(95% CI, 1.00-1.05) for IQR increase	Bell et al. 2007
	NE	Madsen et al. 2010
	AOR=1.03(95% CI, 1.01-1.05) for ppm increase at 3 km monitor distance AOR=1.04(95% CI, 1.03-1.05) for ppm increase at 5 km monitor distance AOR=1.03(95% CI, 1.02-1.04) for ppm increase at 10 km monitor distance	Morello-Frosch et al. 2010
CO	NE	Alderman et al., 1987
	AOR=1.22(95% CI, 1.03-1.44) for > 5.5 ppm increase during the last trimester	Ritz and Yu, 1999
	AOR=1.08(95% CI, 1.04-1.12) for IQR increase in the first trimester	Ha et al. 2001
	AOR=1.31(95% CI, 1.06-1.62) for 1 ppm increase in the third trimester	Maisonet et al. 2001
	NE	Chen et al. 2002
	OR=1.05(95% CI, 1.01-1.09) increase in all trimesters OR=1.04(95% CI, 1.01-1.07) for IQR increase in the first trimester OR=1.03(95% CI, 1.00-1.08) increase in the second trimester	Lee et al. 2003
	NE	Liu et al. 2003
	NE	Gouveia et al. 2004
	NE	Lin et al. 2004
	NE	Salam et al. 2005
	NE	Huynh et al. 2006
	NE	Bell et al. 2007
	AOR=1.06(95% CI, 1.03-1.09) for ppm increase at 5 km monitor distance AOR=1.04(95% CI, 1.02-1.06) for ppm increase at 10 km monitor distance	Morello-Frosch et al. 2010
Ozone(O ₃)	NE	Ha et al. 2001
	NE	Chen et al. 2002
	NE	Liu et al. 2003

	NE	Gouveia et al. 2004
	NE	Lin et al. 2004
	NE	Dugandzic et al. 2006
	NE	Morello-Frosch et al. 2010
PM _{2.5}	AOR=1.14(95% CI, 1.07-1.23) for 17.7-22.1 µg/m ³ increase at any time during the gestation AOR=1.15(95% CI, 1.07-1.24) for > 22.1 µg/m ³ increase at any time during the gestation AOR=1.09(95% CI, 1.01-1.17) for 12.5-18.2 µg/m ³ increase in the first month AOR=1.14(95% CI, 1.06-1.22) for 18.2-23.0 µg/m ³ increase in the first month AOR=1.21(95% CI, 1.12-1.30) for > 23.0 µg/m ³ increase in the first month AOR=1.11(95% CI, 1.04-1.19) for 10.2-15.6 µg/m ³ increase in the last 2 weeks AOR=1.18(95% CI, 1.10-1.19) for 15.6-23.3 µg/m ³ increase in the last 2 weeks AOR=1.17(95% CI, 1.09-1.27) for > 23.3 µg/m ³ increase in the last 2 weeks	Huynh et al. 2006
	OR=1.05(95% CI, 1.02-1.09) for IQR increase	Bell et al. 2007
	NE	Madsen et al. 2010
	AOR=1.05(95% CI, 1.02-1.08) for 10 µg/m ³ increase at 5 km monitor distance AOR=1.04(95% CI, 1.02-1.07) for 10 µg/m ³ increase at 10 km monitor distance	Morello-Frosch et al. 2010
PM ₁₀	NE	Maisonet et al. 2001
	NE	Chen et al., 2002
	OR=1.06(95% CI, 1.01-1.10) for IQR increase in all trimesters OR=1.03(95% CI, 1.00-1.07) for IQR increase in the first trimester OR=1.04(95% CI, 1.00-1.08) for IQR increase in the second trimester	Lee et al. 2003
	AOR=1.25(95% CI, 1.03-1.53) for highest quartile of exposure increase in the second trimester	Gouveia et al. 2004
	NE	Lin et al. 2004
	NE	Salam et al. 2005
	NE	Dugandzic et al. 2006
	NE	Bell et al. 2007
	AOR=1.24(95% CI, 1.02-1.52) for increments (difference between the maximum and minimum concentrations) increase in Pusan AOR=1.19(95% CI, 1.04-1.37) increase in Daegu	Seo et al. 2010
	NE	Madsen et al. 2010

	NE	Morello-Frosch et al. 2010
	AOR=1.13(95% CI, 1.02-1.25) for IQR (7 $\mu\text{g}/\text{m}^3$) increase in the first trimester AOR=1.10(95% CI, 1.00-1.22) for IQR (7 $\mu\text{g}/\text{m}^3$) increase in the second trimester	Xu et al. 2011
TSP	AOR=1.10(95% CI, 1.05-1.14) for 100 $\mu\text{g}/\text{m}^3$ increase	Wang et al. 1997
	NE	Bobak and Leon 1999
	NE	Bobak. 2000
	AOR=2.88(95% CI, 1.16-7.13) for > 56.75 μ/m^3 increase for very LBW infant outcome	Rogers et al. 2000
	ARR=1.04(95% CI, 1.00-1.08) for IQR increase in the first trimester	Ha et al. 2001

Air pollution and LBW

*NE: No effect, **AOR: Adjusted odds ratio

Table 1. Air pollution and low birth weight

2.2 Air pollution and preterm delivery

An association of higher exposure to SO_2 and PTB was reported in seven (Bobak, 2000; Huynh et al., 2006; Leem et al, 2006; Liu et al., 2003; Mohorovic, 2004; Sagiv et al., 2005; Xu et al., 1995) of the eight studies.

The association of NO_2 exposure and PTB was explored in 10 studies (Bobak, 2000; Gehring et al., 2011; Jalaludin et al., 2007; Leem et al, 2006; Liu et al., 2003; Llop et al. 2010; Maroziene and Grazuleviciene, 2002; Ritz et al.,2000, 2007, 2011) (Table 2). Bobak (2000) (first and third trimester), Maroziene and Grazuleviciene(2002) (first trimester), Leem et al (2006), Bobak (2000) (first and third trimester), Llop et al. (2010) (second and third trimester and entire pregnancy) reported an increased risk of PTB; however, others reported no association.

The association between CO exposure and preterm birth was explored in 6 studies (Ritz et al., 2000; Huynh et al., 2006; Leem et al., 2006; Liu et al., 2003; Wilhelm and Ritz, 2005; Ritz et al., 2007). Liu et al. (2003) (last month of the pregnancy), Wilhelm and Ritz (2005) (first trimester), leem et al (2006) (first and third trimester) and Ritz et al. (2007) (first trimester) reported a higher risk of PTB with higher concentration of CO. 4 of 6 studies reported a higher risk of PTB with CO exposure around 1ppm. In particular, Leem et al's study (2006) showed that the relationships between PTB and exposures to CO was dose dependent ($p < 0.001$). But Ritz et al.(2000) and Huynh et al. (2006) did not report the association between CO exposure and preterm birth There was a significant dose-dependent association between gestational age and sulfur dioxide and total suspended particulate concentrations (Xu et al, 1995).

In 3 studies (Ritz et al., 2000; Liu et al., 2003; Ritz et al., 2007, the association between exposure to ozone and PTB was investigated (Table 2). None of these studies reported a statistically significant increase in PTB with higher exposure to ozone.

The effects of $\text{PM}_{2.5}$ on PTB were evaluated in three studies (Huynh et al., 2006; Ritz et al., 2007, 2011) (Table 2). Huynh et al. (2006) and Ritz et al. (2007, 2011) reported an association of high levels of $\text{PM}_{2.5}$ with PTB when the exposure was measured at any time during the gestation.

In 4 studies (Leem et al., 2006; Ritz et al., 2000; Sagiv et al, 2005; Wilhelm and Ritz,2005) , the effects of PM_{10} on PTB were assessed (Table 2). Leem et al. (2006) and Ritz et al. (2000) reported on the association between PTB and high levels in PM_{10} exposure during the first

trimester. But Wilhelm and Ritz (2005) and Sagiv et al (2005) did not report any association between exposure to PM₁₀ and PTB.

Three studies (Bobak, 2000; Bobak and Leon, 1999; Xu et al., 1995) reported on total suspended particles and an association with PTB (Table 2), all of which reported an increased risk of PTB births with higher concentrations.

Some studies reported the association between living near petrochemical industrial complexes or living with 500m of freeway, or living 200m of main roads and PTB. Llop et al. reported the association between benzene exposure > 2.7 µg/m³ and PTB.

Pollutants or exposure variable	Results	Reference
SO ₂	AOR** = 1.21 (95% CI, 1.01-1.45) for 100 µg/m ³ increase	Xu et al. 1995
	NE*	Langren, 1996
	AOR = 1.27 (95% CI, 1.16-1.39) for 50 µg/m ³ increase in the 1st trimester	Bobak 2000
	AOR=1.09(95% CI, 1.01-1.19) for 5.0 ppb increase	Liu et al 2003
	Significantly shorter gestation for SO ₂ exposure during the initial two months of pregnancy	Mohorovic 2004
	AOR=1.15(95% CI, 1.00, 1.32) for 15 ppb increase during 6 weeks before birth	Sagiv et al., 2005
	AOR=2.31(95% CI, 1.29-4.15) for 1 hr maximum in the first trimester	Huynh et al. 2006
	AOR=1.21 (95% CI: 1.04-1.42) in the highest quartiles in the 1st trimester	Leem et al., 2006
NO ₂	AOR= 1.10(95%CI,1.00-1.21) For 50 µg/m ³ increase above mean level in the 1 st trimester	Bobak, 2000
	AOR= 1.08(95%CI,0.98-1.19) For 50 µg/m ³ increase above mean level in the 1 st trimester	
	AOR= 1.11(95%CI,1.00-1.23) For 50 µg/m ³ increase above mean level in the 1 st Trimester	
	NE	Ritz et al. 2000
	AOR= 1.67(1.28-2.18) for 10 µg/m ³ increase in exposure in the first trimester	Maroziene and Grazuleviciene, 2002
	NE	Liu et al. 2003
	AOR=1.24 (95% CI: 1.09-1.41) for 0.77 1.01 ppm in the 1st trimester	Leem et al., 2006
	AOR=1.21 (95% CI: 1.07-1.37) in the highest quartiles in the 3rd trimester	
	Decreasing PTB risk	Jalaludin et al. 2007
	NE	Ritz et al., 2007
AOR=1.16 (95% CI: 1.07-1.26) per inter-quartile range	Ritz et al. 2011	
AOR=1.29(95% CI= 1.13- 1.46) NO ₂ > 46.2 µg/m ³	Llop et al. 2010	

	NE	Gehring et al., 2011
CO	NE	Ritz et al. 2000
	AOR=1.08(95% CI: 1.01-1.15) for a 1.0 ppm increase	Liu et al 2003
	AOR= 1.27 (95% CI: 1.07-1.50) for 1ppm increase in the 1st trimester	Wilhelm and Ritz 2005
	AOR= 1.25 (95%: 0.81-1.91)	Huynh et al. 2006
	AOR=1.26 (95% CI: 1.11-1.44) for 0.77 – 1.01 ppm in the 1 st trimester	Leem et al., 2006
	AOR=1.16 (95% CI: 1.01-1.34) for 0.79 – 1.11 ppm in the 3 rd trimester	
	AOR= 1.25(95% CI: 1.12- 1.38) for CO more than 1.25 ppm in the 1 st trimester	Ritz et al. 2007
PM _{2.5}	AOR = 1.15(95% CI: 1.07- 1.24).	Huynh et al. 2006
	AOR= 1.10(95% CI: 1.01- 1.20) for PM _{2.5} more than 21.36 µg/m ³ in the 1st Trimester	Ritz et al. 2007
	AOR= 1.08 (1.02-1.15) per inter-quartile range	Ritz et al. 2011
PM ₁₀	RR = 1.16 (95% 1.06-1.26) for 50 µg/m ³ increase in the 1st trimester	Ritz et al. 2000
	AOR=1.00(95% CI, 0.90 – 1.12) for 10 µg/m ³ increase in the 1st trimester	Wilhelm and Ritz 2005
	NE	Sagiv et al., 2005
	AOR=1.27 (95% CI: 1.04-1.56)) in the highest quartiles in the 1st trimester	Leem et al.,2006
TSP	AOR = 1.10 (95% CI, 1.01-1.20) for 100 µg/m ³ increase	Xu et al. 1995
	AOR= 1.11(95% CI, 1.02-1.22) for each 50 µg/m ³ increase in the 1st trimester	Bobak and Leon 1999
	AOR= 1.06(95% CI, 0.96-1.16) for each 50 µg/m ³ increase in the 2nd trimester	
	AOR= 1.14(95% CI, 1.03-1.26) for each 50 µg/m ³ increase in the 3rd trimester	
	AOR = 1.18 (95% CI, 1.05-1.31) for 50 µg/m ³ increase in the 1 st trimester	Bobak 2000
O ₃	NE	Ritz et al. 2000
	NE	Liu et al 2003
	NE	Ritz et al. 2007
SO ₂ + NO ₂ + PM ₁₀	AOR = 1.41 (91% CI, 1.08-1.82) comparing petrochemical and control municipalities	Lin et al. 2001
SO ₂ + NO ₂ + PM ₁₀ + CO (Air Pollution Index)	AOR=4.66(95% CI, 1.92-11.32); 95% confidence interval (95% CI), 1.92-11.32 in hispanic mothers	Woodruff et al. 2003
Benzene	AOR=1.29(95% CI= 1.13- 1.46) Benzene > 2.7 µg/m ³	Llop et al. 2010

Living near petrochemical industrial complexes	AOR=1.18 (95% CI=1.04-1.34 for mothers living near petrochemical industrial complexes	Yang et al. 2002
living near industrial districts	AOR=1.11 (95% CI, 1.02-1.21)) for mothers living near industrial districts	Tsai et al. 2003
living near oil refinery plants	AOR=1.14 (95% CI,1.01-1.28) for mothers living near oil refinery plants	Yang et al. 2004
local traffic-generated NO(x) and PM _(2.5) .	AOR= 1.42(95% CI, 1.26-1.59) For highest NO(x) and PM(2.5) quartiles	Wu et al. 2009
living within 500 m of the freeway.	AOR=1.30 (95% CI, 1.03, 1.65)	Yang et al. 2003
Living within 200 m of main roads	AOR= 1.5 (95% CI = 1.2-1.8),	Yorifuji et al. 2011

Air pollution and premature births

*NE: No effect, **AOR: Adjusted odds ratio

Table 2. Air pollution and premature births

3. Considerations to reduce bias or measurement errors

Some studies systemically reviewed published articles about air pollution and LBW or PTB (Bobak, 2005; Bonzini et al., 2010; Pope et al., 2010; Leonardi-Bee et al., 2008; Ghosh et al., 2007; Misra et al., 1999; Sram et al., 2011). Because of different exposure assessments, methods of ascertainment, measurement times and collinearity between pollutants, the results about the association showed heterogeneity and/or an absence of association. We summarized our systemic review of these research papers in tables 1 and 2. Exposure to sulphur dioxide was associated with PTB, and exposure to PM_{2.5} was associated with LBW and PTB. The evidence for NO₂, ozone and carbon monoxide was inconclusive. To investigate the association between air pollutants and adverse birth outcomes is challenging. The following are major issues in clarifying such associations.

3.1 Exposure assessment: reduction of misclassification

Epidemiological studies for APO often had limited spatial and temporal information on pollution sources and concentrations. Misclassification of exposure is often a source of bias in such environmental epidemiologic studies.

Various exposure assessment methods have been applied in different studies. Exposures were assigned to individual subjects based on residential address at delivery using the nearest ambient monitoring station data [CO, NO₂, NO, nitrogen oxides (NO_x), O₃, and PM_{2.5} or less than 10 µm in aerodynamic diameter (PM₁₀)], both unadjusted and temporally adjusted land-use regression (LUR) model estimates, line-source air dispersion model

estimates, and a simple traffic-density measure. Proximity to main roads and photochemical industrialized zones was also applied by using geographic information system (GIS).

Reliable measurements of daily SO₂, NO₂, CO, and PM₁₀ concentrations were available from several air monitoring stations by using various extrapolation method, such as kriging to predict the spatial distribution of the air pollutants (Pikhart et al. 2001; Mulholland et al., 1998; Jerrett et al. 2005b). The kriging method, unlike proximity models (Jerrett et al. 2005a), uses real pollution measurements in the computation of exposure estimates. In case of many monitoring stations, kriging methods are often preferred to other interpolation methods because they are fairly accurate in a variety of situations and avoid the artifacts that often result from the use of IDW, spline, or global/local polynomials (Jerret et al. 2005a; Ritz et al. 2000; Waller and Gotway, 2004).

Even though exposure models, such as kriging method, attempt to decrease misclassification of individual exposures by enhancing exposure assessment through spatially- and temporally-explicit exposure models, the potential remains for misclassification of exposure due to the use of surrogate ambient air pollution data. The only real way to avoid such potential misclassifications is to conduct personal exposure assessments which are often not feasible. LUR models often produced odds ratios somewhat larger in size than temporally adjusted models (Wu J et al. 2011).

Mobility patterns could introduce possible confounding when examining small-scale variations in exposure by using addresses. This could be of importance in future studies (Madsen C et al., 2010).

3.2 Biological mechanism

Interpretation of epidemiological studies reporting an association between air pollution and birthweight needs caution. Although a range of social and behavioural determinants of birthweight or preterm birth have been identified, the biological mechanisms leading to prematurity are not well understood (Berkowitz and Papiernik, 1993) and it is not clear which mechanisms could provide the link between air pollution and birthweight. The biological mechanisms whereby air pollution might influence birth weight remain unexplained, although several theories have been proposed. The pathways could be similar to those of maternal smoking, which can increase PTB risk through premature rupture of membranes and placental abruption and lower birth weight. Air pollution could affect fetal health either through direct effects on the fetus by exposure through the placenta or from effects on the mother's health and multiple mechanisms may occur simultaneously (Glinianaia et al., 2004).

One hypothesized pathway is that placental inflammation may play an important role in the physiological pathway between air pollution exposure and LBW (Lee BE et al., 2003). Although most published reports focus on genitourinary infections, maternal illness due to respiratory infection in pregnancy may also be involved. It is possible that air pollution during pregnancy leads to placental inflammation, which impairs placental function (Dexter et al., 2000). Salafia et al. (1995) reported that chronic inflammation brought about growth restriction, independently of placental vasculopathy. PM₁₀ and SO₂ exposures from first through second trimesters appeared to have the largest effect on LBW. In terms of the biological mechanism on LBW, it is reasonable to consider PM₁₀ and SO₂ together rather than separately because they represent fine particles that are believed to be a risk pollutant (Ha et al., 2001). In addition, these pollutants were correlated strongly with each other and exerted an effect on LBW within similar periods.

Coarse PM ($PM \leq 10\mu M$) is emitted from residential heating and power plants, whereas fine PM ($PM \leq 2.5 \mu M$) is emitted from cars, utilities or wood burning. Both types of PM are comprised of primary and secondary particles: primary particles are emitted directly from a source, such as construction work, and secondary particles are formed after the reaction of primary particles in the atmosphere with chemical pollutants such as SO_2 or NO_2 . When PM enters the lungs it can be absorbed into the blood and hence dispersed into distant organs. Due to their relatively small size, PM escapes phagocytosis (Ritz et al., 2007). Particle exposure in vitro and in exposed animals causes oxidative stress (Kadiiska et al., 1997) and can increase the permeability of lung epithelium, allowing particles access to the endothelial cells and the blood (Donaldson et al., 2001). PM_{10} and gaseous pollutants such as SO_2 and NO_2 lead to pulmonary inflammation with a systemic release of cytokines (Walters et al., 2001; Nemmar et al., 2002) and increased blood viscosity (Peters et al., 1997; Prescott et al., 2000).

Air pollution may affect DNA or its transcription. DNA adducts are more common in areas with higher levels of pollution. Placental DNA adducts were more common among mothers exposed to higher levels of outdoor air pollution (Bobak, 2000). When toxic organic matter such as polycyclic aromatic hydrocarbons (PAH) is adsorbed onto the surface of PM, associated oxidative stress (Leem et al., 2005) and DNA adducts are formed (Perera et al., 1999). High levels of DNA adducts were associated with reduced gestational length (Liu et al., 2003; Perera et al., 1998; Perera et al., 1999), and a correlation has been observed between the adduct levels in the mother's and the newborn's blood (Topinka et al., 2009). Newborns with elevated PAH-DNA adducts (which are used as a proxy to measure individual biologically effective dose to PAH) were found to have significantly reduced birth weight and head circumference suggesting that transplacental exposures to PAHs in ambient air may negatively impact on fetal development. High levels of PAH can interfere with nourishment of the fetus by increasing blood viscosity, and reducing the flow of blood to the placenta and uterus (Liu et al., 2003; Shah PS et al., 2011; Ritz et al., 2000). The effects of air pollution on DNA adducts levels seem similar (although weaker) to the effects of cigarette smoking. There may also be a parallel with maternal smoking, an accepted risk factor for LBW, for which the biologic mechanisms are not well understood. Although the fetal exposures to air pollution are probably lower than to tobacco smoke, the biologic mechanisms (rheologic factors, DNA damage) may be partially similar (Bobak, 2000).

Another potential mechanisms could be related to hematologic factors. Rheologic variables, including blood viscosity, influence the blood perfusion of the placenta. It has been shown that inflammation in the lung caused by air pollutants increases the coagulability of the blood. Production of free radicals induced by pollutants might cause an inflammatory response, contributing to enhanced blood coagulation. Hematologic effects of air pollutants might occur from an initial inflammatory response resulting in increased blood coagulation, and subsequent decreased oxygen supply to the placenta. Human volunteers exposed to diesel particles at $300 \mu g/m^3$ for an hour had increases in peripheral neutrophils and platelets as well as upregulation of endothelial adhesion molecules. Decreased oxygen supply from blood viscosity changes by increasing coagulability may cause chronic hypoxic injury to fetus. This theory is supported by evidence of the role of elevated blood viscosity for impaired efficiency of maternal blood flow (Ha et al., 2001). Increased blood viscosity is associated with decreased oxygen diffusion (Zondervan et al., 1988) and may interfere with the supply of oxygen and nutrients to the fetus. In addition, some toxicants from air pollutants could cross the placenta with direct effects on fetal development (Dejmek et al., 1999).

Alternatively, placental insufficiency may be an important pathway. Basic concepts of the pathophysiology of IUGR are based on different levels of maternal supply, fetoplacental competition, and fetal adaptations. In recent studies knowledge about placental development and function has been increased. Abnormalities in placental development may occur during its formation, and cellular and molecular functions may be changed leading to inadequate implantation and growth. Abnormalities in placental transport may also develop later on, because of problems in the uteroplacental circulation, exchange at the intervillous space, and umbilical and fetal circulation. All these factors lead to problems with fetal adaptation mechanisms, most importantly decreased fetal growth rate and fetal activities. Biologic mechanisms that have been suggested to support the hypothesis of an effect associated with early pregnancy exposures are related to the etiology of IUGR. Although likely multifactorial, one suggested mechanism for IUGR is abnormal placental development in early pregnancy. Placental insufficiency reduces the oxygen and nourishment supplies to the fetus and leads to growth retardation.

Exposure to air pollution in early pregnancy could cause insufficient trophoblast formation, and lead to insufficient placental vascularization (Duvekot et al., 1995). Chronic reductions of uteroplacental circulation due to the effects of air pollution could result in fetal hypoxia and IUGR (Werler et al., 1985).

CO is well known as a reproductive toxicant that can interfere with oxygen delivery to the fetus. CO shifts the oxyhemoglobin dissociation equilibrium and displaces oxygen from hemoglobin for a given partial pressure of oxygen. CO can also cause oxidative injury due to its effects on the endothelium (Hardy and Thom, 1994). CO has also been shown to cross the placental barrier (Sangalli et al., 2003) and the fetus is particularly vulnerable to CO poisoning because of 10–15% higher accumulation in fetal blood than maternal levels. Its elimination is slower in fetal blood than in maternal circulation. Fetal hemoglobin has greater affinity for binding CO than does adult hemoglobin (Longo, 1977). O₂ delivery to fetal tissues is further compromised. The resultant tissue hypoxia has the potential to reduce fetal growth (Bosley et al., 1981; Gabrielli et al., 1995; Ritz and Yu, 1999; Salam et al., 2005). Another possible toxic mechanism of CO is that it can also affect leukocytes, platelets, and the endothelium, inducing a cascade of effects resulting in oxidative injury that contributes to the toxicity of other air pollutants (Ha et al., 2001).

Gaseous pollutants such as SO₂ and NO₂ lead to pulmonary inflammation with a systemic release of cytokines (Walters et al., 2001; Nemmar et al., 2002) and increase blood viscosity (Peters et al., 1997; Prescott et al., 2000). Prenatal exposure to SO₂ can lead to developmental and functional toxicities (Singh, 1989). NO₂ suppresses antioxidant defense systems of the human body (Tabacova et al., 1998). Exposure of experimental animal models to NO₂ during pregnancy induces lipid peroxidation in the placenta and disturbs postnatal development (Tabacova et al., 1985). Exposure to any gas pollutants leads to inflammatory reactions in the lung, leading to systemic release of cytokines that may trigger PTB (Walters et al., 2001). NO₂ may also have direct toxic effects on the fetus (Maroziene and Grazuleviciene, 2002). Particle and NO₂ were correlated strongly with each other and exerted an effect on LBW within similar periods. But considering many published data, the evidence for the association between NO₂ and LBW is inconclusive. Exposure to ozone may have negative effects on birth weight (BW) and neurodevelopment (Dell'Omo et al., 1995), although the mechanism through which ozone can affect pregnancy outcomes is unclear.

Several hypotheses have been postulated to explain the mechanism of triggering PTB. One hypothesis suggests causality between uterine inflammation and PTB. The direct evidence

that infection provokes preterm labor was first shown in an animal study. When Group B streptococci were injected into the amniotic fluid in preterm rhesus monkeys, amniotic fluid cytokine concentrations increased, followed by production of the prostaglandins E_2 and $F_{2\alpha}$ and, finally, uterine contractions (Gravett et al., 1994). Similarly, in humans, preterm labor due to infection is thought to be initiated by cytokines, including interleukin-1 (IL-1), tumor necrosis factor, and interleukin-6, produced by macrophages (Cram et al., 2002; Narahara and Johnston 1993; Mitreski and Radeka 2002).

Additionally, entry of PM into the body by this method may lead to oxidative inflammation in lungs and other organs, including the placenta, thereby increasing the susceptibility of the mother to begin preterm labor (Liu et al., 2003).

Because IL-1 β is not present in the membranes of term-laboring patients, it may be the unique mediator by which intrauterine infection induces preterm labor (Cunningham and William, 1997). Antenatal infection can trigger intrauterine inflammation which then promotes preterm labor. In addition, periodontal disease may be an independent risk factor for preterm labor: postulated mechanisms include translocation of periodontal pathogens to the fetoplacental unit and action of a periodontal reservoir of lipopolysaccharides or inflammatory mediators (McGaw, 2002). Our inability to determine the periodontal status of the mother is a potential confounding factor. Cyclooxygenase-2 inhibitor, developed as an anti-inflammatory drug, also has tocolytic effects (Sakai et al., 2001). A similar inflammatory mechanism has been suggested for the effect of smoking on IUGR, PTB, and perinatal mortality (Klesges et al., 2001). There are reports of increased blood viscosity and plasma fibrinogen during air pollution (Peters et al., 1997). It has been speculated that chronic exposure to high pollution levels may influence placental function (Petruzzelli et al., 1998). The placental dysfunction may lead to IUGR. The effects of air pollution on pregnancy outcomes may differ according to the timing of exposure, with early exposures likely to be important for pregnancy end points such as spontaneous abortion, IUGR and birth defects (Antipenko and Kogut 1993; Dejmek et al., 1999; Dejmek et al., 2000; Hansteen et al., 1987). Intrauterine infection during pregnancy could also lead to brain damage of the developing fetus (Huleihel et al., 2004).

Recent studies suggest that antenatal infection and inflammation can increase the preterm infant's susceptibility to develop chronic lung disease. It may be that exposure of the fetal lung to high concentrations of pro-inflammatory cytokines is the cause of this increased susceptibility (Miralles et al., 2002). Photochemically produced gaseous products influence the toxic responses of cells, such as the production of cytokine, in the absence of particles (Sexton et al., 2004). PM₁₀ is responsible for the production and release of inflammatory cytokines by the respiratory tract epithelium, as well as for activation of the transcription factor Nf κ B (Baeza-Sqiban et al., 1999; Bonvallot et al., 2001). Although fetal exposures to air pollution are probably much lower than exposure to the constituents of cigarette smoke, the biological mechanism of PTB could be through increased prostaglandin levels that are triggered by inflammatory mediators during exposure periods.

The pathophysiology of carbon monoxide may be more complex, involving hypoxic stress on the basis of interference with oxygen transport to the cells and possibly impairment of electron transport. Carbon monoxide can also affect leukocytes, platelets and the endothelium, inducing a cascade of effects resulting in oxidative injury (Hardy and Thom 1994). Carbon monoxide may interfere with metabolic and transport function of the placenta and, after crossing the placental barrier, concentrate more in the fetus than in the

mother (Hardy and Thom, 1994). These placenta insufficiency may be associated with preterm birth.

The causality between air pollution and risk of IUGR, LBW, short birth length, and small head circumference has been suggested through molecular epidemiologic studies where levels of DNA adducts are positively correlated with these outcomes (Sram et al., 2005). With the same biologic mechanism of the DNA damage, high levels of DNA adducts may be a cause of PTB.

3.3 Window periods

The possible biological mechanisms involved in the reduction of birth weight associated with maternal exposure to air pollution vary according to the timing of this exposure. The implantation of the fetus and the formation of the placenta occur during the first trimester while weight gain occurs predominantly during the third trimester. Therefore, exposure during both periods presents the possibility of interference with the final birth weight. In the first trimester, genetic mutations are considered to be the most important element in placental abnormalities, and in the second and third trimesters extremely complex vascular alterations are considered the main cause of placental abnormalities and consequent IUGR. Pollutants are recognized as being able to have an effect on both dimensions (Gouveia et al., 2004).

The possible biological mechanisms of air pollution on birth weight might vary according to the time of pregnancy, such as the implantation of the fetus and the formation of placenta during the first trimester, as well as important weight gain during the third trimester. Placental abnormalities, DNA damage, disruption of the endocrine system and change of blood coagulability are those potential biological mechanisms, which have been reported (Dejmek et al., 2000; Maisonet et al., 2004; Perera et al., 1999, 2002; Whyatt et al., 1998).

The finding of a significant effect of PM exposure on LBW during the first trimester is consistent. Its effect is striking at window periods during the first trimester.

The highest ambient air pollution concentrations during the first trimester were significantly associated with elevated relative risks of PTB. These results are generally consistent with the findings from China, South Korea, the United States, Canada, and the Czech Republic (Bobak 2000; Liu et al., 2003; Mohorovic 2004; Ritz et al., 2000; Tsai et al., 2003; Woodruff et al., 2003; Xu et al., 1995; Yang et al., 2002a; Yang et al., 2002b, Yang et al., 2003; Yang et al., 2004; Leem et al., 2006). These studies reported significant associations between air pollution and PTB during early pregnancy (i.e., first or second month, first trimester) (Mohorovic 2004; Ritz et al., 2000), late pregnancy (i.e., last month, last trimester, 7 days or 6 weeks before birth) (Liu et al., 2003; Xu et al., 1995), or during both early and late pregnancies (Bobak 2000).

3.4 Disease burden from air pollution and smoking

Population-attributable risk (PAR) is used to determine by what percentage the incidence of a disease in a population would be reduced if exposure were eliminated. PAR measures the potential impact of control measures on a population, and is relevant to decisions on public health. PAR is a very important concept in guiding policy decisions regarding the preventive approaches to APO, such as LBW, and PTB (Seo et al., 2010).

PAR measures the potential impact of control measures on a population, and is relevant to decisions on public health. PAR is a very important concept in guiding policy decisions regarding the preventive approaches to many diseases, such as cancer, hypertension, diabetes mellitus, and stroke.

Some studies have reported the PAR levels for LBW attributable to environmental factors, such as smoking (Levi F, 1999; Matsubara et al., 2000; Suzuki et al., 2008) and indoor pollution (Boy et al., 2002). Cigarette smoking during pregnancy is a strong dose-dependent risk factor for LBW (Chiolero et al. 2005; Windham et al. 2000). Women exposed to prenatal secondhand smoke were more at risk for preterm birth (odds ratio [OR]=2.3; 95% Confidence Interval [CI] [.96, 5.96]), and their infants were more likely to have immediate newborn complications (OR=2.4; 95% CI [1.09, 5.33]) than non-exposed women. Infants of passive smoking mothers were at increased risk for respiratory distress syndrome (OR=4.9; 95% CI [1.45, 10.5]) and admission to a Neonatal Intensive Care Unit ((OR=6.5; 95% CI[1.29, 9.7]) when compared to infants of smoking mothers (OR=3.9; 95% CI [1.61, 14.9]; OR=3.5; 95% CI [2.09, 20.4], respectively). Passive smokers and/or women with hair nicotine levels greater than .35 ng/ml were more likely to deliver earlier (1 week), give birth to infants weighing less (decrease of 200-300 g), and deliver shorter infants (decrease of 1.1-1.7 cm) (Ashford et al., 2010). Environmental tobacco smoke (ETS) and traffic-related air pollution share a few characteristics. They are widespread exposures in both developed and developing countries, and they have several chemical components in common. Mothers who smoke during pregnancy are twice as likely to give birth to a LBW newborn. In high-income countries, the mean PAR for tobacco smoking in both genders combined is estimated to be 25-30% of the total cancer mortality. Some studies reported PAR for LBW attributable to environmental factors, such as smoking (Chiolero et al., 2005; Windham et al., 2000; Matsubara et al., 2000; Suzuki et al., 2008) and indoor pollution (Boy et al., 2002). Chiolero et al., (2005) reported that maternal smoking during pregnancy was closely associated with LBW, small-for-gestational age (SGA), and pre-term birth. Comparing smokers to non-smokers, the adjusted odds ratios (AOR) were 2.7 (2.1-3.5) for LBW, 2.1 (1.7-2.5) for SGA, and 1.4 (1.1-1.9) for preterm birth. Past smoking was not associated with the outcomes. In that study, maternal smoking during pregnancy accounted for 22% (15-29%) of all LBW babies in the population, 14% (10-18%) of SGA babies, and 7% (1-12%) of preterm babies. Ojima et al. (2004) reported on the population-attributable proportion of active and passive smoking for LBW. These results showed the population-attributable proportion of smoking among mothers without preeclampsia during pregnancy was 7.0% for active smoking and 15.6% for passive smoking. Leonardi-Bee et al. (2008) reported that exposure of non-smoking pregnant women to ETS reduces mean birth weight by 33 g or more, and increases the risk of birth weight below 2500 g by 22%, but has no clear effect on gestation or SGA risk.

Misra and Nguyen (1999) suggested that there is consistent evidence to relate maternal ETS exposure to an increased APO risk and that this association may be generalized to the work environment. In studies with positive findings, infants exposed to ETS antenatally were 1.5-4 times more likely to be born with LBW, but few studies examined LBW. Most studies looked at measures of IUGR. ETS was associated with reductions in birth weight (adjusted for gestational age) ranging from 25 to 90 g. Infants born to women exposed to ETS were generally 2-4 times more likely to be born SGA. ETS exposure in the workplace can and should be minimized to protect pregnant women from its adverse effects.

Such research is urgently needed so as to calculate the etiologic fractions of the PAR that contribute directly to PTB. This will enable preventive strategies to be established to protect fetuses against air pollutants.

Most studies have reported an association between exposure to air pollution and PTB, with risk ratios from 1.03-1.36. Especially, PM₁₀ air pollution was found to be significantly associated with PTB.

Some studies reported PAR for PTB attributable to environmental factors, such as smoking, outdoor air pollution, and indoor pollution. Maternal smoking during pregnancy was closely associated with LBW, SGA, and PTB. In a study of seven Korean cities, air pollution accounted for 7~18% of all LBW babies (Seo et al., 2010).

PAR to PM₁₀ pollution for LBW was comparable to the figure derived from maternal smoking for PTB. Because air pollution is an important risk factor for PTB, a large proportion of PTB could be prevented if air pollution is reduced.

PAR depends on the strength of the relative risk, but also on the prevalence of the risk factor. Causes for APO may include metals, inhalational of anesthetics, organic solvents, air pollution, radiation, stress, and physical stress. Common risk factors carry larger PARs than do rare risk factors. The PAR attributable to PM₁₀ pollution for LBW was similar to that regarding smoking for LBW because every pregnant woman was exposed to air pollution. Though those who smoke are in the minority, the relative risk due to smoking is greater than air pollution.

Air pollution is an important risk factor for LBW and PTB because every pregnant woman is exposed to air pollution. Thus, a large proportion of LBW and PTB pregnancies could be prevented if air pollution were reduced.

3.5 Gender as effect modifier

Does the effect of air pollution on pregnancy outcomes differ by gender? Gender is known to influence pregnancy outcomes. Recent studies have reported an association between air pollution exposure and APO, but gender differences have not been considered. In order to assess the current evidence of the interactive effects between gender and air pollution on pregnancy outcomes, Ghosh R et al.(2007) undertook a systematic literature review. In total 11 studies were included. Of the 11 studies, four evaluated LBW, one each evaluated very LBW and fetal growth and six examined PTB. Females were at higher LBW risk: AOR ranged from 1.07 to 1.62. Males were at higher risk for PTB: AORs ranged from 1.11 to 1.20. In addition, there was some evidence to suggest that the effect of air pollution on LBW is gender dependent; however, the evidence was available only from four studies.

3.6 Socioeconomic status(SES): health disparity

People with low socioeconomic status (SES) are more vulnerable to air pollution than others. They are exposed to infection, nutritionally deficient, and often lived in more polluted area. Infection in pregnancy is a predictor of premature births (Gibbs RS et al., 1992), and it could be speculated that repeated infections, possibly related to pollution, might play a part. Increased blood viscosity, found during air pollution episodes (Peters A et al., 1997) may be related to impaired placental function (Zondervan HA et al., 1987). Increased concentrations of DNA adducts have been found in the blood (Perera FP et al., 1992; Petruzzelli S et al., 1998) and placentas (Topinka J et al., 1997) of subjects living in polluted areas, and were also found to be related to birthweight (Perera FP et al., 1998). Maternal nutrition status can be acting as a effect modifier between exposures to airborne particulate matter and adverse perinatal outcomes (Kannan et al, 2006). Maternal pulmonary function has been linked to altered placental vascular function and growth retardation in asthmatic pregnancies (Bracken et al. 2003; Clifton et al. 2001; Schatz et al. 1990). Mothers with lowered pulmonary function are more likely to have increased risks of LBW and PTB. Other theories about these associations include a) altered cardiac function from changes in heart rate variability; b)

inhalation by the mother of PAHs that then relate to placental exposure, potentially disrupting endocrine and nervous systems; c) changes in blood viscosity due to alveolar inflammation from PM, which in turn affects placental function; and d) binding of CO to hemoglobin binding sites, preventing the binding of oxygen and subsequent function (Glinianaia et al. 2004; Maisonet et al. 2004; S'ram et al. 2005).

Despite advances in medical care, preterm birth and its associated racial/ethnic disparities remain major public health issues. Environmental exposures may contribute to racial disparities in preterm birth (Burriss HH et al., 2011). Interestingly, a study in South Korea recently demonstrated that SES modifies the association between air pollution and preterm birth (Yi O et al., 2010).

Hispanic, African-American, and Asian/Pacific Islander mothers experienced higher mean levels of air pollution and were more than twice as likely to live in the most polluted counties compared with white mothers after controlling for maternal risk factors, region, and educational status [Hispanic mothers: AOR = 4.66; 95% confidence interval (95% CI), 1.92-11.32; African-American mothers: AOR = 2.58; 95% CI, 1.00-6.62; Asian/Pacific Islander mothers: AOR = 2.82; 95% CI, 1.07-7.39](Woodruff et al. 2003).

PTB increased from 8.3% in counties with low income inequality to 10.0% in counties with high inequality. The Gini Index remained modestly associated with PTB after adjusting for individual level variables and mean county-level per capita income within the total population (AOR: 1.06; 95% CI 1.03-1.09) as well as within most of the racial/ethnic groups. PNM(post-natal mortality) increased from 1.15 deaths per 1000 live births in low inequality counties to 1.32 in high-inequality counties. However, after adjustment, income inequality was only associated with PNM within the non-Hispanic black population (AOR: 1.20; 95% CI 1.03-1.39). These findings may provide some support for the association between income inequality and PTB. Further research is required to elucidate the biological mechanisms of income inequality (Huynh M et al., 2005).

4. Conclusion

The association between air pollution, such PM and SO₂, and APO has been clearly shown in the literature although the mechanisms have not been elucidated. More work is required to fully elucidate the physiologic mechanisms by which air pollution may affect fetal growth and development and to determine if the mechanisms are pollutant specific.

The findings of prior studies of air pollution effects on adverse birth outcomes are difficult to synthesize due to differences in study design, although a few studies have included meta-analysis. Location-specific analyses of air pollution effects on birth weight need to be conducted using a common protocol and a standardized statistical approach to understand how differences in research methods contribute to variations in findings. Study groups such as The International Collaboration on Air Pollution and Pregnancy Outcome (ICPPO) have been formed to perform these kinds of collaboration study. Variability in PM₁₀-LBW relationships among study locations has remained, despite the use of a common statistical approach by a pilot study (Parker et al., 2011). A more detailed meta-analysis and use of more complex protocols for future analysis may uncover the reasons for heterogeneity across locations.

Many studies demonstrated air pollution levels critical to LBW and PTB in humans. These levels are very important because they may be a good indication on how to protect fetuses

against adverse effects from air pollutants. Annual standards for air quality are certainly too high in some countries and do not prevent APO. Many studies showed that statistically significant effects of LBW and PTB are seen below the air quality standards for PM₁₀ and SO₂ and potentially below the standards for CO and NO₂. The adverse effects on pregnancy are increased for smaller particles like PM_{2.5}. Several lines of evidence support the plausibility of a negative effect of CO exposure on birth weight. CO reduces oxygen-carrying capacity of maternal hemoglobin, which could adversely affect O₂ delivery to fetal circulation. Low-concentration exposure to CO, even below 1ppm, increased PTB risk. The current air quality standard for CO is 9 ppm. The air quality standards for PM_{2.5} should be established, and the air quality standards for CO should be lowered to 1ppm to protect fetuses' health against the hazardous toxicities of PM_{2.5} and CO. Many studies may provide supportive evidence that reduction in the current air quality standards may increase the health of pregnancy outcomes.

We observed that exposure to sulphur dioxide was associated with PTB, and exposure to PM_{2.5} was associated with LBW and PTB. The evidence for N₂O, ozone and carbon monoxide was inconclusive. However, the observed adverse effects were generally small. Possible important factors such as maternal activity pattern, diet, smoking and occupation, which are usually not reported on the birth certificate, might have led to exposure misclassification and confounding and could have hidden moderately increased risks. Additional well-conducted studies that include detailed information on maternal risk factors and use validated models for estimating maternal exposure are needed to establish the extent of the association between air pollution and birth outcomes.

In conclusion, several studies showed that relatively low concentrations of air pollution below current air quality standards during critical gestational periods may contribute to increased risk of LBW and PTB. Fetuses in the early and late stages of development are susceptible to air pollutants. Further studies are needed to validate the fetuses' susceptibility to air pollutants with more detailed information on personal exposures, confounders, and effect modifiers. Many investigators reported reductions in ETS exposure and the risk of LBW and very early preterm birth. Clues about potential mechanisms underlying the disparities in LBW and preterm birth can be gained from exploring differences in environmental exposures. Investigators should include environmental variables when studying birth outcomes. Such efforts should result in targeted interventions to decrease the incidence of LBW, preterm birth and its disparities.

5. References

- Alderman BW, Baron AE, Savitz DA.(1987). Maternal exposure to neighborhood carbon monoxide and risk of low infant birth weight. *Public Health Rep* ;102(4):410-4. ISSN: 0033-3549
- Antipenko YeN, Kogut NN. (1993). The experience of mutation rate quantitative evaluation in connection with environmental pollution (based on studies of congenital anomalies in human populations). *Mutat Res* 289(2):145 -155. ISSN: 0027-5107
- Ashford KB, Hahn E, Hall L, Rayens MK, Noland M, Ferguson JE. (2010). The effects of prenatal secondhand smoke exposure on preterm birth and neonatal outcomes. *J Obstet Gynecol Neonatal Nurs*. 2010 Sep;39(5):525-35. . ISSN: 0884-2175

- Baeza-Squiban A, Bonvallot V, Boland S, Marano F. (1999). Airborne particles evoke an inflammatory response in human airway epithelium. Activation of transcription factors. *Cell Biol Toxicol* 15(6):375-380. ISSN: 0742-2091
- Barker DJ.(2007). The origins of the developmental origins theory. *J Intern Med.* 261(5):412-7. ISSN: 0954-6820
- Bell ML, Ebisu K, Belanger K. (2007). Ambient air pollution and low birth weight in Connecticut and Massachusetts. *Environ Health Perspect* 115:1118-24. ISSN: 0091-6765
- Berkowitz GS, Papiernik E.(1993). Epidemiology of preterm birth. *Epidemiol Res* ;15:414-43. ISSN: 0193-936X
- Bibby E, Stewart A. (2004). The epidemiology of preterm birth. *Neuro Endocrinol Lett.* 25 Suppl 1:43-47. ISSN: 0172- 780X
- Bobak M. (2000). Outdoor air pollution, low birth weight, and prematurity. *Environ Health Perspect* 108(2):173-176. ISSN: 0091-6765
- Bobak M. (2005). Ambient Air Pollution and Pregnancy Outcomes: A Review of the Literature. *Environ Health Perspect* 113:375-382. ISSN: 0091-6765
- Bobak M, Leon DA.(1999) Pregnancy outcomes and outdoor air pollution: an ecological study in districts of the Czech Republic 1986-8. *Occup Environ Med.* Aug;56(8):539-43. ISSN: 1351-0711
- Bonvallot V, Baeza-Squiban A, Baulig A, Brulant S, Boland S, Muzeau F, et al. (2001). Organic compounds from diesel exhaust particles elicit a proinflammatory response in human airway epithelial cells and induce cytochrome p450 1A1 expression. *Am J Respir Cell Mol Biol* 25(4):515-521. ISSN: 1044-1549
- Bonzini M, Carugno M, Grillo P, Mensi C, Bertazzi PA, Pesatori AC. (2010). Impact of ambient air pollution on birth outcomes: systematic review of the current evidences. *Med Lav* 101(5):341-63. ISSN: 0025-7818
- Bosley ARJ, Sibert JR, Newcombe RG. (1981). Effects of maternal smoking on fetal growth and nutrition. *Arch Dis Child* 56:727-729 ISSN: 0003-9888
- Boy E, Bruce N, Delgado H. (20002). Birth weight and exposure to kitchen wood smoke during pregnancy in rural Guatemala. *Environ Health Perspect* 110(1):109-114. ISSN: 0091-6765
- Bracken MB, Triche EW, Belanger K, Saftlas A, Beckett WS, Leaderer BP. (2003). Asthma symptoms, severity, and drug therapy: a prospective study of effects on 2205 pregnancies. *Obstet Gynecol.* 102(4):739-52. ISSN:0029-7844
- Burris HH, Collins JW Jr, Wright RO. (2011). Racial/ethnic disparities in preterm birth: clues from environmental exposures. *Curr Opin Pediatr.* 23(2):227-32. ISSN: 1040-8703
- Chen L, Yang W, Jennison BL, Goodrich A, Omaye ST.(2002). Air pollution and birth weight in northern Nevada, 1991-1999. *Inhal Toxicol* 14(2):141-157. ISSN: 0895-8378
- Chiolero A, Bovet P, Paccaud F. (2005). Association between maternal smoking and low birth weight in Switzerland: the EDEN study. *Swiss Med Wkly.* 135(35-36):525-30. ISSN: 1424-7860
- Clifton VL, Giles WB, Smith R, Bisits AT, Hempenstall PA, Kessell CG, Gibson PG. (2001). Alterations of placental vascular function in asthmatic pregnancies. *Am J Respir Crit Care Med.* 164(4):546-53. ISSN: 1073-449X
- Cram LF, Zapata MI, Toy EC, Baker B 3rd. (2002). Genitourinary infections and their association with preterm labor. *Am Fam Physician* 65(2):241-248. ISSN: 0002-838X

- Cunningham FG, Williams JW. (1997). Parturition. In: Williams Obstetrics. 20th ed. Stamford, Conn: Appleton & Lange; 306-313 and 797-821.
- Dejmek J, Selevan SG, Benes I, Solansky I, Sram RJ. (1999). Fetal growth and maternal exposure to particulate matter during pregnancy. *Environ Health Perspect.* 107(6):475-480. ISSN: 0091-6765
- Dejmek J, Solansky I, Benes I, Lenicek J, Sram RJ. (2000). The impact of polycyclic aromatic hydrocarbons and fine particles on pregnancy outcome. *Environ Health Perspect* 108(12):1159-1164. ISSN: 0091-6765
- Dexter SC, Pinar H, Malee MP, Hogan J, Carpenter MW, Vohr BR. (2000). Outcome of very low birth weight infants with histopathologic chorioamnionitis. *Obstet Gynecol* 96(2):172-7. ISSN: 0029-7844
- Dell'Omo G, Fiore M, Petruzzi S, Alleva E, Bignami G. (1995). Neurobehavioral development of CD-1 mice after combined gestational and postnatal exposure to ozone. *Arch Toxicol.* 69(9):608-16. ISSN:0340-5761
- Donaldson K, Stone V, Seaton A, MacNee W. (2001). Ambient particle inhalation and the cardiovascular system: potential mechanisms. *Environ Health Perspect.*109 Suppl 4:523-7. ISSN: 0091-6765
- Dugandzic R, Dodds L, Stieb D, Smith-Doiron M.(2006). The association between low level exposures to ambient air pollution and term low birth weight: a retrospective cohort study. *Environ Health ;5:3.* ISSN: 1476-069X
- Duvekot JJ, Cheriex EC, Pieters FA, Peeters LL. (1995). Severely impaired fetal growth is preceded by maternal hemodynamic maladaptation in very early pregnancy. *Acta Obstet Gynecol Scand.*74(9):693-7. ISSN:0001-6349
- Gabrielli A, Layon AJ. Carbon monoxide intoxication during pregnancy: a case presentation and pathophysiologic discussion, with emphasis on molecular mechanisms. *J Clin Anesth.* 1995 Feb;7(1):82-7.ISSN:0952-8180
- Gehring U, van Eijsden M, Dijkema MB, van der Wal MF, Fischer P, Brunekreef B. (2011).Traffic-related air pollution and pregnancy outcomes in the Dutch ABCD birth cohort study. *Occup Environ Med ;68(1):36-43.* ISSN: 1351-0711
- Gibbs RS, Romero R, Hillier SL, Eschenbach DA, Sweet RL. (1992).A review of premature birth and subclinical infection. *Am J Obstet Gynecol ;166:1515-28.* ISSN: 0002-9378
- Ghosh R, Rankin J, Pless-Mulloli T, Glinianaia S. (2007). Does the effect of air pollution on pregnancy outcomes differ by gender? A systematic review. *Environ Res.* 105(3):400-8. ISSN: 0013-9351
- Glinianaia SV, Rankin J, Bell R, Pless-Mulloli T, Howel D. (2004). Particulate air pollution and fetal health: a systematic review of the epidemiologic evidence.*Epidemiology.* 15(1):36-45.ISSN: 1044-3983
- Gouveia N, Bremner SA, Novaes HM. (2004). Association between ambient air pollution and birth weight in Sao Paulo, Brazil. *J Epidemiol Community Health* 58:11-7.ISSN: 0143-005X
- Gravett MG, Witkin SS, Haluska GJ, Edwards JL, Cook MJ, Novy MJ. (1994). An experimental model of intraamniotic infection and preterm labor in rhesus monkeys. *Am J Obstet Gynecol* 171:1660-1667. ISSN: : 0002-9378
- Ha EH, Hong YC, Lee BE, Woo BH, Schwartz J, Christiani DC.(2001). Is air pollution a risk factor for low birth weight in Seoul? *Epidemiology* 12(6):643-648. ISSN:1044-3983

- Hansteen IL, Heldaas SS, Langard S, Steen-Johnsen J, Christensen A, Heldaas K.(1987). Surveillance of pregnancies as a means of detecting environmental and occupational hazards. I. Spontaneous abortions, congenital malformations and cytogenetic abnormalities in a newborn population. *Hereditas* 107(2):197-203. ISSN: 0018-0661
- Hardy KR, Thom SR. (1994). Pathophysiology and treatment of carbon monoxide poisoning. *J Toxicol Clin Toxicol* 32(6):613-629. ISSN: 0731-3810
- Huleihel M, Golan H, Hallak M.(2004). Intrauterine infection/inflammation during pregnancy and offspring brain damages: possible mechanisms involved. *Reprod Biol Endocrinol* 2(1):17-24. ISSN: 1477-7827
- Huynh M, Parker JD, Harper S, Pamuk E, Schoendorf KC. (2005). Contextual effect of income inequality on birth outcomes. *Int J Epidemiol.* 34(4):888-95. ISSN: 0300-5771
- Huynh M, Woodruff TJ, Parker JD, Schoendorf KC. (2006). Relationships between air pollution and preterm birth in California. *Paediatr Perinat Epidemiol.* 20(6):454-61. ISSN: 0269-5022
- Jalaludin B, Mannes T, Morgan G, Lincoln D, Sheppard V, Corbett S.(2007). Impact of ambient air pollution on gestational age is modified by season in Sydney, Australia. *Environ Health.* 2007 Jun 7;6:16. ISSN: 1476-069X
- Jerrett M, Arain A, Kanaroglou P, Beckerman B, Potoglou D, Sahuvaroglu T, Morrison J, Giovis C. (2005a). A review And evaluation of intraurban air pollution exposure models. : *J Expo Anal Environ Epidemiol.* 15(2):185-204. ISSN:1053-4245
- Jerrett M, Buzzelli M, Burnett RT, DeLuca PF.(2005b). Particulate air pollution, social confounders, and mortality in small areas of an industrial city. *Soc Sci Med* 60(12):2845-2863. ISSN: 0277-9536
- Kadiiska MB, Mason RP, Dreher KL, Costa DL, Ghio AJ. (1997). In vivo evidence of free radical formation in the rat lung after exposure to an emission source air pollution particle. *Chem Res Toxicol.* 10(10):1104-8.ISSN: 0893-228X
- Kannan S, Misra DP, Dvonch JT, Krishnakumar A. (2006). Exposures to airborne particulate matter and adverse perinatal outcomes: a biologically plausible mechanistic framework for exploring potential effect modification by nutrition. *Environ Health Perspect.*114(11):1636-42. ISSN: 0091-6765
- Klesges LM, Johnson KC, Ward KD, Barnard M.(2001). Smoking cessation in pregnant women. *Obstet Gynecol Clin North Am* 28(2):269-282. ISSN: 0889-8545
- Kwon HJ, Cho SH, Nyberg F, Pershagen G. (2001) Effects of ambient air pollution on daily mortality in a cohort of patients with congestive heart failure. *Epidemiology.* 12(4):413-9. ISSN: 1044-3983
- Lee BE, Ha EH, Park HS, Kim YJ, Hong YC, Kim H, Lee JT. (2003). Exposure to air pollution during different gestational phases contributes to risks of low birth weight. *Hum Reprod.* 18(3):638-43. ISSN:0268-1161
- Leem JH, Kaplan BM, Shim YK, Pohl HR, Gotway CA, Bullard SM, Rogers JF, Smith MM, Tylenda CA. (2006). Exposures to air pollutants during pregnancy and preterm delivery. *Environ Health Perspect.* 114(6):905-10. ISSN: 0091-6765
- Leem JH, Kim JH, Lee KH, Hong Y, Lee KH, Kang D, Kwon HJ.(2005). Asthma attack associated with oxidative stress by exposure to ETS and PAH. *J Asthma.* 42(6):463-7. ISSN: 0277-0903

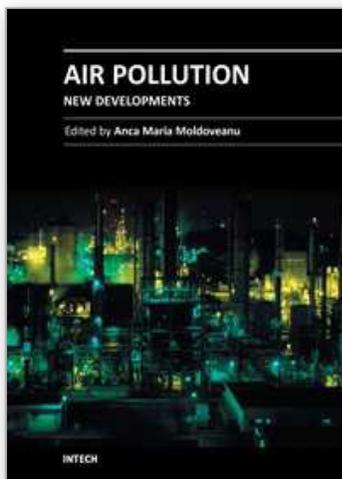
- Leonardi-Bee J, Smyth A, Britton J, Coleman T. (2008). Environmental tobacco smoke and fetal health: systematic review and meta-analysis. *Arch Dis Child Fetal Neonatal Ed.* 93(5):F351-61. ISSN: 1359-2998
- Levi F. (1999). Cancer prevention: epidemiology and perspectives. *Eur J Cancer* 35(7):1046-1058. ISSN: 0959-8278
- Lin CM, Li CY, Yang GY, Mao IF. (2004). Association between maternal exposure to elevated ambient sulfur dioxide during pregnancy and term low birth weight. *Environ Res* 96(1):41-50. ISSN: 0013-9351
- Lin MC, Yu HS, Tsai SS, Cheng BH, Hsu TY, Wu TN, Yang CY. (2001). Adverse pregnancy outcome in a petrochemical polluted area in Taiwan. *J Toxicol Environ Health A* 63(8):565-574. ISSN: 1528-7394
- Liu S, Krewski D, Shi Y, Chen Y, Burnett RT. (2003). Association between gaseous ambient air pollutants and adverse pregnancy outcomes in Vancouver, Canada. *Environ Health Perspect* 111(14):1773-1778. ISSN: 0091-6765
- Llop S, Ballester F, Estarlich M, Esplugues A, Rebagliato M, Iñiguez C. (2010). Preterm birth and exposure to air pollutants during pregnancy. *Environ Res* 110(8):778-85. ISSN: 0013-9351
- Longo LD. (1977). The biological effects of carbon monoxide on the pregnant woman, fetus, and newborn infant. *Am J Obstet Gynecol.* 129(1):69-103. ISSN: 0002-9378
- Madsen C, Gehring U, Walker SE, Brunekreef B, Stigum H, Naess O, Nafstad P. (2010). Ambient air pollution exposure, residential mobility and term birth weight in Oslo, Norway. *Environ Res.* 110(4):363-71. ISSN: 0013-9351
- Maisonet M, Bush TJ, Correa A, Jaakkola JJ. (2001). Relation between ambient air pollution and low birth weight in the Northeastern United States. *Environ Health Perspect* 109 Suppl 3:351-356. ISSN: 0091-6765
- Maisonet M, Correa A, Misra D, Jaakkola JJ. (2004). A review of the literature on the effects of ambient air pollution on fetal growth. *Environ Res* 95(1):106-115. ISSN: 0013-9351
- Maroziene L, Grazuleviciene R. (2002). Maternal exposure to low-level air pollution and pregnancy outcomes: a population-based study. *Environ Health* 1(1):6-12. ISSN: 1476-069X
- Matsubara F, Kida M, Tamakoshi A, Wakai K, Kawamura T, Ohno Y. (2000). Maternal active and passive smoking and fetal growth: A prospective study in Nagoya, Japan. *J Epidemiol* 10(5):335-343. ISSN: 0917-5040
- McGaw T. (2002). Periodontal disease and PTB of low-birth-weight infants. *J Can Dent Assoc* 68(3):165-169. ISSN: 0008-3372
- Miralles RE, Hodge R, Kotecha S. (2002). Antenatal inflammation and infection in chronic lung disease of prematurity. *Child Care Health Dev* 28 Suppl 1:11-15. ISSN: 0305-1862
- Misra DP, Nguyen RH. (1999). Environmental tobacco smoke and low birth weight: a hazard in the workplace? *Environ Health Perspect.* 107 Suppl 6:897-904. . ISSN: 0091-6765
- Mitreski A, Radeka G. (2002). Prostacyclin and hormone levels in patients with symptoms of miscarriage and infection. *Med Pregl* 55(9-10):371-379. ISSN: 0025-8105
- Mohorovic L. (2004). First two months of pregnancy-critical time for PTD and low birth weight caused by adverse effects of coal combustion toxics. *Early Hum Dev* 80(2):115-123. ISSN: 0378-3782
- Morello-Frosch R, Jesdale BM, Sadd JL, Pastor M. (2010). Ambient air pollution exposure and full-term birth weight in California. *Environ Health*;9:44. ISSN: 1476-069X

- Mulholland JA, Butler AJ, Wilkinson JG, Russell AG, Tolbert PE. (1998). Temporal and spatial distributions of ozone in Atlanta: regulatory and epidemiologic implications. *J Air Waste Manag Assoc.* 48(5):418-426. ISSN: 1096-2247
- Narahara H, Johnston JM. (1993). Effects of endotoxins and cytokines on the secretion of platelet-activating factor acetylhydrolase by human decidual macrophages. *Am J Obstet Gynecol* 169:531-537. ISSN: 0002-9378
- Nemmar A, Hoet PH, Vanquickenborne B, Dinsdale D, Thomeer M, Hoylaerts MF, Vanbilloen H, Mortelmans L, Nemery B. (2002). Passage of inhaled particles into the blood circulation in humans. *Circulation* 105(4):411-4.
- Ojima T, Uehara R, Watanabe M, Tajimi M, Oki I, Nakamura Y. (2004). Population attributable fraction of smoking to low birth weight in Japan. *Pediatr Int* 46(3):264-267. ISSN: 1328-8067.
- Parker J, Rich DQ, Glinianaia SV, Leem JH, Wartenberg D, Bell ML, Bonzini M, Brauer M, Darrow L, Gehring U, Gouveia N, Grillo P, Ha E, van den Hooven EH, Jalaludin B, Jesdale BM, Lepeule J, Morello-Frosch R, Morgan GG, Slama R, Pierik FH, Pesatori AC, Sathyanarayana S, Seo J, Strickland M, Tamburic L, Woodruff TJ. (2011). The International Collaboration on Air Pollution and Pregnancy Outcomes: Initial Results. *Environ Health Perspect.* 2011 Feb 9. . ISSN: 0091-6765
- Perera FP, Hemminki K, Gryzbowska E, Motykiewicz G, Michalska J, Santella RM, Young TL, Dickey C, Brandt-Rauf P, De Vivo I. (1992). Molecular and genetic damage in humans from environmental pollution in Poland. *Nature* 360:256-8. ISSN: 0028-0836
- Perera FP, Whyatt RM, Jedrychowski W, Rauh V, Manchester D, Santella RM, Ottman R. (1998). Recent developments in molecular epidemiology: a study of the effects of environmental polycyclic aromatic hydrocarbons on birth outcomes in Poland. *Am J Epidemiol* 147:309-14. ISSN: 0002-9262
- Perera FP, Jedrychowski W, Rauh V, Whyatt RM. (1999). Molecular epidemiologic research on the effects of environmental pollutants on the fetus. *Environ Health Perspect* 107 Suppl 3:451-60. . ISSN: 0091-6765
- Peters A, Doring A, Wichmann HE, Koenig W. (1997). Increased plasma viscosity during an air pollution episode: a link To mortality? *Lancet* 349(9065):1582-1587. ISSN: 0140-6736
- Petruzzelli S, Celi A, Pulera N, Baliva F, Viegi G, Carrozzi L, Ciacchini G, Bottai M, Di Pede F, Paoletti P, Giuntini C. (1998). Serum antibodies to benzo(a)pyrene diol epoxide-DNA adducts in the general population: effects of air pollution, tobacco smoking, and family history of lung diseases. *Cancer Res* 58(18):4122-6. ISSN: 0008-5472
- Pikhart H, Bobak M, Gorynski P, Wojtyniak B, Danova J, Celko MA, Kriz B, Briggs D, Elliott P. (2001). Outdoor sulphur dioxide and respiratory symptoms in Czech and Polish school children: a small-area study (SAVIAH). Small-Area Variation in Air Pollution and Health. *Int Arch Occup Environ Health.* 74(8):574-578. ISSN: 0340-0131
- Pope DP, Mishra V, Thompson L, Siddiqui AR, Rehfuess EA, Weber M, Bruce NG. (2010). Risk of low birth weight and stillbirth associated with indoor air pollution from solid fuel use in developing countries. *Epidemiol Rev.* 32(1):70- 81. ISSN: 0193-936X
- Prescott GJ, Lee RJ, Cohen GR, Elton RA, Lee AJ, Fowkes FG, Agius RM. (2000). Investigation of factors which might indicate susceptibility to particulate air pollution. *Occup Environ Med.* 57(1):53-7. ISSN: 1351-0711

- Reagan PB, Salsberry PJ.(2005). Race and ethnic differences in determinants of preterm birth in the USA: broadening the social context. *Soc Sci Med.* 60(10):2217-2228. ISSN: 0277-9536
- Ritz B, Yu F. (1999). The effect of ambient carbon monoxide on low birth weight among children born in southern California between 1989 and 1993. *Environ Health Perspect.* 107(1):17-25. ISSN: 0091-6765
- Ritz B, Yu F, Chapa G, Fruin S. (2000). Effect of air pollution on preterm birth among children born in Southern California between 1989 and 1993. *Epidemiology* 11(5):502-511. ISSN: 1044-3983
- Ritz B, Wilhelm M, Hoggatt KJ, Ghosh JK. (2007). Ambient air pollution and preterm birth in the environment and pregnancy outcomes study at the University of California, Los Angeles. *Am J Epidemiol.*166(9):1045-52. ISSN: 0002-9262
- Rogers JF, Thompson SJ, Addy CL, McKeown RE, Cowen DJ, Decouflé P. (2000). Association of very low birth weight with exposures to environmental sulfur dioxide and total suspended particulates. *Am J Epidemiol.*151(6):602- 13. ISSN: 0002-9262
- Sakai M, Tanebe K, Sasaki Y, Momma K, Yoneda S, Saito S.(2001). Evaluation of the tocolytic effect of a selective cyclooxygenase-2 inhibitor in a mouse model of lipopolysaccharide-induced PTD. *Mol Hum Reprod* 7(6):595-602. ISSN: 1360-9947
- Sagiv SK, Mendola P, Loomis D, Herring AH, Neas LM, Savitz DA, Poole C. (2005). A time-series analysis of air pollution and preterm birth in Pennsylvania,1997-2001. *Environ Health Perspect.* 113(5):602-6. ISSN: 0091-6765
- Sangalli MR, Mclean AJ, Peek MJ, Rivory LP, Le Couteur DG. (2003). Carbon monoxide disposition and permeability-surface area product in the foetal circulation of the perfused term human placenta. *Placenta.*24(1):8-11. ISSN:0143-4004
- Salam MT, Millstein J, Li YF, Lurmann FW, Margolis HG, Gilliland FD. (2005). Birth outcomes and prenatal exposure to ozone, carbon monoxide, and particulate matter: results from the Children's Health Study. *Environ Health Perspect.*113(11):1638-44. ISSN: 0091-6765
- Salafia CM, Ernst LM, Pezzullo JC, Wolf EJ, Rosenkrantz TS, Vintzileos AM. (1995). The very low birthweight infant: maternal complications leading to preterm birth, placental lesions, and intrauterine growth. *Am J Perinatol.* 12(2):106-10. ISSN: 0735-1631
- Schatz M. Asthma and pregnancy. *J Asthma.* 1990;27(6):335-9. ISSN:0277-0903
- Seo JH, Leem JH, Ha EH, Kim OJ, Kim BM, Lee JY, Park HS, Kim HC, Hong YC, Kim YJ. (2010). Population-attributable risk of low birthweight related to PM10 pollution in seven Korean cities. *Paediatr Perinat Epidemiol.* 24(2):140-8. ISSN: 0269-5022
- Sexton KG, Jeffries HE, Jang M, Kamens RM, Doyle M, Voicu I, Jaspers I. (2004). Photochemical products in urban mixtures enhance inflammatory responses in lung cells. *Inhal Toxicol.* 16 (Suppl 1):107-114. ISSN: 0895-8378
- Shah PS, Balkhair T; (2011). Knowledge Synthesis Group on Determinants of Preterm/LBW births. Air pollution and birth outcomes: a systematic review. *Environ Int.* 2011 Feb;37(2):498-516. ISSN:0160-4120.
- Singh J. (1989). Neonatal development altered by maternal sulfur dioxide exposure. *Neurotoxicology.* 10(3):523-7.ISSN: 0161-813X
- Srám RJ, Binková B, Dejmek J, Bobak M. (2005). Ambient air pollution and pregnancy outcomes: a review of the literature. *Environ Health Perspect* 113(4):375-382. . ISSN: 0091-6765

- Sram JR., BinKova B, Dejmek J, Shah PS, Balkhair T. (2011). Knowledge Synthesis Group on Determinants of Preterm/LBW births. Air pollution and birth outcomes: a systematic review. *Environ Int.* 37(2):498-516. ISSN: 0160-4120
- Suzuki K, Tanaka T, Kondo N, Minai J, Sato M, Yamagata Z. (2008). Is maternal smoking during early pregnancy a risk factor for all low birth weight infants? *J Epidemiol.* 18(3):89-96. ISSN:0917-5040
- Tabacova S, Nikiforov B, Balabaeva L. (1985). Postnatal effects of maternal exposure to nitrogen dioxide. *Neurobehav Toxicol Teratol.*7(6):785-9. ISSN: 0275-1380
- Tsai SS, Yu HS, Liu CC, Yang CY. (2003). Increased incidence of PTD in mothers residing in an industrialized area in Taiwan. *J Toxicol Environ Health A* 66(13):987-994. ISSN: 1528-7394
- Topinka J, Binkova B, Mrackova G, Stávková Z, Peterka V, Benes I, Dejmek J, Leníček J, Pilčík T, Srám RJ. (1997). Influence of GSTM1 and NAT2 genotypes on placental DNA adducts in an environmentally exposed population. *Environ Mol Mutagen* 30:184-95. ISSN: 0893-6692
- Topinka J, Milcova A, Libalova H, Novakova Z, Rossner P Jr, Balascak I, Sram RJ. (2009). Biomarkers of exposure to tobacco smoke and environmental pollutants in mothers and their transplacental transfer to the foetus. Part I: bulky DNA adducts. *Mutat Res.* 2009 Oct 2;669(1-2):13-9. ISSN: 0027-5107
- United Nations Children's Fund and World Health Organization. *Low Birthweight: Country, Regional and Global Estimates.* UNICEF, 2004.
- Waller LA, Gotway CA.(2004). Applied spatial statistics for public health data Wiley series in probability and statistics: John Wiley & Sons, Inc.
- Walters DM, Breyse PN, Wills-Karp M. (2001). Ambient urban Baltimore particulate-induced airway hyperresponsiveness and inflammation in mice. *Am J Respir Crit Care Med.* 2001 Oct 15;164(8 Pt 1):1438-43. ISSN: 1073-449X
- Wang X, Ding H, Ryan L, Xu X. (1997), Association between air pollution and low birth weight: a community-based study, *Environ Health Perspect* 105: 514-520. ISSN: 0091-6765
- Werler MM, Pober BR, Holmes LB. (1985). Smoking and pregnancy. *Teratology.* 32(3):473-81. ISSN: 0040-3709
- Whyatt RM, Santella RM, Jedrychowski W, Garte SJ, Bell DA, Ottman R, Gladek-Yarborough A, Cosma G, Young TL, Cooper TB, Randall MC, Manchester DK, Perera FP. (1998). Relationship between ambient air pollution and DNA damage in Polish mothers and newborns. *Environ Health Perspect.* 106 Suppl 3:821-6. ISSN: 0091-6765
- Wilhelm M, Ritz B. (2005). Local variations in CO and particulate air pollution and adverse birth outcomes in Los Angeles County, California, USA. *Environ Health Perspect.* 113(9):1212-21. ISSN: 0091-6765
- Windham GC, Hopkins B, Fenster L, Swan SH. (2000). Prenatal active or passive tobacco smoke exposure and the risk of preterm delivery or low birth weight. *Epidemiology.* 11(4):427-33.ISSN: 1044-3983
- Woodruff TJ, Parker JD, Kyle AD, Schoendorf KC. (2003). Disparities in exposure to air pollution during pregnancy. *Environ Health Perspect* 111(7):942-946. ISSN: 0091-6765
- Wu J, Ren C, Delfino RJ, Chung J, Wilhelm M, Ritz B. (2009). Association between local traffic-generated air pollution and preeclampsia and preterm delivery in the south

- coast air basin of California. *Environ Health Perspect.* 2009 Nov;117(11):1773-9. ISSN: 0091-6765
- Wu J, Wilhelm M, Chung J, Ritz B. (2011). Comparing exposure assessment methods for traffic-related air pollution in an adverse pregnancy outcome study. *Environ Res.* Mar 29. ISSN: 0013-9351
- Xu X, Ding H, Wang X. (1995). Acute effects of total suspended particles and sulfur dioxides on PTD: a community- Based cohort study. *Arch Environ Health* 50(6):407-415. ISSN: 0003-9896
- Xu X, Sharma RK, Talbott EO, Zborowski JV, Rager J, Arena VC, Volz CD. (2011). PM10 air pollution exposure during pregnancy and term low birth weight in Allegheny County, PA, 1994-2000. *Int Arch Occup Environ Health.*;84(3):251-7. ISSN: 0340-0131
- Yang CY, Cheng BH, Hsu TY, Chuang HY, Wu TN, Chen PC. (2002a). Association between petrochemical air pollution and adverse pregnancy outcomes in Taiwan. *Arch Environ Health* 57(5):461-465. ISSN: 0003-9896
- Yang CY, Chiu HF, Tsai SS, Chang CC, Chuang HY. (2002b). Increased risk of PTD in areas with cancer mortality problems from petrochemical complexes. *Environ Res* 89(3):195-200. ISSN: 0013-9351
- Yang CY, Chang CC, Chuang HY, Ho CK, Wu TN, Tsai SS. (2003) Evidence for increased risks of preterm delivery in a population residing near a freeway in Taiwan. *Arch Environ Health.* 58(10):649-54. ISSN: 0003-9896
- Yang CY, Chang CC, Tsai SS, Chuang HY, Ho CK, Wu TN, Sung FC.(2003). PTD among people living around Portland cement plants. *Environ Res* 92(1):64-68. ISSN: 0013-9351
- Yang CY, Chang CC, Chuang HY, Ho CK, Wu TN, Chang PY.(2004). Increased risk of PTD among people living near the three oil refineries in Taiwan. *Environ Int* 30(3):337-342. ISSN: 0160-4120
- Yi O, Kim H, Ha E. (2010). Does area level socioeconomic status modify the effects of PM(10) on preterm delivery? *Environ Res.*110(1):55-61. ISSN: 0013-9351
- Yorifuji T, Naruse H, Kashima S, Ohki S, Murakoshi T, Takao S, Tsuda T, Doi H.(2011). Residential proximity to major roads and preterm births. *Epidemiology.*22(1):74-80. ISSN: 1044-3983
- Zondervan HA, Oosting J, Hardeman MR, Smorenberg-Schoorl ME, Treffers PE. (1987). The influence of maternal whole blood viscosity on fetal growth. *Eur J Obstet Gynecol Reprod Biol* 1987;25:187-94. ISSN: 0301-2115
- Zondervan HA, Oosting J, Smorenberg-Schoorl ME, Treffers PE. (1988). Longitudinal changes in blood viscosity are correlated with fetal outcome. *Acta Obstet Gynecol Scand.* 1988;67(3):253-7. ISSN:0001-6349



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Today, an important issue is environmental pollution, especially air pollution. Due to pollutants present in air, human health as well as animal health and vegetation may suffer. The book can be divided in two parts. The first half presents how the environmental modifications induced by air pollution can have an impact on human health by inducing modifications in different organs and systems and leading to human pathology. This part also presents how environmental modifications induced by air pollution can influence human health during pregnancy. The second half of the book presents the influence of environmental pollution on animal health and vegetation and how this impact can be assessed (the use of the micronucleus tests on *TRADESCANTIA* to evaluate the genotoxic effects of air pollution, the use of transplanted lichen *PSEUDEVERNIA FURFURACEA* for biomonitoring the presence of heavy metals, the monitoring of epiphytic lichen biodiversity to detect environmental quality and air pollution, etc). The book is recommended to professionals interested in health and environmental issues.

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