

Adverse Effects of Pollutants on Expectant Mothers— *From Womb to Grave: A Retrospective Review*

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ABSTRACT

Aim: The present state-of-art study is an attempt to decipher how adversely the air pollution and its constituents affect the fate of a developing fetus. This involves a detailed study on criteria pollutant and its impact on various pregnancy outcomes, i.e., low birth weight, premature birth, intrauterine growth retardation, and reduction in fetus size.

Materials and methods: All the concerned research and review papers from the virtual dataset were segregated and have been studied specifically.

Results: In relevance to the specific pollutants, the particulate matter (PM) seems to be greatly responsible for causing neonatal deaths and high infant mortality rates, whereas the exposure to nitrogen dioxide (NO₂) reveals low-birth-weight fetus. Proceeding further, sulfur dioxide (SO₂) greatly targets expectant mothers in the second and last trimesters of pregnancy, resulting in low-birth-weight fetuses. The impact of carbon monoxide (CO) during pregnancy was also studied and found to be responsible for structural malformations. Active and passive smoking both boost pregnancy complications in terms of ectopic pregnancy, low birth weight, and infant mortality.

Discussion: Very few studies have been reported that reveal the dependency of pollutant exposure and reproductive outcomes. One strong interpretation is not sufficient enough to meet the complexity related to plethora of information. Due to variation in the number of factors like spatial and temporal variation, maternal thresholds, period of pregnancy, period of exposure, etc., the extrapolation of result is multifaceted. Different epidemiological studies with different adaptation in methodology report diverse consequences.

Conclusion: The evidence is satisfactory enough to reveal that the most potent pollutant seems to be PM. The detailed biologic mechanism regarding how these pollutants find their way to placental membrane and disturb the fetal destiny is still vague. The review suggests that reproductive awareness programs should be initiated by the government and policy analysts should be done to lessen the increasing economic burden on human health.

Keywords: Active and passive smoking, Air pollution, CO, Fetal growth restriction, Low birth weight, NO₂, Particulate matter, Pregnancy outcomes, Preterm delivery, Small gestational age.

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INTRODUCTION

It is cliché to say that air pollution can negatively affect one's health by exacerbating one's respiratory tracts or by triggering one's cardiovascular illness or in extreme cases can contribute to lung cancer. Interestingly, this study shows that we are living and prospering in the literal clouds of pollutants that are toxic in nature and have also found their way into developing fetuses with quantifiable cost later in life. As the world is progressing toward globalization and industrialization, the economic burden on human health is also remarkably increasing. The science community has explored a new area of air pollution in relation to the effective reproductive outcome epidemiology study, where the literature concerned with the reproductive outcome on environmental exposure is extensively surveyed.

From a public health perspective, environmental pollutants are important indicators of environment and human health. In recent decades, environmental pollutants have been stimulating for the research community to gauge their antagonistic effects on cardiopulmonary and respiratory disorders. However, the literature illuminates the effect of pollutants on different pregnancy outcomes.¹ Several studies have reported an association between air pollution and birth outcomes, such as early spontaneous growth restriction, low birth weight,²⁻⁴ premature births,⁵ or intrauterine growth retardation (IUGR). This state-of-art study aims to highlight to what extent environmental pollutants are associated with causing childhood mortality, low birth weight, premature birth, IUGR, and birth defects. Collins et al⁶ found the correlation between air pollution and infant mortality and infant respiratory mortality in association with industrial and domestic pollution. Osmond and Barker⁷ concluded that anomalies

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associated with environmental teratogens in the initial years of life are believed to encourage the consequent poor health status of individuals. The study also found significant correlations between air pollution and infant mortality, particularly infant respiratory mortality. Emergent evidences of ambient pollutant [particulate matter (PM), nitrogen dioxide (NO₂), sulfur dioxide (SO₂), carbon monoxide (CO), and also polycyclic aromatic hydrocarbons] have unpleasant health effects on a developing fetus such as low birth weight, preterm births, IUGR, and fetal mortality and morbidity as reported by Xu et al,⁵ Wang et al,² and Parker et al.

If a health conclusion was considerably associated with more than one pollutant, there is always the subject as to whether the effect of one pollutant is actually screening the impact of another with which it is correlated or it's the single potent pollutant whose exposure is lethal to expectant mothers.

OBJECTIVES

This article is an attempt to highlight the adverse effects of ambient pollutants (PM, SO₂, NO₂, CO, and active and passive smoking) on the variant pregnancy outcomes. It also aims to gauge the most potent pollutant entity among the plethora, which is strongly accountable for a negative pregnancy conclusion. With special emphasis on the spatial and temporal variability outcomes, the available epidemiology literature has also been taken under consideration.

The article primarily focuses on the environmental pollutant's impact on pregnant mothers, whereas factors such as socioeconomic status, race, caste, nutritional availability, and education, which may also have confounding effect on an expectant mother, have not been taken under consideration.

MATERIALS AND METHODS

We searched all the concerned publications available in the electronic databases, i.e., Google Scholar, PubMed, Science Citation Index, BioMed Central, Scopus, etc. We searched for combinations of either of the keywords "air pollution" or "environmental pollutants" or "maternal smoking" with any of the following: "low weight," "infant mortality," "prematurity," "IUGR," "birth defect," and "congenital anomalies." We explored the reference lists of concerned papers for additional publications. We debarred the abstracts of papers presented at conferences because they did not enclose a myriad of information. Since this review imparts importance on criteria pollutants and their effect on maternal and fetal health, so intentionally information on other previously described risk factors was not evaluated.

RESULTS

The impacts of air pollution on variant pregnancy outcomes are a matter of substantial interest to a wide array of researchers and policy analysts. Epidemiologically, it is rational to presume that each individual has diverse thresholds limits, depending on prevailing or preceding environmental exposures as well as genetic vulnerability. However, results varied with the type of pollutants, methodology adapted, and episode of pregnancy, which further complicates the analysis. The results of aforementioned pollutants and its effect have been reviewed individually.

Particulate Matter (PM_{10,2.5}) and Pregnancy Outcomes

Ambient fine particles PM_(10,2.5) are compound mixtures of diverse substances including metal and organic matter such as polycyclic aromatic hydrocarbons (PAHs). Table 1 shows spatial and temporal pregnancy outcomes on maternal exposure to PM. Bobak⁸ explored that the consequence of PM robustly appeared in the first trimester, resulting in prematurity and low birth weight. The Czech-US Environmental Protection Agency reported that the exposure of PM₁₀ in the first month of pregnancy was correlated with prominent risk of IUGR [odds ratio was 2.64 (confidence interval, CI: 1.48–4.71)]; interestingly, exposure in the later months of pregnancy was not related to IUGR.⁹ Dejmeck et al⁹ also investigated the blow of PM_{10,2.5} on IUGR in an extremely tainted vicinity of northern Bohemia. The cases reported with the risk of IUGR were 1.44 times higher (CI: 1.03–2.02) in the group exposed to PM₁₀ (levels >40–50 µg/m³). Srám et al¹⁰ reported that there are satisfactory data available that

Table 1: Spatial and temporal pregnancy outcomes on exposure to particulate matter

Pollutant	Outcomes	Findings	References
PM	Post-neonatal mortality	AOR = 1.10 (95% CI: 1.4–1.1.6) For >40 µg/m ³	Woodruff et al (1997) ¹¹
PM	Infant mortality	(95% CI: 2.5–11.3%) For 10 µg/m ³ increase	Loomis et al (1999) ¹²
PM	Respiratory mortality in post-neonatal period	AOR = 1.18 (95% CI: 1.1–1.21)	Ha et al (2003) ¹³
PM	Low birth weight	(95% CI: 20.3–19.8) For 10 µg/m ³ increase in PM	Chen et al (2002) ¹⁴
PM	Low birth weight	The risk increased by 19% for every 1 ppm increase in the mean concentration	Wilhelm and Ritz (2003) ¹⁵

AOR: Adjusted odds ratio; CI: Confidence interval; PM: Particulate matter

reveal the association between increasing levels of PM and low birth weight.

NO₂ and Pregnancy Outcome

Nitrogen oxide occurs naturally and by anthropogenic activity. In areas of high automobile traffic, the NO₂ is used as a surrogate for traffic-related pollution and contributes to differential pregnancy outcomes. Table 2 has evaluated some of the pregnancy outcomes on exposure to NO₂. Pereira et al¹⁶ reported the associations between intrauterine mortality in Brazil. The risk of IUGR in accordance with NO₂ amplified considerably throughout the entire term of pregnancy as reported by Liu et al in 2007.¹⁷ He also reported that with the increase of 20.0 ppb in ambient cases, there occurred 14% risk in IUGR cases. Ballester et al reported that the increase in 40 µg/m³ NO₂ exposure during first trimester was correlated with a reduction in fetus length approximately [-0.27 cm (95% CI: -0.51 to -0.3)]. He also investigated the decrease in the birth weight of approximately 40.3 gm with an increase in NO₂ exposure.¹⁸

SO₂ and Pregnancy Outcomes

Sulfur dioxide is a colorless, pungent, and highly reactive gas and also one of the common air pollutants upon which the National Ambient Air Quality Standards (NAAQS) are imposed.²³ On exposure to SO₂, the low-birth-weight and

Table 3: Spatial and temporal pregnancy outcome on exposure to sulfur dioxide

Pollutant	Outcomes	Findings	References
SO ₂	Low birth weight	50 µg/m ³ in first trimester (95% CI: 1.11–1.30)	Bobak (2000) ⁸
SO ₂	Low birth weight	During first trimester	Maisonet et al (2001) ²⁴
SO ₂	Premature fetus	On increase in 100 g/m ³ of SO ₂	Xu et al (1995) ⁵
SO ₂	Low birth weight	Increasing 11.4 ppb ambient SO ₂ risk 26% LBW cases	Lin et al (2004) ²⁵
SO ₂	Low birth weight and very low birth weight	Increasing 1 ppb SO ₂ risk LBW and VLBW by 0.5% and 0.4%	Yang et al (2013) ²³

LBW: Low birth weight; VLBW: Very low birth weight; CI: Confidence interval

very-low-birth-weight fetuses were reported as shown in Table 3. Wang et al² reported low birth weight fetus due to maternal exposure to SO₂ during their last trimester in Beijing. Contrastingly, Maisonet et al in 2001²⁴ revealed their correlation in the second trimester. A number of cases of infant mortality were reported by Bobak and Leon³ in Czech Republic due to maternal exposure to SO₂. Ritz and Yu¹⁰ found a strong correlation between elevated SO₂ concentration in ambient environment, which resulted in low-birth-weight fetuses. According to a Chinese report, the last trimester is considered unsafe on prolonged exposure to SO₂, which risks low-birth-weight fetuses.¹⁰

CO and Pregnancy Outcomes

Carbon monoxide is produced both endogenously and from many exogenous sources, i.e., cigarette smoke, automobile exhaust, etc. In many cases, acute CO poisoning during pregnancy still goes undiagnosed. Breslau and Freund were accountable for the first published details of acute CO intoxication in pregnancy. According to Brown and Piantadosi,²⁶ CO may inhibit mitochondrial electron transport in the brain, thereby resulting in toxicity. In France, Elkharrat et al²⁷ found that 4.6% of patients hospitalized due to CO poisoning were pregnant women. According to a review of literature, Norman and Halton²⁸ explored that the first stage of gestation in comparison to the later stages is more prone to anatomical malformations on exposure to CO intoxication. The fetal brain seems to be more sensitive to CO during the late gestational stage as per Okeda et al.²⁹ Table 4 represents the pregnancy defects on exposure to CO.

Active and Passive Smoking

Tobacco smoke is a complex mixture that contains substances such as PAHs and N-nitrosamines. Both are

Table 2: Spatial and temporal pregnancy outcome on exposure to nitrogen dioxide

Pollutant	Outcomes	Findings	References
NO ₂	Reduced birth length	Increase in NO ₂ (11.1 µg/m ³) associated with reduction in crown-heel length (95% CI: -0.25 to -0.05)	Ballester et al (2010) ¹⁸
NO ₂	Reduction in head circumference	-0.31 cm reduction with (> 31.4 µg/m ³) in NO ₂ exposure	Ballester et al (2010) ¹⁸
NO ₂	Small for gestational age (SGA)	During second trimester (95% CI: 0.89–2.25)	Ballester et al (2010) ¹⁸
NO ₂	Reduced fetal weight	Exposure during first trimester is inversely correlated with decreased size (p=0.009) at 32 weeks and with reduced growth (p=0.004) between 32 and 38 weeks	Iñiguez et al (2011) ¹⁹
NO ₂	Low birth weight	95% CI: 7.0–10.8	Bell et al (2007) ²⁰
NO ₂	Small for gestational age (SGE)	During second and third trimesters (95% CI: 1.0–1.2)	Mannes et al (2005) ²¹
NO ₂	Preterm birth	When exposed to NO ₂ >46.2 µg/m ³	Llop et al (2010) ²²

CI: Confidence interval

Table 4: Spatial and temporal pregnancy outcomes on exposure to carbon monoxide

Pollutant	Outcomes	Findings	References
CO	Low birth weight	The risk increased during third trimester	Ritz et al (2002) ³⁰
CO	Risk of cardiac ventricular septal defects	During second month of pregnancy	Ritz et al (2002) ³⁰
CO	Low birth weight	(95% CI: 1.18–1.74) for 1 ppm increase in first trimester	Maisonet et al (2001) ²⁴
CO	Low birth weight	(95% CI: 1.04–1.12) in first trimester	Ha et al (2003) ¹³

CI: Confidence interval

genotoxic and carcinogenic, and their metabolites lead to the formation of deoxyribonucleic acid (DNA) adducts.³¹ Maternal smoking during pregnancy is correlated with low birth weight, risk of prematurity, prenatal mortality, and ectopic pregnancy.² The ill-effect of maternal smoking on the fetus depends upon several factors such as the number of cigarettes smoked by individuals, the extent of inhalation, and the metabolism of smoking components.

Kline et al³² concluded that smoking mothers have 25% increased risk of spontaneous miscarriage. In support of Kline, the Nielsen study³³ also found evidence that show spontaneous miscarriage is correlated with the number of cigarettes inhaled per day. Williams et al³⁴ reported that there is a 2.1 times greater risk of preterm delivery in smoking mothers as compared with nonsmoking mothers. Table 5 shows the various pregnancy defects with respect to maternal smoking.

DISCUSSION

In this review, adverse effects such as low birth weight, prematurity, fetal intrauterine growth restriction, and small gestational age was associated with maternal pollutant exposure. However, the data from these associations varied greatly from study to study; some yielded very significant results and some merely concluded results.

The growth of fetus can be gauged by placental, maternal, and fetal factors. Ambient air pollutant and its potent constituents are inhaled by maternal respiratory tract and could be absorbed into the bloodstream, and consequently intervene in the development of fetus. Rutledge in 2000 reported that there are toxicants that are able to cross the placental membrane and after entering placenta hinder fetal growth.³⁸ The biologic mechanisms of these toxicants that enter into placenta are largely unknown. Tabacova et al³⁹ revealed that there is an increased risk of lipid peroxidation in placenta on maternal exposure to NO₂, elevated post-implantation embryonic lethality, and further disturbed postnatal development. Increased NO₂

Table 5: Spatial and temporal pregnancy outcomes on exposure to smoking

Pollutants	Outcomes	Findings	References
Nicotine	Preterm birth	Smoking increased the risk of preterm birth by a factor of 1.4. The crude relative risk for birth before 32 weeks was 3.7 and for 28 weeks was 7.2	Wickström (2007) ³⁵
Nicotine	Preterm birth	Shorter gestational age	Wickström (2007) ³⁵
Nicotine	Birth weight and preterm delivery	Mean birth weight was reduced in smokers by 190 gm (95% CI: 178–202 gm) and preterm delivery was increased by a factor of 1.57 (95% CI: 1.38–1.80)	England et al (2003) ³⁶
Tobacco	Reduction in gestational age	Reduction in gestational age by 3.0–9.4 days	Gupta et al (2004) ³⁷

CI: Confidence interval

level in ambient environment lessens maternal antioxidant reserves and triggers the formation of cell-damaging lipid peroxides. From the aforementioned results we can decipher that NO₂ hampers fetal birth weight, head circumference, and gestational growth.^{18–20}

In 1976, Longo⁴⁰ described the CO biological mechanism on maternal exposure, which results in tissue hypoxia by causing elevated carboxyhemoglobin concentrations and hampering fetal oxygen tensions. Carbon monoxide affects fetus greatly with respect to oxygenation of tissues as compared with mothers. As already mentioned, the prolonged CO exposure increases the risk of low birth weight during the third trimester.³⁰ The cardiac ventricular septal defects were also reported in the second month of pregnancy due to CO exposure.³⁰

Particulate matter during pregnancy affects the fetus by in utero exposure or indirectly by maternal toxicity. Exposure to particulate matter has been associated with adverse effects such as low birth weight, infant mortality, post-neonatal mortality, etc., by Chen et al,¹⁴ Woodruff et al,¹¹ and Ha et al.¹³ On prolonged exposure to PM, there is an increased formation of DNA adducts, which is responsible for embryotoxicity.¹⁰

When SO₂ impact was reviewed, interesting results were obtained. Wang et al² reported that on exposure to SO₂ in the last trimester, low-birth-weight fetuses were obtained, whereas Maisonet et al²⁴ obtained the same results in the second trimester. Bobak⁸ found the strongest relationship between SO₂ and preterm births.

The present state-of-art study contributes to a large scale on the domain of maternal exposure to ambient air pollution during pregnancy. The important conclusive

data is presented in a tabular format to make the study more interesting. This review article has tapered down further future research doors and also possesses several strengths. First, the data covers a wide population across different countries. A wide spatial and temporal variation has been studied under this review article. Second, criteria pollutants have been studied widely and their impact on variant reproductive outcomes has been established with respect to severity, maternal threshold, and period of pregnancy. Third, unlike others, this article also highlights the impact of active and passive maternal smokers on fetal health and development.

The extrapolation of environmental health impacts on reproductive outcomes is a conflicting study, because of wide spatial and temporal variation, different individual thresholds, differences in environmental exposure, variation in the pollutant sources, active and passive maternal smoking patterns, etc. All these factors make it difficult for the study complex to reach an appropriate conclusion. A persistent lacuna in the available data as well as this review suggests some future research priorities. First, it is of utmost importance to identify the most potent pollutants, which have the most detrimental effects on maternal exposure. The synergistic and antagonistic effects of criteria pollutant phenomenon should be established. Second, to avoid the unintended maternal exposure to ambient irritants, the most vulnerable period of pregnancy should be known. Third, the biologic metabolic pathways should be studied more and with concern for fetal health.

An important limitation of this review article is that the pollutant biological metabolism has not been discussed in a wider scope. The biological mechanism how environmental toxicants enter the placenta and influence the destiny of the developing fetus is largely unknown. Furthermore, to focus the results on the pollutant exposure, parameters such as socioeconomic factors, maternal age, educational status, race, and nutritional availability, which may also influence fetal health and growth, have been excluded from the study. Despite these limitations, satisfactory evidence determines that air pollution has confrontational effects on variant pregnancy outcomes.

CONCLUSION

Prima facie, there is sufficient evidence to conclude that air pollution has adverse effects on variant pregnancy outcomes. There is satisfactory evidence that reveals that the most potent pollutant seems to be particulate matter. The detailed biologic mechanism regarding the entry of these pollutants into the placental membrane and fetus destiny still remains ambiguous. The study of

environmental pollutant in correlation with maternal and fetal well-being is a subject of concern and has captured huge attention from the science community over the recent decades. Putting together all the data reviewed in this article, we can suggest that the criteria pollutants have detrimental effects on maternal and fetal well-being. Due to the persisting lacuna in the studies of air pollution and fetal health, the data available is suggestive, not conclusive.

Environmental concerns should be included both in pre-conceptional and prenatal care. To prevent any fetal hazards, prolonged exposure to pollutant teratogens should be avoided before conception is recognized. Appropriate prenatal services like screening and counseling should be introduced. The expectant mothers should be addressed regarding environmental issue and its much exposure. The government and policy analysts should initiate reproductive awareness programs from remote areas to urban cliffs to protect the innocent child's health.

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