

**PRETERM BIRTH IN INDUSTRIAL CITY OF INDIA, KANPUR: A CASE STUDY OF
THE EFFECT OF AIRBORNE PARTICULATE MATTER OF PM_{2.5} OR LESS**Anindita Bhattacharya¹ and Alka Tangri*²¹Department of Chemistry, Christ Church College, Kanpur – 208001.²Department of Chemistry, Brahmanand College, Kanpur – 208004.***Corresponding Author: Alka Tangri**

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ABSTRACT

Scarcely any examinations from western countries have connected pre-birth to particulate matter < 2.5 µm (PM_{2.5}) with increased risk of congenital anomalies. However, the outcomes are of mixed opinion. In this review study, the information of all pregnant ladies women laboured in public hospitals during 2017–2018 in Kanpur, an industrial city of the country were matched with the data of daily average PM_{2.5}, nitrogen dioxide (NO₂), sulphur dioxide (SO₂) and ozone (O₃) concentrations of the nearest monitoring station. A time-dependent exposure over the entire pregnancy for each woman was calculated. The study used a time varying Cox proportional hazards model to explore the association between PM_{2.5} exposure and the risk of congenital anomalies, after adjusting for individual confounders and other pollutants. A total of 9386 singleton live births were included in the study, and 127 (1.35%) were with congenital anomalies. An increase of every 10 µg/m³ in PM_{2.5} exposure over the entire pregnancy was significantly associated with increased risk of congenital anomalies, with hazard ratio (HR) of 1.35. For subtype analyses, PM_{2.5} exposure exhibited a significant association with cardiac anomalies and other unclassifiable anomalies with HRs of 1.60 and 1.42 respectively. The impacts of PM_{2.5} exposure on orofacial anomalies and musculoskeletal anomalies were not significant. The results indicate high concentration of PM_{2.5} could increase the risk of congenital anomalies among Indians, especially for cardiac anomalies. Self-protective measures involving reducing PM_{2.5} pollution exposure during pregnancy as well as environmental policies aiming to restrict PM_{2.5} emission could be helpful to reduce the burden of congenital anomalies.

KEYWORDS: PM_{2.5} exposure; Congenital anomalies; Cardiac anomalies.**INTRODUCTION**

The last 20 years or so have provided a lot of epidemiological evidence that being exposed to ambient particulate matters (PM) during pregnancy is associated with adverse birth outcomes. These include phenomena such as preterm birth and low birth weight (Li et al., 2017; Wang et al., 2018). Apart from these two conditions, another adverse outcome, known as congenital anomalies or birth defects, also increases vulnerability to infant mortality and childhood and adult morbidity.

It has been established that particulate matters with aerodynamic diameters ≤10 µm (PM₁₀) or ≤2.5 µm (PM_{2.5}) could enter human airways, resulting in the creation of reactive oxygen species, oxidative stress and inflammation, and cell damage, DNA damage and alterations in cellular signalling.^[1] It may hamper placental development and affect normal processes of gestation, and result in premature birth.^[2] Previous study had observed that exposure to PM during early pregnancy substantially modified DNA methylation

levels in placental tissues (Janssen et al., 2013). As the placenta is crucial in nutrient transfer to the embryo, this may result in abnormal embryonic development, which has been linked to adverse pregnancy outcomes as well as non-communicable disease across the lifespan, according to the Developmental Origins of Health and Disease (DoHaD) theory (Haugen et al., 2015; Janssen et al., 2013; Zhong et al., 2017). As preterm birth is an adverse pregnancy outcome, the epigenetic modifications in early pregnancy may confirm the link between air pollution on preterm birth.

MATERIALS AND METHODS

The maternal information and birth outcomes of all the pregnant women who had delivered from January 1, 2018 to December 31, 2019 were obtained from public and private hospitals of Kanpur city. After excluding women with multiple births, with genetic history of congenital anomalies and without record for gestational length, we finally included 9386 singleton live births in the study. Maternal information included each pregnant woman's home address, age, nationality, education and

parity. Birth outcome information included sex, gestational week, date of labour and diagnosed congenital anomalies.

Each pregnant woman's exposure was estimated by using the nearest monitor approach. The study area was the city of Kanpur with a population of about 3.2 million and is situated in north-central part of India (longitude 88° 22' E and latitude 26° 26' N). About 250,000 vehicles ply daily on these roads around the sampling sites. Kanpur has various types of industries such as coal-based 200MW thermal power plant, textiles, leather and leather products and chain. The data of daily average concentrations of PM_{2.5}, nitrogen dioxide (NO₂), sulphur dioxide (SO₂) and ozone (O₃) from each monitoring station in Kanpur city was obtained. There were 6 monitoring stations covering the entire city as shown in Figure 1. Local weather data, including temperature and relative humidity, was taken from Air Force Meteorological Station, Chakeri, Kanpur. The average outdoor temperature, relative humidity and wind speed were 30.51 ± 9°C, 33.27 ± 17.70% and 2.93 ± 1.32 m/s.

Each pregnant woman's home address was matched to the nearest monitoring station. The majority (80%) of participants lived within 10 km from the nearest monitors. Each woman's moving average exposure to PM_{2.5}, NO₂, SO₂ and O₃, respectively was assessed during the entire pregnancy for each week, based on the date of last menstrual period (LMP) and the date of delivery. Given the variability among exposure length (gestational week) of each birth, a Cox proportional hazards model was fitted with time dependent exposure to explore the associations between PM_{2.5} exposure over the entire pregnancy and the risk of congenital anomalies. In the model, gestational age was fitted as time scale, and in each week, a woman could either remain pregnant or give birth to an infant with congenital anomalies (defined as event) or not (defined as censoring).

RESULTS AND DISCUSSIONS

A total of 9386 singleton live births were included in the study, and 127 (1.35%) were with congenital anomalies. Table 1 shows the characteristics of pregnant women and children. Most pregnant women were aged 25 to 29 years. The mean concentrations of PM_{2.5}, NO₂, SO₂ and O₃ over the entire pregnancy for all participants were 50.07 µg/m³, 39.40 µg/m³, 73.17 µg/m³ and 86.97 µg/m³, respectively.

Figure 2 shows the unadjusted and adjusted associations between PM_{2.5} exposure over the entire pregnancy and the risk of congenital anomalies. In the crude model, it was found that PM_{2.5} exposure over the entire pregnancy was related to congenital anomalies, while the association was not significant with a HR of 1.05 (95% CI: 0.96, 1.16). In the model adjusted for individual characteristics, a 10 µg/m³ increase in PM_{2.5} exposure

over the entire pregnancy was marginally associated to increased risk of congenital anomalies, with a HR of 1.10 (95% CI: 1.00, 1.22). When NO₂, SO₂ or O₃ were included, it was found that significant associations between PM_{2.5} exposure and the risk of congenital anomalies with HRs ranged from 1.24 (adjusted for O₃) to 1.40 (adjusted for NO₂). In the full adjusted model, we found a 10 µg/m³ increase in PM_{2.5} exposure over the entire pregnancy was significantly associated with increased risk of congenital anomalies, with a HR of 1.35 (95% CI: 1.16, 1.58).

Figure 3 shows the estimated effects of PM_{2.5} exposure on the risk of congenital anomalies with a time-varying coefficients model. The proportional hazards assumption was satisfactory when performed Schoenfeld residuals check ($p = 0.47$). The pregnant women at early gestation probably appear to be more sensitive to PM_{2.5} exposure than later gestations.

Figure 4 provides the associations between PM_{2.5} exposure and the risks for each subgroup of congenital anomalies. It was found that a 10 µg/m³ increase in PM_{2.5} exposure over the entire pregnancy was significantly associated with increased risk of cardiac anomalies and other unclassifiable anomalies, with HRs of 1.60 (95% CI: 1.24, 2.08) and 1.42 (95% CI: 1.07, 1.89), respectively. PM_{2.5} exposure over the entire pregnancy was related to increased risks of orofacial anomalies and musculoskeletal anomalies, but not statistically significant. It was also found that cardiac anomalies were more sensitive to the PM_{2.5} exposure than orofacial and musculoskeletal anomalies.

The effects appeared to be stronger among the vulnerable women coming from rural areas, working as farmers, being overweight before pregnancy, whose mate was smoking during her pregnancy and having conception in autumn. An increase of every 10 µg/m³ in PM_{2.5} exposure over the entire pregnancy period was significantly associated with increased risk of congenital anomalies with hazard ratio (HR) of 1.35. For subtype analyses, PM_{2.5} exposure exhibited a significant association with cardiac anomalies and other unclassifiable anomalies with HRs of 1.60 and 1.42 respectively. The impacts of PM_{2.5} exposure on orofacial anomalies and musculoskeletal anomalies were not significant. The results indicate high concentration of PM_{2.5} could increase the risk of congenital anomalies among Indians, especially for cardiac anomalies.

Table 1: Characteristics of the study population and the distribution of pregnancy exposures.

Variable	Cases	Congenital anomalies (%)	Mean concentration during pregnancy ($\mu\text{g}/\text{m}^3$)			
			PM _{2.5}	NO ₂	SO ₂	O ₃
Age						
< 25	883	1.02	49.3	39.8	75	87.4
25–29	1770	50.2	39.3	72.7	72.7	86.8
30–34	4227	1.48	50.4	39.3	72.7	86.7
≥ 35	2506	2.08	50.2	39.4	72.9	87.4
Educational Qualification						
≤ 9	535	0.26	49.7	40.5	77.9	86.7
10–12	4156	2.39	50.1	39.7	75	86.6
> 12	4695	1.66	50.3	38.6	69.5	87.3
Gestational weeks						
< 28	263	65.78	49.2	36.9	62.5	93
28–32	647	4.64	50.3	38.9	72	87.2
32–37	6354	1.52	49.9	39.4	72.9	87.2
> 37	2122	0.76	50.1	39.4	73.3	86.9
Baby's sex						
Male	3120	1.42	50.1	39.4	73.3	87
Female	6266	1.13	50.1	39.4	73.1	87
Overall	9386	1.35	50.1	39.4	73.2	87

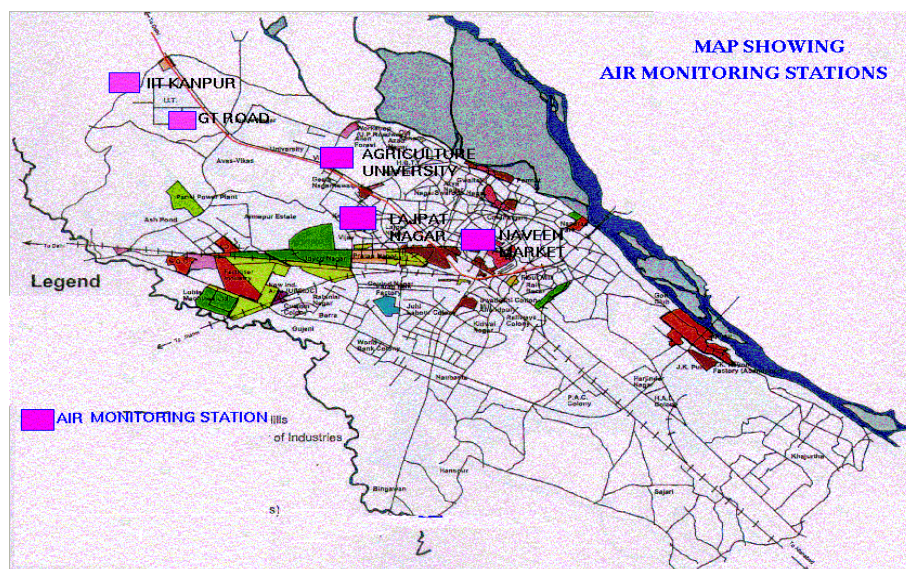
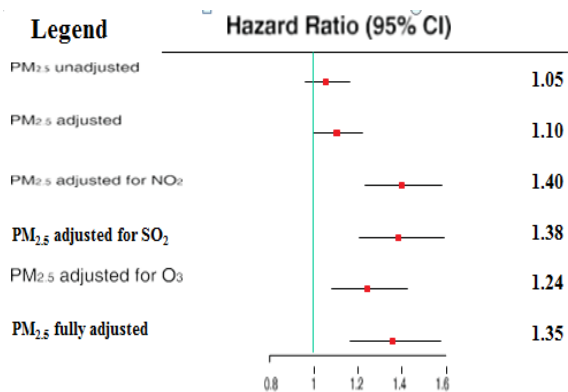
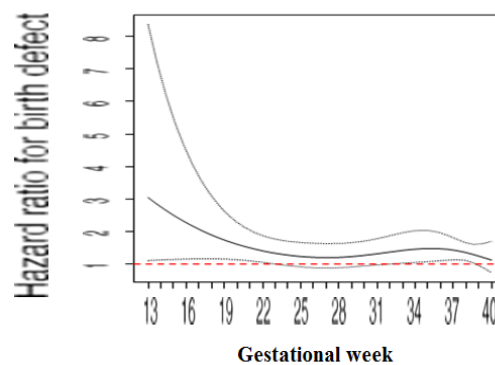


Figure 1: Air Monitoring Stations in Kanpur, India.

Figure 2: Hazard ratios and 95% confidence intervals of all congenital anomalies, associated with a 10 $\mu\text{g}/\text{m}^3$ increase in PM_{2.5} exposure during entire pregnancy in unadjusted and adjusted models.Figure 3: Hazard ratios (and 95% confidence intervals) of all congenital anomalies, associated with a 10 $\mu\text{g}/\text{m}^3$ increase in moving average PM_{2.5} exposure for each gestational week.

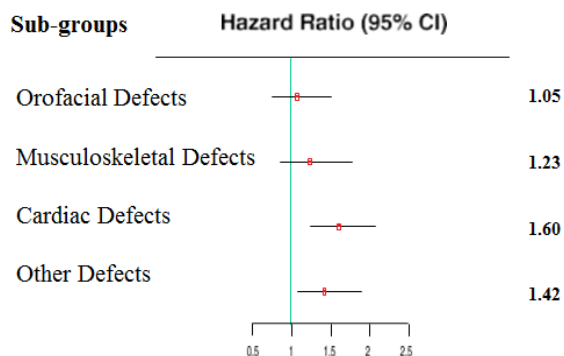


Figure 4: Hazard ratios (and 95% confidence intervals) of congenital anomalies by subgroups associated with a 10 $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ exposure during entire pregnancy.

CONCLUSION

As far as we know, this is the first study that provides evidence that exposure to $\text{PM}_{2.5}$ during pregnancy is linked to increased risk of congenital anomalies in Indian pregnant women. Exposure to $\text{PM}_{2.5}$ throughout the pregnancy period results in an increased risk of congenital anomalies. Cardiac issues were more sensitive to the $\text{PM}_{2.5}$ exposure than orofacial and musculoskeletal problems. There is an urgent need to frame policies to reduce $\text{PM}_{2.5}$ pollution. At an individual level, measures such as wearing a mask or using air purifier during pregnancy could reduce the risk of congenital anomalies.

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