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Birth defects and prenatal exposure to particulate matter in a Colombian population

Defectos congénitos y exposición prenatal a material particulado en una población colombiana

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ABSTRACT

Introduction: Air pollution is associated with adverse obstetric events. There is evidence of an association between exposure to high levels of particulate matter less than 10 microns (PM10) and birth defects. Objective: To determine the existence of an association between birth defects and prenatal exposure of pregnant women to PM10 in a Colombian population. Methods: Retrospective case-control study. Cases of mothers of newborns with postnatally confirmed congenital defects and controls without congenital defects were included. Emission exposure was determined by temporo-spatial disaggregation using ArcGIS® and georeferencing using gvSIG®, Google Earth® and Google Street View®, using previously published and validated estimates for the city. Statistical analysis was performed using Jamovi-Stats Open now®. Results: A total of 101 patients were included, corresponding to 31 cases and 70 controls. There was an increased risk of developing birth defects after exposure to PM10 emissions above 2.23 Ton/year/250m2 (OR: 8.17; 95% CI: 1.61 – 41.46; *p* = 0.011). Conclusions: There was a relationship between exposure to high levels of PM10 and increased risk of birth defects in the population studied. Future research on the relationship between environmental contamination and adverse obstetric events is suggested.

Key words: Congenital abnormalities, Particulate matter, Air pollution, Traffic-related pollution.

RESUMEN

Introducción. La contaminación atmosférica se asocia a eventos obstétricos adversos. Existe evidencia de asociación entre la exposición a niveles elevados de material particulado menor a 10 micras (PM10) y defectos congénitos. Objetivo. Determinar la existencia de asociación entre defectos congénitos y la exposición prenatal de mujeres gestantes a PM10 en una población colombiana. Métodos. Estudio retrospectivo de casos y controles. Se incluyeron casos de madres de recién nacidos con defectos congénitos confirmados posnatalmente y controles sin defectos congénitos. La exposición a emisiones se determinó mediante disgregación temporo-espacial mediante ArcGIS® y georreferenciación mediante gvSIG®, Google Earth® y Google Street View®, usando estimaciones previamente publicadas y validadas para la ciudad. El análisis estadístico se realizó utilizando Jamovi-Stats Open now®. Resultados. Se incluyeron un total de 101 pacientes, correspondiendo a 31 casos y 70 controles. Existió un aumento del riesgo de desarrollar defectos congénitos tras la exposición a emisiones de PM10 superiores a 2,23 Ton/año/250 m2 (OR: 8,17; IC 95%: 1.61 a 41.46; *p* = 0,011). Conclusiones. Existió relación entre la exposición a niveles elevados de PM10 y aumento en el riesgo de defectos congénitos en la población estudiada. Se sugiere la realización de futuras investigaciones sobre la relación entre contaminación medioambiental y eventos obstétricos adversos.

Palabras clave. Anomalías congénitas, Material particulado, Contaminación del aire, Contaminación por tráfico vehicular

Introduction

Congenital defects (CD) are those alterations that occur during fetal formation and development. They appear in about 5% of births[1,2] and can affect different systems and organs, from mainly aesthetic alterations to lethal entities or those incompatible with life such as organ agenesis[2,3]. They are one of the main causes of perinatal mortality and are related to disability, prolonged hospitalization, and surgical procedures, representing an important cost for the health system[4,5].

Among the etiologies and risk factors, genetic alterations, infections, exposure to teratogens and environmental conditions stand out[1,5,6]. Prenatal exposure of pregnant women to environmental pollution emissions is associated with different adverse obstetric events, such as hypertensive disorders, low fetal weight, preterm delivery, and congenital defects. The agents that stand out as generators of these events are carbon monoxide, ozone, sulfur or nitrogen derivatives and particulate matter[7-9].

Particulate matter (PM) is a mixture of liquid and solid particles suspended in the air. It is composed mainly of nitrates, sulfates, carbon derivatives, metals and other organic compounds resulting from human activity. They are classified based on their diameter as less than 10 microns (PM10), 2.5 microns (PM2.5) or 0.1 microns (PM0.1)[9,10]. Exposure to high concentrations of particulate matter is associated with the development of multiple pathologies[10,11].

It is postulated that PM has the capacity to cross the placental barrier, producing inflammation and free radicals that in turn generate epigenetic alterations in embryogenesis[11-13]. There is evidence linking the increased risk of birth defects with exposure to high levels of particulate matter[8,9,11].

The aim of this study was to determine the existence of an association between the development of congenital malformations and prenatal exposure of pregnant women to particulate matter less than 10 microns (PM10) of vehicular origin in a Colombian population. The present publication is based on the results obtained from the degree work of the main researcher to access the title of specialist in gynecology and obstetrics at the University of Caldas. Additional data can be consulted in the repository of the university library.

Methods

A correlational, retrospective, case-control study was conducted, including pregnant women residing in the urban area of Manizales, Colombia, with delivery care in a high complexity maternity center, between July 2014 and June 2015. Cases were considered to be mothers of newborns with clinically confirmed postnatal diagnosis of a congenital defect. Controls corresponded to the following three newborns born alive in the institution without a diagnosis of congenital malformation, with the same demographic condition. Subjects with clinical findings of TORCH spectrum infections, chromosomopathies or exposure to teratogenic agents were excluded, in order to subtract possible additional factors to the appearance of congenital malformations. Subjects with incomplete data in the records or whose address could not be correctly georeferenced using gvSIG®, Google Earth® and Google Street View® applications were also excluded. Sociodemographic, clinical and georeferencing information was collected from the medical history record.

The geographic distribution of PM10 exposure was obtained through the description of results published by Gómez et al[14], with which a grid with a definition of 250 x 250 meters was created using the ArcGIS® application, with the respective PM10 concentration in tons per year (Ton/year/250m2). On this tool, the subjects' addresses were georeferenced. Two definitions were used for PM exposure, after classifying the PM10 concentration in quartiles: 1- the lower quartile was compared with the upper quartiles (Q1 vs. Q2-Q4) and, 2- the highest quartile was compared with the lower quartiles (Q4 vs. Q1-Q3).

The data obtained were included in a bivariate analysis, calculating the corresponding odds ratio (OR). For the multivariate analysis, a logistic regression model adjusted for marital status, socioeconomic stratum and maternal education was applied. Statistical significance was established with a p-value < 0.05 and a 95% confidence interval was estimated. The Jamovi-Stats Open now statistical package (free license) was used.

Ethical considerations

The study was evaluated and approved by the Research Ethics Committee of the hospital center and the University of Caldas. It was guided by the ethical and legal frameworks for health research in Colombia, where it was considered low-risk research.

Results

A total of 101 patients were included, 31 cases and 70 controls (after exclusion of patients who did not meet the criteria). The descriptive analysis of sociodemographic, clinical and PM10 and CO exposure variables is shown in Table 1. No statistically significant differences were found for educational level, marital status, and socioeconomic stratum.

Exposure to particulate matter is described in Table 2. No statistically significant difference was observed in the distribution of cases and controls (*p* = 0.99). In the bivariate analysis, there were no statistically significant associations between the presence of congenital malformations and exposure to PM10 (Table 3).

The binomial logistic regression model for exposure to PM10 (see Table 4) adjusted for marital status, education and socioeconomic stratum determined an association as a protective factor between belonging to high socioeconomic strata and developing a congenital defect, with statistical significance in the group belonging to the middle stratum, compared to the low stratum (OR: 0.22; 95%CI: 0.66-0.74; *p*: 0.15). A trend of association was identified between the presence of birth defects as the degree of exposure to PM10 increases, showing a 7.17-fold increase in the risk of fetal malformations (OR: 8.17, 95% CI: 1.61-41.46; *p*= 0.011) when exposed to high levels of PM10 (Q3) versus the lower quartile.

Table 1. Sociodemographic characteristics of the population.

Variable		Cases n (%)	Controls n (%)	Total n (%)	X^2	*p*
Marital status	Single mother	15 (48)	37 (53)	52 (51)	0.17	0.68
	Lives with partner	16 (51)	33 (47)	49 (48)		
Education	Elementary	1 (3)	2 (3)	3 (3)	1.54	0.68
	Secondary	12 (39)	33 (47)	45 (44)		
	Technical	10 (32)	24 (34)	34 (34)		
	Professional	8 (26)	11 (16)	19 (19)		
Socioeconomic stratum	Low (1,2)	18 (58)	27 (38.6)	45 (44)	4.21	0.12
	Medium (3,4)	10 (32)	38 (54.3)	48 (47)		
	High (5,6)	3 (10)	5 (7.1)	8 (8)		

It is represented in absolute and relative frequencies for cases, controls and for the total sample.
p-value. χ2 test.

Table 2. Quartile distribution of exposure to PM10 vehicle emissions.

Variable		Cases	Controls	Total	X^2	*p*
		n (%)	n (%)	n (%)		
PM10	Q1 (0.41 Ton/year/250 m2)	5 (16)	21 (30)	26 (25)	3.37	0.33
(quartiles)	Q2 (0.95 Ton/year/250 m2)	8 (25)	18 (25)	26 (25)		
	Q3 (2.23 Ton/year/250 m2)	10(32)	13 (18)	23 (23)		
	Q4 (7.98 Ton/year/250 m2)	8 (25)	18 (25)	26 (26)		

It is represented in absolute and relative frequencies for cases, controls and for the total sample.
p-value. χ2 test. Shapiro Wilk test p = < 0.001 (non-normal distribution).

Discussion

The results of this study made it possible to determine the association between exposure to particulate matter emissions of less than 10 microns and the development of birth defects. Exposure to PM10 was determined using temporal-spatial disaggregation based on the results of the study carried out by Gómez et al[14], where the concentration of emissions in the city of Manizales, Colombia, was determined by indirect measurement techniques (vehicle counting, traffic density, estimation of emissions by type of vehicle). These data were collected through the determination of disaggregation factors, performing vehicle counts of buses, cabs, trucks, cars, and motorcycles per hour, considering the estimated emissions according to the type of vehicle and the proximity to the main and secondary roads. Using cloud movement and emission models, it was possible to create a distribution grid of vehicle emissions with a definition of 250 square meters.

There was a tendency for the risk of presenting a congenital defect to increase as exposure to PM10 increased. When comparing the risk of pregnant women exposed to concentrations in the lower quartile (Q1) versus the quartiles with higher contamination, an increase in risk of 1.9 times was found with respect to quartile 2 (Q2), 7.1 times in quartile 3 (Q3) and 2.5 times in the upper quartile (Q4).

These results coincide with other published works in which an association was found between the variables studied. For example, Yu and collaborators found an association between PM10 exposure and increased risk for the development of congenital heart disease, neural tube

Table 3. Bivariate analysis.

Variable		Cases n (%)	Controls n (%)	OR	p	CI 95%
PM10 (quartiles)	Q1 (0,41 Ton/year/250 m2)	5 (16)	21 (30)	Reference		
	Q2 (0,95 Ton/year/250 m2)	8 (25)	18 (25)	1.86	0.34	0.5 - 6.7
	Q3 (2,23 Ton/year/250 m2)	10 (32)	13 (18)	3.23	0.07	0.9 - 11.6
	Q4 (7,98 Ton/year/250 m2)	8 (25)	18 (25)	1.86	0.34	0.5 - 6.7
Exposed to PM10	No (less than 7,98 Ton/year/250 m2)	23 (74)	52 (74)	Reference		
	Yes (7,98 or more Ton/year/250 m2)	8 (25)	18 (25)	1.01	0.99	0.4 - 2.6
Exposed to PM10	No (less than 0,41 Ton/year/250 m2)	5 (16)	21 (30)	Reference		
	Yes (0,41 or more Ton/year/250 m2)	26 (83)	49 (70)	2.22	0.14	0.7 - 6.6

It is represented in absolute and relative frequencies for cases, controls and for the total sample. The p-value of the χ2 test for comparison between cases and controls, OR and 95%CI.

Table 4. Multivariate logistic regression analysis of the association between birth defects and exposure to PM10 at the mother's place of residence (Q2, Q3, Q4 vs. Q1).

Variable		OR*	p	CI 95%
PM10 (quartiles)	Q1 (0.41 Ton/year/250 m2)	Reference		
	Q2 (0.95 Ton/year/250 m2)	2.95	0.15	0.67 - 13
	Q3 (2.23 Ton/year/250 m2)	8.16	0.01**	19.2 - 41.4
	Q4 (7.98 Ton/year/250 m2)	3.541	0.11	0.75 - 16
Socioeconomic stratum	Low	Reference		
	Medium	0.22	0.015	0.66 - 0.74
	High	0.46	0.43	0.66 - 3.2
Education	Elementary	Reference		
	Secondary	0.79	0.87	0.04 - 13.7
	Technical	0.99	0.99	0.05 - 18.5
	Professional	2.06	0.66	0.078 - 54.7
Marital status	Lives with partner	Reference		
	Single mother	1.25	0.66	0.45 - 3.5

Multivariate model by logistic regression, 95%CI.
** Adjusted for socioeconomic stratum, education and marital status.*
*** Statistically significant findings.*

defects and cheilopalatoschisis(15). Similarly, in a paper published in 2021, Sun and coworkers determined that exposure to elevated levels of PM10 between 4-14 weeks of gestation was associated with congenital defects(16), providing evidence supporting the theory of deleterious intervention of PM10 in embryogenesis(7,8,11-13). This study contrasts with the report by Narváez et al, in which, using the same estimate of concentration of vehicle emissions for the city of Manizales, did not identify an association between the exposure of pregnant women to high concentrations of PM10 and carbon monoxide with the development of obstetric alterations (preeclampsia)(17).

Our study showed the association between low economic level and the presence of birth defects, with statistically significant results when comparing pregnant women living in areas with a higher poverty index (OR 0.22; 95%CI: 0.66 -0.74; *p*: 0.015). This coincides with multiple reports that identify poverty as a risk factor related to congenital defects(1,2,4,5,26).

The main weakness of the present work lies in the determination of the calculation of PM10 exposure with the use of indirect measurements made by Gómez(14). Therefore, it is not possible to precisely state the concentration of PM10 in each home nor the amount inhaled or absorbed by the research subjects(11,18). In the absence of chemical analysis of PM10 emitted in the city, it is not possible to determine the impact of each compound on embryogenesis(18). Furthermore, in the present study only emissions from vehicles were estimated, without including other sources such as industrial emissions and natural sources that cause fetal malformations(9,10,18-22).

These results are difficult to compare or extrapolate with similar studies, since most studies use mobile or fixed measurements of air quality, where the concentration is estimated in micrograms per cubic meter (μg/m3), a measurement that is neither comparable nor comparable to the one used in our work, since it refers to the behavior of dilution and transport in the air. Meanwhile, the unit used in this study (Ton/year/250m2) refers to the production of PM10 during a given period and area[18,19]. Future studies should be carried out considering both measures and their impact.

The limited sample size was due to the low incidence of congenital defects in the selected institution, generating high variance in the data and not obtaining more statistically significant results. Therefore, it is recommended to carry out studies where the sample universe is larger in order to reduce statistical biases. However, strategies were used to reduce the impact of bias in the selection of controls by including the newborn immediately after the case. This avoids selection or convenience biases, a methodology frequently used for the sample selection of low prevalence entities such as congenital anomalies, included and validated in epidemiological surveillance studies such as the ECLAMC (Latin American Collaborative Study of Congenital Malformations)[27].

The results of this study allow us to infer a possible relationship between the degree of pollution associated with vehicular emissions of PM10 to which pregnant women in a given area are exposed and the increased frequency of congenital malformations.

Conclusions

A relationship was found between exposure to high levels of PM10 and increased risk of congenital defects in the population studied, a result that coincides with that found in the literature, being one of the first to address this issue in the region.

Future research is needed to clarify this and other associations between environmental pollution and adverse obstetric events.

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