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Research Article
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Risk of Low Birth Weight and Very Low Birth Weight from Exposure to Particulate Matter ($PM_{2.5}$) Speciation Metals during Pregnancy

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Abstract

Purpose: To examine the association between maternal exposures to particulate matter speciation metals during pregnancy and the risk of Low Birth Weight (LBW) or Very Low Birth Weight (VLBW) in offspring.

Methods: This retrospective population-based cohort study involved two linked databases: the Florida birth certificate records for births for Hillsborough and Pinellas Counties from 2004 to 2007, and the Environmental Protection Agency (EPA) particulate matter speciation data. Exposure values of speciation chemicals for pregnant mothers were allocated based on their residential proximity to monitoring sites. Primary outcomes of interest were LBW and VLBW. Adjusted odds ratios (OR) and 95% Confidence Intervals (CI) were computed using multivariable logistic regression.

Results: Exposure to particulate matter sodium and aluminum during first trimester and the entire pregnancy period were associated with the odds of having LBW and VLBW. Exposure to $PM_{2.5}$ sodium increased the risk of LBW by more than 35% for both the first trimester and the entire pregnancy period (OR=1.41, 95% CI=1.19-1.68 and OR=1.35, 95% CI=1.02-1.79 respectively). $PM_{2.5}$ sodium exposure was also associated with the risk of VLBW for the entire pregnancy exposure (OR=2.06, 95% CI=1.07-3.96). $PM_{2.5}$ aluminum exposure during the whole pregnancy also was associated with an increased the risk of low birth weight (OR=1.08, 95% CI= 1.01-1.15) but not associated with the risk of very low birth weight (OR=1.02, 95% CI= 0.97-1.06).

Conclusion: Maternal exposure to $PM_{2.5}$ aluminum and sodium during pregnancy increases the risk of both low birth weight and very low birth weight, which suggests a need for further research to be conducted on the health effects of exposure to $PM_{2.5}$ speciation metals in general, and aluminum and sodium in particular.

Keywords: Low birth weight; Very low birth weight; Normal birth weight; Particulate matter; Metals; Air pollutants; Sodium; Aluminum

Introduction

Toxicological and epidemiological studies have attempted to establish relationships between measured Particulate Matter (PM) mass and adverse health effects [1]. Exposure to fine particles, less than 2.5 micrometers in diameter ($PM_{2.5}$) are believed to pose the greatest risk [2].

Rapid industrial development enhances the possibility of occupational and environmental exposure to various air pollutants (including metals and particulate matter) among women, a situation that has been shown to have adverse effects on pregnant mothers [3]. According to Semczuk and Sikora, pollution resulting from industrial products and wastes, increased motorization, and the chemization of agriculture has given rise to an increased amount of toxic metals and air pollutants in the environment [4]. Continuous exposure of pregnant women to small concentrations of heavy metals such as lead, mercury and cadmium demonstrate cumulative characteristics, and can result in irreversible disorders in the course of fetal growth and development. Although these heavy metals have been shown to be teratogenic and embryotoxic, the placenta serves as a natural barrier that decreases feto-maternal transmission of some heavy metals [4]. Studies of four counties in Connecticut and Massachusetts found associations between PM 2.5 components of aluminum, elemental carbon, nickel, silicon, vanadium, and zinc and risk of LBW [5]. Increases in air pollutants and subsequent exposure to low-levels of contaminants place expectant mothers at risk for adverse birth outcomes [6]. Negative health effects of particulate matter and gaseous pollutants have been established in studies involving laboratory animals, controlled human exposures, and population-based epidemiologic studies [7-12].

Low Birth Weight (LBW) or infants weighing less than <2500 g and Very Low Birth Weight (VLBW) or infants weighing less than <1500 g are major health issues in public health. Epidemiologic studies commencing in the 1990's to date have shown that exposure to ambient air pollution during the gestational or prenatal period could intensify the risk of Low Birth Weight (LBW), Small-for-Gestational Age (SGA) and preterm infants [10,13-16]. Studies done in different geographic regions have reported associations between air pollution and birth outcomes such as LBW, SGA and preterm delivery and increased infant morbidity and mortality [6,17]. Exposure to higher concentrations of Carbon monoxise (CO), Nitrogen dioxide (NO_2), Sulfur dioxide (SO_2), Total Suspended Particles (TSP) and PM_{10} during the first trimester to mid pregnancy periods were associated with an increased risk of LBW [9,18]. Several $PM_{2.5}$ chemicals such as aluminum, elemental carbon, nickel and titanium were found to be associated with LBW [19]. Darrow et al. found that exposure to various concentrations of air pollutants in the latter stages of pregnancy causes slight decreases in the birth weights of full term infants [11].

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There has been a strong association between PM and its subsequent effects on LBW and preterm birth. However, there is yet to be an agreement on the causative pollutants [12]. The pathophysiological mechanisms that may contribute to effects of air pollution on birth outcomes remain uncertain even though various hypotheses exist. Particulate matter of aero-dynamic diameter less than 2.5 micrometers is a complex mixture of several chemicals, including metals of varying toxicity to humans. This requires relating the level of exposure to the particular chemical characteristics of $PM_{2.5}$ to individual health outcomes in the same locale, to identify which components are hazardous and which are not. Our study examines the connection between level of exposure to $PM_{2.5}$ speciation metals during pregnancy and the risk of having LBW or Very Low Birth Weight (VLBW) in offspring, by relating individual exposure to individual maternal outcome for each pregnant woman in our study.

Methods

Geographic coverage

Hillsborough County, Florida is situated midway by the west coast of Florida, covering about 1020 square miles. It is among the most populated counties in the United States (US) with a population of about 1.2 million. Pinellas county, also located on the Florida's west coast, covers 273.80 square miles with a population size of about 917,000 [20]. Hillsborough County is a fragment of a greater pollution monitoring area which includes Pinellas and Pasco Counties [21]. It is home to Florida's largest seaport, the Port of Tampa which produces considerable amounts of pollution. Expectedly, an estimated 20 percent of all Florida's industrial air pollution sources are located in Hillsborough County. The Pinellas County Resources Recovery Facility is one of the nation's largest waste-to-energy trash incinerators and has been included on the US Environmental. Protection Agency's (EPA) watch list due to the quantity and nature of air pollutants produced by the plant [22]. In addition other pollution sources such as traffic, power point for electricity generation and non-road mobile sources are great contributors in the two counties.

Study design and data sources

We conducted a population-based retrospective cohort study on all singleton live births born between 2004 and 2007 to residents of Hillsborough and Pinellas counties. The study database was created by linking birth vital records to $PM_{2.5}$ chemical speciation data. Birth certificate data was ascertained from the Florida Office of Vital Statistics, and was the source of a wealth of maternal personal and pregnancy history information, as well as perinatal outcomes. Socio-demographic and health-related characteristics included in the database included, but was not limited to maternal age, education, race, and marital status, pre-pregnancy Body Mass Index (BMI), and tobacco use during pregnancy. In our analyses, we coded maternal age in years into three groups (<18, 18 to 35 and above 35), marital status as yes or no, race as white or black, education as less than 12 years and 12 years or greater and maternal smoking during pregnancy as yes or no. Gestational age at delivery was calculated as the number of completed weeks between the first day of the last menstrual period of the expectant mother and the infant's date of birth. Maternal health history, previous pregnancy history, current pregnancy conditions, and complications of labor and delivery were captured from dichotomous (yes/no) indicators present on the birth certificate. Examples of these conditions and complications include anemia, placental abruption, pre-pregnancy diabetes mellitus, myocardial infarction, chronic hypertension, placenta previa, gestational diabetes, and gestational hypertension.

$PM_{2.5}$ chemical speciation data for Hillsborough and the Pinellas counties were obtained from the EPA. These data were used to approximate county-level concentrations of PM speciation metals that include the following, which contribute substantially to $PM_{2.5}$ total mass and have been suspected to have potential adverse health consequences: aluminum, ammonium ion, arsenic, cadmium, calcium, chlorine, elemental carbon, lead, mercury, nickel, nitrate, organic carbon matter, silicon, sodium, sulfur, titanium, vanadium, and zinc [23-27]. Estimates of maternal exposure during pregnancy were assigned based on the 24-hours pollutant readings obtained from the three monitoring stations located in the Hillsborough and Pinellas counties. Each maternal zip code of residence was assigned to one of the three monitoring sites based on maternal residential proximity to the monitoring stations. The distances were then calculated between maternal residences center zip code and the monitoring sites. The derived distances assisted in generating the exposure values [28,29]. As in, we have to depend on estimations of exposure assessment by the use of distances from residential areas to the monitor sites within an area, since assessing exposure per pollutant for each individual is potentially difficult at the population level and there were no individual exposure data available and we did not use any regression models or Community Multi-scale Air Quality Model (CMAQ) [28-32]. Exposure estimates as daily reading averages for the first trimesters and entire pregnancy duration were generated for this study using the gestational age and the delivery dates. All exposure estimates were used as continuous variables.

Our first steps in conducting the analysis was to relate the occurrence of LBW and VLBW to sociodemographic and medical risk factors using chi-square tests and logistic regression to determine which factors have a significant effect on their occurrence before accounting for the effects of speciation chemicals. All $PM_{2.5}$ speciation metals as continuous covariates have been included and investigated in the analysis for possible association. During the analysis, we added first individual metal to the initial model of sociodemographic and medical risk factors to an ascertain individual significance. Next, several metals combination based on their correlation were considered and we retained metals that show significant association with birth outcomes in consideration.

The R statistical package (version 2.15.1) was used for the analysis. All hypothesis testing was carried out with a type 1 error rate set at 5%. This study was approved by the institutional review board at the University of South Florida.

Results

Correlation coefficients between some selected metals are shown in Table 1. In particular aluminum is highly correlation calcium, iron, and titanium, while sodium is correlated with nickel and iron. Table 2 shows the summary statistics in nanogram per cubic meter: mean (standard error), IQR and proportion of non-detectable values of $PM_{2.5}$ speciation

	Aluminum	**Calcium**	**Copper**	**Iron**	**Manganese**	**Nickel**	**Tantalum**	**Sodium**
Aluminum	1.00	0.44	-0.02	0.82	0.32	0.07	0.72	-0.30
Calcium		1.00	0.01	0.60	0.12	0.60	0.34	0.14
Copper			1.00	0.01	0.17	-0.04	0.05	-0.11
Iron				1.00	0.39	0.16	0.61	-0.33
Manganese					1.00	-0.18	0.39	-0.19
Nickel						1.00	0.06	0.38
Tantalum							1.00	-0.06
Sodium								1.00

Table 1: Correlation coefficients of some selected monitor level PM speciation metals.

Chemical	Mean(SE)	IQR	% Non-detectable
Aluminum	43.70 (0.086)	31.30	37.95
Barium	17.49 (0.028)	42.60	61.07
Cadmium	01.81 (0.003)	02.90	69.25
Calcium	56.03 (0.031)	39.20	00.33
Chromium	01.64 (0.003)	01.76	31.71
Cobalt	00.18 (0.000)	00.04	65.98
Copper	04.49 (0.010)	03.07	11.56
Cesium	03.15 (0.008)	07.91	78.95
Gallium	00.62 (0.001)	01.27	58.23
Iron	62.30 (0.055)	39.20	00.33
Hafnium	01.89 (0.004)	03.76	71.97
Lead	02.93 (0.003)	03.66	37.51
Indium	02.15 (0.003)	03.63	69.90
Manganese	01.31 (0.001)	02.20	32.23
Iridium	00.96 (0.001)	02.74	72.63
Molybdenum	00.71 (0.001)	01.74	83.75
Nickel	02.69 (0.017)	02.06	13.63
Magnesium	11.51 (0.030)	13.16	60.20
Mercury	01.29 (0.002)	02.23	60.52
Gold	01.05 (0.001)	02.53	62.60
Lanthanum	06.51 (0.012)	14.30	70.56
Niobium	00.47 (0.001)	00.93	78.95
Tin	06.41 (0.007)	14.42	63.25
Titanium	05.52 (0.007)	04.75	31.08
Scandium	00.17 (0.000)	00.11	87.13
Vanadium	02.73 (0.002)	02.99	16.58
Silver	02.30 (0.002)	04.55	61.18
Zinc	05.21 (0.005)	04.77	06.54
Strontium	01.18 (0.004)	01.28	42.53
Tantalum	05.10 (0.007)	19.42	72.19
Rubidium	00.37 (0.001)	00.47	56.92
Potassium	92.77 (0.282)	42.21	00.11
Yttrium	00.41 (0.001)	00.47	67.72
Sodium	130.11 (0.113)	194.00	22.79
Zirconium	00.89 (0.003)	00.89	70.45

Table 2: Mean (SE), first quartile, third quartile in nanogram/m^3 and proportion of non-detectable values of every 6 day measurement of $PM_{2.5}$ Speciation metals and elemental carbon of the three monitoring stations in Tampa MSA.

Characteristics	LBW[a] n (%)	VLBW[a] n (%)	NBW[a] n (%)	P Value
Age				
Below18 years	397 (5.8)	73 (6.2)	2964 (3.2)	
18-35 years	5693 (83.0)	987 (83.3)	80129 (85.6)	<0.0001
Above 35 years	767 (11.2)	125 (10.5)	10543 (11.3)	
Education level completed				
less than 12 years	1613 (23.8)	260 (22.6)	14419 (15.5)	<0.0001
12 years or above	5153 (76.2)	890 (77.4)	78694 (84.5)	
Race				
White	3651 (62.5)	539 (53.8)	63263 (79.0)	<0.0001
Black	2193 (37.5)	463 (46.2)	16788 (21.0)	
Marital Status				
No	3785 (55.2)	680 (57.5)	37786 (40.4)	<0.0001
Yes	3070 (44.8)	503 (42.5)	55850 (59.6)	
Smoking Status				
No	5669 (86.2)	991 (88.5)	84011 (92.2)	<0.0001
Yes	910 (13.8)	129 (11.5)	7124 (7.8)	

LBW: Low Birth Weight; NBW: Normal Birth Weight

[a] Columns do not tally due to missing data

Table 3: Chi-squared Analysis and Maternal Characteristics as a Percentage of LBW and NBW Infants.

metals. It shows that the most abundant metals are: aluminum, calcium, iron, potassium and sodium and least abundant are: cobalt, niobium and rubidium. Chemicals with most measurement below detection limit yielded unreliable crude odd ratios and were excluded for further analysis. Table 3 presents descriptive characteristics of the study population with respect to LBW, VLBW and Normal Birth Weight (NBW) delivery outcomes. There were 100,493 deliveries included in our analyses, with 6,857 (6.8%) of infants born LBW and 1185 (1.2%) of infants born VLBW. Among women who delivered LBW babies, 5,693 (83.0%) are aged between 18 to 35 years, 767 (11.2%) are over 35 years old and 397(5.8%) are less than 18 years old. Blacks constituted 37.5% of LBW deliveries compared to 62.5% whites. Of the pregnant mothers that delivered LBW babies, 5,153 (76.2%) had high school or above level of education. Maternal background characteristics comparison between mothers who had LBW and NBW infants showed a significant difference in relation to race, age, education, marital status and prenatal smoking status. Similar results were observed as in the case of LBW (Table 3).

The rates of pregnancy and labor complications amongst pregnant women who delivered LBW or VLBW babies compared to those with NBW are represented in Table 4. Rates were higher for mothers who delivered babies weighing over 2500 g or normal birth weight babies. Significant difference between rates were observed among mothers experiencing anemia, diabetes mellitus, placental abruption, gestational hypertension, chronic hypertension, placenta previa, renal disease, myocardial infarction and gestational diabetes.

Table 5 presents the crude odds of having LBW and VLBW associated with exposure to some PM speciation metals per IQR increase of the chemicals. For LBW and during the first trimester, only sodium (OR=1.35, 95% CI=1.22-1.49) show a significant increased odd of having LBW, while manganese (OR=0.73, 95% CI=0.64-0.82) and vanadium (OR=0.88, 95% CI=0.81-0.96) show significant decreased odd of LBW. During the whole pregnancy period, aluminum (OR=1.08, 95% CI=1.04-1.10), iron (OR=1.11, 95% CI=1.02-1.20) and sodium (OR=1.38, 95% CI=1.17-1.62) are associated with an increased odd of LBW. Manganese (OR=0.71, 95% CI=0.59-0.90) is the only one

Labor Complications	LBW (%)	VLBW (%)	NBW (%)	P value
Anemia	0.78	0.18	8.73	<0.0001
Diabetes mellitus	0.09	0.02	0.73	<0.0001
Placenta abruption	0.41	0.16	0.47	<0.0001
Gestational hypertension	0.41	0.04	4.32	<0.0001
Chronic hypertension	0.32	0.09	1.46	<0.0001
Placenta previa	0.14	0.03	0.41	<0.0001
Renal	0.02	0.01	0.07	<0.0001
Myocardial infarction	0.07	0.01	0.37	<0.000
Gestational diabetes	0.35	0.06	5.42	<0.02

LBW: Low Birth Weight; NBW: Normal Birth Weight

Table 4: Chi-Squared analysis and Rates of Labor Complications of LBW and NBW Infant Mothers.

Chemical	First Trimester	Entire Period	First Trimester	Entire Period
	LBW vs NBW	LBW vs NBW	VLBW vs NBW	VLBW vs NBW
Aluminum	1.00 [0.98-1.02]	1.08 [1.04-1.10]	0.94 [0.90-0.99]	1.08 [0.97-1.19]
Calcium	0.94 [0.86-1.05	1.20 [0.98-1.46]	0.67 [0.53-0.84]	1.23 [0.82-1.85]
Chromium	0.94 [0.87-1.02]	1.08 [0.95-1.22]	0.90 [0.75-1.10]	1.06 [0.79-1.42]
Copper	1.01 [0.98-1.04]	0.99 [0.95-1.04]	1.01 [0.95-1.07]	1.07 [0.96-1.18]
Iron	0.97 [0.93-1.00]	1.11 [1.02-1.20]	0.84 [0.77-0.92]	1.06 [0.87-1.29]
Lead	0.89 [0.79-1.01]	0.95 [0.83-1.10]	0.86 [0.65-1.15]	1.00 [0.71-1.41]
Manganese	0.73 [0.64-0.82]	0.71 [0.59-0.90]	0.42 [0.32-0.57]	0.45 [0.29-0.68]
Nickel	0.90 [0.78-1.04]	0.86 [0.72-1.06]	1.18 [0.85-1.65]	0.84 [0.53-1.32]
Titanium	0.96 [0.93-1.00]	1.02 [0.94-1.10]	0.84 [0.77-0.91]	0.92 [0.77-1.10]
Vanadium	0.88 [0.81-0.96]	0.90 [0.80-1.01]	0.72 [0.59-0.88]	0.74 [0.56-0.98]
Zinc	1.01 [0.95-1.08]	1.00 [0.91-1.11]	1.22 [1.05-1.42]	1.05 [0.83-1.33]
Potassium	0.99 [0.98-1.01	1.00 [0.97-1.02]	0.94 [0.90-0.99]	1.01 [0.95-1.08]
Sodium	1.35 [1.22-1.49]	1.38 [1.17-1.62]	2.00 [1.60-2.50]	2.73 [2.00-3.73]

Table 5: Crude odds ratios of some $PM_{2.5}$ speciation chemical risk factors that predict LBW and VLBW for the first trimester and entire pregnancy, Hillsborough and Pinellas counties, Florida, 2004-2007.

Outcome Variables	First Trimester [b]		Average pregnancy period[c]	
	VLBW vs. NBW		VLBW vs. NBW	
	OR	95% CI	OR	95% CI
Sodium	1.41	[1.19-1.68]	1.35	[1.02-1.79]
Aluminum	1.02	[0.97-1.06]	1.08	[1.01-1.15]
Preterm	3.08	[2.68-3.53]	3.59	[3.14-4.10]
Infarction	2.19	[1.41-3.38]	2.15	[1.39-3.32]
Tobacco use	2.27	[2.01-2.55]	2.29	[2.04-2.57]
High school and above	0.72	[0.65-0.80]	0.74	[0.67-0.82]
Black	2.03	[1.84-2.22]	2.04	[1.86-2.23]
Married	0.75	[0.68-0.82]	0.74	[0.68-0.81]
Gestational Hypertension	1.74	[1.49-2.02]	1.72	[1.48-1.99]
Placenta abruption	2.05	[1.56-2.70]	2.10	[1.61-2.74]
Male	0.64	[0.59-0.70]	0.65	[0.60-0.70]
Placenta previa	1.43	[1.01-2.01]	1.50	[1.07-2.09]
Preeclampsia	2.82	[2.47-3.22]	2.83	[2.49-3.21]
Gestation in weeks	0.52	[0.50-0.54]	0.55	[0.53-0.57]
Pre pregnancy BMI	0.96	[0.95-0.97]	0.96	[0.95-0.97]
Diabetes mellitus	0.58	[0.40-0.85]	0.69	[0.48-0.98]
Temperature	1.00	[0.99-1.02]		NA

OR: Odds Ratio; CI: Confidence Interval; LBW: Low Birth Weight; NBW: Normal Birth Weight

[b] Adjusted maternal characteristics and labor complications for first trimester.

[c] Adjusted maternal characteristics and labor complications for average pregnancy period.

Table 6: Adjusted Odds Ratio from Logistic Regression Models for Maternal Risks of LBW (n=6847) from Speciation Chemicals of Metals in the first trimester and entire pregnancy period.

Outcome Variables	First Trimester [b]		Average pregnancy period[c]	
	VLBW vs. NBW		VLBW vs. NBW	
	OR	95% CI	OR	95% CI
Sodium	1.32	[0.81-2.14]	2.06	[1.07-3.96]
Aluminum	0.93	[0.82-1.06]	1.09	[0.92-1.30]
Preterm	2.23	[1.39-3.57]	2.44	[1.56-3.83]
Black	1.59	[1.27-1.99]	1.65	[1.32-2.05]
Placenta Abruption	1.84	[1.28-2.63]	1.80	[1.27-2.55]
Renal	3.55	[1.14-11.02]	3.46	[1.14-10.46]
Male	0.75	[0.60-0.93]	0.76	[0.61-0.94]
Preeclampsia	3.86	[3.02-4.93]	3.69	[2.92-4.67]
Gestation in weeks	0.47	[0.45-0.49]	0.48	[0.46-0.50]
Temperature	1.00	[0.96-1.04]	NA	

OR: Odds Ratio; CI: Confidence Interval; VLBW: Very Low Birth Weight; NBW: Normal Birth Weight

[b] Adjusted maternal characteristics and labor complications for first trimester

[c] Adjusted maternal characteristics and labor complications for average pregnancy period

Table 7: Adjusted Odds Ratio from Logistics Regression Models for Maternal Risks of VLBW (n=1185) from Speciation Chemicals of Metals in the first trimester and entire pregnancy period.

associated with reduced odds of LBW. For VLBW, iron, manganese titanium, vanadium and potassium are associated with reduced odd per IQR increase during the first trimester, while sodium is the only metal associated with an increased odd. For the whole pregnancy exposure, sodium is again the only metal associated with an increased odd of VLBW, while manganese and vanadium show a reduced odd of VLBW (Table 5).

Estimates of the adjusted odds ratio depicting association between LBW and particulate matter sodium and aluminum after controlling for maternal risk factors during the first trimester and the entire pregnancy period are given in Table 6. Exposure to particulate matter sodium in both the first trimester and during the entire pregnancy period was found to be associated with the highest increase risk of 41% and 35% respectively among metals of having a LBW infant per IQR increased in sodium (OR=1.41, 95% CI=1.19-1.68 and OR=1.35, 95% CI=1.02-1.79 respectively). A moderate increase risk (8%) of LBW is found with the exposure to particulate matter aluminum during the entire pregnancy period per IQR increase in aluminum (OR=1.08, 95% CI=1.01-1.15). But that association was no longer statistically significant if exposure happened only during the first trimester of pregnancy (OR=1.02, 95% CI=0.97-1.03). Among maternal risk factors, preterm delivery was associated with the highest increased risk of LBW in both exposure periods (OR=3.08, 95% CI=2.68-3.53 and OR=3.59, 955 CI=3.14-4.10 respectively). It is followed by preeclampsia (OR=2.82, 95% CI=2.47-3.22 and OR=2.83, 95% CI=2.49-3.21) and tobacco use (OR=2.27, 95% CI=2.01-2.55 and OR= 2.29, 95% CI=2.04-2.57). Other maternal risk factors found to increase the incidence of LBW includes; infarction, black mothers, gestational hypertension, placental abruption and placental previa. The risk of LBW was reduced if mothers have completed at least high school (OR=0.72, 95% CI=0.65-0.80 and OR= 0.74, 95% CI=0.67-0.82) and were married (OR=0.75, 95% CI=0.68-0.82 and OR=0.74, 95% CI=0.68-0.81). Other reduced risk factors include; male babies, have high gestational age, have high pre-pregnancy BMI and for mothers diagnosed with diabetes mellitus (Table 6).

Summary estimates of the adjusted odds ratios for association between VLBW and particulate matter sodium and aluminum after controlling for maternal risk factors are represented in Table 7. Among metals, exposure to $PM_{2.5}$ sodium during the entire pregnancy period shows the highest risk of delivering very low birth weight babies (OR=2.06, 95% CI=1.07-3.96). But that risk was no longer present if mothers were exposed to $PM_{2.5}$ aluminum (OR=1.09, 95% CI=0.92-1.30). Exposure to $PM_{2.5}$ sodium (OR=1.32, 95% CI=0.81-2.14) and $PM_{2.5}$ aluminum (OR=0.93, 95% CI=0.82-1.06) during the first trimester were found not to be associated with the risk of having VLBW babies. Among maternal risk factors, the highest risk of delivering very low birth weight babies were associated with preeclampsia (OR=3.86, 95% CI=3.02-4.93 and OR=3.69, 95% CI=2.92-4.67), followed by renal disease (OR=3.55, 95% CI=1.14-11.02 and OR=3.46, 95% CI=1.14-10.46). Other maternal risk factors found to increase the risk of having very low birth weight babies includes; preterm delivery, being black and placental abruption. The risk of delivering very low birth weight babies were reduced if babies were males and with high gestational age (Table 6).

Discussion

This study examined the association between particulate matter of aerodynamic less than 2.5 micro-meters of diameter speciation metals and the risk of LBW and VLBW in offspring after mother's exposure either during the first trimester or the entire pregnancy period. Our findings show a 41% increased odds of LBW for maternal exposure to $PM_{2.5}$ sodium during the first trimester and 35% during the entire pregnancy period per IQR increase. It also show that exposure to particulate matter sodium particles during the entire pregnancy period increases the risk of VLBW infants by more than two times. Likewise, an 8% increased risk of LBW was found if an expectant mother were exposed during the entire pregnancy period to $PM_{2.5}$ aluminum.

Metals like lead, copper and arsenic have been associated with the risk of increasing low birth weight [33-35]. Also, elevated levels of zinc, elemental carbon, silicon, aluminum, vanadium and nickel from $PM_{2.5}$ constituents are responsible for decreasing birth weight in newborns [5]. Our study confirms the negative effect of aluminum and unlike it shows a negative effect on birth weight of sea salt (sodium). Our findings were consistent with studies which reported maternal exposure to air pollutants as being responsible for negative birth outcomes; LBW and preterm [5,19,36]. Ozone and carbon monoxide pollutants are known to reduce the birth weight of infants [37,38]. However, a study by observed maternal exposure to NOx and traffic density as a protective factor rather than increasing the risk for preterm birth [29].

The biological mechanisms that may contribute to effects of air pollution on birth outcomes are uncertain, and various hypotheses exist [19]. For instance, NO_2 exposure during pregnancy may limit placental vascular function and disturb fetal growth [39]. CO may react with oxygen on hemoglobin-binding sites, reducing oxygen delivery [10]. Fetal growth may be retarded by direct toxic effects of air pollution, similar to effects of smoking [11]. The mechanism of PM effects on birth outcomes could be related to the transfer of toxic components to the fetus from PM that has accumulated in the mother's lungs [16].

PM has a complex chemical composition, and its chemical components may affect outcomes through different biological pathways. One possible explanation is that exposure to $PM_{2.5}$ metal-related components, including aluminum and titanium, increases oxidative stress burdens leading to adverse health outcomes [40]. PM exposures may also lead to changes in hemoglobin, platelets, and white blood cells [41], which may potentially contribute to the association between PM and adverse fetal growth [42]. PM exposure may contribute to systemic oxidative stress [43]. Direct effects from oxidative activities of combustion-derived particles or by transition-metal constituents (e.g., iron, copper, chromium, and vanadium) [44,45] may adversely affect the embryo in its earliest phase of growth [46].

Researchers, who included a team from the UK, found that babies were smaller even in areas with relatively low levels of air pollution, well below the limits considered acceptable in European Union guidance. For every increase of 5 micrograms per cubic meter in exposure to fine particulate matter during pregnancy, the risk of low birth weight in the baby rose by 18%. Exposure to ambient air pollutants from traffic during pregnancy is associated with restricted fetal growth.

Diabetes mellitus is a frequent diagnosable complication during pregnancy and a major risk factor for the mother and fetus [47], and both maternal and paternal race and ethnicity is responsible for the increased rates of gestational diabetes mellitus [48]. Our study showed that diabetes mellitus was associated with a modest risk of LBW. It also indicates a reduced risk of LBW and VLBW with well-educated mothers (high school graduates and above). As cited by [49], women with education above high school were less likely to have preterm babies. The use of tobacco products is responsible for about 32,000 to 61,000 LBW infants delivered annually [50]. It is also important to note that our results for mothers who used tobacco was consistent with findings of [51] which estimated the risk of LBW to be higher among babies born to women who smoked. Maternal gestational hypertension was also associated with a higher risk of LBW. Findings from our study are consistent with other studies findings, which suggest the risk of LBW to be differential with regards to the sex of the infant. Female babies are reported to be at a greater risk of having a lower birth weight and this confirms air pollutants as affecting the fetus; males and females differently [29,52]. Results from our study, suggest males to be at a reduced risk of being born with a low or very low birth weight. In other words being a male served as a protective factor.

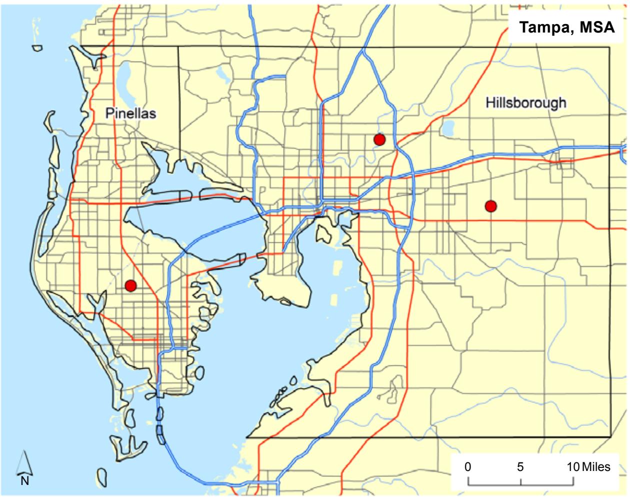

Figure 1: Map of the study area with the three PM speciation monitoring stations.

This study is very important since not many studies have studied the effects of particulate matter metals speciation exposure during pregnancy. In addition, our study uses a population-based data. Like any retrospective study, our study had some limitations. The exposure assessments for this study were based on data derived from the closest monitoring stations to the residence of mothers at the time of delivery, and residential mobility during this period may have occurred [53] (Figure 1). Studies have confirmed about 12-33% of pregnant women to move addresses during pregnancy [54,55]. About 12% of pregnant women who move address during pregnancy, a significant amount of them (62%) usually move within the same municipalities [54]. Factors including low family income, lower maternal age, marital status (single) and tobacco use are reported with the increased movement during pregnancy [54]. Studies using maternal address at time of delivery are plausible to be a major source of exposure misclassification due to maternal mobility during pregnancy [54-57]. As a result, exposure level classification may have been affected. Additionally as for all air pollution data, some measurements could be below the minimum detection limit that could affect study findings. Despite that, our study has some strength. The major strength of the study is the availability of the large population based data. The Florida birth certificate records for births in Hillsborough and Pinellas Counties contained significant amount of information, which made it possible for a wide range of the known confounders to be adjusted for.

There is evidence in our study to suggest that maternal exposure to particulate matter metals such as sodium and aluminum increases the risk of LBW and VLBW. Nonetheless, maternal socio demographics and pregnancy complications could also intensify the risk. Ebisu and Bell reported that most exposure levels in their study area were in compliance with U.S [19]. Environmental Protection Agency air pollution standards; however, they identified associations between $PM_{2.5}$ components and LBW. Their findings suggest that some $PM_{2.5}$ components may be more harmful than others, and that some groups may be particularly susceptible.

Aluminum is the most abundant metal and the third most abundant element in the earth's crust, comprising about 8.8% by weight (88 g/kg). It is never found free in nature and is found in most rocks, particularly igneous rocks as aluminosilicate minerals [58,59]. Aluminum enters environmental media naturally through the weathering of rocks and minerals. Anthropogenic releases are in the form of air emissions, waste water effluents, and solid waste primarily associated with industrial processes, such as aluminum production. Because of its prominence as a major constituent of the earth's crust, natural weathering processes far exceed the contribution of releases to air, water, and land associated with human activities [60]. As for sodium, a substantial amount of particulate exists in the atmosphere because emission sources of sodium are widely spread on the Earth's surface. Concentrations of sodium in the urbanized area are related mainly to the anthropogenic sources of their emission [60].

There is a definite need for further detailed analysis relating exposure to particulate matter speciation metals in general and aluminum and sodium in particular during pregnancy and the risk of low birth weight to validate our findings. Better exposure assessment models that could take personal characteristics such as breathing rate, and body mass into account could be helpful in establishing the association in future research.

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