HHS Public Access

Author manuscript

Pediatr Obes. Author manuscript; available in PMC 2019 June 01.

Published in final edited form as:

Pediatr Obes. 2018 June ; 13(6): 348–356. doi:10.1111/ijpo.12248.

Prenatal Traffic-Related Air Pollution Exposures, Cord Blood Adipokines, and Infant Weight

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Abstract

Objective—Studies suggest that prenatal exposure to traffic-related air pollution (TRAP) may contribute to childhood obesity. While exact mechanisms for this association are unknown, circulating adipokines are hypothesized to contribute to early-life weight gain.

Methods—The Maternal and Child Health Study birth cohort included 136 women from the Los Angeles County + University of Southern California Medical Center. This study estimated prenatal residential TRAP exposure and used linear regression analysis to examine associations between adipokines with TRAP exposure and infant weight change (birth to 6 months).

Results—A one standard deviation (1-SD: 2 ppb) increase in prenatal non-freeway NOx was associated with 33% (p=0.01) higher leptin and 9% higher high molecular weight (HMW) adiponectin levels (p=0.07) in cord blood. Leptin levels were 71% higher in mothers who lived <75 meters than those living >300 meters from major roadways (p=0.03). A 1-SD (10 ng/ml) increase in leptin was associated with a significant increase in infant weight change in females (0.62 kg, p=0.02) but not males (0.11 kg, p=0.48).

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Author Contributions

T.L. Alderete conceived the research question, assisted with analysis, wrote the manuscript, and approved the final manuscript as submitted. C. Breton, T. Bastain, F.D. Gilliland., and M.T. Salam conceived the primary study design and approved the final manuscript as submitted. A. Song conducted the analyses, generated the results and assisted with manuscript preparation. C.M. Toledo-Corral and R. Habre contributed to analysis, writing of methods, and reviewed data. C. Breton, T. Bastain, and F. Lurmann assembled residential data, guided geocoding efforts, designed and created the final analysis dataset and contributed to manuscript writing. T.L. Alderete, A. Song, and C. Breton are the guarantors of this work, and as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

All authors declare that they have no conflict of interest.

Conclusions—Higher TRAP exposures were associated with higher cord blood levels of leptin and HMW adiponectin. These adipokines were associated with increased infant weight change in females, which may have implications for future obesity risk.

Keywords

air pollution; cord blood; adipokines; leptin; high molecular weight adiponectin

Introduction

In the United States, approximately 23% of children are overweight or obese (1). Despite substantial policy efforts, there is no evidence of a decline in childhood obesity prevalence in any age group (2). Beyond poor diet and lack of physical activity, studies suggest that early life exposures to environmental pollutants may also contribute to childhood obesity (3–6). Exposures to traffic-related air pollution (TRAP) and ambient nitrogen dioxide (NO_2) and particulate matter have been shown to independently contribute to childhood obesity (5–7). The prenatal period represents a critical developmental window (8) where maternal exposure to air pollutants may influence infant and childhood growth trajectories. Recent studies have shown that increased prenatal air pollution exposure is associated with childhood obesity (9, 10). Further, cord blood adipokines have been shown to be positively associated with infant birthweight and adiposity (11–13). Therefore, prenatal exposures to environmental toxins may contribute to excess adiposity and childhood obesity through alterations in fetal exposure to cord blood adipokines.

One previous study has examined associations between cord blood adipokines with ambient air pollution exposure (14). In the Maternal-Infant Research on Environmental Chemicals Study, increased maternal exposure to residential NO_2 and particulate matter with an aerodynamic diameter ≤2.5 μm ($PM_{2.5}$) were associated with increased cord blood leptin and adiponectin levels (14). Leptin and adiponectin are hormones secreted by adipocytes and have been shown to correlate with fetal adiposity and childhood weight gain (11, 12). The primary aim of this study was to determine whether prenatal exposures to TRAP, NO_2, and/or $PM_{2.5}$ were associated with leptin, high molecular weight (HMW) adiponectin, and the ratio of leptin to HMW adiponectin in cord blood in 136 mother-infant pairs. As a secondary aim, this study investigated whether cord blood adipokines were associated with changes in infant weight from birth to 6 months, which may be predictive of future obesity. We hypothesized that increased prenatal exposure to TRAP and ambient air pollution are associated with higher levels of cord blood leptin and HMW adiponectin. We further hypothesized that these higher levels of adipokines in cord blood are associated with a greater increase in infant weight at 6 months of age.

Research Design and Methods

Study Population

The current study included 136 mother-infant pairs with available cord blood samples from the ongoing University of Southern California Maternal and Child Health Study (MACHS). Women were recruited on the labor and delivery ward at the Los Angeles County+University

of Southern California Medical Center between 2012–2016 and a subset of infants was followed by phone and medical abstraction until 6 months after birth (n=46). Written informed consent was obtained from each pregnant woman prior to any testing. Exclusion criteria included <18 years of age, HIV positive status, physical, mental, or cognitive disabilities that prevented participation, current incarceration, or multiple pregnancies. Medical record information pertaining to pregnancy complications and delivery was obtained and infant medical records were requested from pediatricians for information related to growth.

Traffic-Related and Ambient Air Pollution Exposure Assessment

TRAP and ambient air pollution exposures were estimated based on participant's residential address reported at study entry. Street-level residential addresses of participants were standardized and geocoded at the parcel level and match codes were obtained using the Texas A&M Geocoder (http://geoservices.tamu.edu/Services/Geocode/). Addresses that did not match to a parcel centroid were corrected based on the best available knowledge of the participant's residence location.

Distance from residences to the nearest roads was considered a surrogate for TRAP. Residential distance to the nearest freeways/highways was classified as <500, ≥500 to <1000, ≥1000 to ≤1500, and >1500 meters. Residential distance to major roads was classified as <75, ≥75 to <150, ≥150 to ≤300, and >300 meters. Freeways/highways and major roadways represent different traffic-related exposures and these distance categories have been shown to capture important effects of TRAP on childhood health outcomes (15, 16). Exposure to local TRAP for the 9 months prior to delivery was estimated using modeled nitrogen oxides (NOx) at homes by applying the CALINE4 ("California Line Source") model (17). The CALINE4 dispersion model is an air quality model designed to estimate the incremental ambient concentration contributed by vehicle emissions on local roadways. It uses meteorological data, roadway geometry, traffic volumes, and vehicle emission factors as inputs and has been shown to be the best single predictor of local-scale spatial variation in NO_2 in Southern California (18).

Ambient air pollution concentrations for the 9 months prior to delivery were used to assess prenatal exposures. Hourly and daily air quality data (NO_2, ozone, $PM_{2.5}$, and PM_{10}) from ambient monitoring stations were downloaded from the U.S. Environmental Protection Agency's Air Quality System (http://www.epa.gov/ttn/airs/airsaqs) for the relevant time period and the hourly data were averaged to daily level. In urban Southern California, air monitors stations are spaced 20–30 km apart and provide a monitoring network with good characterization of the pollution gradients. The gases were measured using Federal Reference Method (FRM) continuous monitors while PM data were restricted to FRM or Federal Equivalent Method (FEM) monitors. Non-FEM $PM_{2.5}$ data were used only when FRM/FEM measurement data were not available. Daily exposure values were spatially interpolated from the four closest air quality monitoring station's locations to the residence locations using an inverse distance-squared weighting algorithm as previously described (19). Monthly average exposures were calculated from the daily data using a 75% completeness criterion.

Adipokines

Cord blood was collected and stored at room temperature for up to 24 hours until processing where serum was stored at −80°C until analysis. Plasma levels of leptin and HMW adiponectin were assayed in duplicate using ELISA (R&D Systems) and the average coefficient of variation for each assay was less than 10%. The ratio of leptin to HMW adiponectin (L/A) has been used as a marker of insulin resistance among children and adults (20); however, no studies have examined the use of this ratio in cord blood. Adiponectin is a circulating protein produced by adipocytes that is present in high and low molecular weight oligomers. HMW adiponectin binds to its receptors with high affinity and is one of the key molecules mediating various metabolic actions (21).

Maternal and Infant Assessments

Maternal information was assessed via interviewer-administered questionnaire and included: maternal age, gestational age at delivery, race, parity, stress level during pregnancy, annual family income, maternal education, and maternal pre-pregnancy body mass index (BMI). Maternal stress was evaluated using questions from the Perceived Stress Scale (22). Infant birthweight was extracted from hospital medical records for all 136 infants. In the sub-study, weight at 6 months of age was obtained from medical records for 46 infants. Infant sex-specific weight-for-age z-score was calculated based on the Centers for Disease Control and Prevention 2000 growth chart at birth and 6 months.

Statistical Analysis

Categorical variables were presented as frequencies and continuous variables were examined using mean and standard deviation (SD). Differences in maternal and infant characteristics by infant sex were examined using independent t-tests. Multivariate linear regression models were used to explore the relationships between adipokines in cord blood with TRAP, ambient air pollution exposure, and infant weight change from birth to 6 months of age. Potential confounders were identified from the literature and retained in the final models if a ≥10% change in the coefficient estimate was observed. Models examining the associations between air pollutant exposures with cord blood adipokines were adjusted for maternal age, gestational age, parity, race/ethnicity, annual family income, and maternal pre-pregnancy BMI. Models examining associations between cord blood markers with infant weight change included the same covariates with the addition of infant sex, birthweight (as indicated), and removal of family income. Pre-term birth and maternal smoking status were examined but were not identified as confounders. Infant outcomes were stratified by infant sex due to known differences in growth rates and effect modification by infant sex and maternal pre-pregnancy BMI was examined using interaction terms and evaluated for significance. The natural log transformation was used to normalize the distribution of leptin and HMW adiponectin when evaluating their associations with exposures. Results are presented as percent change per a 1-SD increase in prenatal TRAP and/or ambient air pollution exposure. A two-sided p-value <0.05 was considered statistically significant. All statistical analyses were performed using SAS 9.4 (SAS Institute, Cary, NC).

Results

Baseline characteristics of the 136 mother-infant pairs and the average distribution of air pollutants and adipokines are shown in Table 1 for the entire cohort and by infant sex. Mothers were predominantly Hispanic (90%) and more than 33% were below the Los Angeles County poverty line based on a reported annual income of <$15,000 per year (23). Infants were approximately half female and mothers of female infants were approximately three years older (p=0.002) and less likely to be nulliparous (p=0.01). Male infants were heavier at 6 months of age and also had a greater increase in weight from birth to 6 months (both p=0.01). Those with 6-month follow-up data (n=46) were approximately one week younger in gestational age and had a slightly lower birthweight compared to the full cohort (Table S1). Among infants with 6-month weight, mothers of male infants were 5.4 years younger than mothers of female infants (p=0.002) (Table S2).

Associations Between TRAP and Ambient Air Pollution Exposures with Adipokines

TRAP exposures during pregnancy were positively associated with adipokines in cord blood (Table 2). A 1-SD (2 ppb) increase in non-freeway NOx was associated with a 33% higher leptin level (p=0.01), 9% higher HMW adiponectin level (p=0.07), and 23% higher L/A ratio (p=0.05). Cord blood leptin levels were higher in mothers who lived near major roadways. Compared to mothers who lived >300 meters from major roadways, cord leptin levels were 71%, 47%, 29% higher in those who lived <75 m, 75–150 m, and 150–300 m from major roadways, respectively (P_{trend}=0.05). These findings were consistent with the CALINE4 modeled non-freeway NOx, which was significantly and positively associated with cord leptin levels. Ambient air pollutants were not significantly associated with adipokines. For example, a 1-SD increase in ambient O_3 (26 ppb) was associated with a 15% higher HMW adiponectin level (p=0.07), but this finding did not reach statistical significance (Table S3). Lastly, associations between ambient and TRAP exposures with cord blood adipokines were not modified by maternal pre-pregnancy BMI (data not shown).

Associations Between Adipokines with Infant Weight

Cord blood adipokines were associated with increased weight and weight-for-age z-score change from birth to 6 months (Table 3). As an example, a 1-SD increase in leptin (10 ng/ml) and a 1-SD increase in the L/A ratio (0.5) was associated with a 0.21 kg (p=0.08) and 0.18 kg (p=0.09) increase in infant weight from one to 6 months. These associations were supported by the observation that a 1-SD increase in leptin and the L/A ratio was associated with a 0.25 (p=0.07) and 0.22 (p=0.07) change in weight-for-age z-score, respectively. Associations between leptin with change in infant weight varied by sex (interaction p=0.03). Higher cord blood leptin levels were associated with an increase in infant weight from birth to 6 months. For example, from birth to 6 months, a 1-SD (10 ng/ml) increase in cord blood leptin was associated with a 0.62 kg increase in weight in females (p=0.02) and a 0.11 kg increase in weight (p=0.48) in males. The interaction between sex and HMW adiponectin was non-significant (p=0.20), yet stratification revealed that a 1-SD (8 ug/ml) increase in cord blood HMW adiponectin was significantly associated with a 0.53 kg increase in weight in females (p=0.02) and a 0.07 kg decrease in weight in males (p=0.68) from birth to 6 months. As shown in Table 3, sex-specific results observed in infant weight change were

consistent with change in infant weight-for-age z-score from birth to 6 months and larger effect sizes were observed without adjustment for birthweight (Table 3). Associations were similar when excluding preterm infants and after adjusting for birthweight-for-gestational age z-score (Table S4–5). Leptin and HMW adiponectin levels in cord blood were not associated with infant birthweight (Table S6) and were not modified by infant sex (interactions ≥0.10).

Discussion

Our results demonstrate that TRAP exposures during pregnancy were associated with higher cord blood levels of leptin, HMW adiponectin, and the L/A ratio. These findings suggest that prenatal TRAP exposure may have the potential to alter cord blood adipokine levels. Consistent with previous work (11, 12), the current study found evidence that cord blood adipokine levels were associated with increased growth from birth to 6 months of age. However, these associations were only observed among female infants, suggesting that cord blood levels of leptin, HMW adiponectin, and the L/A ratio may have sex-specific effects on changes in body weight. Findings from this study add to the growing body of literature that suggests that increased prenatal exposure to TRAP may alter cord blood levels of adipokines, which have the potential to contribute to infant growth and have implications for future obesity risk.

One previous study has investigated associations between air pollution exposure during pregnancy with cord blood levels of leptin and adiponectin. This study utilized land use regression to estimate prenatal, residential NO_2 exposures and kernel density functions were incorporated to capture the fine-scale variation due to vehicle emissions. The authors found that 13.6 ppb increase in NO_2 exposure, a marker of primary traffic emissions, was associated with a 12% and 13% higher cord blood leptin and adiponectin levels, respectively (14). Consistent with these findings, we found that a 2 ppb increase in non-freeway NOx exposure was associated with a 33% higher leptin and a 9% higher HMW adiponectin in cord blood. Lastly, cord blood leptin and HMW adiponectin were positively associated with non-freeway NOx but not freeway or total NOx. These results suggest that residential proximity to smaller, busy roadways may represent exposures to non-exhaust particles (e.g., brake wear) that increase maternal adipokine levels. It is also possible that non-freeway NOx exposures capture other neighborhood characteristics (e.g., housing, income) that introduce some residual confounding. Future studies should incorporate personal monitoring to examine which specific components of TRAP are associated with increased levels of cord blood adipokines.

Studies suggest that early-life exposures to environmental pollutants contribute to obesity (5–7), yet few studies have examined prenatal air pollution exposure with risk for childhood obesity. One study found that mothers exposed to the highest category of polycyclic aromatic hydrocarbons, a family of air pollutants generated during incomplete combustion, had children with a greater risk of obesity at age seven (9). In a U.S. cohort, higher third trimester traffic-related air pollution exposure (e.g., black carbon, roadway proximity) was associated with reduced fetal growth and more rapid postnatal weight gain (24). These studies suggest that increased TRAP exposures may establish a “thrifty phenotype” that

contributes to future increased weight gain and adiposity (25). The current study builds upon this work by demonstrating that cord blood adipokines were associated with increased prenatal TRAP exposure as well as infant change in weight and weight-for-age z-score in females. Furthermore, removal of preterm infants strengthened these associations. One possible explanation for this finding is that preterm infants start at a lower birthweight and have an overall slower rate of growth, thereby reducing the effect size in the entire sample over the 6-month period. While the exact mechanisms underlying these associations are unknown, increased TRAP exposure may contribute to increased production of placental leptin (26) through lower placental leptin promoter methylation (27) and/or increased production of adiponectin from maternal adipocytes (28). Leptin and its receptors are present in fetal tissues and contribute to infant development during the pre- and neonatal periods (26). Additionally, adiponectin is thought to be involved in the expansion of fat mass following birth and enhance the growth-promoting effects of insulin (29).

The strengths of this study include the examination of cord blood adipokines in relation to residential estimates of prenatal TRAP and ambient air pollution exposures in low-income and predominately Hispanic pregnant women who, on average, experience some of the highest exposure burden in urban Los Angeles, California (30). This study is also strengthened by the examination of adipokines with infant birthweight and change in weight from birth to 6 months. Additionally, important confounder information was abstracted from medical records and was not subject to potential self-report errors. Despite the study strengths, it may be limited by potential exposure misclassification of air pollutants since information about work locations, time spent at home, and residential mobility during pregnancy was unavailable. However, exposure estimates were based on residential addresses and any exposure misclassification would likely result in systematic non-differential exposure estimate errors that would diminish any observed associations. This study is also limited by the sample size available to assess infant growth by 6 months of age, which may have decreased our power to detect associations between infant weight and cord blood adipokines among males. Future studies should examine these associations in a larger sample and would benefit from the inclusion of measures of adipokines as well as body fat percent at various developmental stages. Finally, findings from this study may only be generalizable to Hispanic mothers mostly of a lower socio-economic status (SES), yet these findings have significant public health implications since lower SES and minority communities have some of the largest environmental toxin burden and suffer from the greatest health disparities in maternal and childhood obesity (1, 30).

The present study found that higher prenatal TRAP exposure may alter cord blood levels of leptin and HMW adiponectin. This work also identified associations between these cord blood adipokines with infant growth from birth to 6 months of age among female infants. These findings suggest that prenatal TRAP exposures may increase childhood obesity risk by altering levels of cord blood adipokines that have been shown to alter postnatal growth. Future studies should validate and expand upon these results by investigating whether increased maternal TRAP exposure leads to increased cord blood adipokines, thereby contributing to alterations in infant weight, body composition, and fat distribution. In conclusion, results from this study support the growing body of literature that has found

important associations between environmental exposures and maternal health, which may have significant implications for the risk of childhood obesity in vulnerable populations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Grants

This work was supported by the Southern California Environmental Health Sciences Center (P30ES007048) funded by the National Institute of Environmental Health Sciences (NIEHS) (PI Gilliland), NIEHS grant numbers R01ES021801 (PI Gilliland) and R21ES025870 (PI Breton), the Hastings Foundation, the USC Diabetes and Obesity Research Institute (DORI) Pilot Funds, NIEHS grant number K99ES027853 (PI Alderete), and the Ruth L. Kirschstein National Research Service Award (NRSA) Institutional Research Training Grant (T32ES013678).

References

1. Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of childhood and adult obesity in the United States, 2011–2012. JAMA. 2014; 311:806–814. [PubMed: 24570244]
2. Skinner AC, Perrin EM, Skelton JA. Prevalence of obesity and severe obesity in US children, 1999–2014. Obesity. 2016; 24:1116–1123. [PubMed: 27112068]
3. La Merrill M, Birnbaum LS. Childhood obesity and environmental chemicals. Mt Sinai J Med. 2011; 78:22–48. [PubMed: 21259261]
4. McConnell R, Shen E, Gilliland FD, et al. A Longitudinal Cohort Study of Body Mass Index and Childhood Exposure to Secondhand Tobacco Smoke and Air Pollution: The Southern California Children's Health Study. Environ Health Perspect. 2014; 123:360–366. [PubMed: 25389275]
5. Jerrett M, McConnell R, Wolch J, et al. Traffic-related air pollution and obesity formation in children: a longitudinal, multilevel analysis. Environ Health. 2014; 13:49. [PubMed: 24913018]
6. Dong GH, Qian ZM, Liu MM, et al. Ambient air pollution and the prevalence of obesity in chinese children: The seven northeastern cities study. Obesity. 2014; 22:795–800.
7. Toledo-Corral CM, Alderete TL, Habre R, et al. Effects of air pollution exposure on glucose metabolism in Los Angeles minority children. Pediatr Obes. 2016 Epub ahead of print.
8. Dietz WH. Critical periods in childhood for the development of obesity. The American Journal of Clinical Nutrition. 1994; 59:955–959. [PubMed: 8172099]
9. Rundle A, Hoepner L, Hassoun A, et al. Association of childhood obesity with maternal exposure to ambient air polycyclic aromatic hydrocarbons during pregnancy. Am J Epidemiol. 2012; 175:1163–1172. [PubMed: 22505764]
10. Mao G, Nachman RM, Sun Q, et al. Individual and Joint Effects of Early-Life Ambient PM2.5 Exposure and Maternal Pre-Pregnancy Obesity on Childhood Overweight or Obesity. Environ Health Perspect. 2016 Epub ahead of print.
11. Tsai PJ, Yu CH, Hsu SP, et al. Cord plasma concentrations of adiponectin and leptin in healthy term neonates: positive correlation with birthweight and neonatal adiposity. Clin Endocrinol (Oxf). 2004; 61:88–93. [PubMed: 15212649]
12. Mantzoros CS, Rifas-Shiman SL, Williams CJ, Fargnoli JL, Kelesidis T, Gillman MW. Cord blood leptin and adiponectin as predictors of adiposity in children at 3 years of age: a prospective cohort study. Pediatrics. 2009; 123:682–689. [PubMed: 19171638]
13. Marchini G, Fried G, Ostlund E, Hagenäs L. Plasma leptin in infants: relations to birth weight and weight loss. Pediatrics. 1998; 101:429–432. [PubMed: 9481009]
14. Lavigne E, Ashley-Martin J, Dodds L, et al. Air Pollution Exposure During Pregnancy and Fetal Markers of Metabolic function: The MIREC Study. Am J Epidemiol. 2016; 183:842–851. [PubMed: 27026336]

15. McConnell R, Berhane K, Yao L, et al. Traffic, Susceptibility, and Childhood Asthma. Environ Health Perspect. 2006; 114:766–772. [PubMed: 16675435]
16. Gauderman WJ, Vora H, McConnell R, Berhane K. Effect of exposure to traffic on lung development from 10 to 18 years of age: a cohort study. The Lancet. 2007; 369:571–7.
17. Benson PE. A review of the development and application of the CALINE3 and 4 models. Atmospheric Environment Part B Urban Atmosphere. 1992; 26:379–390.
18. Franklin M, Vora H, Avol E, et al. Predictors of intra-community variation in air quality. J Expo Sci Environ Epidemiol. 2012; 22:135–147. [PubMed: 22252279]
19. Wong DW, Yuan L, Perlin SA. Comparison of spatial interpolation methods for the estimation of air quality data. J Expo Sci Environ Epidemiol. 2004; 14:404–415.
20. Finucane FM, Luan J, Wareham NJ, et al. Correlation of the leptin:adiponectin ratio with measures of insulin resistance in non-diabetic individuals. Diabetologia. 2009; 52:2345–2349. [PubMed: 19756488]
21. Hara K, Horikoshi M, Yamauchi T, et al. Measurement of the high-molecular weight form of adiponectin in plasma is useful for the prediction of insulin resistance and metabolic syndrome. Diabetes Care. 2006; 29:1357–1362. [PubMed: 16732021]
22. Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. J Health Soc Behav. 1983; 24:385–396. [PubMed: 6668417]
23. Proctor, BD., Semega, JL., Kollar, MA. Income and Poverty in the United States: 2015. 2016. http://www.census.gov/content/dam/Census/library/publications/2016/demo/p60-256.pdf
24. Fleisch AF, Rifas-Shiman SL, Koutrakis P, et al. Prenatal exposure to traffic pollution: associations with reduced fetal growth and rapid infant weight gain. Epidemiology. 2015; 26:43–50. [PubMed: 25437317]
25. Hales CN, Barker DJ. The thrifty phenotype hypothesis. Br Med Bull. 2001; 60:5–20. [PubMed: 11809615]
26. Hoggard N, Haggarty P, Thomas L, Lea RG. Leptin expression in placental and fetal tissues: does leptin have a functional role? Biochem Soc Trans. 2001; 29:57–63. [PubMed: 11356127]
27. Saenen ND, Vrijens K, Janssen BG, et al. Lower Placental Leptin Promoter Methylation in Association with Fine Particulate Matter Air Pollution during Pregnancy and Placental Nitrosative Stress at Birth in the ENVIRONAGE Cohort. Environ Health Perspect. 2017; 125:262–268. [PubMed: 27623604]
28. Shehzad A, Iqbal W, Shehzad O, Lee YS. Adiponectin: Regulation of its production and role in human diseases. Hormones. 2012; 11:6–18.
29. Mantzoros C, Petridou E, Alexe D-M, et al. Serum adiponectin concentrations in relation to maternal and perinatal characteristics in newborns. European Journal of Endocrinology. 2004; 151:741–746. [PubMed: 15588241]
30. OEHHA. Analysis of Race/Ethnicity - California Communities Environmental Health Screening Tool (CalEnviroScreen 2.0). 2014 Aug 14.:1–7.

Table 1

Maternal and Infant Characteristics

N=136	Mean ± SD Entire Cohort	Mean ± SD Males (N=70)	Mean ± SD Females (N=66)	p-value
Maternal Characteristics				
Age (years)	27.1 ± 6.4	25.4 ± 5.6	28.7 ± 6.7	**0.002**
Pre-Pregnancy BMI (kg/m^2)	29.1 ± 7.8	28.8 ± 7.0	29.3 ± 8.7	0.70
Hispanic / Other, %Hispanic	123 / 13, 90.4%	64/5, 91.4%	59/7, 89.4%	0.69
Nulliparous	62, 45.6%	39, 55.7%	23, 34.8%	**0.01**
Annual Family income (N, %)				
Less than $15,000	45, 33.1%	25, 35.7%	20, 30.4%	0.28
$15,000 – $29,999	36, 26.5%	15, 21.5%	21, 31.8%	
$30,000 – $49,999	7, 5.2%	5, 7.1%	2, 3.0%	
$50,000 to $99,999	2, 1.5%	0, 0%	2, 3.0%	
Don't know	46, 33.8%	25, 35.7%	21, 31.8%	
Maternal Education (N, %)				
Less than 12th grade	48, 35.3%	22, 31.4%	26, 39.4%	0.73
Completed grade 12	49, 36.0%	28, 40.0%	21, 31.8%	
Some college or technical school	32, 23.5%	17, 24.3%	15, 22.7%	
Completed college or higher	7, 5.2%	3, 4.3%	4, 6.1%	
Infant Characteristics				
Male / Female, %Male	70/66, 51.5%			
Gestational Age (weeks)	38.4 ± 2.2	38.6 ± 1.7	38.1 ± 2.7	0.18
Birthweight (kg)	3.2 ± 0.6	3.3 ± 0.4	3.1 ± 0.6	0.14
Weight at 6 Months (kg)[a]	7.7 ± 1.1	7.9 ± 0.9	7.1 ± 1.1	**0.01**
6-Month Weight Change (kg)[a]	4.4 ± 0.8	4.7 ± 0.7	4.1 ± 0.9	**0.01**
z-score at Birth	−0.4 ± 1.0	−0.4 ± 0.8	−0.5 ± 1.2	0.76
z-score at 6 Months[a]	−0.4 ± 1.2	−0.3 ± 0.9	−0.4 ± 1.3	0.75
6-Month z-Score Change[a]	0.2 ± 1.0	0.3 ± 0.8	0.3 ± 1.2	0.96
Cord Blood Adipokines				
HMW Adiponectin (ug/ml)[b]	22.5 ± 7.8	23.5 ± 8.1	21.1 ± 7.3	0.40
Leptin (ng/ml)[c]	11.8 ± 10.6	11.6 ± 10.1	12.0 ± 11.1	0.38
Leptin / Adiponectin (L/A) Ratio[c]	0.58 ± 0.56	0.55 ± 0.51	0.62 ± 0.61	0.71
Traffic-Related Air Pollution				
Freeway NOx	10.4 ± 8.4	10.4 ± 9.1	10.4 ± 7.5	0.37
Non-Freeway NOx	3.3 ± 1.6	3.3 ± 1.5	3.3 ± 1.7	0.93
Total NOx	13.7 ± 8.7	13.6 ± 9.4	13.7 ± 7.9	0.46
Ambient Air Pollutants				
NO_2 (ppb)	18.7 ± 2.2	18.5 ± 2.1	18.9 ± 2.3	0.93
O_3 (ppb)	25.4 ± 2.5	25.6 ± 2.4	25.2 ± 2.6	0.56
$PM_{2.5}$ (ug/m^3)	12.3 ± 0.8	12.4 ± 0.7	12.3 ± 0.8	0.23

N=136	Mean ± SD Entire Cohort	Mean ± SD Males (N=70)	Mean ± SD Females (N=66)	p-value
PM_{10} (ug/m^3)	31.5 ± 2.0	31.5 ± 1.9	31.4 ± 2.2	0.21

Maternal and infant characteristics as well as prenatal exposures are shown as mean with SD unless otherwise noted.

[a]Average infant weight at 6 months (N=46).

Sample sizes correspond to [b]N=136 and [c] N=135.

P-values for adipokines, traffic-related air pollution (TRAP), and ambient air pollutants were derived from t-tests using log-transformed variables. Prenatal exposures to ambient and TRAP in the nine months prior to delivery are shown as mean with standard deviation.

Table 2

Association Between Prenatal TRAP Exposures and Adipokines in Cord Blood

	HMW Adiponectin[b]		Leptin[c]		L/A Ratio[c]	
	% diff	95% CI	% diff[b]	95% CI	% diff[b]	95% CI
Traffic-Related Air Pollution						
Freeway NOx	5.0	−2.4, 12.8	2.8	−12.4, 20.5	−2.1	−16.3, 14.4
Non-Freeway NOx	8.9	−1.0, 19.8	**33.4**	**8.9, 63.5**	**22.7**	**0.2, 50.3**
Total NOx	5.8	−1.3, 13.6	6.7	−8.5, 24.4	0.75	−13.4, 17.2
Distance to Freeways/Highways[a]						
<500 m	15.1	−4.4, 38.5	23.5	−18.3, 86.6	7.1	−28.5, 60.3
500–1000 m	−12.0	−29.5, 9.8	18.3	−28.4, 95.6	32.6	−18.9, 116.8
1000–1500 m	−5.6	−23.9, 17.1	27.6	−21.0, 106.3	35.0	−15.6, 115.9
>1500 m	*Ref*		*Ref*		*Ref*	
Distance to Major Roadways[a]						
<75 m	20.6	−3.8, 51.1	**71.1**	**4.8, 179.3**	41.9	−12.5, 130.3
75–150 m	4.2	−14.6, 27.2	47.3	−4.4, 127.1	41.3	−7.8, 116.6
150–300 m	21.2	−1.4, 48.9	29.0	−17.7, 102.3	5.1	−32.6, 63.8
>300 m	*Ref*		*Ref*		*Ref*	

Estimated exposures to traffic-related air pollution (TRAP) correspond to the 9-month average prior to delivery. Estimated percent difference with 95% confidence intervals (CI) in adipokines for a 1-SD or category difference in exposure. Models were adjusted for maternal age, gestational age, race/ethnicity, parity, annual family income, and maternal pre-pregnancy BMI. Distance to major freeways/highways as well as distance to major roadways are shown in meters. Sample sizes in each category (from furthers to closest distance) are as follows:

[b] Freeways/highways (N=46, 25, 26, and 39) and major roadways (N=25, 40, 38, and 33),

[c] Freeways/highways (N=46, 24, 26, and 39) and major roadways (N=25, 40, 37, and 33).

Table 3

Associations between Adipokines in Cord Blood and Infant Growth from Birth to 6 Months with and Without Adjustment for Birthweight

Associations between Adipokines and Infant Growth with Adjustment for Birthweight

	Males + Females[a]		Males[a]		Females[a]		
	Weight Change		Weight Change		Weight Change		
Adipokines	**β**	**95% CI**	**β**	**95% CI**	**β**	**95% CI**	**$p_{interaction}$**
HMW Adiponectin (ug/ml)	0.01	−0.25, 0.27	−0.07	−0.41, 0.27	0.53	0.08, 0.98	0.20
Leptin (ng/ml)	0.21	−0.03, 0.45	0.11	−0.22, 0.44	0.62	0.09, 1.15	0.03
L/A Ratio	0.18	−0.04, 0.41	0.11	−0.18, 0.39	0.42	−0.12, 0.97	0.09

	Males + Females[a]		Males[a]		Females[a]		
	z-score Change		z-score Change		z-score Change		
Adipokines	**β**	**95% CI**	**β**	**95% CI**	**β**	**95% CI**	**$p_{interaction}$**
HMW Adiponectin (ug/ml)	0.04	−0.26, 0.33	−0.07	−0.42, 0.30	0.61	0.06, 1.17	0.22
Leptin (ng/ml)	0.25	−0.02, 0.53	0.09	−0.26, 0.44	0.74	0.09, 1.39	0.02
L/A Ratio	0.22	−0.04, 0.47	0.10	−0.20, 0.41	0.52	−0.13, 1.18	0.07

Associations between Adipokines and Infant Growth Without Adjustment for Birthweight

	Males + Females		Males		Females		
	Weight Change		Weight Change		Weight Change		
Adipokines	**β**	**95% CI**	**β**	**95% CI**	**β**	**95% CI**	**$p_{interaction}$**
HMW Adiponectin (ug/ml)	0.08	−0.16, 0.31	−0.05	−0.37, 0.27	0.55	0.20, 0.89	0.07
Leptin (ng/ml)	0.24	0.01, 0.45	0.04	−0.24, 0.31	0.71	0.31, 1.11	0.004
L/A Ratio	0.19	−0.02, 0.40	0.05	−0.20, 0.31	0.53	0.10, 0.96	0.03

	Males + Females		Males		Females		
	z-score Change		z-score Change		z-score Change		
Adipokines	**β**	**95% CI**	**β**	**95% CI**	**β**	**95% CI**	**$p_{interaction}$**
HMW Adiponectin (ug/ml)	0.13	−0.16, 0.42	0.01	−0.36, 0.38	0.63	0.16, 1.09	0.16
Leptin (ng/ml)	0.34	0.07, 0.61	0.11	−0.20, 0.42	0.91	0.39, 1.43	0.01
L/A Ratio	0.26	0.004, 0.52	0.09	−0.20, 0.38	0.71	0.15, 1.26	0.02

Estimated effects (β) with 95% confidence intervals (CI) are shown for a 1-SD increase in adipokines. Weight change was defined as the difference in weight between birth and 6 months (kg). The sex-specific weight-for-age z-score calculated based on CDC 2000 growth chart. Models were adjusted for maternal age, gestational age, race/ethnicity, sex (where appropriate), parity, maternal pre-pregnancy BMI, and

[a]birthweight as indicated. $P_{interaction}$ tests effect modification of sex. Sample sizes for males/females were HMW adiponectin (n=23/23), leptin (n=22/23), and leptin / HMW adiponectin (L/A) ratio (n=22/23).