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Early pregnancy particulate matter exposure, pre-pregnancy adiposity and risk of gestational diabetes mellitus in Finnish primiparous women: An observational cohort study

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A R T I C L E I N F O

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A B S T R A C T

Aims: To evaluate the association between the exposure of particulate matter with an aerodynamic diameter of $\leq 2.5\mu m$ ($PM_{2.5}$) and with an aerodynamic diameter of $\leq 10\mu m$ (PM_{10}) over the first trimester and the risk of gestational diabetes mellitus (GDM), and to assess whether maternal pre-pregnancy body mass index (BMI) modified the GDM risk.

Methods: All Finnish primiparous women without previously diagnosed diabetes who delivered between 2009 and 2015 in the city of Vantaa, Finland, composed the study cohort (N = 6189). Diagnosis of GDM was based on a standard 75 g 2-hour oral glucose tolerance test. The average daily concentration of $PM_{2.5}$ and PM_{10} over the first trimester was calculated individually for each woman. The relationship between exposure of $PM_{2.5}$ and PM_{10} and GDM was analyzed with logistic models.

Results: No association was observed between the average daily concentrations of $PM_{2.5}$ and PM_{10} over the first trimester and the GDM risk. When simultaneously taking BMI and PM_{10} into account both mean daily PM_{10} concentration ($p = 0.047$) and pre-pregnancy BMI ($p = 0.016$) increased GDM risk independently and an interaction ($p = 0.013$) was observed between PM_{10} concentration and pre-pregnancy BMI.

Conclusions: Even globally low PM_{10} exposure level together with elevated maternal pre-pregnancy BMI seems to increase the GDM risk.

1. Introduction

Globally during the last decade, the burden of gestational diabetes mellitus (GDM) has increased rapidly and today it is estimated that one in six pregnant women has GDM [1–3]. GDM increases the risk of both short- and long-term adverse outcomes to the pregnant woman and her

Abbreviations: BMI, body mass index; CI, confidence intervals; GDM, gestational diabetes mellitus; PM, particular matter; $PM_{2.5}$, particular matter $\leq 2.5\mu m$ in aerodynamic diameter; PM_{10}, particular matter PM $\leq 10\mu m$ in aerodynamic diameter; SD, standard deviation.

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offspring [4,5]. Classic risk factors for GDM include increased maternal childbearing age, maternal obesity, genetic predisposition for diabetes and non-Caucasian ethnicity [3,6].

In addition to the classic risk factors for GDM, it has been suggested that environmental factors such as air pollution and more specifically particulate matter (PM) may predispose for GDM [7–21]. Further, the study findings are contradictory regarding to the associations between PM and the risk for GDM varying from negative associations to no associations to positive associations [9–13,15–21]. PM is often classified by their mass concentration ($\mu g/m^3$) on the basis of their aerodynamic diameter and the most commonly used classes are PM with aerodynamic diameter 2.5 μm or less ($PM_{2.5}$) and PM with aerodynamic diameter 10 μm or less (PM_{10}) [22]. Both of them are inhalable PM. In Europe, the main sources for $PM_{2.5}$ are combustion of fuels, especially in small combustion of wood, whereas the main sources for PM_{10} are resuspension of industrial dust and soil tracked onto roads and streets the dust raised by traffic [22]. Previous studies have focused on the association between the exposure of $PM_{2.5}$ and/or PM_{10} and GDM, or on the association in different maternal age groups or the association between exposure during different periods of gestation and GDM. To the best of our knowledge, none of previous studies have evaluated whether the maternal degree of pre-pregnancy adiposity modifies the association between the exposure of $PM_{2.5}$ and/or PM_{10} and GDM.

Our study hypothesis was that increased maternal pre-pregnancy adiposity together with increased exposure of $PM_{2.5}$ /PM_{10} during the first trimester would increase the risk of GDM. The aim of this study was to evaluate the association between the exposure of $PM_{2.5}$ and/or PM_{10} during the first trimester and the risk of GDM and whether maternal degree of pre-pregnancy adiposity modified the risk of GDM in primiparous women.

2. Methods

2.1. Design, setting and population of the study

The study is an observational cohort study. The study population consists of all Finnish primiparous women without previous diagnosed diabetes mellitus who lived in the city of Vantaa, Finland, and who delivered between January 1st 2009 and December 31st 2015 (N = 6189). In 2015, the city of Vantaa located in the Helsinki metropolitan area was the fourth biggest city in Finland having 211 000 habitants. Women were defined as Finnish if they were born in Finland and their native language was Finnish or Swedish.

2.2. Data on deliveries and maternal characteristics

In Finland, each delivery hospital sends data from all live births and stillbirths from 22 gestational weeks or 500 g onwards to the Finnish Medical Birth Register kept by the Finnish Institute for Health and Welfare (THL). From this register we obtained data on women's age, status of cohabiting and smoking, pre-pregnancy weight and height, number of previous pregnancies (including induced abortions, miscarriages, and ectopic pregnancies), number of previous deliveries, number of fetuses, use of infertility treatments, and the duration of pregnancy at the day of delivery (http://www.thl.fi/en/statistics/parturients). The Finnish Medical Birth Register is considered to be of high quality [23]. Pre-pregnancy body mass index (BMI) was calculated as pre-pregnancy weight (kg) divided by height (m) squared. The conception date was calculated by reducing the duration of pregnancy from the day of delivery.

Data on women's educational attainment was obtained from Statistics Finland. Educational attainment was defined according to years of highest attained schooling (http://www.stat.fi/meta/luokitukset/koulutus/001–2016/kuvaus).

We obtained data on primiparous women's chronic diseases over three years before conception from the Finnish Social Insurance Institution (http://www.kela.fi/web/en/reimbursements-for-medicine-expenses). In Finland, medication for certain chronic diseases entitles to 65% or 100% reimbursement. For receiving reimbursement, the treating physician composes a medical certificate with the history and status observations of the person with a chronic disease. At the Finnish Social Insurance Institution, expert physicians check the certificates. If the reimbursement criteria for a chronic disease are met, the applicant receives a right to a reimbursable medication and the entitlement is entered into a nationwide register at the same time.

In Finland since 2008 according to the current care guidelines for GDM, GDM has been screened using a 75 g 2-hour oral glucose tolerance test between 24 and 28 weeks of gestation in all pregnant women, with the exception of those who are at low risk (http://www.kaypahoito.fi). Low risk nulliparous women are defined as women aged under 25 years with BMI 18.5 – 24.9 kg/m^2 and without a first-degree family history of diabetes. Further, the women with high risk are recommended to test for the first time at 12–16 weeks of gestation. High risk nulliparous women are defined as women with BMI 35 kg/m^2 or more, glucosuria, first- or second-degree family members with type 2 diabetes, continuous use of oral corticosteroid medication, or polycystic ovary syndrome. One or more pathological glucose value in the oral glucose tolerance test lead to GDM diagnosis with the following diagnostic thresholds: fasting plasma glucose ≥ 5.3 mmol/L, 1-hour glucose ≥ 10.0 mmol/L, and 2-hour glucose ≥ 8.6 mmol/L (http://www.kaypahoito.fi). Screening for GDM is mainly made in communal antenatal clinics in primary health care centers and it is free-of-charge for women.

2.3. Particulate matter exposure assessment

The ambient particulate concentrations are monitored by Helsinki Region Environmental Services Authority. In Vantaa, there has been one monitoring site operating continuously during the study period between 2008 and 2015. At this Tikkurila Neilikkatie (60.28995, 25.03953) site hourly concentrations of $PM_{2.5}$ and PM_{10} have been recorded. Monitoring has been performed according to the requirements set by the European Union Air quality directive (Directive 2008/50/EC of the European Parliament and of the Council of 2008 on ambient air quality and cleaner air for Europe). Tikkurila Neilikkatie site is located in a busy traffic environment and as such can be considered to represent rather the upper estimate of the particulate pollution in Vantaa area 250km2. Hourly concentrations of $PM_{2.5}$ and PM_{10} mass were available from April 24th 2008 to July 17th 2015. The data were downloaded from Finnish Meteorological Institute's open interface (en.ilmatieteenlaitos.fi/open-data). Based on this data, an average daily concentration of $PM_{2.5}$ and PM_{10} over the first trimester of pregnancy was calculated individually for each woman. The follow-up of daily concentration of $PM_{2.5}$ and PM_{10} was initiated at the conception date and it continued over the first trimester, thus it was possible to take account the seasonal variation.

2.4. Statistical analyses

Data are shown as means with standard deviation (SD) or counts with percentage (%). Between primiparous women without GDM and with GDM, the differences in characteristics were compared with t-test for continuous variables and with a chi-square test for categorical variables.

The relationship of GDM and PM was modeled with logistic regression adjusted for age, educational attainment and smoking. We also included into models an interaction term between PM and BMI (effect modification). For restricted cubic splines, also known as natural splines, knot locations are based on Harrell's recommended percentiles [24]. Normal distributions were evaluated graphically and with the Shapiro–Wilk W test. Stata 16.0 (StataCorp LP; College Station, Texas, USA) statistical package was used for the analysis.

3. Results

The mean age of the primiparous women was 28.5 (SD 5.2) years and mean pre-pregnancy BMI was 24.1 (SD 4.6) kg/m^2. Further, of the women 18.5% were smokers and 2.5% had chronic pulmonary diseases. The prevalence of GDM was 16.2%. Table 1 shows the characteristics of the 6 189 primiparous women divided into women without and with GDM.

In the city of Vantaa, Finland, between April 24th 2008 and July 17th 2015, mean daily concentration of $PM_{2.5}$ was 7.9 (SD 1.8) μg/m^3 and, respectively, mean daily concentration of PM_{10} was 14.6 (SD 4.0) μg/m^3.

Over the first trimester mean daily concentration of $PM_{2.5}$ was 7.95 (SD 1.80) μg/m^3 in primiparous women without GDM and 7.89 (SD 1.83) μg/m^3 in women with GDM, respectively ($p = 0.32$). The corresponding mean daily concentration of PM_{10} in women without GDM was 14.68 (SD 3.98) μg/m^3 and in women with GDM 14.48 (SD 3.99) μg/m^3 ($p = 0.16$), respectively. The distribution of GDM according to different $PM_{2.5}$ and PM_{10} concentrations is shown in Fig. 1.

The Odds Ratio (OR) for GDM was 0.98; (95% confidence interval [CI] 0.91–1.05) per one SD increase in $PM_{2.5}$ after adjustment for age, BMI, smoking and educational attainment. The corresponding adjusted OR for GDM per one SD increase in PM_{10} was 0.95; (95% CI 0.89–1.03). Impact of mean daily concentration of $PM_{2.5}$ and PM_{10} over the first trimester and pre-pregnancy BMI and their interaction on the risk for GDM adjusted for age, smoking and educational attainment is shown in Fig. 2. Over the first trimester mean daily PM_{10} concentration and pre-pregnancy BMI both independently increased the risk for GDM (p-value for mean daily PM_{10} concentration $p = 0.047$ and for pre-pregnancy BMI $p = 0.016$) and mean daily PM_{10} concentration and pre-pregnancy BMI showed an interaction ($p = 0.013$), all adjusted for age, smoking and educational attainment. No significant interaction ($p = 0.14$) was observed with mean daily $PM_{2.5}$ concentration over the first trimester and pre-pregnancy BMI on the risk for GDM.

4. Discussion

As expected mean daily concentrations of $PM_{2.5}$ and PM_{10} were low and the prevalence of GDM was high. No association was observed between the exposure of $PM_{2.5}$ and PM_{10} over the first trimester and the risk for GDM. Simultaneously taking into account maternal pre-pregnancy adiposity and PM_{10}, we found that maternal pre-pregnancy adiposity together with increasing concentrations of PM_{10} over the first trimester showed a positive association with GDM risk.

According to our study findings from the urban area of southern Finland, mean daily concentrations of $PM_{2.5}$, 7.9 μg/m^3, and PM_{10}, 14.6 μg/m^3, were low. These findings are in line with the WHO reports that in the European urban area mean concentration of $PM_{2.5}$ is between 15 and 20 μg/m^3, and mean concentration of PM_{10} is between 22 and 43 μg/m^3, respectively, and in addition in high income areas of Europe these concentrations are even lower [22]. We found a high prevalence of GDM, 16%, in primiparous Finnish women. This study finding is in concordance with data on the nationwide GDM prevalence 21% in Finland in 2019 including both primiparous and multiparous women (http://urn.fi/URN:NBN:fi-fe2020112092125). Commonly in Europe the prevalence of GDM is lower with an estimate of 6% [25]. In Finland since 2008, screening for GDM has been comprehensive according to the recommendations of current care guidelines for GDM (http://www.kaypahoito.fi), which explains at least partly the differences in the prevalence rates. Our previous study findings from the same cohort showed no association between the month of conception and risk of GDM [26].

We observed no association between the exposure of $PM_{2.5}$ and PM_{10} during the first trimester and the risk for GDM in primiparous women. Regarding the association between exposure of $PM_{2.5}$ during the first trimester and the risk for GDM, our study findings are in line with a U.S. and China study observations in primiparous women as well as with some other studies including both primiparous and multiparous women [9,10,14,15,17,21]. Further, some studies reported a positive association between the exposure of $PM_{2.5}$ during pregnancy and GDM risk [11,20,21]. Our study observation of no association between the exposure of PM_{10} over the first trimester and the risk for GDM in primiparous women endorses study findings from studies from the U.S., China and Taiwan [10,12,17]. Interestingly, there is also reports on an inverse association between the exposure of PM_{10} over the first trimester and the risk of GDM [14]. The reasons for these contradictory findings in the literature are not know but could be due to study design, sample sizes, geographical location of the study as well as measured levels of exposure.

The novelty of this study was to assess whether maternal pre-pregnancy BMI modifies the association between the exposure of PM over the first trimester and the risk for GDM. We found a positive association with maternal pre-pregnancy BMI together with an increasing exposure of PM_{10} over the first trimester and the risk of GDM.

Several studies have reported an association between exposure to PM and precursors of GDM including insulin resistance, dyslipidemia and systemic metabolic dysfunction [19,27–34]. In addition, it has been shown that there is an association between air pollution and elevated levels of C-reactive protein in healthy adults, in people with diabetes as well in women with GDM [19,35–38]. C-reactive protein is one of the markers for systemic inflammation and elevated levels of C-reactive protein are associated with gestational glucose intolerance [39]. Further, in animal studies it has been observed that diet-induced obesity promotes the influence of PM on diabetes risk [40,41].

Study strengths and limitations. Our study cohort from the city of Vantaa, Finland, is large and comprehensive including all Finnish primiparous women delivering over seven years. Diagnosis of GDM is trustworthy on the basis of a 75 g standard 2-hour oral glucose tolerance test and the recommendations for GDM screening have been the same during the whole study period. Data on maternal pre-pregnancy BMI based on data from antenatal clinics, which are free of-charge for women and, in practice, every pregnant woman use the service of antenatal clinics. The register data from the Finnish Medical Birth Register, Statistics Finland, the Finnish Social Insurance Institution, and Finnish Meteorological Institute are comprehensive. Average daily concentration of $PM_{2.5}$ and PM_{10} over the first trimester of pregnancy was

Table 1
Characteristics of the primiparous women divided into women without and with GDM.

	Women without GDM N = 5186	Women with GDM N = 1003	P-value
Age (years), mean (SD)	28.2 (5.1)	30.0 (5.2)	< 0.001
Cohabiting, n (%)	4108 (79.2)	824 (82.2)	0.034
Smokers*, n (%)	958 (18.5)	184 (18.3)	0.92
Years of education, mean (SD)	13.5 (2.6)	13.5 (2.4)	0.96
Pre-pregnancy BMI (kg/m^2) mean (SD)	23.5 (4.1)	27.0 (5.7)	< 0.001
Previous pregnancies**, n (%)			0.016
None	4186 (80.7)	774 (77.2)	
1	712 (13.7)	154 (15.4)	
≥ 2	288 (5.6)	75 (7.5)	
Fertility treatment, n (%)	422 (8.1)	121 (12.1)	< 0.001
Number of fetuses ≥ 2, n (%)	64 (1.2)	19 (1.9)	0.096
Chronic diseases, n (%)			
Pulmonary diseases	119 (2.3)	38 (3.8)	0.006
Rheumatoid diseases	38 (0.7)	17 (1.7)	0.003
Inflammatory bowel diseases	31 (0.6)	9 (0.9)	0.28
Hypertension	2 (0.0)	3 (0.3)	0.033

BMI = body mass index; GDM = gestational diabetes mellitus; SD = standard deviation.

* including those who quitted during the first trimester.

** including induced abortions, miscarriages, and ectopic pregnancies.

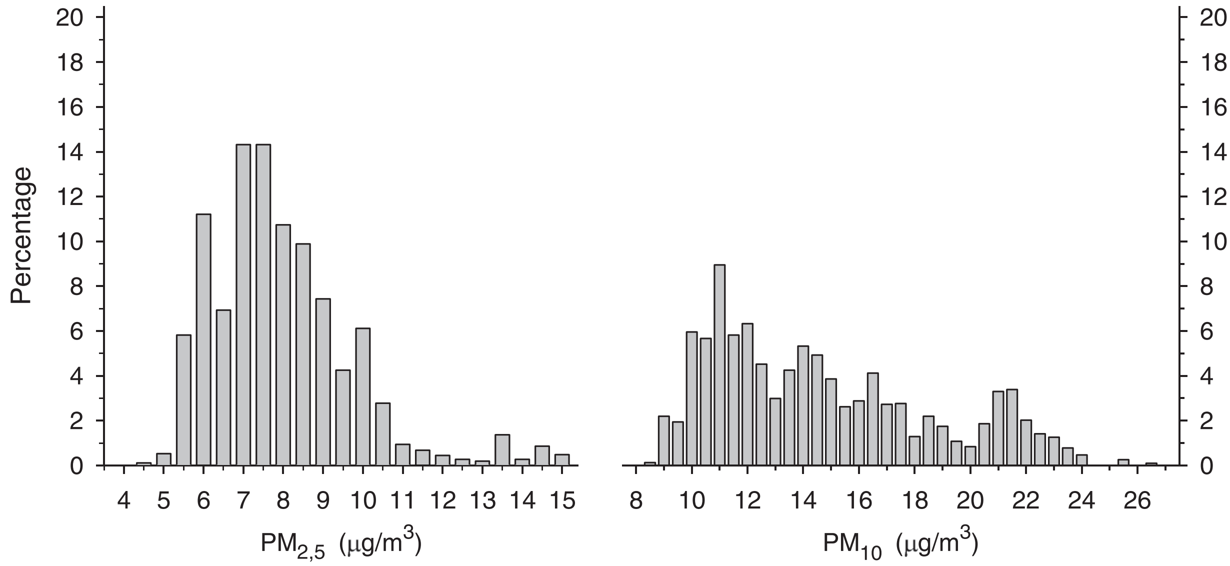

Fig. 1. Distribution of gestational diabetes in different mean daily $PM_{2.5}$ and PM_{10} concentrations. The mean concentration of $PM_{2.5}$ and PM_{10} over the first trimester of pregnancy was calculated individually for each woman. $PM_{2.5}$ =particulate matter with aerodynamic diameter under 2.5 μm or less; PM_{10} =particulate matter with aerodynamic diameter under 10 μm or less.

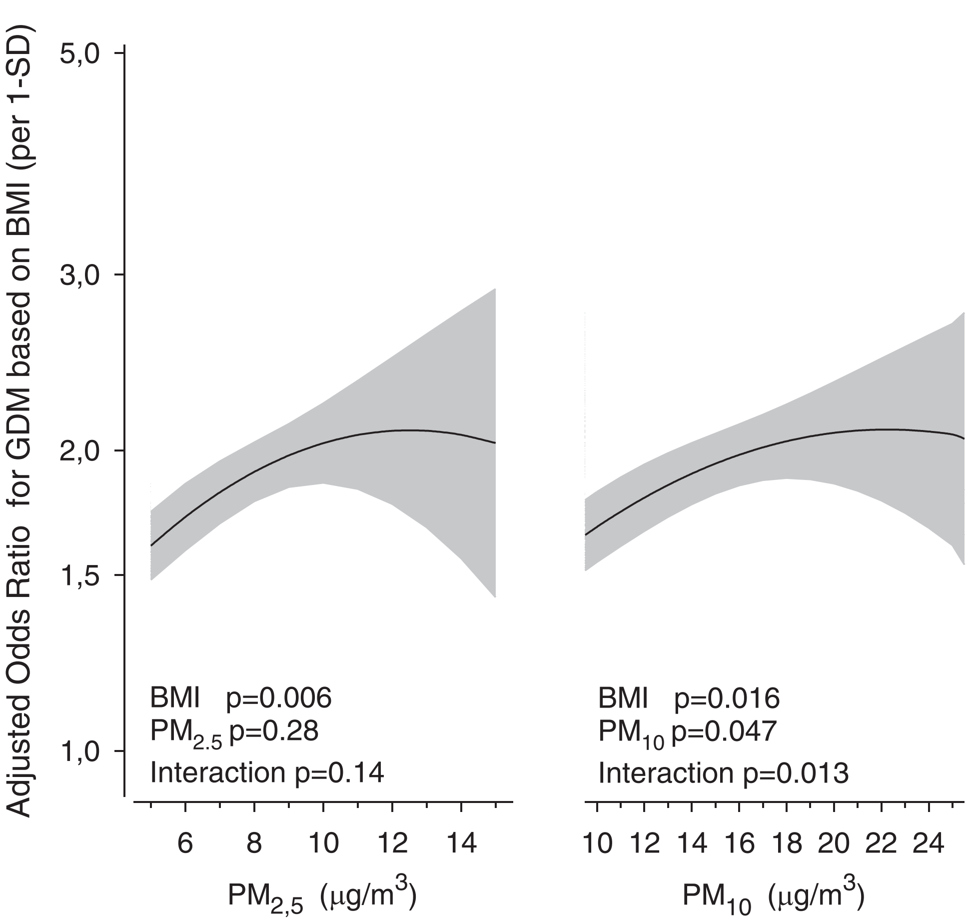

Fig. 2. Impact of mean concentration of $PM_{2.5}$ and PM_{10} over the first trimester and pre-pregnancy BMI and their interaction on the risk for GDM in primiparous women adjusted for age, smoking and educational attainment. The mean concentration of $PM_{2.5}$ and PM_{10} over the first trimester of pregnancy was calculated individually for each woman. The solid line illustrates adjusted Odds Ratio for GDM based on BMI (per 1-SD) and shaded area 95% confidence intervals. The Odds Ratios were derived from a 4-knot-restricted cubic splines logistic models. BMI=body mass index; GDM=gestational diabetes mellitus; $PM_{2.5}$ =particulate matter with aerodynamic diameter under 2.5 μm or less; PM_{10} =particulate matter with aerodynamic diameter under 10 μm or less.

calculated individually for each woman. In Finland, every person has a unique personal identification number. With the personal identification number, it is possible to combine the register data from several administrative registers on a personal level. There are also some study limitations. Like any register-based study, we are missing information on potential confounding factors such as physical activity, diet and sleeping patterns as well as the study participants' time spent outside the city of Vantaa, Finland. Although our study cohort was large and the follow-up time was long, the study observations should be verified within larger cohorts. Further, the study was performed in one city and all participants were Finnish-born, so there is limited generalization.

5. Conclusions

In a high-income European area, the mean daily concentrations of $PM_{2.5}$ and PM_{10} were low and no linear association was found between the exposure of $PM_{2.5}$ and/or PM_{10} over the first trimester and the risk of GDM in primiparous women. However, an increasing maternal pre-pregnancy BMI and increasing exposure of PM_{10} elevate the risk of GDM. Thus, reducing the burden of GDM will require multipronged public health strategies including reducing exposure to air pollution.

Declarations

Ethics approval and consent to participate: The study has been approved by the ethics committee of the Hospital District of Helsinki and Uusimaa, Finland (356/13/03/03/2015, 2 November 2015), and the health authority of the city of Vantaa, Finland. Finnish Institute for Health and Welfare (THL), Social Insurance Institution, and Statistics Finland has given permission to use register data in the study. Informed consents were not required because this is an observational cohort study based on register data and no study participants were contacted.

Consent for publication

Not applicable.

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Authors' contributions

MKL wrote the manuscript. MKL, HK and JGE contributed to study design, data collection and researched data. All authors contributed to the interpretation of the results and to the discussion, reviewed the paper critically and approved the final version of the manuscript.

Declarations of interest

None.

Data availability

Data cannot be shared for both legal and ethical reasons. Data from the Finnish Institute for Health and Welfare (THL), Statistics Finland, and the Finnish Social Insurance Institution can only be used for the purpose stated in the license granted, scientific research on society by the license applicant, and can therefore not be shared with third parties.

References

[1] V. Anna, H.P. van der Ploeg, N.W. Cheung, R.R. Huxley, A.E. Bauman, Sociodemographic correlates of the increasing trend in prevalence of gestational diabetes mellitus in a large population of women between 1995 and 2005, Diabetes Care 31 (2008) 2288–2293.

[2] J.A. Lavery, A.M. Friedman, K.M. Keyes, J.D. Wright, C.V. Ananth, Gestational diabetes in the United States: temporal changes in prevalence rates between 1979 and 2010, BJOG 124 (2017) 804–813.

[3] ADA (American Diabetes Association), 14. Management of diabetes in pregnancy: standards of medical care in diabetes 2020, Diabetes Care 43 (Suppl 1) (2020) S183–S192, https://doi.org/10.2337/dc20-S014.

[4] J. Malcolm, Through the looking glass: gestational diabetes as a predictor of maternal and offspring long-term health, Diabetes Metab. Res. Rev. 28 (2012) 307–311.

[5] D. Mitanchez, C. Yzydorczyk, B. Siddeek, F. Boubred, M. Benahmed, U. Simeoni, The offspring of the diabetic mother – short- and long-term implications, Best Pract. Res. Clin. Obstet. Gynaecol. 29 (2015) 256–269.

[6] C. Zhang, S. Rawal, Y.S. Chong, Risk factors for gestational diabetes: is prevention possible? Diabetologia 59 (2016) 1385–1390.

[7] E.H. Van den Hooven, V.W. Jaddoe, Y. de Kluizenaar, A. Hofman, J. P. Mackenbach, E.A. Steegers, et al., Residential traffic exposure and pregnancy-related outcomes: a prospective birth cohort study, Environ. Health 8 (2009) 59, https://doi.org/10.1186/1476-069X-8-59.

[8] E. Malmqvist, K. Jakobsson, H. Tinnerberg, A. Rignell-Hydbom, L. Rylander, Gestational diabetes and preeclampsia in association with air pollution at levels below current air quality guidelines, Environ. Health Perspect. 121 (2013) 488–493.

[9] A.F. Fleisch, D.R. Gold, S.L. Rifas-Shiman, P. Koutrakis, J.D. Schwartz, I. Kloog, et al., Air pollution exposure and abnormal glucose tolerance during pregnancy: the project Viva cohort, Environ. Health Perspect. 122 (2014) 378–383.

[10] C. Robledo, P. Mendola, E. Yeung, T. Männistö, R. Sundaram, D. Liu, et al., Preconception and early pregnancy air pollution exposures and risk of gestational diabetes mellitus, Environ. Res. 137 (2015) 316–322.

[11] H. Hu, S. Ha, B.H. Henderson, T.D. Warner, J. Roth, H. Kan, X. Xu, Association of atmospheric particulate matter and ozone with gestational diabetes mellitus, Environ. Health Perspect. 123 (2015) 853–885.

[12] A.F. Fleisch, I. Kloog, H. Luttmann-Gibson, D.R. Gold, E. Oken, J.D. Schwartz, Air pollution exposure and gestational diabetes mellitus among pregnant women in Massachusetts: a cohort study, Environ. Health 15 (2016) 40, https://doi.org/10.1186/s12940-016-0121-4.

[13] S.C. Pan, C.C. Huang, S.J. Lin, B.Y. Chen, C.C. Chan, Y.L. Leon Guo, Gestational diabetes mellitus was related to ambient air pollutant nitric oxide during early gestation, Environ. Res. 158 (2017) 318–323.

[14] M.C. Lu, P. Wang, T.J. Cheng, C.P. Yang, Y.H. Yan, Association of temporal distribution of fine particulate matter with glucose homeostasis during pregnancy in women of Chiayi City, Taiwan, Environ. Res. 152 (2017) 81–87.

[15] A.M. Padula, W. Yang, F.W. Lurmann, J. Balmes, S.K. Hammond, G.M. Shaw, Prenatal exposure to air pollution, maternal diabetes and preterm birth, Environ. Res. 170 (2019) 160–167.

[16] H. Jo, S.P. Eckel, J.-C. Chen, M. Cockburn, M.P. Martinez, T. Chow, et al., Associations of gestational diabetes mellitus with residential air pollution exposure in a large Southern California pregnancy cohort, Environ. Int. 130 (2019), 104933, https://doi.org/10.1016/j.envint.2019.104933.

[17] M. Yao, Y. Liu, D. Jin, W. Yin, S. Ma, R. Tao, et al., Relationship between temporal distribution of air pollution exposure and glucose homeostasis during pregnancy, Environ. Res. 185 (2020), 109456, https://doi.org/10.1016/j.envres.2020.109456.

[18] X. Tang, J.B. Zhou, F. Luo, Y. Han, Y. Heianza, M.A. Cordoso, L. Qi, Air pollution and gestational diabetes mellitus: evidence from cohort studies, BMJ Open Diabetes Res. Care 8 (2020), e000937, https://doi.org/10.1136/bmjdrc-2019-000937.

[19] H.H. Zhang, Q. Wang, S.M. He, K.P. Wu, M. Ren, H.T. Dong, et al., Ambient air pollution and gestational diabetes mellitus: a review of evidence from biological mechanisms to population epidemiology, Sci. Total Environ. 719 (2020), 137349, https://doi.org/10.1016/j.scitotenv.2020.137349.

[20] Q. Lin, S. Zhang, Y. Liang, C. Wang, C. Wang, X. Wu, et al., Ambient air pollution exposure associated with glucose homeostasis during pregnancy and gestational diabetes mellitus, Environ. Res. 190 (2020), 109990, https://doi.org/10.1016/j.envres.2020.109990.

[21] B. Ye, C. Zhong, Q. Li, S. Xu, Y. Zhang, X. Zhang, X. Chen, L. Huang, H. Wang, Z. Zhang, J. Huang, G. Sun, G. Xiong, X. Yang, L. Hao, N. Yang, S. Wei, The associations of ambient fine particulate matter exposure during pregnancy with blood glucose levels and gestational diabetes mellitus risk: a prospective cohort study in Wuhan, China, Am. J. Epidemiol. 189 (11) (2020) 1306–1315, https://doi.org/10.1093/aje/kwaa056.

[22] WHO, 2013. 〈http://www.euro.who.int/_data/assets/pdf_file/0006/189051/Health-effects-of-particulate-matter-final-Eng.pdf〉. Accessed 12 Oct 2020.

[23] M. Gissler, J. Teperi, E. Hemminki, J. Meriläinen, Data quality after restructuring a national medical registry, Scand. J. Soc. Med. 23 (1995) 75–80.

[24] F.E. Harrell Jr, ISBN 978-1-4757-3462-1. Regression Modeling Strategies with Applications to Linear Models, Logistic Regression, and Survival Analysis, Springer, New York, 2001.

[25] Y. Zhu, C. Zhang, Prevalence of gestational diabetes and risk of progression to type 2 diabetes: a global perspective, Curr. Diabetes Rep. 16 (2016) 7.

[26] M.K. Laine, H. Kautiainen, M. Gissler, P. Pennanen, J.G. Eriksson, Impact of sunshine on the risk of gestational diabetes mellitus, Int. J. Circumpolar Health (2019), https://doi.org/10.1080/22423982.2019.1703882.

[27] Z.J. Andersen, O. Raaschou-Nielsen, M. Ketzel, S.S. Jensen, M. Hvidberg, S. Loft, et al., Diabetes incidence and long-term exposure to air pollution: a cohort study, Diabetes Care 35 (2012) 92–98.

[28] K.J. Chuang, Y.H. Yan, S.Y. Chiu, T.J. Cheng, Long- term air pollution exposure and risk factors for cardiovascular diseases among the elderly in Taiwan, Occup. Environ. Med. 68 (2011) 64–68.

[29] P.F. Coogan, L.F. White, M. Jerrett, R.D. Brook, J.G. Su, E. Seto, et al., Air pollution and incidence of hypertension and diabetes mellitus in black women living in Los Angeles, Circulation 125 (2012) 767–772.

[30] R. Kelishadi, N. Mirghaffari, P. Poursafa, S.S. Gidding, Lifestyle and environmental factors associated with inflammation, oxidative stress and insulin resistance in children, Atherosclerosis 203 (2009) 311–319.

[31] J.H. Kim, Y.C. Hong, GSTM1, GSTT1, and GSTP1 polymorphisms and associations between air pollutants and markers of insulin resistance in elderly Koreans, Environ. Health Perspect. 120 (2012) 1378–1384.

[32] U. Krämer, C. Herder, D. Sugiri, K. Strassburger, T. Schikowski, U. Ranft, W. Rathmann, Traffic-related air pollution and incident type 2 diabetes: results from the SALIA cohort study, Environ. Health Perspect. 118 (2010) 1273–1279.
[33] R.C. Puett, J.E. Hart, J. Schwartz, F.B. Hu, A.D. Liese, F. Laden, Are particulate matter exposures associated with risk of type 2 diabetes? Environ. Health Perspect. 119 (2011) 384–389.
[34] Z. Sun, B. Mukherjee, R.D. Brook, G.A. Gatts, F. Yang, Q. Sun, et al., Air-Pollution and Cardiometabolic Diseases (AIRCMD): a prospective study investigating the impact of air pollution exposure and propensity for type II diabetes, Sci. Total Environ. 448 (2013) 72–78.
[35] D.Q. Rich, H.M. Kipen, W. Huang, G. Wang, Y. Wang, P. Zhu, et al., Association between changes in air pollution levels during the Beijing Olympics and biomarkers of inflammation and thrombosis in healthy young adults, JAMA 307 (2012) 2068–2078.
[36] M.A. Khafaie, S.S. Salvi, A. Ojha, B. Khafaie, S.S. Gore, C.S. Yajnik, Systemic inflammation (C-reactive protein) in type 2 diabetic patients is associated with ambient air pollution in Pune City, India, Diabetes Care 36 (2013) 625–630.
[37] E.H. van den Hooven, F.H. Pierik, Y. de Kluizenaar, A. Hofman, S.W. van Ratingen, P.Y. Zandveld, et al., Air pollution exposure and markers of placental growth and function: the generation R study, Environ. Health Perspect. 120 (2012) 1753–1759.
[38] P.C. Lee, E.O. Talbott, J.M. Roberts, J.M. Catov, R.K. Sharma, B. Ritz, Particulate air pollution exposure and C-reactive protein during early pregnancy, Epidemiology 22 (2011) 524–531.
[39] L.P. Lowe, B.E. Metzger, W.L.Jr Lowe, A.R. Dyer, T.W. McDade, H.D. McIntyre, HAPO Study Cooperative Research Group. Inflammatory mediators and glucose in pregnancy: results from a subset of the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study, J. Clin. Endocrinol. Metab. 95 (2010) 5427–5434.
[40] Q. Sun, P. Yue, J.A. Deiuliis, C.N. Lumeng, T. Kampfrath, M.B. Mikolaj, et al., Ambient air pollution exaggerates adipose inflammation and insulin resistance in a mouse model of diet-induced obesity, Circulation 119 (2009) 538–546.
[41] Y.H. Yan, C.C. Chou, C.T. Lee, J.Y. Liu, T.J. Cheng, Enhanced insulin resistance in diet-induced obese rats exposed to fine particles by instillation, Inhal. Toxicol. 23 (2011) 507–519.