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Maternal exposure to ambient air pollution and fetal growth in North-East Scotland: A population-based study using routine ultrasound scans

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ABSTRACT

Background: Maternal ambient air pollution exposure is associated with reduced birthweight. Few studies have examined the effect on growth in utero and none have examined the effect of exposure to particulates less than 2.5 μm ($PM_{2.5}$) and possible effect modification by smoking status.
Objectives: Examine the effect of maternal exposure to ambient concentrations of PM_{10}, $PM_{2.5}$ and nitrogen dioxide (NO_2) for in utero fetal growth, size at birth and effect modification by smoking status.
Methods: Administratively acquired second and third trimester fetal measurements (bi-parietal diameter, femur length and abdominal circumference), birth outcomes (weight, crown heel length and occipito-frontal circumference) and maternal details were obtained from routine fetal ultrasound scans and maternity records (period 1994–2009). These were modelled against residential annual pollution concentrations (calendar year mean) adjusting for covariates and stratifying by smoking status.
Results: In the whole sample ($n = 13{,}775$ pregnancies), exposure to PM_{10}, $PM_{2.5}$ and NO_2 was associated with reductions in measurements at birth and biparietal diameter from late second trimester onwards. Among mothers who did not smoke at all during pregnancy ($n = 11{,}075$), associations between biparietal diameter and pollution exposure remained significant but were insignificant among those who did smoke ($n = 2700$). Femur length and abdominal circumference were not significantly associated with pollution exposure.
Conclusions: Fetal growth is strongly associated with particulates exposure from later in second trimester onwards but the effect appears to be subsumed by smoking. Typical ambient exposures in this study were relatively low compared to other studies and given these results, it may be necessary to consider reducing recommended "safe" ambient air exposures.

1. Introduction

Air pollution is a major component of the total global burden of disease (Lim et al., 2012) associated with, for example, approximately 40,000 deaths per year and associated annual healthcare costs of around £20 billion in the UK (Royal College of Physicians, 2016). The harmful effects of ambient air pollution are apparent at birth with associations between pollution exposures, particularly fine particulate matter with a diameter less than ten microns (PM_{10}) and nitrogen oxides, and adverse neonatal outcomes such as reduced birthweight, prematurity and birth head circumference (Dibben and Clemens, 2015; Hjortebjerg et al., 2016; Malley et al., 2017; Pedersen et al., 2013; Rich et al., 2015; Stieb et al., 2016). Some studies have used ultrasound scans to examine when in utero exposure to air pollution may be linked to growth restriction (Aguilera et al., 2010; Carvalho et al., 2016; Hansen et al., 2008; Iñiguez et al., 2012; Malmqvist et al., 2017; Ritz et al., 2014; Slama et al., 2009; van den Hooven et al., 2012). Collectively these studies show some evidence of an association between increased maternal exposures and reduced fetal head size however there are limitations with some of these studies and also variations in methodology that may be important. Some of the studies are based on fairly small sample sizes and there are potential differences in how pollution exposure is assigned. One study used, for example, a nearest static monitor approach (Hansen et al., 2008), which may introduce a bias to the null hypothesis (Butland et al., 2013), and others use modelled concentrations from land use regression techniques(Aguilera et al., 2010; Ritz et al., 2014; van den Hooven et al., 2012). The main determinant of poor quality ambient air is combustion of fossil fuels where PM_{10}, $PM_{2.5}$ (particulates with a diameter < 2.5 μm) and nitrogen dioxide (NO_2) arise. Importantly, of those previous studies, that have looked specifically at in utero fetal growth, only three have examined PM_{10} and NO_2 exposure (Aguilera et al., 2010; Ritz et al., 2014;

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van den Hooven et al., 2012) and none have examined $PM_{2.5}$ which may be an important determinant of birth outcomes (Sun et al., 2016).

In this paper we extend existing research by examining the effect of $PM_{2.5}$ as well as PM_{10} and NO_2 on in utero fetal growth in the relatively low pollution environment of North-East Scotland. Using a whole population cohort of pregnancies and associated routine ultrasound sonography information from North-East Scotland, we aim to test the hypothesis that maternal ambient outdoor air exposures to increased $PM_{2.5}$, PM_{10} and NO_2 concentrations are associated with reduced fetal size and growth. This large cohort also allows us to examine models stratified by smoking status to determine possible differences in the effect of pollutant exposure among smokers and non-smokers.

2. Methods

2.1. Study population

We use maternal and fetal data from the Aberdeen Maternity and Neonatal Databank (AMND) which has archived routinely acquired data from clinical activity at Aberdeen Maternity Hospital (AMH) since 1950 (Ayorinde et al., 2016). This hospital is the delivery unit for approximately 80% of the population of North East Scotland and 95% of deliveries in Aberdeen City (Thompson et al., 2010). Ultrasound scan assessments started at AMH in the mid-1980s but only scans occurring in the period for which pollution data were available were used for the present analysis (2002 – 2011). Because only 1.5% of the population of North East Scotland is minority ethnic (as recorded at the 2011 census) we did not consider ethnicity in the study. Furthermore, only singleton births were considered.

2.2. Exposure assessment

To estimate outdoor air pollution exposure, we use modelled concentration estimates that are based on calendar year emissions totals and so represent annual average concentrations. These data are available UK wide at a spatial resolution of 1 km × 1 km from 2002 onwards for $PM_{2.5}$, PM_{10} and NO_2 and are supplied by the United Kingdom Department for the Environment, Food and Rural Affairs (DEFRA) (Brookes et al., 2011; NETCEN, 2005). The concentration estimates are generated from a Pollution Climate Mapping (PCM) approach which takes local and distant point and area sources and sums the annual concentration values. For NO_2, the National Atmospheric Emissions Inventory (*NAE*I) is used to determine concentration values for point sources. Distant sources are modelled with a combination of dispersion models and rural background static monitors. Area concentration sources are modelled with dispersion kernels and *NAE*I data (Brookes et al., 2011). Because the composition of PM pollution is more heterogeneous, different approaches are used details of which can be found in Brookes et al. (2011, pp. 17–18).

Full address location was unavailable in the dataset and so we allocate exposure values to each mother on the basis of the centroid of the postcode of residence, recorded at the time of delivery. Postcodes vary in size from single apartment blocks in urban centres (< 100 m^2) to much larger areas in rural locations (up to around 200 km^2 in the very sparsely populated upland areas of Western North East Scotland). However, pollution levels in rural scotland are low and spatially homogenous and therefore larger postcode areas further from urban centres are unlikely to introduce significant exposure misclassification. We use the population weighted postcode centroid coordinates and a geographical information system to determine an exposure estimate from the gridded concentration data based on the grid cell within which the centroid point is located. To adjust for unmeasured annual variation in the modelled concentrations, we include a dummy term for year of birth in the models. We calculated frequency quartiles of each pollutant and used these as well as continuous measures as exposure variables.

Table 1
Descriptives for maternal characteristics and fetal measurements.

N (Pregnancies)	13,775	
Categorical variables	Number	%
Parity		
Nulliparous	6731	48.86
One previous pregnancy	4820	34.99
Two previous pregnancies	1541	11.19
3 or more previous pregnancies	683	4.96
Age		
19 and under	717	5.21
20–40	12,803	92.94
Over 40	254	1.84
Offspring sex		
Female	6706	48.68
Male	7069	51.32
Smoking		
Ex smoker, non-smoker	11,075	80.40
Smoker	2700	19.60
Social class		
Professional	2193	15.92
Managerial and technical	3883	28.19
Skilled non-manual	1932	14.03
Skilled manual	1425	10.34
Partly skilled	1345	9.76
Unskilled	322	2.34
Not available	2675	19.42
Continuous variables	Mean	
Maternal height (cm)	163.75	
Maternal weight (kg)	68.60	

Table 2
Descriptive statistics for outcomes.

Fetal characteristics trimester 2	Mean (SD in brackets)	Mean gestational age (SD in brackets)
Bi-parietal diameter (mm) (14,172 scans)	47.6 (9.3)	19.5 (2.8)
Femur length (mm) (15,417 scans)	33.0 (7.6)	19.6 (2.7)
Abdominal circumference (mm) (12,606 scans)	165.9 (31.3)	20.5 (2.8)
Fetal characteristics trimester 3		
Bi-parietal diameter (mm) (5728 scans)	84.6 (7.0)	33.3 (3.1)
Femur length (mm) (6258 scans)	64.7 (6.5)	33.5 (3.2)
Abdominal circumference (mm) (9171 scans)	296.4(35.0)	33.4 (3.2)
Birth characteristics (pregnancies in brackets)		
Crown heel length (cm) (13,667 pregnancies)	49.5 (3.0)	39.0 (2.3)
Occipitofrontal circumference (cm) (13,714 pregnancies)	34.5 (1.9)	39.0 (2.3)
Birthweight (kg) (13,756 pregnancies)	3339.8 (630.5)	39.0 (2.3)

2.3. Birth outcomes, fetal ultrasound measurements and growth curves

First trimester scans (i.e. ≤ 13 weeks gestation) are typically made at 10–12 weeks gestation to determine the gestational age of the pregnancy. Second trimester scans (i.e. 13– < 28 weeks) take place close to 20 weeks gestation in order to screen for fetal anomalies. Third trimester scans (i.e. ≥ 28 weeks gestation) are conducted for obstetric indications such as breech presentation or in uterine growth retardation. Some pregnancies were scanned multiple times in each trimester. At the first trimester, crown rump length (CRL) is recorded and during second and third trimester scans abdominal circumference (AC), femur length (FL) and bi-parietal diameter (BPD) are recorded. All measurements are recorded in mm. Gestational age is estimated from maternal