Title: Spontaneous very preterm birth in relation to social class, and smoking : A temporal-spatial analysis of routinely collected data in Aberdeen, Scotland (1985 – 2010)

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Running title: Social determinants of spontaneous very preterm birth

Abstract

Objective: To examine trends of spontaneous very preterm birth (vPTB) and its relationship with maternal socioeconomic status and smoking

Methods: This was a population-based cohort study in Aberdeen Maternity Hospital, UK. The cohort was restricted to spontaneous singleton deliveries occurring in Aberdeen from 1985-2010. The primary outcome was very preterm birth which was defined as <32 weeks gestation and the comparison group was deliveries ≥37 weeks of gestation. The main exposures were parental Social Class based on Occupation, Carstairs' deprivation index and smoking during pregnancy. Logistic regression was used to estimate the association between vPTB and the exposures.

Results: There was an increased likelihood of vPTB in those with unskilled-occupations compared to professional-occupations [aOR:2.77 (95%CI:1.54-4.99)], in those who lived in the most deprived areas compared to those in the most affluent [aOR:1.74 (95%CI:1.36-2.21)] and in women who smoked compared to those who did not [aOR: 2.16 (95%CI: 1.27-3.67)]. The association with Carstairs index was no longer statistically significant when restricted to smokers but remained significant when restricted to non-smokers.

Conclusion: The strongest risk factor for vPTB was maternal smoking while socioeconomic deprivation showed a strong association in non-smokers. Smoking cessation interventions may reduce vPTB. Modifiable risk factors should be explored in deprived areas.

Introduction

The UK government has the ambitious aim to reduce perinatal mortality by 50% by 2030. National rates of perinatal mortality vary by geographic region with the Grampian region of Scotland having a neonatal mortality rate up to 10% lower than the UK average with a perinatal mortality rate of 5.36 per 1000 births (95%CI: 4.79 to 6.52).[1] However, compared to maternal mortality, perinatal mortality remains a relatively common event. Identifying the modifiable risk factors for perinatal mortality may be crucial to reducing this rate. Perinatal mortality increases with lower gestational age.[2] Very preterm birth, defined as infants born at less than 32 weeks of gestation, is a major risk factor for severe neonatal morbidity, perinatal mortality and future childhood and adult health impairment.[3]

The association between perinatal mortality and deprivation is clear as the recent MBRRACE reports show that infants who died were 1.5 times more likely to be born to the most deprived mothers.[1] While the aetiology of preterm birth is multifactorial and somewhat unclear, the literature has shown a consistent relationship between preterm birth and socioeconomic status.[3,4] Furthermore, individual level factors such as parental smoking, education, ethnicity and neighbourhood effects are all shown to increase the risk of preterm birth.[4-8] There is limited evidence examining the complex interaction between smoking, socioeconomic status and very preterm birth.

There is varying incidence of very preterm birth over time. An ecological study in Trent showed that the incidence of very preterm birth increased from 11.9 per 1000 births in 1994 to 13.7 per 1000 births in 2003.[6] While in a study using national Scottish data there appeared to be no clear trend over time for very preterm birth, although an increase in all preterm births was noted.[4] Spatial distribution of very preterm birth outside of measures that capture socioeconomic status has yet to be examined. This study aimed to describe the temporal and spatial distribution of spontaneous very preterm birth and to examine the risk factors of

spontaneous very preterm birth, in particular the interaction between smoking and socioeconomic status.

Methods

Data source

This was a population based cohort study using routinely collected data from the Aberdeen Maternity Neonatal Databank (AMND) between 1985-2010. The details of the AMND have previously been described.[9] In brief, Aberdeen hospital is the only maternity hospital in Aberdeen and 97% of the births from the Grampian area occur there. Information on 5000 births per year on average is recorded in the database from the case notes after each delivery. The data were extracted by the Data Management Team, University of Aberdeen. The extracted variables included: mother's age at delivery, gestational age, smoking status, ethnicity, maternal and paternal social class based on occupation (SC), Carstairs index, labour type (whether spontaneous or induced), year of birth and postcode sector. Gestational age at delivery was recoded into a binary variable – very preterm birth (yes/ no). Year of birth (five year periods), ethnicity (white and other ethnicities) and smoking status (current smoker, former smoker and non-smoker) were all categorised. Gestational age is based on the ultrasound estimates from 1985 onwards when it became universally available. Date of the last menstrual period is also collected but the ultrasound dates are accepted if the two estimates differ by more than 7 days.

Outcome

The main outcome of interest was very preterm birth. This was defined as a spontaneous singleton first live birth prior to 32 weeks of gestation. The comparison group was births ≥37 weeks of gestation. The primary aim of this study was to examine very preterm birth, thus

infants born between 32 weeks and <37 weeks of gestation were excluded from the analysis, however remained part of the denominator. Multiple births were excluded to the increased likelihood of early induction of labour and elective caesarean section. In addition, iatrogenic births were also excluded, as a result, the study sample included singleton spontaneous births.

Exposures

The main exposures of interest were parental social class recorded in the database as the Registrar General's Occupation-based social class, Carstairs Index and smoking status. Social class was calculated using predominately the paternal social class and was further supplemented with the maternal social class if the paternal social class was missing thereby allowing for a more complete exposure variable. Social class was made up of six categories classifying occupations as either: professional (I), managerial (II), skilled non-manual (IIInm), skilled manual (IIIm), semi-skilled (IV), unskilled (V).

The second measure of socioeconomic status was the Carstairs index, an area-based measure, based on Census data. As each maternal record in the database has a postcode this allows a deprivation score to be assigned to each mother (postcodes classify areas helping to identify the area for mail delivery). The Carstairs index is a relative measure, which uses four unweighted indicators (unemployment, car ownership, crowding and social class providing a score for each area in Scotland. The scores are ranked from one (least deprived) to eight (most deprived), no postcode area in Aberdeen has a score below six.

The third exposure was smoking which was categorised as current smokers, ex-smokers and never smokers. The reference categories for each of the exposures were: social class I , least

deprived/most affluent category and never-smokers. Other covariates included ethnicity (white or other), age at delivery (analysed as a continuous variable) and year of birth (categorised into five year periods).

Missing data

Gestational age was missing in 0.1% of deliveries but was distributed randomly through time and in the different social classes. As this was the key variable for calculating the outcome of interest, we excluded cases with missing gestational age. Complete case analysis was used in this analysis.

Statistical analysis

Statistical analyses were performed using STATA V.13SE (STATA Corp, Texas, USA). Counts and proportions of characteristics were presented in the very preterm birth and non-preterm group. A global chi square test was used to assess difference between the groups. Collinearity was assessed between smoking and measure socioeconomic status prior to multivariable analysis, using Pearson's correlation coefficient. These exposures were not highly collinear (coefficient <23%). Logistic regression models were used to estimate odds ratios and 95% confidence intervals for the effect on very preterm birth of smoking, social class and area level deprivation. Each exposure was modelled separately with very preterm birth. Both an unadjusted model and a model adjusted for mother's age and ethnicity were presented. A secondary analysis was completed by stratifying the fully adjusted social class and Carstairs model by smoking status. The population attributable fraction was calculated to assess the impact of smoking on very preterm birth.

Spatial analysis was done using ESRI's ArcGIS 10 Geographical Information System (GIS) software. The proportion of very preterm birth was mapped according to each postcode sector

in Aberdeen City, and this allowed a thematic map to be created. The map was shaded using the Carstairs index. The postcode boundary data was provided using the 2011 Census, Output Area Boundaries (Crown copyright 2003).[10] The spatial examination was restricted to 1995 as postcodes changed prior to this period. In order to assess the distribution within the city centre, a global Chi Square test was used to determine statistical difference between the distribution of very preterm birth inside the city centre and outside the city centre.

Ethics approval

No ethical approval required for the secondary analysis of data. Approval for the use of anonymised data was gained from the Aberdeen Maternity Neonatal Databank steering committee.

Results

Description of the sample

In 39,373 live births there were 388 spontaneous singleton very preterm births during the period 1985-2010, which provided a prevalence of 9.9 per 1000 live birth (95% CI: 8.9 -10.9). Table 1 highlights the characteristics of the sample from the AMND. A higher proportion of women who delivered at less than 32 weeks of gestation were older and smokers compared to those who delivered at ≥37 weeks. A higher proportion of mothers in the very preterm birth group were from the most deprived area compared to those delivered at 37 weeks or greater and this difference was not statistically significant.

Multivariable analysis

Table 2 presents the unadjusted and adjusted odds ratios with 95% confidence intervals for very preterm birth. VPTB was 3 times more likely to occur in households with unskilled occupations compared to the professional occupations [adjusted odds ratio (aOR): 2.77

(95%CI: 1.54-4.99). There was nearly a doubling of the odds of vPTB in smoking mothers compared to those who did not [aOR:1.74 (95% CI:1.36-2.21)]. Similarly, living in the most deprived area compared to the most affluent was associated with a doubling of the odds of vPTB [aOR: 2.16 (95% CI: 1.27-3.67)].

Table 3 presents the association between very preterm birth and occupational social class and the Carstairs index by smoking status (current smokers or never). The association between occupational social class and vPTB in those who smoked was not statistically significant. Similarly, in mothers who smoked, those in the least deprived area compared to the most deprived were not at an increased risk of preterm birth. While in those who did not smoke, the relationship between those in the lowest category of social class and the most deprived Carstairs index with very preterm birth remained statistically significant. The population attributable fraction of smoking was 14.5% (95% CI: 7.6-20.8%), indicating that 14% of very preterm births might be eliminated if maternal smoking was stopped.

Exploratory temporal and spatial analysis

The proportion of very preterm birth increased over time from 0.9% in 1985-1989 to 1.2% in 2005-2010, although this increase was not statistically significant in the bivariate analysis (Supplementary table 1).

The spatial distribution of very preterm birth in Aberdeen City was mapped using the Carstairs index categories as background shading (Figure 1). There appeared to be a spatial pattern with very preterm birth in Aberdeen City. The highest levels of very preterm birth tended to be located in the inner city areas where the postcode sectors are the smallest, which suggest it occurs in more densely populated areas. The bivariate analysis showed there was a significantly larger proportion of very preterm birth distributed within the city centre in

comparison to the surrounding areas suggesting spatial clustering of very preterm birth (70% vs 30%, p value <0.05) within the city centre.

Discussion

Main findings of this study

Smoking was an important risk factor of very preterm birth, where socioeconomic status was not a risk factor for very preterm birth in those who smoked. In contrast an association remained between socioeconomic status and very preterm birth in non-smokers. Over time the risk of very preterm birth has increased and spatial analysis showed that there was clustering of very preterm birth within Aberdeen city.

What is already known

Smoking

The association shown in the study between smoking and very preterm birth is consistent with previous research. A systematic review examining the social determinants of birth outcomes including nine prospective studies showed a positive relationship between preterm birth and smoking.[12] Furthermore, a number of studies have shown the strong relationship between maternal smoking and spontaneous preterm birth.[13,14] Kyrklund-Blomberg and Cnattingius[13] suggested the biological plausibility for premature onset of labour resulting in preterm birth is multifactorial and could be as a result of inflammatory response due to impaired immunity which has been shown to be associated with mothers who smoke.[15] This finding is important as it identifies a modifiable risk factor which could prevent future very preterm births.

Socioeconomic status

The association between area-based deprivation measures and very preterm birth index were also consistent with other studies. Grey et al.[4] showed that the relative risk for very preterm birth and extremely preterm birth was highest in the most deprived quintiles of the Carstairs

index. Similarly, Smith et al.[6] showed there were social inequalities in the incidence of very preterm birth with the most deprived decile having the largest risk of very preterm birth. The biological mechanisms connecting socioeconomic status and very preterm birth are unknown. Green et al.[16] hypothesised that maternal stress caused by an environmental or psychosocial problem would result in changes in the neuroendocrine pathways, resulting in the release of oestrogen and the corticotrophin releasing hormone initiating premature labour. Grey et al.[4] argued that smoking rates and maternal age may account for the disparities seen between the deprivation categories. However, this study showed that socioeconomic status was not associated with very preterm birth in smokers, while the association with deprivation remained in those who were non-smokers. A possible explanation has been suggested that there are other social and environmental factors such as pollution and overcrowding as well as poor nutrition that drive disparities between regions that have remained undiscovered.[12] Suggesting the association may be driven by factors other than deprivation and the aetiology of very preterm birth is far more complex with multiple factors at different levels of a conceptual framework.

Temporal trend

These findings are consistent with previous research that has shown an increase in the incidence of very preterm birth. Smith et al.[6] showed an increase in the incidence of very preterm birth from 11.9 per 1000 births in 1994 to 13.7 per 1000 births in 2003 in Trent, UK. Gray et al.[4] showed that from 1980-84 to 2000-03 the incidence of very preterm birth has increased by 0.6 per 1000 live births. However, there was not a clear trend over this period, shown by a declining trend in 1985-89 and 1995-99.

A worldwide study examined the incidence and potential reasons for preterm births. It suggested that increased maternal age, assisted conception techniques and co-morbidities such as obesity and diabetes may be risk factors for increased spontaneous preterm birth.[17]

The increase in preterm birth has also been mirrored by a decline in perinatal mortality which reflects the high quality of neonatal care in recent decades.

Spatial clustering

To support the hypothesis of spatial clustering of very preterm birth further work should attempt to reproduce similar patterns in order to encourage future investigation of these patterns. Furthermore, a mechanism for this urban-rural disparity must also be established, in order to be able to support any causal association between environmental determinants and increased very preterm birth. This study has highlighted the association between very preterm birth and the area based Carstairs index yet the aetiology still largely remains unknown making it difficult to design public health interventions. In contrast, smoking is a modifiable lifestyle factor, and future public health interventions should continue to emphasise the importance of avoiding smoking during pregnancy.

What this study adds

This study has been able to address the issues with some of the previous research that was unable to control for parity, labour type and multiple pregnancy.[5,6] These other potential explanations were excluded by selecting singleton first spontaneous deliveries; thus this study will have presented a truer reflection of the association between very preterm birth and socioeconomic status.

This study has also benefitted from the availability of high quality registry data provided by the AMND. The AMND has data quality checks to ensure the data is both valid and reliable. Previous research has highlighted limited data surrounding very preterm birth and socioeconomic status.[4,6] Thus the AMND provides a unique way to examine the relationship with individual level social class and area based measures over time, while adjusting for other covariates such as smoking which are shown to be on the causal pathway.

Limitations of this study

A number of potential limitations may have arisen from this research, as this study is susceptible to residual confounding. The aetiology of very preterm birth is multifactorial making it difficult to measure the true risk factors of very preterm birth over time. This may be the case as this study showed spatial clustering in the city centre that may be explained by unmeasured environmental factors rather than deprivation per se. The study may also be susceptible to misclassification as the Carstairs index is a proxy of deprivation using postcodes. Postcodes themselves are not designed for this purpose but rather to allow efficient delivery of mail, so the association between very preterm birth and the Carstairs index may be better explained by unmeasured environmental factor(s) other than deprivation. Further exploration of the geospatial clustering was not possible due to the ethical issues surrounding disclosure of full postcodes and the small number of events in each area.

Conclusion

Smoking is an important modifiable risk factor for very preterm birth. Over 14 % of preterm births could have been prevented if women did not smoke which has important implications for public health. Socio-economic status remained a risk factor of very preterm birth in those who did not smoke.

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Nothing to disclose.

Contribution to authorship:

SJM contributed to the study design, data analysis and interpretation and prepared the first manuscript. SB helped with study design, data acquisition and revised the manuscript. DRG helped with the mapping element of the paper and revised the manuscript. GJM contributed to study design, data interpretation and revised the manuscript.

Details of Ethics Approval:

No ethical approval was required for the secondary data analysis. We gained approval from the AMND steering committee that has ethical approval to provide access to the database.

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Table 1. The comparison of sample characteristics across

		Pregnancies ≥37 weeks	Very preterm birth	P-value
n= 37 (0.1% missing)		38985 (98.9)	388 (1.0)	
Age n=39342	<20	4761 (12.2)	73 (18.8)	<0.001
	20-24	10276 (26.4)	94 (24.2)	
	25-29	13319 (34.2)	113 (29.1)	
	30-34	8087 (20.8)	68 (17.5)	
	35-39	2264 (5.8)	37 (9.5)	
	≥40	247 (0.6)	3 (0.8)	
Ethnicity n= 39371	White	36405 (93.4)	360 (92.8)	0.634
	Other	2578 (6.6)	28 (7.2)	
Smoking n= 37510	Non - smoker	24641 (66.3)	199 (56.7)	<0.001
	Previous smoker	3263 (8.8)	23 (6.6)	
	Smoker	9255 (24.9)	129 (36.8)	
Social Class based on Occupation n= 29607	I	3740 (12.8)	28 (10.2)	0.203
	II	6100 (20.8)	48 (17.5)	
	III NM	3515 (12.0)	40 (14.5)	
	III M	7278 (24.8)	70 (25.5)	
	IV	6884 (23.5)	65 (23.6)	
	V	1815 (6.2)	24 (8.7)	
Carstairs Index n= 33621	Most affluent	4906 (14.7)	30 (9.0)	0.015
	2	10055 (30.2)	99 (29.8)	
	3	6675 (20.1)	62 (18.7)	
	4	6557 (19.7)	23.8 (79)	
	5	2805 (8.4)	30 (9.0)	
	Most deprived	2291 (6.9)	32 (9.6)	

Location* n=9915	City centre	5759 (58.6)	63 (70.0)	0.029
	Outside city centre	4066 (41.4)	27 (30.0)	

*Only from 1995 onwards. Carstairs index is an area measure of socioeconomic status

Table 2. Independent associations between social class, smoking and carstairs index with very preterm birth

		Unadjusted			Adjusted		
		Odds ratio	95% CI	P-value	Odds ratio	95% CI	P-value
Social Class based on Occupation	I	1			1		
	II	1.03	(0.65-1.61)	0.91	1.03	(0.64-1.64)	0.92
	III NM	0.97	(0.59-1.57)	0.89	1.01	(0.60-1.68)	0.98
	III M	1.35	(0.86-2.13)	0.19	1.44	(0.90-2.32)	0.13
	IV	1.28	(0.80-2.04)	0.3	1.27	(0.78-2.07)	0.34
	V	2.5	(1.43-4.36)	<0.001	2.77	(1.54-4.99)	<0.001
Smoking	Non-smoker	1			1		
	Previous smoker	0.88	(0.57-1.36)	0.56	0.9	(0.58-1.40)	0.65
	Smoker	1.74	(1.40-2.18)	<0.001	1.74	(1.36-2.21)	<0.001
Carstairs index	Most affluent	1			1		
	2	1.62	(1.07-2.44)	0.02	1.62	(1.07-2.47)	0.02
	3	1.54	(0.99-2.38)	0.05	1.56	(1.00-2.44)	0.05
	4	2.01	(1.32-3.06)	<0.001	2.01	(1.30-3.12)	<0.001
	5	1.76	(1.06-2.93)	0.03	1.72	(1.02-2.93)	0.04
	Most deprived	2.31	(1.40-3.81)	<0.001	2.16	(1.27-3.67)	<0.001

Smoking, social class and carstairs index were modelled separately with very preterm birth. Adjusted for age at delivery and ethnicity. I Professional, II Managerial and technical, III NM (Skilled non-manual), III M (Skilled manual), IV (Semi-skilled), V (Unskilled).

Table 3. The association between very preterm birth and measure of socioeconomic status stratified by smoking status.

		Non-smokers				Smokers			
		Total number of observations	Odds ratio	95% CI	P-value	Total number of observations	Odds ratio	95% CI	P-value
Social Class based on Occupation	I	3,144	1			236	1		
	II	5,009	0.97	(0.56-1.68)	0.91	1,007	0.77	(0.25-2.39)	0.65
	III NM	3,140	1.01	(0.54-1.87)	0.98	1,080	0.67	(0.21-2.14)	0.5
	III M	3,020	1.51	(0.85-2.67)	0.16	1,455	0.64	(0.21-2.00)	0.45
	IV	2,887	1.14	(0.63-2.07)	0.67	1,210	0.8	(0.25-2.39)	0.69
	V	567	2.87	(1.32-6.23)	0.01	431	1.56	(0.46-5.31)	0.48
Carstairs index	Most affluent	3,777	1			468	1		
	2	6,529	1.85	(1.10-3.12)	0.02	1,662	0.8	(0.31-2.06)	0.64
	3	4,029	1.6	(0.90-2.85)	0.11	1,452	1.19	(0.48-2.99)	0.7
	4	3,324	2.43	(1.38-4.27)	<0.001	1,933	1.34	(0.55-3.27)	0.52
	5	1,370	1.87	(0.89-3.92)	0.1	1,032	1.13	(0.43-2.99)	0.8
	Most deprived	933	2.34	(1.06-5.16)	0.04	983	1.57	(0.61-4.06)	0.35

Figure 1. Aberdeen City – proportion of very preterm birth by postcode and mapped by Carstairs Index

vPTB: very preterm birth