Ethnic differences in the association between maternal vitamin D status and offspring asthma and wheeze

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Ethnic differences in the association between maternal vitamin D status and offspring asthma and wheeze: Findings from the Born in Bradford cohort study

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Introduction

Maternal vitamin D deficiency [1] and childhood asthma and wheeze [2] are common health problems. Risk factors for low vitamin D levels include dark skin [3], and ethnic variations in the prevalence of asthma have previously been reported [4, 5]. Whilst it is known that rates of both circulating vitamin D levels and childhood asthma differ by ethnicity, to our knowledge, no UK study as previously investigating ethnic differences in their association with each other. Our aims were to quantify maternal vitamin D levels and the prevalence of asthma and wheeze in a bi-ethnic cohort of UK-born children, and to explore the relationship between them.

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Methods

Our sample comprised 1204 (553 White British and 651 Pakistani) participants from the Born in Bradford study [6]. Ethics approval was granted by Bradford National Health Service Research Ethics Committee (ref 07/H1302/112). Maternal serum concentrations of 25(OH)D were measured in fasting serum samples at pregnancy booking at ~26 weeks gestation. Detection of 25(OH)D was achieved using mass spectrometry. Diagnosis of asthma and wheeze, and prescription information was extracted from primary care records. We examined three outcomes: (1) GP-diagnosed asthma that is not treated with asthma-controlling medication; (2) GP-diagnosed asthma that is treated with asthma-controlling medication (antimuscarinic bronchodilators, selective β2 agonists, leukotriene receptor antagonists and nasal corticosteroids); and (3) GP-diagnosed wheeze on at least one occasion without diagnosis of asthma.

The association of maternal 25(OH)D levels with childhood asthma and wheeze was explored using two logistic regression models, which were applied to the full sample and then repeated separately in White British and Pakistani participants, and tested for an interaction between ethnicity and exposure: model 1 was unadjusted, and model 2 was adjusted for maternal BMI, maternal education and in receipt of means-tested benefits and smoking during pregnancy. Associations between 25(OH)D and asthma are presented as change per 1 standard deviation (SD) increase. Multiple imputation using chained equations were used to impute missing covariable values. Sensitivity analysis was performed on complete cases and the results were similar. All analyses were performed using STATA/SE software (Stata/SE 13.1 for Windows, StataCorp LP, College Station, TX, USA).

Results and Discussion

Table 1 shows the distribution of the outcomes, exposure and confounders for the full sample and stratified by ethnicity. 25(OH)D levels were significantly lower in Pakistani women compared to White British women. A higher prevalence of untreated asthma was observed in Pakistani children and they tended to be diagnosed at a younger age. However, there was little difference in the proportion of White British and Pakistani children who were diagnosed with asthma and receiving treatment, or with wheeze, though Pakistani children tended to be diagnosed with wheeze at an older age compared to White British children. The odds ratios

(ORs) with 95% confidence intervals (CI) for the association between an offspring diagnosis of untreated and treated asthma, and wheeze with maternal 25(OH)D levels are presented in table 2. In the adjusted analysis there was a null association with untreated asthma in both ethnic groups, and the parallel lines in figure S1 shows that maternal vitamin D levels had the same effect on the probability of developing asthma that was not treated was the same in both ethnic groups. For asthma treated with medication there was an 18% relative reduction in odds in White British children and a 21% increase in Pakistani, and though there was no evidence of a statistically significant interaction. Figure S2 shows that the lines diverge with increasing maternal vitamin D levels, leading to a greater probability developing asthma requiring medication in Pakistani children but not in White British children, in whom the probability slightly decreases. Whilst there was a weak positive association of 25(OH)D with wheeze in White British children, 25(OH)D was inversely association with wheeze in Pakistani children, with each 1 SD greater level associated with a 36% relative reduction in odds, together with evidence of an interaction between ethnicity and exposure. Figure S3 shows that whilst lower maternal 25(OH)D levels increase the probability of wheeze in Pakistani children, this decreases with higher levels; the converse was observed in White British children.

Our findings replicate those of other studies which have found that whilst South Asian children have a higher rate of medical consultations for asthma compared with White children [7], their use of inhaled corticosteroids is lower [8]. The reduced use of inhaled medications amongst Pakistani children in our cohort may be due to a range of factors such as cultural health beliefs and attitude towards medication, language barriers, and migration status (e.g. unfamiliarity with preventative treatment and asthma management plans in first-generation and recent migrants) [9]. These barriers highlight the importance of the clinician's approach when managing asthma in different ethnic groups.

Maternal vitamin D appears to be important in the development of the immune system and for optimal lung growth and maturation [10]. However, despite observing lower vitamin D levels in Pakistani women and higher prevalence of asthma in their offspring we found no association between the two in our stratified analysis, possibly suggesting differing underlying mechanisms between the two ethnic groups. We found that higher maternal vitamin D levels were shown to be protective against wheeze in Pakistani children only. As wheeze is frequently viral-induced, it may be that maternal vitamin D exerts a protective

effect against viral infections in the offspring but this is modified by ethnic variability in genetic and environmental factors.

In conclusion, despite highly significant ethnic differences in maternal 25(OH)D and asthma prevalence, our analyses do not provide evidence that low maternal vitamin D levels increase the risk of offspring developing asthma. However, we did observe a possible protective effect of maternal vitamin D levels and offspring wheeze which appears to be limited to Pakistani children only.

	All (N=1204)	White British (N=553)	Pakistani (N=651)
Outcomes			
GP diagnosed, untreated asthma	132 (11.0)	49 (8.9)	83 (12.8)
Age at asthma diagnosis (months)[a]	47.0 (18.8)	52.0 (20.7)	44.0 (17.1)
GP diagnosed and treated asthma	69 (5.7)	26 (4.7)	43 (6.6)
Age first diagnosed with asthma or prescribed asthma-related drugs (months)[b]	34.8 (23.3)	34.1 (25.1)	35.3 (21.8)
Wheeze, no diagnosis of asthma	131 (10.9)	57 (10.3)	74 (11.4)
Age at first wheeze (months)[a]	31.9 (22.6)	27.8 (20.8)	34.3 (23.3)
Exposure			
25(OH)D, nmol/L[b]	22.6 (11.9, 40.5)	36.8 (26.5, 55.8)	13.0 (8.5, 20.8)
Confounders			
BMI[a]	26.0 (5.7)	27.1 (6.1)	25.1 (5.2)
Missing	121 (10.0)	40 (7.2)	81 (12.4)
Smoked during pregnancy			
No	930 (77.2)	354 (64.0)	576 (88.5)
Yes	204 (16.9)	181 (32.7)	23 (3.5)
Missing	70 (5.8)	18 (3.3)	52 (8.0)
In receipt of benefits			
No	665 (55.2)	344 (62.2)	321 (49.3)
Yes	469 (39.0)	191 (34.5)	278 (42.7)
Missing	70 (5.8)	18 (3.3)	52 (8.0)
Maternal education			
<A level equivalent	702 (58.3)	343 (62.0)	359 (55.2)
A level and above	430 (35.7)	192 (34.7)	238 (36.6)
Missing	72 (6.0)	18 (3.3)	56 (8.3)

Table 1: Maternal and child characteristics for all participants and by ethnic groups. Values are n (%) unless otherwise indicated: [a] Mean (SD); [b] Median (IQR)

	Odds Ratio (95% CI) per 1 SD of 25(OH)D			
	All (n=1204)	White British (n=553)	Pakistani (n=651)	$P_{interaction}$ [a]
Asthma – diagnosed, untreated				
Model 1	0.87 (0.71, 1.06)	0.94 (0.70, 1.27)	0.98 (0.70, 1.38)	0. 488
Model 2	0.86 (0.70, 1.06)	0.92 (0.68, 1.25)	0.98 (0.70, 1.38)	0.903
Asthma – diagnosed, treated				
Model 1	0.92 (0.71, 1.20)	0.85 (0.55, 1.30)	1.23 (0.85, 1.77)	0.199
Model 2	0.92 (0.71, 1.20)	0.82 (0.53, 1.27)	1.21 (0.83, 1.77)	0.207
Wheeze				
Model 1	0.93 (0.76, 1.12)	1.11 (0.85, 1.43)	0.63 (0.38, 1.04)	0.050
Model 2	0.93 (0.77, 1.14)	1.15 (0.88, 1.49)	0.64 (0.39, 1.05)	0.043

Table 2 Associations between maternal 25(OH)D with childhood asthma and wheeze overall and stratified by ethnicity. Model 1: Unadjusted. Model 2: Adjusted for maternal BMI, smoking during pregnancy, maternal education and in receipt of means-tested benefits. [a] P-value for interaction between ethnicity and exposure.

Author contributions

GS designed the study with input from JW and AS. JW was involved in the design and data collection of the Born in Bradford Study. GS developed the analysis protocol and conducted the analysis. GS wrote the first draft of the paper and JW and AS contributed to the final submitted version.

Declaration of interests

We declare no competing interests.

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