

MATERNAL VITAMIN D IN PREGNANCY AND THE RISK OF ASTHMA IN THE OFFSPRING: THE VITAMIN D IN PREGNANCY STUDY

Hyde NK¹, Vuillermin P², Wark JD², Hosking SM¹, Pasco JA^{1,2}

¹Deakin University, Geelong, VIC, Australia; ²The University of Melbourne, Parkville, VIC, Australia

BACKGROUND

- It has been hypothesised that vitamin D deficiency may contribute to the observed increase in incidence of asthma.
- Studies in both human and animal models have reported that vitamin D is involved in lung maturation and development *in utero*¹.
- Thus, given that the developing foetus is reliant on maternal vitamin D (25(OH)D) stores to cross the placenta, it is plausible that maternal 25(OH)D levels may be implicated in child asthma risk.
- Separate meta-analyses have provided inconsistent results^{2,3}, however one meta-analyses reported a U-shaped relationship where maximal protective effects were seen at 70nmol/L².
- Previously, we have reported that there was an association between maternal vitamin D in late pregnancy and asthma and wheeze risk in girls, but not boys at one and six years of age in the Vitamin D in Pregnancy (VIP) cohort.
- In the VIP study maternal 25(OH)D levels greater than 70nmol/L were protective against asthma in the children and the effect was more pronounced in girls than boys, at six years of age.
- Thus, we aimed to determine whether the association persisted in offspring at age 11 years.

METHODS

- Women were recruited from VIP⁴ before 16 weeks gestation from the Geelong Hospital antenatal clinic (2002-04)(n=475), which resulted in 402 mother child pairs at birth.
- 209 (52%) when children were aged approximately 11 years, and 178 children had complete data for the current analyses.
- Venous blood samples were taken into serum gels and EDTA tubes, centrifuged before 2 hours and stored at -70°C at recruitment. Assays were undertaken in fully accredited laboratories (Royal Children's Hospital, Melbourne) and 25(OH)D was measured by radioimmunoassay (Immunodiagnosics Systems, Tyne and Wear, UK). The co-efficient of variance was 10.2 and 10.1% at 30 and 100 nmol/L, respectively. For statistical analysis purposes, high 25(OH)D was categorised as >70nmol/L
- Asthma status was parentally reported using the International Study of Asthma and Allergies in Childhood Questionnaire (Has your child ever had asthma? Yes/No; defined as lifetime asthma, and Has your child ever had wheeze or whistling in the past 12 months? Yes/No; defined as current asthma).
- Logistic regression models were built predicting asthma and wheeze outcomes. The final models were adjusted for maternal age, BMI and gestational smoking.
- Interactions between maternal 25(OH)D status and sex were tested by the inclusion of a 25(OH)D*sex term in to the model.



Figure 1: A Vitamin D in Pregnancy Study mother completing questionnaires

RESULTS

- 45 (24%) of the offspring had parent-reported 'asthma ever'; and 26 (15%) had parent-reported 'wheeze/whistling in the last 12 months', respectively.
- Demographics of the sample by child sex are presented in Table 1.
- The association between 25(OH)D and asthma ever varied by sex (25(OH)D (p for interaction=0.01).
- In adjusted models, girls, but not boys, who were born to mothers with high 25(OH)D in late pregnancy were significantly less likely to report 'asthma ever' (Table 2).
- Sex*25(OH)D interaction terms were unable to be explored in 'current asthma' models due to quasi separation.
- In sex-pooled models there was a trend for children born to mothers with high 25(OH)D in late pregnancy to be less likely to report 'current asthma' (Table 2).
- There was no associations with 25(OH)D in early pregnancy with 'asthma ever' or 'current asthma' in either sex (Table 2).

Table 1: Demographic and anthropometric measures of the participants

	Girls n=80	Boys n=98	p for difference
<i>Child measures</i>	Median (IQR), Mean (SD) or n(%)	Median (IQR) or Mean (SD) or n(%)	
Height (cm)	149.6 (7.45)	148.7 (8.12)	0.46
Weight (kg)	40.85	39.55	0.28
Lifetime asthma (%) yes	21	24	0.79
Current asthma (%) yes	9	17	0.25
<i>Maternal measures</i>			
25(OH)D recruitment	54.45	59.45	0.34
25(OH)D 28-32 weeks	52.0	57.4	0.50
BMI (recruitment)	25.59	24.90	1.0
Gestational smoking status (recruitment) n (%) yes	10 (12.5)	22 (22.4)	0.09

Table 2: Regression modelling after stratification by glucose challenge test results (GCT)

Asthma ever (girls)	aOR (95% CI)	p
25(OH)D recruitment	0.69 (0.15,3.30)	0.64
25(OH)D 28-32 weeks	0.08 (0.008,0.82)	0.006
Asthma ever (boys)	aOR (95% CI)	p
25(OH)D recruitment	1.33 (0.48,3.72)	0.59
25(OH)D 28-32 weeks	1.10 (0.36,3.32)	0.87
Current asthma (pooled)	aOR (95% CI)	p
25(OH)D recruitment	1.12 (0.42,3.03)	0.82
25(OH)D 28-32 weeks	0.21 (0.05,0.97)	0.02

DISCUSSION

- High maternal 25(OH)D in late pregnancy was associated with decreased risk of lifetime asthma in girls, but not boys.
- There was also a decreased risk of current asthma in sex pooled sample.
- There are several plausible mechanisms on which vitamin D may act to decrease asthma risk. The first is a direct impact on lung development. The second may be a complex role in immune system development⁵.
- There was also no association between maternal 25(OH)D in early pregnancy and offspring asthma and wheeze, which would suggest that this association is temporally reliant. These results, however contradict the findings of a previous meta-analyses which suggested that 25(OH)D levels were more important in early pregnancy.
- Thus, these findings suggest we should be ensuring that pregnant women maintain optimal 25(OH)D levels into late pregnancy.
- These findings should be confirmed in randomised control trials in 25(OH)D deficient pregnant populations.

REFERENCES

1. Pfeffer PE et al. 2018, Chest, 153:1229-1239
2. Song et al. 2017, Mol Nutr Food Res, 61, 1600657
3. Wei et al. 2016, Pediatr Allergy Immunol, 27: 612-619.
4. Morley et al. 2006, J Clin Endocrinol Metab 91(3):906-12
5. Litonjua AA. 2019, Curr Opin Allergy Clin Immunol, 19(2):126-131