Prevalence of vitamin D deficiency and insufficiency in Malaysian infants

Dear Editor,

Vitamin D deficiency, a worldwide health problem, is also prevalent in tropical countries.¹ It is estimated that 15% of the world's population are either vitamin D deficient or insufficient.¹ In a study on the state of Kelantan in Malaysia (2010–2012), 60% of pregnant women were vitamin D deficient.² Maternal vitamin D deficiency predisposes infants to vitamin D deficiency especially if they are exclusively breastfed. The prevalence of vitamin D deficiency in Malaysian infants is unknown. We conducted a cross-sectional study to ascertain the prevalence and risk factors predisposing to vitamin D deficiency in Malaysian neonates.

We recruited term neonates (gestational age ≥ 37 weeks; aged 2 to 4 weeks) followed up for neonatal jaundice in a well-baby clinic from December 2016 to December 2017. Written informed consent was obtained from parents. Ethical approval was obtained (Ethics Number: 20161115-4600). No blood samples were obtained purely for the purpose of the study. We excluded neonates with the following: prematurity (gestational age < 37 weeks), neonatal cholestasis (conjugated bilirubin > 17 mmol/L if total bilirubin < 85 mmol/L, or conjugated bilirubin $> 20\%$ if total bilirubin > 85 mmol/L), infants who were on diuretics or vitamin D supplements, and infants with feeding difficulties. Infants whose mothers had renal, liver, thyroid and gastrointestinal disorders or taking anti-epileptic medications were excluded.

We collected data on age, gender, ethnicity, gestational and feeding history. Daily sun exposure of the infants was determined via a set of sunshine exposure behaviour in a questionnaire adapted from Barger and Heaney.³ Blood was collected for liver function, serum 25-hydroxy vitamin D (25(OH)D) and bone profile tests. Serum 25(OH)D level was assayed using Siemens Advia Centaur Analyser, which has a within-run precision coefficient of variation (CV) of $\leq 8\%$ and a total CV of $\leq 12\%$. Maternal vitamin D level was not assayed. We defined vitamin D status of the infants according to Munns et al.⁴—25(OH)D > 50 nmol/L as sufficient, 25(OH)D 30.0–50.0 nmol/L as insufficient, and 25(OH)D < 30.0 nmol/L as deficient.

T-test and Mann-Whitney U test were used to compare the mean quantitative variables while the differences

between mean qualitative variables were analysed with Pearson's chi-square or Fisher's exact test. A *P* value of < 0.05 was considered statistically significant. For the ease of statistical analysis, infants with vitamin D insufficiency and sufficiency (non-deficient) were grouped together.

Of the 110 term neonates (mean age: 2.5 [± 0.9] weeks; 60.0% males; Malay 70.0%, Chinese 20.9%, Indian 8.2%, other ethnicities 0.9%), 79.1% (*n*=87) were exclusively breastfed, including 80.5% (62/77) of the Malays and 75.8% (25/33) of the non-Malays (*P*=0.574). None of the 110 neonates had a serum vitamin D level of < 20 nmol/L; 47 (42.7%) were 20.1–30.0 nmol/L, 33 (30.0%) 30.1–40.0 nmol/L, and 11 (10.0%) 40.1–50.0 nmol/L. Only 17.3% (*n*=19) were vitamin D sufficient. The overall mean (SD) serum vitamin D level of all neonates was 36.9 (± 15.3) nmol/L. No correlation between serum calcium level and degree of vitamin D deficiency was observed. None of the neonates had clinical symptoms or signs of vitamin D deficiency.

On univariate analysis, the only factor significantly associated with vitamin D deficiency was a shorter duration of sunlight exposure (mean [$\pm$ SD] duration of exposure, hour/week; deficient versus non-deficient: 2.00 [± 1.40] vs 2.60 [± 1.63], *P*=0.043).

Our results showing vitamin D deficiency and insufficiency is common in Malaysian neonates are consistent with studies from other tropical countries.⁵ We did not find any correlation between exclusive breastfeeding and vitamin D deficiency, possibly due to the small number of study subjects and a high exclusive breastfeeding rate in the present cohort. Other authors have observed that exclusive breastfeeding without adequate sunlight exposure and vitamin D supplementation were risk factors for vitamin D deficiency in neonates.⁶ It is likely that changes in lifestyle related to urbanisation, increased indoor activities and use of sunscreen have increased the prevalence of hypovitaminosis D in tropical countries, including pregnant mothers.

We found that the only significant risk factor for vitamin D deficiency was a shorter duration of sunlight exposure. A possible effective strategy to improve vitamin D level in the newborn is having adequate sunlight exposure. A study from India showed

Table 1. Factors associated with vitamin D deficiency in 110 Malaysian neonates

Factors	Total N=110	Vitamin D deficient (<30nmol/L) n=41	Vitamin D non-deficient (≥30nmol/L) n=69	P value
Sex, no. (%)				
Male	66 (60.0)	21 (51.2)	45 (65.2)	0.147
Female	44 (40.0)	20 (48.8)	24 (34.8)	
Ethnicity, no. (%)				
Malay	77 (70.0)	29 (70.7)	48 (69.6)	0.897
Non-Malay	33 (30.0)	12 (29.3)	21 (30.4)	
Gestational age, median (IQR), weeks	38.0 (0)	38.0 (0)	38.0 (2.0)	0.715
Birth weight, mean (SD), g	2920 (456)	2940 (467)	2907 (451)	0.715
Birth weight <2500g, no. (%)	17 (15.5)	6 (14.6)	11 (15.9)	0.854
Feeding method, no. (%)				
Exclusive breastfeeding	87 (79.1)	35 (85.4)	52 (75.4)	0.212
Non-exclusive breastfeeding	23 (20.9)	6 (14.6)	17 (24.6)	
Feeding frequency per day, median (IQR)	8.0 (3.0)	8.0 (4.0)	8.0 (3.0)	0.832
Current weight, median (IQR), g (N=107)	3420 (715)	3390 (820)	3430 (639)	0.873
Weight gain from day 14, median (IQR), g/day (N=107)	73 (83)	66 (90)	92 (96)	0.136
Laboratory parameters, median (IQR)				
ALP, mean (SD), U/L	287.00 (100.14)	289.15 (113.06)	285.72 (92.47)	0.863
Intact parathyroid hormone, pmol/L (n=109)	2.4 (2.6)	2.4 (3.8)	2.3 (2.2)	0.610
Calcium, mmol/L	2.57 (0.16)	2.54 (0.18)	2.58 (0.15)	0.178
Phosphate, mmol/L	2.25 (0.38)	2.23 (0.21)	2.25 (0.43)	0.757
Child sun exposure, mean (SD), hours/week	2.38 (1.57)	2.00 (1.40)	2.60 (1.63)	0.043 ^a

ALP: alkaline phosphatase; IQR: interquartile range; SD: standard deviation

^a $P < 0.05$

that a minimum of 30 minutes weekly sunlight exposure in the afternoon between 10am and 3pm, over 40% of the body area with the infant clothed in diapers in prone position for at least 16 weeks, was all that was required to achieve sufficient vitamin D levels by 6 months of age.⁷ In the present study, the mean duration of sunlight exposure for the whole cohort was 2.38 hours/week, but the 19 neonates who had sufficient vitamin D (>50nmol/L) had a mean duration of 3.21 (1.39) hours/week of sunlight exposure. Unfortunately data on the body area and the timing of day the neonates were exposed to sunlight were unavailable.

Other possible strategies to prevent neonatal vitamin D deficiency include supplementing high-dose vitamin D (4,000 or 6,400IU/day) to lactating mothers with

limited sunlight exposure,⁸ or supplementing vitamin D to all newborn babies irrespective of their breastfeeding status. Selective supplementation of vitamin D to breastfed infants,⁹ however, should be avoided as it is associated with concerns that lactating mothers would switch to infant formula due to the potential negative perception with breastfeeding.¹⁰

Drawbacks of the present study include a lack of maternal vitamin D level and the small sample size. Data on breastfeeding jaundice, caused by inadequate breastmilk leading to inadequate vitamin D intake in the first few days of life, were also not collected. Finally, data on phototherapy for neonatal jaundice, which may increase the level of vitamin D in babies with low levels of vitamin D, were unavailable.

In summary, in this cohort of Malaysian neonates, we found a very high prevalence of vitamin D deficiency and insufficiency. Supplementing pregnant and lactating mothers, and all newborn infants with vitamin D as well as ensuring adequate sunlight exposure a few months after birth are possible strategies to prevent neonatal vitamin D deficiency.

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