Large anterior fontanelle and low vitamin D in neonates: a potential early recognition sign

Vitamin D is an essential nutrient that regulates the amount of calcium and phosphate in the body and is necessary for healthy bones, teeth and muscles. This audit of practice demonstrates that a majority of neonates with low vitamin D have a large anterior fontanelle. A large anterior fontanelle could be identified prior to discharge during the newborn and infant physical examination to aid with early detection and treatment of vitamin D deficiency.

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Key points

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1. Large anterior fontanelles in neonates could be an early sign of low vitamin D.
2. The practice of testing for vitamin D levels in infants at Sandwell and West Birmingham Hospital NHS Trust was audited and the clinical implications are discussed.
3. Early detection and treatment can prevent severe deficiency, especially in breastfeeding infants.

Vitamin D can be obtained from the diet and is synthesised in the skin by exposure to sunlight, however, inadequate vitamin D is common and an important worldwide issue. High risk groups for vitamin D deficiency include:[1]

- pregnant and breastfeeding women
- infants
- infants of twin and multiple pregnancies
- adolescents
- obese individuals
- those with reduced sun exposure, eg living in the northern latitude, Asian and African descent, wearing concealing clothing, immobility, excessive use of sun block.

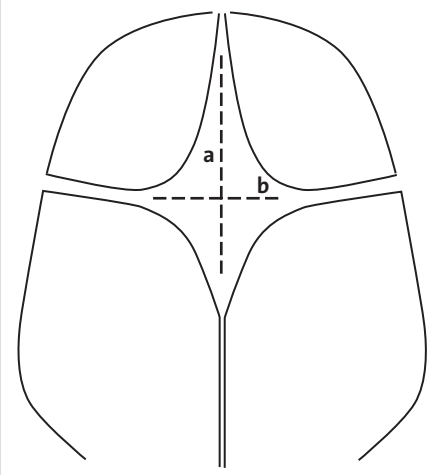
A US study showed that breastfeeding without supplementation among infants and lower milk intake among toddlers were significant predictors of vitamin D deficiency.[2] Chronic disease may also increase risk of vitamin D deficiency, including chronic renal disease, chronic liver disease and malabsorption syndromes (eg coeliac disease, Crohn's disease and cystic fibrosis).

Routine testing of vitamin D levels in infants is not recommended. Vitamin D deficiency or insufficiency should be considered and checked only if infants are symptomatic, have other risk factors, and where other causes for symptoms have been excluded. Signs and symptoms in infants included seizures, tetany and cardiomyopathy. In children, symptoms include aches and pains, myopathy causing delayed walking, rickets (lack of vitamin D) with bowed legs, knock knees, poor growth and muscle weakness.[1] Gordon et al demonstrated that about one-third of vitamin D-deficient participants exhibited demineralisation, highlighting the deleterious skeletal effects of this condition.[2]

The anterior fontanelle

Fontanelles are soft membrane-covered gaps at the junction of the sutures between the cranial bones of an infant or fetus. There are six fontanelles in a newborn at birth: the anterior and posterior, two sphenoid and two mastoid, with the largest being the anterior fontanelle.[3]

The anterior fontanelle can range



Anteroposterior (a) and transverse (b) diameters

$\frac{a+b}{2}$ = anterior fontanelle size

FIGURE 1 Measuring the size of the anterior fontanelle.

between 0.6cm and 3.6cm, with a mean of 2.1cm but can increase up to 4.7cm in dark-skinned infants.[3,4] The anterior fontanelle is palpated during all newborn and infant physical examinations (NIPE). Measurement of the anterior fontanelle should be performed as an average of the anterior-posterior and the transverse measurements, as shown in **FIGURE 1**.[4,5]

Delayed closure of the anterior fontanelle is associated with vitamin D deficiency, however, not much is known about the association of vitamin D deficiency with large anterior fontanelles in newborns. Furthermore, there is no clear guidance on procedure for infants with a large anterior fontanelle. Common causes of large anterior fontanelle include Down's syndrome, congenital hypothyroidism, achondroplasia, rickets and increased intracranial pressure.[3]

Methods

The practice of testing for vitamin D levels in infants less than six months of age was audited in Sandwell and West Birmingham Hospital NHS Trust.

A retrospective audit was carried out between January 2015 and December 2015. A list of all infants under six months of age who were tested for vitamin D levels was obtained from the Biochemistry Department. Data included birth gestation, birth weight, ethnicity, reason for vitamin D testing, maternal vitamin D status and method of feeding. The treatment of infants with low vitamin D levels was also audited. The data were obtained through hospital computerised medical records and medical notes. The infants were dichotomised to normal and low vitamin D.

Results

A total of 84 infants were tested for vitamin D in the study period. Three infants were excluded due to missing data. The infants were divided into two groups according to the flow diagram in **FIGURE 2**:
1. low vitamin D levels (<50nmol/L; n=45)
2. normal vitamin D levels (n=36).

Of the cohort categorised as low vitamin D, the majority of infants were term gestation, breastfed and from an ethnic background of Asian or African (**TABLE 1**), in keeping with the literature. The finding of a large anterior fontanelle in 24 infants was the most common reason to check the vitamin D level.

These 24 infants were all neonates with a mean age of three days (ranging from 0 to 14 days). Of the 24 neonates with a large anterior fontanelle, 18 had deficient vitamin D levels (<25nmol/L) and six had insufficient vitamin D levels (25-50nmol/L). It was found that, of those with deficient vitamin D levels, 11 (61%) had very low vitamin D with levels <15nmol/L. There were two infants aged two days and 21 days in the normal vitamin D group that had a large anterior fontanelle; neither of these had any of the common causes of a large anterior fontanelle.

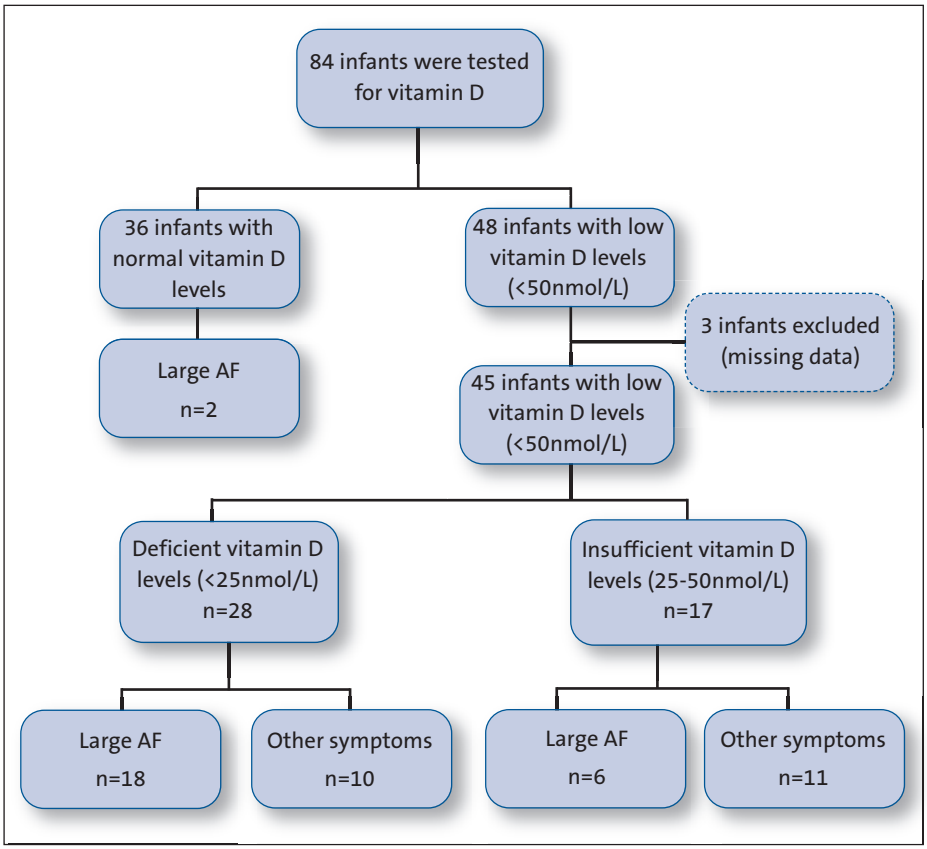


FIGURE 2 The total number of infants tested for vitamin D and their subsequent categorisation. Key: AF = anterior fontanelle.

The Sandwell and West Birmingham Hospital NHS Trust protocol for the treatment of infants with low vitamin D levels is shown in **APPENDIX 1**. The treatment of infants with low vitamin D levels, as per the Trust protocol, was audited. It was found that 50% of infants with deficient vitamin D levels were not treated according to the Trust protocol guidelines. These infants did not receive either the correct dose or the correct treatment duration (**TABLE 2**).

Discussion

Current practice in the UK, as recommended by the British Paediatric and Adolescent Bone group, is to define vitamin D deficiency as the serum level of vitamin D below 25nmol/L and insufficiency as between 25 and 50nmol/L. It is known that clinically, insufficiency can cause muscle aches and pains and deficiency can cause seizures, cardiomyopathy, myopathy, rickets and poor growth. A vitamin D level test is recommended when an infant or child is symptomatic and has risk factors.[1]

In this study, 36 out of 45 (80%) of the infants in the low vitamin D group were neonates with an age range 0 to 24 days and the majority of infants in the audit were breastfed. Over two thirds of these neonates were of Asian or African descent. Elucidating signs and symptoms of vitamin D deficiency in infants and particularly in neonates can be challenging. As such, clinicians should be more vigilant especially when examining infants with risk factors for low vitamin D. The majority of our infants from the low vitamin D group (53%) were tested due to the finding of a large anterior fontanelle.

A limitation of our study was that evaluation of the size of the anterior fontanelle was made subjectively as per standard practice within our unit. A more objective measurement (as depicted in **FIGURE 1**) may help standardise the definition of a large anterior fontanelle and

	Low vitamin D levels (n=45)	Normal vitamin D levels (n=36)
Birth gestation:		
Preterm	13	23
Term	32	13
Mean birth weight (g)	2,648 (range: 780-3,640)	2,464 (range: 640-3,840)
Ethnicity		
Asian	21	15
African	12	8
Caucasian	4	9
Mixed	7	4
Unknown	1	0
Reasons for vitamin D testing		
Poor weight gain	3	7
Large fontanelle/craniotabes*	24*	2
Abnormal blood test/X-ray	7	6
Abnormal movements	2	3
Maternal or paternal low vitamin D	2	1
Genu varum (bow leg)	1	0
Unknown	3	6
Abnormal head size/shape	0	4
Carried out with routine bloods/ incidental finding	3	7
Maternal vitamin D status		
Deficient	4	2
Insufficient	9	1
Normal	4	1
Unknown/not tested	28	32
Infant nutrition		
Breastfed	29	8
Formula	6	13
Mixed	6	3
Unknown	4	12

TABLE 1 The characteristics of the babies in the low and normal vitamin D categories. *Craniotabes is a softening of the skull bones, which can occur normally in premature infants and those younger than six months of age. Only two babies out of the 24 in the low vitamin D group had craniotabes.

Low vitamin D status / treatment given	Low vitamin D levels (n=45)	Treated as per protocol (yes/no)
Deficient/cholecalciferol for eight weeks	**14**	**Y**
Deficient/cholecalciferol for three weeks	**6**	**N**
Deficient/cholecalciferol for unknown weeks	**3**	**N**
Deficient/Abidec	**2**	**N**
Deficient but no treatment given (no follow-up)	**3**	**N**
Insufficient/cholecalciferol	**3**	**Y***
Insufficient/Abidec	**11**	**Y**
Insufficient/no treatment given	**3**	**N**

TABLE 2 Infants with low vitamin D and the treatment they received. Note, Abidec is a multivitamin supplement, cholecalciferol is vitamin D3. *These three babies received cholecalciferol because they were symptomatic.

possibly refine its use as a screening tool. Currently there is limited data on the normal range of anterior fontanelle sizes in the UK population and further work is recommended.

A study by Uzukwu-Edeani et al in 2013 looked at the normal anterior fontanelle sizes in newborn Igbo babies in south-eastern Nigeria.[6] They produced a percentile value chart of the anterior fontanelle measurements in term babies. Using a percentile chart would help determine whether an anterior fontanelle would be considered large, and may help determine if vitamin D testing is warranted. There are currently no guidelines and a variation in practice exists in the management of a large anterior fontanelle.

Previous studies raised concerns that infants at birth with vitamin D deficiency acquired this deficit *in utero*.[7,8] In the cohort of low vitamin D infants presented here, maternal vitamin D levels were not checked in 28 out of 45 cases (62%). Screening mothers in pregnancy is not routinely performed and only those with risk factors and signs and symptoms are tested. Maternal vitamin D status has been suggested to have long-term effects on an infant.[9] There is a relationship between the breastfeeding mother's vitamin D status and the vitamin D content of her breast milk.[7,10] As previously mentioned, the majority of infants from the low vitamin D cohort were breastfed. Daaboul et al described cases of infants with symptomatic vitamin D deficiency; all were breastfeeding or had poor diet lacking vitamin D. All the mothers had vitamin D deficiency and they recommended that vitamin D supplementation should be given to at-risk breastfeeding mothers and their infants.[11]

The American Academy of Pediatrics recommends 400IU of oral vitamin D daily beginning in the first days postpartum, but subsequent studies[12,13] showed only about 20% compliance to this recommendation. A prospective randomised trial demonstrated that 6400IU of daily maternal Vitamin D3 for six months maintains maternal vitamin D status, producing sufficient vitamin D levels for breastfeeding infants.[10] In addition, Cooper et al showed that vitamin D supplementation of 1000IU daily, compared to placebo, in pregnant women in the UK allowed a significant increase in bone mineral content of neonates, however, only when they were born in the winter.[14]

Conclusion

From our audit, the subjective sign of a large anterior fontanelle in neonates appears to be a simple early recognition sign for low vitamin D with the potential for being utilised as a screening tool. A larger study comparing vitamin D levels in infants with risk factors versus those without risk factors and having a large anterior fontanelle is suggested. Early detection and treatment of vitamin D deficiency can prevent severe deficiency, especially in breastfeeding infants.

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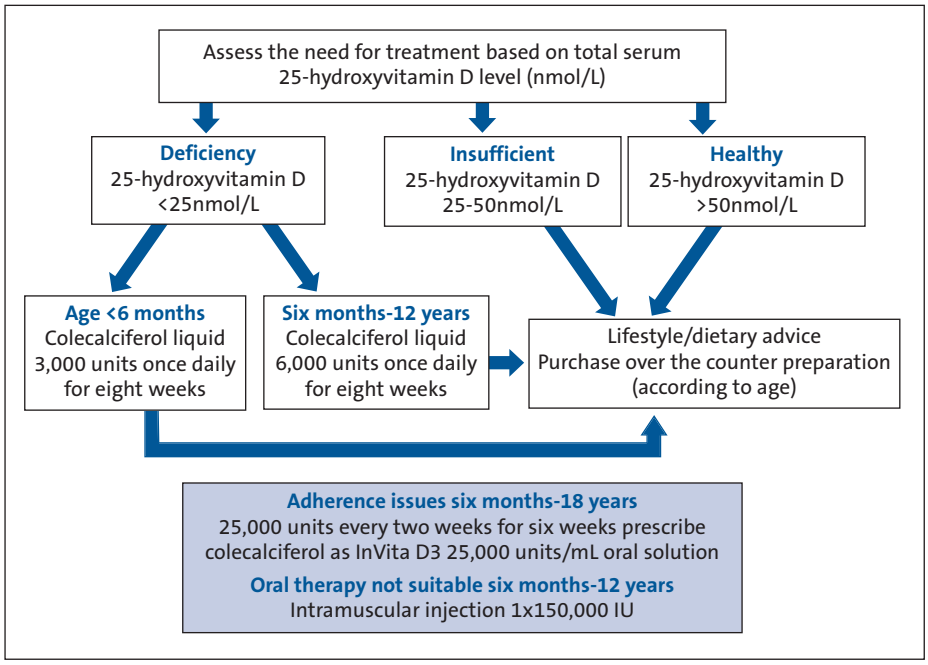

APPENDIX 1 The treatment pathway for children with suspected vitamin D deficiency (Sandwell and West Birmingham Hospitals NHS Trust).

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