Prevalence Estimates of Vitamin A Deficiency in India by NNMB Surveys

We read with interest the manuscript entitled "Relevance of Continuation of Universal Vitamin A Supplementation Program in India" [1]. The following pertinent aspects need to be carefully considered prior to interpreting the findings in relation to national policy on VAD.

It was reported by authors that the prevalence of clinical vitamin A deficiency (VAD) has declined considerably in India, as compared to previous years [2]. However, they found a high prevalence of blood vitamin A deficiency (<20 µg/dL), a criteria for sub-clinical VAD [3]. In their data, 61% preschool children had sub-clinical VAD, and with this criterion, a public health problem was diagnosed in all the NNMB states surveyed, ranging from 52% in Maharashtra to 88% in Madhya Pradesh. The proportion of severe blood VAD (<10 µg/dL) was 21.5%, again indicating a severe public health problem in all the NNMB states [4].

This NNMB survey [2] was conducted in the year 2000-2001 in rural areas of eight States viz., Andhra Pradesh, Karnataka, Kerala, Madhya Pradesh, Orissa, Tamil Nadu, Maharashtra and West Bengal. The Blood vitamin A levels were assessed in a subsample of preschool children by dry blood spot technique (DBS), using HPLC at the National Institute of Nutrition (NIN) [5]. There was an average gap of 220 days between the collection of sample and analysis due to delay in commissioning of analytic facility. [4]. The findings of this NNMB survey [4] were reviewed by an expert committee constituted by the ICMR to explain the contradictory scientific findings on VAD. For example, the prevalence of Bitot's spots among preschoolers in the State of Kerala was nil; however, the prevalence of sub-clinical form of vitamin A deficiency was the maximum [2]. This committee recommended a resurvey on a sub-sample of 50 children of 1-5 year age group (@ 10 children per village, from 5 villages) in the States of Kerala, Madhya Pradesh (high prevalence of sub-clinical VAD) and Andhra Pradesh (low prevalence) by covering one district each during the same season. The clinical signs of vitamin A deficiency and blood vitamin A levels were documented simultaneously. It was also suggested that in each of these district, all those villages surveyed earlier be covered in a repeat survey, by adopting similar sampling procedures. The Repeat surveys were carried out in the districts of Mallapuram in Kerala, Srikakulam in Andhra Pradesh and Seoni in Madhya Pradesh. The children were examined for prevalence of clinical signs of vitamin A deficiency, and blood vitamin A levels were estimated from Finger prick blood samples by DBS method, as was done in the earlier survey. The median blood vitamin A levels in all the three states during the repeat survey were around 20 µg/dL.

The prevalence of children having blood vitamin A levels of <20 µg/dL was about "half" of that observed earlier in the States of Kerala (52% *vs* 93%), Andhra Pradesh (45% *vs* 80%) and Madhya Pradesh (50% *vs* 100%) [4].

Validity of serum retinol estimated by DBS is low because the children from whom DBS samples are collected, acute-phase proteins like serum C reactive protein levels (CRP) are not done. Hence, no adjustments can be made in the final value of Serum retinol levels values obtained by DBS method. The changes in vitamin A metabolism during the acute phase response have been reviewed extensively and documented [6,7]. Reductions in plasma retinol have been described during the acute phase of a wide range of infections [8]. In light of frequent sub-clinical infections, these NNMB surveys have probably overestimated the prevalence of VAD because concomitant CRP levels were not used for correcting blood vitamin A levels.

Scientists in India has been advocating targeted distribution of synthetic vitamin A to the areas where there is significant clinical VAD. Thus, the conclusion of the authors that there is no need "to stop supplementation of vitamin A to pre-school children hastily" are subject to misinterpretation and likely to create confusion with regards to vitamin A supplementation policy in country.

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REFERENCES

1. Arlappa N, Ravikumar BP. Relevance of continuation of universal vitamin A supplementation program in India. Indian Pediatr. 2011;48:246-7.
2. Toteja GS, Singh P, Dhillon BS, Saxena BN. Vitamin A deficiency disorders in 16 districts of India. Indian J Pediatr. 2002;69:603-5.
3. World Health Organization (WHO). Indicators for assessing Vitamin A deficiency and their application in monitoring and evaluating intervention programs. Geneva: WHO;1996.

4. National Nutrition Monitoring Bureau (NNMB). Prevalence of Vitamin A Deficiency among Rural Preschool Children. Hyderabad, India: National Institute of Nutrition, Indian Council of Medical Research. Report No 23;2006.
5. Craft NE. Retinol analysis in dried blood spots by HPLC. J Nutr. 2000;130:882-5.
6. Filteau SM. Vitamin A and the acute-phase response. Nutrition. 1999;15:326–328.
7. Christian P, Schulze K, Stoltzfus RJ, West KP Jr. Hyporetinolemia, illness symptoms, and acute phase protein response in pregnant women with and without night blindness. Am J Clin Nutr. 1998;67:1237-43.
8. Filteau SM, Tomkins AM. Micronutrients and tropical infections. Trans R Soc Trop Med Hyg. 1994;88:1-3.

Evaluation of Phototherapy Devices

The recent paper by Subramanian, *et al*. [1] evaluating phototherapy devices used for treating neonatal hyperbilirubinemia contains several flaws that limit the practical relevance and interpretation of the measurements.

1. The authors fail to distinguish adequately between photodegradation, in which bilirubin is degraded to substances of lower molecular weight, and photoisomerization, in which the pigment's structure changes but no degradation occurs. Both processes contribute to the effects of phototherapy in humans, but their relative contributions are presently unknown. However, in the Gun rat animal model photoisomerization is more important than photodegradation and the same is likely to hold for humans. In the article the authors focus largely on photodegradation, the pathway of least importance.

2. The relative effectiveness of the different lights tested was determined by comparing their effects on methanolic solutions of bilirubin *in vitro*. Residual bilirubin was measured after 15-120 min of exposure, by which time a substantial fraction of the original bilirubin had been bleached and degraded. Preparation of the methanolic solutions was not described. Aside from the fact that bilirubin is insoluble in methanol, the photochemistry of bilirubin in organic solvents is rather different from that in serum or aqueous albumin solutions. Therefore, methanolic solutions of bilirubin are inappropriate for comparative testing of phototherapy lights.

3. The test solutions were clearly over-irradiated and not sampled early enough to detect the relative rates of formation of the physiologically important photoisomers of bilirubin. Bleaching of bilirubin has been used in previous studies of the relative efficacy of phototherapy lights, but there is no evidence that this is a valid method, especially when bleaching is allowed to continue to a point where secondary reactions of no relevance to phototherapy may be taking place. Measuring initial rates of formation of bilirubin photoisomers would probably provide a more valid and clinically relevant method.

4. The authors claim to have developed a novel high precision HPLC/MS technique for measuring bilirubin photoisomers, yet presented no examples of typical separations. Samples were extracted with a solvent containing formic acid. Configurational photoisomers of bilirubin, the most rapidly formed isomers in humans, are highly sensitive to acids, undergoing reversion to unisomerized bilirubin. Therefore, it seems unlikely that these important photoproducts would have survived the HPLC conditions. Reference standards were prepared by irradiating bilirubin in methanolic solution, but no details were provided of how specific photoisomers or other photoproducts were identified and characterized.

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1. Subramanian S, Sankar MJ, Deorari AK, Velpandian T*, Kannan P, Prakash GV, *et al*. Evaluation of phototherapy devices used for neonatal hyperbilirubinemia. Indian Pediatr. 2010; Nov 30 (E-pub ahead of print).

REPLY

We thank the reader for the interest shown in our article published recently in the Journal (Epub). The questions raised by the reader are indeed valid. However, they