RESEARCH BRIEF

Vitamin A Status of Low and Normal Birth Weight Infants at Birth and in Early Infancy

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Received: December 18, 2012; Initial review: December 20, 2012; Accepted: March 12, 2013.

Serum retinol levels of low birth weight (LBW; birth weight <2500g) and normal birth weight (NBW; birth weight ≥2500g) infants were evaluated at birth and 3 months using high performance liquid chromatography. At birth, levels were 13.3±8.2 µg/dL in LBW (*n*=146) and 14.0±6.2 µg/dL in NBW infants (*n*=79; p=0.51), with 41.1% of LBW and 24.1% of NBW infants having vitamin A deficiency (VAD, <10 µg/dL; *P*=0.01). At follow up, levels were 18.0±9.4 µg/dL in LBW (*n*=83) and 20.0±7.3 µg/dL in NBW infants (*n*=51; *P*=0.19), with 18.1% of LBW and 3.9% of NBW infants having VAD (*P*=0.02).

Keywords: *Infant, Low Birth Weight, Retinal, Vitamin A.*

Vitamin A is an important micronutrient required for maintaining adequate growth and development, epithelial cell integrity and visual, reproductive and immune functions. The prevalence of subclinical vitamin A deficiency (VAD) in India is quite high, ranging from 31% to 57% among preschool children [1]. Limited data is available on vitamin A status of specific high risk groups like low birth weight (LBW; birthweight <2500 g) infants. We herein report the vitamin A status of LBW infants from Delhi, compared to the normal birth weight (NBW; birthweight ≥2500 g) infants, at birth and at 3 months of age.

METHODS

The present results are part of a larger study which evaluated micronutrient status of LBW and NBW infants at birth and in early infancy [2,3]. This was a prospective observational study conducted in 2009-2010 at three hospitals of Delhi. Ethics Committee of all collaborating hospitals approved the protocol.

All live born, clinically stable infants were enrolled consecutively in LBW and NBW categories following informed consent from parents. Venous blood samples of the enrolled mothers and infants were drawn within first 48 hours of birth. Mothers received routine iron and calcium supplementation and no additional multivitamin/ micronutrient supplementation as part of the study. Infants were also not provided any multivitamin/ micronutrient supplementation as part of the study. Follow up samples were taken at 14±4 weeks of corrected age. Detailed methodology has been given in a previous publication [3].

Primary outcome was serum retinol as measured by high performance liquid chromatography; (Shimadzu LC-6AD Binary Gradient System). VAD was defined as serum retinol level of less than 10 µg/dL [4,5,6]. Data were analyzed using Stata 11.0 (College Station, Texas, USA). Continuous normally distributed data were analyzed using Student's t-test, and categorical data using chi square test. The change in retinol values from birth to follow up was analyzed using multiple linear regression and proportions deficient were compared using multiple logistic regression.

RESULTS

A total of 220 LBW and 119 NBW infants were enrolled. Of these, serum retinol levels were available for 146 LBW and 79 NBW infants and their mothers at birth and of 83 LBW and 51 NBW infants at follow up. The baseline characteristics of study infants at birth and follow up are outlined in ***Table* I**. Serum retinol levels of mothers and infants are shown in ***Table* II**, along with proportion of subjects deficient in serum retinol.

The change in the serum retinol levels from birth to follow up visit was comparable in both groups with increasing age. The proportion of deficient infants did not increase significantly with increasing age, but the LBW infants had significantly higher chance of being deficient

TABLE I DEMOGRAPHIC AND INFANT VARIABLES AT BIRTH AND FOLLOW UP*

Variables	*Low Birth Weight infants (n=146)*	*Normal Birth Weight infants (n=79)*	*P*
Demographic variables			
Maternal education (completed years)	10 (0 -15)	8 (0 -15)	0.58
Family income (thousand Rs./month)	3.8 (2-10)	4 (2-20)	0.11
Infant variables at birth			
Male gender	70 (47.9%)	38 (48.1%)	<0.01
Birth weight (g)	1920±328	2988±312	<0.01
Gestation (wk)	36.0±2.4	38.7±1.1	< 0.01
Infant variables at follow-up visit#			
No. of infants with retinol results available	83 (56.8%)	51 (64.5%)	0.26
Postnatal age (wk)	12.0 (8.0-37.0)	13.0 (6.0-34.0)	0.87
Micronutrient/multivitamin supplementation received	23/83 (27.7%)	8/51 (15.7%)	0.04
Exclusive/predominant breastfeeding	72/83 (86.7%)	47/51 (92.2%)	0.55

Data expressed as number (percentage), or median (interquartile range).

(OR=5.3; 95% CI 1.2, 24.2) compared to the NBW infants at follow up (*P*=0.03).

The mean maternal levels of LBW and NBW infants were 39.0 µg/dL (*n*=122) and 38.1 µg/dL (*n*=78), respectively (*P*=0.69); with 11.5% of LBW and 9.0% of NBW infants' mothers having VAD (serum retinol <20 µg/dL; *P*=0.57). There was no correlation between maternal and infant serum retinol levels at birth (r=0.26).

DISCUSSION

The mean serum retinol levels of LBW infants in our study were low, though comparable to NBW infants at birth as well as at follow up in early infancy. All infants are born with low vitamin A stores, including those born to well-nourished mothers with abundant vitamin A stores [7]. The reported proportion of infants with serum retinol below 20 µg/dL at birth is very variable, ranging from 0-89% in developing countries, as against 0-29% in industrialized countries [7]. This has been proposed to be due to higher rates of preterm deliveries and LBW in developing countries [7], as both these factors have been shown to be associated with low neonatal serum retinol levels [8].

Breast milk is the primary source of vitamin A in first months of life, and it has been shown that even infants fed by vitamin A-deficient mothers whose breast milk provides as little as 120 ± 15µg RE/day grow normally and have no clinical signs of VAD [9]. Most of our infants whose follow up results are available were exclusively/ predominantly breastfed, and most mothers had adequate levels of vitamin A. The proportion of deficient infants therefore decreased with increasing age in our study. However, the proportion of LBW infants with VAD was significantly higher compared to NBW infants at birth as well as at follow up in early infancy. It therefore suggests that exclusive breastfeeding might not be sufficient to maintain serum retinol levels of LBW infants during early infancy. Current recommendations do not support daily oral vitamin A supplementation to human milk fed LBW infants due to lack of evidence of benefit [10]. However, looking at the deficiency status among these infants, it might be worth examining the role of such supplementation to these infants.

Another relevant point to note is that zinc and vitamin A concentrations tend to co-vary in marginally nourished individuals with co-existing zinc and vitamin A deficiencies, and zinc deficiency might limit the health and nutritional effect of vitamin A interventions in a population [11]. It is therefore important to note that our study population also had significant zinc deficiency (present in 51.0% and 79.0% of LBW and 42.4% and 66.7% of NBW infants at birth at follow-up, respectively) [3].

We targeted a study population representative of neonatal population in developing countries at highest risk of nutritional deficiencies. We followed these infants till three months of age and reported how the levels evolved during early infancy, with simultaneous comparison with normal birth weight infants, thereby providing a comparative picture. Our study had limitations in terms of being based on a sample size of convenience and a significant loss to follow-up. However, the baseline characteristics of infants who were followed up *versus* those who were lost to follow up were comparable.

WHAT THIS STUDY ADDS?

- Information on vitamin A status of low birthweight infants at birth and in early infancy.

TABLE II SERUM RETINOL LEVELS OF MOTHER-INFANT DYAD AT BIRTH AND OF INFANTS AT FOLLOW UP VISIT

Variables	*Low Birth Weight infants*		*Normal Birth Weight infants*		*P*
	n	*Results*	*n*	*Results*	
Infant levels at birth					
Serum Retinol (µg/dL)	146	13.3±8.2	79	14.0±6.2	0.51
Serum Retinol <10 µg/dL		60/146 (41.1%)		19/79 (24.1%)	0.01
Infant levels at follow up visit					
Serum Retinol (µg/dL)	83	18.0±9.4	51	20.0±7.3	0.19
Serum Retinol <10 µg/dL		15/83 (18.1%)		2/51 (3.9%)	0.02
Maternal levels at birth					
Serum Retinol (µg/dL)	122	39.0±15.5	78	38.1±16.3	0.69
Serum Retinol <20 µg/dL		14/122 ((11.5%)		7/78 (9.0%)	0.57

Data expressed as number (percentage) or mean±SD.

Contributors: RA, DV, MLJ,GST designed research (project conception, development of overall research plan, and study oversight) and shall be the overall guarantor; RA, DV, MLJ,GST conducted research; GST additionally carried out the laboratory analysis; SG, RA: analyzed data, performed statistical analysis; SG, RA: wrote paper.

Funding: Indian Council of Medical Research, Delhi; *Competing* interests: None stated.

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