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ORIGINAL ARTICLE

Vitamin A, E, and D Deficiencies in Tunisian Very Low Birth Weight Neonates: Prevalence and Risk Factors

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Key Words
pre-eclampsia;
preterm neonate;
very low birth weight;
vitamin deficiency

Background: Preterm neonates are at high risk of vitamin deficiencies, which may expose them to increased morbidity and mortality. This study aimed to determine the prevalence and risk factors for vitamin A, E, and D deficiencies in Tunisian very low birth weight (VLBW) neonates.
Methods: A total of 607 VLBW and 300 term neonates were included in the study. Plasma vitamins A and E were assessed by high performance *liquid chromatography* and vitamin D was assessed by radioimmunoassay.
Results: Prevalence of vitamin A, E, and D deficiencies were dramatically elevated in VLBW neonates and were significantly higher than term neonates (75.9% vs. 63.3%; 71.3% vs. 55.5%; and 65.2% vs. 40.4%, respectively). In VLBW neonates, the prevalence of vitamin deficiencies was significantly higher in lower classes of gestational age and birth weight. Vitamin E deficiency was associated with pre-eclampsia [odds ratio (OR) (95% confidence interval, 95% CI), 1.56 (1.01–2.44); $p < 0.01$] and gestational diabetes [4.01 (1.05–17.0); $p < 0.01$]. Vitamin D deficiency was associated with twin pregnancy [OR (95% CI), 2.66 (1.33–5.35); $p < 0.01$] and pre-eclampsia [2.89 (1.36–6.40); $p < 0.01$].

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Conclusion: Vitamin A, E, and D deficiencies are very common in Tunisian VLBW neonates and are associated with pre-eclampsia. Improved nutritional and health support for pregnant women and high dose vitamins A, E, and D supplementation in VLBW neonates are strongly required in Tunisia.

1. Introduction

Vitamins A, E, and D are vital nutrients for humans. Vitamin A (VA) is involved in vision, immune function, and cell growth and differentiation.[1] Vitamin E (VE) is a powerful antioxidant protecting cellular structures and functions against harmful effects of free radicals. It also acts as a regulator of signal transduction and gene expression.[2] Vitamin D (VD) is involved in phosphate and calcium homeostasis, bone metabolism, and immune function.[3] Deficiencies in these vitamins are considered to be risk factors for various diseases such as cardiovascular, infectious and bone diseases, and cancer.[1,3,4]

Preterm neonates, especially very low birth weight (VLBW) neonates, are at high risk of nutritional deficiencies, which could alter their development and health during the neonatal period and for their whole life. Preterm infants have inadequate vitamin status, which may expose them to increased risk of morbidity and mortality.[4–9] Accordingly, vitamin supplementation is strongly recommended in these neonates.[10] Most data about vitamin status, its relationship with health, and vitamin requirement in preterm infants are based on studies from Western populations that differ from those of undeveloped and developing countries in terms of living standards, nutritional habits, and genetic factors.

Few data suggest that vitamin deficiencies are more frequent in preterm neonates from developing countries.[11–13] Tunisia is a developing country where prematurity affects 5% of under-fives and low birth weight is approximately 5.4%.[14] During recent years, socioeconomic level, nutrition, and health have improved.[15,16] However, micronutrient deficiencies such as iron deficiency remain frequent in Tunisian neonates and children.[14] A recent study showed a low prevalence of vitamin A and E deficiencies in Tunisian children aged 5–7 years.[17] However, no data are available on vitamin status in neonates. This study was designed to determine the prevalence and risk factors for vitamin A, E, and D deficiencies in VLBW neonates. Results will provide the first data on vitamin status in Tunisian infants and will permit making recommendations to counter vitamin deficiencies in preterm infants from developing countries.

2. Participants and Methods

2.1. Participants

The study included 607 preterm VLBW neonates (birth weight $<$ 1500 g and gestational age $<$ 37 weeks) admitted at the Department of Neonatology and Neonatal Intensive Care and 300 term neonates (birth weight between 2500 g and 3500 g) as controls. All neonates were born between 2005 and 2008 in The Center of Maternity and Neonatology of Tunis. This Center is the most important public maternity hospital in the Great Tunis region and draws pregnant women of low to average socioeconomic rank. Malformed neonates, those with chromosomal abnormality, of birth weight $<$ 650 g or gestational age $<$ 27 weeks were excluded. The study protocol was approved by the Ethics Committee of The Maternity Center and informed consent was obtained from each mother.

2.2. Data collection

Relevant information was collected from medical records. It included maternal age, medical and obstetrical history, and the course of the current pregnancy, term of delivery, and infant anthropometrical measures. All mothers had been taking habitual Tunisian foods during pregnancy and no one had adopted a special diet or had received vitamin A, E, or D supplements. Pre-eclampsia and gestational diabetes are defined according to the American College of Obstetricians and Gynecologists criteria.[18,19]

2.3. Collection of blood samples

Blood was drawn from neonates within the first hours of life into EDTA-containing tubes. Blood was collected following medical prescription for cell count analysis or ABO Rhesus grouping. After completion of the prescribed analysis, the tube was recovered (within 2 hours), centrifuged at 1500*g* for 20 minutes and plasma was stored at −40°C for vitamin analysis (within 6 months). Vitamins A and E were measured in all neonates, and vitamin D was measured in 279 VLBW and 156 term neonates.

2.4. Analytical methods

Plasma vitamin A and E concentrations were measured by reverse phase high performance liquid chromatography (HPLC) as described by Driskell et al[20] using a Shimadzu HPLC system (Shimadzu, Kyoto, Japan) and a C18 column (Shimpack ODS-M; Shimadzu). The method sensitivity was 0.175 μmol/L for VA and 1.16 μmol/L for VE. The long-term (n = 30) imprecision (coefficient of variation) was 6.1% and 5.6% at concentrations of 1.65 μmol/L and 2.60 μmol/L, and 5.8% and 5.1% at concentrations of 26.7 μmol/L and 32.5 μmol/L for VA and VE, respectively. Plasma 25-hydroxy vitamin D (25-OHD) concentration was measured by radioimmunoassay (IDS GmbH, Frankfurt, Germany). The sensitivity of the assay method was 3 nmol/L and the