# Vitamin A Status Among Infants At Nine Months of Age

Thesis

For Partial Fulfillment of MSc Degree in Pediatrics

By

## Rasha Mahmoud Abdel Moawad Hamed

**Supervisors** 

**Prof. Magd Ahmed Kotb** 

**Professor of Pediatrics** 

Faculty of Medicine – CairoUniversity

**Prof. Manal Michel Wilson** 

Professor of Clinical Pathology

Faculty of Medicine – Cairo University

Dr. Christine William Shaker

Lecturer of Pediatrics

Faculty of Medicine – Cairo University

**Department of Pediatrics** 

**Faculty of Medicine** 

**Cairo University** 

2013

### Acknowledgment

I am deeply thankful to **Allah**, by grace of whom, the progress and success of this work was possible.

I express my deep appreciation and great thanks to **Dr Magd Ahmed Kotb**, Professor of Pediatrics, Faculty of Medicine, Cairo University for her meticulous supervision, encouragement & valuable advice throughout the work.

My deepest thanks to **Dr Manal Michel Wilson,** Professor of clinical and Chemical Pathology, Faculty of Medicine, Cairo University for her outstanding advices and keen interest throughout the work.

Also, I would like to express my deepest appreciation to **Dr Christine William Shaker,** Lecture of Pediatrics, Faculty of Medicine, Cairo University for her great efforts, helpful suggestions, support and genuine help.

Also, I would like to thank the parents of infants for being cooperative.

Last but not the least, I am deeply thankful and always indebted to the (soul of my Father), my mother, my husband, brothers, daughter and my aunt who were always supporting and encouraging me.

#### **Abstract**

**Background:** Vitamin A is required for normal functioning of the visual system, and maintenance of cell function for growth, epithelial integrity, red blood cell production, immunity and reproduction, its deficiency is considered of one of the major public health problems but also toxicity from vitamin A witch occurs after consuming large amounts of vitamin A over a short period of time, typically within a few hours or days or when large amounts of vitamin A build up in the body over a long period of time is considered hepatotoxic and because of the long half-life of vitamin A in the liver (50 days to 1 year), the fibrotic process may continue due to the slow release of hepatic vitamin A stores despite discontinuation of oral intake of the vitamin.

**Objective:** To assess the level of vitamin A status in infants at 9 months of age who were not supplemented by vitamin A, and in infants at 9 months who were supplemented with 100,000 IU of vitamin A.

**Methods:** A hundred healthy breast fed infants were enrolled in this cross-sectional study, 50 of them received a compulsory doses of 100.000 IU of vitamin A.

We assessed growth by anthropometric measurements and clinical examination. We assessed retinol level by high frequency liquid chromatography.

**Results:** The mean of serum retinol was 53.18±8.74 in the non -supplemented group and a mean of 59.78±7.07 supplemented group (p value=0.00) which is all within the normal range (11.3 and 64.7 mcg/dL). The mean of serum AST, ALT and albumin in un-supplemented group was 4.83±2.57, 7.83±2.81 and 3.55±0.41 respectively while the mean of serum AST, ALT and albumin in supplemented group was 6.37±2.28, 19.96±3.42 and 3.91±0.46 respectively and There was a positive statistically correlation between serum retinol level and liver functions (AST, ALT and albumin) between both groups (p value =0.000, 0.002, 0.000, 0.0000) respectively. All values are also within the normal range of liver function. There was no correlation between the serum retinol level and the sex, weight and height of the studied groups (p value =1.000, 0.672, 0.338) respectively.

**Conclusion:** This study showed that level of serum retinol was within normal range before and after the vitamin A supplementation in infants at nine months of age. The study found the need for vitamin A at 9 months is questionable, yet the sample size and its confinement to a small geographic area that is not representative of Egyptian variance call for more prospective trials to define timing of decline of serum retinol and support need for its supplementation and time of supplementation if needed.

**Key words:** Vitamin A, serum Retinol level, Retinol Binding Protein, vitamin A supplementation.

## **List of contents**

Title	page
	No.
List of abbreviations	II
List of Tables	V
List of Figures	VI
Introduction	1
Aim of Work	3
Review of Literature	
• Overview of vitamin A	4
• Clinical manifestations of vitamin A deficiency and	
hypervitaminosis	25
■ Rationale of vitamin A supplementation	37
Subject and Methods	58
Results	62
Discussion	77
Summary	87
Conclusion	90
Recommendations	91
References	92
Appendix	115
Arabic summary	1

#### **List Of Abbreviations**

**AI** : Adequate Intake

**ALT** : Alanine transaminases

**APC** : Antigen presenting cells

**APL** : Acute promyelocytic leukemia

**AML** : Acute myeloid leukemia

**AST** : Aspartate transaminases

**ATRA** : All-trans retinoic acid

**B cell** : B lymphocyte

**BMI** : Body mass index

**Cox-2** : cyclooxygenase-2

**CAD** : Coronary artery disease

**c-AMP** : Cyclic adenosine monophosphate

**C-cells** : Parafollicular cells

CD40L : CD40 ligand

**CSA** : Cross-sectional area.

**DC** : Dendritic cells.

**DEMPU**: Diabetic Endocrine Metabolic Pediatric Unit.

**DNA** : Deoxyribonucleic acid.

**DHS** : Demographic and Health Survey

**EAR** : Estimated average requirement

**EGFR** : Epidermal Growth Factors Receptor

**ELISA** : Enzyme-linked immunosorbent assay

**FNB** : Food and Nutrition Board

**HIV** : Human immunodeficiency virus

**HPLC**: High performance liquid chromatography

**HR-NBL** : High risk neuroblastoma

**HSCs** : Hepatic Stellate Cells

Ht : Height

**IBD** : Inflammatory bowel diseases

**IgA-ASC** : Immunoglobulin A-antibody secreting cells

IL1 : Interleuken 1

IU : International units

**Kcal** : Kilocalories

**MDGs** : The Millennium Development Goals

**MRDR** : Modified relative dose response

NBL : Neuroblastoma

**NDHS** : Nepal Demographic and Health Survey

LC-MS : Liquid chromatography-mass spectroscopy

LICs : Leukemia initiating cells

**PEM** : Protein energy malnutrition

**PML-RARA** : protein promyelocytic leukemia-retinoic acid receptor

alpha

**RA** : Retinoic acid

**RAE** : Retinol activity equivalents

**RAR** : Retinoic acid receptor

**RBP** : Retinol binding protein

**RDA** : Recommended dietary allowance

**RDIs** : Recommended dietary intakes

**RE** : Retinol equivalents

**RCT** : Randomized controlled studies

**RPE** : Retinal pigment epithelium

**RXR** : Retinoid X receptor

SPSS : Statistical Package for Social Science

Tc : Cytotoxic T cell

T cell : T lymphocyte

Th : T helper cell

TNF-alpha : Tumor necrosis factor alpha

T(reg) cells : Regulatory T cells

VA : Vitamin A

**VAD** : Vitamin A deficiency

**VEGF** Vascular endothelial growth factor

**UNICEF**: The United Nations International Children's

**Emergency Fund** 

**UL** : Upper Intake Level

**WHO** : World Health Organization

Wt : Weight

13-cis-RA : 13-cis retinoic acid

## **List of Tables**

Table No.	Title	Page
T-1-1- (1)	Vita min A a super de	5
Table (1)	Vitamin A compounds	3
Table (2)	Recommended Daily Allowance (RDA) for Vitamin A as	18
	Preformed Vitamin A (Retinol Activity Equivalents)	
Table (3)	Tolerable Upper Intake Level (UL) for Preformed Vitamin	31
	A (Retinol).	
Table (4)	Suggested vitamin A supplementation scheme for infants	57
	children 6–59 months of age.	
Table (5)	Demographic data of studied cases.	63
Table (6)	The anthropometric measurements of studied groups.	65
Table (7)	Retinol level, ALT, AST and Albumin of studied cases.	66
Table (8)	Difference between males and females in group A in their	67
	retinol level, ALT, AST and Albumin.	
Table (9)	Difference between male and female in group B in their	68
	retinol level, ALT, AST and Albumin.	

# List of figures

Figure No.	Title	Page
Fig. (1)	Metabolism of vitamin A.	10
Fig. (2)	Bitot's spots.	28
Fig. (3)	Picture of Xerophthalmia.	28
Fig. (4)	Picture of papilledema.	32
Fig. (5)	Hyperostosis of the ulna and the tibia.	34
Fig. (6)	Ranges of serum retinol level (µg/dl) and vitamin A supplementation (100.000IU).	69
Fig. (7)	Correlation between serum retinol level ( $\mu g/dl$ ) and serum ALT (U/L) for the 100 infants of the studied group.	70
Fig. (8)	Correlation between serum retinol level ( $\mu g/dl$ ) and serum AST (U/L) for the 100 infants of our study group.	70
Fig. (9)	Correlation between serum retinol level (µg/dl) and serum Albumin (g/d) for the 100 infants of the studied group.	71
Fig. (10)	Correlation between vitamin A supplementation (100.000IU) and serum ALT (U/L).	71
Fig. (11)	Correlation between vitamin A supplementation (100.000IU) and serum AST (U/L).	72
Fig. (12)	Correlation between vitamin A supplementation (100.000IU) and serum Albumin (g/d).	72
Fig. (13)	Correlation between weight (kg) and serum retinol level ( $\mu g/dl$ ) for the 100 infants of the studied group.	73
Fig. (14)	Correlation between weight (kg) and serum ALT (g/l) for the 100 infants of the studied group.	73
Fig. (15)	Correlation between weight (kg) and serum AST (g/l) for the 100 infants of the studied group.	74

Fig. (16)	Correlation between weight (kg) and serum albumin (g/d) for the 100	74
	infants of the studied group.	
Fig.(17)	Correlation between height (cm) and serum retinol level (µg/dl) for the	75
	100 infants of the studied group.	
Fig.(18)	Correlation between height (cm) and serum ALT (U/L) for the 100	75
	infants of the studied group.	
Fig.(19)	Correlation between height (cm) and serum AST (U/L) for the 100	76
	infants of the studied group.	
Fig.(20)	Correlation between height (cm) and serum albumin (g/d) for the 100	76
	infants of the studied group.	

#### Introduction

Vitamin A is the name of a group of fat-soluble retinoids, including retinol, retinal, retinoic acid, and retinyl esters. It is involved in immune function, vision, reproduction, and cellular communication. It is an essential component of rhodopsin, a protein that absorbs light in the retinal receptors, and because it supports the normal differentiation and functioning of the conjunctival membranes and cornea and also supports cell growth and differentiation. It plays a critical role in the normal formation and maintenance of the heart, lungs, kidneys, and other organs (Johnson and Russell, 2010).

In developing countries, vitamin A deficiency typically begins during neonatal period, when the neonates do not receive adequate supplies of colostrum or breast milk. The most common symptom of vitamin A deficiency in young children is xerophthalmia. One of the early signs of xerophthalmia is night blindness, or the inability to see in low light or darkness. Vitamin A deficiency also increases the severity and mortality risk of infections particularly diarrhea and measles even before the onset of xerophthalmia (Mayo et al., 2011).

In developed countries, the amounts of vitamin A in breast milk are sufficient to meet infants' needs for the first 6 months of life. The prevalence of vitamin A deficiency in developing countries begins to increase in young children just after they stop breastfeeding (Oliveira et al., 2010).

Vitamin A is fat soluble, the body stores excess amounts, primarily in the liver, and these levels can accumulate, the manifestations of hypervitaminosis A depend on the amount and rapidity of the excess intake. The symptoms of

hypervitaminosis as nausea, irritability, anorexia, vomiting, blurry vision, headaches, hair loss, muscle and abdominal pain and weakness, drowsiness, and altered mental status, follow sudden, massive intakes of vitamin A and with consumption of too much vitamin A. The tissue levels take a long time to fall after they discontinue intake, and the resulting liver damage is not always reversible. The tolerable upper intake levels for preformed vitamin A for the age from 0–12 months in males and females is 600 mcg retinol activity equivalents (RAE) (2,000 IU) which is a unit of measurement that researchers have developed for evaluating the degree to which carotenoid forms of vitamin A can be converted into retinoid forms (Ross, 2010).

Combining the administration of bolus vitamin A supplements with immunization is a part of the effort done for the elimination of vitamin A deficiency. Since 1987, WHO has advocated the routine administration of vitamin A with measles vaccine in countries where vitamin A deficiency is a problem (Burton et al., 2009).

## Aim of the work

The aim of this work is to address the need for bolus vitamin A at 9 months by assessing the level of vitamin A status in infants at 9 months of age before and after receiving the compulsory dose of vitamin A.

#### Physiology of vitamin A

#### Introduction

The term "vitamin A" makes it sound like there is one particular nutrient called "vitamin A," but that is not true. Vitamin A is a broad group of related nutrients. Each of these nutrients provides us with health benefits, but these benefits may be quite different and they may be provided in different ways (**Bailey et al., 2012**).

Vitamin A is a lipid-soluble vitamin that is essential for cellular differentiation. It is ingested either as the preformed retinyl ester or carotenoid provitamins (including beta-carotene) from plant sources and stored in the liver. It is transported from the liver to the rest of the body by retinol binding protein (RBP) and gains entry into cells via a specific receptor. Once intracellular, it is transformed to retinoic acid and modulates gene regulation and transcription. Overt deficiency occurs when hepatic retinol stores are exhausted (**Sommer, 2009**).