

Comparison of Vision Restoration Time With Vitamin A Levels in Pregnant Nigerian Women

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Abstract

Background: Vitamin A deficiency, subclinical or otherwise is associated with adverse maternal fetal and neonatal outcome, ditto excess vitamin A. The challenge in pregnancy is to detect subclinical vitamin A deficiency in patients for whom supplements or dietary manipulation will be of benefit.

Objective: To compare the usefulness of the vision restoration time with biochemical methods in the determination of vitamin A status in pregnancy.

Study Design And Setting: A cross sectional case controlled study in a University teaching hospital.

Methods: Data was collected from Antenatal patients (142). Using serum Biochemistry three categories of patients were recognised. Patients with normal vitamin A levels (N = 100 with blood vitamin A within two standard deviation of the mean) Twenty four patient (24) had low vitamin A levels (blood vitamin A level at less than 2 standard deviation below the mean). Eighteen patients (18) had high vitamin A levels (blood vitamin A levels at greater than two standard deviation above the mean).

Outcome Measures: The vision restoration time was compared for all three groups of patients.

Results: The vision restoration time (VRT) was found to have a high degree of sensitivity (80%) and a high specificity (83%) in detection of patients with vitamin A deficiency. The positive predictive value was 90% with a negative predictive value of 83%. The VRT was unable however to differentiate patients with normal and high vitamin A.

Conclusion: The vision Restoration time is a cheap effective method to detect subclinical vitamin A deficiency in pregnancy. It is an easy cost effective screening tool to select patients for whom dietary manipulation and or vitamin A supplementation will be beneficial.

Keywords: Vitamin A, Nutrition, Supplementation
Pregnancy, Vision.

Introduction

Vitamin A is a general term, which covers all compounds with the biological activity of retinol. These include dehydroretinol (vitamin A₂) retinal and , carotene. Vitamin A occurs as retinal or retinal esters in animal food and as provitamin, A carotenoid primarily in plant food. It cannot be synthesised within the body. The bioavailability is more in foods of animal origin. The vitamin A status in pregnancy is influenced by age, parity and diet^{1,2,3,4,5,6,8,9,10}. Socio-economic circumstance is particularly important because of the availability and cost of vitamin A rich foods^{1,2,11,12}. The vitamin A status is also influenced by increased demands of pregnancy and lactation to cater for the need of the fetus. Other factors include malnutrition, measles and respiratory infection^{1,13,14} food taboos and food preparation methods such as prolonged frying at high heat is likely to decrease the amount of vitamin A contained in these foods.

Vitamin A is required for growth and development. Maternal retinol level parallels fetal and consequently childhood vitamin A status. Both excess of vitamin A and vitamin A deficiency are associated with adverse fetal and neo-natal outcomes^{15,16} vitamin A is also required for the maintenance of the immune status (both innate and acquired immunity). It is also essential for epithelial defences^{17,18,19,20,21}. Vitamin A deficiency is associated with adverse fetal and maternal outcome while hypervitaminosis A affects mainly the fetus and the neonate. Deficiency occurs, in the setting of malnutrition, poverty and adverse socio-economic and

cultural practices common in the third world countries²⁴. It is also associated with micronutrient deficiency, anaemia and consequent adverse pregnancy outcome^{17,26,27}.

Different qualitative and quantitative approaches are used to assess vitamin A status. These include conjunctival impression cytology^{1,28} liver biopsy, xerophthalmia prevalence, physical signs, biochemical survey and the vision restoration time. Biochemical method is the only direct of all these methods. It uses a cut-off point of 0.7-1.5umol/litre as normal levels for serum vitamin^{2,30,22,31,32,33}. The main drawback is the fact that it is invasive and it is not cost-effective, especially for community screening^{5,22}. The conjunctival impression cytology assesses epithelial cells of tear film in order to evaluate clinical impression of vitamin A deficiency. It is also invasive. It is therefore not ideal as a screening tool as it is lacking in sensitivity and specificity. Liver biopsy assesses vitamin storage in the liver. It is also invasive and it is not for community screening. Xerophthalmia prevalence assesses disease progression rather than screening for vitamin A deficiency, ditto night blindness. The importance of vitamin A in maternal health and consequently child health makes estimation of it in pregnancy of vital importance.

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The vision restoration time is a relatively new test. In studies where it has been used it has been found to have a high degree of sensitivity and specificity^{13,25,28,29}. It is a simple cost effective means of screening for vitamin A deficiency in the population. An abnormal vision restoration time merits further investigation with fundoscopy and biochemical means. This is because an abnormal V.R.T. is also seen in retinitis pigmentosa.

The basis of the test is this: The retina contains 2 photosensitive pigment rhodopsin in the rod cells and iodopsin in the cone cells. They are formed by binding of vitamin A aldehyde pro-retinal to the protein opsin. Rhodopsin and to a lesser extent iodopsin is primarily responsible for ability to see in dim illumination. Exposure to light causes cleavage of the photopigments into opsin and retinal (bleaching).

In the dark adapted eye rhodopsin is resynthesised. The vision restoration time is the earliest test of vitamin A deficiency. The vision restoration time is the time taken for the subject to identify letters illuminated by a fixed dim light. The rate of rhodopsin and iodopsin regeneration is dependent on vitamin A store in the retina. In the presence of replete stores and in hypervitaminosis, the vision restoration time is normal while it is abnormal in deficiency state. The purpose of this study is to compare the vision restoration time (V.R.T) with Biochemical method in evaluation of vitamin A levels. A finding of a significant correlation would indicate that determination of the vision restoration time (a simple non-invasive easily performed evaluation) may be useful as a screening test for the determination of vitamin A status in pregnancy. The challenge in pregnancy is to maintain an optimal vitamin A millieu.

Materials and Methods

This was a cross sectional case controlled study conducted in the department of obstetrics and Gynaecology of the University of Benin Teaching Hospital between November 1999 July 2000. The department has 42 gynaecological and 84 obstetrical beds and undertakes about 2000 deliveries annually. A total of 142 consecutive patients attending the Antenatal

Clinic were recruited. They were fairly well spread across all the three trimesters of pregnancy. All patients had.

A. Venepuncture for biochemical analysis

B. A dark adaptation test (vision restoration time)

The sample size required was calculated using Epi-info (stat calc). The sample size using 95% confidence level with an expected frequency of 10% yielded a sample size of 132.

A Blood Biochemistry

Determination of vitamin A in serum was done using the modified Bessey, Lowry, Brock and Lopez method of 1946.

B Vision Restoration Time (Dark Adaptation Testing)

The test was done in a dark room containing a table and two chairs.

The patient was made to sit at a distance of 3 metres from the chart (The log man chart was used because it contains letters of uniform characters and the letters used were 10 non-serif letters). The light source i.e. the dark adaptometer was placed 50cm from the subject. The intensity of light was about 100-10,000cd/m². The candela (cd) is a measure of the luminous intensity of light. The light flashed from a distance of 50cm. The test was done binocularly and this was done for 2 minutes, for the first 2 minutes the photoreceptors of the eyes were expected to have been bleached. The bright light was then replaced by dim light with a reduced illumination and immediately, after the patient was asked to read the first line of the logman chart. The time interval between turning on the dim light and the verbal identification of the letter was recorded as the dark adapted time or vision restoration time. A vision restoration time (VRT) of less than or equal to 150 seconds is regarded as normal. A VRT of greater than 150 seconds is regarded as abnormal. The test was completed in 4-10 minutes.

Statistical Analysis

Statistical analysis was done using epi-info 2002 Revision 1. The chi-square test was used with a P value of <0.05 being regarded as statistically significant.

Table 1 Clinical summary of age, parity and social class.

Clinical/Social variables	Group I n = 100	Group II n = 24	Group II n = 18	P value
Mean Age	30+ 4.36	31 + 4.31	32 +4.87	} P > 0.05 N/S
Mean parity	3 + 1.85	1 + 0 .685	2 + 1.035	
Social class				} N/S
I	25(25%)	4(16.7%)	2(11%)	
II	21(21%)	2(8.3%)	8(44.4%)	
III	23 (23%)	4(16.7%)	2(11%)	
IV	16 (16%)	6(25%)	4(22.2%)	
V	15 (15%))	8(33.3%)	3(16.7)	

Results

A total of one hundred and forty two patients were recruited. They were categorized into three groups based on the result of serum vitamin A levels. The mean level of serum vitamin A in the 142 patients recruited was 1.54umol/litre with a standard deviation of 1.25 i.e. (1.54 ± 1.25umol/L). Patients with blood vitamin A levels within 2 standard deviation of the mean were grouped as having Average vitamin A levels (Group I). Patients with blood vitamin A at less than 2 standard deviation below the mean were assessed as having low vitamin A (Group II) while patients with blood vitamin A at two standard deviation above the mean were classified as having high vitamin A (Group III). One hundred patients (100) were in-group I, 24 patients in group II while 18 patients were in group III.

The clinical and social³⁴ characteristics of the 142 patients were as shown in Table I. There was no statistically Significant differences between the three with regard to age, parity, and social class. The average age for the three groups was 30 and the mean parity was 2.

Eighty nine of the 142 patient (62.6%) assessed had a vision restoration time of less than or equal to 150 seconds. Fifty three patients (37.3%) had a vision restoration time of greater than 150 seconds. Only one patient volunteered a history of night blindness. All patients had normal funduscopy. A vision restoration time of less or equal to 150 seconds was present in 69% of patients in group I, 20% of patients in group II and 83% of patients in group III. Patients in group II (low vitamin A) had a statistically significant proportion of patients with an abnormal vision restoration time (VRT > 150 seconds). The vision restoration time (VRT) had a sensitivity of 80% and a specificity of 83% in patients with low vitamin A, with a positive predictive value of 90% and a negative predictive value of 83%.

Discussion

Vitamin A is a fat soluble vitamin derived from both plant and animal sources. It plays a very important role in human reproduction. Vitamin A status of pregnancy is influenced by age, parity and diet^{1,2,3,4,5,6,7,23,24}.

The methods of assessment of vitamin A status in this study was by xerophthalmia prevalence (night blindness), the vision restoration time and biochemical means. Other ways to assess vitamin A level which were not utilized here include conjunctiva impression cytology and liver biopsy^{2,11,22,35}.

The study confirms the high degree of sensitivity of the vision restoration time in patients with subclinical vitamin A deficiency. However unlike biochemical analysis it was unable to differentiate between patients with normal and high vitamin A levels (Table I). The sensitivity was 80% while the specificity was 83%. This is similar to similar observation by other authors^{2,11,22,28,29,35}. The positive predictive value was similarly high at 90% while the negative predictive value was

83% with a false negative rate of 20% and a false positive rate of 17%. This result indicates that V.R.T. is one of the earliest test of vitamin A deficiency^{2,22,24,28,29,35}. The vitamin A storage in the rods and the cones is an indication of vitamin A stores in the body. An abnormal V.R.T. may in some cases pre-date low blood levels of vitamin^{24,27,28,29}.

Detection of vitamin A deficiency is probably of more importance in a socially and economically deprived third world environment like Nigeria. Diet rich in vitamin A are either not accessible or not affordable to a large segment of the Nigerian populace. On the other hand, hypervitaminosis A is a condition prevalent in Western industrialised countries. In these countries habitual vitamin A intakes exceed at least three times the RDA (about 30000 i.u or 2,400ug RE). The advantage of the vision restoration from this study is immediately obvious it is indicative of vitamin A deficiency. Again it is safe, cheap and acceptable. It is easily learnt and can be taught to community health workers and can be quite useful as a screening tool for vitamin A deficiency in pregnancy. It only requires a room, a logman chart and a dark adaptometer. (in the rural setting a torch light can suffice). These characteristics are unlike other tools of detection of vitamin A status which are expensive, invasive and require specialist knowledge and skill to analyse and interpret. Findings are similar to the observations of various other authors^{22,23,24,28,29}.

In conclusion although the series is small and follow up interval brief. Vitamin A deficiency as detected by vision restoration appears to be a useful tool of detection of Vitamin A deficiency. It is suggested that advantage be taken of its usefulness in screening for vitamin A deficiency in pregnancy. This will enhance good antenatal management. Intervention programmes by dietary manipulation and or direct supplementation can be designed based on results of the V.R.T. This is especially important considering the known adverse maternal and neonatal effects of vitamin A deficiency.

References

1. Hermus RT, Severs AH clinical significance of extra vitamin Supplements and enriched food products. Med. Tidsschr Geneesled April 24:143(17): (1999): 889- 92.
2. Collins MD, Mao GE Teratology of retinoids. Annu. Rev. Pharmacol. Toxicol. (1999): 39: 395-430.
3. Rao VG, Suqunam AP, Schqal SC Nutritional deficiency disorders and high mortality among children of the Great Andmanestribes. In: Natl. Med.J. India (1998)11(2): 65-8
4. Lindblad BS, Patel M; Hamadash M; Helmyani, Ahmad I, Dawodu A, et al: Age and sex are important factors in determining normal retinal levels. J. Trop. Pediatr. (1998)44(2): 96-9
5. Ocampo MB, Monya E: A comparative study of nutrition and health of mothers in Japan and the Philippines. Southeast Asian J. Trop. Med Public Health (1997) 28(3): P645-56.
6. Bohm V, Peiker G, Starker A, Wesket, Schaarmen G, Schubert R, et al: Vitamin Ba, B2, A and E and Beta carotene content in transitional breast milk and

- comparative studies in maternal and umbilical cord blood. In: *Z. Ernährung Swiss* (1997) 36 (3)b 214-9.
7. Coutsoudis A, Moodley D, Pillay K, Harrigan R, Stone C, Moodley J, et al: Effects of vitamin A supplementation on viral load in HIV-I infected pregnant women. *J. Acquir. Immune Defic. Syndr. Hum. Retrovirol.* 1(1997) 15 (1): 86-7.
 8. Roy SK, Islam A, Molla A, Akramuzzaman SM, Jahan F, Fanchs G: Impact of a single, megadose of vitamin A at delivery on breast milk of Mothers and morbidity of their infants. *Eur.J. Nutr.* (1997) 51(5): 302-7.
 9. Monga M: Vitamin A and its congeners. In: *Semin. Perinatol.* (1997) 21(2): 135-42.
 10. ACOG: Vitamin A supplementation during pregnancy. ACOG Opinion committee on obstetric maternal and fetal medicines. *International J. of Gynecology and Obstetrics.* (1993) 40: 175.
 11. Trugo NM: Micronutrient regulation in pregnant and lactating women from Rio de Janeiro. *Arch. Catinaam Nutr.* (1997) 47 (2 suppl.1) 30-4
 12. Miller RK, Hendricks AG, Mills JH, Hummter H, Wiegand VW: Periconceptional Vitamin A Use: How Much is teratogenic. *Reprod. Toxicol.* (1998) 12(1): 75-88.
 13. ACOG Committee opinion vitamin A supplementation during pregnancy. *Int. J. Gynaecol. Obstet.* (1998) 61 (2): d205-6
 14. Worthington-Roberts B: The role of maternal nutrition in the prevention of birth defects. *J. Am. Diet. Assoc.* (1997) (10, Suppl.2) 5184-5.
 15. Milk JL, Simpson JL, Cunningham GC, Cunley MR, Rhuade GG: P Vitamin A and birth defects *Am. J. Obstet. Gynecol.* (1997) 177 (1): 31-6.
 16. Semba RD: Overview of the potential role of vitamin A in mother to child transmission of HIV-I. *Acta Paediatr. Suppl.* (1997) 421: 107-12.
 17. Christian P, Bentley ME, Pradhan R, West KP Jr: an ethnographic study of night blindness "ratauni" among women in the Terai of Nepal. *Soc. Sci. Med.* (1998) 46 (7): 879-89.
 18. Chemukhuna LA, Danchenko GV, Zadorna OV, Kuzmenko IV, Khmetevstal UV: Vitamin provision in children of some Ukraine regions. *Ukr. Biochem. Zh.* (1997) 69 (2) 214-9.
 19. Hautvast JG: Adequate nutrition in pregnancy does matter. *Eur. J. Obstet. Gynecol. Reprod. Biol.* (1997) 75(1): 33-5.
 20. Marutinez RM, Ortega RM, Andres P: Vitamin A conception in Maternal milk: the effect of intake and serum levels of vitamin A during the third trimester of pregnancy. *Med. Cli. (Barek)* (1997) 109 (15): 573-6
 21. Ortega RM, Andres P, Martinez RM, Lopez-Sobaler AM: Vitamin A status during the third trimester of pregnancy in spanish women influence on concentrations of vitamin A in breast milk. *Am. J. Clin. Nutr.* (1992) 66 (3): 564-8.
 22. Christian P, West KP Jr., Khatri Sk, Katz I, Lecelerqs SI, Pradhan EK, et al: Vitamin A or beta carotene supplementation reduces but does not eliminate maternal night blindness in Nepal. *Jr. Nnutre* (1998) 128 (4k): 1458-63.
 23. Semba RD, Matti PG, Chipnanqwi JD, Dallabetha GK, Yang CP, Saah A, Hoover D: maternal vitamin A deficiency and infant mortality in Malawi. *J. Trop. Pediatr.* Aug: 44 (4): (1998): 232-4.
 24. 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. Nutre.* (1998) 67 (6): 1237-43.
 25. Nimmagaddo A, O'Brien WA, Goets MB: The significance of vitamin A and carotenoids in persons infected by the human immunodeficiency virus. *Clin. Infect. Dis.* (1998) 26 (3): 711-8
 26. Christian P, West KP Jr, Khatri SK, Katz J, Shrestha SR, Pradhan Ek, Nigh blindness of pregnancy in rural Nepal. Nutritional and Health risks. *Int. J. epidemiol.* (1998) 27 (2): 231-7.
 27. Christian P, Thorn-Lyman AL; West KP Jr, Bentley ME, Khatri SK, Pradhan et al Working after the sun goes down: exploring how night blindness impairs women's working activities in rural Nepal. *Eur. J. Clin. Nutr.* (1998) 52 (7): 517-24.
 28. Deconsi A, Torrisi R; Polizzi A, Gesi R, Brezzo V, Rolando M, et al Effect of the synthetic retinoid fenretinide on dark adaptation and the ocular surface. *J Nat. Cancer Inst.* Jan. 1988(2) (1994): 105-10.
 29. Vernon SA: Vitamin A deficiency with non-invasive dark adaptometry to screen children and adolescents. *British Medical journal.* Jul 8; 311(1999): (1995): 124.
 30. Dolk HM; Nau H, Hummler H, Barlow SM: Dietary vitamin A and teratogenic risk. European Teratology Society discussion paper. *European J. Obstet. Gynaecol. Reprod. Biol.* (1999): March: 83 (1) 31-6.
 31. West KP Jr, Katz I, Khatri SK, Leclercq SC, Pradhan EK, Shrestha SR, et al: Double blind cluster randomised trial of low dose supplementation with vitamin A or beta carotene on mortality related to pregnancy in Nepal. The NNIPS-2 study Group. *British Medical Journal.* Feb. 27: 318 (7183): (1999) 570-5
 32. Mastroiacovo P, Mazzome T; Addis A; Elephant E, Carlier P; Vial; et al High vitamin A intake in early pregnancy and major malformation: a Multicenter prospective controlled study in Teratology. (1998) 59 (1): 7-11.
 33. Wiegand UW; Hartmann S; Hammler H: Safety of vitamin A: Recent results. In: *Int. J. Vitamin Nutr. Res.* (1998) 68(6): 411-6.
 34. Olusanya O, Okpere E, Ezimokhai M: The importance of Social Class in Voluntary fertility in a developing country. *West African Journal of Medicine:* (1985) 205 212.
 35. Czeizel AE, Rockenbauer M: prevention of congenital abnormalities by vitamin A. *Int. J. vitamin. Nutr. Res.* (1998) 68 (4) 219-8
 36. Rosen DS, Haselow NJ, Sloan NL: How to use the Helen Keller International Food Frequency method to assess community risk for Vitamin A deficiency. *Helen Keller International Vitamin. A Technical Program.* (1993) 34 35.