

Serum retinol, carotenoids, vitamin E, and cholesterol in Nigerian women

Lucile L. Adams-Campbell, Martin U. Nwankwo, Flora A. Ukoli,
Jackson A. Omene, and Lewis H. Kuller

*University of Pittsburgh, Graduate School of Public Health, Department of
Epidemiology, Pittsburgh, PA, USA; and University of Benin, College of Medical
Sciences, Benin City, Nigeria, West Africa*

An epidemiologic study was conducted to assess serum levels of retinol, carotenoids, vitamin E, and their associations with cholesterol in an indigenous African population. The study population consisted of 116 black Nigerian women representing a response rate of 74%. The ages ranged from 17–32 years with a mean age of 22.6 years. The beta-carotene, total carotenoids, alpha-tocopherol, and cholesterol levels for the Nigerian women were 3.93 $\mu\text{mol/L}$, 7.03 $\mu\text{mol/L}$, 18.78 $\mu\text{mol/L}$, and 4.01 mmol/L, respectively. The beta-carotene levels of the Nigerian women ranged from 1.2–13 times greater than the United States population, and the total carotenoid levels were 2.5 times greater in the Nigerians compared with the United States population. On the contrary, the cholesterol levels of the Nigerians ranged from 5%–24% lower than similarly aged United States populations. Significant positive associations were observed between cholesterol and the following: 1) beta-carotene ($r = 0.31$, $P < 0.001$); 2) total carotenoids ($r = 0.43$, $P < 0.001$); and alpha-tocopherol ($r = 0.72$, $P < 0.001$). The findings suggest that dietary intake may not be the key factor in the vitamin A-cholesterol relationship, because this relationship has been observed in populations with significantly lower vitamin A and higher saturated fat intake.

Keywords: vitamin A; retinol; cholesterol; blacks; carotenoids

Introduction

In recent years the interest in vitamin A status has increased considerably because of the epidemiologic evidence linking intake of vitamin A, both preformed vitamin A and provitamin A carotenoids, with the possible prevention of various types of cancer.^{1–13} It is hypothesized that beta-carotene, through the conversion to retinoids and its antioxidant properties, may act as a cancer protector.¹⁴

The role of vitamin E has also been linked to the carcinogenesis process. It is hypothesized that vitamin E may inhibit carcinogenesis via its function as an intracellular antioxidant.^{15,16} Vitamin E is the major lipid-soluble antioxidant in plasma, and this vitamin,

as well as cholesterol, is transported in plasma almost exclusively by lipoproteins. Lipoproteins, particularly low-density lipoproteins (LDL), are the major plasma transport molecules for both cholesterol and vitamin E.^{17–19}

A few plausible explanations have been offered to support the cholesterol-vitamin A relationship. Because vitamin A and serum cholesterol are transported in association with liver-derived serum proteins, the correlations between these two factors may be attributed to the mutual associations of these factors with the serum-transport proteins.²⁰ Another possible explanation is that cholesterol and vitamin A, which are known to be absorbed in conjunction with chylomicrons, may reflect the association between dietary retinol and cholesterol. A final suggestion is that there exists a mutual association between serum cholesterol and vitamin A with LDL, because the majority of circulating cholesterol and carotene (provitamin A) is transported in conjunction with LDL.

There is a dearth of information on the vitamin A-cholesterol association among healthy, free-living populations, particularly blacks (United States and Af-

Address reprint requests to Dr. Lucile L. Adams-Campbell, Howard University Cancer Center, Division of Epidemiology and Cancer Control, 2041 Georgia Avenue, N.W., Washington, DC 20060, USA.

Dr. Lucile Adams-Campbell was supported under the National Heart, Lung, and Blood Institute, Grant No. HL39788.
Received July 25, 1990; accepted June 11, 1991.

rica). Therefore, the present study is designed to assess serum levels of retinol, carotenoids, vitamin E, and their associations with cholesterol in an indigenous African population.

Materials and methods

The study population consisted of Nigerian women, who were attending either Nursing or Mid-wifery school at the University of Benin Teaching Hospital in Benin City, Nigeria, West Africa. Complete ascertainment of the population was attempted. Dietary information was obtained on a subsample of the study population which included the number of meals eaten each day and a food frequency questionnaire. The food frequency questionnaire was developed by Nigerians so that foods specific to the culture were included. There were 60 food items on the survey which focussed on the major sources of vitamin A, carotenoids, and vitamin E.

Twelve-hour fasting blood samples were obtained from all subjects who were not using vitamin supplements within a 1-week period in June and the samples were stored at -47°C . All samples were analyzed within 2 months. Beta-carotene, carotenoids, retinol, alpha-tocopherol, and total cholesterol were analyzed by the Heinz Nutrition Laboratory at the Graduate School of Public Health, University of Pittsburgh (Pittsburgh, PA, USA). The Heinz Laboratory participates routinely in standardization and quality assurance programs conducted by the Center for Disease Control, the National Bureau of Standards, the National Cancer Institute, and others.

Serum beta-carotene levels were determined using Perkin-Elmer (Norwalk, CT, USA) high-performance liquid chromatography (HPLC) employing the serum extraction procedure of Driskell et al.²¹ and the HPLC eluants of Nierenberg.²² Total carotenoids were measured using a Micro-Medic spectrophotometer (ICN Micro-Medic System, Inc, Horsham, PA, USA).²³ Total cholesterol was obtained by enzymatic determination.^{24,25}

Statistical analysis

Descriptive statistics were used to provide means, standard deviations, and ranges for the vitamin and cholesterol serum levels. Pearson product-moment correlation coefficients were computed to examine the associations between the selected vitamins and cholesterol.

Results

One hundred-sixteen black Nigerian (predominantly Igbo) college women participated in the study representing a response rate of 74% (116/157). The ages ranged from 17–32, with a mean age of 22.6 years. These Nigerian women were considered more affluent than the typical Nigerian, based on educational attainment. In terms of lifestyle factors, none of the college women reported cigarette smoking.

The most frequently consumed foods (based on daily consumption) are reported in *Table 1*. Because of the known limitations associated with food frequencies, the food data were not quantifiable. However, it is of interest to note that palm oil, which was used daily by the majority of the students (78%), is considered one of the richest sources of provitamin A activity varying from 65,000 to 113,000 IU per 100 gm oil.²⁶

The means and ranges for serum levels of retinol, carotenoids, vitamin E, total cholesterol, and the

Table 1 Frequency distribution of foods consumed daily by sample of Nigerian women (n = 67)

Food group & constituents	Frequency
Meats	69%
beef	
chicken	
Seafood	54%
fish	
Dairy products	40%
eggs	
whole milk	
Grains and nuts	54%
rice	
fufu	
groundnuts	
Vegetables	85%
spinach	
tomatoes	
yams	
Fruits	33%
mangos	
Oils	78%
palm oil	

Table 2 Mean serum levels of vitamins and total cholesterol in Nigerian women (n = 116)

Variable	Range	Mean	S.D.
Retinol ($\mu\text{mol/L}$)	0.48–1.64	1.61	0.35
Alpha-tocopherol ($\mu\text{mol/L}$)	8.13–30.18	18.78	3.94
Beta-carotene ($\mu\text{mol/L}$)	0.86–9.42	3.93	1.52
Carotenoids ($\mu\text{mol/L}$)	1.96–14.34	7.03	2.20
Cholesterol ($\mu\text{mol/L}$)	1.63–6.91	4.01	0.83
Alpha-tocopherol/ total cholesterol	3.68–7.88	5.27	0.80

S.D., standard deviation.

alpha-tocopherol/total cholesterol ratio are presented in *Table 2*. The beta-carotene and carotenoids levels were 3.93 $\mu\text{mol/L}$ and 7.03 $\mu\text{mol/L}$, respectively. Yet the mean cholesterol level of the Nigerian women was 4.01 mmol/L. The alpha-tocopherol/total cholesterol ratio ranged from 3.68–7.88.

The correlation coefficient matrix of vitamins A and E, and total cholesterol are presented in *Table 3*. Significant positive associations were demonstrated between cholesterol and retinol, alpha-tocopherol, beta-carotene, and carotenoids ($P < 0.001$, for all comparisons).

Discussion

The results of the present study reveal that the Nigerians have high levels of beta-carotene (3.93 $\mu\text{mol/L}$) and total carotenoids (7.03 $\mu\text{mol/L}$) compared with United States populations. More specifically, in previously reported data by Comstock et al.,²⁷ the beta-carotene levels of U.S. females, median age of 58.1 years, was only 0.68 $\mu\text{mol/L}$. In a chemopreventive

Table 3 Correlation coefficient matrix of vitamins A, E, and total cholesterol (n = 116)

	Alpha-tocopherol	Beta-carotene	Carotenoids	Cholesterol	Ratio ^a
Retinol	0.41	0.04	0.09	0.30	0.21
α-tocopherol		0.28	0.39	0.72	0.38
β-carotene			0.96	0.31	-0.05
Carotenoids				0.43	-0.06
Cholesterol					-0.34

^a Ratio is alpha-tocopherol:total cholesterol.

All correlation coefficients ≥ 0.28 are statistically significant at $P < 0.001$.

trial using 15 mg of beta-carotene daily over a 4-month period, it was observed that the mean beta-carotene levels at baseline, 2 months, and 4 months, were 0.3, 2.9, and 3.3 $\mu\text{mol/L}$, respectively,²⁸ never equalling or exceeding that of the Nigerians. Adams et al²⁹ found that the mean total carotenoid level of similarly aged United States college females was 2.5 times less than that observed among the Nigerians; 7.02 $\mu\text{mol/L}$ and 2.97 $\mu\text{mol/L}$, respectively. Also, the cholesterol levels of the Nigerians were observed to be between 5%–24% lower than their US counterparts.^{29,30}

Another important finding was the significant positive association observed among the Nigerians between cholesterol and serum vitamins A and E, and carotenoids. These findings were consistent with previously reported studies, although the United States comparison groups had significantly lower beta-carotene and carotenoid levels.^{4-6,8,29,31} The findings are of particular interest and suggest that dietary intake may not be the key factor in the vitamin A-cholesterol relationship. Since the Nigerian diet is associated with a high intake of palm oil (one of the richest sources of provitamin A activity varying from 65,000 to 113,000 IU per 100 gm oil),²⁶ the data demonstrate that the vitamin A-cholesterol relationship persists across a wide distribution range of serum cholesterol levels.

It is hypothesized that the vitamin A-cholesterol association may be attributed to the mutual associations of these factors with the serum-transport proteins. There has been some concern that the absorption of the fat-soluble vitamins will be poor, as well as their transport in the serum, if the serum cholesterol levels are low. Results of the present study suggest that even in a population in which the serum total cholesterol levels are lower than that observed in United States populations, it is apparent that a high carotenoid intake results in very high levels of beta-carotene in the serum.

References

- 1 Menkes, M.S., Comstock, G.W., Vuilleumier, J.-P., et al. (1986). Beta-carotene, vitamins A and E, and selenium and risk of lung cancer. *N. Engl. J. Med.* **315**, 1250–1254
- 2 Friedman, G.D., Blaner, W.S., Goodman, D.S., et al. (1986). Serum retinol and retinol-binding protein levels do not predict subsequent lung cancer. *Am. J. Epidemiol.* **123**, 781–789
- 3 Peleg, I., Heyden, S., Knowles, M., et al. (1984). Serum retinol and risk of subsequent cancer: Extension of the Evans County, Georgia, study. *JNCI* **73**, 1455–1458
- 4 Stahelin, H.R., Rosel, F., Buess, E., et al. (1984). Cancer, vitamins, and plasma lipids: *Prospective Basel study*. *JNCI* **73**, 1463–1468
- 5 Willett, W.C., Polk, B.F., Underwood B.A., et al. (1984). Relation of serum vitamins A and E and carotenoids to the risk of cancer. *N. Engl. J. Med.* **310**, 430–434
- 6 Wald, N.J., Boreham, J., Hayward, J.L., et al. (1984). Plasma retinol, β-carotene and vitamin E levels in relation to the future risk of breast cancer. *Br. J. Cancer* **49**, 321–324
- 7 Wald, N., Idle, M., Boreham, J., et al. (1980). Low serum-vitamin-A and subsequent risk of cancer. *Lancet* **2**, 813–815
- 8 Kark, J.D., Smith, A.H., Switzer, B.R., et al. (1981). Serum vitamin A (retinol) and cancer incidence in Evans County, Georgia. *JNCI* **66**, 7–16
- 9 Shekelle, R.B., Lepper, M., Liu, S., et al. (1981). Dietary vitamin A and risk of cancer in the Western Electric Study. *Lancet* **2**, 1185–1190
- 10 Hirayama, T. (1979). Diet and cancer. *Nutr. Cancer* **1**, 67–81
- 11 Bjelke E. (1975). Dietary vitamin A and human lung cancer. *Int. J. Cancer* **15**, 561–565
- 12 Graham, S. (1983). Results of case-control studies of diet and cancer in Buffalo, New York. *Cancer Res.* **43**, s2409–2413
- 13 Ziegler, R.G. (1989). A review of epidemiologic evidence that carotenoids reduce the risk of cancer. *J. Nutr.* **119**, 116–122
- 14 Krinsky, N.I., and Dencke S.M. (1982). The interaction of oxygen and oxy-radicals with carotenoids. *JNCI* **69**, 205–210
- 15 Tappel, A.L. (1980). Vitamin E and selenium protection from in vivo lipid peroxidation. *Ann. NY Acad. Sci.* **355**, 18–29
- 16 Bieri, J.G., Carash, L., and Hubbard, V.S. Medical uses of vitamin E. *N. Engl. J. Med.* **308**, 1063–1071
- 17 Davies, T., Kelleher, J.V., and Losowsky M.S. (1969). Inter-relationship of serum lipoproteins and tocopherol levels. *Clin. Chim. Acta* **24**, 431–436
- 18 Haga, P., Johan, E., and Kran, S. (1982). Plasma tocopherol levels and vitamin E/β-lipoprotein relationships during pregnancy and in cord blood. *Am. J. Clin. Nutr.* **36**, 1200–1204
- 19 Vatassery, G.T., Krezowski, A.M., and Eckfeldt, J.H. (1983). Vitamin E concentrations in human blood plasma and platelets. *Am. J. Clin. Nutr.* **37**, 1020–1024
- 20 Flaim, E., Williford, W.O., Muller, J.L., et al. (1986). The relationship of serum cholesterol and vitamin A in hospitalized patients with and without cancer. *Am. J. Clin. Nutr.* **44**, 370–378
- 21 Driskell, W.J., Bashor, M.M., and Neese, J.W. (1983). Beta-carotene determined in serum by liquid chromatography with an internal standard. *Clin. Chem.* **29**, 1042–1044
- 22 Nierenberg, D.W. (1985). Serum and plasma beta-carotene levels measured with an improved method of high-performance liquid chromatography. *J. Chromatogr.* **339**, 273–284
- 23 Neeld, J.B. and Pearson, W.N. (1963). Macro- and the micro-methods for the determination of serum vitamin A using trifluoroacetic acid. *J. Nutr.* **79**, 454–462
- 24 Allain, C.C., Poon, L.S., Chou, C.S.G., et al. (1974). Enzymatic determination of total serum cholesterol. *Clin. Chem.* **20**, 470–475

- 25 Copper, G.R., Duncan, G.H., Hazlehurst, J.S., et al. (1982). Cholesterol enzymatic methods. In: *Selected Methods for the Small Clinical Chemistry Laboratory* (Faulkner WR and Meites S, eds.), pp. 165-174, American Association for Clinical Chemistry, Inc., Washington, DC
- 26 Goodhart, R.S. and Shils, M.E. (1980). *Modern Nutrition in Health Disease*. Lea and Feilbiger, Philadelphia
- 27 Comstock, G.W., Menkes, M.S., and Schober, S.E., et al. (1988). Serum levels of retinol, beta-carotene, and alpha-tocopherol in older adults. *Am. J. Epidemiol.* **127**, 114-123
- 28 Constantino, J.P., Kuller, L.H., Begg, L., et al. (1988). Serum level changes after administration of a pharmacologic dose of β -carotene. *Am. J. Clin. Nutr.* **48**, 1277-1283
- 29 Adams, L.L., LaPorte, R.E., Watkins, L.O., et al. (1985). The association of lipoprotein cholesterol with vitamin A. *Cancer* **56**, 2593-2597
- 30 The Lipids Research Clinics. Population Studies Data Book Vol 1: The prevalence study. US Department of Health and Human Services, PHS, NIH Publication No. 80-1527, July 1980
- 31 Desai, I.D., and Lee, M. (1974). Plasma vitamin E and cholesterol relationship in Western Canadian Indians. *Am. J. Clin. Nutr.* **27**, 334-338