THE ASSOCIATION OF PLASMA FATTY ACIDS WITH PROSTATE CANCER RISK IN NIGERIANS

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Purpose: To investigate the role of fatty acids (FAs) in prostate cancer (PCa) risk in Nigeria, a country in transition to westernized diet high in animal fats, and currently experiencing rising rates of prostate cancer.

Methods: Men ≥40 years were recruited from surgery/urology clinics, University of Benin Teaching Hospital and from 2 rural and 2 urban communities. Personal information, urological symptom history and anthropometrics were recorded, digital rectal examination performed, and 30 mLs of fasting blood collected for prostatic specific antigen and fatty acid (FA) analysis. Odds ratio (OR) of PCa risk was determined by unconditional logistic regression with the plasma FA 1st quartile as reference, controlling for age, education, waist-to-hip ratio, and family history.

Results: Mean ages for 66 (22.6%) cases and 226 (77.4%) controls were 71.9±11.47 and 56.7±12.69 years, $P<.001$, and median (25th, 75th percentile) fasting plasma FA were 2,447 (2,087, 3,024) and 2,373 (2,014, 2,751) μg/mL, respectively. PCa risk trend was observed for total ω-6 FA, adjusted $OR_{Q3vs.Q1}$ 2.33 (95%CI,0.77–7.07), $P<0.05$. Unadjusted $OR_{Q4vs.Q1}$ for behenic and nervonic acids were 2.79 (95%CI,1.27–6.10) and 2.40 (95% CI,1.19–4.85), and unadjusted $OR_{Q2vs.Q1}$ for erucic and arachidonic acids were 4.20 (95%CI,1.79–9.82) and 3.81 (95%CI,1.50–9.70) respectively. Unadjusted $OR_{Q2vs.Q1}$ for ω-3 FAs eicosapentaenoic (EPA) and docosapentaenoic (DPA) were 0.39 (95%CI, 0.18–0.85) and 0.79 (95%CI, 0.35–1.79) respectively.

Conclusions: In this population with high total plasma ω-3, we observed modest positive PCa risk trend with total plasma ω-6 (2.3), inverse risk reduction with EPA (0.4), and strong positive risk associations with behenic (2.8), erucic (4.2), and nervonic (2.4) acids. Total plasma ω-6 is highest in the educated high-income group. These findings should be confirmed in a larger study because of the potential serious implication of dietary transition particularly in a region designated as low-incidence for PCa. (*Ethn Dis.*2009;19:454–461)

Key Words: Prostate Cancer, Fatty Acids, Omega-3, Omega-6, Nigerians, Case-Control

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INTRODUCTION

The incidence of prostate cancer (PCa) varies widely across the world. African ancestry, increasing age, and family history are recognized significant risk factors.[1–3] Based on global age-standardized PCa incidence data, Sub-Saharan Africa is designated low-incidence, less than 24.5 per 100,000 inhabitants.[4] Without routine screening in Nigeria, PCa diagnosis is on the rise, becoming the most diagnosed male cancer.[5,6] Comparative studies of African-Americans in Washington, DC and Nigerian men in Ibadan demonstrated similar incidence of latent PCa, although African-Americans recorded 10-fold higher incidence of clinical PCa.[7] Growth and differentiation of the prostate is under androgen control, and differences in estrogen and androgen metabolites and urinary steroid levels observed between healthy Africans and African-Americans were reported to depend on their respective diets, which could explain disparate PCa rates.[8,9] A possible ecological link between PCa and diet was originally based on international differences in PCa mortality rates and national average dietary fat.[10] The role of diet in PCa etiology has been reported in numerous studies including a multicenter study of dietary factors that demonstrated that 10–15% of the ethnical differences in PCa incidence were accounted for by the differences in saturated fat intake,[11] and that diets rich in red meats and fat from animal sources are associated with increased PCa risk.[12–14] Recent increase in PCa incidence among Nigerians has been attributed to improved diagnosis, transition to a more westernized diet high in meat and animal fat, and the increase in the number of older men at risk for PCa resulting from increased longevity.[6,15] Most case-control studies associated high intakes of animal fat and saturated FAs with increased PCa risk based on dietary assessments using food-frequency questionnaires (FFQ), while a few reported objective biomarker information that did not rely on the precision of food composition databases, accuracy of self-reports or the appropriateness of FFQ items.[16,17] The plasma phospholipids sub-fraction better reflects type of dietary fat eat-

We examined PCa risk association of plasma FAs… sub-group totals and individual fasting plasma FA concentrations among Nigerians in a case-control design.

en,[18–20] and fasting plasma concentration reflects usual essential FA intake.[21] We examined PCa risk association of plasma FAs by estimating odds ratio (OR) across quartiles of total, sub-group totals, and individual fasting plasma FA concentrations among Nigerians in a case-control design.

METHODS

Study Population

Apparently healthy men aged ≥40 years were recruited house-to-house in two rural and two urban communities of Edo and Delta states of southern Nigeria. Men presenting with prostate-related symptoms at the surgery/urology clinics, University of Benin Teaching Hospital (UBTH), Benin-City, were also recruited. Participants signed appropriately administered informed consent. Cases were histologically diagnosed with PCa and controls had normal prostate on digital rectal examination (DRE) and serum prostate specific antigen (PSA) <4 ng/mL. Trained and certified research assistants collected demographic and urology history information, FFQ diet assessment by interview, and anthropometric measurements (height, weight, waist, hip, mid-arm circumference, biceps, triceps, and sub-scapular skin-fold thickness) using standard protocols with participants wearing light clothing and without shoes. Participants were instructed to eat dinner before 9:00 pm the previous night, and to fast until their blood was drawn the next morning before 9:00 am by a certified phlebotomist/registered nurse. This was followed by a medical consultation that included a DRE by a general surgeon/urologist. The 30 mL fasting venous blood was drawn into red-, yellow-, and lavender-top vacutainer tubes, centrifuged after standing for 30–60 minutes, sub-fractions were separated into accurately labeled microvials, and samples were stored at −20°C until shipped quarterly, on dry ice, to the United States where they were stored at −40°C. Serum PSA was measured at a reference laboratory in Nashville and the result forwarded to the attending surgeon/urologist within five working days. An aliquot of plasma from each participant was shipped to a specialized research laboratory for FA analyses. The capillary gas chromatography-electron-capture negative-ion mass spectrometry (GC/MS) method was used for the quantitative determination of plasma C8–C26 total FAs.[22]

Table 1. Characteristics of Nigerian study population

Characteristics	Frequency (%)	
	Cases (*n*=66)	Controls (*n*=226)
Recruitment site*		
Community	8(12.1)	165(73.0)
Urology/surgery clinics	58(87.9)	61(27.0)
Age (Years)*		
< 54	2(3.0)	106(46.9)
55–74	40(60.6)	104(46.0)
≥ 75	24(36.4)	16(7.1)
Education status		
< High school	44(66.7)	133(58.8)
High school	6(7.6)	36(15.9)
Some college	8(12.1)	26(11.5)
College/post-grad	8(12.1)	21(9.3)
Not recorded	1(1.5)	10(4.4)
Socioeconomic status		
Low	52(78.8)	157(69.5)
Middle	7(10.6)	16(7.1)
High	4(6.1)	15(6.6)
Not recorded	3(4.5)	38(16.8)
Obesity (BMI)		
Normal weight (<24.9)	45(68.2)	153(67.7)
Overweight (25.0–29.9)	14(21.2)	52(23.0)
Obese I (30–34.9)	2(3.0)	15(6.6)
Obese II (≥35.0)	0(0.0)	1(0.4)
Not recorded	5(7.6)	4(1.8)
Family history of PCa	3(4.5)	4(1.8)
Urology history		
BPH no symptom	4(6.1)	52(23.0)
BPH with symptom	27(40.9)	27(11.9)

BPH - Benign prostatic hyperplasia.
* $P<.001$.

Statistics

Summary statistics for plasma FA (μg/mL) were reported as mean ± standard deviation (SD) and median (25^{th} percentile, 75^{th} percentile). The Chi-squared and non-parametric tests for independent samples were used to compare cases and controls as appropriate, and unconditional logistic regression was used to estimate OR (95% confidence intervals) of PCa risk across quartiles of plasma FA relative to the lowest quartile (Q1), with *P* calculated with FA as continuous data in each quartile. ORs were adjusted for age, education, family history of PCa, and waist-hip ratio. Income was appropriately stratified as low, middle, and high, and educational status as low (≤6), middle (6–12), and high (≥13) formal years of education. Data analysis was performed using SPSS, v14.0 (SPSS, 2001, Chicago, Ill.). Study participants with elevated PSA≥4 ng/mL who did not have any prostate biopsy informa-

Table 2. Plasma fatty acids (μg/ml) of Nigerians by educational status

	Mean (SD)				
	Primary or less	Some/complete secondary	Post secondary or college	*P*-value	
Fatty acids	*n*=182	*n*=82	*n*=69	Group*	Linear†
Total	2,486.7(589.4)	2,341.6(612.6)	2,658.4(764.0)	.01	.20
Saturated total	892.6(217.1)	855.5(247.9)	958.1(289.5)	.03	.16
ω-9 total	685.4(218.6)	603.8(179.9)	675.4(234.0)	.02	.31
ω-7 & ω-5 total	115.4(51.9)	102.2(54.0)	116.0(65.0)	.17	.70
ω-6 total	661.6(181.6)	658.1(181.7)	766.9(216.4)	.0001	.001
ω-3 total	116.6(60.6)	107.9(57.7)	127.6(86.3)	.19	.42
Trans total	16.6(6.2)	14.2(6.1)	18.2(8.5)	.004	.46
Lauric	8.0(20.3)	7.1(9.2)	10.1(14.2)	.53	.50
Myristic	28.5((20.8)	27.7(14.9)	34.8(26.6)	.07	.07
Palmitic	615.1(144.2)	582.9(176.1)	647.4(203.5)	.06	.39
Stearic	183.9(44.6)	179.3(51.1)	196.9(53.9)	.07	.13
Behenic	16.2(4.9)	16.5(4.9)	20.8(6.8)	.0001	.0001
Palmitoleic	68.9(38.0)	60.5(39.9)	68.1(46.4)	.28	.60
Vaccenic	45.0(33.6)	38.6(13.9)	43.4(19.6)	.21	.42
Palmitelaidic	2.2(1.4)	1.9(1.1)	2.3(1.5)	.18	.60
Elaidic	9.2(3.7)	7.9(3.7)	10.1(4.9)	.006	.60
Oleic	625.3(213.9)	551.5(170.9)	615.5(221.6)	.03	.32
Mead	4.6(3.5)	3.6(2.6)	3.9(3.1)	.05	.07
Erucic	0.9(2.2)	0.7(0.2)	0.8(0.3)	.46	.40
Nervonic	32.3(9.0)	30.7(9.7)	35.5(11.7)	.01	.08
Linoleic	492.8(134.8)	493.4(128.0)	560.7(162.8)	.002	.002
γ-linolenic	7.9(5.2)	7.8(5.0)	9.3(5.2)	.11	.08
Di-homo-γ-linolenic	28.7(11.5)	27.7(11.5)	33.5(14.2)	.007	.018
Arachidonic	116.5(46.0)	114.2(53.3)	145.6(62.1)	.0001	.001
α-linolenic	6.0(4.0)	5.7(3.2)	6.6(4.8)	.35	.37
Eicosapentaenoic	28.7(20.2)	29.9(24.4)	32.2(31.1)	.58	.31
Docosapentaenoic	3.4(2.1)	3.1(2.1)	4.1(2.8)	.03	.12
Docosahexaenoic	69.0(36.0)	60.1(29.2)	74.8(48.6)	.05	.60

* Between-group difference.
† Linearity across group difference.

tion at the time of data analysis were excluded from the risk analysis.

RESULTS

Of 340 consenting participants, 66 (19.4%) were confirmed PCa cases, 48 (14.1%) with elevated PSA, and 226 (66.5%) were controls, with mean ages of 71.9±11.47, 67.0±11.12, and 56.7±12.69, respectively, $P<.001$. Prostate cancer cases were more likely to report a family history compared to controls, 3 (4.5%) to 4 (1.8%), present with symptoms, 27 (40.9%) to 27 (11.9%), and have enlarged prostate on DRE without symptoms, 4 (6.1) to 52 (23.0), $P<.001$. Cases and controls were similar by marital, educational, socioeconomic, and obesity status (Table 1). Total FA was 2,526±781 μg/mL, 2,236±526 μg/mL, and 2,778±710 μg/mL, $P<.04$, across low, middle, and high income groups, respectively (not displayed). Total, saturated, all ω-6 except γ-linolenic, trans FAs, behenic, trans elaidic, nervonic, docosapentaenoic acid (DPA) and docosahexaenoic acid (DHA), but not total ω-3 FAs, were highest in the more educated men. Total ω-9 FAs, specifically oleic and mead, were higher in men with low education (Table 2).

All saturated FAs were similar for cases and controls except for behenic acid with a median of 18.4 (14.8, 22.6) μg/mL to 15.8 (12.7, 19.8) μg/mL, respectively, $P<.001$. Monounsaturated FAs were similar for cases and controls except for erucic acid with a median of 0.8 (0.7, 0.9) μg/mL to 0.7 (0.5, 0.8) μg/mL, respectively, $P<.001$, and nervonic acid with median 38.0 (32.7, 48.9) μg/mL to 28.8 (24.3, 34.7) μg/mL, respectively, $P<.001$. Arachidonic acid was higher in cases, 132.0 (105.9, 160.6) μg/mL to 104.5 (76.6, 143.4) μg/mLl, $P<.001$. Regarding ω-3 FAs, eicosapentaenoic (EPA) was lower in cases, DPA higher in cases, and DHA was similar for cases and controls. Essential ω-6 linoleic acid and essential ω-3 α-linolenic acid were similar for cases and controls (Table 3). Adjusted OR trend was significant across quartiles of total ω-6 FA with $OR_{Q3vs.Q1}$ 2.33 (95%CI, 0.77–7.07), but not for total saturated nor trans FAs. Unadjusted and adjusted OR trends were not

Table 3. Plasma fatty acids (μg/mL) of Nigerian prostate cancer cases and controls

Fatty acids	Median (25^{th}, 75^{th} percentile)	
	Cases	Controls
Total	2446.8 (2,087.4, 3,024.2)	2,373.5 (2,013.6, 2,750.6)
Saturated	886.5 (728.2, 975.1)	846.2 (728.2, 975.1)
n-9 total	624.6 (532.3, 875.4)	602.7 (517.4, 750.2)
n-7 & n-5 total	95.9 (80.4, 130.0)	101.0 (76.8, 135.3)
n-6 total	694.4 (564.8, 880.1)	654.0 (550.4, 779.5)
n-3 total	97.1 (67.3, 145.0)	104.9 (75.3, 152.4)
Trans total	15.1 (10.6, 20.9)	15.5 (12.2, 20.0)
Lauric	4.4 (2.5, 9.0)	4.2 (2.7, 8.0)
Myristic	21.6 (16.2, 37.2)	24.1 (16.5, 38.3)
Palmitic	603.0 (539.2, 744.1)	572.0 (503.6, 658.5)
Stearic	188.0 (152.0, 229.6)	175.4 (150.0, 209.1)
Behenic	18.4 (14.8, 22.6)	15.8 (12.7, 19.8)†
Palmitoleic	53.0 (42.3, 73.4)	58.8 (40.2, 85.0)
Vaccenic	41.2 (33.0, 52.5)	38.1 (30.3, 48.3)
Palmitelaidic (trans)	1.8 (1.1, 2.7)	2.1 (1.3, 2.9)
Elaidic (trans)	8.7 (5.9, 12.1)	8.6 (6.5, 11.0)
Oleic	568.0 (471.9, 809.0)	550.3 (471.7, 687.7)
Mead	3.5 (2.1, 5.2)	3.5 (1.9, 5.6)
Erucic	0.8 (0.7, 0.9)	0.7 (0.5, 0.8)†
Nervonic	38.0 (32.7, 48.9)	28.8 (24.3, 34.7)†
Linoleic	513.4 (436.3, 658.7)	491.8 (417.1, 585.6)
γ-linolenic	6.7 (4.2, 11.3)	7.0 (4.6, 10.1)
Di-homo-γ-linolenic	30.6 (21.1, 38.6)	26.4 (20.5, 34.5)
Arachidonic	132.0 (105.9, 160.6)	104.5 (76.6, 143.4)†
α-linolenic	5.2 (3.9, 7.4)	5.0 (3.6, 6.9)
Eicosapentaenoic	16.7 (11.5, 32.3)	26.2 (14.0, 40.4)*
Docosapentaenoic	3.2 (2.3, 4.9)	2.7 (1.8, 3.9)*
Docosahexaenoic	58.8 (42.7, 78.7)	58.6 (42.6, 80.1)

* $P<.05$.
† $P<.001$.

significant for total ω-3 FA (Table 4). Unadjusted risk trend was significant for behenic acid, $OR_{Q4vs.Q1}$ 2.79 (95%CI, 1.27–6.10) and nervonic acid, 2.40 (95%CI, 1.19–4.85), and for erucic acid, 4.20 (95%CI, 1.79–9.82) and arachidonic acid, 3.81 (95%CI, 1.50–9.70). For EPA unadjusted and adjusted $OR_{Q2vs.Q1}$ were 0.39 (95%CI, 0.18–0.85) and 0.39 (95%CI, 0.15–0.97), respectively (Table 5).

DISCUSSION

Early epidemiological studies suggested possible causal association between dietary fat and PCa risk as demonstrated by dramatic changes in PCa incidence among men who moved from PCa low-incidence regions with low dietary fat intake to PCa high-incidence regions with high dietary fat intake, alluding to the overriding importance of increased exposure to environmental risk factors.[23,24] Western diet, fat in general, meat and animal fat specifically, is associated with increased PCa risk, whereas diets high in fish content are associated with reduced PCa risk,[25–27] and an African high-fiber, low-fat diet is associated with reduced risk for atherosclerosis and cancer of the large bowel.[28] Lower PCa incidence in southeast Nigeria could be related to their high-fish, low-meat diet.[6] Differences in the dietary content of oils, fats, and protein from plant versus animal sources account for a large part of nutrient diversity across African countries.[29] Although microethnic dietary diversity was minimized by conducting the study in a limited ethnogeographic region of southern Nigeria, a wide range of fasting plasma FA, 891.7 μg/mL to 7,828.8 μg/mL, with a mean of 2,527.7±752.4 μg/mL, confirmed the wide range in dietary fat intake.

Nutrition transition to high-fat diets in low-income nations is a result of human preference for palatable dishes, availability of cheap vegetable oils and fats, and urbanization,[30,31] accounting for similar FA profile across diverse economic groups in this study. Differences for some and not all FA subgroups across education rather than income strata indicate a dietary transition, particularly in the more educated group who can afford more meat and animal products and who now record higher levels of saturated, ω-6 and trans FAs. This dietary transition has been alluded to as a contributing factor to increasing cancer rates in Nigerians,[15] although no attempt has been made to compare PCa rates across socioeconomic stratification. Comparable levels of monounsaturated FAs across education and income groups can be explained by popular consumption of readily available palm fruit, palm kennel, and coconut oils, and comparable total ω-3 attributed to readily available fish. Omega-3 FAs DPA and DHA are higher in the postsecondary/college group probably because they eat the more desirable and expensive fresh water fish, rather than the cheaper commonly available frozen fishes like mackerel. Fish remains the main source of animal protein in this population,[32] a relic of the historical eating pattern of shoreline Africans.[33] Oleic and mead acids derived from animal and plant sources were highest among men with low education, suggesting deficiency of dietary essential FA.[34]

Plasma and tissue FA compositions are more objective exposure measures than dietary assessment estimations from FFQs, and concentrations in the plasma phospholipids and cholesterol

Table 4. Odds ratios and 95% confidence interval for prostate cancer risk across quartiles of sub-group plasma fatty acids in Nigerians

Sub-group fatty acid quartiles	Unadjusted OR (95% CI)	*P**	Adjusted OR† (95% CI)	*P**
Total				
Q1	1.00		1.00	
Q2	1.52 (0.70–3.30)		0.78 (0.30–2.03)	
Q3	1.66 (0.76–3.63)		1.30 (0.50–3.39)	
Q4	1.19 (0.55–2.53)	.57	0.80 (0.32–1.98)	.70
Total saturated				
Q1	1.00		1.00	
Q2	1.82 (0.80–4.17)		1.14 (0.42–3.07)	
Q3	1.16 (0.54–2.52)		1.14 (0.46–2.87)	
Q4	1.00 (0.47–2.15)	.46	1.02 (0.41–2.54)	.99
Total ω-9				
Q1	1.00		1.00	
Q2	1.44 (0.66–3.15)		0.76 (0.28–2.04)	
Q3	1.35 (0.62–2.92)		0.82 (0.32–2.10)	
Q4	1.22 (0.56–2.64)	.81	0.79 (0.31–2.03)	.95
Total ω-6				
Q1	1.00		1.00	
Q2	1.39 (0.64–3.01)		0.65 (0.24–1.76)	
Q3	2.30 (0.98–5.38)		2.33 (0.77–7.07)	
Q4	0.91 (0.44–1.88)	.14	0.55 (0.22–1.36)	.05
Total ω-3				
Q1	1.00		1.00	
Q2	0.65 (0.30–1.40)		0.50 (0.20–1.28)	
Q3	0.87 (0.40–1.93)		0.69 (0.26–1.81)	
Q4	1.07 (0.48–2.42)	.58	0.88 (0.34–2.30)	.49

* Calculated with fatty acid in each quartile as a continuous variable.
† OR adjusted for age, education, family history of prostate cancer, and waist-hip ratio.

Plasma total ω-3 FA is high across all socioeconomic groups in this population, while plasma ω-6 is significantly higher among educated men with higher income.

ester fractions better reflect medium-term (weeks to months) dietary intake. We measured fasting FAs in the combined triglycerides and phospholipids fractions rather than the more expensive sub-fraction analysis.[35] We observed that total FA per se did not explain PCa risk probably because the percentage of energy derived from fat varied widely, and we cannot confirm the 20–25% reported for rural and urban West Africa[36,37] in the absence of Nigerian food composition tables for indigenous Nigerian soups and sauces which are the major sources of dietary fats and oils. Our findings are consistent regarding ω-3 and ω-6 polyunsaturated FAs, which are reported to be associated with reduced and increased PCa risk, respectively.[38,39] There is a significant risk trend across quartiles of total ω-6 FA but the 2-fold PCa risk observed between the 3rd and 1st quartile is not statistically significant. Reports about the role of ω-6 FAs is mixed, with a significant positive association across tertiles, adjusted OR 3.6 (95%CI, 1.3–9.7),[40] but unconfirmed in human dietary intake studies,[41] while laboratory evidence remains very strong.[42] We did not observe convincing protective association for total ω-3 FAs as in studies of marine FAs,[43,44] however, the evidence for a protective effect for EPA is consistent in this data. It is possible that storage and preparation methods of fish can interfere with FA composition like other nutrient contents; fresh fish retaining a higher nutritional value than frozen fish.[45] The fact that diets rich in fish are not always associated with reduced PCa risk[46] underscores the influence of entire diets over single food items, and interactions with genetic and other environmental factors. Unlike the RR of 2.21 (95%CI, 1.14–4.29), $P<.06$ reported in a United States study,[47] our data did not show PCa risk association with trans FAs probably because of very low plasma trans FA in this population, resulting from infrequent intake of processed foods high in partially hydrogenated vegetable oils.

Regarding saturated FAs, we did not observe PCa risk association with myristic acid like other reports,[39,48] but observed significant risk trends and 2 to 6-fold PCa risk association across quartiles of behenic acid. Lack of association with palmitic acid is in agreement with the Physicians' Health Study,[46,49] but in contrast with a Norwegian study that reported a 2-fold risk with palmitic acid.[48] Our data did not show protective association with monounsaturated oleic acid as expected, given the popular report of the protective effect of diets rich in olive oil, the major source of oleic acid.[50] Rather nervonic and erucic FAs demonstrated 4-fold and 2-fold PCa risk associations, respectively, for which we have no biological explanation. Although essential linoleic (ω-6) and α-linolenic (ω-3) FAs are associated with PCa risk,[41,46,49] this was not observed in our study. However arachidonic acid, a metabolite of linoleic acid, did show a 2-fold significant risk comparing the 2nd to the 1st quartile.

One strength of our study is that we have reported pilot data from an

Table 5. Odds ratios and 95% confidence interval for prostate cancer risk across quartiles of selected plasma fatty acids among Nigerians

Fatty acid quartiles	Unadjusted OR (95% CI)	*P**	Adjusted OR† (95% CI)	*P**
Behenic				
Q1	1.00		1.00	
Q2	6.75 (2.58–17.63)		5.40 (1.79–16.36)	
Q3	1.53 (0.76–3.08)		1.32 (0.54–3.21)	
Q4	2.79 (1.27–6.10)	.000	2.47 (0.97–6.27)	.01
Erucic				
Q1	1.00		1.00	
Q2	4.20 (1.79–9.82)		2.16 (0.81–5.72)	
Q3	4.26 (1.82–9.96)		2.15 (0.82–5.64)	
Q4	1.06 (0.52–2.16)	.000	0.94 (0.40–2.20)	.16
Nervonic				
Q1	1.00		1.00	
Q2	13.6 (4.88–37.8)		5.32 (1.74–16.29)	
Q3	8.89 (3.57–22.1)		4.78 (1.76–12.97)	
Q4	2.40 (1.19–4.85)	.000	1.78 (0.79–4.00)	.003
Linoleic				
Q1	1.00		1.00	
Q2	1.15 (0.53–2.54)		0.47 (0.17–1.34)	
Q3	1.43 (0.64–3.21)		0.96 (0.34–2.72)	
Q4	0.82 (0.39–1.73)	.57	0.38 (0.15–0.99)	.12
Arachidonic				
Q1	1.00		1.00	
Q2	3.81 (1.50–9.70)		2.59 (0.85–7.86)	
Q3	1.75 (0.79–3.87)		1.93 (0.73–5.14)	
Q4	0.74 (0.36–1.50)	.003	0.75 (0.32–1.74)	.06
α- linolenic				
Q1	1.00		1.00	
Q2	1.38 (0.63–3.05)		1.04 (0.39–2.73)	
Q3	1.08 (0.50–2.31)		0.80 (0.33–1.98)	
Q4	1.19 (0.55–2.56)	.87	0.98 (0.40–2.40)	.95
Eicosapentaenoic				
Q1	1.00		1.00	
Q2	0.39 (0.18–0.85)		0.39 (0.15–0.97)	
Q3	0.57 (0.25–1.30)		0.48 (0.18–1.28)	
Q4	0.82 (0.35–1.91)	.08	1.09 (0.40–2.96)	.07
Docosapentaenoic				
Q1	1.00		1.00	
Q2	0.79 (0.35–1.79)		0.36 (0.13–1.00)	
Q3	1.55 (0.63–3.83)		0.44 (0.16–1.22)	
Q4	1.49 (0.62–3.61)	.35	0.44 (0.17–1.19)	.24

* Calculated with fatty acid concentration in each quartile as a continuous variable.
† OR adjusted for age, education, family history of prostate cancer, and waist-hip ratio.

understudied population and have provided adequate storage conditions to allow the FAs to remain stable.[51–53] Study limitations include: plasma FAs may not accurately reflect prostate levels;[41] measuring FAs only in the plasma phospholipids and triglycerides sub-fractions; and consenting PCa cases with localized or metastatic disease. A larger sample size is necessary to accommodate the wide variance in FA measures, allowing for more detailed risk analysis stratified by education status. Restricting recruitment to newly diagnosed cases will improve the precision of our findings. As we increase sample size we intend to expand our studies to simultaneously investigate genetic and antioxidant effects that have been shown in animal and in-vitro studies to have complex physiologic and cellular relationship with a number of FAs,[16] which can confound findings.

CONCLUSIONS

Plasma total ω-3 FA is high across all socioeconomic groups in this population, while plasma ω-6 is significantly higher among educated men with higher income. This data supports modest positive PCa risk association with total plasma ω-6 FA and a consistent inverse risk association with EPA, but not total ω-3 FA. Strong PCa risk association was observed for unsaturated behenic, and monounsaturated erucic and nervonic acids. Transition to diets rich in animal fat can potentially increase PCa risk even in a population on a high-fish diet, and the potential for serious implications should be viewed carefully, particularly in a region designated as low-incidence for prostate cancer. These are preliminary findings and increasing our sample size will provide adequate statistical power for risk estimations adjusted for more relevant variables within population sub-groups. Furthermore in-vitro investigations are warranted to clarify the roles and mechanisms of action of behenic, nervonic and erucic FAs in prostate carcinogenesis.

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REFERENCES

1. American Cancer Society. *Cancer Facts & Figures 2006*. Atlanta, GA, Available at http://www.cancer.org/docroot/STT/stt_0_2006.asp. Last accessed December 10, 2007.
2. Crawford ED. Epidemiology of prostate cancer. *Urology*. 2003;62(6 Suppl l):3–12.
3. Grönberg H. Prostate cancer epidemiology. *Lancet*. 2003;361(9360):859–864.
4. Ferlay J, Bray F, Pisani P, Parkin DM. *GLOBOCAN 2002: Cancer Incidence, Mortality and Prevalence Wworldwide. IARC CancerBase No. 5. version 2.0*. Lyon: IARCPress; 2004.
5. Ogunbiyi JO, Shittu OB. Increased incidence of prostate cancer in Nigerians. *J Natl Med Assoc*. 1999;91(3):159–164.
6. Ekwere PD, Egbe SN. The changing pattern of prostate cancer in Nigerians: current status in the southeastern states. *J Natl Med Assoc*. 2002; 94(7):619–627.
7. Kovi J, Heshmat MY. Incidence of cancer in Negroes in Washington, D.C. and selected African cities. *Am J Epidemiol*. 1972;96(6): 401–413.
8. Hill P, Wynder EL, Garbaczewski L, Garnes H, Walker AR. Diet and urinary steroids in Black and White North American men and black South African men. *Cancer Res*. 1979;39(12):5101–5105.
9. Haas GP, Sakr WA. Epidemiology of prostate cancer. *CA Cancer J Clin*. 1997;47(5):273–287.
10. Armstrong B, Doll R. Environmental factors and cancer incidence and mortality in different countries, with special reference to dietary practices. *Int J Cancer*. 1975;15(4):617–631.
11. Whittemore AS, Kolonel LN, Wu AH, et al. Prostate cancer in relation to diet, physical activity, and body size in blacks, whites, and Asians in the United States and Canada. *J Natl Cancer Inst*. 1995;87(9):652–661.
12. Giovannucci E, Rimm EB, Colditz GA, et al. A prospective study of dietary fat intake and risk of prostate cancer. *J Natl Cancer Inst*. 1993;85(19):1571–1579.
13. Veierød MB, Laake P, Thelle DS. Dietary fat intake and risk of prostate cancer: a prospective study of 25,708 Norwegian men. *Int J Cancer*. 1997;73(5):634–638.
14. Hayes RB, Ziegler RG, Gridley G, et al. Dietary factors and risks for prostate cancer among blacks and whites in the United States. *Cancer Epidemiol Biomarker Prev*. 1999;8(1):25–34.
15. Solanke TF. Cancer in the Nigerian setting (with particular reference to Ibadan). *Archives of Ibadan Medicine*. 2000;1(2):3–5.
16. Kolonel LN, Nomura AM, Cooney RV. Dietary fat and prostate cancer: current status. *J Natl Cancer Inst*. 1999;91(5):414–428.
17. Cantwell MM. Assessment of individual fatty acid intake. *Proc Nutr Soc*. 2000;59(2):187–191.
18. Tholstrup T. Dairy products and cardiovascular disease. *Curr Opin Lipidol*. 2006;17(1):1–10.
19. Sun Q, Ma J, Campos H, Hu FB. Plasma and erythrocyte biomarkers of dairy fat intake and risk of ischemic heart disease. *Am J Clin Nutr*. 2007;86(4):929–937.
20. Hodge AM, Simpson JA, Gibson RA, et al. Plasma phospholipid fatty acid composition as a biomarker of habitual dietary fat intake in an ethnically diverse cohort. *Nutr Metab Cardiovasc Dis*. 2007;17(6):409–482.
21. Baylin A, Kim MK, Donovan-Palmer A, et al. Fasting whole blood as a biomarker of essential fatty acid intake in epidemiologic studies: comparison with adipose tissue and plasma. *Am J Epidemiol*. 2005;162(4):373–381.
22. Lagerstedt SA, Hinrichs DR, Batt SM, Magera MJ, Rinaldo P, McConnell JP. Quantitative determination of plasma c8–c26 total fatty acids for the biochemical diagnosis of nutritional and metabolic disorders. *Mol Genet Metab*. 2001;73(1):38–45.
23. Kolonel LN. Racial and geographic variations in prostate cancer and the effect of migration. In: Fortner JG, Sharp PA, eds. *Accomplishments in Cancer Research, 1996*. Philadelphia: Lippincott-Raven, 1997;221–230.
24. Committee on Diet, Nutrition and Cancer, National Research Council. *Diet, Nutrition and Cancer*. Washington, DC: National Academy Press; 1982.
25. Kolonel LN. Fat, meat, and prostate cancer. *Epidemiol Rev*. 2001;23(1):72–81.
26. Mettlin C, Selenskas S, Natarajan N, Huben R. Beta-carotene and animal fats and their relationship to prostate cancer risk. *Cancer*. 1989;64(3):606–612.
27. Yatani R, Shiraishi T, Nakakuki K, et al. Trends in frequency of latent prostate carcinoma in Japan from 1965–1979 to 1982–1986. *J Natl Cancer Inst*. 1988;80(9):683–687.
28. Osuntokun BO. Nutritional problems in the African region. *Bull Schweiz Akad Med Wiss*. 1976;31(4–6):353–376.
29. Burlingame B. The food of Near East, North West and Western African regions. *Asia Pac J Clin Nutr*. 2003;12(3):309–312.
30. Drewnowski A, Popkin BM. The nutrition transition: new trends in the global diet. *Nutr Rev*. 1997;55(2):31–43.
31. Sokolov R. *Why We Eat What We Eat*. New York: Summit; 1991.
32. Ukoli FA, Khandaker T, Egbagbe E, Lomotey M, Oguike T, Akumabor P, Osime U, Beech D. Association of self-reported consumption of cooked meat, fish, seafood and eggs with prostate cancer risk among Nigerians. *Infect Agent Cancer*. 2009;4(Suppl):S1–S6.
33. Robson A. Shellfish view of omega-3 and sustainable fisheries. *Nature*. 2006;444:1002.
34. Edward N. Siguel, Kew M. Chee, Junxian-Gong, Ernst J. Schaefer. Criteria for essential fatty acid deficiency in plasma as assessed by capillary column gas-chromatography. *Clin Chem*. 1987;33(10):1869–1873.
35. Riboli E, Rönnholm H, Saracci R. Biological markers of diet. *Cancer Surv*. 1987;6(4):686–718.
36. Cole AH, Taiwo OO, Nwagbara NI, Cole CE. Energy intakes, anthropometry and body composition of Nigerian adolescent girls: a case study of an institutionalized secondary school in Ibadan. *Br J Nutr*. 1997;77(4): 497–509.
37. Mazengo MC, Simell O, Lukmanji Z, Shirima R, Karvetti RL. Food consumption in rural and urban Tanzania. *Acta Trop*. 1997;68(3): 313–326.
38. Yang YJ, Lee SH, Hong SJ, Chung BC. Comparison of fatty acids profiles in the serum of patients with prostate cancer and benign prostatic hyperplasia. *Clin Biochem*. 1999; 32(6):405–409.
39. Männisto S, Pietinen O, Virtanen MJ, et al. Fatty acids and risk of prosate cancer in a nested case-control study in male smokers. *Cancer Epidemiol Biomarker Prev*. 2003; 12(12):1422–1428.
40. Godley PA, Campbell MK, Gallagher P, Martinson FE, Mohler JL, Sandler RS. Biomarkers of essential fatty acid consumption and risk of prostate carcinoma. *Cancer Epidemiol Biomarkers Prev*. 1996;5(11): 889–895.
41. Jacobsen BK, Trygg K, Hjermann I, Thomassen MS, Real C, Norum KR. Acyl pattern of adipose tissue triglycerides, plasma free fatty acids, and diet of a group of men participating in a primary coronary prevention program (the Oslo Study). *Am J Clin Nutr*. 1983;38(6): 906–913.
42. Connolly JM, Coleman M, Rose DP. Effects of dietary fatty acids on DU 145 human prostate cancer cell growth in athymic nude mice. *Nutr Cancer*. 1997;29(2):114–119.
43. Chavarro JE, Stampfer MJ, Li H, Campos H, Kurth T, Ma J. A prospective study of polyunsaturated fatty acid levels in blood and prostate cancer risk. *Cancer Epidemiol Biomarkers Prev*. 2007;16(7):1364–1370.
44. Parkinson AJ, Cruz Al, Heyward WL, et al. Elevated concentrations of plasma omega-3 polyunsaturated fatty acids among Alaskan Eskimos. *Am J Clin Nutr*. 1994;59:384–388.
45. Omotosho JS, Olu OO. The effect of food and frozen storage on the nutrient composition of some African fishes. *Rev Biol Trop*. 1995;43(1–3):289–295.
46. Newcomer LM, King IB, Wicklund KG, Stanford JL. The association of fatty acids with prostate cancer risk. *Prostate*. 2001;47(4): 262–268.
47. Chavarro JE, Stampfer MJ, Campos H, Kurth T, Willett WC, Ma J. A prospective study of

trans-fatty acid levels in blood and risk prostate cancer. *Cancer Epidemiol Biomarkers Prev*. 2008;17(1):95–101.

48. Harvei S, Bjerve KS, Tretli S, Jellum E, Robsahm TE, Vatten L. Prediagnostic level of fatty acids in serum phospholipids: Omega-3 and omega-6 fatty acids and the risk of prostate cancer. *Int J Cancer*. 1997;71(4):545–551.
49. Gann PH, Hennekens CH, Sacks FM, Grodstein F, Giovannucci EL, Stampfer MJ. Prospective study of plasma fatty acids and risk of prostate cancer. *J Natl Cancer Inst*. 1994;86(4):281–286.
50. Hodge AM, English DR, McCredie MR, et al. Foods, nutrients and prostate cancer. *Cancer Causes Control*. 2004;15(1):11–20.
51. Stanford JL, King I, Kristal AR. Long-term storage of red blood cells and correlations between red cells and dietary fatty acids: Results from a pilot study. *Nutr Cancer*. 1991;16(3–4):183–188.
52. Jellum E, Andersen A, Lund-Larsen P, Theodorsen L, Orjasaeter H. The JANUS serum bank. *Sci Total Environ*. 1993;139–140:527–535.
53. Marangoni F, Colombo C, Martiello A, Negri E, Galli C. The fatty acid profiles in a drop of blood from a fingertip correlate with physiological, dietary and lifestyle parameters in volunteers. *Prostaglandins Leukot Essent Fatty Acids*. 2007;76(2):87–92.