A Study on Serum Carotenoid Levels in Breast Cancer Patients of Indian Women in Chennai (Madras), India

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Two-hundred and six breast cancer cases were histologically confirmed breast cancer diagnoses at the Cancer Institute in Chennai (Madras), India. One-hundred and fifty hospital controls were patients who had cancer at any site other than breast and gynecological organs, and 61 healthy controls were persons accompanying patients in the Cancer Institute. Serum levels of carotenoids such as \( \beta \)-carotene, lycopene, cryptoxanthin, and zeaxanthin \& lutein were determined by HPLC. Serum levels of total carotenes and total carotenoids including \( \beta \)-carotene, which reflects food intake of colored vegetables and fruits and has a protective role for certain sites of cancer, were significantly lower among breast cancer cases and hospital controls compared to healthy controls, especially in post-menopausal women. Serum carotenoid levels appeared to change with menopausal status. Serum \( \beta \)-carotene levels tended to be lower among breast cancer cases than among hospital controls in premenopausal women. Serum xanthophyll levels were significantly lower among breast cancer cases than among healthy controls in post-menopausal women, but not in premenopausal women. Serum levels of retinol and \( \alpha \)-tocopherol among breast cancer cases were not significantly different from those in post-menopausal healthy controls, but were higher than those in hospital controls.

Serum estrone levels were significantly higher among breast cancer cases than among healthy controls, but serum levels of estradiol and estriol were not.

In conclusion, Indian women with cancer of breast or of other sites might have low intake of green-yellow vegetables rich in fiber and carotenoids such as \( \beta \)-carotene and zeaxanthin \& lutein. 

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Several observational studies have shown that green-yellow vegetables and some colored fruits which are rich in \( \beta \)-carotene play a protective role against certain cancers such as those of lung, stomach, and colon 14). The concentration of \( \beta \)-carotene in the serum is a well known indicator for consumption of carotenoids since \( \beta \)-carotene is the principal component of carotenoids found in green yellow vegetables and some colored fruits 57). In almost all epidemiological studies, serum levels of \( \beta \)-carotene and other carotenoids were lower in patients with lung or stomach cancer 8-10). In contrast, there were no reports on significant inverse associations between \( \beta \)-carotene intake or serum \( \beta \)-carotene levels and the risk of breast cancer among Americans 11-15) and others 16-20). However, it was reported that high intakes of vegetables and some fruits might have a synergistic effect on breast cancer risk 20) since there were some reports that high intake of vegetables rich in fiber 13, 14, 19) and \( \beta \)-carotene 20, 22) tends to reduce the risk for breast cancer. Recently, intakes of \( \alpha \)- and \( \beta \)-carotenes reported to offer protective role for breast cancer 20) No study of serum levels of carotenoids among Asians with breast cancer has been reported.

This study was carried out to investigate serum carotenoid levels...
levels for breast cancer among women in Chennai (Madras), India, in where cancer registration is actively conducted and the incidence of breast cancer is about 20% for all cancer cases.

SUBJECTS AND METHODS

Subjects
Breast cancer cases in this study were recruited at the Cancer Institute (W.I.A.) in Chennai (Madras), which has a central cancer clinic hospital and cancer registry covering the area. Cases were histologically confirmed breast cancer patients diagnosed at the Institute from July 1992 to February 1993. Controls selected during the same period were of two types. Hospital controls recruited in the same hospital were patients who had cancer at any site (mainly stomach and esophagus) other than breast, thyroid and gynecological organs. Healthy controls were persons accompanying patients with cancer other than in breast, thyroid and gynecological organs. Cases and controls were matched by age to within 5 years. Two-hundred and six breast cancer patients, 150 hospital controls and 61 healthy controls were enrolled in this study. Healthy controls were fewer than one-third of the number of breast cancer cases. Several subjects, including hospital controls, were excluded due to inability to measure serum levels of carotenoids and estrogens in them.

Methods
A fasting serum sample was collected from all study subjects at a luteal menstrual phase. The collected serum was immediately separated from blood cells in Chennai (Madras) and packed on dry ice for analysis of carotenoids and estrogens at a laboratory in Japan.

Biochemical tests were carried out using a biochemical analyzer (SMAC, Technicon Co. Ltd.). Serum estrogen levels were determined by radioimmunoassay. Serum levels of estrogens were separated into estrone (E1), estradiol (E2) and estriol (E3). Serum levels of carotenoids, retinol and α-tocopherol were simultaneously determined using the HPLC method previously reported. Serum levels of zeaxanthin & lutein and provitamin A were represented as the sum of zeaxanthin and lutein levels, α-carotene, β-carotene and cryptoxanthin levels, respectively. Those of total carotenes, total xanthophylls, and total carotenoids represented the sum of α- and β-carotenes and lycopene levels, cryptoxanthin, canthaxanthin and zeaxanthin & lutein levels, and total carotenes and total xanthophylls levels, respectively. Serum levels of lipid peroxides (TBARS) and superoxide dismutase (SOD) activity were estimated using the thiorbituric acid reaction method and the NADPH cytochrome c reductase-NTB method. Almost subjects measured serum TBARS levels were excluded because serum samples were in small quantities. The information about alcohol consumption and smoking status was collected individually by trained interviewers.

Statistical analysis for the differences between means were tested by the ANOVA statistical method after adjusting for age. The odds ratio on healthy controls against breast cancer cases was calculated by the logistic regression model in controlling of age, which was conducted using the independent variable divided into four equal categories of the analyzed subjects (breast cancer cases and healthy controls) by serum component levels. Statistical analyses for the ANOVA and the logistic regression model were conducted using a StatView statistical package.

RESULTS

Comparison of serum levels of carotenoids and estrogens between breast cancer cases and controls in Indians.

The age range of cases and controls was 22 yrs to 80yrs. None of healthy controls smoked and drank (Table 1). The percentages of current smokers and of regular drinkers were less among breast cancer cases than among hospital controls.

| Table 1. Number of subjects classified according to age intervals, and smoking and alcohol drinking status. |
|-----------------|-----------------|-----------------|-----------------|
| Item            | Breast Cancer Cases | Hospital Controls | Healthy Controls |
| Age             |                  |                  |                  |
| 20 - 29         | 4 (1.9)          | 4 (2.7)          | 2 (3.3)          |
| 30 - 39         | 43 (20.9)        | 14 (9.3)         | 10 (16.4)        |
| 40 - 49         | 41 (19.9)        | 44 (29.3)        | 11 (18.0)        |
| 50 - 59         | 82 (39.8)        | 60 (40.0)        | 27 (44.3)        |
| 60 - 69         | 28 (13.6)        | 23 (15.3)        | 9 (14.8)         |
| 70 - 80         | 8 (3.9)          | 5 (3.3)          | 2 (3.3)          |
| total           | 206 (100.0)      | 150 (100.0)      | 61 (100.0)       |
| Current smokers | 2 (1.0)          | 5 (3.3)          | 0 (0.0)          |
| Regular alcohol drinkers | 1 (0.5) | 2 (1.3) | 0 (0.0) |

Data represented as the number and percentage in parenthesis.
Serum levels of albumin, uric acid, total cholesterol and triglyceride were lower among hospital controls than among breast cancer cases (Table 2). Serum levels of total protein, uric acid, total cholesterol and triglyceride were not significant.

### Table 2. Comparison of serum component levels between breast cancer cases and the controls in Indians. *

| Serum component        | Breast Cancer Cases | Hospital Controls(1) | Healthy Controls(2) | Probability       |
|------------------------|---------------------|----------------------|---------------------|-------------------|
| Total protein g/dl     | 7.7 (0.7)           | 7.8 (0.8)            | 7.8 (0.6)           | 0.193             |
| Albumin g/dl           | 4.1 (0.4)           | 3.8 (0.5)            | 4.4 (0.3)           | <0.0001           |
| Uric acid mg/dl        | 4.3 (1.3)           | 4.0 (1.2)            | 4.3 (0.8)           | 0.032             |
| Creatinine mg/dl       | 0.8 (0.1)           | 0.8 (0.2)            | 0.8 (0.2)           | 0.502             |
| Calcium mg/dl          | 9.4 (0.6)           | 9.5 (0.7)            | 9.7 (0.5)           | 0.041             |
| Total cholesterol mg/dl| 194.7 (44.7)        | 186.2 (44.7)         | 206.9 (49.3)        | 0.096             |
| Triglyceride mg/dl     | 121.2 (67.6)        | 110.2 (44.4)         | 122.3 (68.3)        | 0.102             |

Number 185 140 54

TBARS nmol/ml 4.66 (1.57) 5.09 (2.14) 4.54 (1.27) 0.310 0.763 0.305 0.025 0.245 0.0001

SOD activity unit 0.52 (0.55) 0.31 (0.17) 0.70 (0.55) 0.310 0.763 0.305 0.025 0.245 0.0001

Number 40 40 19

TBARS: Thiobarbituric acid-reactive substances; SOD: Superoxide dismutase.

# Data represented as the mean value and standard deviation in parenthesis.

Probability was calculated by the ANOVA analyses after adjusting for age.

### Table 3. Comparison of serum levels of carotenoids, retinol, a -tocopherol, and estrogens between breast cancer cases and the controls in Indians. 

| Component                          | Breast Cancer Cases | Hospital Controls(1) | Healthy Controls(2) | Probability       |
|------------------------------------|---------------------|----------------------|---------------------|-------------------|
| 
| $\beta$-Carotene $\mu$ mol/L      | 0.162 (0.105)       | 0.161 (0.132)        | 0.267 (0.225)       | 0.972             |
| a-Carotene $\mu$ mol/L             | 0.052 (0.034)       | 0.041 (0.044)        | 0.075 (0.051)       | 0.013             |
| Lycopene $\mu$ mol/L               | 0.084 (0.060)       | 0.074 (0.056)        | 0.149 (0.102)       | 0.139             |
| Total carotenol $\mu$ mol/L        | 0.295 (0.166)       | 0.276 (0.190)        | 0.490 (0.299)       | 0.306             |
| Cryptoxanthin $\mu$ mol/L          | 0.116 (0.080)       | 0.090 (0.100)        | 0.156 (0.109)       | 0.010             |
| Canthaxanthin $\mu$ mol/L          | 0.037 (0.029)       | 0.031 (0.019)        | 0.074 (0.023)       | 0.022             |
| Zeaxanthin lutein $\mu$ mol/L      | 0.395 (0.170)       | 0.327 (0.186)        | 0.488 (0.216)       | 0.001             |
| Total xanthophylls $\mu$ mol/L     | 0.548 (0.211)       | 0.448 (0.247)        | 0.691 (0.282)       | <0.0001           |
| Provitamin A $\mu$ mol/L           | 0.331 (0.185)       | 0.293 (0.215)        | 0.498 (0.317)       | 0.110             |
| Total carotenoids $\mu$ mol/L      | 0.847 (0.334)       | 0.725 (0.387)        | 1.181 (0.526)       | 0.004             |
| Retinol $\mu$ mol/L                | 1.660 (0.537)       | 1.500 (0.654)        | 1.790 (0.575)       | 0.012             |
| a-Tocopherol $\mu$ mol/L           | 16.75 (5.29)        | 15.41 (5.20)         | 18.90 (7.33)        | 0.027             |
| Estrone (E1) pmol/L                | 281.0 (169.5)       | 194.2 (96.6)         | 214.9 (145.5)       | <0.0001           |
| Estradiol (E2) pmol/L              | 156.5 (227.3)       | 64.2 (107.1)         | 149.4 (226.6)       | <0.0001           |
| Estriol (E3) pmol/L                | 7.7 (4.1)           | 6.8 (4.1)            | 8.2 (5.0)           | 0.091             |
| Age number                         | 49.2 (11.1)         | 50.5 (10.2)          | 50.7 (10.5)         | 0.250             |

# Data represented as mean value and standard deviation in parenthesis.

Probability was calculated by the ANOVA analyses after adjusting for age.
different between breast cancer cases and healthy controls, whereas serum levels of calcium and albumin levels were significantly lower among breast cancer cases and hospital controls compared to healthy controls. Serum TBARS levels tended to be highest among hospital controls, followed by breast cancer cases and healthy controls, while serum SOD activities appeared to be lowest among hospital controls, followed by breast cancer cases.

Table 3 shows that mean age of cases and controls were comparable. The mean serum estrone (E1) levels were significantly higher among breast cancer cases than among hospital controls and healthy controls. The mean serum estradiol (E2) and estriol (E3) levels among hospital controls were lower than that seen among healthy controls and breast cancer cases.

Serum levels of β-carotene and lycopene among breast cancer cases were not significantly different from those among hospital controls, whereas they were significantly lower among breast cancer cases than among healthy controls. Serum levels of carotenoids such as α-carotene, cryptoxanthin, canthaxanthin and zeaxanthin & lutein were lowest among hospital controls, followed by breast cancer cases and then healthy controls. Those of provitamin A, total carotenes, total xanthophylls and total carotenoids were also lowest among hospital controls, followed by breast cancer cases and healthy controls. Serum retinol levels were not significantly different between breast cancer cases and healthy controls, while those were significantly lower among hospital controls than among breast cancer cases. Serum α-tocopherol levels were lowest among hospital controls, followed by breast cancer cases and healthy controls.

Mean age of cases and controls was also comparable in both premenopausal (breast cancer:36.2y, hospital controls:36.1y) and post-menopausal (breast cancer:57.0y, hospital controls:57.0y). The trends of carotenoid levels appeared to differ by menopausal status (Table 4,5).

Serum levels of α-tocopherol and carotenoids, except for xanthophylls were significantly lower among breast cancer cases than among healthy controls in premenopausal, but not significantly among hospital controls. In contrast, serum levels of carotenoids, including xanthophylls were significantly lower among breast cancer cases and hospital controls than among healthy controls in post-menopausal. Serum retinol levels were not significantly different between breast cancer cases and healthy controls. Serum levels of E1 and E2 among breast cancer cases were significantly lower in post-menopausal than in premenopausal, as same as those among hospital controls and healthy controls. Moreover, serum E1 levels in both pre-

### Table 4. Comparison of serum levels of carotenoids, retinol, α-tocopherol, and estrogens between breast cancer cases and the controls in premenopausal.

| Component | Subjects | Breast Cancer Cases | Hospital Controls(1) | Healthy Controls(2) | Case vs Control(1) | Case vs Control(2) | Control(1) vs Control(2) |
|-----------|----------|---------------------|----------------------|----------------------|-------------------|-------------------|------------------------|
| β-Carotene | μmol/L   | 0.164 (0.119)       | 0.182 (0.119)        | 0.235 (0.094)        | 0.498             | 0.029             | 0.137                  |
| α-Carotene | μmol/L   | 0.055 (0.041)       | 0.058 (0.075)        | 0.089 (0.056)        | 0.801             | 0.030             | 0.076                  |
| Lycopene   | μmol/L   | 0.096 (0.071)       | 0.086 (0.080)        | 0.160 (0.086)        | 0.543             | 0.003             | 0.002                  |
| Total carotenes | μmol/L | 0.316 (0.195)     | 0.326 (0.206)        | 0.484 (0.184)        | 0.812             | 0.002             | 0.010                  |
| Cryptoxanthin | μmol/L | 0.127 (0.101)     | 0.099 (0.053)        | 0.151 (0.079)        | 0.141             | 0.320             | 0.053                  |
| Canthaxanthin | μmol/L | 0.038 (0.035)     | 0.037 (0.025)        | 0.050 (0.018)        | 0.820             | 0.168             | 0.162                  |
| Zeaxanthin & lutein | μmol/L | 0.411 (0.179)   | 0.380 (0.195)        | 0.444 (0.103)        | 0.414             | 0.509             | 0.241                  |
| Total xanthophylls | μmol/L | 0.577 (0.237)    | 0.515 (0.241)        | 0.645 (0.149)        | 0.219             | 0.278             | 0.066                  |
| Provitamin A | μmol/L | 0.347 (0.220)      | 0.339 (0.200)        | 0.475 (0.112)        | 0.862             | 0.026             | 0.034                  |
| Total carotenoids | μmol/L | 0.893 (0.380)     | 0.841 (0.388)        | 1.129 (0.266)        | 0.521             | 0.020             | 0.012                  |
| Retinol    | μmol/L   | 1.646 (0.473)      | 1.517 (0.594)        | 1.887 (0.706)        | 0.280             | 0.110             | 0.029                  |
| α-Tocopherol | μmol/L | 15.85 (5.04)       | 14.66 (3.38)         | 20.24 (9.61)         | 0.330             | 0.005             | 0.002                  |
| Estrone (E1) | pmol/L | 413.2 (222.2)      | 248.9 (115.2)        | 287.8 (193.3)        | 0.003             | 0.029             | 0.534                  |
| Estradiol (E2) | pmol/L | 353.1 (274.2)      | 164.8 (163.5)        | 332.2 (353.2)        | 0.028             | 0.777             | 0.044                  |
| Estriol (E3) | pmol/L | 7.8 (4.2)          | 7.4 (4.2)            | 10.2 (5.5)           | 0.742             | 0.071             | 0.059                  |
| Total cholesterol | mg/dL | 192.6 (52.7)       | 177.6 (42.8)         | 200.4 (35.6)         | 0.202             | 0.589             | 0.156                  |
| Triglyceride | mg/dL  | 114.9 (92.2)       | 107.8 (45.3)         | 116.0 (82.4)         | 0.702             | 0.963             | 0.747                  |

Number | 66 | 30 | 16

#: Data represented as mean value and standard deviation in parenthesis.
Probability was calculated by the ANOVA analyses after adjusting for age.
Table 5. Comparison of serum levels of carotenoids, retinol, \( \alpha \)-tocopherol, and estrogens between breast cancer cases and the controls in postmenopausal#.

| Component          | Serum Levels | Probability |
|--------------------|--------------|-------------|
|                    | Breast Cancer Cases | Hospital Controls(1) | Healthy Controls(2) | Case vs Control(1) | Case vs Control(2) | Control(1) vs Control(2) |
| \( \beta \)-Carotene | 0.157 (0.099) | 0.157 (0.130) | 0.258 (0.242) | 0.993 | 0.0002 | 0.0003 |
| \( \alpha \)-Carotene | 0.049 (0.029) | 0.039 (0.034) | 0.070 (0.051) | 0.046 | 0.002 | <0.0001 |
| Lycopene           | 0.075 (0.052) | 0.072 (0.050) | 0.146 (0.114) | 0.773 | <0.0001 | 0.0001 |
| Total carotenes    | 0.281 (0.149) | 0.269 (0.184) | 0.474 (0.336) | 0.654 | <0.0001 | 0.0001 |
| Cryptoxanthin      | 0.106 (0.067) | 0.087 (0.117) | 0.140 (0.083) | 0.127 | 0.042 | 0.002 |
| Canthaxanthin      | 0.035 (0.023) | 0.029 (0.017) | 0.046 (0.025) | 0.056 | 0.009 | 0.0001 |
| Zeaxanthin & lutein| 0.378 (0.161) | 0.329 (0.198) | 0.516 (0.256) | 0.069 | 0.0002 | <0.0001 |
| Total xanthophylls | 0.520 (0.192) | 0.445 (0.269) | 0.701 (0.331) | 0.032 | <0.0001 | 0.0001 |
| Provitamin A       | 0.313 (0.164) | 0.284 (0.219) | 0.468 (0.335) | 0.343 | 0.0002 | <0.0001 |
| Total carotenoids  | 0.801 (0.297) | 0.714 (0.404) | 1.176 (0.619) | 0.123 | <0.0001 | <0.0001 |
| Retinol            | 1.655 (0.628) | 1.529 (0.700) | 1.740 (0.462) | 0.161 | 0.476 | 0.089 |
| \( \alpha \)-Tocopherol | 17.06 (5.49) | 15.59 (5.70) | 18.67 (6.36) | 0.068 | 0.132 | 0.006 |
| Estrone (E1)       | 214.2 (86.5) | 172.6 (77.5) | 165.6 (90.1) | 0.001 | 0.033 | 0.685 |
| Estradiol (E2)     | 44.1 (58.9)  | 26.9 (29.9)  | 64.0 (71.6)  | 0.027 | 0.045 | 0.004 |
| Estril (E3)        | 7.6 (4.1)    | 6.4 (4.1)    | 7.1 (4.4)    | 0.090 | 0.587 | 0.521 |
| Total cholesterol  | 198.6 (38.9) | 188.0 (42.6) | 208.8 (47.2) | 0.081 | 0.225 | 0.017 |
| Triglyceride       | 124.7 (52.2) | 108.5 (42.1) | 131.8 (65.2) | 0.032 | 0.492 | 0.030 |

| Number | 118 | 88 | 38 |

# Data represented as mean value and standard deviation in parenthesis. Probability was calculated by the ANOVA analyses after adjusting for age.

DISCUSSION

The population of the study area remains steady about 4 million in recent years. The most frequent cancer among women in south India is cancer of cervix uteri (44/100,000) followed by breast cancer (21.7/100,000) according to the population based cancer registry in Madras. In western India, it is cancer of the breast followed by cancer of the uterine cervix. The racial and international differences in breast cancer incidence rates and changes in their rates with migration and time, suggest that diet may influence breast cancer risk. The majority of Indians belong to the Hindu religion and do not eat beef. Eating raw vegetables is uncommon in south India. Cooking practices vary from region to region.

Although reports of the relation between high fat intake and the risk for breast cancer do not agree, there was a report that serum uric acid levels tended to be higher in breast cancer. In this study, serum levels of total cholesterol and triglyceride tended to be higher among breast cancer cases than among healthy controls, but they were not always higher than among healthy controls. In addition, serum albumin levels were significantly and inversely associated with breast cancer cases by the logistic regression analyses. These results suggest that high intake of animal foods rich in protein might play a protective role for breast cancer in Indian women.

It has been reported that high intake and high serum levels of \( \beta \)-carotene diminishes the risk for developing cancer of the lung, stomach and colon. However, few reports fail to
demonstrate a significant association between high serum levels of β-carotene and low risk for breast cancer\textsuperscript{11,12,15,17}. Betacarotene intake has been reported to play a preventive role for breast cancer in certain western population studies\textsuperscript{21-23}. In this study, serum levels of carotenoids, including xanthophylls, were significantly lower among breast cancer cases and inversely associated with breast cancer cases by the logistic regression analyses.

Seasonal variation in serum levels of carotenoids were reported to be small; errors related to determining serum levels of carotenoid were found to be small, as well\textsuperscript{20,49}. The variation in serum levels of carotenoids such as β-carotene, lycopene, zeaxanthin & lutein and α-tocopherol was less than 6.5% in repeatability and less than 10% of this variation was ascribable to serum storage\textsuperscript{20}. Moreover, variations throughout the menstrual cycle is less than 9%-12% for β-carotene, zeaxanthin & lutein and lycopene\textsuperscript{41}.

Serum levels of carotenoids, especially, β-carotene and zeaxanthin & lutein, were less than one-half of those among healthy controls in Indian women, comparing our results among Japanese female residents\textsuperscript{25,42}. High intakes of green yellow vegetables rich in β-carotene, fiber and minerals such as calcium are well known to elevate serum levels of β-carotene and zeaxanthin & lutein\textsuperscript{5-7}. The results obtained in this study suggest that low consumption of these foods relate to lower serum levels of β-carotene and calcium among breast cancer cases, especially in postmenopausal women, compared to the healthy controls.

The carotenoids such as β-carotene and zeaxanthin play a role as antioxidant\textsuperscript{43,44}. Serum lipid peroxides, thiobarbituric acid-reactive substances (TBARS), are a biomarker of lipid peroxidation\textsuperscript{45}. In a case-control study, breast adipose tissue concentrations of some carotenoids such as β-carotene were reported to be significantly lower among breast cancer cases than among controls\textsuperscript{46}, whereas serum TBARS levels increased a proportion to tumor sizes in young breast cancer patients\textsuperscript{47}. In this study, serum TBARS levels were the highest among hospital controls, followed by the breast cancer cases and the healthy controls. They inversely corresponded to serum levels of carotenoids and serum SOD activities, substances with protective roles against lipid peroxidation by activated oxygen\textsuperscript{48}. It seems that high rates of oxidative activities, such as lipid peroxidation in cancerous organs, may prevail among breast cancer cases as compared to healthy controls, as well as to hospital controls.

We obtained similar results in this study as in the literature\textsuperscript{49,50} that serum levels of E1 and E2 were higher among breast cancer patients, especially in premenopausal women, while a study on high dietary fiber intake\textsuperscript{51} found decreased serum levels of E1 and E2 in premenopausal women.

### Table 6. Logistic regression analyses on serum component levels between breast cancer cases and healthy controls.

| Components         | Odds ratio | (95% Confidence interval) | Number |
|--------------------|------------|----------------------------|--------|
| β-Carotene         | 0.569      | (0.427-0.767)              | 266    |
| α-Carotene         | 0.564      | (0.413-0.771)              | 266    |
| Lycopene           | 0.531      | (0.399-0.709)              | 266    |
| Total carotenes    | 0.484      | (0.353-0.662)              | 266    |
| Cryptoxanthin      | 0.634      | (0.474-0.847)              | 266    |
| Zeaxanthin & lutein| 0.549      | (0.400-0.754)              | 266    |
| Total Xanthophylls | 0.502      | (0.360-0.699)              | 266    |
| Provitamin A       | 0.591      | (0.439-0.795)              | 266    |
| Total carotenoids  | 0.498      | (0.362-0.687)              | 266    |
| Retinol            | 0.861      | (0.655-1.133)              | 266    |
| α-Tocopherol       | 0.826      | (0.638-1.069)              | 266    |
| Estrone (E1)       | 1.685      | (1.255-2.262)              | 259    |
| Total cholesterol  | 0.857      | (0.651-1.270)              | 239    |
| Triglyceride       | 1.057      | (0.806-1.385)              | 239    |
| Albumin            | 0.381      | (0.248-0.584)              | 239    |
| Calcium            | 0.541      | (0.395-0.741)              | 239    |
| TBARS              | 0.893      | (0.529-1.505)              | 59     |
| SOD activity       | 0.470      | (0.261-0.846)              | 59     |

Odds ratio was calculated by the logistic regression model conducted using the independent variable divided into quarter parts of serum component levels in healthy controls against breast cancer cases after adjusting for age.
Moreover, the significant inverse relationship between serum zeaxanthin & lutein levels and serum E1 levels in postmenopausal closely agreed with a report ⁵⁰ of the strong and independent relationships between carotenoid intake or plasma lutein concentration and estrogen receptor status. Dietary fiber intake was inversely associated with the risk of breast cancer ⁵³ ⁵⁴ and with improved survival among breast cancer patients ⁵⁵. Some components found in vegetables might have a synergistic effect on breast cancer risk since a low risk for breast cancer appeared in studies on dietary intake of vegetables rich in carotenoids and fiber ²¹ ²² ³³ ³⁴.

In conclusion, our study demonstrated that serum levels of carotenoids such as β-carotene were significantly lower among breast cancer cases, especially in post-menopausal women, it appears that low intake of green yellow vegetables might relate to the risk for breast cancer among Indian women.

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REFERENCES

1. Peto R, Doll R, Buckley JD, Sporn MB. Can dietary beta-carotene materially reduce human cancer rates? Nature, 1980;290:201-208.
2. Beyers T, and Graham S. The epidemiology of diet and cancer. Adv Cancer Res, 1984;41:1-69.
3. Ziegler RG. Vegetables, fruits, and carotenoids and the risk of cancer. Am J Clin Nutr, 1991;53:251S-259S.
4. van Poppel G, Goldbohm RA. Epidemiologic evidence for β-carotene and cancer protection. Am J Clin Nutr, 1995;62:1393S-1402S.
5. Brown ED, Rose A, Craft N, Seidel KE, Smith JC. Concentrations of carotenoids, retinol, and tocopherol in plasma, in response to ingestion of a meal. Clin Chem, 1989;35:310-312.
6. Micoczi MS, Brown ED, Edwards BK, Bieri JG, Taylor PR, et al. Plasma carotenoid response to chronic intake of selected foods and β-carotene supplements in men. Am J Clin Nutr, 1992;55:1120-1125.
7. Yeum K-J, Booth SL, Sadowski JA, Liu C, Tang G, Krinsky NI, Russell RM. Human plasma carotenoid response to the ingestion of controlled diets high in fruits and vegetables. Am J Clin Nutr, 1996;64:594-602.
8. Menkes MS, Comstock GW, Vuilleumier JP, Helsing KJ, Rinder AA, Brookmeyer R. Serum beta-carotene, vitamins A and E, selenium, and the risk of lung cancer. New Eng J Med, 1986;315:1250-1254.
9. Comstock GW, Bush TL, Helzlsouer K. Serum retinol, beta-carotene, vitamin E, and selenium as related to subsequent cancer of specific sites. Am J Epidemiol, 1992;135:115-121.
10. van Poppel G. Carotenoids and cancer: an update with emphasis on human intervention studies. Eur J Cancer, 1993;29:1335-1344.
11. Willett WC, Polk BF, Underwood BA, Stampfer MJ, Pressel S, et al. Relation of serum vitamins A and E and carotenoids to the risk of cancer. New Eng J Med, 1984;310:430-434.
12. Marubini E, Decarli A, Costa A, Mazzoleni C, Andreoli C, et al. The relationship of dietary intake and serum levels of retinol and beta-carotene with breast cancer. Results of a case-control study. Cancer, 1988; 61:173-180.
13. van’t Veer P, Kolb CM, Verhoef P, Kok FJ, Schouten EG, Hermus RJJ, Sturmans F. Dietary fiber, beta-carotene and breast cancer: results from a case-control study. Int J Cancer, 1990;45:825-828.
14. Graham S, Zielezny M, Marshall J, Priore R, Freudenheim J, Brasure J, Haughey B, Nasca P, Zdeb M. Diet in the epidemiology of postmenopausal breast cancer in the New York State cohort. Am J Epidemiol, 1992 ; 136 : 1327-1337.
15. London SJ, Stein EA, Henderson IC, Stampfer MJ, Wood WC, et al. Carotenoids, retinol, and vitamin E and risk of proliferative benign breast disease and breast cancer. Cancer Causes and Control, 1992;3:503-512.
16. Wald NJ, Boreham J, Hayward JL, Bulbrook RD. Plasma retinol, β-carotene and vitamin E levels in relation to the future risk of breast cancer. Brit J Cancer, 1984;49:321-324.
17. Smith AH, Waller KD. Serum beta-carotene in persons with cancer and their immediate families. Am J Epidemiol, 1991;133:661-671.
18. Katsouyanni K, Willett W, Trichopoulos D, Boyle P, Trichopoulos A, et al. Risk of breast cancer among Greek women in relation to nutrient intake. Cancer, 1988 ; 61 : 181-185.
19. Verhoeven DTH, Assen N, Goldbohm RA, van der Waerden B, Vink M, Veer P, et al. Vitamins C and E and breast cancer. Brit J Cancer, 1994;70:1805-1811.
20. Freudenheim LJ, Marshall JR, Vena JE, Laughlin R, Brasure JR, Swanson MK, Nemoto T, Graham S.
30. Parkin DM, Muir CS, Whelan SL, Gao YT, Ferlay J, et al. Cancer registration in five continents: Volume VI, IARC Scientific Publication, International Agency for Research on Cancer Lyon, 1992 (No. 120): 454-455.

31. Willett WC, Stampfer MJ, Colditz GA, Rosner BA, Hennekens CH, Speizer FE. Dietary fat and the risk of breast cancer. New Eng J Med, 1989;321:67-74.

32. Kushi LH, Sellers TA, Potter JD, Nelson CL, Munger RG, Key SA, Folsom AR. Dietary fat and postmenopausal breast cancer. J Natl Cancer Inst, 1992;84:1092-1099.

33. Giovannucci E, Stampfer MJ, Colditz GA, Manson JE, Rosner BA, Longnecker M, Speizer FE, Willett WC. A comparison of prospective and retrospective assessments of diet in the study of breast cancer. Am J Epidemiol, 1993;137:502-511.

34. van den Brandt PA, van't Veer P, Goldbohm RA, Dorant E, Volovics A, Hermus RJ, Sturmans R. A prospective cohort study on dietary fat and the risk of postmenopausal breast cancer. Cancer Res, 1993;53:75-82.

35. Coliditz GA. Epidemiology of breast cancer. Cancer, 1993;71:1480-1489.

36. Jain M, Miller AB, To T. Premenopausal breast cancer risk and intake of vegetables, fruits, and related nutrients. J Natl Cancer Inst, 1996;88:340-348.

37. Hunter DJ, Willett WC. Nutrition and breast cancer. Cancer Causes and Control, 1996;7:56-68.

38. Burgaz S, Torun M, Sargin H, Orman MN, Ozdamer NY. Serum carotenoids and uric acid levels in relation to cancer. J Clin Pharm Ther, 1996;21:331-336.

39. Olemedilla B, Granado F, Blanco I, Rojar-Hidalgo E. Seasonal and sex-related variations in six serum carotenoids, retinol, and \( \alpha \)-tocopherol. Am J Clin Nutr, 1994;60:106-110.

40. Craft NE, Brown ED, Smith JC. Effects of storage and handling conditions on concentrations of individual carotenoids, retinol, and tocopherol in plasma. Clin Chem, 1988;34:44-48.

41. Forman MR, Beecher GR, Muesing R, Lanza E, Olsen B, Campbell WS, et al. The fluctuation of plasma carotenoid concentrations by phase of the menstrual cycle: a controlled diet study. Am J Clin Nutr, 1996;64:559-565.

42. Ito Y, Sasaki R, Suzuki S, Yasui T, Hishida H, Otani M, Aoki K. Serum carotenoid levels and its sex differences. Vitamins (Japan), 1994;60:106-110.

43. Burton GN, Ingold KV. \( \beta \)-Carotene: an unusual type of lipid antioxidant. Science, 1984;224:569-573.

44. Bendich A, Olsen JA. Biological actions of carotenoids. FASEB J, 1989;3:1927-1932.

45. Janero DR. Malondialdehyde and thiobarbituric acid-reactivity as diagnostic indices of lipid peroxidation and peroxidative tissue injury. Free Rad Biol Med, 1990;9:515-540.

46. Zhang S, Tang G, Russell RM, Mayzel KA, Stampfer MJ, Willett WC, Hunter DJ. Measurement of retinoids and carotenoids in breast adipose tissue and a comparison of concentrations in breast cancer cases and control subjects. Am J Clin Nutr, 1997;66:626-632.

47. Gerber M, Segala C. Aging and cancer: Plasma antioxidants and lipid peroxidation in young and aged breast cancer patients.” in “Free Radical and Aging”, ed Emerit I & Chance B, Basel/Switzerland, Birkhause Verlag, 1992:235-246.

48. McCord JM, Fridovich I. Superoxide dismutase. J Biol Chem, 1969;244:6049-6055.

49. Bernstein L, Ross RK. Endogenous hormones and breast cancer risk. Epidemiol Rev, 1993;15:48-65.

50. Rosenberg CR, Pasternack BS, Shore RE, Koenig KL, Toniole PO. Premenopausal estradiol levels and the risk of breast cancer: a new method of controlling for day of the menstrual cycle. Am J Epidemiol, 1994;140:518-525.

51. Rose DP, Goldman M, Connolly JM, Strong LE. High-fiber diet reduces serum estrogen concentrations in premenopausal women. Am J Clin Nutr, 1991;54:520-525.

52. Rock CL, Saxe GA, Ruffin IV MT, August DA,
Schottenfeld D. Carotenoids, vitamin A, and estrogen receptor status in breast cancer. Nutr Cancer, 1996;25:281-296.

53. Stefani ED, Correa P, Ronco A, Mendilaharsu M, Guidobono M, Deneo-Pellegrini H. Dietary fiber and risk of breast cancer: a case-control study in Uruguay. Nutr Cancer, 1997;28:14-19.

54. Rock CL, Flatt SW, Wright A, Faerber S, Newman V, Kealey S, Pierce JP. Responsiveness of carotenoids to a high vegetable diet intervention designed to prevent breast cancer recurrence. Cancer Epidemiol Biomark Prev, 1997;6:617-623.

55. Ingram D. Diet and subsequent survival in women with breast cancer. Brit J Cancer, 1994;69:592-595.