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# Nutritional Aspects of Mammary Carcinogenesis: a Case-Control Study

Pages with reference to book, From 118 To 120

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## Abstract

Dietary factors are believed to play an important role in mammary carcinogenesis. International correlations, case-control and cohort studies have associated the incidence and mortality from breast cancer with high fat consumption in the form of meat, gravy and dairy products. Most of these studies have been conducted in the developed countries. Due to paucity of data from developing countries, we conducted a case-control study to evaluate the role of nutritional factors in mammary carcinogenesis. This prospective study was conducted in the oncology clinic at a university hospital. On a detailed questionnaire, information was collected from 80 patients with histologically proven breast cancer (cases) and 80 normal healthy subjects (controls). Information was collected on several patients characteristics as well as intake of 44 different food items. Special care was taken to exclude any recent changes in diet, induced in cases since learning the diagnosis of breast cancer. Interviews were conducted by the same interviewer and lasted approximately 20 minutes. Analysis of data reveal no significant difference in patients characteristics between cases and controls. Similarly, no significant difference was found in the intake of most dietary items including meat and dairy products. However, a significant difference was observed in the consumption of fish, vegetable and fruits ( $P=0.05$ ). We conclude that our study fails to support the fat-breast cancer hypothesis. It also suggests a potential role of other dietary items such as fish, vegetables and fruits in mammary carcinogenesis (JPMA 43: 118, 1993).

## Introduction

There is a marked geographic variation in the incidence of breast cancer. Incidence rates are generally higher in more industrialized countries with the notable exception of Japan. Japan, China and some Afro-Asian countries have the lowest rates<sup>1</sup>. Results of studies on Japanese migrants to Hawaii indicate that Japanese-Americans have incidence rates intermediate between those of Japan and the United States and at younger ages their rates closely resemble those of America rather than Japan<sup>2-4</sup>. Similar shifts in incidence rates have been shown for Chinese migrants to the United States as well as for Blacks<sup>1,5</sup>. These dramatic changes can best be explained by the influence of environmental factors. One of the most important environmental factors is diet. Changes in the incidence of breast cancer after migration and the rising incidence of breast cancer in Japan since the fifties, can be correlated with increasing westernization of their traditional diet<sup>6</sup>. Similarly Eskimo women who originally had a very low incidence of breast cancer have rising incidence rates that correlate with dietary patterns becoming more westernized<sup>7,8</sup>. Many international correlations, case-control and cohort studies have been carried out to evaluate the influence of dietary factors on mammary carcinogenesis<sup>9-15</sup>. Most of the case-control studies have been reported from more affluent societies. In Pakistan, breast cancer is the commonest malignancy in females<sup>16</sup>. Due to the magnitude of this problem and paucity of data from under-developed world, we conducted a case-control study of nutritional factors in mammary carcinogenesis.

## Patients and Methods

The study was conducted on eighty females with histologically proven breast cancer. Controls were eighty females matched for age, socio-economic status and menopausal status who were otherwise completely healthy and were visitors to the hospital out-patient clinics. A detailed nutritional questionnaire was used. It includes information about age, surface area, ethnic background, marital status, education, known risk factors for breast cancer, smoking and 44 different food items. Dietary history obtained was of recent past to exclude any changes in the present diet that may have been induced by the disease or the knowledge acquired afterwards. Quantitative assessment of intake was made by explaining standard serving size. Interviews were conducted by the same interviewer to prevent inter-individual variability and lasted for approximately 20 minutes.

## Results

Personal characteristics of the cases and controls are provided in Table I.

**Table I. Nutritional aspects of mammary carcinogenesis.**

**Personal characteristics of the cases and controls.**

Characteristics	Cases mean $\pm$ SD	Controls mean $\pm$ SD
Age (years)	46.6 $\pm$ 11.3	46.8 $\pm$ 10.5
Weight (kg)	65.6 $\pm$ 16.0	64.0 $\pm$ 11.3
Height (cm)	52.5 $\pm$ 8.2	56.8 $\pm$ 5.2
<b>Socio-economic status</b>	<b>%</b>	<b>%</b>
Lower	13	10
Lower middle	5	6
Middle	41	31
Upper middle	21	30
Upper	20	23
<b>Ethnic background</b>		
Urdu	55	51
Gujrati	22	15
Punjabi	15	19
Others	8	15
<b>Occupational status</b>		
Housewife	89	90
Occupied outside the home	11	10

Two groups are well matched for age, height and weight, socio-economic status, ethnic background and occupation and no significant difference exists in any of these parameters. Some of the well known risk factors for getting breast cancer were investigated in the cases as well as controls. Age at menarche, age at menopause, age at first full term pregnancy, number of pregnancies, frequency of lactation and use of estrogens is comparable between the two groups (Table II).

**Table II. Nutritional aspects of mammary carcinogenesis.****Personal history of cases and controls**

Characteristics	Cases mean $\pm$ SD	Controls
Age at menarche (years)	13.0 $\pm$ 2.3	13.2 $\pm$ 2.3
Age at menopause (years)	43.8 $\pm$ 6.0	44.9 $\pm$ 4.9
Age at 1st pregnancy	21.0 $\pm$ 5.5	20.8 $\pm$ 5.4
Number of pregnancies	5.6 $\pm$ 3.9	5.6 $\pm$ 3.5
Lactation	16.4 $\pm$ 12.5	14.4 $\pm$ 9.3
Usage of estrogens	16%	14%
II/O benign breast disease	30%	8.8%*
Relatives with cancer	48.8%	30.0%**

\* P &lt; 0.05

\*\* P &lt; 0.05

As expected, two groups are significantly different in the history of prior breast disease and family history of breast cancer ( $P > 0.05$ ). Comparison of the dietary histories revealed no significant difference in the frequency of intake of milk and milk products except more often consumption of dahi/lassi by the controls ( $P > 0.05$ ). Similarly, no significant difference was observed in the intake of meat and meat products. Consumption of fish, however, was significantly different between cases and controls ( $P > 0.05$ ). As compared to cases (12.5%), controls more often ate fish at a frequency of once to twice per week (27.5%). There was a significant difference ( $P > 0.05$ ) in the intake of fruits (except apples) and vegetables between cases and controls. This study suggests that the dietary pattern of the cases and controls did not differ significantly except that controls had a higher intake of fish, vegetables and fruits.

**Discussion**

International correlation, case-control and cohort studies have associated the incidence of breast cancer with high fat consumption<sup>9-14</sup>. A significantly increased risk of breast cancer has been shown with increased consumption of milk and dairy products, gravy, beef and pork<sup>15</sup>. Many recent studies however, have questioned the role of fats in causing breast cancer<sup>17-19</sup>. There appears to be no consensus on the role of fats in mammary carcinogenesis<sup>19-23</sup>. Our study fails to correlate fat intake with the occurrence of breast cancer. In our study, decreased intake of fish by cases is an interesting finding. Japanese and Eskimos have some of the lowest rates of getting breast cancer<sup>1,7</sup>. Both consume diets traditionally based on fish and other marine animals. Recent changes in the traditional diet of Japanese and Eskimos have been associated with the rising incidence of breast cancer. These changes may well involve decreased consumption of fish. Some previous case-control studies have shown a negative effect of fish consumption on the incidence of breast cancer<sup>15,24</sup>. Animal studies also indicate that unlike other fats, fish oils inhibit mammary tumorigenesis<sup>25,26-29</sup>. This inhibitory effect on mammary carcinogenesis may be related to the inhibitory effect of fish oils on prostaglandin synthesis<sup>30</sup>. Eicosanoid activity has been associated<sup>30</sup> with the development, aggressiveness, extent and mortality from breast cancer<sup>31,32</sup>. Our study also reveals increased consumption of green leafy

vegetables and carotene rich fruits by controls as compared to cases. Many other case-control studies have assessed the relationship between breast cancer and consumption of fruits and vegetables<sup>33-39</sup>. Although vegetables including green leafy vegetables and carotenoids were reported to be protective in some studies<sup>33-35,38,39</sup>, no association was reported by others<sup>40,41</sup>. Iscovich et al also reported a significant protective effect of citrus fruit consumption<sup>33</sup>. In a re-analysis of combined data from nine different studies, Howe et al reported a significant protective effect of fruits and vegetables against breast cancer<sup>43</sup>. It may be that the fruits and vegetables contain desirable chemo-preventive agents<sup>43,44</sup>. They may also be an important source of essential micronutrients, vitamins and minerals. Case-control studies are fraught with many pitfalls<sup>45</sup>. Dietary habits of cases may change after the diagnosis of breast cancer is made. These changes may be induced by the disease, its treatment, or newly acquired knowledge regarding the role of dietary factors in mammary carcinogenesis. In our study, information recorded was not of the present dietary habits but the recent past. This was done specifically to exclude these recent changes. This, however, may create the problem of validity of data based upon recall. It has previously been demonstrated that recall of past diet maybe affected by the present dietary habits. However, reproducibility of recall past diet is acceptable in most of the studies with less than 20 percent variation. We have not yet analyzed the reproducibility of our data, although such a study is in progress at our institution. Breast cancer is the commonest cancer in females. In the United States, more than 150,000 new cases of breast cancer are diagnosed annually and this disease results in approximately 45,000 cancer deaths per year<sup>46,47</sup>. The incidence of this disease has increased by almost one percent per year. Presently there are no known methods to decrease this rising incidence. If nutritional factors are indeed casually related to the incidence of breast cancer, dietary changes based upon the findings of this and other similar studies may be a simple and inexpensive way to decrease the incidence of breast cancer.

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## References

1. Waterhouse, 3., Muir, C., Shanmugaratnam, K., Powell, 3. eda. Cancer incidence in five continents. VoL IV. Lyon: IARC Sci. PubI. No.42,1982.
2. Mortality from cancer and other diseasea amongJapanee in the United States. 3. NatI. Cancer Inst., 1968;40:43-68.
3. Dunn, G.E. Breast cancer among American-Japanese in the San Francisco Bay area. NstI. Cancer Inst. Monogr., 1977;47:157-60.
4. Buell, P. Changing incidence of breast cancer in Japanese- American wOmen.). NatI. Cancer Inst., 1973; 51:1473-79.
5. Gray, G.E., Henderson, B.E., Pike, MC. Chsngingratio ofbresst cancerincidence rates with age of black femalee compared with white females in the United States. 3. NatI. Cancer Inst., 1980;64:461-63.
6. Hiroyama, T. Epidemiology of breast cancer with special reference to the role of diet Prey. Med., 1978;7:173-95.
7. Shaefer, O., Hildes, J.A., Medd, L.M., Cameyon, D.G. The changing pattern of neoplastic diseases in Canadian Eskimos. Can. Med. Assoc. 3., 1975;112:1399-1404.
8. Hildes, J.A., Shaefer, O. The changing picture of neoplastic diseases in tbewestern and central Canadian Artic (1950-1980). Can.Med. Assoc. 1, 1984;130:25-32.
9. Armstrong, B., Doll, R. Environmental factors and cancer incidence and mortality in

- different countries with special reference to dietary practices. *Int. J. Cancer*, 1975;15:617-31.
10. Gray, G.E., Pike, M.C., Henderson, B.E. Breast cancer incidence and mortality rates in different countries in relation to known risk factors and dietary practices. *Br. J. Cancer*, 1979;39:1-7.
  11. Gaskill, S.P., McGuire, W.L., Osborn, C.K., Stern, M.P. Breast cancer mortality and diet in the United States. *Cancer Res.*, 1979;39:3628-37.
  12. Kolonel, L.N., Hsin, J.H., Lee, J., Chu, S.Y., Nomura, A.M.Y., Hinds, M.W. Nutrient intakes in relation to cancer incidence in Hawaii. *Br. J. Cancer*, 1981;44:332-39.
  13. Hirshyama, T. Epidemiology of breast cancer with special reference to the role of diet. *Prey. Med.*, 1978;7:173-95.
  14. National Research Council, National Academy of Sciences. *Diet, Nutrition and Cancer*. Washington, DC., National Academy Press, 1982.
  15. Hislop, T.G., Coidman, A., Elwood, J.M., Brauer, O., Kan, U. Childhood and recent eating patterns and risk of breast cancer. *Cancer Detect. and Prey.*, 1986;P.47-58.
  16. Jafarey, N.A., Zsidi, S.H.M. Cancer in Pakistan. *Pat. Med. Assoc.*, 1987;37:178-83.
  17. Hirohata, T., Nomura, A.M.Y., Hankin, J.H. et al. An epidemiologic study on the association between diet and breast cancer. *Nati. Cancer Inst.*, 1987;78:595-600.
  18. Willett, W.C., Stampfer, M.J., Colditz, G.A. et al. Dietary fat and the risk of breast cancer. *N. Engl. J. Med.*, 1987;316:22-28.
  19. Phillips, R.L., Snowdon, D.A. Association of meat and coffee use with cancers of the large bowel, breast and prostate among Seventh Day Adventists: preliminary results. *Cancer Res.*, 1983;43: S. 2403-8.
  20. Pariza, M.W. Dietary fat and cancer risk: Evidence and research needs. *Annu. Rev. Nutr.*, 1988;8:167-83.
  21. Prentice, R.L., Pepe, M., Self, S.G. Dietary fat and breast cancer: a quantitative assessment of the epidemiological literature and a discussion of methodological issues. *Cancer Res* 1989;261:3147-56.
  22. Schatzkin, A., Greenwald, P., Byar, D.P., Clifford, C.I. The dietary fat-breast cancer hypothesis is alive. *JAMA.*, 1989;261:3284-87.
  23. Simopoulos, A.P. Diet and health: Scientific concepts and principles. *Am. J. Clin. Nutr.*, 1987;45:1027.
  24. Decarli, A., La Vecchia, C. Environmental factors and cancer mortality in Italy: Correlational exercise. *Oncology.*, 1986;43:116-26.
  25. Hayashi, Y., Nagao, M., Sugimura, T. et al (eds). *Diet and nutrition and cancer*. Tokyo and Utrecht, Japan Scientific Societies Press and VNU Sciences Press, BV., 16:P3-345.
  26. Jurkowski, U., Cae, W.T.J. Dietary effects of menhaden oils on the growth and membrane lipid composition of rat mammary tumours. *J. Natl. Cancer Inst.* 1985;74:1145-50.
  27. Krsmsli, R.A., Marsh, S., Fuchs, C. Effect of omega-3 fatty acids on growth of a rat mammary tumour. *J. Natl. Cancer Inst.*, 1984; 73:457-61.
  28. Carroll, K.I., Brsden, L.M. Dietary fat and mammary carcinogenesis. *Nutr. Cancer*, 1985;6:254-9.
  29. Karmali, R.A. n-3 fatty acids and cancer. *Intern. Med. Suppl.*, 1989;225:197-200.
  30. Culp BR., Titus, B.G., Lant, W.E. Inhibition of prostaglandin biosynthesis by eicosapentaenoic acid. *Prostaglandins*, 1979;3:269-78.
  31. Karmali, R.A. Review: Prostaglandins and cancer. *Prostaglandins*, 1980;5:11-28.
  32. Watson, D.M.A., Kelley, L.W., Hawkins, R.A., Miller, W.R. Prostaglandins in human mammary cancer, *Br. J. Cancer*, 1984;49:459-64.
  33. Iscovich, J.M., Iscovich, R.B., Howe, G. et al. A case control study of diet and breast cancer in Argentina. *Int. J. Cancer*, 1989;44:770.
  34. Katsouyanni, K., Trichopoulos, D., Boyle, P. et al. Diet and breast cancer: a case control study in Greece. *Int. J. Cancer*, 1986;38:815.
  35. La Vecchia, C., Decarli, A., Franceschi, S. et al. Dietary factors and the risk of breast cancer. *Nut*

Cancer, 1987;10:205.

36. Lubin, F., Wax, Y., Modan, B. Role of fat, animal protein and dietary fiber in breast cancer etiology: a case control study. Nat Cancer Inst. 1986;77:605-12.
37. Pryor, M., Slattery, M.L., Robinson, L.M. et al Adolescent diet and breast cancer in Utah. Cancer Res., 1989;49:2161-67.
38. Rohan, T.E., McMichael, A.J., Baghurst, P.A. A population-based case control study of diet and breast cancer in Australia. Am. J. Epidemiol., 1988;128:478-89.
39. Katsouyanni, IC, Willett, W., Trichopoulos, D. et al. Risk of breast cancer among Greek women in relation to nutrient intake. Cancer, 1988;61:181.
40. Marubini, E., Decarli, A., Costa, A. 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.
41. Toniolo, P., Riboli, E., Protta, F. et al. Calorie providing nutrients and risk of breast cancer. Natl. Cancer Inst., 1989;81:278.
42. Howe, G.R., Hirohata, T., Hislop, T.G. et al. Dietary factors and risk of breast cancer: combined analysis of 12 case control studies. J. Natl. Cancer Inst., 1990; 82:561-69.
43. Mettlin, C. Level of epidemiologic proof in studies of diet and cancer with a special reference to dietary fat and vitamin A. Prog. Clin. Biol. Res., 1988; 259:149-59.
44. Moon, T., Micozzi, M.S. (eds). Nutrition and cancer prevention: investigating the role of micronutrients. New York, Marcel Dekker, 1989, p.3-588.
45. Block, G. A review of validations of dietary assessment methods. Am. J. Epidemiol., 1985;125:164.
46. Rohan, T.E., Potter, J.D. Retrospective assessment of dietary intake. Am. J. Epidemiol., 1984; 120: 876-77.
47. Boring, C., Squires, T., Tong, T. Cancer Statistics 1991. CA., 1991;41:19-36.