



CLINICAL AND NUTRITIONAL STATUS OF BREAST CANCER PATIENTS: A CROSS-SECTIONAL STUDY

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ABSTRACT

Mortality due to breast cancer is high due to detection at advanced stages. The investigation was carried out to determine the prevalence of risk factors among breast cancer patients. A cross-sectional survey on 98 subjects enrolled from two purposively selected government hospitals in the cities of Kota and Vadodara was carried out. Information pertaining to their socio-economic status, anthropometric measurements, dietary profile and medical history were recorded using a semi-structured pre-tested questionnaire. Majority of the subjects enrolled were in the age range of 41-60 years (59.2%) and were in stage II of cancer (65.3%). Most of the subjects (78.6%) in the study were physically inactive. Family history for cancer, obesity, diabetes, hypertension and coronary heart disease was absent in 90-95% of the subjects. Reproductive and menstrual history variables were normal among the subjects. Around 46% of the subjects were found to be overweight or obese. Chemotherapy and radiotherapy were the primary modes of treatment received by the subjects. Around 98% of the subjects had low consumption of fruits and vegetables (<4 times/week). The dietary intake of calories, protein and iron was low. Dietary fat contributed >30% towards the calorie intake. Baseline hemoglobin levels revealed a large number of the subjects to be anaemic (84.4%). In conclusion, the results obtained indicated that in the absence of heredity, and with normal reproductive and menstrual history, lifestyle variables could play a decisive role in precipitating the clinical condition, thus necessitating lifestyle modifications focussing on healthy diets and physical activity in order to optimize health.

Keywords: Breast cancer, Lifestyle variables, Nutritional status.

1. INTRODUCTION

Breast cancer has become a major health problem over the last 50 years. In 2018, 2,088,849 new cases of breast cancer (11.6% of total new cases) were identified and 626,679 cases of deaths (6.6% of total deaths) due to breast cancer occurred in the world. Breast cancer was reported to be the most common cancer in women, accounting for 24.2% of new cases in 2018 [1]. The burden of cancer is increasing in countries of all income levels. Approximately 70% of deaths from cancer occur in low- and middle-income countries [2]. With rapid industrialization and urbanization, the incidence of breast cancer is rising fast among Indian women. According to the National Cancer Registry Programme three year report (2012-2014), among females, cancer of the breast is the leading site of cancer in 19 registry areas. In terms of age adjusted incidence rates, Delhi (41.0), Chennai (37.9), Bangalore (34.4) and Thiruvananthapuram District (33.7) occupied the top four places among all the

population based cancer registries [3]. GLOBOCAN 2018 data also ranks breast cancer as the number one cancer among females in India with 1,62,468 new cases in 2018 making up 27.7% of total new cases [4].

The aetiology of breast cancers is multifactorial with a complex interplay of genetic and environmental factors. Tobacco use, alcohol use, unhealthy diet, and physical inactivity are major cancer risk factors worldwide [2]. The burden of cancer is expected to increase with population growth. In addition to this, the cancer burden is also increasing among women in low and middle income countries as the countries experience economic transition due to changes in the prevalence of cancer risk factors that include smoking, excess body weight, physical inactivity, and changes in reproductive patterns, such as a later age at first childbirth and fewer childbirths [5]. Between 30-50% of cancers can currently be prevented by avoiding risk factors and implementing existing evidence-based prevention strategies [2].

Nutrition is an important aspect of multimodal cancer care as patients with cancer are at a particularly high risk for malnutrition because both the disease and its treatments threaten their nutritional status [6]. Diet has been proposed to have a significant impact on breast cancer outcomes. Adoption of healthful dietary patterns that include healthier foods such as fruits, vegetables, whole grains, and poultry and less consumption of red meat and refined foods might improve overall prognosis and survival in women diagnosed with early-stage breast cancer [7]. There is a growing body of evidence that suggests that physical activity is important in improving survival following breast cancer diagnosis and should be encouraged both pre- and postdiagnosis and perhaps more crucially so in women who were insufficiently active prediagnosis [8].

The present study was planned with an objective to carry out nutritional assessment of breast cancer patients in relation to anthropometry, diet history, medical history and biochemical parameters.

2. MATERIAL AND METHODS

In this cross-sectional study, subjects were enrolled from two purposively selected government hospitals in the cities of Kota (Rajasthan, India) and Vadodara (Gujarat, India). In all 98 subjects were enrolled with equal numbers from both the government hospitals. Information regarding their economic status, level of education, physical activity, family history of non-communicable diseases, medical history, general dietary profile was collected using a semi-structured pre-tested questionnaire. Anthropometric measurements of height, weight, waist circumference (WC) and hip circumference were taken using standard methods. Comprehensive medical history of patients was obtained by reviewing hospital case papers, treatment summaries and test reports. In order to obtain detailed dietary information, 24 hr dietary recall method was used and nutrient intake was calculated using Indian food composition tables [9]. Results are expressed as Mean $\pm$ S.D and percentages. The statistical analysis was carried out using Microsoft® Office Excel 2003. The study was approved by the Institutional Ethics Committee for Human Research.

3. RESULTS AND DISCUSSION

Majority of the subjects (59.2%) were in the age range of 41-60 years. The majority of the patients (83.9%) in a study conducted in patients admitted to a tertiary care hospital of North India were also reported to be in the

fourth to sixth decade of their life [10]. The age distribution within the population of breast cancer patients is also quite characteristic as reported by Kamińska *et al.* [11]. The study reported that eighty percent of the cancer cases were diagnosed in women aged 50 and more and 50% of breast cancers occurred in women aged 50 to 69 years. These observations imply that there is a need to screen women especially post-menopausal women for breast cancer. There is also a need to sensitize the middle-aged women about screening and good nutritional practices to optimize health.

Around 86.7% of the subjects were married. Education is a key component of socioeconomic status and breast cancer risk may be influenced by many reproductive, lifestyle and behavioural factors associated with education [12]. Nearly half (49.0%) of the subjects enrolled were illiterate and 42.9% of the subjects had studied only up to school. A study carried out to assess the association between education level and *in situ* and invasive breast cancer risk and invasive breast cancer survival, using the 2006 update of the Swedish Family-Cancer Database reported that compared to women completing less than 9 years of education, university graduates were more likely to be diagnosed with *in situ* and invasive breast cancer, and were associated with the highest survival following a breast cancer diagnosis [12]. Most of the subjects enrolled were in stage II of cancer (65.3%) followed by stage III (27.5%). A lack of awareness regarding the disease and delay in the first visit to the doctor could be responsible for late detection in women with breast cancer. Therefore, it is important to create awareness which can help in earlier identification of breast cancer cases thus leading to good prognosis and increased chances of survival.

Table 1: Information Regarding Lifestyle Variables of Breast Cancer Subjects (N=98)

	N	%
Use of Addictive Substances		
Tobacco Chewing in the Past	14	14.3
Never Indulged	84	85.7
Physical Activity		
Physically Inactive	77	78.6
Physically Active	21	21.4
<3 Hrs / Week	20	95.2
>3 Hrs / Week	1	4.8

Data pertaining to the use of addictive substances and physical activity pattern is given in Table 1. A major proportion (85.7%) of the subjects reported never having

used any addictive substance. Physical activity has been linked with a lower risk of breast cancer. Most of the subjects (78.6%) in the study were physically inactive. Physical inactivity could have been a contributing factor in increasing the risk of breast cancer and may have a negative impact on prognosis of the disease. In the Sister Study cohort of 50,884 women who had a sister with breast cancer but no prior breast cancer themselves at enrolment, it was found that higher hours/week and metabolic equivalent-hours/week of physical activity were associated with reduced postmenopausal breast cancer risk, but not premenopausal breast cancer risk and was not modified by extent of family history [13]. In a 2012 review of 76 studies, 40 (53%) of the studies reviewed reported a protective effect of physical activity on breast cancer risk. The mechanisms responsible for the protective effect of physical activity on breast cancer risk and recurrence were reported to be likely through changes in sex hormone levels, immune function, adiposity, and insulin-related factors [14]. Thus, it becomes imperative to sensitize the breast cancer patients about the importance of physical activity for better prognosis and survival.

It was observed that family history for cancer, obesity, diabetes, hypertension and coronary heart disease was absent in majority (90-95%) of the subjects (Table 2). Breast cancers resulting from familial or genetic predisposition are thought to account for only 15% to 20% of all diagnosed cases indicating that 80% to 85% of breast cancers occur in women with no family history of the disease [15]. This data may thus signify the role of lifestyle variables in precipitating the condition.

Table 2: Family History for Non-Communicable Diseases in Breast Cancer Subjects (N=98)

Disease/Condition	No History	Positive History*
	N (%)	N (%)
Cancer	94(95.9)	4(4.1)
Obesity	93(94.9)	5(5.1)
Diabetes	89(90.8)	9(9.2)
Hypertension	90(91.8)	8(8.2)
CHD	93(94.9)	5(5.1)

Note: CHD=Coronary Heart Disease; * Positive history denotes presence of disease or condition in parents/siblings grandparents of the subjects

Information was collected regarding the reproductive and menstrual history of the subjects (Table 3). Early menarche and late menopause result in a substantial

cumulative exposure to estrogens and the simultaneous presence of progesterone, an exposure theorized to increase the risk of breast cancer [16]. The average age at menarche was found to be 14.3 years and average age at menopause was 44.5 years. In a study conducted to analyze the clinical presentation and outcome of early breast cancer patients at a major cancer center in North India, median ages at menarche and menopause were reported to be 14 years and 46 years respectively [17].

Table 3: Reproductive and Menstrual History of Breast Cancer Subjects

Variables	N	Mean $\pm$ SD
Age at Menarche	98	14.3 $\pm$ 1.2
Age at Menopause	79	44.5 $\pm$ 5.1
Age at First Delivery	94	21.6 $\pm$ 4.6
Consumption of OCP	N	%
Yes	4	4.1
No	94	95.9
Parity	N	%
Nulliparous	6	6.1
≤ 2	46	46.9
3 – 5	41	41.8
6 – 8	5	5.1
Gravida	N	%
≤ 2	33	35.1
3-5	45	47.9
6 – 8	16	17.0

Note: OCP= Oral Contraceptive Pills

Only 4.1% of the subjects reported having used oral contraceptive pills while the rest had no history of oral contraceptive pill usage. The population at risk of breast cancer due to oral contraception in our country is smaller when compared to the western world [18]. Nulliparity has for decades been known to be associated with increased reproductive cancer risks including breast, ovarian and uterine cancers [19]. Among the subjects very few were nulliparous (6.1%). In a study conducted in patients admitted to a tertiary care hospital of North India only 20.37% of the patients were nulliparous, whereas, others had three or more children [10]. Thus, the reproductive and menstrual history variables were normal among the subjects.

Obesity and weight gain are negative prognostic factors for breast cancer survival. Based on the Asia Pacific Classification [20], the prevalence of overweight (Body Mass Index (BMI) ≥ 23) and obesity (BMI ≥ 25) among the subjects was found to be 22.4% and 23.5% respectively (Table 4).

Table 4: Nutritional Status of Breast Cancer Subjects Based on Anthropometry

Status	N (%)
Underweight	14(14.3)
Normal	39(39.8)
Overweight (BMI $\geq$ 23)	22(22.4)
Obesity (BMI $\geq$ 25)	23(23.5)
Waist Circumference $\geq$ 80 cm	66(67.3)
Waist Hip Ratio $>$ 0.85	48(49.0)

Note: BMI = Body Mass Index

Obesity has been found to be associated with increased breast cancer risk in women. A secondary analysis of the Women's Health Initiative Randomized Clinical Trials revealed that women who were overweight and obese had an increased invasive breast cancer risk vs women of normal weight. Greatest risk was reported for obesity grade 2 plus 3 (BMI >35.0). Obesity grade 2 plus 3 was also associated with advanced disease, including larger tumor size, positive lymph nodes, regional and/or distant stage, and deaths after breast cancer [21]. A strong association of overweight and obesity with breast cancer has also been revealed in the Indian population. In a hospital-based matched case-control study which included three hundred and twenty newly diagnosed breast cancer patients and three hundred and twenty normal healthy individuals it was observed that the patients had a statistically higher mean weight, BMI, and mid upper arm circumference as compared to the controls. It was also observed that the risk of breast cancer increased with increasing levels of BMI with overweight and obese women having an Odd's ratio of 1.06 and 2.27, respectively, as compared to women with normal weight [22]. Overweight and obesity have been shown to be independently associated with poorer prognosis for breast cancer patients. In a retrospective analysis of 1017 breast cancer patients where the clinicopathological characteristics and clinical outcomes of patients within 5 years following breast cancer diagnosis were analyzed, it was found that the 5-year disease-free survival and overall survival decreased in overweight and obese patients. Both overweight and obesity were found to be independent predictors for increased risks of breast cancer relapse and death [23]. Central obesity has been suggested to be a key risk factor for breast cancer. WC values of majority (67.3%) of the subjects were found to be higher than the normal cut off ($\geq$ 80 cm for females) indicating the presence of abdominal obesity. Higher waist hip ratio and WC have

been associated with a threefold increased risk of premenopausal and postmenopausal breast cancer in Indian women [24]. Overall adiposity in women adversely affects breast cancer risk mainly by greater exposure of mammary epithelial tissue to endogenous estrogen. Upper abdominal adiposity appears to involve an additional effect related to the presence of insulin resistance [25]. All treatment modalities for breast cancer such as surgery, radiotherapy, chemotherapy and hormonal treatment may be adversely affected by the presence of obesity [26]. The prevalence of underweight among the subjects was 14.3% which could be the result of deteriorating nutritional status during breast cancer (Table 4). Being underweight may increase the risk of breast cancer recurrence or death. In a study that investigated the impact of BMI on the prognosis for patients with breast cancer within the context of race (African-American versus Caucasian) and ethnicity (Hispanic versus Non-Hispanic), multivariate analysis revealed that breast cancer death rate was increased over 2.6-fold for underweight patients ubiquitously, regardless of race or ethnicity [27].

On the basis of the diagnostic reports, the size of tumor and location of cancer were studied and the findings are shown in Table 5. Around 72.4% of the breast cancer subjects had a tumor of size 2 to 5 cm before being operated upon while 17.3% subjects had a tumor of size >5 cm. Women have been known to be more likely to develop cancer in the left breast than the right [28]. However, with regard to location it was seen that about 61.0% subjects had the tumor on the right breast, 32.6% had the tumor on the left breast and in 6.3% subjects bilateral breast involvement was observed. Similar results have been reported by Saha *et al* where 51.7% of the subjects showed involvement of the right breast [29].

Table 5: Medical History of Breast Cancer Subjects

Tumor Size	N	%
< 2 cm	4	4.1
2-5 cm	71	72.4
> 5 cm	17	17.3
Tumor of any size with direct extension to chest wall or skin	3	3.1
No Tumor	3	3.1
Location of Cancer		
Right Breast	58	61.0
Left Breast	31	32.6
Bilateral	6	6.3

Table 6: Treatment History of Breast Cancer Subjects

Therapy Type	Received N (%)	Not Received N (%)	No of Sessions Mean $\pm$ SD
CT	87(88.8)	11(11.2)	4.2 $\pm$ 2.8
RT	47(48.0)	51(52.0)	10.6 $\pm$ 11.8
CT & RT	37(37.8)	61(62.2)	-

Note: CT = Chemotherapy RT= Radiotherapy

Table 7: Side Effects Due to Treatment Among Breast Cancer Subjects

Side Effects Due to CT	N (%)	Side Effects Due to RT	N (%)
Any Side Effect	87(100)	Any Side Effect	39(83.0)
Anorexia	75(86.2)	Anorexia	12(30.8)
Nausea	68(78.2)	Nausea	13(33.3)
Vomiting	52(59.8)	Vomiting	8(20.5)
Vertigo	40(46.0)	Heart Burn	9(23.1)
Pain in Limbs	39(44.8)	Vertigo	8(20.5)
Mouth Ulcers	24(27.6)	Mouth Ulcers	2(5.1)
Hair Loss	87(100)	Skin Discoloration	39(100)

Note: CT = Chemotherapy RT= Radiotherapy

Cancer and its treatment modalities can have side effects that lead to changes in eating habits and might endanger the nutritional status of patients. Table 6 shows the type of treatment received by the subjects. Around 88.8% of the subjects underwent chemotherapy for treatment of breast cancer and all the subjects who underwent chemotherapy reported presence of side effects (Table 7). The reported side effects of chemotherapy included hair loss, anorexia, nausea, vomiting, vertigo, pain in limbs and mouth ulcers. Approximately 48% of the subjects received radiotherapy as treatment of which, 83.0% reported presence of side effects like skin discoloration, nausea, anorexia, heartburn, vomiting, vertigo and mouth ulcers. Thus, it is evident that the treatment lines followed for breast cancer have varied and highly prevalent side effects. Anorexia, nausea and vomiting constitute a spectrum of symptoms and signs whose net result is a reduction of food intake. This is an undesirable state of affairs, particularly in cancer patients who suffer both a decreased ability to withstand treatment and an impaired quality of life [30].

From the analysis of data collected on dietary pattern of the subjects it was seen that 98% of the subjects had low consumption of fruits and vegetables (*i.e.* <4 times a week). Block et al reviewed about 200 studies of cancer and fruit and vegetable intake [31]. In 128 of 156 studies in which results were expressed in terms of relative risks, a statistically significant protective effect of fruits and vegetables was found. For most cancer sites, people in the lower quartile of the population who ate the least amount of fruits and vegetables experience about twice

the risk of cancer compared to those with high intake of fruits and vegetables. More recently, the Italian section of the European Prospective Investigation into Cancer and Nutrition study showed an inverse association between breast cancer risk and consumption of all vegetables and according to subtypes of vegetables, an inverse association emerged for increasing consumption of leafy vegetables, fruiting vegetables and raw tomatoes [32].

Table 8: Mean Nutrient Intake of Breast Cancer Subjects

Nutrient	Mean $\pm$ SD
Energy (Kcal)	1132 $\pm$ 383
Carbohydrate (g)	154 $\pm$ 79.6
Fat (g)	42.8 $\pm$ 16.5
Protein (g)	32.6 $\pm$ 12.1
Iron (mg)	9.5 $\pm$ 6.0
Vitamin C (mg)	86.1 $\pm$ 109.6
β -carotene (μ g)	101 $\pm$ 228.3

The mean nutrient intake of subjects as evaluated by a 24-hour dietary recall is given in Table 8. Cancer patients with anorexia/cachexia syndrome have increased energy needs, and increased proteolysis depletes essential as well as nonessential amino acids, the latter of which may become conditionally essential [33]. Subjects in the present study consumed diets inadequate in calories and protein meeting only around 60% of the recommended dietary allowance (RDA) of 1900Kcal and 55g protein for a sedentary adult Indian

female. Carbohydrates, proteins and fats contributed 54.4%, 11.5% and 34.0% of the calories respectively. Calories from protein (11.5%) were inadequate since the protein requirement of cancer patients is high. In a study conducted to assess the intake of proteins before, during and after chemotherapy treatment in a cohort of women with non-metastatic breast cancer (stage I, II), protein consumption was reported to decrease in the women during treatment, and even more after the end of treatment [34]. A modest survival advantage with higher intake of protein has been reported in women with breast cancer. In a study, where data from 6348 women with stage I to III breast cancer diagnosed between 1976 and 2004 was analyzed, during follow-up, there were 1046 cases of distant recurrence and an inverse association between energy-adjusted protein intake and recurrence was reported [35]. Percentage calories coming from fat (34.0%) were on the higher side which may have a negative impact on prognosis. Saturated fat intake has been reported to negatively impact upon breast cancer survival. In a meta-analysis of dietary fat and breast cancer mortality, breast-cancer-specific death was higher for women in the highest versus lowest category of saturated fat intake [36]. Results from a systematic literature review conducted to assess the epidemiological evidence on the impact of total dietary fat and fat subtypes, measured pre- and/or postcancer diagnosis, in relation to breast cancer-specific and all-cause mortality among breast cancer survivors suggested that higher saturated fat intake prediagnosis was associated with increased risk of breast cancer-specific and all-cause mortality [37].

Iron consumption among the subjects was also poor with the subjects meeting only 45.2% of the RDA of 21mg. Iron deficiency, highly prevalent in young women because of menstruation, has been shown to contribute to poor prognosis in young breast cancer patients [38]. Thus, dietary data revealed that the diet was inadequate in terms of both, macronutrients and micronutrients.

Anaemia is a major problem in cancer patients as a consequence of the disease itself or its treatment. The prevalence of anaemia among the breast cancer subjects was assessed using the WHO classification based on baseline blood haemoglobin levels [39]. The data revealed that a large number of subjects were anaemic (84.4%). When severity of anaemia was considered, it was found that more than one fourth of the subjects (27.1%) were in the category of moderate anaemia. The

presence of anaemia may have a negative impact on treatment outcome and overall survival in patients with cancer. In a retrospective analysis of 2123 breast cancer patients who underwent surgery between 2002 and 2008 it was found that preoperative anaemia was independently associated with poor prognosis of patients with breast cancer [40]. In another study, a total of 655 patients with operable or locally advanced breast cancer who underwent neoadjuvant chemotherapy before definitive surgery were reviewed. About 25.3% of the women were reported to be anaemic before treatment and pretreatment anaemia was found to be associated with worse pathological response to neoadjuvant chemotherapy as well as survival status in breast cancer [41].

4. CONCLUSIONS

In the present study, heredity did not contribute significantly to breast cancer. Lifestyle and dietary factors of the study subjects appear to be the dominant factors influencing the risk of breast cancer and its prognosis. With normal reproductive history and minimal number of subjects using oral contraceptive pills, the major contributors appear to be BMI, WC, fat intake contributing >30% of calories, low intake of fruits and vegetables and low physical activity levels. Fruits and vegetables not only contribute towards micronutrients but also provide antioxidants which are protective in nature. There is a need to encourage consumption of local fruits and vegetables in the daily diet to improve dietary diversity and to also improve the nutrient adequacy ratio for micronutrients and antioxidants. Thus, from the study it is clear that lifestyle factors need to be given due recognition to optimize health and screening strategies need to be devised to detect breast cancer cases early so as to reduce the complications and the financial burden associated with the condition. Health promotion strategies focussing on healthy diets and physical activity could go a long way in improving the quality of life of breast cancer patients.

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