Introduction:
Breast cancer is the most common cancer in women worldwide with a widely variable incidence rate between countries and regions. In developed countries, which accounts for a small proportion of the world population, about 50% of breast cancers are diagnosed (1,2). The lowest breast cancer incidences were reported in far Eastern and South East Asian countries (3,4). However, the burden of health care costs on the account of breast cancer has been steadily increasing in the developing countries of Asia. In the coming decades, developing countries will account for a majority of new breast cancer patients developing on a global level. Further, more than 100,000 new breast cancer cases and 540 age matched controls were selected from various hospitals of Chennai. Women, of all ages, were given a questionnaire that evaluated, familial cancer, age of diagnosis, stages of cancer, laterality of breast cancer, types of treatment, and psychological counseling. The collected data were analyzed using Karl Pearson statistical test and student’s t-test.

Results: In Tamil Nadu, only a fraction, 13%, of breast cancer patients had familial breast cancer history compared to the 87% with non-familial breast cancer. The occurrence of breast cancer cases in age groups, 41-45, 46-50 and 51-60 years are significantly higher than other age groups ($\chi^2 = 60.6719, P < 0.001$). Notably, we observed an age shift in breast cancer cases from 45-50 to 35-45 years, indicating that an increased number of women in younger age brackets are being afflicted with the disease. Breast cancer stages I and II were significantly higher than stages III and IV ($p < 0.001$). Further, incidences of breast cancer on the left side were more prevalent than on the right side of the breast with significantly higher positive axillary lymph node at the time of diagnosis.

Conclusion: The study revealed that there is a very low familial breast cancer incidence in Chennai, including a shift in cancer rates to women of a younger age, implying that the risk factors such as environmental, dietary habits, and lifestyle may possibly be involved in the genesis of breast cancer rather than genetic factors. Thus, lifestyle modifications and educating the population of risk factors may be better avenues for future studies to pursue in order to reduce the risk of breast cancer.

Keywords: Breast cancer – TNM stages – Axillary Lymph node – Age shift – Dietary habits – Lifestyle.
than women in other religious sects (31). Considering high prevalence of intra-caste marriages (consanguineous) in South India (6), our study aimed to discover patterns of familial inheritance, stages of breast cancer, and age shift, if any, among the breast cancer cases in Chennai, Tamil Nadu, India.

Materials and Methods:
To evaluate the familial and clinical stages of breast cancer, a case-control design was conducted, involving two groups, one group of breast cancer patients and a control group of women (non-cancer) from the same geographical area from February 2013 to January 2015. For this study, 512 breast cancer patients (cases) from different hospitals of Metropolitan City, Chennai were enrolled as the case group. For the control group, 540 age-matched, non-cancer women in and around Chennai were enrolled. Informed consent was obtained from all study subjects that participated in this study. A well-formulated English questionnaire was given to each patient, in both control and case group and their answers recorded. The patients who did not volunteer to respond to the questions were not included in this study. The questionnaire, originally written in English, was translated to regional languages for the patients who did not understand English language.

Preparation of questionnaire
The questionnaire was prepared in consultation with an oncologist to cover the family cancer, clinical stages of breast cancer, and other relevant information. General descriptions of the questionnaires and data collection procedures were followed (32). The family history of breast cancer (whether their mother, father, grandmother, grandfather, aunt and uncle were affected or not) was noted. In the control group, women with familial cancer were excluded, and only women without any familial history were considered. The age of breast cancer diagnosis was taken into consideration. Similarly, the stage at which the cancer was diagnosed was recorded, which included TNM stages I to IV (33). Based on the available reports, the involvement of axillary lymph nodes (left or right breast), current treatment, period of treatment, and psychological counseling, if any, were noted from the medical history of breast cancer cases, and was approved by the Institutional Ethical Committee of the respective hospitals (Cancer Institute (WIA) Adyar, Chennai; Cancer Care Centre, Kuman Hospital, Chennai and Kamatchi Memorial Hospital, Chennai).

Statistical analysis:
Data on the various risk-factors were collected from (breast cancer patients, n = 512) and controls (randomly selected non-breast cancer women, n = 540) and were tabulated. Karl Pearson's chi-square test was performed to determine the overall association between a particular risk factor and breast cancer. When there was a significant association (P < 0.05), post hoc chi-square test (2 x 2 table) was performed (1) to compare any two categories of a risk factor and (2) to compare the proportion of breast cancer patients and the proportion of non-breast cancerous subjects in a specific category of a risk factor. Post hoc multiple comparisons of proportions were made by the Marascuilo's procedure and any absolute difference between two proportions (test statistics) that exceeds the critical value, \( \gamma \), was considered significant at that level of significance. All the calculations were performed either in Excel (34) or in Winpepi 11.43.

Results
Family history of cancer
The results of familial history of breast cancer in case and control women are given in Table 1. Among the breast cancer cases, majority of them (86.72%) did not have history of the breast cancer in the family tree that included parents and close relatives. A similar trend was observed in the control group. Women with familial cancer were excluded, and only women without any familial history were considered. The age of breast cancer diagnosis was taken into consideration. Similarly, the stage at which the cancer was diagnosed was recorded, which included TNM stages I to IV (33). Based on the available reports, the involvement of axillary lymph nodes (left or right breast), current treatment, period of treatment, and psychological counseling, if any, were noted from the medical history of breast cancer cases, and was approved by the Institutional Ethical Committee of the respective hospitals (Cancer Institute (WIA) Adyar, Chennai; Cancer Care Centre, Kuman Hospital, Chennai and Kamatchi Memorial Hospital, Chennai).

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cases, respectively. A positive association between family history of cancer and risk of breast cancer was also reported in the studies of Japanese women (41), Iranian women (42), and in the Cypriot (Eastern Mediterranean country) population (43).

According to the 1992-1993 National Family Health Survey (NFHS) that was conducted, consanguineous marriage has dropped from 12.9% to 11.9% in India. In Mangalore (Karnataka) 12.3% of consanguineous marriage was reported in urban areas (44). The highest incidence of consanguineous marriage was reported in Tamil Nadu (38%), followed by Andhra Pradesh (30.8%) and Karnataka (29.7%). Further, higher rates of consanguineous marriage were observed in rural areas (45) and notably, in the present study, breast cancer rates were also observed to be significantly higher in rural women than in urban women in Chennai. In this context, it is inferred that where there is a higher percentage of intra community marriage (38% in Tamil Nadu and 30.8% in Andhra Pradesh), there was a higher percentage of breast cancer with hereditary origin of 13.2% in Chennai as observed in the current study, and 17% in Andhra Pradesh (13), implying that there is a circumstantial relationship between intra community marriage and occurrence of hereditary breast cancer. In New Delhi, where a low percent (4.3%) of consanguineous marriage was recorded, a higher percentage of (20.7%) hereditary breast cancer was reported that may be attributed to genetic mutations from exposure to chemicals in urbanized and industrialized settings (16).

The low rate of familial pattern of breast cancer in the Indian patients has been reported by many researchers (2). Further, in most populations, 6-10% of patients with cancer have mutations in BRCA gene irrespective of family history. Nevertheless, a number of Indian studies pertaining to germ line mutation analysis of BRCA 1 and BRCA 2 genes in breast cancer reported that BRCA mutation makes up 9-25% of familial breast cancer cases (9,46,47,48). Three novel BRCA1 mutations including the founder Ashkenazi BRCA1 mutation have been reported in breast cancer patients in India (48). Studies have shown that 60% breast cancer family cases with site-specific female breast cancer cannot be explained by BRCA 1 and BRCA 2 (49,50). Moreover, population studies have demonstrated that these genes only account for 15% of the overall familial risk of breast cancer (51). These studies revealed that very low proportion of breast cancer cases are due to genetic inheritance further proving that other factors are involved in the genesis of non-familial breast cancer. Although it has not been verified, one may draw the conclusion that the human genetic profile has not changed over the past 10,000 years, whereas major changes have taken place in our food supply, energy expenditure, and physical activity (52).

In our investigation, the risk for breast cancer in age groups, 41-45, 46-50, and 51-60 are significantly higher than the age groups 35-40 or 61-70 among breast cancer cases in Chennai (P<0.001). A peculiarity is that there is shift in the age group of women affected by breast cancer from 45 to 50 to 35 to 45, which indicates that young women are more affected by breast cancer and coincides with other studies (53). The mean age of breast cancer diagnosis was 47.73 years in Delhi (11), 40 years in Chennai and Trivandrum (54), and 48 years in North Karnataka (14). In Chandigarh (a union territory of India), the rate of breast cancer in those less than 40 years of age was 34%, followed by 23% in the 41-45 age group, 7.4% in the 46-50 age group, and 25.3% in the 50 plus years age group (10). Chopra et al (15) reported higher proportions of breast cancer in the age group of 41-50 years and less in 51-60 years in Punjab state, India. The incidence of breast cancer in women younger than 25 years is rare and it represents 2% of all cases in the Western population. However, the incidence of younger women affected has increased in the Indian population. For instance, breast cancer incidences in younger women <35 years of age has been reported in Bangalore at11.25% (53), and in New Delhi at 5.5%, and 8% (55,56).

In our study, the frequencies of breast cancer patients with stage II (46%) was significantly higher followed by stage I (23%), III (21%), and stage IV (10%). In Haryana, 4.2% of cancer diagnoses presented in stage IV, and it is attributed to lack of literacy of breast cancer risk factors among the study population (57). Meshram et al., (58) reported more than 90% were in the late stages of breast cancer in Nagpur (Maharashtra). Similar late stages of (III and IV) breast cancer were reported in Manipal (Karnataka) (59) and in Kerala (60).

In Brazil, rates of stage II breast cancer was 42.5%, followed by stage I (32.5%), and stage III (20%) (61). Similar trends of incidence were reported in Singapore (62). In Iran, 50% of the breast cancer cases were diagnosed in a stage III, 30% in stage II, 5% in stage I, and 5% in stage IV (63). Our findings of breast cancer in stages I, II, and III are in agreement with the above reports. Therefore, it is suggested that an awareness and screening program for early detection of breast cancer in women is created, which may aid in higher curative rates with shorter treatment time periods, thus resulting in higher survival rates.

In our study, the positivity of axillary lymph node in breast cancer cases was significantly higher than the negative cases and the results are in concurrence with the other reports (64,65). A similar observation of lymph node involvement was reported in New Delhi, India (16) and in Tirupati (A.P.) (13). In Singapore, 35.8% of cases were found to be node positive and the percent of breast cancer varies with different races, 86.1% in Chinese, 8% in Malay, 4.0% in Indian, and 1.9% in other races (62).

Our study revealed that most patients had breast cancer on left side (54%) than right side of breast (46%), which are in concurrence with the other studies (14,64,66) and is attributed to the bulkier characteristics of the left breast in which the upper outer quadrant has a relatively larger volume of breast tissue compared to right breast (22). Similar trends in the rate of cancer in the left-side of breast were reported in women in several countries including Turkey (67), Iran (63), Iceland (68), and in Egypt (69). Three types of treatment namely viz., chemotherapy, radiotherapy, and surgery were commonly noted among breast cancer patients in our study and a similar types of treatment have been noted among breast cancer patients in other studies (54,61,62,63).

The stress due to cancer, household problems, and in the workplace was significantly noted among the breast cancer cases. Hence it is suggested that practicing yoga, meditation, and having a daily routine for physical exercise to overcome the stress in breast cancer cases is needed. Further, the patients enrolled in this study attended breast cancer survivor meetings to get both psycho-oncological counseling and treatment. It is therefore suggested that routine counseling sessions may be necessary to avoid any further complications. Overall, breast cancer cases undergoing treatment for less than 6 months was higher than the patients who are treated more than 6 months based on the stages of breast cancer and types of treatment (chemotherapy, surgery and radiation).

Due to the risk of cancer found in both those who had a family history of cancer and those who did not, lifestyle factors such as dietary habits, smoking, alcohol consumption and infection, may have a profound influence on development of cancer and imply that many types of the cancers are not due to hereditary factors (20,70). According to Doll and Peto (24), only 5-10% of all cancer cases are due to genetic defects and the remaining 90-95% is due to environment and lifestyle and suggested that cancer deaths can be prevented by modifying the diet. Epidemiological studies indicate that a western diet and/or westernization of diet act as a probable cause of the increasing incidence in breast cancer in India (71). It has been suggested that vegetarian diets are inversely related to overall cancer incidence (72). Vegetarian diets seem to confer protection against cancer and specifically the risk of female specific cancers when compared with non-vegetarian diets (73). It is, therefore, concluded that modification of lifestyle and food habit may need to study in order to determine its role in preventing the risk of breast cancer, as the majority (87%) of breast cancer diagnoses were not due to genetic inheritance.

Conclusion:
Our study suggests that familial breast cancer is very low in the female population in Chennai and the results are in line with the many studies globally. The results of investigation imply that genetic inheritance of breast cancer is limited to 5-10% and the non-genetic factors such as environment, dietary habits and lifestyle factors play a major role in the genesis of breast cancer. Early screening and awareness programs for women along with diet, counseling, and an integrated preventive approach may decrease the rates of breast cancer in the future.

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Declaration of Conflict of Interest:
The authors declare no conflicts of interest.

Table 1: Studies on Familial cancer and clinical stages of breast cancer cases and control women in Chennai.

<table>
<thead>
<tr>
<th>No.</th>
<th>Study groups</th>
<th>Cases (n=512)</th>
<th>Control (n=540)</th>
<th>J2 -P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cancer history</td>
<td>No cancer family in history</td>
<td>Breast cancer history</td>
<td>444</td>
</tr>
<tr>
<td>2</td>
<td>Age at breast cancer was Diagnosed (Years)</td>
<td>35 – 39</td>
<td>39</td>
<td>7.62</td>
</tr>
<tr>
<td>3</td>
<td>Cancer stages</td>
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<td>118</td>
<td>23.05</td>
</tr>
<tr>
<td>4</td>
<td>Axillary lymph nodes</td>
<td>Positive</td>
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<td>84.38</td>
</tr>
<tr>
<td>5</td>
<td>Side of Cancer</td>
<td>Left</td>
<td>274</td>
<td>53.52</td>
</tr>
<tr>
<td>6</td>
<td>Types of treatment</td>
<td>Chemo therapy</td>
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<td>7</td>
<td>Psychological Counseling</td>
<td>Yes</td>
<td>292</td>
<td>57.03</td>
</tr>
<tr>
<td>8</td>
<td>Period of treatment (Months)</td>
<td>&lt;6</td>
<td>273</td>
<td>53.52</td>
</tr>
</tbody>
</table>

Note: '*' = Not applicable; Controls are free from breast cancer, hence, S. No. 2 & 8 are marked as NIL

References:


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