ORIGINAL ARTICLE

RELATIONSHIP BETWEEN INCIDENCE OF BREAST CARCINOMA AND FIRST DEGREE RELATIVE POSITIVITY

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ABSTRACT

Objective: This study aims to find out a relationship between incidence of breast carcinoma & first degree relative positivity.

Methodology: A case control study was conducted to compare the Ca breast patients with positive first degree relative (group A) to Ca breast patients having negative first degree family relative positivity (group B), alongside the presence of secondary malignancies. Patients of age groupof 20-70 were assessed clinically with in the hospital outpatient department (OPD) setting from 2017 to 2023. The diagnosed cases were filtered, using the triple parameters (mammogram, fnac/trucut or physical asses.A Pre-prepared questionnaire was used to collect the initial information and patients were asked to follow up post treatment to continue the momentum.

*Results***:** The total numbers of participants partaking this research study were 158 in number. However,the highest incidence of first degree relative positivity was noted in 45-60years of age being about 5 first degree positive cases in 64 primary cases while the lowest was recorded in 20-30 years of age being null in 5 primary cases .The secondary malignancies were lowest in 20-30 at about 7 among the 5 primary cases and peaked at 60-70 and >70 age group being about 13 incidences among 29 primary cases. Albeit,al l age groups lacked daughter being the positive first degree relative

*Conclusion***:** Presence of first degree family relative strongly influences the incidence of breast Ca and as well as the secondary malignancies that manifest 60 years of Age above. The age group (45 till 60 yrs) as being the highest percentage of first degree relative positivity should be screened biannually.

Keywords: First degree family history, Incidence of Breast CA, CA=carcinoma, secondary malignancies, IDC= Invasive ductal Ca, ILC=invasive lobular Ca, malignant phylloides, PAEC- Pakistan Atomic Energy Commission.

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INTRODUCTION

This study was conducted in Pakistan that ranks amongst the 1st country with the highest incidence of Breast carcinoma in South east Asia and the 18th amongst the global ranking [1]. So far all variants and classified grades of breast carcinoma have expressed themselves in the subjects of this study, making it an interesting approach to results and a unique study in itself.

The occurrence of Ca breast worldwide and inPakistan is 1 in 8 among cancers .Its steep trajectory over the years evidently sirens the need for prevention and prompt treatment.There is a high mortality vs. morbidity ratio pinned to it. As of 2022,2.3 million

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patients mostly women were diagnosed among which 684996 deaths from breast cancer globally was recorded by WHO in women [2]. The mortality rate in 2022-23 is 1.1% and an estimated recurrence rate of 20-30% amidst these patients recorded [3].

The multitude of factors contributing to the above statistics include age, BMI, marital status, multiparity, sedentary lifestyle choices, menopausal status and strong predisposition to aberrant genetic lineage , hormonal therapies, Ocp use, breastfeeding & the focal one being familial first degree relative positivity [4]. These all are focal determinants of breast cancer worldwide and in Pakistan.

Breast carcinoma has growingly become quite a diagnostic & prognostic ordeal in today‘s time. The timely diagnosis, accurate Precaution, precisely devised treatment plan & valid nomination for adjunct therapy are all the key factors in its treatment journey .Given the multiplying incidence & surging cases of Breast carcinoma more so today than ever has compelled us to undertake this research and decipher the root key aetiology. We shall profoundly entail the relationship, incidence and the repercussions of the aforementioned in the research as it unfolds fact by fact.

Considering the magnitude of the incidence in Pakistan, it is worthwhile to consider and pinpoint the detrimental factors aiding the rapid progression and fatality of breast carcinoma in women of all age in Pakistan.Acknowledging, very few studies in Pakistan have undertaken this study on relationship between first degree relative positivity and various secondary malignancies in 2nd degree relatives of Ca breast patient. Hence the aim is to highlight this aspect of Ca breast incidence, directed at improving patient care, early screening of the vulnerable age group, prevention, cure & treatment. This study can also press need for a thorough screening and annual checkups in suspects, thereby mitigating the quality of life over all for such diagnosed patients. Breast carcinoma occurs at a younger age group with predominance of high-grade lesions and with frequent lymph node metastasis as in supported by many prior studies [5].

METHODOLOGY

The study was conducted during the period of year 2017-2022 at PAEC hospital from outpatient department(OPD) of Surgery. Pre designed questionnaires were formulated and every patient diagnosed with breast Ca is included in this study, their data was entered in questionnaire form &archived safely for follow up on Opd basis. Their data was briefly noted down and all follow up routines & progress weremeticulously entered tofacilitate from later .The total number of patients registered during the time were 158 in total with female to male ratio of 157:1. With age range from 20 years old to 82 years old (Median-51 years age).The patients were categorized according to the type of tumor (IDC=Invasive Ductal Carcinoma, ILC=Invasive Lobular Carcinoma and malignant Phyloides) and its grade variant (Grade 1-2-3) with grade 1 being well differentiated, grade 2 moderately differentiated and grade 3 being poorly differentiated.

It was a retrospective case control study in nature between the groups with Positive first degree relative (A) and those with breast carcinoma but without the first degree relative positivity (B).The data translated shows that a large number of patients between 30-60 years of age presented with Invasive ductal carcinoma. Very few among them had malignant phyloides carcinoma. Mucinous and neuroendocrine were none in number. The involvement of first degree family positivity stood true for all the age categories except 20-30 years of age and the higher occurrence was noted in age category 30-45 & 45-60 years of age with Invasive ductal carcinomas.

Along with it the secondary malignancies in 2nd degree relatives were also noted and assessed , most of them were found to amount up under breast cancers in age group 60-70 and <70.

RESULTS

All 158 patients were evaluated as having full-fledged breast carcinoma with signs and symptoms. Under this section, we will compare the incidence

of Ca breast with first degree family positivity and secondary malignancy among the extended 2nd degree family relatives.

Among these the 20-30 years of age group had a low incidence of Ca breast 5/158 i.e. 0.03 % risk incidence with all of them falling under Invasive ductal carcinoma Grade 2. Age group 45-60 had the highest incidence of ca breast 64/158 in total i.e., 40.5%, with majority amounting up in IDC grade 2 (table 1).

Table 1: Bio-data of the participants who enrolled in research

Age (years)	n(158)	Tumor type	Grade
20-30	5	IDC	G-2 5/5
30-45	47	IDC	G-1=2/47 G-2=28/47 G-3 =13/47 G-2=2/47
		ILCI Phyloides	G-2=2/47
45-60	64		G-1=1/64 G-2=46/64
		IDC	G-3=15/64
		ILCI	G-2=1/64
		Phyloides	=1/64
60-70	29	IDC	G-1=4/29 G-2=17/29 G-3=7/29
		ILCI Phyloides	G-1=1/29 0
>70	13	IDC	G-1=0 G-2=9/13 G-3=2/13
		ILCI Phyloides	G-2=2/13 0

There was no first degree family positivity in this age i.e 20-30 years of age group .However in 45-60 years of age group, first degree relative positivity was imminent in sister and mother. It was observed that the sisters of CA breast diagnosed patients were mostly positive for IDC grade 2 and grade 3, grade 1 being the least and the positivity incidence being only 1 in ILC grade 2 .The mothers in first degree family were positive for Ca breast tumor type IDC grade 2 and 3 only. The daughters weren't found to be positive in any single category (table 2).

Table 2: First degree relative positivity

Age	Sister	Mother	Daughter
20-30	0	0	0
30-45	IDC G1=1/47 G-2 1/47 G-3=1/47	IDC G-2=1/47 IDC G-3=1/47	0
45-60	IDC G-2=2/64 IDC G-3=1/64 ILC G-2 =1/64	IDC G-2=1/64	0
60-70	IDC G1= 1/29 IDC- G2=3/29	0	0
>70	IDC G2=3/13	0	0

The secondary malignancies in 2nd degree relative were enumerated between Colon, lung, stomach, breast, brain, Ca tongue, leukemia and thyroid. Among these breast Carcinoma took the lead and manifested the most in age group 60-70, with thyroid being the least secondary malignancy and only eminent in age group 30-45. The secondary malignancy (breast, stomach carcinoma and leukemia) in extended 2nd degree relatives was 100 % among the patients in age group 20-30 years of age (table 3).

Strong predilection for a positive family history in first degree relative increased the risk of breast cancer in the controlled subjects. The crude odds ratio was 0.3977 (95% confidence interval 0.25-0.65). Multiple logistic regression analysis showed that Invasive ductal carcinoma grade II was the predominant type in such patients who had at least one positive first degree relative history and in about 25 % of such patients, presence of other coexisting carcinomas was a key factor. Second most occurring carcinoma was IDC –grade 3 with about 60-70 years age group being the targeted window for increased incidence along with second most number of first degree relative positivity for breast carcinoma in

this age group and Grade 1 being the 3rd most evident in line.

On the other hand, Invasive lobular & Dcis (Ductal Carcinoma Insitu) was evenly divided among the remainder, while malignant phyloides accounted to about 1% in rare setting where as mucinous was next to nil.

Table 3: Secondary malignancy in the 2nd degree family relatives

Age	Colon	Lung	Breast	Stomach	Leukemia	Thyroid	Ca Tongue	Brain
20-30	0	0	2	4	1	0	0	0
30-45	0	0	7	0	0	1	0	0
45-60	1	2	5	0	3	0	0	0
60-70	0	0	8	1	0	0	1	3
70+	1	0	3	0	0	0	1	0

DISCUSSION

From the above extensive research study we can conclude with fair understanding that the incidence of breast carcinoma takes an inverse " U" dip in the aforementioned age groups ranging between 0.03%, 29.7%, 40%, 18.3% & 0.082% in percentage among the respective 20-30, 30-45, 45-60, 60-70 & 70+ age groups with in Paksitan's female population. The types of breast carcinomas categorized up till now are Invasive ductal carcinomas, Invasive lobular carcinomas, malignant phyloides carcinoma & mucinous carcinoma.

The results were formulated in a tabulated form and shall figuratively convey the incidence, risk and correlation between breast carcinomas, first degree family positivity and other carcinomas / malignancies in the extended 2nd degree relative. IDC being the most common carcinoma with in which the grade 2 being the most abundantly graded one for all age groups but specifically in 30-45 and 45-60 [6].

Presence of constant positive family history in sisters for age group above 30 was found. We notice the exceeding risk of other malignancies in age group 60-70 and 70 + at about 44% and 39 % respectively. Presentation at advanced stage is more common and particularly of Invasive ductal carcinoma being the commonest type. Early menarche (<12 years) and late menopause (>60 years) are also indefinite contributing factors [7]. Also no correlation with the occurrence in daughter in all the above mentioned age groups was acknowledged. It is noted that the disease experience in patients below 50 years of age was significant in relation to relatives diagnosed less than 50 years of age where as above 50 years; it was of roughly equal importance for all ages [8]. Thus, having a first degree family history of breast cancer was associated with an increased risk of breast cancer with a magnitude of association being higher in middle and younger age groups but exhausting towards the old age groups.

The presence of other secondary carcinomas also signified that the genetic pool strongly favors the incidence and risk of breast cancer being higher in the same lineage with aggressive outcome. Awareness among the masses remains an important issue. Like the red ribbon of AIDS, the 'pink ribbon' has become the symbol of reverence and care for the sufferers

of breast cancer. The symbol is the brain-child of Evelyn H. Lauder, founder and president of the Breast Cancer Research Foundation and Alexandra Penney, invented in 1991. It helps those already diagnosed and creates awareness for screening and early detection among those who are still spared. The Pakistan Chapter is most active in Punjab while activities in other provinces have not been so pronounced as yet. Self-examination, clinical examination and mammography remain the basis of screening and early diagnosis. This triple approach has brought about marked changes in the early detection of disease in the asymptomatic women in the UK, Sweden etc. where cancer registries are now witnessing a breast cancer mass being detected at a much smaller size and, therefore, more amenable to therapy. Mammography in a particular is said to be as near-example of a perfect screening test as possible with high sensitivity, specificity, negative predictive value particularly in the fatty breast, reproducibility and feasibility [9].

*Strengths / Limitations***:** Patient cooperation has been the biggest achievement in this research, specially, with follow ups since it's a semi government setup and the readily access to data has just aided enough to reach the finishing lines. Fully financed diagnostic tests and rapid identification by qualified consultants, the onco-surgical panel meetings and decisive judgment has all fuelled up the creation of this research.

As for limitations, the current models of breast cancer risk assessment are limited. Exploring the progression from healthy tissue to malignancy through techniques such as fine needle aspiration, ductal lavage, and nipple aspiration may lead to more precise individualized risk prediction. Lack of awareness on the issue, its diagnosis early management and complications have instilled an unhealthy fear in the minds of patients leading to reluctance and refusal to treatment. Cultural and ethnic factors also come into play building the resistance towards a male surgeon/radiologist. Sometimes the mechanical disruption and upgrading of diagnostic tools has also been a hindrance, owing the delay to treatment. Late consultation for a chronic disease has been the biggest impedance that left us with little choice and time to maneuver.

CONCLUSION

The incidence of breast carcinoma is strongly linked with familial predisposition of the first degree relative positivity and is influenced by the presence of other secondary malignancies in the first and second degree relatives that become aggressive and pronounced in later ages above >60. It is there by strongly recommended to evaluate and examine oneself monthly post cycle for women between 20-45 years of age & those among these who have a positive first degree family relative should also bi annually get themselves examined by a Gp/surgeon & investigated, to negate and nip the tumor in the bud before the likelihood of it. Those above 45, with a positive first degree family history should be investigated for secondary malignancies prophylactically.

Authors Contribution:

AS: Concept & design, edited, review and approved the manuscript.

TF: Data analysis, interpretation, and wrote the manuscript.

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