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# Insight into deviating breast cancer; East vs west: hurdle in achieving the global Millennium sustainability goal

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**Abstract**

**Background:** Global sustainable health is an important target of the United Nations Organization. While talking globally, the variable scenario of breast cancer incidence is an important hurdle in achieving the said goal. Throughout the last few years, the incidence of breast cancer (BC) has been increasing fast in East Asia, and now BC became most common in several countries. The increasing incidence of breast cancer (BC) is more likely to change in lifestyle and environmental factors and increase the awareness and screening of BC at early diagnosis. We are working on different angles of breast cancer incidence and sustainable approaches.
**Material & Methods:** We report the epidemiology and biology of breast cancer in Pakistani women and its deviations from the West. The study was conducted based on Helsinki-consented questionnaires filled by 150 female breast cancer patients from two city hospitals; Shaukat Khanum Memorial Hospital and Mayo Hospital, Lahore. The epidemiological, biological, and clinical factors were studied and compared.
**Conclusions:** Adaption with change of strategy is important. The present study impacts the diagnosis, prevention, and breast cancer management of ethnic diversity.

**Keywords:** Paternalistic Leadership, Organization Citizenship Behavior, Effectiveness

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## 1 Introduction

Breast cancer (BC) is the most common cancer of women in many countries of the world(American Cancer Society, n.d.). Regarding to the report by GLOBOCAN in 2018, the overall age standardized of BC incidence rate in Southeast Asia is 1/100 000 which is less than half of that in Australia, New Zealand, Europe and America (I. Aziz et al., 2013). However, in contrast, incidence rate of BC is decreasing in west from 1990 to 2008, while it is rising in Asia. Pakistan has highest incidence of breast cancer in Asia (S. Aziz et al., 2003).

Mainly the BC management and understanding in east is currently depending on western research (Farhana Badar, Shahid Mahmood, Raqib Faraz, Aneel Yousaf, Ain ul Quader, 2015). But reported work proved that eastern epidemiology and cancer biology of BC may have deviations from west (Bhoo-Pathy et al., 2013). Not only the epidemiology; in eastern women; prevalence of different BC subtypes, more immune active microenvironment and different spectra of germ line mutations is also deviating from western approach (Bhurgri1 et al., 2007). Moreover, difference in tolerance of certain cytotoxic agents (which affects BC treatment), lower body mass (which affects drugs administered with fix doses), lower breast volume (which affects type of surgery) and increased breast density (which may affects the sensitivity to mammography) are main differences from western subjects (BOICE, 1996). Currently it is considered that life style changes, environmental changes, lack of awareness and delayed screening are important causes of rising incidence of BC (Freddie Bray, Jacques Ferlay ME, Isabelle Soerjomataram, Rebecca L. Siegel MPH, Lindsey A. Torre, 2020). Our present study is one step of cascade studies on breast cancer in Pakistan. Presently, we pondered and compared the epidemiology and biology of BC in Pakistani women which may have deviations to western reports. Keeping in view the renown reported work; we compared our research work with authentic reported work of International Agency for Research on Cancer, Shoukat Khanum Hospital and Research Centre, GLOBOCAN report, American cancer society and other advance data in relation to the researched topic (Beral et al., 2002; Bingham et al., 1989; Cheng SA, Liang LZ, Liang QL, Huang ZY, Peng XX, Hong XC, Luo XB, Yuan GL, Zhang HJ, 2018; Collaborative Group on Hormonal Factors in Breast Cancer., 2012). Our research work may impact the process of diagnosis, prevention and management of breast cancer strategies.

### Materials and methods

Data was extracted from Helsinki-consented questionnaires filled by 150 breast cancer female patients (fully informed about research) who were recruited at two metropolitan hospitals; Shukat Khanum Memorial Hospital and Mayo Hospital, Lahore. Ethical committees of both hospitals have consented positively. This medical research followed set criteria for the process of data collection. Parameters such as epidemiological, biological and clinical factors (Geographical variations; Educational status; socio-economic level and feeding choice; smoking status; exposure to environmental and biomass emissions and age at visitation, menarche; marital status were recorded. Besides, use of contraceptives and menstruation regularity; number of children (parity), abortion and breast feeding; Size, grade of tumor and lymph node involvement; Hormonal level, nature of carcinoma and laterality and familial history) were compared and discussed in this research. ICD-O-3 classification was used for grading. Hormone receptor classification was also described.

## 2 Results

### 2.1 Geographical variations

Pakistan is divided into four provinces. In present study, mostly patients (92%) were belonging to rural areas of Punjab province. It may be due to present study venue (Mayo and Shoukat Khanum Hospital, Lahore, Punjab, Pakistan). Remaining 7% were from Khyber Pakhtunkhwa (NWFP) and

only 1% was from Baluchistan and study followed research protocols of social sciences and medical settings. There was no patient from Sindh province (Figure 1) for the population of the study.

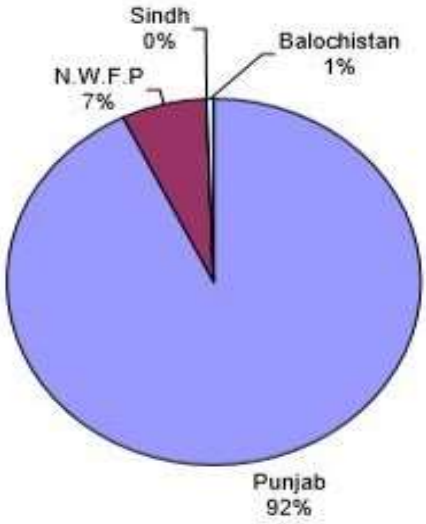


**Figure 1:** Geographical representation of patient ethnicity of four provinces

## 2.2 Educational status

Educational status (Uneducated, primary, secondary, and higher) was studied. Figure 2 shows that 51% of breast cancer patients were uneducated (no formal education in school), 19% of patients had primary education (studied till class 2-5), 20% had secondary level (undergraduates) and 10% were educated till university level (>/graduation).

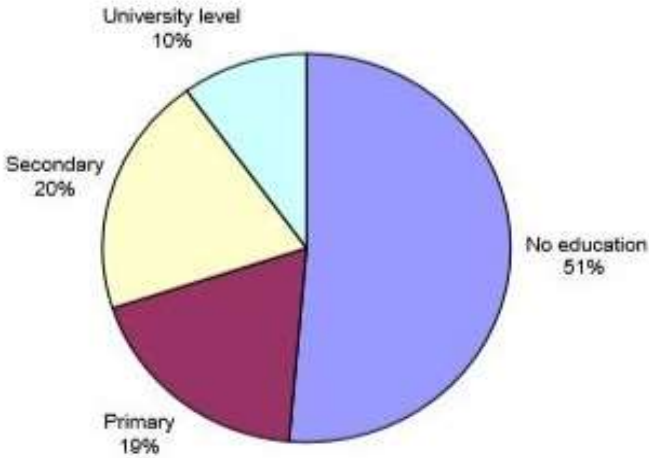


**Figure 2:** Educational levels of selected patients in the current study

## 2.3 Socio-economic level and feeding choice

The income per month in Pakistani currency has been taken as a tool for measuring socioeconomic level of patients. One Pakistani rupee is equal to 0.0064 dollars (presently). Figure 3A shows that only 7% patients belonged to high income level (<20,000 RS/month), 33% belonged to middle (=20,000/month) and 60% belonged to lower income level (>20,000/month). Feeding choice of breast cancer patients was studied. Figure 3B represents the feeding choice of BC patients. It shows that only 13% of patients prefer vegetables in their diet and remaining (87%) preferred red meet and products made up of animal fat.

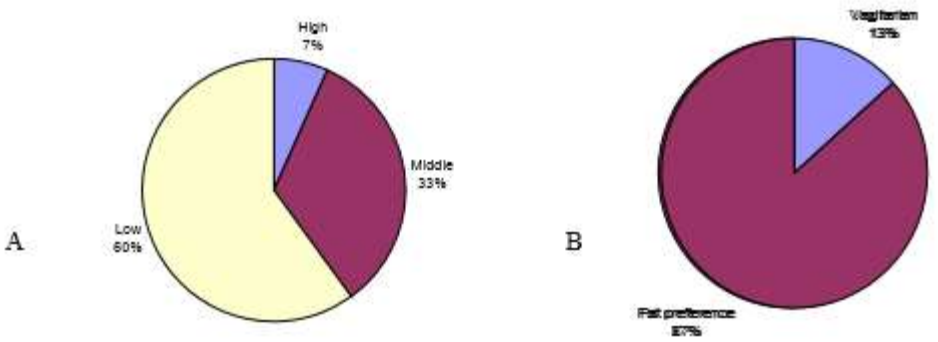


**Figure 3:** (A) Percentage of economic status of patients show three groups (High, Middle and Low) & (B) Representation of feeding choice of patients

## 3 Smoking status

Figure 4(A & B) shows the smoking status of breast cancer patients. Figure 4A shows that 3 % were smokers and 97% nonsmoker breast cancer patients participated in the concerned study. In case of passive smoking, Figure 4B shows that 36% patients with close relatives (husband, son and father) were smokers and 64% patients were not even the passive smokers.


Figure 4: (A) Representation of smoker patients and (B) passive smoking status selected in current study

## 4 Exposure to environmental and biomass emissions

It has been reported that the emissions from biomass (wood) and X-rays are also probably

carcinogens for humans 29. So, information about the way of cooking food the patients and exposure to environmental emissions was collected. Figure 5A shows the information on the type of fuel used for cooking food while Figure 5B shows the exposure to X-rays and other carcinogens. Figure 5A shows that 40% of the patients used wood as fuel and 60% used gas. Figure 5B shows that 6% have worked under intense sunlight, 7% patients had exposure to X-rays and 3% had exposure to power station or electric cables passing over their residences.

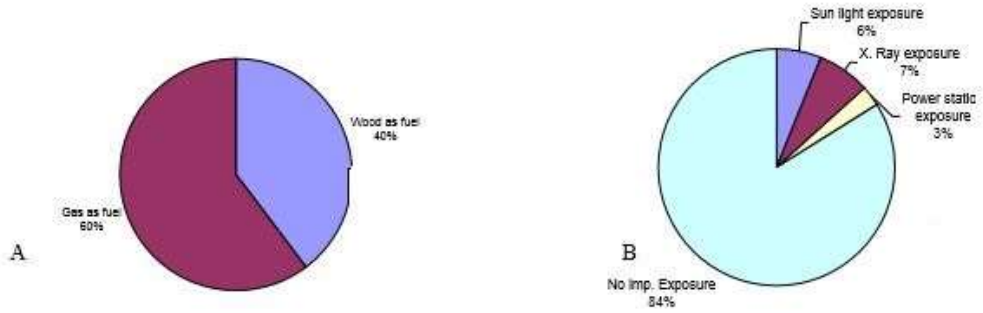


**Figure 5**: (A) Represent the type of fuels used by patients while (B) represents the exposure of patients to environmental carcinogens

## 5 Age at visitation

The information on the age group who visit doctors for seeking advice has been shown in Figure 6. It was observed that 19 % of patients came to see doctor first time at the age of 30 years, 36% of patients at the age of 40 years, 19 % of patients at the age of 50 years, 10 % of patients at the age of 60 years and 16 % of patients at the age of 70 years. So, majority of patients (74%) visited the physicians in early age, i.e. 30-50 years.

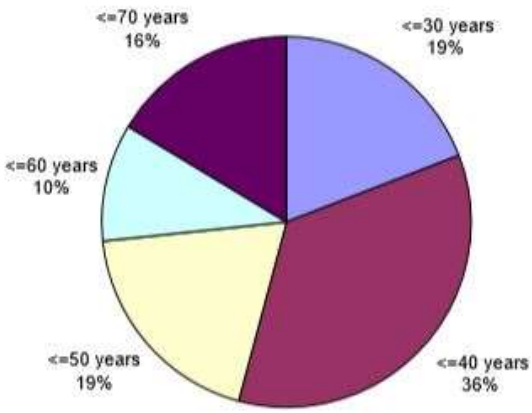


**Figure 6**: Different ages of patients who visited doctor for diagnosis of breast cancer

## 6 Menarche

Figure 7 shows the age at which the menarche was started. It was 12 years for 11% of patients, 13 years for 42% of patients, 14 years for 28% of patients, 15 years for 11% of patients, 16 years for 0% patients and 17 years for 1% of patients and 18 years for 10% of patients. It was concluded

that early age of menarche was more prominent in present study.

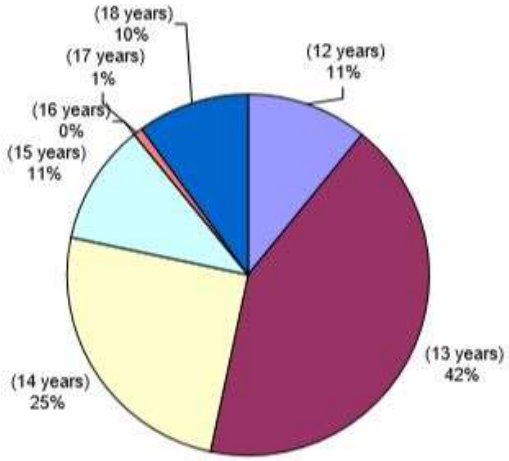


**Figure 7**: Representation of patient's age at which menarche was started

8. Marital status, use of contraceptives and menstruation regularity

Figure 8(A) shows that out of all breast cancer patients only 5% were unmarried. Figure 8(B) shows that only 8% had used and 92% had not used any type of contraceptives. Figure 8(C) shows that among all, 7% patients had no regular menstruation and 93% had regular menstrual cycle.

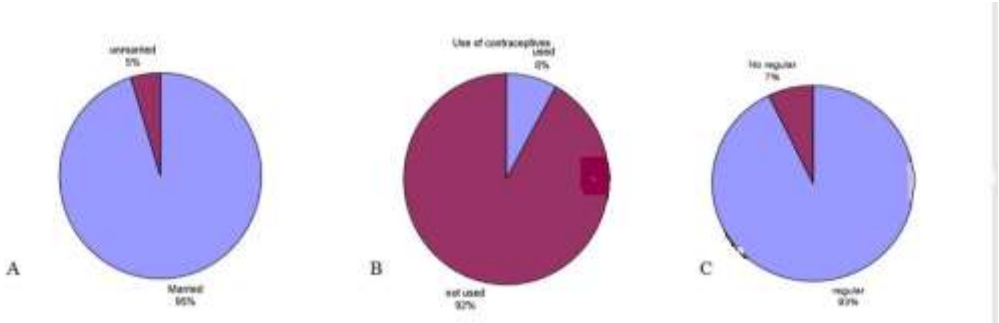


**Figure 8:** (A) Represent the marital status of patients, (B) using contraceptives, and (C) represents the regularity of the menstrual cycle

## 7 Number of children (parity), abortion and breast feeding

Figure 9A shows that 5% of breast cancer patients had 1 child, 29% had 2-3 children, 46% had 4-6 children, 7% had 7-9 children, 5% had 10-12 children and 8% were nulliparous. Figure 9B shows that 49% patients experienced the child death before or after birth whereas those of 51% patients' children were all alive. Figure 9C shows that 81% patients had breast fed their children, whereas; 19% had not breast fed any of their child.

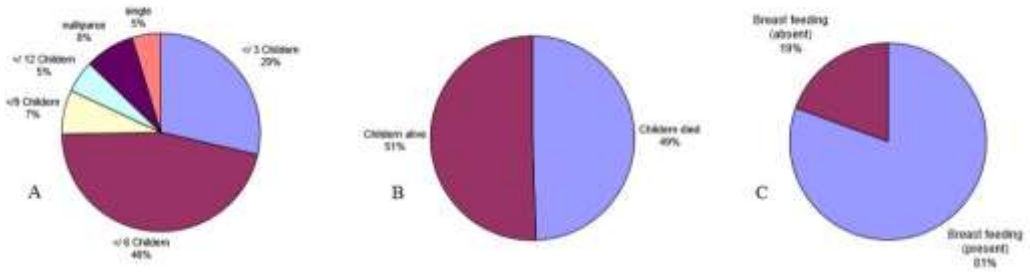


Figure 9: (A) Represent the number of children of patients, (B) abortion status and (C) show the patients that had breast feeding to their children

## 8 Size, grade of tumor and lymph node involvement

Figure 10 shows the status of breast cancer. Figure 10A shows that 15% patients had breast tumor size of 0.5-2 cm, 47% of the patients had 2.1- 3.5 cm, 19% had 3.6- 4.5 cm, 12% had 4.6- 6 cm and 7% of patients had size of 6.1- 9 cm. Figure 10B shows the tumor grade: only 2% patients had their tumors at grade 1, 47% had tumor grade 2 tumors and 51% had grade 3 tumors. While 62% breast cancer patients showed lymph node involvement whereas 38% patients have not shown lymph node involvement [Figure 10C].

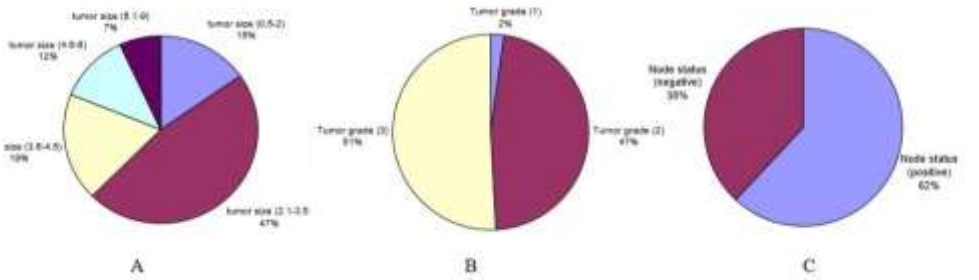


**Figure 10**: Represent different positions and statuses of breast cancer in patients (A) show size (B) show grade and (C) show involvement of lymph nodes in patients

## 9 Hormonal level, nature of carcinoma, and laterality

Figure 11A shows that 51% of patients were ER+/ PR+, 37% were ER-/ PR-, 4% of patients were ER-/ PR+, and 8% of patients were of ER+ / PR- status. Figure 11B shows that 86% of patients were suffering from in situ ductal carcinoma, 9% had invasive lobe carcinoma and 5% of patients had both types of breast cancer. Figure 11C shows that 41% of patients had left breast involvement, 51% of patients had right breast involvement, whereas only 1% of patients show both sides of involvement in breast cancer. The data about 7% of patients was not available in this regard.

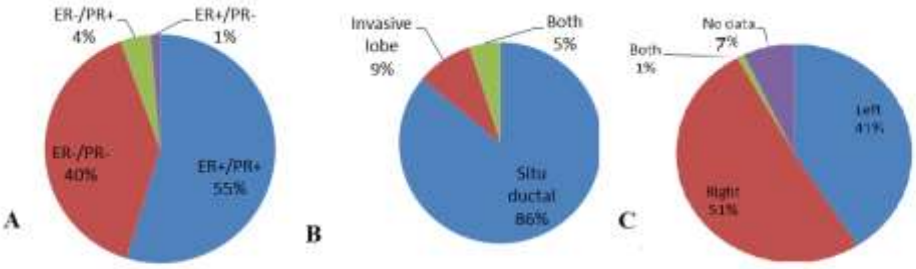


**Figure 11**: (A) shows the status of hormonal level in patients, (B) shows type of cancer and (C) show laterality of breast

## 10 Familial history

Figure 12 shows that out of 150 patients 98% had sporadic breast cancer and only 2% had familial background of breast carcinoma.

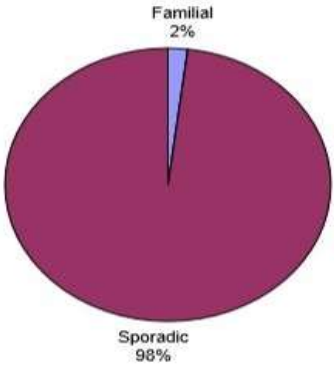


**Figure 12:** Representation of familial and sporadic breast cancer in patients participating in this study

## 11 Discussion

The rate of incidence vs mortality of breast cancer in Asian countries is different to west.5 South-Asian country; Pakistan has same scenario (Figure 13).

Figure 13: Inequality in incidence vs mortality of breast cancer (per 100 000 population of Pakistan in comparison with western world). Left map shows the rate of incidence of breast cancer in Pakistan is lesser than other western countries e.g. Australia; Right map shows the rate of mortality of breast cancer is more than western countries

It is generally considered that the risk factors for breast cancer as studied in west are same worldwide. However, we could not negate the gene-gene and gene-environment relation, which may affect disease from diagnosis to treatment. Presently, we studied the breast cancer in Pakistan; epidemiology to biology as discussed under:

The hypothesis for present study is "Breast cancer in Pakistan has deviations to west". Now we will discuss each risk factor individually, studied in present research:

Rural disparity of BC incidence was found in present research. Rural vs urban disparity is studied worldwide. One belief is that the rural women is more blessed for living in nature and second is that the rural women is cursed for living in nature (Hoffman et al., 1989). Such as living beyond the facilities including early diagnosis, advanced screening techniques and treatment (*Department of Health. Interim Advice to GPs on Familial Breast Cancer. London: Department of Health.*, 2000). In west, more urban more prone to breast cancer is considered. The overall age standardized BC incidence rate in Southeast Asia is 1/100 000 (Devesa & Diamond, 1980).Women are less than half of those in Australia, America, Europe and New Zealand (Ewertz, 1988). Many studies have also reported similar type of habitat of cancer patients in Pakistan (Faggiano et al., 1994; Fan et al., 2014).

Low income community was surveyed with higher incidence of breast cancer in present study. While high income community is considered with more incidence of breast in west. National Health Epidemiologic Follow-up Survey (NHEFS) of United States of America (USA) reported; higher the socioeconomic level higher the BC incidence. Other reported data from USA also confirms the said correlation (Farley & Flannery, 1989; Ferlay et al., 2018; Freddie Bray, Jacques Ferlay ME, Isabelle Soerjomataram, Rebecca L. Siegel MPH, Lindsey A. Torre, 2020; Fritz et al., 2000; Gaudet et al., 2013; Gomes et al., 1995). Studies conducted in other western countries e.g. Brazil Finland, Italy, Denmark and Australia suggests the same disparity (Hedau et al., 2004; Helmrich et al., 1983). International Agency for Research on Cancer (IARC) are also favors the present study (Huang et al., 2019).

Comparative study for observing the association between breast cancer incidence and community income in two neighbor countries; Canada and United States shows higher incidence of BC in economically strong communities. While; it is interesting that India has likewise geographical and cultural similarities with Pakistan, but many Indian studies are not in favor of present study. Most

of studies show that BC was a disease of high socio-economic community (Parkin, 1985). Differences in reproductive, high fat diet and lifestyle factors may be the reasons of BC incidence link to high socioeconomic community (Jussawalla & Jain, 1977).

Less educated community was found more prone to BC incidence in present research. This is an interesting factor that in west; BC is reported more incident in higher educated women. Studies in United States, Canada indicates that women with more than 12 years of education have significantly increased risk of breast cancer (Kang et al., 2018). Israel is also in favors of positive relation (Krieger, 1990).

Low food transition was found in present study. Although 87% of BC patients were fat lovers but due to low socio-economic as well as rural traditions; abundance of cereal, fiber and other traditional food are ingredient of their daily intake of food. As compared to present study in west food transition has been evolved from prudent to western style.

Low environmental exposure is reported in present study. As compared to western life style, urban environmental exposures (chemicals, carcinogens and auto mobile carbons) were not significantly informed in present study. Basing on American Environment protection agency's data, reported various hazardous environmental exposures which are threat for breast cancer patients (Kurebayashi et al., 2015).

However, emissions from biomass, wood (household combustion) and working in sun (geography) were recorded as usual events in present study. It has been reported that the household coal combustion emissions are carcinogenic to humans and that emissions from biomass and wood are also probable human carcinogens (Lawson, 1999). In case of other radiation exposure; a study has reported that frequent exposure to X-rays and other radiations may increase the risk of breast cancer. In the present study, 7% patients passed through intense x-rays exposure and 3% had power station exposure due to their residence near power stations which may prove a risk factor (C. Lin et al., 2012)

Null alcohol consumption, lower passive and lowest active smoking in breast cancer patients was recorded in present study. According to western researchers, women having 2-3 drinks per day have 20% more chances of getting BC (C.-H. Lin et al., 2014). As alcohol consumption is not recorded so it may not a prominent risk factor in Pakistan. While passive smoking (36%) recorded in present research may have alarming importance. Because, many studies reported passive smoking as risk factor for BC in western women especially when the event takes place during childhood and premenopausal age (Liu et al., 2015). In case of active smoking; is not in-vogue in Pakistan (only 3% patients with active tobacco smoking) so western research may not in agreement with Pakistani situation. Regarding to researchers of American Cancer Society, the women, started smoking 10 years before their first pregnancy have 18% more chances of BC (Mackillop et al., 2000).

Low use of contraceptives was studied in present research. Minor use of oral contraceptives (8%) was recorded in present study. According to western studies 20% BC is linked to use of contraceptives with diminish effect of low quantity.

**12 Biological factors**

Young age at time of visitation was recorded in present study which is in contrast of western studies. The median age of white women is 63 years and it is slightly low in black women.i.e.60 years (Madigan et al., 1995). While in present study, only 10% BC patients were presented in said group (<=60 years). It is considered that young age at time of BC diagnosis is major difference in BC epidemiology in east vs west. Published data from China, Taiwan, Japan and Korea shows that BC onset is between 45-49 years in comparison to United States with 70 years (Martínez et al.,

2017). However, with the consideration of age-cohort effect, it may possible that the age onset may become more similar in east and west with time (Ghosh et al., 2011).

No problematic menstruation cycle was recorded in present study. Age of menarche was recorded between 13-14 years in 67% BC patients with normal menstruation. According to western studies early menarche than 11 years of age is linked to breast cancer (20%) while menarche at the age of 14 years and more is considered normal (Collaborative Group on Hormonal Factors in Breast Cancer). Many researches agree with current study while breast cancer is a post-menopausal disease in the West (Nasca et al., 1992; Onitilo et al., 2009; Orsini et al., 2016).

Married status, parity, and prolonged breastfeeding are studied in a high percentage with no protective role in the present research. In the case of single/unmarried factor as a risk for breast cancer; studied the magnitude of the differences in incidence rates between single American black women and other marital statuses (widowed, married, and divorced) ranging from 1.2-1.4 times higher for breast cancer (Paffenbarger Jr et al., 1980). Another study has also found higher mortality in unmarried breast cancer patients as compared to married ones (Parkin, 1985). While considering parity as a protective factor, reported a higher frequency of breast cancer in nulliparous females (Pervaiz et al., 2015).

Likewise, it is commonly reported from the West that breastfeeding is the strongest protective factor against breast cancer. The risk of breast cancer has been studied reduced to 4% with every 12 months of breastfeeding (Polednak, 1990).

No Family history was studied in 98% of BC patients. Only 2% of patients have a first-degree family history. While in Brittan, this ratio is between 6-19% (Pukkala, 1995). According to a cross reference of American cancer society; facts and Figures, the risk of having breast cancer get doubled with more than one first degree relatives (Rana F, Younus J, Muzammil A, Raza S, Siddiqui S K, Khan U, 1997).

Large tumor size was studied presently. Most of the patients reported to the hospital with large tumor size even up to 9cm and only 15% of patients came to the hospitals with 0.5-2 cm tumor size. This data coincides with the findings of two studies, who worked on morphological features of breast carcinoma in Pakistan and found that most patients were presented with tumors greater than 5cm. Due to awareness about BC in the West and early diagnosis, tumor size also has been seen as small on the first encounter. It is considered in the west that with 5.1 cm the survival rate is 50% and with 0.5-2 cm the crude 5 years survival rate is about 90% (Setiawan et al., 2009; Shiyanbola et al., 2017).

Advance tumor grade has been seen in present study. Most of the Breast cancer patients (82%) presented themselves with advance tumor grade (II-III). Reasons for late presentation were i.e. unavailability of physicians, no female physicians, being shy to discuss or show the breast lesions to physicians and lump being painless. While a study shows the difference of breast cancer in U.S. residing Indian-Pakistani versus non-Hispanic white women and concluded larger tumor size and higher tumor grade in Indian-Pakistani group (Siddiqui et al., 2000).

Node involvement has been observed in present study in greater percentage (62%). Many studies clear differences in East and West with more node involvement in Indian-Pakistani breast cancer patients (Sivasubramaniam et al., 2015; "SKH&RC," 2019; Sung et al., 2016).

Laterality of right breast was studied in present research. The difference was not significant however right breast showed higher percentage (51%) of involvement. Many studies find same results in China and related the right breast laterality to younger aged BC incidence (Sung et al., 2015; Swanson et al., 1985; Thakur et al., 2017; Usmani et al., 1996; Wagener & Schatzkin, 1994).Research studied laterality in USA and found that left breast involvement in significant

number of breast cancer patients of any race or of any stage of cancer (Weiss et al., 1996).

Estrogen/ Progesterone (ER/PR) status was positive. A higher frequency of ER+/PR+ status of hormones (Estrogen and Progesterone) was observed in the present study. Some studies from coincide with us (Wells & Horm, 1992; Westhoff & Pike, 2018; White et al., 2017; White & Sandler, 2017).This study carried out a multiethnic Cohort Study and found significant differences even within the same tumor stage. The same group has found ER-/PR- tumors significantly high in the African-American group (Williams et al., 1991; Xiao et al., 2019; Yap et al., 2019; Youlden et al., 2014).

Infiltrating/invasive Ductal Carcinoma (IDC) was observed in 86% of patients. The results of these studies from Pakistan coincide with us (Youlden et al., 2014). Many studies analyzed the epidemiology of breast cancer at Shukat Khanum Hospital Lahore, Pakistan, and confirmed that 85.2% of BC patients (mean age 48.6 years) were suffering from IDC. While according to American Cancer society in American women (40-49 years of age), only 14% invasive cases were observed (American Cancer Society, n.d.).

## 13 Conclusions

It is concluded that as Pakistani women have deviations to western acquaintance so Pakistani women should include in the international clinical trials to provide insight into effectiveness of treatment.

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