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**INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES**Available online at: <http://www.iajps.com>**Research Article****CLINICAL PRESENTATION AND LIFESTYLE RELATED RISK
FACTORS OF BREAST CANCER AMONG DIFFERENT AGE
AND ETHNIC GROUPS****Asma Yousafzai^{1*}, Nisar Ahmed¹, Muhammad Luqman, Hafiz Khush Naseeb², Neelam Hashmi, Kiran Rani³, Muhammad Murad¹, Muneza Arbab¹, Mahnoor Ejaz⁶, Umair Ahmed⁵, Abdul Wali¹, Naheed Sajjad³, Abdul Hameed Baloch⁴, Jamil Ahmad¹**¹ Department of Biotechnology, Balochistan University of Information Technology and Management Sciences (BUITEMS), Quetta.² CENAR Hospital (Center for Nuclear Medicine and Radiotherapy)³ Department of Biotechnology, Sardar Bahadur Khan Women University, Quetta, Pakistan⁴ Department of Animal Breeding and Genetics, Lasbela University of Agriculture, Water and Marine Sciences, Uthal, Pakistan⁴⁵ Department of Chemistry, Balochistan University of Information Technology and Management Sciences (BUITEMS), Quetta.⁶ COMSATS Institute of Information Technology, Islamabad, Pakistan.**Abstract:**

Breast cancer (BC) is one of the most frequent and leading cause of malignancies in females globally. In Pakistan, breast cancer is most frequently found in younger individuals and late stage presentation is the key feature for clinical diagnosis. Numbers of genetic factors are reported to be significantly associated with the manifestation of breast cancer. A number of factors including gender, age, genetic predisposition, familial vertical history, ethnicity and life style eventually leading to the development of the cancer. Therefore, we identified the role of biochemical characteristics of all participants in the development of breast cancer. 50 breast cancer patients were enrolled in this study. A written informed consent was taken from each of the patients prior to data collection through questionnaire. People belonging to different ethnic groups: Pashtoon was found to be the highest noteworthy figure of breast cancer patients with an overall of 14 (28%) followed by Afghani ethnic group with 7 (14%), Baloch 15 (30%), Hazara 8 (16%), Punjabi 3 (6%) and Sindhi 3 (6%).

Key words: Breast cancer, Ethnic groups, Cenar Hospital, Balochistan.**Corresponding Author:****Asma Yousafzai,**

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INTRODUCTION:

Breast cancer (BC) is a single disease characterized by uncontrolled growth and spread of atypical cells which if not restrained eventually leads to death. Breast cancer is a malignant breast neoplasm originates from breast tissue. The most common form of breast cancers are ductal carcinoma originate from ducts and lobular carcinoma originate from the lobules; milk producing glands [1]. BC is the most frequent malignancy of females worldwide and is known to be the second leading cause of cancer death among females. Asia and Africa experienced a rapid increase in the annual incidence rates of breast cancer than Europe and North America in the years, from 1975 to 1990 [2]. In Pakistan, the burden of breast carcinoma is high with the late stage demonstration being a common feature. It has been noticed that more than half of the patients are diagnosed in advanced stages (stages III and IV) [3]. BC is a first-degree relative i.e. Parents or siblings have a significantly increased risk of the cancer disease, but any breast cancer case in the family should be studied as a factor for increased chances of the disease. Roughly 5 to 10 percent of breast cancer cases will be due to inherited mutations. Especially for female with positive family history of breast cancer, tests for genetic susceptibility will be usable.

The breast cancers are classified histologically based on characteristics examined from biopsy specimens through light microscopy. They are classified as ductal or lobular carcinoma when they are developed from the epithelium of the ducts or lobules [4] and are further divided into carcinomas in situ i.e. ductal carcinoma in situ and lobular carcinoma in situ. Among non-infiltrating breast cancers Ductal carcinoma in situ (DCIS) is the commonest type and is a heterogeneous disease defined as a neoplastic proliferation within the ductal structure of the breast. In DCIS cancer cells have not yet invaded through the walls of the ducts and remain inside the ducts. Women affected with DCIS would be at high risk to develop invasive ductal carcinoma [5]. The other type is Lobular Carcinoma in situ (LCIS) which is considered as a marker of cancer that may mature into an invasive lobular breast carcinoma. It is also called as lobular neoplasia. LCIS starts in lobules but it does not grow through the wall of the lobules [6]. Of all breast cancers, 55% cases are reported to be invasive ductal carcinoma, whereas 5% cases are of invasive lobular carcinoma and about 13% cases are reported to be of ductal carcinoma in situ [7].

There are several risk factors that lead to the development of breast carcinoma such as age, gender and genetic risk factors. Other risk factors include;

positive family history, race and ethnicity, personal history of hormonal imbalances and breast lumps and lifestyle factors (American Cancer Society). Instead of their ethnic or racial heritage and origin all women are at higher risk of develop breast cancer in their lives [8]. Although men may also be affected by breast cancer but it is very rare and more common in women than men [9]. In female breast cancer risk is highest who give birth to the first child after the age of 35. Becoming pregnant at young age and having many pregnancies decrease the risk of breast cancer, because life time menstrual cycles of women are reduced due to pregnancy that could be a reason to that effect. Menopause at older age greater than 55 years and early menarche at the age of less than 12 years increase the lifetime exposure of reproductive hormones to a woman that can elevate the threat of evolving breast cancer in her lifespan [10]. Breast cancer with distinct hormonal status presents a different prognostic and treatment implications. Previous benign breast disease, radiation, oral contraceptive drugs, hormone replacement therapy, lifestyle including diet, weight, alcohol intake and smoking are also risk factors of breast cancer. The frequency of breast cancer in other Asian states like India, China, Japan, Philippines is much less as compared to Pakistan even though prevalence of the risk factors is similar [3, 11]. Whereas among high-income countries, the incidence rate of breast carcinoma is high in Japan [12]. Therefore, we aim to identify the risk factors that contribute towards the development of BC in Pakistani population.

METHODOLOGY:**Development of a Questionnaire**

A well-informed consent documented in a structured questionnaire was designed to record all the necessary information regarding the breast cancer patients and normal subjects, like socioeconomic status, ethnicity, family and personal history of breast cancer and other related diseases, Age, Sex, BMI, Life style and other associated information.

Study Area

Current study was conducted in Balochistan Pakistan. Balochistan constitutes about 44% of the total area of Pakistan but smallest province with lowest population. Balochistan bordering with Iran southwest, to north and north-west with Afghanistan, to south is the Arabian Sea, FATA and Khyber Pakhtunkhwa to the north east, Punjab and Sindh provinces are to the east. Main ethnic groups of Balochistan are Baloch followed by Pashtoon including both the local and the Afghan refugees. Other ethnic groups are Hazara, Punjabi, Sindhi, Hindus and others. Quetta is the biggest and capital

city of Balochistan, Populated by Baloch, Pashtoon, Hazara, Punjabi and other ethnic groups. There is a single cancer hospital, naming CENAR (Center for Nuclear Medicine and Radiotherapy). The breast cancer patients from different ethnic groups enrolled in current study were registered patients in CENAR.

Enrollment of Breast Cancer Patients and Normal Subjects

In this study 50 breast cancer patients were enrolled, already registered in Center for Nuclear Medicine and Radiotherapy (CENAR) Quetta, Balochistan for treatment and 50 normal individuals from different ethnic groups of Balochistan Pakistan. Clinical history, family history positive for breast or other cancer, age at diagnosis and age of onset of breast cancer, menopausal age in older female patients, marital status, past history of exposure to radiations, usage of contraceptive drugs, breast feeding, hormonal imbalances, hormonal therapy, history of other prevalent diseases both present and past like HBV, HCV, TB, reproductive disorders and others. All the related information was taken from patients. Biopsy reports and other related laboratory diagnosis were collected from the patients files registered in CENAR. Normal subjects were enrolled who were found not to have any special and family history of breast and other cancers. Body Mass Index (BMI) was measured by calculating height and weight of the patients and normal subjects using the metric

measures. BMI Categories included <18.5 to be Underweight, 18.5-24.9 range was considered normal, 25-29.9 index was considered Over weight, whereas BMI of 30 or greater was declared obese. Statistical analysis was performed on all the demographic data using online software's.

RESULTS:

A total of 50 patients of breast cancer were investigated from different ethnic groups. All of the patients were females. Among these, 3 were unmarried. Patients from different classes were included in the study. 10 patients were from the high class, 20 were from the middle class and 20 were from the lower-class families. Out of these 50, 4 patients were working women while the rest of the patients were house wives.

Ethnicity

Ethnicity is an important risk factor of breast cancer. Several factors make the ethnic groups differ from each other i.e. socioeconomic status, geographical variations, lifestyle, genetic makeup etc. Considering the ethnic differences, 7 (14%) patients were Afghani, 15 (30%) were from Baloch ethnic group, 8 (16%) were from Hazara ethnic group, 14 (28%) were Pashtoon, 3 (6%) were Punjabi and 3 (6%) patients were from other ethnic groups as represented in Table 1.

Table 1: Ethnic distribution of breast cancer patients
Ethnicity

	Frequency	Percent	Valid Percent	Cumulative Percent
Afghani	7	14.0	14.0	14.0
Baloch	15	30.0	30.0	44.0
Hazara	8	16.0	16.0	60.0
Pashtoon	14	28.0	28.0	88.0
Punjabi	3	6.0	6.0	94.0
Sindhi	3	6.0	6.0	
Total	50	100.0	100.0	100.0

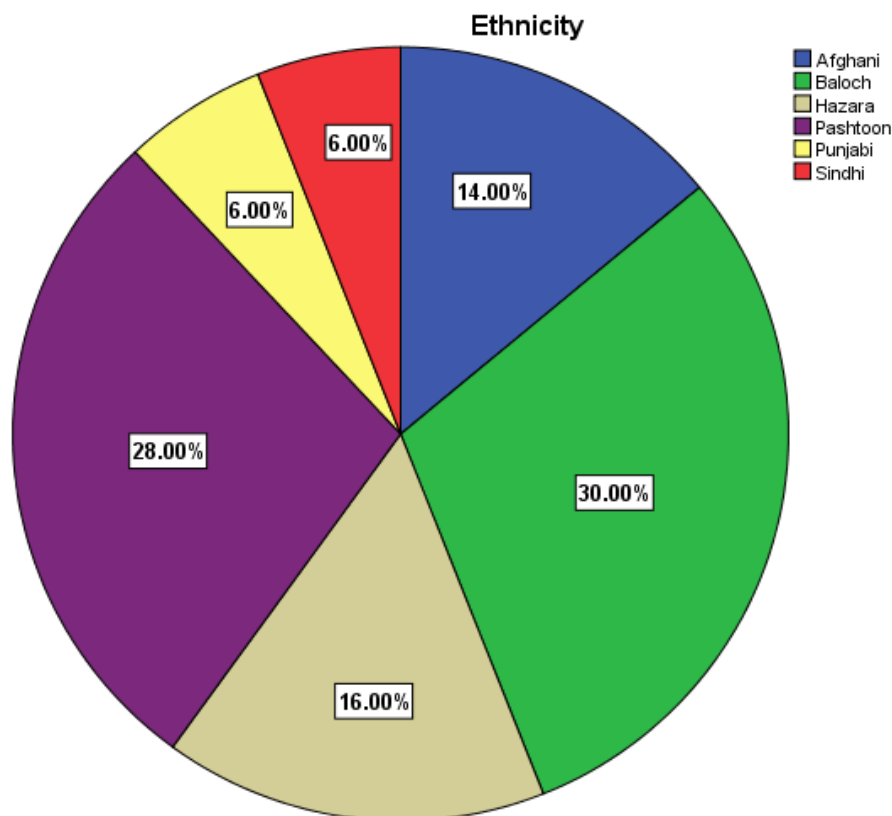


Fig. 1: Showing the percentage of breast cancer patients among different ethnic groups

Age:

Age was found to be a major risk factor for breast cancer as the threat of BC is increased with the increase in age. In current study, there were 8 (16%) patients from 21-30 age group, 18 (36%) were from 31-40 age group, 13 (26%) were from 41-50, 7 (14%)

from 51-60 and 4 (8%) were from 61-70 as represented in table 2. The mean age was 42.72, median age was 40.00, mode was 40.0 and standard deviation was 11.05. Statistics of age are shown in table 3, and cross comparison of age and ethnicity is shown in table 4.

Table 2: Distribution of breast cancer patients in different age groups

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	21 - 30 years	8	16.0	16.0	16.0
	31- 40 Years	18	36.0	36.0	52.0
	41- 50 Years	13	26.0	26.0	78.0
	51 - 60 Years	7	14.0	14.0	92.0
	61- 70 Years	4	8.0	8.0	100.0
Total		50	100.0	100.0	

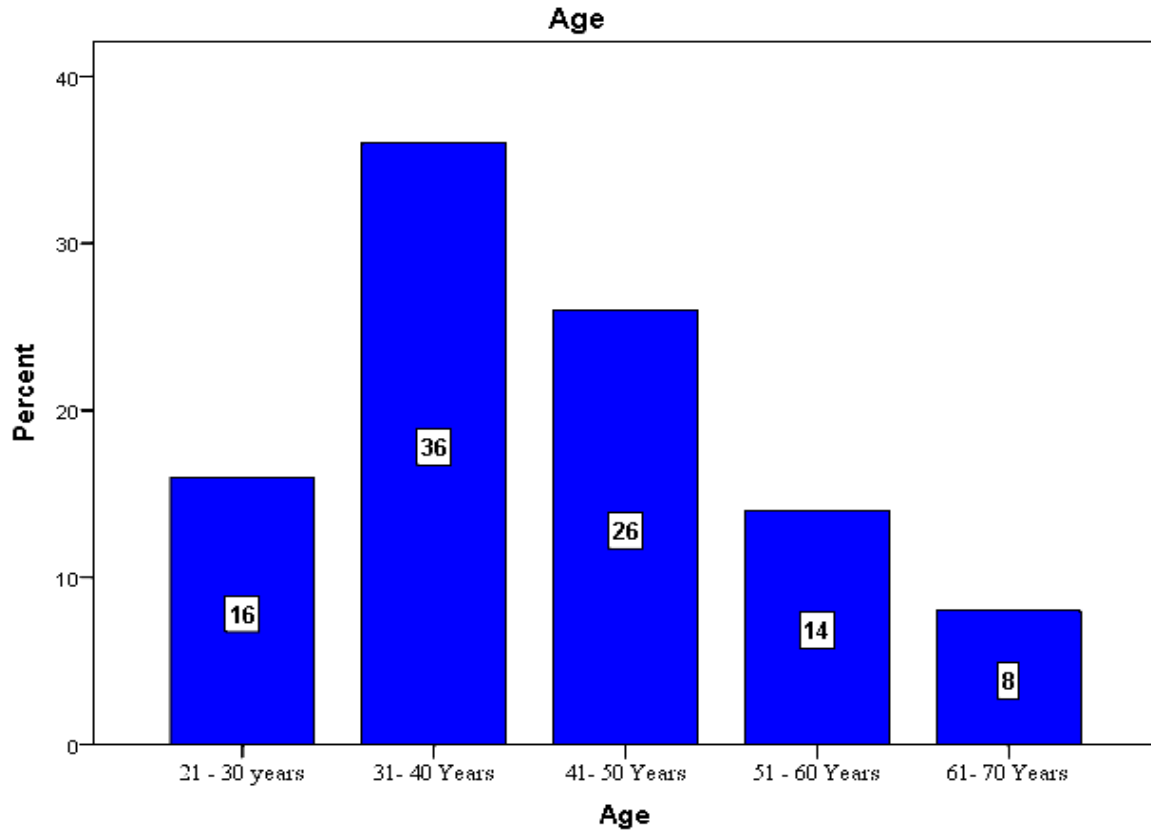


Fig. 2: Showing the percentage of breast cancer patients among different age group

Table 3: Statistics of Age of the BC

N	Valid	50
	Missing	0
Mean		42.72
Median		40.00
Mode		40
Std. Deviation		11.057
Variance		122.247
Range		44

Table 4: Showing the ethnicity and age wise distribution of breast cancer patients

		Age					Total
		21-30	31-40	41-50	51-60	61-70	
Afghani	Count	2	1	2	2	0	7
	% within Ethnicity	28.6%	14.3%	28.6%	28.6%	0.0%	100.0%
	% within Age	25.0%	6.2%	14.3%	22.2%	0.0%	14.0%
Baloch	Count	2	5	6	1	1	15
	% within Ethnicity	13.3%	33.3%	40.0%	6.7%	6.7%	100.0%
	% within Age	25.0%	31.2%	42.9%	11.1%	33.3%	30.0%
Hazara	Count	2	4	0	1	1	8
	% within Ethnicity	25.0%	50.0%	0.0%	12.5%	12.5%	100.0%
	% within Age	25.0%	25.0%	0.0%	11.1%	33.3%	16.0%
Pashtoon	Count	2	4	5	2	1	14
	% within Ethnicity	14.3%	28.6%	35.7%	14.3%	7.1%	100.0%
	% within Age	25.0%	25.0%	35.7%	22.2%	33.3%	28.0%
Punjabi	Count	0	2	0	1	0	3
	% within Ethnicity	0.0%	66.7%	0.0%	33.3%	0.0%	100.0%
	% within Age	0.0%	12.5%	0.0%	11.1%	0.0%	6.0%
Sindhi	Count	0	0	1	2	0	3
	% within Ethnicity	0.0%	0.0%	33.3%	66.7%	0.0%	100.0%
	% within Age	0.0%	0.0%	7.1%	22.2%	0.0%	6.0%
Total	Count	8	16	14	9	3	50
	% within Ethnicity	16.0%	32.0%	28.0%	18.0%	6.0%	100.0%
	% within Age	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

Body Mass Index (BMI)

Body Mass Index (BMI) is reported to be linked with breast cancer. BMI was calculated by measuring the height and weight of the subjects using the metric represented in table 6.

measures. Among 50 breast cancer patients 0 (0%) were underweight, 2 (4 %) were normal, 4 (8 %) were overweight and 44 (88 %) were obese as shown in table 5 and further statistics is

Table 5: BMI of the BC patients (<18.5 represent the underweight, 18.5-24.9 normal, 25- 29.9 overweight and >30 represent the obese).

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	> 30	44	88.0	88.0	88.0
	25-29.9	4	8.0	8.0	96.0
	18-24.9	2	4.0	4.0	100.0
	Total	50	100.0	100.0	

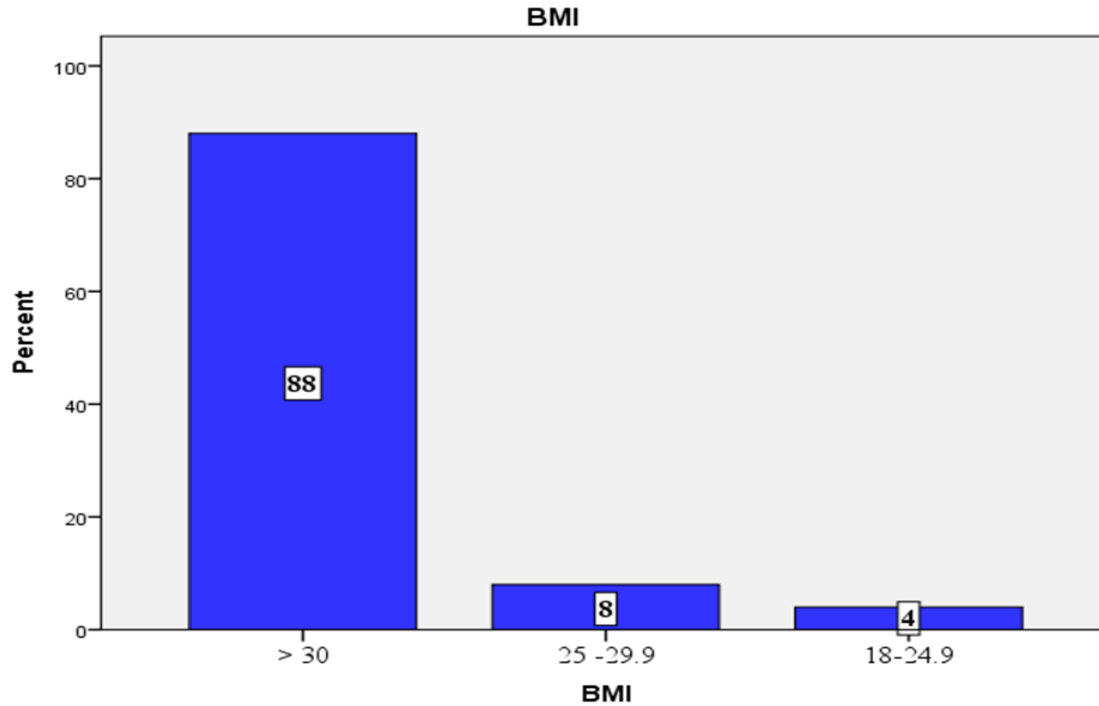


Fig.5: Graphical presentation of BMI among breast cancer patients

Table 6: Statistics of BMI of the BC patients

N	Valid	50
	Missing	0
Mean		38.5340
Std. Error of Mean		1.16159
Median		38.7211
Mode		40.00
Std. Deviation		8.21370
Variance		67.465
Range		40.65

Stage

1 (2%) patients were recorded with stage I, 20 (40%) with stage II, 22 (44 %) with stage III and 7 (14%)

patients with stage IV were recorded as table 7 shows. The stage of cancer among ethnic group was also statistically significant with p-value 0.02.

Table 7: Distribution of the patient according to the cancer stage

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	I	1	2.0	2.0	2.0
	II	20	40.0	40.0	42.0
	III	22	44.0	44.0	86.0
	IV	7	14.0	14.0	100.0
	Total	50	100.0	100.0	

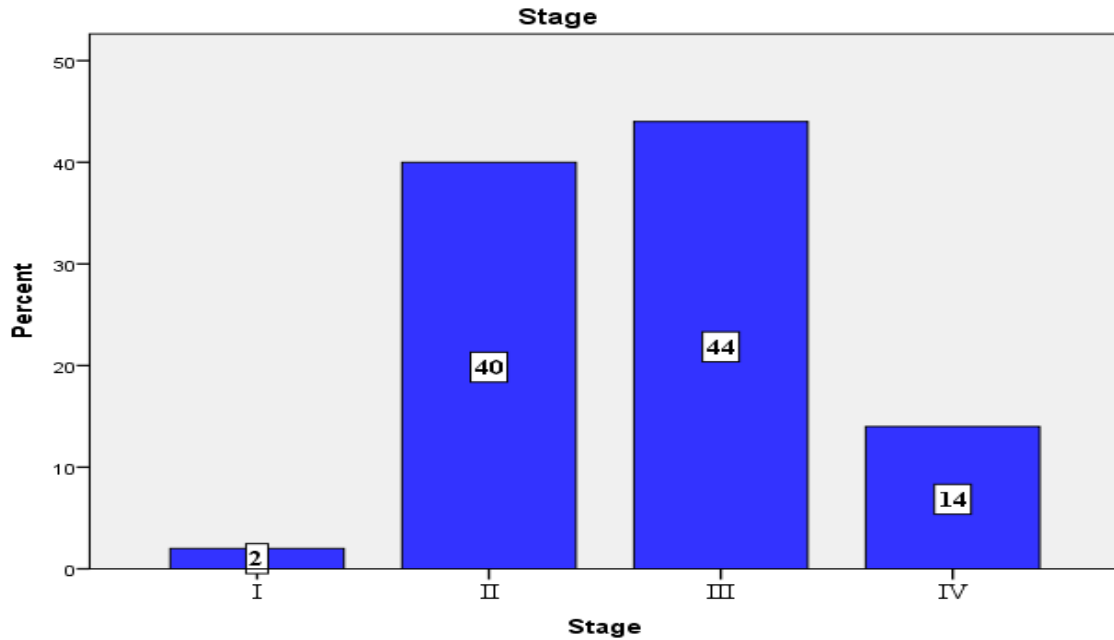


Fig. 7: Graphical presentation of stage of cancer observed in breast cancer patients.

Tumor Location: There were 21(42 %) patients affected by cancers at left side and 29 (58 %) were affected at right side as presented in table 8.

Table 8: Tumor Location

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid Left side	21	42.0	42.0	42.0
Valid Right side	29	58.0	58.0	100.0
Total	50	100.0	100.0	

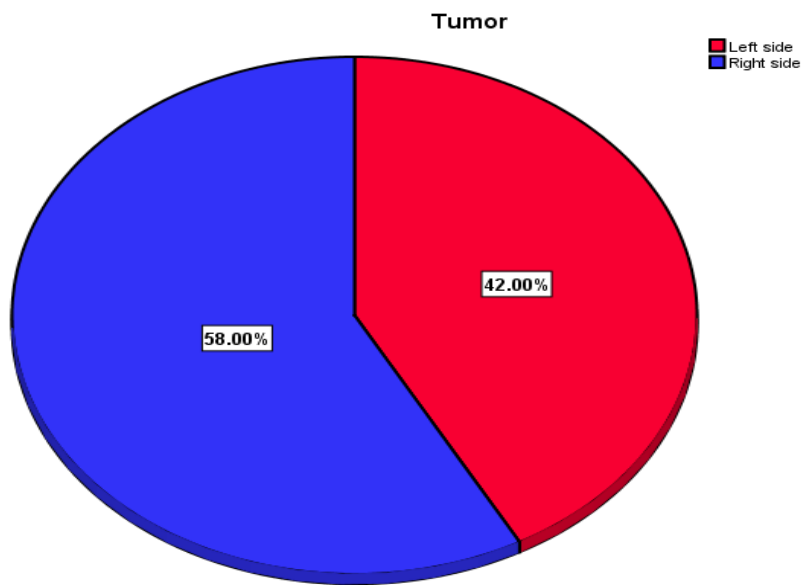


Fig. 8: Tumor Location

Types of breast cancer

Types of BC's were also studied as indicated in table 9, where majority of the patients 37 (74 %) were affected with IDC, others including 7 (14 %) were affected with ILC and 6 (12 %) were recorded with ductal carcinoma in situ (DCIS).

**Table 9: Types of breast cancer
Histopathology Report**

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	DCIS	6	12.0	12.0	12.0
	ILC	7	14.0	14.0	26.0
	IDC	37	74.0	74.0	100.0
	Total	50	100.0	100.0	

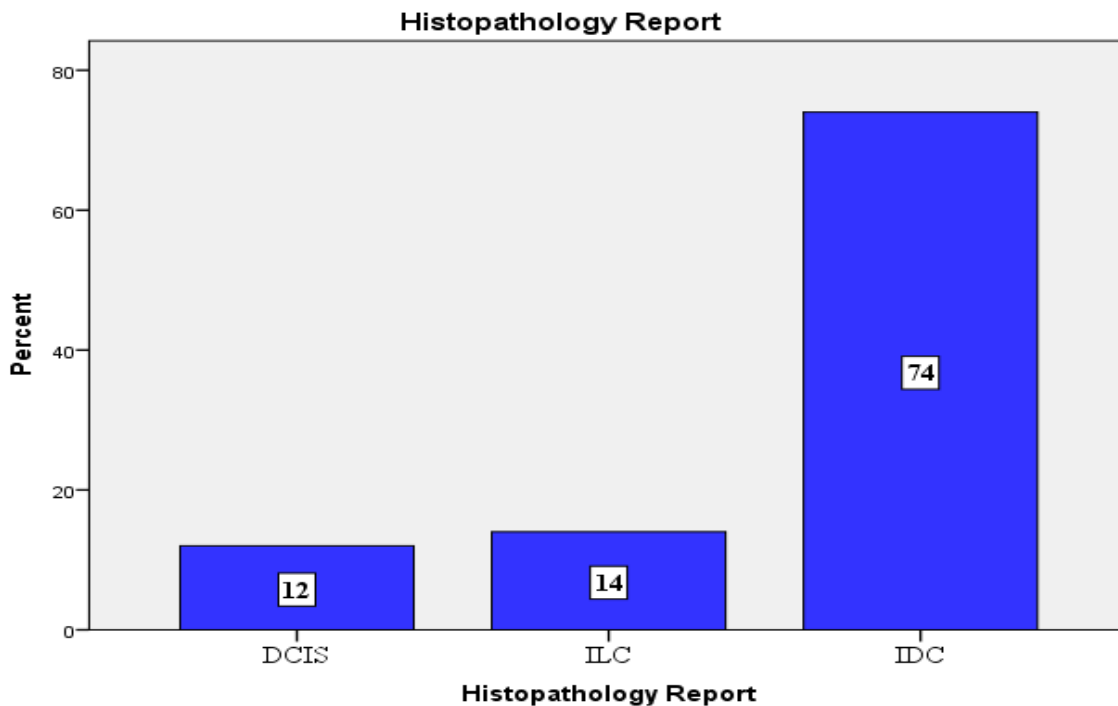


Fig. 9: Graphical presentation of types of cancer observed in breast cancer patients.

DISCUSSION:

Breast cancer is particularly the most diagnosed cancer type in United States and in Europe with estimated rate of cases of this cancer is about 606,380 in 2007, a health associated issue. Representative of 23-26% of all types of cancers with a significant rate of death of 14-15% [13, 14]. A total of 50 female breast cancer patients were investigated in present study. Primary lymphoma of breast was found responsible for affecting both the patients diagnosed at the ages of 48 and 60 years.

In present study, we investigated breast cancer patients from different ethnic groups of Balochistan. People belonging to ethnic group of Pashtoon was with the highest noteworthy figure of breast cancer patients with an overall of 14 (28%) followed by Afghani ethnic group with 7 (14%), Baloch 15 (30%), Hazara 8 (16%), Punjabi 3 (6%) and Sindhi 3 (6%). The survival rates from breast cancer and stages of tumor progression are influenced by Characteristics of tumor, socioeconomic status, life style factors, ethnicity and race [15]. Lifestyle and environmental factors contribute to incidence of breast cancer adjusted to age and varies internationally [16]. In our study the age adjusted occurrence of breast cancer in all ethnic groups were almost same. Patients among all ethnic groups diagnosed with breast cancer were highly between the ages of 31 - 40 years, whereas second age group was 21 - 30 years in Hazara (Pashtoon) and Baloch ethnic groups and in Punjabi, Sindhi and Afghani ethnic groups the second age group with more patients was 51-60 years. Risk factors are almost the same among the ethnic groups like early age menarche, older age of menopause and first child birth at older age are almost same for individual woman (BCERF, Fact sheet No. 47, 2003). Studies suggest that breast cancer in ethnic groups with low awareness have high barriers to high grade and advance stage presentation [17]. It is possible to decline the burden of cancer by spread over the awareness related to cancer control knowledge. A study carried out in South East England found that the black and Asian women diagnosed with more metastatic breast cancer than white women [18]. Among ethnic and racial groups the occurrence of breast cancer is varying considerably showed in their study that cases among white women was 140.8/100,000 yearly based on age-adjusted occurrence rate from 1996 to 2000, 121.7 among African Americans, 97.8 among Asian American/Pacific Islanders, 89.8 in Hispanics and 58 in American Indians/Alaska Natives. White women got inferior incidences of age adjusted breast cancer in contrast to women in ethnic minority. High grade

negative estrogen receptor with greater size of tumor and more advanced stages were mostly identified in African American women compared to that of white women [19]. Age adjusted occurrence of breast cancer is varying globally. In western world, the frequency of age-linked breast cancer occurs at the age of 50 years and above are 81% of cases and about 48% of breast cancers diagnosed in age group 50-69 years (Breast Cancer-UK incidence Statistics, 2011) [20]. But in our study, there is a fluctuation in the incidence of breast cancer among age groups. The age group 31 - 40 years is the highest risk group with more breast cancer patients followed by 41 - 50 years' age group is the second highest risk group, 21 - 30 years' age group is comparatively lesser with that of the 41 - 50 years' age group and in 61 and onward age group is decreasing with very few breast cancer patients. Studies suggest that in younger women, breast cancer is more advanced and aggressive than older women [21]. In present study 41-50 years' age group was diagnosed with mostly high grade (III) tumor followed by 31-40 years' age group and similarly age group 41-50 years also diagnosed with advanced stage (III) breast cancer with more patients followed by stage IV and second highest age group with advanced stages of cancer was 31-40 years. It is also proposed that larger tangible mass with metastasis in many lymph nodes were diagnosed clinically in younger women with breast cancer, more negative hormone receptor compared to older women [22]. American and European Studies have also shown that breast cancer diagnosed at younger age provides data about poor survival [23]. Whereas women of young age can survive better compared to the women of old age influenced by breast cancer presented by Chia *et al* in their study. After tobacco use one of the chief control able risk factor for malignances in humans has been acknowledged as obesity. BMI is also reported to be associated with breast cancer [24]. Studies suggest that obesity may increase the risk of many cancers. Post-menopausal breast cancer, gallbladder cancer, colon cancer, prostate cancer, cancers of kidneys and thyroid, and cancer of endometrium have been linked with obesity [25]. In present study, we investigated 50 (34%) breast cancer patients that were overweight and (16%) were obese. Obesity is connected in dual manner; first one is risk of breast cancer in addition to clinical appearance of the incidence and increased risk of breast cancer of about two-fold in post-menopausal women [26]. Excessive fatty tissues are found guilty to store toxins that act as unceasing cause of carcinogens. Likewise, endogenous estrogen produced by body fat can increase breast cancer risk. Studies suggest that obese women mostly obese at

abdomen raises free level of estrogens. Post-menopausal women with increase BMI are at risk to develop breast cancer [27]. Breast cancers are classified based on characteristics examined histologically on light microscopy. The disease is multifaceted with diverse biological subtypes and natural history. The pathological, clinical and molecular features of all the subtypes of the breast cancer are varying with distinct prognostic and therapeutic implications. In present study, we identified 37 (74%) patients affected with IDC of breast, 7 (14%) were with ILC and 6 (12%) cases were recorded with DCIS. Studies suggest that IDC is the commonest type of breast cancer with diverse subtypes account for about 65-85% of all breast cancers, ILC accounts for about 10% of all breast cancers and DCIS accounts for about 13% of all breast cancers [28]. Reproductive factors including hormone-related risk factors influence the risk of histological types of breast cancer differently [29]. Etiology of breast cancers differs with different histological type for example lobular tumors are mostly associated with age at first birth which is stronger than for other histological types. Clinical features, hormone receptor status and prognosis vary among histological types [30]. Women having age group above than 50 years have rising incidences of ILC may be due to post-menopausal hormonal therapy [31] As compared to invasive ductal carcinoma ILC shows an additional advanced stage for the reason that of capability of the ILC to avoid the early detections [32]. DCIS is a pre-malignant in addition considered to be intensified into invasive cancer conducted study which suggests that several DCIS cases never develop into invasive disorder, raising question regarding development of the IDC from DCIS. Whereas maximum of the studies has suggested that DCIS detected women have shown to be at high risk to grow thorough breast cancer [33]. The pathogenicity of breast cancer is influenced by reproductive hormones. Clinical research of breast cancer patients was also conducted. Out of 50 patients, all of the patients were females. Among these, 3 were unmarried. Patients from different classes were included in the study. 10 patients were from the high class, 20 were from the middle class and 20 were from the lower-class families. Out of these 50, 4 patients were working women while the rest of the patients were house wives. Ethnicity is an important risk factor of breast cancer. Several factors make the ethnic groups differ from each other i.e. socioeconomic status, geographical variations, lifestyle, genetic makeup etc. Women with diverse ethnic backgrounds have different rates of breast cancer occurrence and survival from breast cancer. In current study 7 (14%) patients were Afghani, 15

(30%) were from Baloch ethnic group, 8 (16%) were from Hazara ethnic group, 14 (28%) were Pashtoon, 3 (6%) were Punjabi and 3 (6%) and 3 (6%) were Sindhi patients were from other ethnic groups, were observed. Age is another major risk factor for breast cancer. The threat of breast cancer is increased with the increase of age. In current study, there were 8 (16%) patients from 21-30 age group, 18 (36%) were from 31-40 age group, 13 (26%) were from 41-50, 7 (14%) from 51-60 and 4 (8%) were from 61-70. Body Mass Index (BMI) is reported to be linked with breast cancer. BMI was calculated by measuring the height and weight of the subjects using the metric measures. Among 50 breast cancer patients 0 (0%) were underweight, 2 (4 %) were normal, 4 (8 %) were overweight and 44 (88 %) were obese. 1 (2%) patients were recorded with stage I, 20 (40%) with stage II, 22 (44 %) with stage III and 7 (14%) patients with stage IV were recorded. The locality of the tumor which is an alarming factor found according to our study, there were 21 (42 %) patients affected by cancers at left side and 29 (58 %) were affected at right side. Majority of the patients 37 (74 %) were affected with IDC, others including 7 (14 %) were affected with ILC and 6 (12 %) were recorded with ductal carcinoma in situ (DCIS).

CONCLUSION:

Breast cancer is among the foremost causes of mortality in advanced countries and second biggest cause of deaths in developing countries. Globally breast cancer is a communal cancer in women; however geologically there is unpredictable demonstration of breast cancer. There are several characteristics that contribute in the progress of breast cancer such as age, sex, adaptation of certain life style or inherited risk factors like history of breast cancer running in family, germline mutations, race, ethnicity, and others.

As compared to western population, incidence of breast cancer at younger age is more communal in Pakistan. About $\geq 50\%$ of the reported cases of breast cancer in Pakistan were in advanced stages at the time of diagnosis. As the rate of recurrence is greater in Pakistan as compared to well-populated intra-Asian countries like India and China. The endorsement of breast cancer in women of Pakistan with advance phase has held responsible to conservative society, lack of education and unavailability of national screening programs and others.

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