

A Histopathological Study of the Breast Cancer Cases Registered at Benghazi Medical Center from 2016 to 2018

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المخلص:

الخلفية: سرطان الثدي هو ثاني أكثر أنواع السرطانات شيوعاً بين النساء وهو السبب الرئيسي للوفاة لدى الإناث في جميع أنحاء العالم. **الهدف** من هذا العمل هو دراسة حالات سرطان الثدي المشخصة والمسجلة بمركز بنغازي الطبي من مختلف مناطق شرق ليبيا في الفترة من 1 يناير 2016 إلى 31 ديسمبر 2018. **الموضوعات والأساليب:** جمعت البيانات والدراسة المقطعية من أرشيف قسم الأورام بمركز بنغازي الطبي بالإضافة إلى العينات النسيجية من قسم علم الأمراض بكلية الطب بجامعة بنغازي ومعمل النون الخاص. درست على مدى ثلاث سنوات كان عدد الحالات المصابة 515 حالة حيث تمت دراستها احصائياً لتحديد مدى تكرار الحالات، تحديد الفئات العمرية، ودرجات التمايز المرضية. كما تم اعداد قطاعات نسيجية مصبوجة للتحليل النسيجي. **النتائج:** أظهرت النتائج أن أغلب الحالات (66%) من بنغازي تليها البيضاء (9.1%). ومتوسط اعمار المريضات كان 50 سنة. من خلال التشخيص، 76.9% من الحالات كانت مصابة بسرطان الاقنية وكانت 56% منهم في المرحلة الثالثة وفي الدرجة الثانية 54.2%. سجلت مستقبلات هرمون الاستروجين الموجب في 72.2% من الحالات مقابل 66% من البروجسترون الإيجابي. علاوة على ذلك 61.6% من المرضى لديهم مستقبل عامل نمو البشرة البشري 2 سلبي. **الخلاصة:** معظم مرضى سرطان الثدي في مركز بنغازي الطبي. يزداد التواتر بين سن 46 و 56، ومعظم الحالات- كانت في المرحلة الثالثة، والدرجة الثانية. سرطان الاقنية هو أكثر أنواع الأنسجة المرضية انتشاراً. وكانت معظم الحالات سلبية HER2 مستقبل عامل نمو البشرة البشري 2 و (ER) مستقبل هرمون الاستروجين إيجابية و (PR) مستقبل هرمون بروجسترون إيجابية، ومعظم الحالات كان مستوى (Ki-67) تحميل التلوي لتقييم النشاط التكاثري لسرطان الثدي. (21- 40%).

الكلمات المفتاحية: سرطان الثدي، شرق ليبيا، أرشيف قسم الأورام، مركز بنغازي الطبي.

Abstract

Background: Breast cancer (BRC) is the second most common cancer in the world, the most frequent cancer among women, and the leading cause of cancer death in females worldwide. **Aims** to study the pattern of breast cancer in all the patients who were presented to the Oncology Department at Benghazi Medical Center (BMC) from various parts of eastern Libya from the 1st of January 2016 to the 31st of December 2018. **Subjects and Methods:** This is a retrospective, cross-sectional and histopathological study to determine the frequency of the (BRC) malignancy type, in addition to stages and age groups. The data was collected from the Oncology Department at Benghazi Medical Center which receives cancer patients from Benghazi and the whole eastern part of Libya. Data was also collected from the Pathology Department at the Faculty of Medicine, University of Benghazi and Alnon, a private laboratory. There were 515 registered patients with breast cancer including demographic and clinic-pathological data. The data was analyzed using the SPSS Program Version 20. **Results:** Out of 515 breast cancer patients registered at the Oncology Department (BMC), geographically 66% were from Benghazi, followed by Albaida at 9.1%. **Conclusion:** The majority of cases were between 46 and 56 years old. Invasive ductal carcinoma was diagnosed among most of the cases, (Grade II and stage III). Most of the breast cancer cases collected from BMC were from Benghazi, frequency is higher among the age range (46-56) and most cases were Stage III, and grade II. Invasive ductal carcinoma is the most predominant histopathological type. Most cases were HER2 negative, ER positive and PR positive, and most cases had Ki-67 levels (21- 40%).

Keywords: Breast Cancer, Eastern Part of Libya, Pathology Department, Benghazi Medical Center.

1. INTRODUCTION

Breast cancer is the most common cancer among women, impacting 2.1 million women each year around the world, and it is the leading cause of cancer death in women (15%). In 2018, it is estimated that 627,000 women died from breast cancer⁽¹⁾. It is the most common cause of cancer-related death in industrialized countries, and the third in developing countries⁽²⁾.

However, its incidence varies from areas of high incidence including North America, Australia, New Zealand, and Northern and Western Europe; to intermediate in Central and Eastern Europe, Latin America, and the Caribbean, and low incidence in most of Africa and Asia⁽³⁾⁽⁴⁾. For example, in the US, less than 0.9 new cases per 1000 women were reported in the 1990s, and more than 1.4 new cases per 1000 women were reported in 2006⁽⁵⁾⁽⁴⁾.

The incidence of breast cancer has also shown a steady increase during the last 30 years in Nordic countries. In the UK, approximately one in nine females is likely to develop the disease during her lifetime. An increase has even been noted in areas of lower incidence of breast cancer in Eastern Europe and Japan⁽⁶⁾⁽⁷⁾. Various studies in the US found that females of African

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descent have a lower breast cancer incidence but higher breast cancer mortality rates than Caucasian women. Poor survival may be related to the fact that female individuals of African descent are more likely to be diagnosed at an early age but with an advanced stage of disease ^{(8) (9)}.

In Eastern Mediterranean regions, the incidence rate recorded an obvious rise and the frequencies were higher for younger females ⁽¹⁰⁾. In Northern Africa, the data of the regional registries of Algeria, Morocco, and Tunisia show that breast cancer is the most common cancer in women representing 25% of all cancers, which is similar to the frequency in Libya (25.6%). ^{(11) (12) (13)}.

The incidence of breast cancer in Arab countries is significantly lower than that in Western nations, but it has been rising. This increase in incidence is contributed to many factors including lifestyle changes adopted by Arab women, such as late marriage, delayed first pregnancy, having fewer children, taking oral contraceptives, lack of physical activity, obesity, and smoking ⁽¹⁴⁾. It is also possible that this increase is partly due to improved detection and diagnosis in some Arab countries and population growth and aging ^{(15) (14)}.

Breast cancer has different histopathological and biological features that lead to different treatment responses and also need different therapeutic strategies ⁽¹⁶⁾. The early detection of breast cancer produces higher survival rates, increased treatment options, and improved quality of life ⁽¹⁷⁾.

This study was conducted to determine the frequency, pattern, age and stage of breast cancer cases from the eastern part of Libya that were referred to the Oncology Clinic in Benghazi Medical Center in the period from the 1st of January 2016 to the 31st of December 2018. The Oncology Clinic in the Department of Oncology in BMC was the only clinic in the eastern part of Libya that received all adult cancer patients.

2. SUBJECTS AND METHODS:

This study is a descriptive, retrospective cross-sectional type, and data was collected from the Oncology Department at Benghazi Medical Center which receives cancer patients from Benghazi and the whole eastern part of Libya as well as data from the Pathology Department at the University of Benghazi. A convenience sample of 517 file records of breast cancer patients who registered in the hospital from 1st January 2016 to 31st December 2018 was selected. Inclusion criteria were all Libyan patients from the eastern part of Libya who were registered during the study in Benghazi Medical Center as a case of breast cancer, with a confirmed diagnosis of breast cancer by histopathology. The following conditions excluded non-Libyan patients or Libyan patients not from the eastern part of Libya.

Demographic, clinical, pathological, and biological information including sex, age at diagnosis, address, histopathological type, grade, staging, biomarkers (estrogen receptor [ER], progesterone receptor [PR], proliferation (Ki67) status, and human epidermal growth factor receptor 2 (HER2) status), were extracted from medical file records. Marital status, occupation and family history are important information but not recorded in the files.

Collected data was sorted, coded, and analyzed by IBM SPSS Statistics for Windows, Version 20 (IBM Corp., Armonk, N.Y., USA). Descriptive statistics including frequency, percentage, and mean $\pm$ standard deviation, were obtained for all variables as appropriate.

3. RESULTS:

515 patients with breast cancer were included in our study. 340 patients (66%) were from Benghazi, 47 patients (9.1%) were from Albaida, 35 patients (6.8%) from Ejdabia, 32 patients (6.2%) from Darna, 30 patients (5.8%) from Almarj, 20 patients (3.9%) from Tubruk, and 11 patients (2.1%) from Shahat (Table 1 & Figure 1).

The mean age was 50 years old. However, 196 (38.1%) were in the age range between 46 & 56 years (Table 2 & Figure 2).

The highest number of recorded cases was 212 patients in 2018, followed by 199 patients in 2017 and 104 patients in 2016. The most common type determined microscopically was ductal carcinoma (DC) in 396 patients, followed by invasive lobular carcinoma (IDC) in 32 patients (Table 3 & Figure 3).

Regarding the tumor grade, 291 patients were in grade 2 and 188 patients in grade 3 (Table & Figure 4). According to the AJCC system, the frequencies were 31, 131, 279 and 74 for stages I, II, III and IV respectively (Table & Figure 5). Ki-67 level (21-40%) was recorded in most cases (52.8%) and followed by level (<20%) at (23.9%)

Positive ER (ER+) was (72.2%) and Negative ER (ER-) was (27.8%) compared to PR positive (PR+) was (66%) and negative (PR-) was (34%) (Table & Figures 7). Furthermore (61.6%) of cases were HER2 negative, and (38.4%) were positive. The tumor marker Ki67 compared to IDC was the most common range between 20%-40% in 211 patients (77.6%) out of 272 patients (Table & Figure 8).

Metastasis in Stage IV was highest in the lungs in 32 patients, followed by the bones in 22 patients, and then the liver in 20 patients. Present significant statistical relationship, p-value ($P = 0.001$) between stages and biomarker (ER). ER was positive in most cases compared with stage II, with 182 patients among 372 cases. Also, biomarker PR had a significant statistical relationship p-value ($P = 0.001$) positive PR, most cases compared with stage II in 166 patients among 340 cases. Biomarker (HER2) negative was most common in 246 patients among 317 cases compared with stage II.

Table 1: Geographical distribution of breast cancer patient per city

City	Number	%
Benghazi	340	66
Albiada	47	9.1
Darna	32	6.2
Tubruk	20	3.9
Almarg	30	5.8
Ejdabia	35	6.8
Shahat	11	2.1
Total	515	100

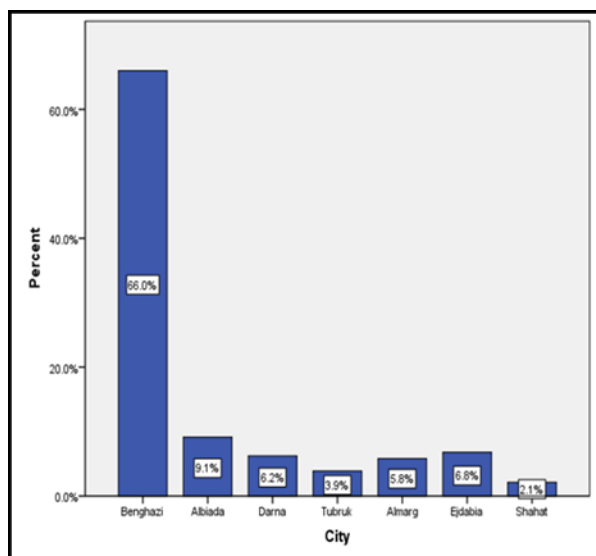


Figure 1: Geographical distribution of breast cancer patient

Table 2: Distribution of patients according to age groups

Age groups	Number	%
24-34	38	7.4
35-45	149	28.9
46-56	196	38.1
57-67	94	18.3
68-78	32	6.2
79-89	6	1.2
Total	515	100

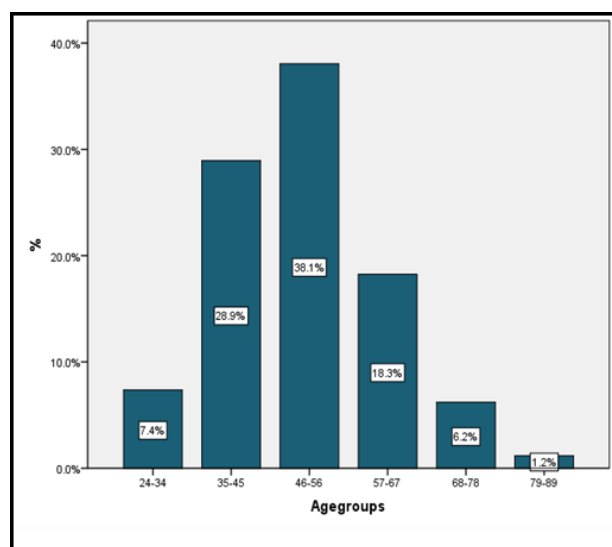


Figure 2; Distribution of patients according to age groups

Table 3-Incidence of breast cancer according to Histo-pathological diagnosis

Diagnosis	Number	%
Invasive Ductal Ca.	396	76.9
Invasive Lobular Ca.	32	6.2
Invasive Papillary Ca.	11	2.1
Invasive Medullary Ca.	4	0.8
Mixed Invasive Lobular Ca.& Invasive Ductal Ca.	23	4.5
Intra ductal Ca. well differentiated	7	1.4
Intra ductal Ca. poor differentiated	31	6.0
Invasive Muciod Ca.	11	2.1
Total	515	100

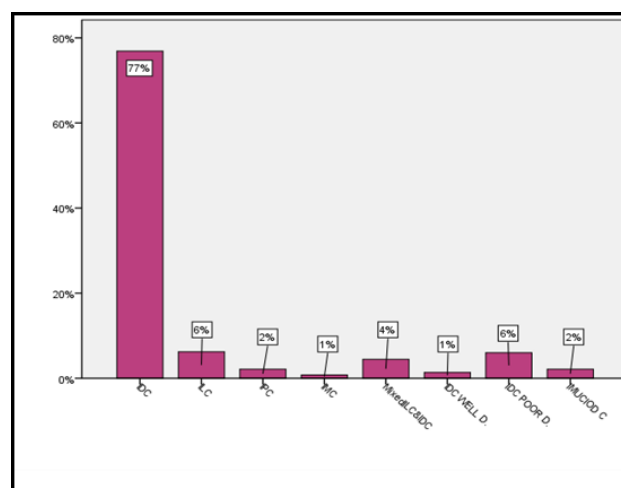


Figure 3-Incidence of breast cancer according to Histo-pathological diagnosis

Table 4; Distribution of patients according to the grade of the tumor

Grads	Number	%
One	36	7.0
Two	291	56.5
Three	188	36.5
Total	515	100

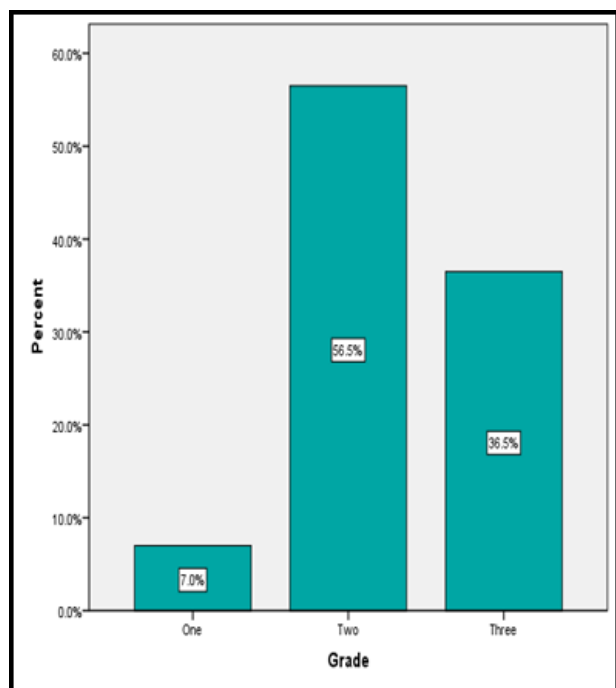


Figure 4-Distribution of patients according to the grade of the tumor

Table 5- Distribution of patients according to the stage of the tumor

Stage	Number	%
I	31	6.0
II	131	25.4
III	279	54.2
IV	74	14.4
Total	515	100

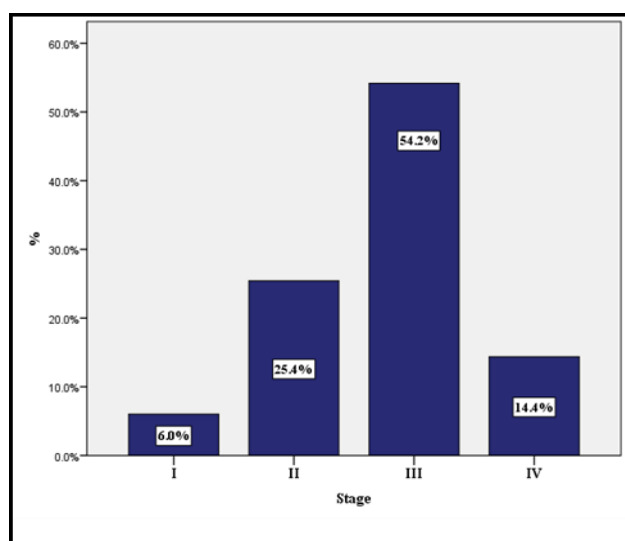


Figure 5- Distribution of patients according to the stage of the tumor

Table 6: Distribution of patients according to the site of the tumor

Site of tumor	Number	%
Right	300	58.3
Left	203	39.4
Bilateral	12	2.3
Total	515	100

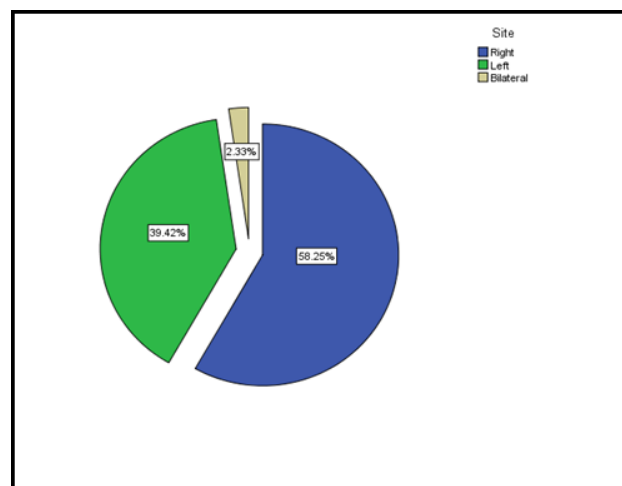


Figure 6: Distribution of patients according to the site of the tumor

Table 7: Biomarker distribution of patients

Biomarker	Positive No. (%)	Negative No. (%)	Total
ER	372 (72.2%)	143 (27.8%)	515 (100%)
PR	340 (66%)	175 (34%)	515 (100%)
HER2	198 (38.4%)	317 (61.6%)	515 (100%)

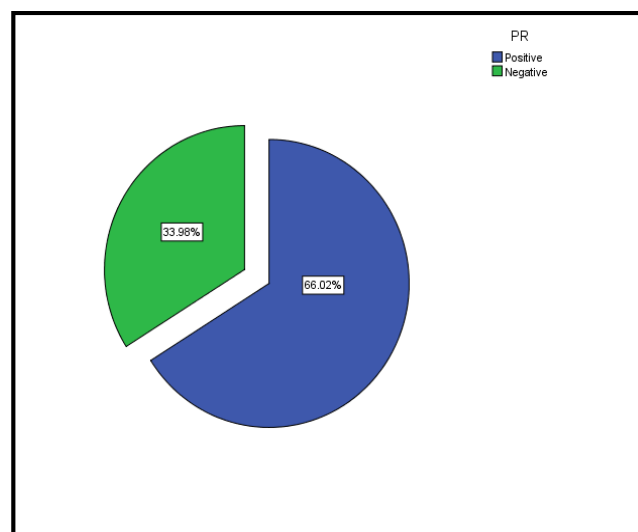


Figure 7a: Biomarker (PR) distribution of patients.

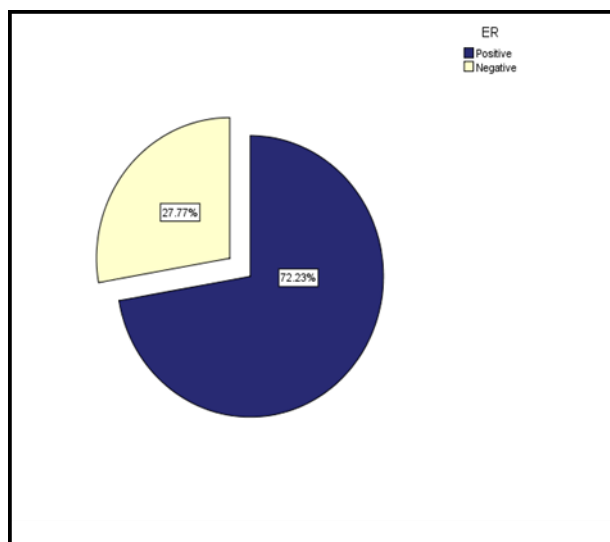


Figure 7b: Biomarker (ER) distribution of patients

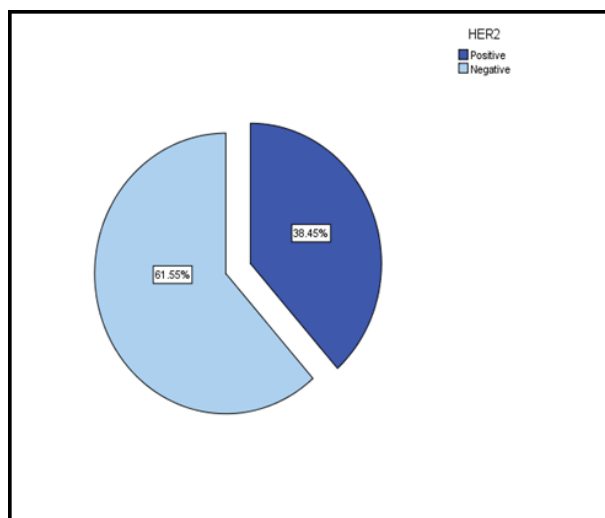


Figure 7c: Biomarker (HER2) distribution of patients

Table 8-Distribution of patients according to KI67 Biomarker

Biomarker KI67	Number	%
< 20%	123	23.9
21-40%	272	52.8
41-60%	58	11.3
61- 80%	50	9.7
> 80%	12	2.3
Total	515	100%

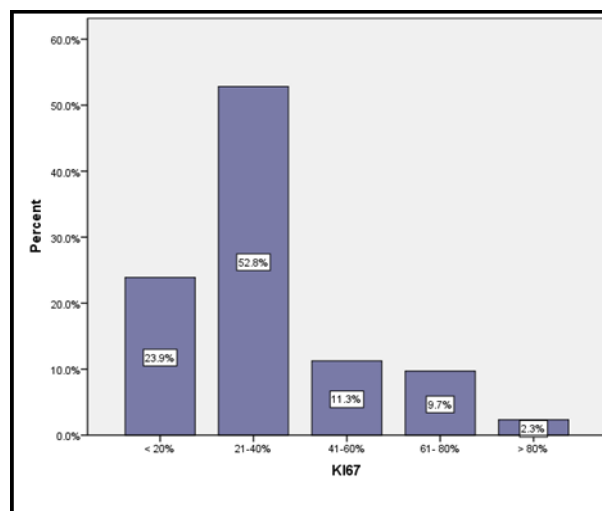


Figure 8-Distribution of patients according to KI67 Biomarker

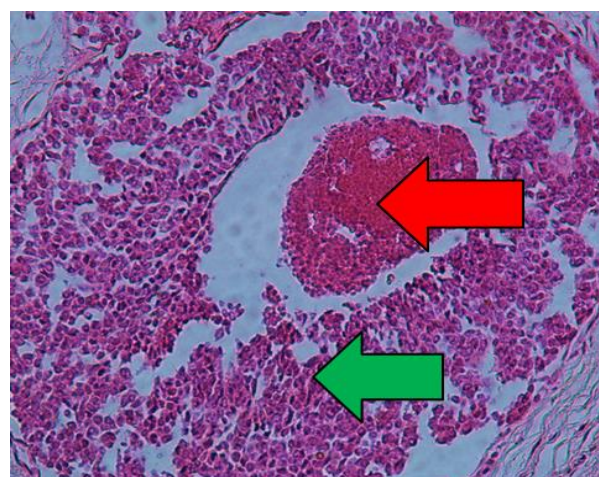


Figure 9; A section of ductal carcinoma in situ with central comedo-type necrosis (red arrow), noninvasive because the cancer cells (green arrow) have not spread out of the ducts and glands into the surrounding breast tissues. H&E stain (200x)

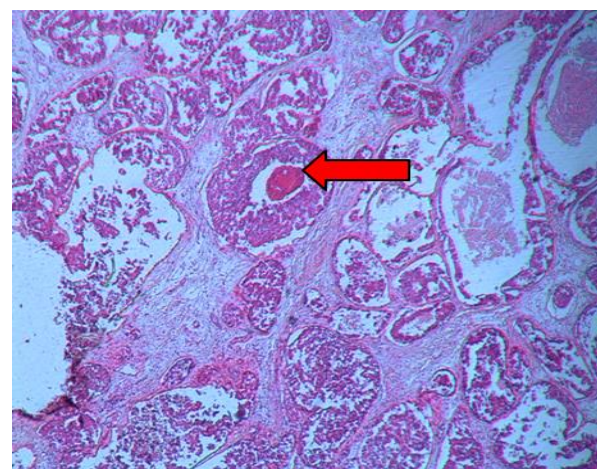


Figure 10; A section of invasive ductal carcinoma (IDC) grade three with ductal carcinoma in situ (DCIS) with central necrosis (yellow arrow). IDC with no specific histologic characteristics, no special type (NST). H&E stain (x100)

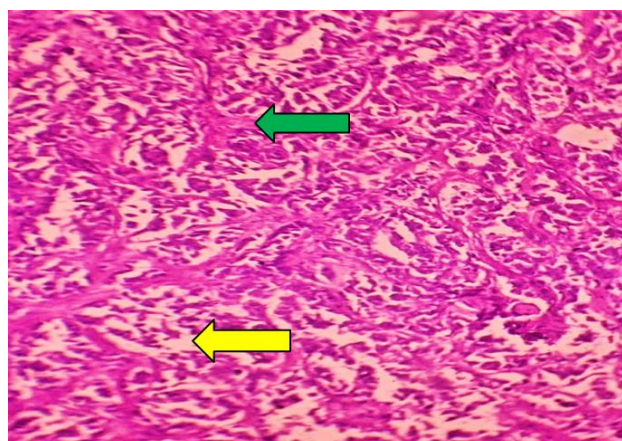


Figure 11: A section of invasive ductal carcinoma grade three (IDC) with high degree pleomorphic nests malignant cells invasion basement membrane to stroma, no tubule formation (yellow arrow) malignant cells (green arrow) fibrous septa separate tumor cells, H&E stain (x200)

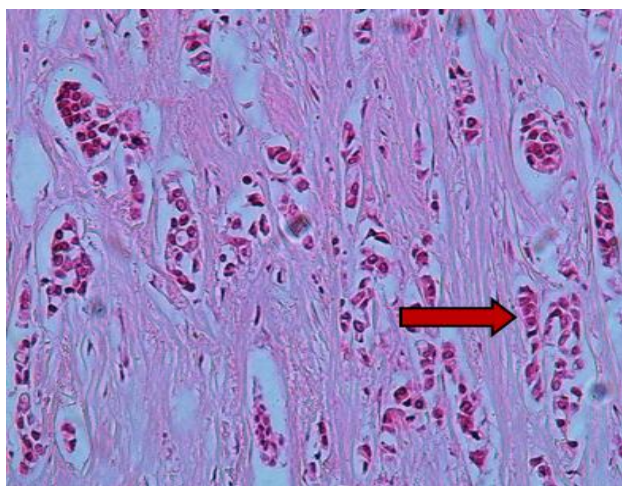


Figure 12: A section of invasive lobular carcinoma grade two with cells exhibiting moderate nuclear pleomorphism but maintaining a single file growth pattern (red arrow) H&E stain (x200)

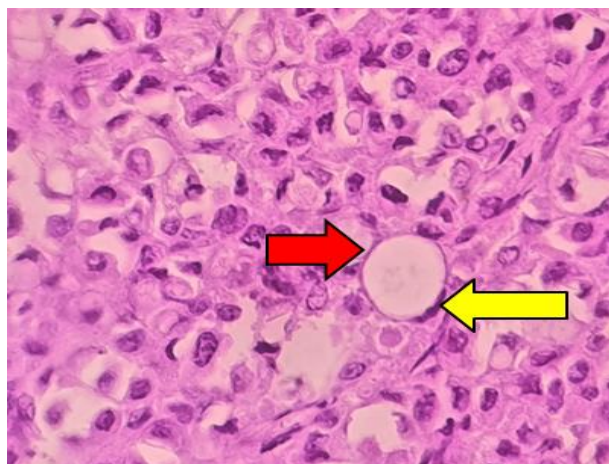


Figure 13: A section of invasive signet ring mucinous carcinoma. Malignant mucinous cell (red arrow), with peripheral nucleus (yellow arrow) pushed by mucin. H&E stain (x400)

4. Discussion

Breast cancer is the most common cancer in women in Libya & worldwide. In Libya, patients often present with advanced disease, have early disease recurrence and are associated with high mortality⁽¹⁸⁾ Prediction of this disease depends on various factors such as histological type, stage, grade, size of the tumor, lymph node metastasis, and the biomarker of the tumor⁽¹⁹⁾.

In the present study, most of the cases were from Benghazi and the mean age was 50 years old compared with a study done in Egypt where

the mean age was 31 years old⁽²⁰⁾. In most cases of tumors, 76.9% were ductal carcinoma, followed by lobular carcinoma at 6.2%, which is in accordance with what was reported from Saudi Arabia, where the incidence percentage was 81.80%, followed by lobular carcinoma at 3.40%⁽²¹⁾.

The tumor stage is considered an important factor in local and distant recurrences, survival rates, and having an effective early diagnosis program. About half of the tumors in the present study were detected at stage III (54.2 %), and this is slightly higher than what was reported by a study in India where detection was at stage IV (45.7%),⁽²²⁾.

Concerning the grade of tumor in the present study, the results illustrated that (56.5%) of tumors were in grade two and (36.5%) in grade three which is in agreement with a study done by⁽¹⁷⁾ which revealed that

out of 909 tumor cases, 12.9% were grade one, 53.7% were grade two, and 33.4% were grade three.

In our results, 72.2% were positive for ER and 66% were positive for the progesterone receptor, and HER2 was 38.4% positive. This is compared with a study conducted in Pakistan, where ER+ve cases were 62%, PR+ve cases were 47%, and HER2 +ve cases were 49%⁽²³⁾.

Our study is in line with studies by Arpino⁽²⁴⁾, Ellis⁽²⁵⁾, Blanco⁽²⁶⁾ & Jalava⁽²⁷⁾, which showed that positive expression of ER and PR correlate with better survival and response to estrogen antagonists such as tamoxifen. Breast cancers with HER2 protein overexpression or HER2 gene amplification are called HER2-positive. HER2-negative breast cancers tend to grow slowly and are less likely to spread and recur compared to HER2-positive breast cancers. These are associated with a poorly differentiated tumor, less hormone receptor expression, high proliferation ability, positive lymph node, and a higher risk of recurrence. HER2 is also considered a prognostic and predictive factor for breast cancer⁽²⁸⁾.

Tumors with both ER and PR negative have a relatively poorer prognosis than cancers with either ER or PR positivity. The main factor in planning breast cancer treatment is the hormone receptor status, ER+, PR+; HER2-tumors have the best prognosis and response to hormone therapy. ER-PR-HER2+ and ER-PR-HER2-tumors are poorly differentiated, show aggressive behavior and poor outcome, and are least likely to respond to hormone therapy⁽²⁹⁾.

The Ki-67 level is considered a valuable biomarker in breast cancer patients and is used in treatment and follow-up. Patients with Ki-67 >20% are more likely to develop recurrence and distant metastasis than those with Ki-67 <20%. Higher levels of Ki-67 correlate with more rapid tumor growth and tumor

aggressiveness. In the present study, a Ki-67 level of $> 20\%$ was recorded in 23.9 % of the cases while, in the western part of Libya, the Ki-67 level > 15 was 19.1% ^{(30), (31), (32)}. This reflects a higher frequency of Luminal A phenotype (86.6%) and less rates of Luminal B (65.4%), Triple Negative (36.5%) and HER2 overexpression (25.2%) ⁽³³⁾. Molecular subtype analyses revealed that Luminal A was the commonest molecular subtype (61.1%), followed by Luminal B, Triple Negative and HER2 Luminal B subtype had a poorer prognosis than Luminal A, tending to spread more aggressively, suggesting the importance of anti-HER2 therapy. Luminal A had the best prognosis and response to hormone therapy.

Most of the age groups were between 46 –56 years old in Benghazi which corresponds to a study by ⁽³⁴⁾, comparing breast cancer in Libya and European countries with 70.9% of cases occurring in females, who are 50 years or younger. Suggesting that in the African population, characterized by African genomic haplotypes, the premenopausal type of breast cancer is more common than the postmenopausal type. In Europe, where the population is characterized by European genomic haplotypes, the contrary is the case. The factors responsible for this are not fully understood, although it could be due to the breast cancer genes (BRCA 1 and 2) and their variant ⁽³⁵⁾.

Similar to other studies, the most frequent histological type of breast cancer in young women was invasive ductal carcinoma 36.1% ⁽³⁶⁾ also common in Benghazi 39.7 %. Genetic factors may be involved. However, no evidence currently exists that breast cancer genes (BRCA1 and BRCA2) are more often involved in breast cancer cases in Africa. ⁽³⁷⁾. Comparing the stage of the disease with age, we found that most of the stage III cases (39.8%) were in the age group 46-56 which corresponds to a study by ⁽³⁸⁾, regarding breast cancer in Gharbiah, Egypt and the United States, the majority of Egyptian breast cancer patients were in stage III, with higher rates in all age groups. Additionally, stage III was common in Benghazi (62%). The total number of Libyan patients with breast cancer from all other types of cancers in the Eastern region was 10.1% in 2016, 19.1% in 2017, and 20.9% in 2018. The large percentage of patients in advanced stages indicates delayed presentation and late diagnosis, as noted in the study by Ikpat ⁽³⁹⁾ on Nigerian breast cancer. Mammographies were not performed in Nigeria but have been performed in Libya, although not in screening programs. However, mammographies have not been able to improve early diagnosis. The reason includes the difficulties involved in obtaining an early mammographic diagnosis of premenopausal breast cancer ⁽⁴⁰⁾. The biological aggressiveness of the premenopausal type also appears to limit the value of early screening ⁽⁴¹⁾. Moreover, the reason for the advanced presentation in Africa could be due to the lack of healthcare coverage especially in remote rural areas and poverty as healthcare is not free in most countries. On the contrary, in most European countries, healthcare is easily accessible and free. In addition, public awareness is high and screening is available in most European countries. Diagnosis delay is preventable and has major effects on patients' prognosis and outcome. It is necessary to investigate diagnosis delay and to understand the causes to reduce delays and improve early diagnosis. Perhaps this trend can be attributed to low awareness of health issues among women, poor information campaigns, and the absence of screening programs for early detection of breast cancer in Libya.

Regarding tumor grades, the most common was grade two (38.5 %) in ages between 46 – 56 years old and again also common in Benghazi (66.0%) followed by Albiada (11.3%). There is a significant statistical relationship between grade two and common histological type IDC (76.3%). $P = 0.037$. Another study found that Libyan and Nigerian patients had a higher tumor grade than Finnish ones. Results in African patients are in concordance with those of African-American patients ⁽⁸⁾. One explanation for the grade differences may involve the more active proliferation in the premenopausal type of breast cancer, which is more common in Africa.

Comparison between the most common histological type of breast cancer IDC and biomarkers ER ve+ 74.7%, PR ve+ 75.3%, HER2 ve- 77.6%, and KI67 average between 21-40% (77.6%) were most common. There was a significant statistical relationship between the most common histological type IDC and PR $P = 0.010$. There was also a significant statistical relationship between ER with stage $P = 0.029$ and between PR with stage $P = 0.020$. In a study by ⁽⁴²⁾, DCIS was more likely to be of the Luminal B and HER2 phenotypes than invasive tumors. Because HER2-positive DCIS lose HER2 expression when they progress to invasive cancers, invasive carcinomas may arise more frequently from HER2-negative DCIS than from HER2-positive DCIS ⁽⁴³⁾. In a study conducted by ⁽⁴⁴⁾ about Libyan breast cancer health services and biology, patients assumed that symptoms were benign and would disappear without medical interference. In agreement with other studies ^{(45), (46)}, this was the most important reason for the delay in seeking doctors' advice. Some patients believed that breast cancer could not be cured, so there was no point in having it diagnosed and treated ⁽⁴⁷⁾. Fear of divorce or remarriage of the husband could lead some women to decide not to get their symptoms diagnosed if they suspected breast cancer. Negative information, such as side effects and expected toxicity of chemotherapy led to fear and refusal of therapy. Diagnosis delay was also related to a belief that mastectomy causes disfigurement and disability ⁽⁴⁸⁾. In addition, shame and a personal need to keep symptoms secret was one of the reasons for diagnosis delay, particularly among older women > 50 ⁽⁴⁴⁾.

The discovery of a breast lump reduces the patient delay as confirmed in other studies ⁽⁴⁹⁾. Mammography is a sensitive means for early detection of breast cancer, but both clinical breast examination (CBE) and breast self-examination (BSE) have the potential to advance the diagnosis of breast cancer without the expenses of a mammography facility ⁽⁵⁰⁾. The role of education on breast cancer symptoms has been reported in several studies ^{(51), (49)}. Lack of knowledge about breast cancer is an important factor in Libya as observed in a study by ⁽⁴⁴⁾. There is a need for public educational programs especially for less educated women.

In our study, important information was missing in patients' files at the Benghazi Medical Center such as marital status, family history, history of menstrual cycle and breastfeeding, which affects the prognosis of breast cancer. In comparison, another study conducted by ⁽³²⁾ about the western part of Libya found that this information was present. As regards marital status, 78.6% of patients were married, 82.1% were from the western region and more than half were employed. More than half of the patients had ≥ 4 children and 46.2% had not breastfed, 16.5% were breastfed for 12 months or more. The majority 64.3% of female cases reported early age of menarche > 12 years. Oral contraceptive use and hormonal treatment were reported in 62%

of female patients. Since the customs are similar in eastern and western Libya, we can take advantage of the results found in the previous research to match them with the missing information in our study, such as breastfeeding, the number of children and the use of contraceptives, which can also be compared with Arab countries. This increase in the incidence may be partly due to lifestyle changes being adopted by Arab women, such as late marriage, delayed first pregnancy, having fewer children, taking oral contraceptives, lack of physical activity/obesity, and smoking ⁽⁵²⁾, ⁽⁵³⁾.

It is also possible that this increase is partly due to improved detection and diagnosis in some Arab countries over the past 26 years. Population growth and aging could also be possible factors contributing to the increase ⁽⁵²⁾. Although the incidence of breast cancer in Arab countries is rising, it is still less than the global average and only one-fifth of that in Western Europe. In general, the high rates of breast cancer in developed countries are the consequence of a higher prevalence of the known risk factors for the disease, many of which – early age at menarche, null parity, late age at the first born child, late age at any birth, low parity, and late menopause – relate to the hormonal (largely estrogen) milieu to which the breast is exposed from menarche to the cessation of ovulation at menopause ⁽⁵⁴⁾. The higher parity and earlier age at first pregnancy of women seen in many developing countries might account for much of the lower incidence of breast cancer in these regions relative to developed countries. The long-standing hypothesis that breastfeeding of longer duration is protective ⁽⁵⁵⁾ has been affirmed again recently ⁽⁵⁶⁾.

In our study we are looking for ways to reduce the incidence of breast cancer and advanced cases in the stages, and to increase early detection of the disease, through educational programs and lifestyle changes that encourage breastfeeding, for example. Additionally, knowing the symptoms of the disease for early diagnosis, awareness of risk factors such as the use of contraceptives, and support for breast cancer research are all important measures that need to be addressed to reduce morbidity.

5. CONCLUSIONS

Breast cancer in Libya is the most frequent cancer among women and the most common area is Benghazi, with a mean age of 50 years, whereas in other cities the age group was (35-45). Most cases were stage III (279), followed by stage II (131), stage IV (74), and stage I (31). Regarding tumor grades, grade II (291) patients were the most common, followed by grade III (188), and grade I (36). Most cases were stage III, and grade II in all age groups and in all cities. Invasive ductal carcinoma was the predominant histopathological type, and the second most common type was invasive lobular carcinoma. Most cases were HER2 negative, ER positive and PR positive, and most cases had Ki-67 levels (21- 40%). Most cases were highest in the year 2018, (212) patients, followed by 2017, with 199 patients, and then 2016, with 104 patients.

Improvements in public awareness, lifestyle change, and the establishment of screening programs especially for women in the age risk group. Early detection and diagnosis using new technologies, improving access to affordable treatment, and more palliative care and support for breast cancer research, are all important measures that need to be addressed to reduce morbidity and mortality.

Updating electronic archives to facilitate data collection of comprehensive information about the patients and ease follow-up to cases.

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