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## Clinical and Histopathological Features of Breast Cancer in Iraqi Patients between 2018-2021

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### Abstract

Breast cancer (BC) is the most common malignancy in women worldwide and a major cause of cancer-related deaths for women in Iraq. This assignment was created to investigate the characteristics of BC diagnosed in Baghdad from 2018 to 2021. A total of eighty-nine of paraffin embedded tissue blocks of different breast tissue tumors (71 females and 18 males) with their data, were collected from archive of Histopathology Department, Teaching Laboratories of Medical City, Al-Yarmouk Teaching Hospital, and a private laboratory in Baghdad-Iraq. The clinical information regarding age, gender, tumor size, tumor stage and grade, lymph nodes metastasis, in addition to the findings of estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor (HER)-2 and molecular subtypes were obtained from reviewed patients medical records and pathologic reports. Results revealed a high incidence of BC in patients at sixth and seventh decades of age, with a rate of 37.78% and 28.89% respectively. The dominant tumor size was 2–5 cm in malignant cases, and 91.11% of cases were in females. Regarding the histological type, the majority of malignant cases (60%) were IDCs. Whereas 53.33% of cases had metastasis to lymph nodes. Stage III was the most common tumor stage and grade II was the most common grade, comprising 64.44%. Furthermore, the hormone receptor status was 46.67% ER positive, while PR results were equally positive and negative comprising 42.22% per each, 62.22% of HER2 status was negative, and luminal subtypes accounted for 46.67% of all molecular subtypes.

**Keywords:** Breast tumors, Risk factors, Epidemiology, Clinicopathological features.

## الخصائص السريرية والنسجية المرضية لسرطان الثدي في المرضى العراقيين بين 2018–2021

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### الخلاصة

سرطان الثدي هو أكثر أنواع السرطانات شيوعاً في العالم والسبب الرئيسي للوفاة المتعلق في السرطان لدى النساء في العراق. تم تصميم هذه الدراسة لتقييم الصفات التشخيصية لسرطان الثدي في بغداد، العراق بين 2018–2021. تم جمع 89 عينة من انسجة أورام الثدي المظومة في شمع البرافين (71 امراه و 18 رجل) مع بياناتهم والتي جمعت من ارشيف قسم الانسجة المرضية / المختبرات التعليمية / مدينة الطب و مستشفى اليرموك التعليمي و مختبرات خاصة في بغداد/ العراق. المعلومات السريرية شملت العمر، الجنس، حجم الورم،

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موقع الورم، الانتشار العقدي للمفاوي، مرحلة الورم، درجة الورم، بالإضافة الى حالة مستقبلات الاستروجين والبروجيسترون و مستقبل عامل النمو البشري والانواع الفرعية الجزيئية. كشفت نتائج هذه الدراسة عن ارتفاع معدل الأصابة بسرطان الثدي بين المرضى في العقدین السادس والسابع من العمر و بنسبة %37.78، %28.89 على التوالي، وان غالبية احجام الاورام كانت بين 2-5 سم في الحالات الخبيثة وشكلت النساء %91,11 من مجموع الاصابات مع نسبة اصابات اعلى في الثدي الأيمن، بينما بلغ النوع القنوي الغازي نسبة %60 من الحالات الخبيثة. بينما ظهر ان %53.33 من الحالات لديها نقائل العقد المفاوية، في حين كانت اكثر مراحل الورم انتشارا بين الاورام الخبيثة هي المرحلة الثالثة III ، بينما كانت نسبة %64.44 من الاورام الخبيثة ضمن الدرجة الثانية II ، وفيما يتعلق بحالة مستقبلات الهرمون فقد بلغت نسبة مستقبلات الايستروجين الايجابية %46,67، بينما تساوت المستقبلات الايجابية والسلبية للبروجيسترون وبنسبة %42.22 لكل منها، بينما كانت الغالبية سالبة وبنسبة %62.22 فيما يخص مستقبل عامل النمو البشرية-2 ، أما فيما يخص الأنواع الفرعية الجزيئية شكلت الانواع المعمية %46.67.

## Introduction:

Breast cancer (BC) is the major cause of human suffering and untimely deaths in women across the world [1]. This cancer is responsible for 25% of new cancer cases in women worldwide, with an estimated 2,088,849 female BC malignancies occurring globally in 2018 (46.3 per 100,000 women) [2]. BC is a major cause of death among Iraqi women, accounting for around one-third of all cancer cases registered in the country in 2019 [3, 4], and there are high rates of breast, lung, and bladder cancer, as well as a growing burden from many other cancers [5]. Between 2006 and 2014, the Iraqi province Sulaymaniyah had the highest incidence rate of BC in females, and it was found to be the most frequent malignancy in Basra, Iraq, in 2017 [6]. The incidence rate of new cancer cases increased in Iraq from the year 2000 (52.00/100,000) to the year 2019 (91.66/100,000). Many factors, either individually or collectively, contribute to the onset of BC, particularly in women who have a genetic predisposition to the disease or come into contact with high-risk factors [7]. The risk factors include advanced age, early menarche, late menopause, first full-term pregnancy at a late age, the use of hormonal therapy, such as oral contraceptives, obesity, lack of exercise, diet, smoking, drinking alcohol, low physical activity, and early life exposure to high doses of radiation [8]. Researchers have also looked into whether psychological aspects might be associated with breast cancer incidence, with inconsistent results. An early study after examining "cancer-prone" personality traits discovered no difference between breast carcinoma subjects and controls on measures of immature, and neurotic defense style; locus of control of behavior; emotional expression-in, emotional expression-out, and emotional control; self-esteem; anxiety; or depression [9]. In addition, the tumor phenotype in terms of molecular subtype in BC patients differs based on gene expression profiles: luminal epithelial/estrogen receptor (ER) positive, HER2 positive, triple negative, and normal breast-like [10]. In this study, we investigated the epidemiology of breast tumors in malignant and benign breast tumors among Iraqi patients, and its correlation with clinicopathological features (age, tumor site, size, grade, lymph node involvement, histological type, pathological stage, grade, (ER-PR and HER2 receptors if data is available) and molecular subtypes.

## Materials and Method:

### *Samples Preparation and Staining:*

A total of eighty-nine of paraffin embedded tissue blocks of different breast tissue tumors (71 females and 18 were males), with their data, were collected from archive of Histopathology Department, Teaching Laboratories of Medical City, Al-Yarmouk Teaching Hospital, and a private Laboratory in Baghdad-Iraq, for the years 2018, 2019, 2020 and 2021. The patients' cases were distributed as follows: Forty-one of cases were females' malignant breast lesions,

thirty of cases were females' benign, fourteen cases were males benign and the last four cases were males malignant tissues. Additionally, eleven cases of health breast biopsies were collected from Forensic Medicine Department in Baghdad as a control after taking the required ethical consents. The samples were preserved in 10% formalin and then subjected to tissue processing series and before transforming them into paraffin blocks. The clinical information regarding age, gender, tumor size, tumor stage, and grade, lymph nodes metastasis, and lab results of ER, PR, and HER-2, molecular subtypes were obtained from reviewed patients medical records and pathologic reports. A section from each paraffin block was cut at a thickness of 5 $\mu$ m by a microtome cutter (Leica RM2125RTS). Sections were placed on a water bath (Electrothermal Cat No. MH 8501) heated at 40°C and before carrying them on a standard slide and staining with Hematoxylin and Eosin (H&E).

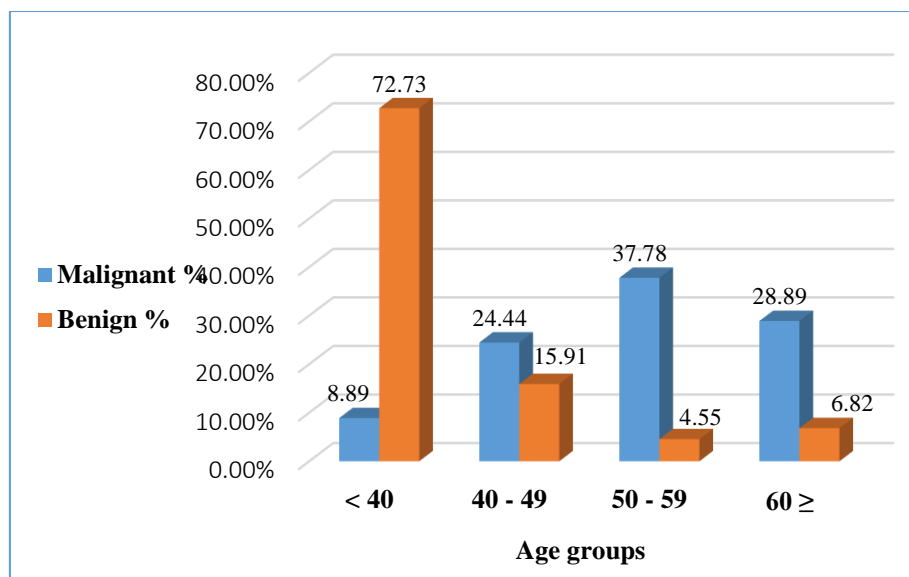
#### Statistical analysis:

The Statistical Packages for Social Sciences—(SPSS), version 22 was used to detect the effects of different factors on study parameters that were tested using the Pearson Chi-square test, with application of Yate's correction or the Fisher Exact test wherever applicable. Data was presented in simple measures of frequency, percentage, mean, standard deviation, and range (minimum-maximum values).

### Results and Discussion:

#### Age

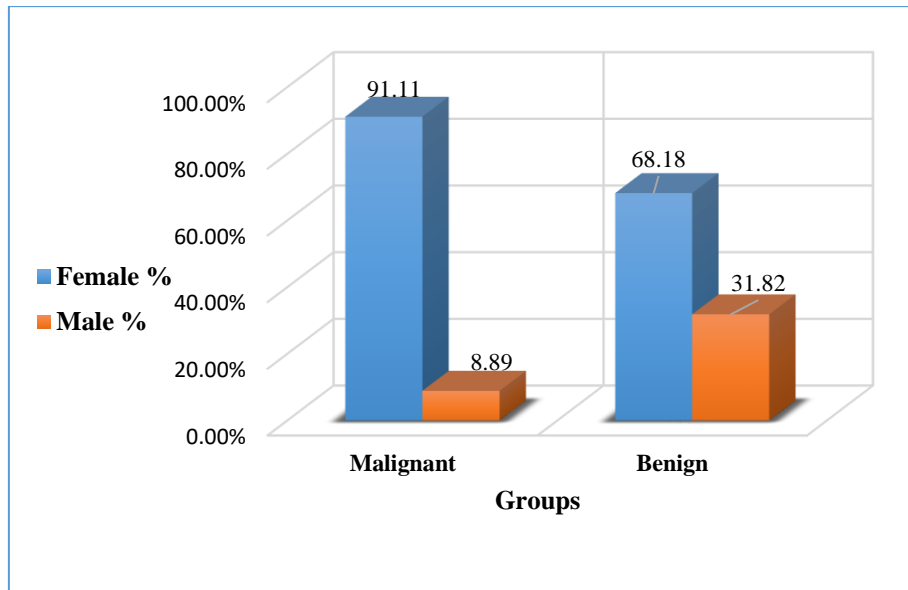
Patients ages ranged from 15-84 years with a mean of  $54.93 \pm 14.33$  years of malignant group, while the mean age of benign group was  $32.39 \pm 14.7$ . The package frequency in benign group was within the age category <40 which comprised 72.73% of the total studied benign cases. While the highest frequency of malignant cases appeared in the sixth and seventh decade which constituted 37.78 % and 28.89% of the total malignant cases respectively (Figure 1).



**Figure 1:** Distribution of malignant and benign cases according age groups.

#### Gender

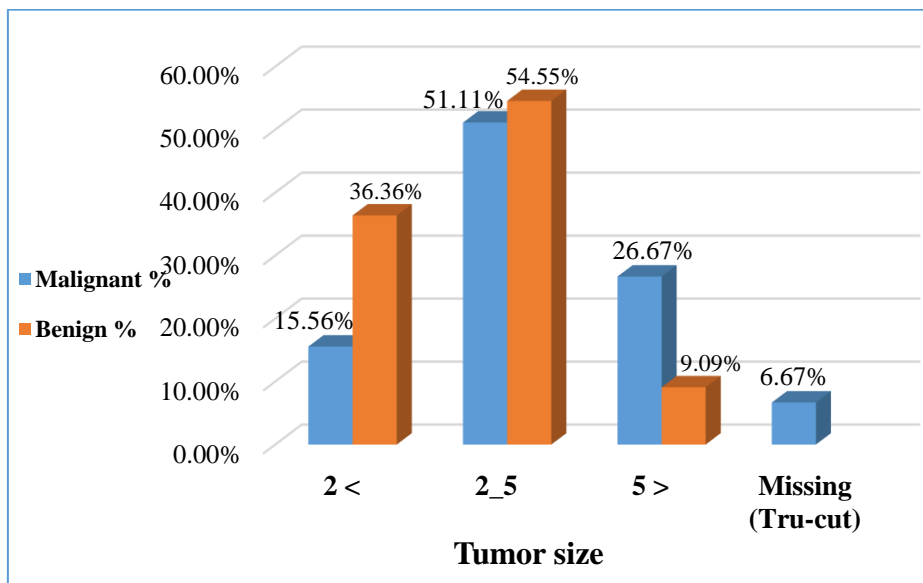
Of the total 45 cases of malignant breast tissues, 91.11% (41 cases) were females and 8.89% (4 cases) males. While for benign cases, 68.18% (30 cases) were females versus 31.82% (14 cases) males (Figure 2).



**Figure 2:** Distribution of study samples according to gender in different groups.

*Tumor Diameter*

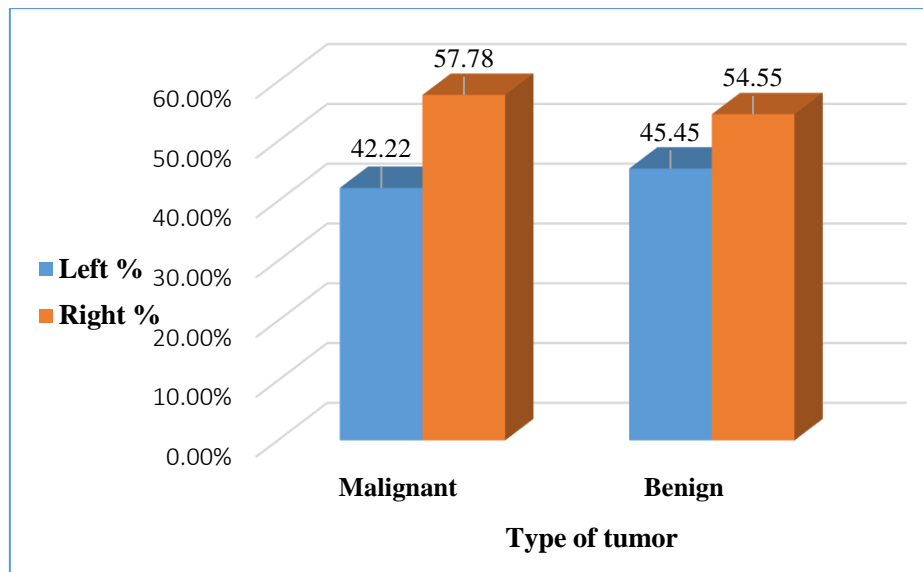
The mean size and standard deviation in malignant cases was  $4.25 \pm 2.90\text{cm}$ . Whereas that for benign cases the readings came to be  $2.66 \pm 1.90\text{cm}$ . All breast tumors were classified into three groups;  $2\text{cm} <$ ,  $2 - 5 \text{ cm}$  and  $5\text{cm} >$ . The average tumor diameter from  $2 - 5\text{cm}$  was observed in both benign and malignant respectively with the highest percentage, constituting 54.55% (24 cases) in benign group, and 51.11% (22 cases) of total malignant cases (Figure 3).



**Figure 3 :** Distribution of different breast tumors according to tumor diameter.

*Tumor side*

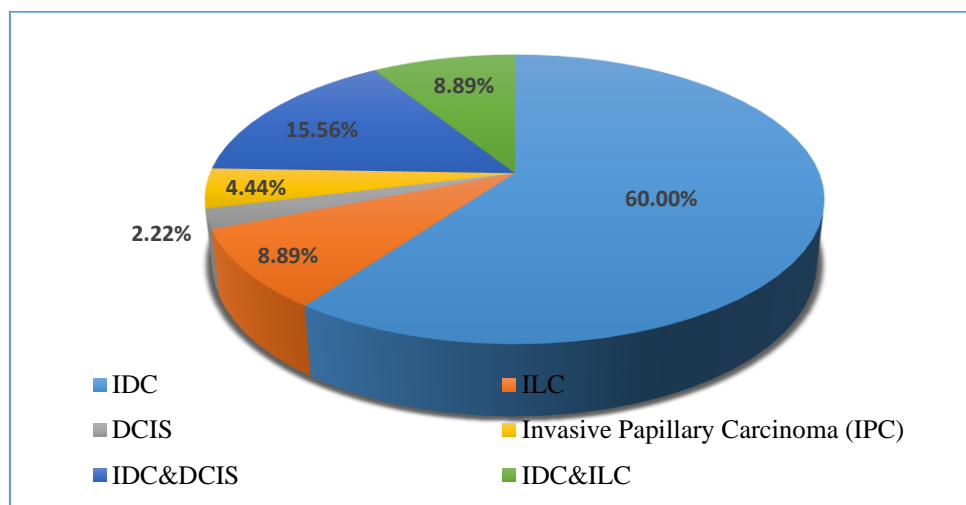
The highest incidence site of tumor in malignant group was seen in the right side comprising 57.77% of total cases. Also 54.55% of benign cases appeared in the right side (Figure 4).



**Figure 4 :** Distribution of malignant and benign according to tumor side.

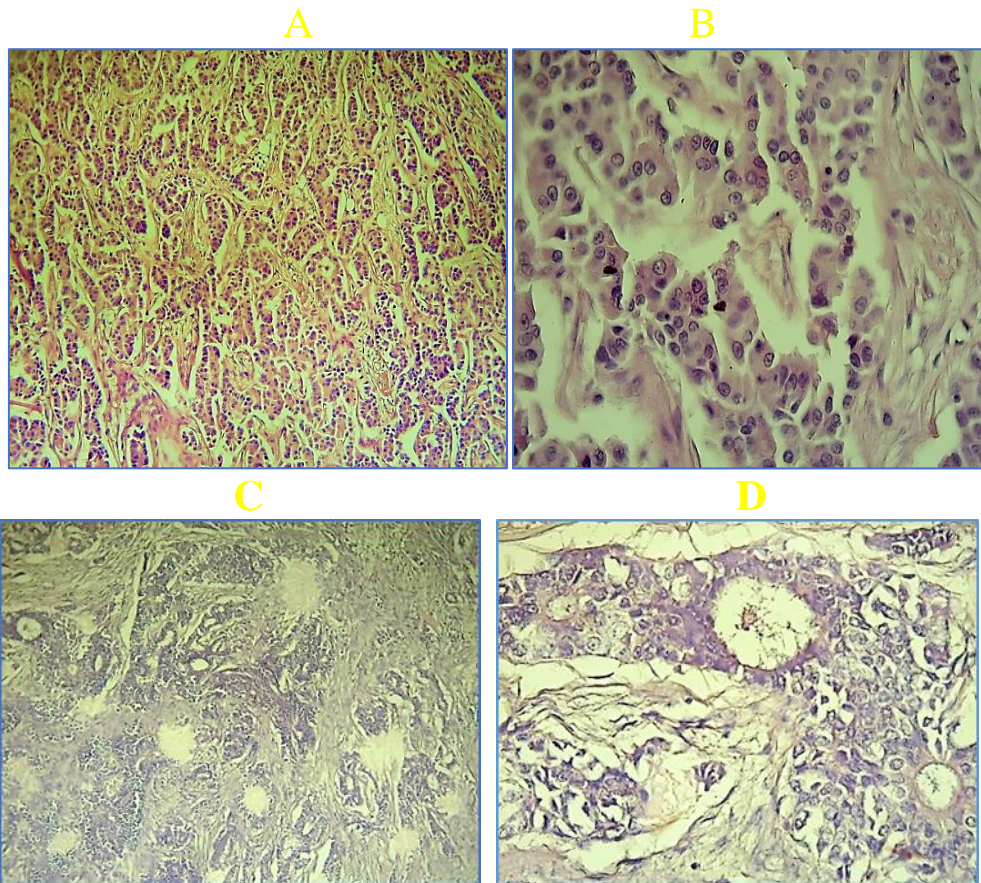
*Histological type of tumor*

In histological types for malignant cases, 60% (27 of the 45) of breast cancer cases were invasive ductal carcinoma (IDC) and 15.56% (7 cases) IDC and ductal carcinoma in situ (DCIS) (Figure 5 & 6). In benign situations, the fibrocystic changes (FCC) were 18.18% and fibro adenoma was 13.64%. Whereas in the other cases, more of one type was present in the same lump (Figure 7).

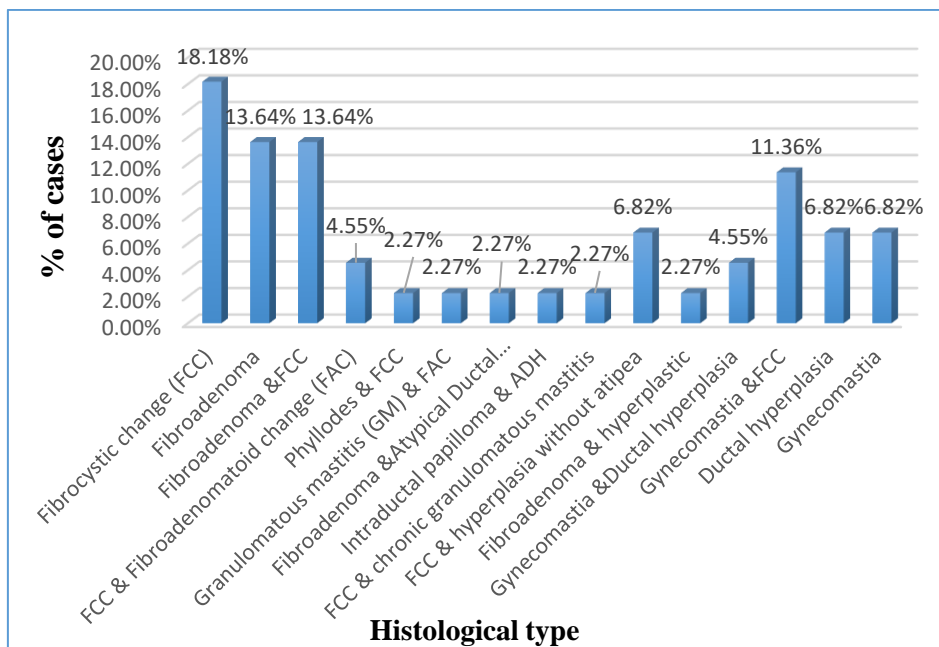


**Figure 5 :** Distribution of malignant cases according to histological types.





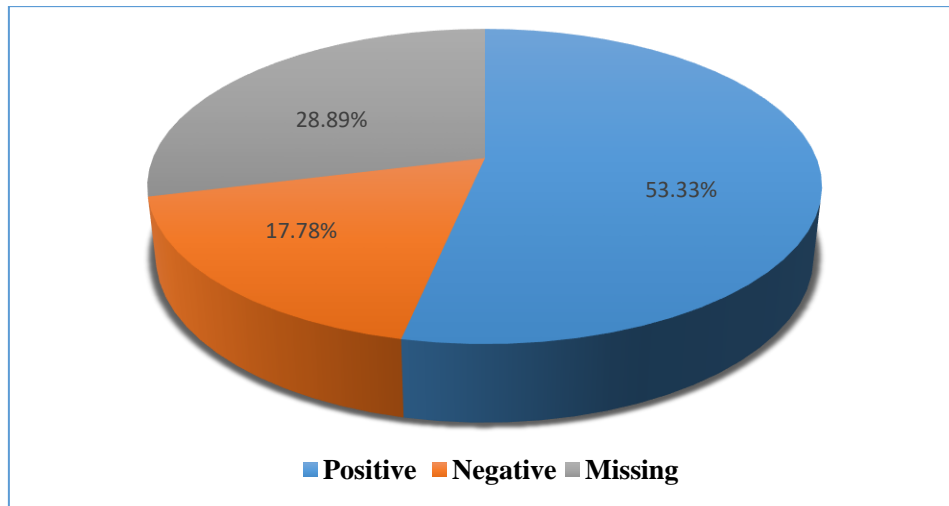
**Figure 6:** Tissue sections stained with hematoxylin and eosin (H&E) for malignant cases, A&B: IDC & ILC (A.10X; B.40X). C&D: IDC & DCIS (C.10X; D.40X).



**Figure 7:** Distribution of benign cases according to histological types.

*Lymph node metastasis*

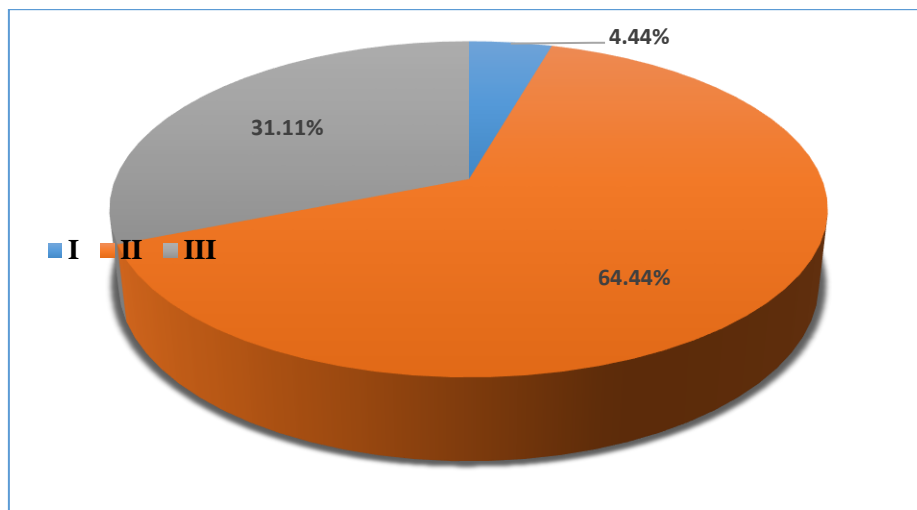
The histological examination of the lymph nodes showed that 53.33% of malignant cases had positive lymph node tumor metastasis (Figure 8).



**Figure 8 :** Distribution of malignant cases according lymph node metastasis.

*Grading of malignant cases*

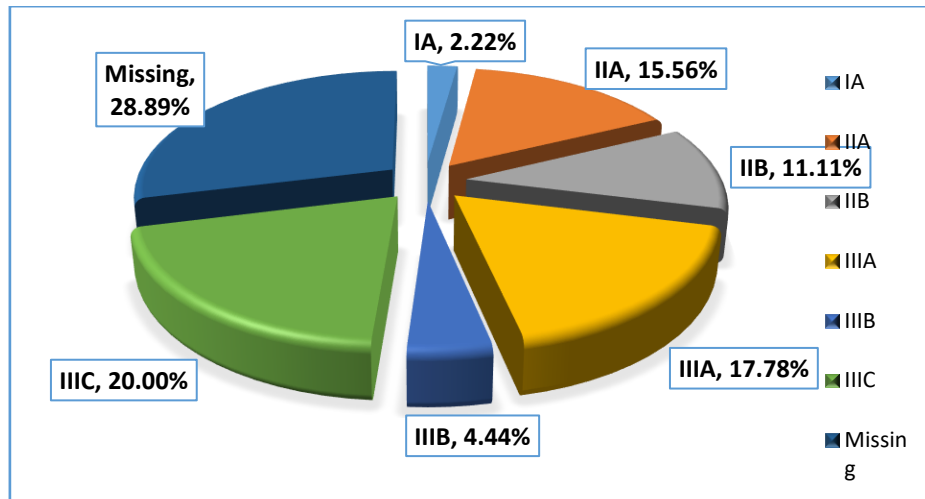
Tumor grading, done according to the Nottingham modification of Bloom and Richardson system, showed that 4.44% of malignant cases were in grade I; 64.44% grade II and 31.11% had grade III (Figure 9).



**Figure 9:** Distribution of malignant cases according to Bloom Richardson grading system.

*Pathological stage*

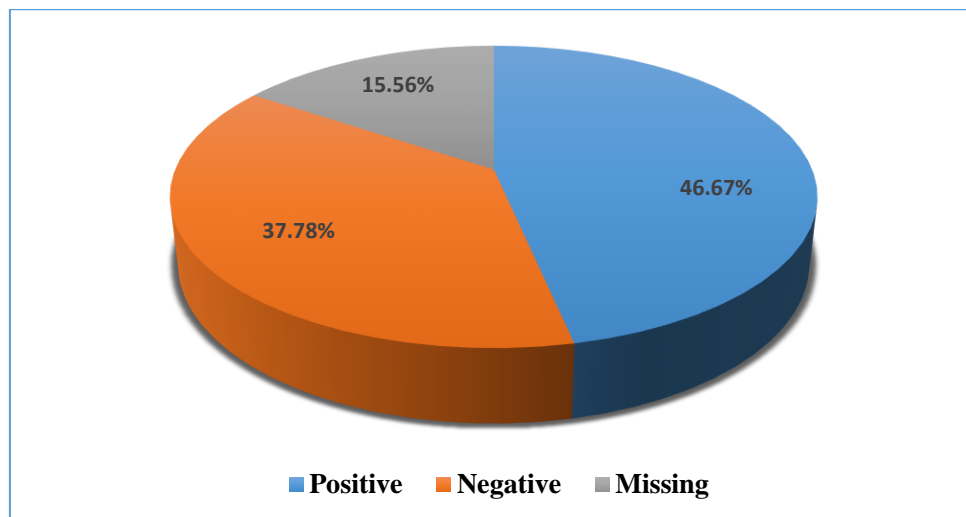
The staging of malignant cases was done according to AJCC staging system. Results revealed that stage III had the highest rate. The distribution of cases according to stages was: 20.00% of cases within IIIC, 17.78% for IIIA and 4.44% for IIIB. followed by stage II, 15.56% for IIA, and 11.11% for IIB. And cases in stage IA comprised 2.22% of cases (Figure 10).



**Figure 10 :** Distribution of malignant cases according to pathological stage.

*ER expression*

Results showed that malignant cases with positive ER results formed 46.67% (21 cases), while ER negative was detected in (17) cases comprising (37.78%) of total (Figure 11).

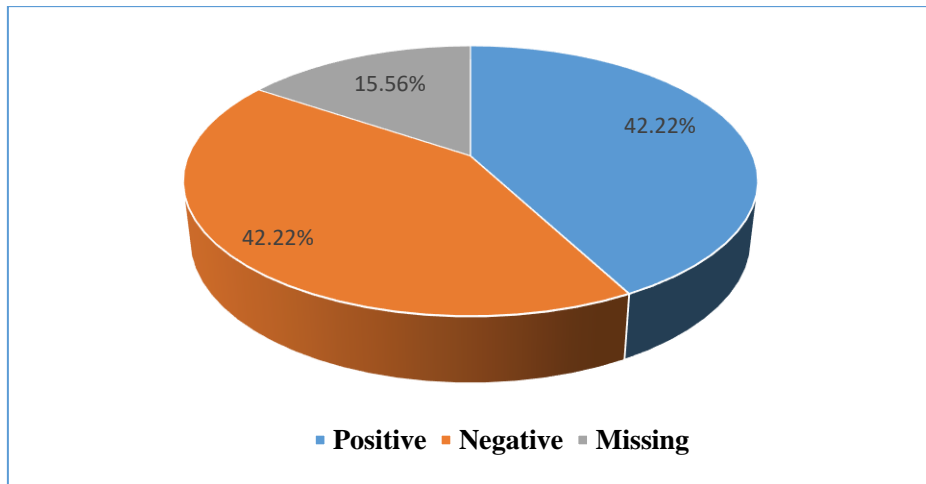


**Figure 11:** Distribution of malignant cases according to ER.

*PR expression*

Data displayed that of the total malignant instances had HR tests, the number of cases with positive PR results made up 42.22% (19 cases) which was equal to those with negative PR findings comprising 42.22% of total (Figure 12).

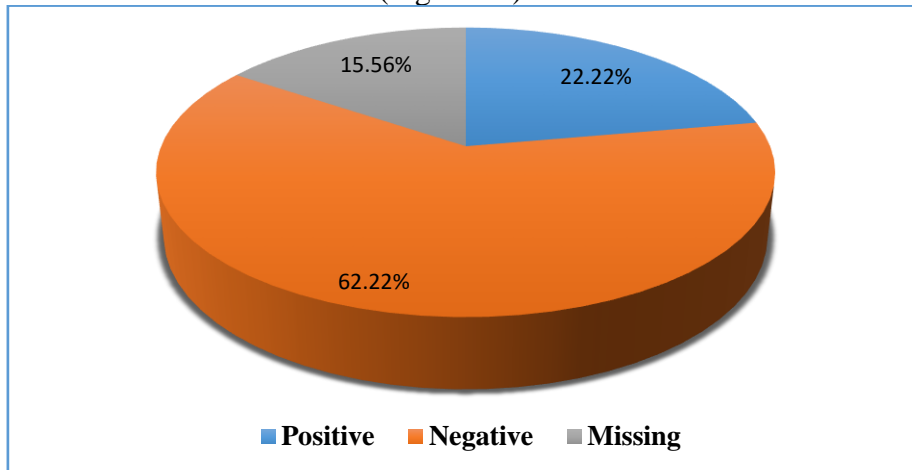




**Figure 12:** Distribution of malignant cases according to PR.

*HER2*

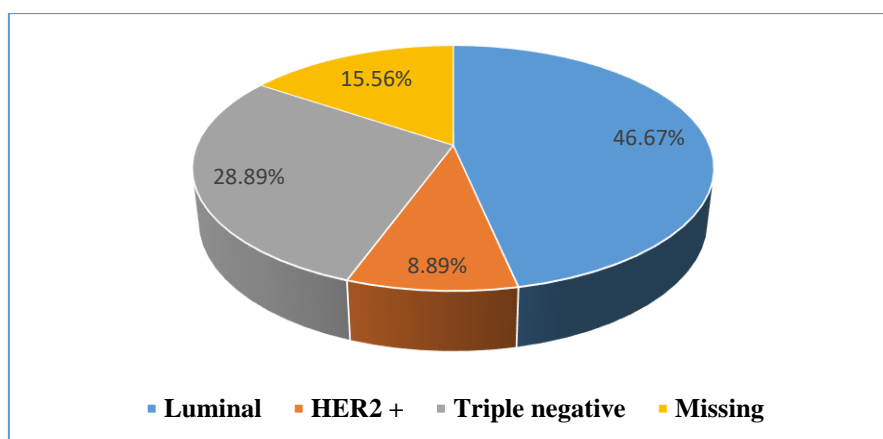
Results revealed that HER2 positive results were detected in 22.22% of cases, while HER2 negative outcome was found in 62.22% (Figure 13).



**Figure 13:** Distribution of malignant cases according HER2.

*Molecular subtype*

Results showed that luminal type formed 46.67% (21 cases), triple negative constituted 28.89% and HER2+ comprised 8.89% of the total (Figure 14).



**Figure 14:** Distribution of malignant cases according to molecular subtype.

The results of this study showed that the highest frequency of the breast cancer occurred in sixth decade of life with incidence of 35.56% and the mean age was  $54.93 \pm 14.33$  years in malignant group. This finding corresponds with Fadhil *et al.* who found that the average age of BC patients was  $52.0 \pm 8.96$  years [11]. Also it was found that the mean age was 50 years with range of 22-85 years in Basra [12]. As well as, this result is similar with data recorded by Al-Gburi and Alwan who mentioned that 54.6% of the study population was aged  $\geq 50$  years [13]. Ali Ghalib *et al.* recorded that the average age of BC in Iraqi Kurdish women patients was between 23-80 years with mean of  $47 \pm 11.0$  years [14]. Also Farra *et al.* (2019) found that the age of BC patients ranged between 27-69 years with mean of  $47.2 \pm 10.4$  years [15].

On the other hand, according to an incidence report published by the Saudi Cancer Registry in 2017, BC ranked top among women and with median age of 51 years (ranging between 20-117 years) at the time of diagnosis [16]. Another study by Salih *et al.* from Saudi recorded that the average age at diagnosis was  $48.14 \pm 14.4$  years with a range between 18 to 85 years [17]. Also, Halbony *et al.* from Jordan reported that the mean age of 115 BC patients was  $56.5 \pm 12.0$  [18]. Similarly, another study from Jordan found that the mean of age was 50 years with ages ranging between 22-79 years [19]. Conversely, the median age and range of BC women patients in Syria at diagnosis was 47yrs [20]. In a separate study carried out in Palestine on 170 patients, it was found that the mean age was  $51.71 \pm 11.11$  years, of these 39.4% patients aged between 50 and 59 years [21]. In China, a study recorded the mean age  $57.2 \pm 7.3$  years with age ranging between 39-69 years [22]. The risk of BC increases with age, but women between 50–69 years are the most frequently affected and only 2–7% of all cases are diagnosed in the age under 40 [23].

As epidemiological studies have explained, the risk of BC increases with age [24]. In women there is an increased risk of breast cancer with age as a result of longer exposure to estrogen. The risk is even greater if a woman also begins menstruating before age 12 years. In postmenopausal patients, the risk factors for both pre and postmenopausal breast cancer have been found to be similar [25]. Postmenopausal women's breast adipose and stromal cells are responsible for increasing the amount of the enzyme aromatase which is responsible for converting testosterone and testosterone into estrogen and estradiol. Because of this age-related increase in aromatase production, estrogen levels in postmenopausal women's mammary glands may be practically identical to those in premenopausal women. In this manner, estrogen produced intra-tumor can significantly influence tumor growth via its receptors [26]. Also, a risk factor for BC of less than 10% can be attributed to an inherited genetic mutation. BC is more commonly associated with environmental, reproductive, and lifestyle factors, some of which are potentially modifiable [24].

Another aspect in the current study is gender which revealed that the highest rate of BC was among females (91.11%) versus only 8.89% in males. This agrees with Ishii *et al.* from Japan who showed in their study of 142,636 BC patients that only 0.61% of cases were male breast cancer patients [27]. Less than 1% of all BCs are male BCs, making them a relatively uncommon malignant tumor [28-31]. Cancer incidence differences between the sexes are thought to be regulated at the genetic/molecular level and by sex hormones like estrogen [32]. In males, BC occurs more often in older adult males who have had hormonal changes, radiation exposure or a family history, and mutations in the *BRCA2* gene [33].

Regarding tumor size, the mean size was 3.92 cm in the malignant cases of the current study. Tumors smaller than 2 cm were observed in 11.11% of patients only, while 48.89% had tumor sizes between 2–5 cm, and 26.67% were larger than 5 cm. Our results are in consistency with Liu *et al.* who showed that the mean tumor size was 3.08 cm and the largest proportion of the size appeared in the size ranging 2–5 cm [34]. Also, Livingston-Rosanoff *et al.* from United States showed in their study that 55% of cases were between 2-5 cm [35].

Likewise, Kakudji *et al.* showed in their study that 49.3% of patients presented with tumors measuring histologically between  $2 \leq 5$  cm. Whereas, 39.1% of patients presented with tumors measuring histologically  $> 5$  cm [36]. This study is also comparable with an Indian study which reported that the tumor size of 3-5 cm was observed in the majority of cases (35, 71.43%), followed by a tumor size of  $> 5$  cm in 14 cases (28.57%) [37]. Tumors larger than 2 cm are classified as big tumors that can be determined by a clinical exam. However, tumors that are smaller than 2 cm are impalpable tumors that a clinical examination cannot confirm and can only be determined by screening mammography [38]. The patients who had a tumor greater than 2 cm may have had this due to a lack of cancer screening, inadequate breast cancer awareness, or non-compliance with breast cancer screening recommendations as a result of either distance from the health centers or difficulty accessing medical treatment. In that regard, social, economic, and psychological factors, as well as the population's age and the high percentage of less educated people, may all play a role in why women don't participate in screening drives. Moreover, women who live in rural areas have lower levels of education, are unemployed or have no known relatives with breast cancer, are more likely to have tumors larger than 2 cm [39].

Axillary involvement is one of the most important prognostic factors for BC that is associated with a 28–40 % of reduction in overall survival [40]. Our study showed that 53.33% had positive lymph nodes metastasis, while 17.78% had negative lymph nodes outcome. This corresponds to several studies, of them, Eric *et al.* reported that positive lymph nodes formed 56.6% of all cases [41]. Obeidat *et al.* (2018) from Jordan reported that the positive axillary lymph nodes comprised 64.5% of total cases [19]. Moreover, a study from Turkey recorded that 67.99% of patients had positive lymph nodes whereas 32.1%, had no lymph nodes involvement [42]. A study from China reported that 44.7% of cases had axillary lymph nodes metastasis, while 55.3% showed no evidence of axillary lymph nodes metastasis [43]. Conversely, Chung *et al.* from Korea found that nodal status was negative in 72.5 % and positive in 27.5 % of patients [44]. Axillary lymph nodes are the most typical location of breast cancer metastasis [45]. Tumor size and estrogen receptor status are frequent variables affecting axillary lymph nodes involvement in breast cancer patients. Since the number of affected lymph nodes is closely related to tumor size, routine screening programs for all women may detect the cancer at an earlier stage and smaller size, improving prognosis and survival rates [46].

Another finding of this assignment is that the right breast had more tumors(57.77%) than the left breast (42.23%). This outcome agrees with Ntekim *et al.* who found 56.25% of the tumors on the right side, while the left side tumors were 43.75% [47]. Sisti *et al.* stated in their study on patients of breast carcinoma that 50.6% of malignant tumors were in the left breast, and the right breast tumors were found in 49% of patients [48]. According to Abdou *et al.* , a previous research has revealed that BC tends to occur more frequently in the left breast, with the left-to-right ratio ranging from 1.05 to 1.26. They found in their study that 50.8 % of the left and 49.2 % of the right breasts had BC respectively. They also observed that the pathology and biology of the left breast are more aggressive compared to the right breast, However, in both laterals, there were no clinicopathological differences or changes [49].

Furthermore, IDC comprised 60% of cases in this study, and involved ILC and mixed IDC & ILC 8.89%, while mixed IDC & DCIS were 15.56%. IPC was 4.44% and DCIS 2.22%. This outcome agrees with Fadhil *et al.* from Baghdad, Iraq, who found that IDC comprised 64.6% and DCIS was 17.7%, while other histological types were 17.7% [11]. These findings are similar to that reported by Ramin *et al.* who discovered that 75.4% of cases were ductal carcinoma, 8.3% were lobular carcinoma, 7.1% were mixed, and 9.2% were other types [50]. Yang *et al.* from China also found IDC at 68.3%, ILC at 15.1%, and mixed DCIS/LCIS was 8.1% [51]. According to Cormedi *et al.* infiltrating ductal carcinoma (86.112%), in situ ductal carcinoma (2.81%), and lobular carcinoma were the three most prevalent histological types among young adults with BC (1.82%) [52]. Invasive lobular carcinoma (ILC), a less frequent histologic form, accounted for 10-15% of all invasive BCs [53], while the most common was IDC-NST which accounted for 70% to 80% of all invasive cancers, [54, 55]. In Iraq, ILC was the second most frequent histopathological type of breast cancer cases after IDC, with IDC accounting for 72.66 % of all breast cancer cases. According to an Iraqi article, the majority of breast cancer cases (60–80%) are discovered when they are already in advanced stages [55]. According to Saadat [56], between 60 and 80 percent of Arab women had advanced diseases. Women may be too hesitant or afraid to seek medical attention until the lump has grown larger. The patient may present cutaneous redness or ulceration. Asymmetry or nipple retraction may also occur in early breast cancer. The primary complaint could be a bloody discharge and patients with inflammatory breast cancer have inflamed, red and thicker breast skin.

In this study, breast carcinoma was graded into 3 major groups according to the Nottingham modification of the Bloom and Richardson system. Our findings showed that most cases were in grade II, comprising 64.44% of cases, and grade III was 31.11%, while grade I was 4.44%. The results of this study were similar to the results found in a comparative study on the clinicopathological profiles of breast cancer among Iraqi and British patients. In both countries, grade II was the highest (Iraq, 67.6% and British 48.3%), followed by grade III (Iraq, 25.7% and British 35.1%), and then grade I (Iraq, 6.7% and British 16.6%) [57]. Chung *et al.* showed in their study that the higher percentage of patients were 61.3% in grade II, 31.9% in grade III, and 6.9% in grade I [44]. Likewise, similar studies recorded that grade II tumors constituted the highest number of cases [58-60]. While another study revealed that a greater proportion of cases were in grade III, constituted 77.6% [61], and 52.5% in a study by Yoshikawa *et al.* [62]. According to studies on other types of cancers in Iraq, the tumor grade most common in ovarian cancer was grade 3 which constituted 40.7%, and in colorectal cancer it constituted 67% of grade 2 [63, 64].

The grading process consists of three factors: (1) the percentage of cancer cells formed into tubules; (2) the difference in the nucleus size between healthy and malignant cells; and (3) the rate of cancerous cells division. Pathologists classify tumors into three categories based on these parameters, with the higher the grade, the greater the difference in histological structures

between cancerous and healthy tissue [65]. The grading systems utilized and the patient cohorts, including age distribution, symptomatic versus screening population, early versus advanced breast cancer groups, and specifics of tissue fixation, can explain the variation in the proportion of each grade reported in the various studies [66]. In general, a lower grade number suggests slower-growing cancer that is less likely to spread and has a better prognosis, whereas a higher grade number indicates faster-growing cancer that may require immediate or more severe treatment [67].

In this study, malignant cases were staged according to the 7th AJCC TNM staging system. The findings of this study revealed that the highest proportion of cases were reported at stage III of disease (20.18% for IIIC, 17.93% for IIIA, 4.44% for IIIB). Then, stage II (11.11% for IIB, 15.69% for IIA), and the lowest frequencies were in stage IA comprising 2.22%. *Mutar et al.* (2019) from Iraq found that the highest frequency also occurred in stage III (28.6% for IIIA) [4]. While in another study in Iraq by *Jamel et al.* reported that the highest frequencies were in stage II (25.00% for IIA and 23.86% for IIB), then in stage III (21.59% for IIIA) [68]. While two studies from China and Korea found that the highest proportion of patients was in stage I (52.9% and 45.1% for IA respectively) [69, 70].

However, if the patients experience distant metastasis, their chance of survival is significantly reduced. The total 5-year relative survival rate for localized illnesses is 99%, for regional illnesses it is 86%, and for distant-stage illnesses it is 27% [71]. According to data from developing countries such as Pakistan and India, as well as other local studies, less than 10% of patients had stage I cancer. The rest of the patients had stage II or advanced diagnoses. The lack of health education and awareness, false beliefs about cancer therapy, and a firm belief in conventional medicine are the major causes of the delay [72].

Hormone receptor status is recognized to be a prognostic factor and a predictor of hormone therapy response in patients with breast cancer. Therefore, a thorough investigation of the status of the ER and PR is crucial for the management of breast cancer [73]. In the current study, 46.67% of patients had positive ER, while 37.78% had negative ER. In the PR, negative and positive cases were equal and made up the same ratio of 42.22% per each. This agrees with *Yang et al.* who reported that the positive ER rate was 50.5% against 49.5% negative, as well as the PR positive was 44.1% but the PR negative was 55.9% [51]. According to *Sun et al.*, the PR result of the positive and negative cases was very close to each other, comprised of about 50.4% positive and 49.6% of negative [74].

Also *Ligorio et al.* found in their report that the high ratio of ER was positive and comprised 63.8%, while negative ER was 36.2%, as well as PR was negative in 57.6%, while it was positive in 42.4% [75]. On the other hand, *Kim and Park* also showed in their research that the ER positive was highest from the negative and comprised 63.2%, but the positive PR represented the highest value and constituted 48.3% [76]. This was also observed in other studies [36, 44, 77]. The results in this study may be considered low-expression when compared with the United States where there are about 250,000 new cases of breast cancer every year, and nearly 80% of them have estrogen receptors that are active (ER+) [78]. The low level of hormone receptor expression may indicate a high grade and advanced stage of the disease when it is first checked [79].

Moreover, the human epidermal growth factor receptor 2 (HER2) is a well-known negative prognostic factor in BC [80]. It is connected to a high mortality and recurrence rate, and is a predictor of chemotherapy response in breast cancer patients [81]. In this task, the great majority of cases were HER2 negative, constituting 62.22% of patients, while only 22.22% were HER2

positive. This was similar to the findings of Wang *et al.* who found that HER2 was negative in 76.8%, while it was positive in 23.2% [82]. These values also agree with several studies [41, 43, 76, 83]. About 20–25% of all breast cancers overexpress HER2 and are referred to as HER2-positive, and this also agrees with this study [84]. HER-2/neu and HR status typically have an inverse relationship [85]. According to the results of many studies, overexpression or amplification of the HER-2/neu gene has been linked to lymph node metastasis, high proliferative, tumor grade, HR negative, and p53 positivity [86].

Finally, according to the molecular type, our results showed that among the malignant cases, the luminal type formed 46.67%, followed by triple negative which constituted 28.89%, and HER2+ which constituted 8.89% of the total cases. Mutar *et al.* from Iraq, found that the highest frequency was also within the luminal type (luminal B, 36.7% and luminal A 21.6%) followed by triple negative which constituted 21.6%, and HER2, (20.1%) [4]. Another study found that the luminal types formed a high ratio in molecular subtype, then triple negative, and a low ratio in HER2+ [83]. While recent research from Basra, Iraq, indicates that HER2+ formed ratio of (33.6%) and the triple negative comprised 16% [87]. Another study in Saudi Arabia showed that the most common subtype was luminal A (58.5%), followed by triple negative (16%), luminal B (14%), and HER2-positive 11.5% [88]. Approximately 75% of breast cancers are ER and/or PR positive. ER-positive tumors express ER, PR, ER responsive genes, and other genes that encode luminal epithelial cell proteins, so are referred to as the luminal group [89]. The luminal subtype is classified into luminal A and B, with luminal A breast tumors having the best prognosis in terms of distant metastasis [90]. According to a study conducted in Brazil, the distribution of BC molecular subtypes varies by geographical location, as it should, taking the continental dimension and the racial variation of the regions in consideration [91].

## Conclusion

In this study, the incidence of BC was higher within the sixth and seventh decades of age, with a high incidence in the right breast. The prevalent tumor diameter was 2–5 cm in malignant cases. The majority of cases were IDC and had positive lymph node tumor metastasis. Most malignant cases were detected at late stages of disease (stage III). A large proportion of malignant cases were grade II tumors. The hormone receptor status was mostly ER positive, while PR results came equally positive and negative, even though the majority of HER2 was negative, and luminal subtypes accounted for nearly half of all molecular subtypes.

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