

## STUDY OF SOME RISK FACTORS IN PATIENTS WITH UNTREATED BREAST CANCER IN ERBIL CITY

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### Summary

This study was carried out in Rizgary and Hawler Teaching hospital in Erbil city, from the period of August 2010 to June 2011. A total of 115 women patients with breast tumor (55 malignant and 60 benign) and 40 females as a control group with age ranged (18-71) in both patients and control group were participated, they were matched with patients by age group without any history of breast problem or neoplastic disease and not had any other cancer. Data were collected by interview with patients and control group, a questioner form were provided to each patients which include (age, age at menarche, regularity of menstruation, etc.) and clinical file made for each patient who attends to these two hospitals for each patients for the first time, in spite of histopathological diagnosis. Results indicated obvious relation between risk factor and breast cancer (BC), among these factors is the age; the most frequent age for breast cancer was that at age group (38- 47).Percentage of patients starting age menarche after 12 year was higher when compared with patients starting at or before 12 year. The results showed higher percentage of BC in patients who have regularity menses when compared with irregular menstrual cycle. Age of first pregnancy in 20 years and greater which was higher than other group. The results indicated that the percentage of BBD patients which diagnosed premenopausal was higher than postmenopausal. Higher percentage of breast feeding found in BC patients when compared with bottle feeding. Oral contraceptive pills users occupied higher percentage in patients. Patients which not used hormone replacement therapy (HRT) have higher percentage when compared with patients used HRT. About half of the patients recorded positive family history. The numbers of patients diagnosed as stage third and fourth were higher compared with those stage two, unknown and first stage. According to the type of benign breast disease, the unknown cause showed higher percentage when compared with other types.

**Keywords:** Breast cancer, risk factors, epidemiological study.

This study is a part of M.Sc. Thesis.

### Introduction

Cancer is the leading cause of death in economically developed countries and the second leading cause of death in developing countries (World health organization, 2008). It is the most frequently diagnosed cancer and the leading cause of cancer death in females worldwide according to global statistics (2008), accounting for 1.38 million of the total new cancer cases and 458,400 of the total cancer deaths annually (Jemal *et al.*, 2011). Breast cancer is the second most common type of cancer after lung cancer. One woman in ten will develop the disease and one in 29 will die as a direct result of it (Wernberg *et al.*, 2009). Generally, breast cancer refers to cancer originating from breast tissue (Martini *et al.*, 2006). In Iraq, breast cancer is the commonest type of female malignancy, accounting for approximately one- third of the registered female cancers according to the latest Iraqi Cancer Registry (Iraqi Cancer Registry, 2007). The incidence of breast cancer in Erbil city was more

common than the other type of cancers (Iraqi Cancer Registry, 2005).

### Aim of the study

The present study was aimed to shed light on the risk factors which may use for detection and they are related with breast cancer.

### Materials and methods

The study was include 115 female patients presented with breast mass (55 malignant and 60 benign) attended Rizgary and Hawler teaching hospital in Erbil city from August 2010 to June 2011. The age of the patients ranged from 18-71 years and the mean was 44.5 years. A total of forty women selected as control group, they were matched with patients by age group without any history of breast problem or neoplastic disease and not had any other cancer. Data were collected by interview with patients and control group, a questioner form were provided to each patients which include (age, age at menarche, regularity of menstruation, etc.) and clinical file made for each patient who attends to these two hospitals for each patients

for the first time, in spite of histopathological diagnosis.

## Results

### Age groups of the patients

The highest number of breast cancer patients were found at age interval (38- 47) year, while the lower or minimum record was at aged 58 and older. The higher number about benign breast disease patients was found at the table age interval (28- 37), as well as the minimum number was found in the last age interval.

### Patients and age at menarche

In fig: 2 about 45.46% of the breast cancer patients have got their menarche at or before 12, while 54.54% of them got it after 12 years old. However, about the BBD the data is different, 16.67% got their menarche at or before 12 years, and 83.33% got it after 12 years old. Women with early age at menarche or late menopause have an increased risk of developing BC.

### Regularity of menstruation and patients

In this study, regularity of menses is considered as a risk factor for BC as showed in (Fig. 3). This study showed 74.54% of BC patients had regular menses, while only 25.46% of them had irregular menstrual cycle. The result for BBD patients showed that 76.66% had regular and 23.34% had irregular menstrual cycle.

### Age at first pregnancy of the patients

In fig: 4 about 16.36% and 16.66% of breast cancer and BBD patients were single or infertile, 27.27% of breast cancer patients had first pregnancy before 20 years old, while 56.36% were at 20 or older. However, 36.66% of the BBD patients had first pregnancy before 20 and 46.66% had it at or after 20. About 55% of our patients had their first pregnancy at age 20 or older.

### Patients and age at diagnosis

Menopausal age used as a point for this risk factor. 65.46% of the breast cancer patients was diagnosed premenopausal, while it was higher in BBD patients which were 80%. Therefore, 34.54% of the BC patients were diagnosed postmenopausal, whereas for BBD patients were 20% as shown in (fig. 5).

### Relation between BC and oral contraceptive pills

In this study, using of oral contraceptive pills (OCP) was a good risk factor for breast cancer. 78.18% of BC patients were using the OCP, while 21.82% did not used it. About the BBD

patients the data showed that about 33.3% used OCP, and 66.7% neglected the OCP (fig. 6).

### Patients and hormone replacement therapy

In fig: 7 (16.36%) breast cancer patients were taking HRT and 83.64% were not taking HRT, while for the BBD patients 8.3% were taking HRT and 91.7% were not taking HRT

### Relation of BC to having family history

The higher number recorded for this risk factor in both BC and BBD patients were from patients who had no family history (55%, 75%) respectively. 29% and 8.33% of the patients had first degree family history relation for both BC and BBD patients respectively. In BC 9% had second degree, while 16.66% of BBD patients had second degree, regarding the third degree 7% of BC was found, while there was no record about third degree for BBD patients, (fig. 8).

### Distribution of patients according to type and stage of disease

Breast cancer patients were 100% had invasive ductal carcinoma, first stage showed zero percentage, while in the second, third and fourth stages, the percentages were 25, 30, and 30% respectively, and 15% of them had unknown stage of BC. About the BBD patients 35% had unknown type of the disease, 30% had lipoma, 15% had fibroadenoma, 5% had fat necrosis, 10% had fibrosis, and 5% had duct ectasia shown in (fig. 9 and 10).

### Body mass index and breast cancer

Body mass index is an important risk factor for BC. There were 40.45% of the BC patients had BMI  $\geq 30$  which were obese females, while 40.63% of them had BMI (25- 29.9), 15.54% of the patients had BMI=18.5- 24.9, and only 3.63% of them had BMI < 18.5. In BBD patients 33.33% had obesity (BMI  $\geq 30$ ), 45% of the examined patients had over weighted BMI (25- 29.9), only 21.66% had BMI=18.5-24.9, and no patient has BMI < 18. While 80.78% of patients had BMI more than 25, which was considered as overweight and obese women as shown in (fig. 11).

### Marital status of the patients

Fig: 12 showed 9% and 11.66% of breast cancer and BBD patients were single respectively, 78.18% and 76.66% of BC and BBD patients were married respectively, while 12.72% and 11.66% of BC and BBD patients were widowed respectively. Our results showed about 7.5% of patients were single, while all of the remaining was married.

## Discussion

### Age groups of the patients

Our study was in agreement with Montazeri *et al.* (2003) and Rennert (2009) which showed that the Iraqi BC patients had an age distribution that was nearly the same as that seen in Iran, Egypt and Jordan. In Sulaimanyiah- Iraq also agreed with our findings they found that currently diagnosed at advanced clinical stages with 60% of patients being under 50 years of age (Majid *et al.*, 2010). In contrary with our study, in the United States, more than three- fourth of all breast cancers occurred in women aged 50 or older (Palmer *et al.*, 2003). The greatest risk of BC occurs with increasing age, with incidence doubling every 10 years until menopause (McPherson *et al.*, 2000). This increasing risk may be indicative of the lifetime accumulation of exposures to those risk factors, as well as genetic events throughout the lifetime (Alwan, 2010).

### Patients and age at menarche

A woman who began menstruating before 12 years old has a 10- 20% increased risk of BC compared to one whose menstruation started when she was older than 14 years of age (Berkey *et al.*, 1999). In addition, women who experience a delayed natural menopause (after the age of 55) are twice as likely to develop BC compared to women who experience menopause before the age of 45 (McPherson *et al.*, 2000) which is in agreement with our study. Older age at menarche typically is reported to be associated with reduced BC risk, while older age at menopause is associated with increased risk. These relationships are believed to be mediated through estrogen production (Henderson *et al.*, 1996).

### Regularity of menstruation and patients

This study showed only one-fourth of the BC patients had irregular menstruation to the extent that irregular menstrual cycles reflect an ovulatory cycles, our findings support the hypothesis that the cumulative number of regular ovulatory cycles increases BC risk (den Tonkelaar and de Waard, 1996). Rockhill *et al.* (1996) found little support for the hypothesis that a longer time until onset of regular menstrual cycling was associated with reduced risk of BC, which is in contrast with our study. Parazzini *et al.* (1993) reported an increased risk among women who had menstrual cycles lasting 31 days or longer, but those women whose cycle

was too irregular to estimate were at reduced risk.

### Age at first pregnancy of the patients

Other reproductive events have also shown a linear association with risk for BC, specifically, women who gave birth for the first time before age 18 experience one- third the risk of women who have carried their first full- term pregnancy after age 20 (Yoo *et al.*, 2002). Women who have their first full- term pregnancy at a relatively early age have a lower risk of BC than those who never have children or those who have their first child relatively late in life (Wohlfahrt and Melbye, 2001). There is also consistent evidence that first pregnancy completed before age 30- 35 lowers risk of BC and that first full- term pregnancy after age 30- 35 raises risk (Helmrich *et al.*, 1983). It has been observed that five to seven years after pregnancy, women, especially older women are at increased risk of BC. This increase in risk is thought to be attributable to the increase in gestational hormone levels that occur during the first pregnancy (Bernstein, 2002 and Dumitrescu and Cotarla, 2005).

### Patients and age at diagnosis

A 2- to 4- fold higher risk was found for women who experienced menopause after 50 years of age; meanwhile, the time from menarche to menopause is an interesting factor in considering its relation to the mechanism of breast carcinogenesis (Suh *et al.*, 1996). Women who have menopause after the age of 55 years are twice as likely to develop BC as women who experience the menopause before the age of 45 years (Khalid *et al.*, 2009). Furthermore, the increased cumulative exposure from the combined effect of early menarche and late menopause has been associated with elevated risk (Lipworth, 1995).

### Relation between BC and oral contraceptive pills

Other study attempting to link oral contraceptives with increased BC have been inconclusive (Marchbanks *et al.*, 2002). A case control study was done in Basrah in 2005 found that there was no association between the use of OCP and development of BC (Dahooz and Hawaz, 2005). Some studies suggest that past use of OCP may increase risk of BC in postmenopausal women, especially in those with a long history (more than 10 years) of OCP use (Van Hoften *et al.*, 2000). The association of OCP use with BC is related to the duration,

dosage, pattern of usage, type of OCP and the age of first use (McPherson *et al.*, 2000).

#### **Patients and hormone replacement therapy**

Use of estrogen replacement therapy is another factor associated with increased hormone levels and it has been found to confer a modest (less than two-fold), elevation in risk when used for 10-15 years or longer (Kelsey, 1993). The long-term (more than five years) use of postmenopausal estrogen therapy (ERT) or combined estrogen/progestin hormone replacement therapy (HRT) may be associated with an increase in BC risk (Downing *et al.*, 2007).

#### **Relation of BC to having family history**

Similar to our findings, others found most women who get BC (approximately 80 percent) have no such family history of the disease (Porch *et al.*, 2002). There was an increased risk of BC among Kurdish patients who had a positive family history compared to case controls.

#### **Distribution of patients according to type and stage of disease**

According to the WHO classification (World health organization, 2008), the most common histological type determined microscopically was invasive ductal carcinoma. According to the AJCC system, the frequencies were 7.6%, 45.1%, 31.5% and 15.7% for stages I, II, III and IV respectively (Alwan, 2010). For patients with a designated stage, there was no significant relationship between tumor stage and age nor was the relationship significant when patients whose stage was unknown were included (Majid *et al.*, 2010).

#### **Body mass index and breast cancer**

Some studies agreed with our results which they had shown that a high BMI was positively related with BC (Helmrich *et al.*, 1983). A study done in Basrah in 2005 showed significant association between increase body mass index and risk of BC (Dahooz and Hawaz, 2005). Obesity is another known risk factor for BC. Obese women have an increased risk for postmenopausal but not premenopausal BC. The association between obesity and BC risk has been proposed to be largely due to increased estrogenic activity in overweight women. Increased body weight results in elevated circulating estrogens from peripheral aromatization of androgens in adipose tissue. Breasts, which are estrogen-sensitive tissues, are therefore exposed to more estrogen stimulation in obese women, leading to an

increased risk for BC (Kelsey, 1993 and McTiernan, 1997).

#### **Marital status of the patients**

Study by Ibarluzea *et al.* (2004) agreed with our results which documented that BC is common in married females. Other study also found higher ratio of BC among married females (Montazeri *et al.*, 2003), while Pharoah *et al.* (1997) was disagree with our results which showed that never married women were at higher risk for BC which may be due to exposure of married women to many hormonal changes like parity, and this factor showed to be protective factors against breast cancer.

#### **Conclusions:**

- Age group (38- 47) was the most susceptible group for breast cancer.
- In breast cancer patients, some risk factors like (regularity of menstruation, age at diagnosis, BMI, age at first pregnancy, OCP and family history) were more prevalent than BBD.

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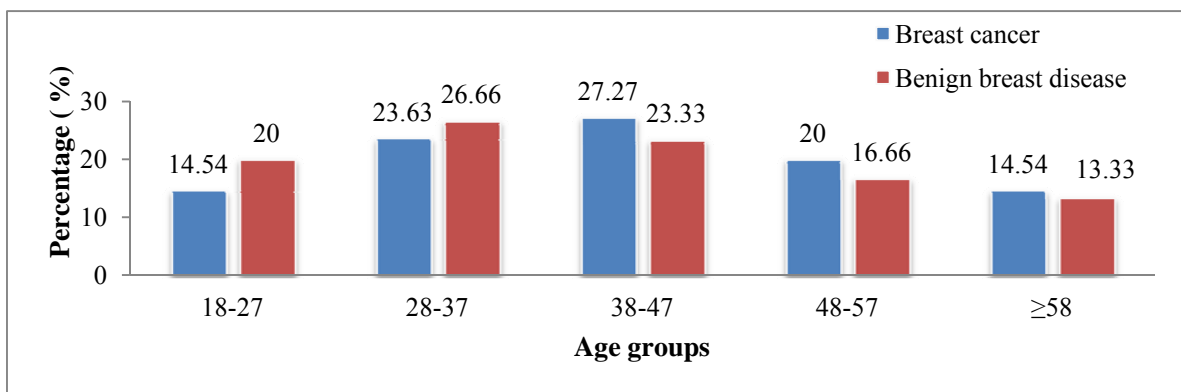


Figure (1): Age groups of the patients.

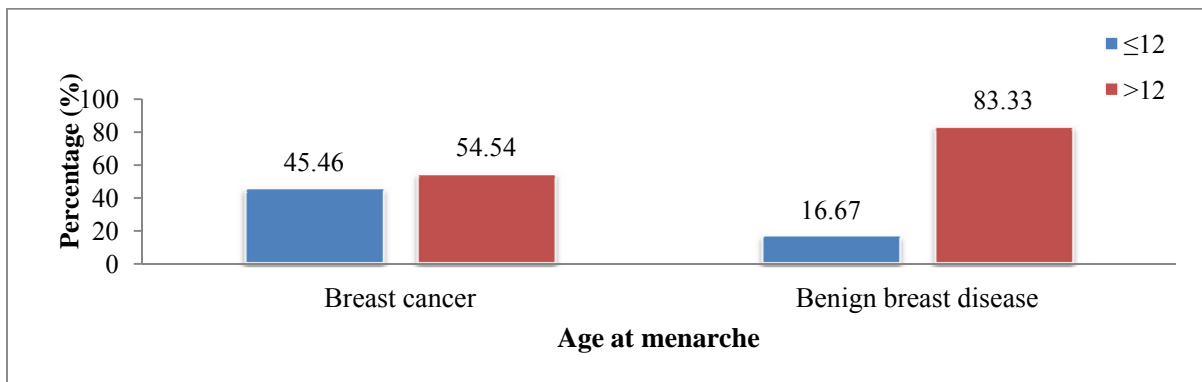


Figure (2): Patients and age at menarche.

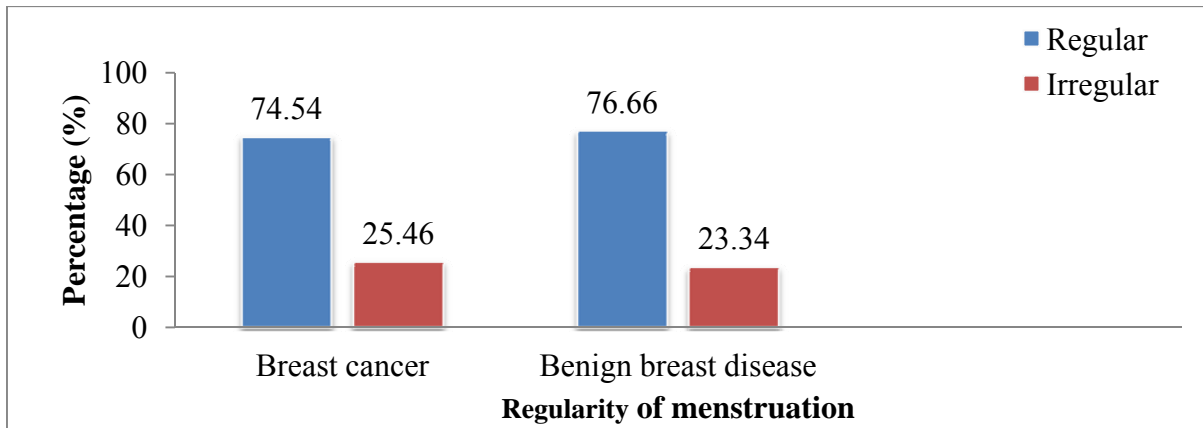


Figure (3): Regularity of menstruation and patients.

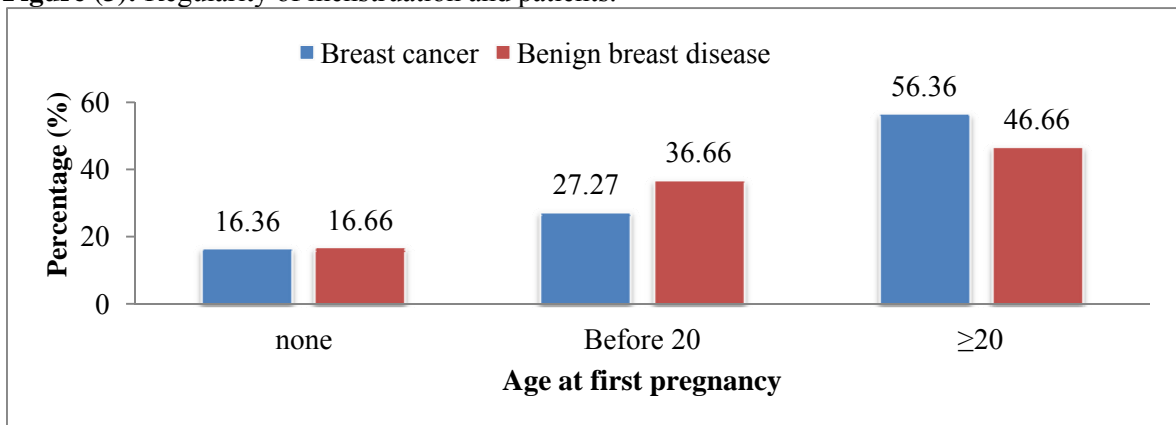


Figure (4): Age at first pregnancy of the patients.

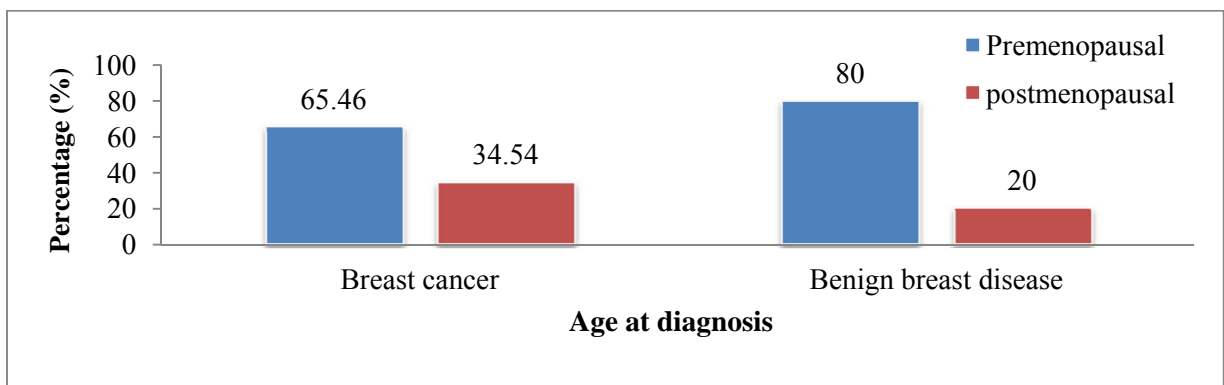
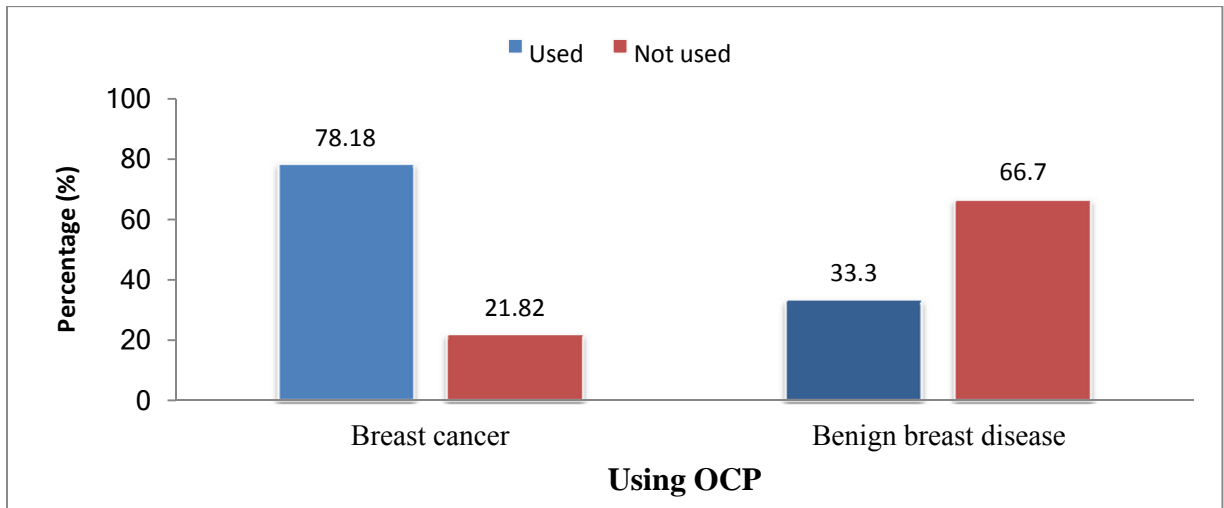
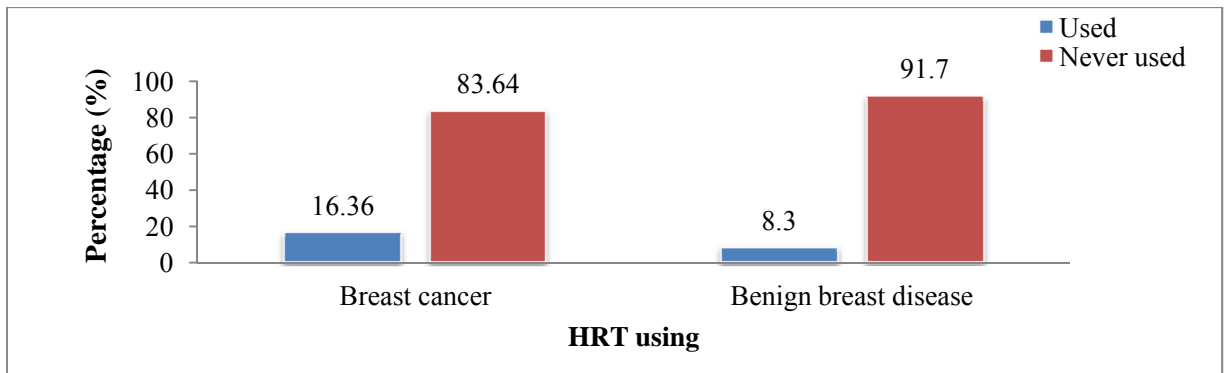


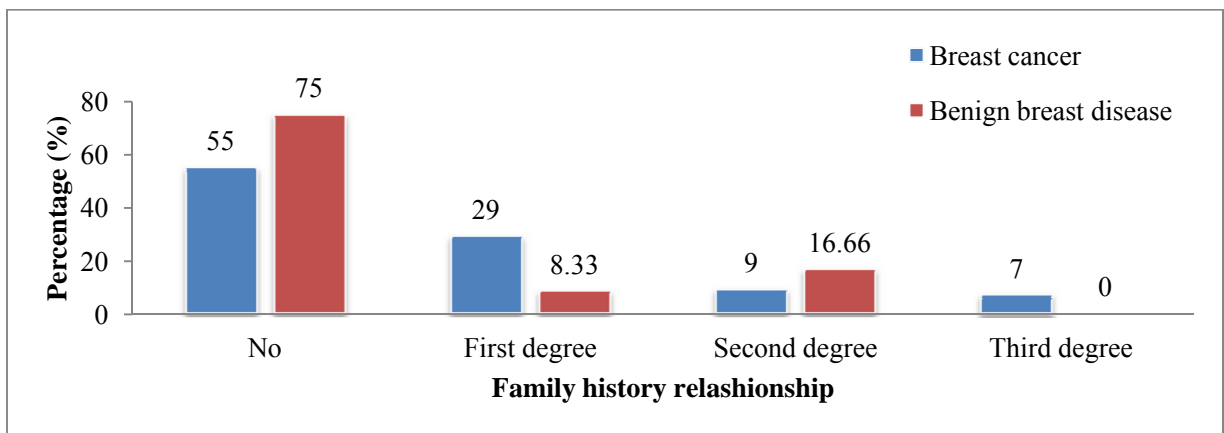
Figure (5): Patients and age at diagnosis.



**Figure (6):** Distribution of patients according to using OCP.

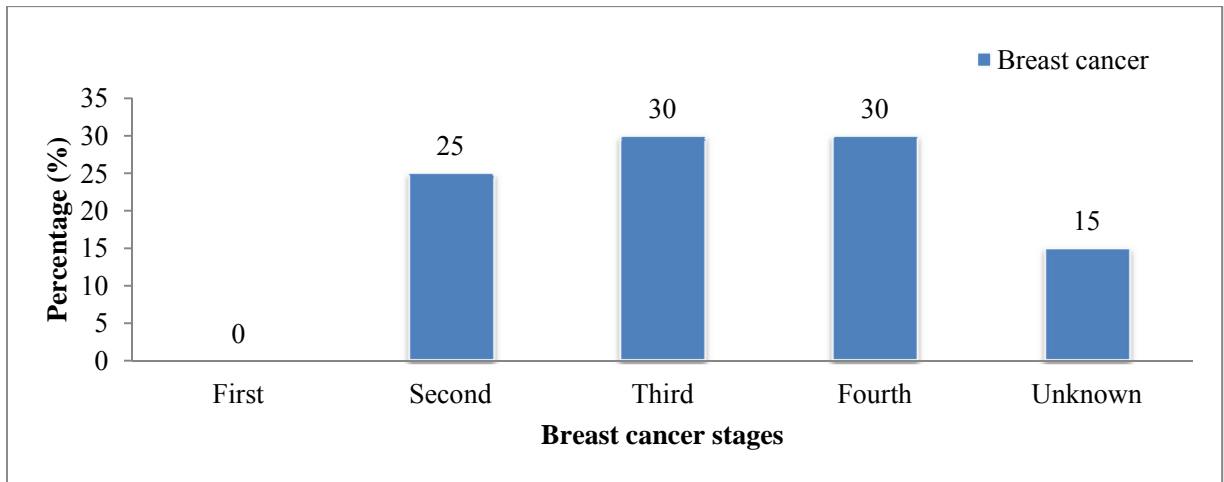


**Figure (7):** Patients and hormone replacement therapy.

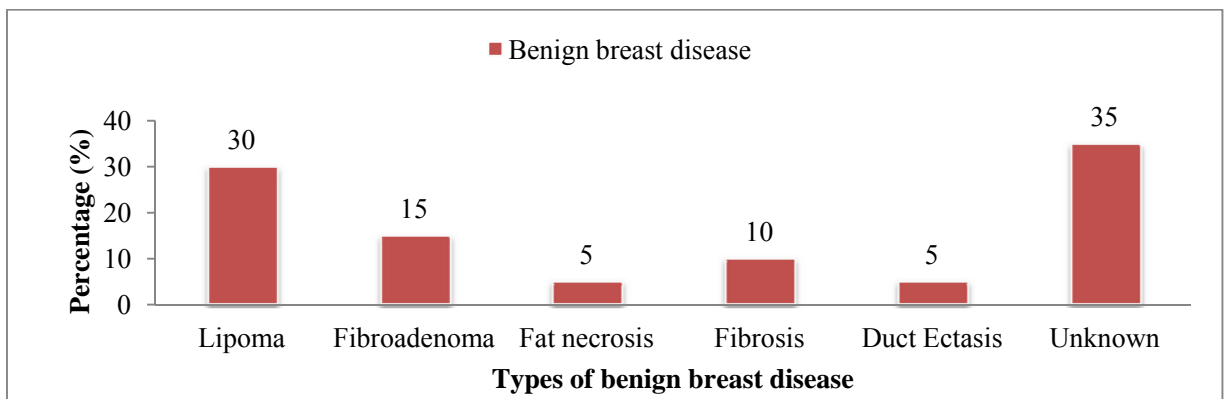


**Figure (8):** Percentage of patients according to family history relationship.

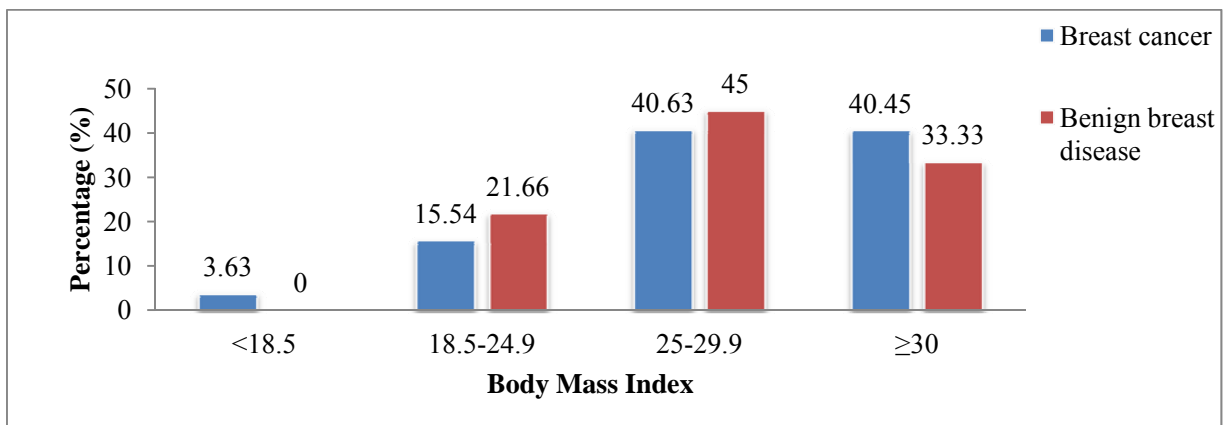




**Figure (9):** Percentage of stages of the infiltrative ductal carcinoma.



**Figure (10):** The percentage of types of BBDs.



**Figure (11):** Patients and body mass index.

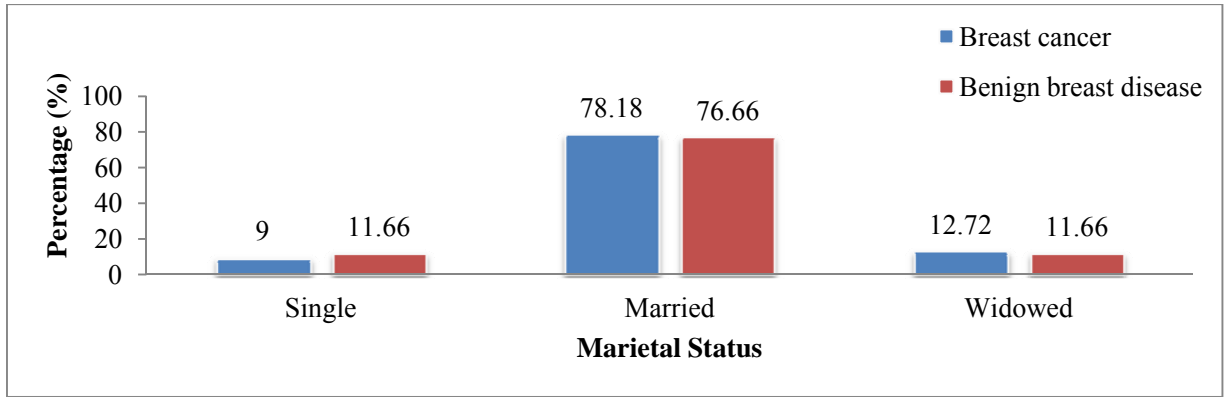


Figure (12): Percentage of the patients according to the marital status

### دراسة بعض عوامل الخطورة في السرطان الثدي قبل معالجة في مدينة اربيل

#### الخلاصة

اجريت هذه الدراسة في مستشفى رزكري و اربيل التعليمي في محافظة اربيل من الفترة آب ٢٠١٠ الى حزيران ٢٠١١ , شملت ١١٥ مريضة مصابة بورم الثدي (٥٥ ورم خبيث و ٦٠ ورم حميد) مع ٤٠ امرأة سليمة اعتبرن كمجموعة السيطرة.

أظهرت النتائج عدة علاقات بين عوامل الخطورة وسرطان الثدي ومن هذه العوامل العمر، حيث تشير الدراسة الى ان معظم الحالات كانت بين الفئة العمرية (٣٧-٤٨) سنة عند مقارنتها بالفئات العمرية الأخرى. عدد المريضات اللاتي بدأن الدورة الشهرية بعد ١٢ سنة كان أعلى مقارنة بالنساء اللاتي بدأن عند أو قبل ١٢ سنة. اظهرت النتائج ان النساء اللاتي لديهن الدورة الشهرية بشكل منتظم اظهرت أعلى ارتفاع عند مقارنتهن بالنساء اللاتي لديهن الدورة الشهرية غير منتظمة. كذلك النساء اللاتي ولدن اول طفل عند سنة ٢٠ او أكثر شكلن اعلى نسبة اصابة بالسرطان مقارنة ببقية النساء. النساء اللاتي يستخدمن حبوب منع الحمل كان لهن اعلى نسبة اصابة بسرطان الثدي مقارنة بالاصابة بالاورام الحميدة بينما النساء اللاتي لم يستخدمن معالجة بديلة بالهرمون سجلن أعلى نسبة مقارنة بالنساء اللاتي يستخدمن هذه المعالجة. واظهرت نصف المريضات لهن تاريخ عائلي للمرض.

## لێكۆلینهوهی هەندێك له هۆكاره مەترسیه كانی شێرپهنجەیی مەمك پێش چارهسەر كردن له شاری ههولێر

پوخته

ئەم توێژینهوهیه له نهخۆشخانهی رزگاری و نهخۆشخانهی ههولێری فێرکاری له شاری ههولێر ئەنجامدراوه له نیوان (ئاب ۲۰۱۰ - حوزەیران ۲۰۱۱). کۆی ۱۱۵ ئافرەت وەرگیراوه به شیوهیهك (۵۵ نهخۆشی شێرپهنجەیی مەمك (زیان بهخشی) ، ۶۰ نهخۆشی گریی مەمکی خاویڤن (بی زیان). و ۴۰ ئافرەت وەك کۆنترۆل وەرگیراوه. ئەنجامی ئەم توێژینهوهیه دەریخست کەوا پەيوەندیهکی بههێز ههیه له نیوان هۆكاره كانی مەترسی توشبوونی شێرپهنجەیی مەمك، یه كێك لهم هۆكارانه تەمەنه، دەرکەوت کەوا زۆربهی توشبوانی شێرپهنجەیی مەمك له نیوان تەمەنی (۳۸-۴۷) سالی بوون به بهراورد له گەل تەمەنه كانی تر. رێژهی توشبووان به نهخۆشی شێرپهنجەیی مەمك لهو ئافرهتانهی كەدهگه نه ههزره كاری (دەستپێکی سووری مانگانه) رێژهی توشبوون دواي ۱۲ سالی زیاتره لهو ئافرهتانهی كە ههزره كاریان له ۱۲ سالی یان زووتر. دەست پێدهكات. نهخۆشی شێرپهنجەیی مەمك لهو ئافرهتانهی كە سووری مانگانهیان رێك و پێكه زیاتره لهوانهی سووری مانگانهیان نارێكه. رێژهی توشبوون لهو نهخۆشانهی كەوا یه كەم منداڵ یان سكهپری تهواویان تەمەنی ۲۰ سالی یان گهورهترهوه بووه زیاتره لهو نهخۆشه كانی تر. ئەو ئافرهتانهی كەوا حهبی دژی سكهپریان بهكارهیناوه زۆرتترین رێژهیان ههبووه بۆ توشبوون به شێرپهنجەیی مەمك، به بهراورد له گەل گریی مەمکی خاویڤن. ئەو ئافرهتانهی كەوا چارهسەری هۆرمۆنیان وەر نهگرتوه زۆرتترین رێژهیان تۆمار كردهوه به بهراورد له گەل ئەو ئافرهتانهی كەوا ئەم چارهسەریانهیان وەرگرتوه. نیوهی توشبووان میژووی شێرپهنجەیی مەمکیان ههبووه له خهزاندا. ژمارهیی نهخۆشه كانی توشبوو به شێرپهنجەیی له قوئاعی سی یهه و چوارهم زیاتر بوو وەك له قوئاعی یه كەم و دووهم و قوئاع نهزانراوهكان. دەربارهی توشبوونی گریی مەمکی خاویڤن، هۆكاری توشبوونی نهزانراو زۆرتترین رێژهی تۆمار كردهوه.