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RESEARCH ARTICLE

BREAST CANCER AMONG WOMEN OF ERBIL.IRAQ'S KURDISTAN REGION.

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Abstract

Background and objectives:-The incidence of breast cancer is increasing and considered as the top cancer in women in both of the developed and the developing world. Study of the incidence and early detection are necessary for breast cancer control. In this study we assessed the incidence and the risk factors of breast cancer among females.

Methods:- A retrospective study in a descriptive and analytic design based on findings from the statistical department of Erbil Directorate of Health. The database was prepared by our research partner and used by specialized physicians in surgery who had interviewed 549 women with breast cancer from the period between 1st of January 2009 to 31st of December 2009. Descriptive and inferential statistics were used through the Microsoft Access Database and the Statistical Package for Social Sciences (SPSS, Version 21). Bivariate correlations were used for data analysis. The P value of ≤ 0.05 was considered as statistically significant.

Results:- The mean (±SD) age of the 549 studied women was 32.71 ± 10.64 years ranging from 13 to 73 years. The most registered age group 201 (36.6%) by breast cancer was between 21 to 30 years old females. The peak incidence 37 (6.7%) of the disease was at the age 40 years. The least 5 (0.9%) registered age group was more than 60 years. The majority 465 (84.7%) of the patients were housewives. More than one third 40 (7.21%) of them were cigarette smokers. About one third 193 (35.2%) were nulliparousfemales. The least number [3 (0.5%), 1 (0.2%)] of registered women by breast cancer were in the groups of Para 13 and 15 respectively. One quarter 142 (25.88%) of the patients were using contraceptive pills. Two thirds 66 (12.05%) had breast cancer in their family histories. About one quarter 151 (27.51%) of the study sample had breastfed their children.

Conclusions:-Breast cancer incidence was higher among the registered young females than older ages with exception to the age 40 which recorded the highest incidence of the disease. The disease was very rare among Para 13 and 15 women. Being housewife, cigarette

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smoking, nulliparity, using oral contraceptive pills, and presence of breast cancer in the family history among the studied women can be considered as risk factors for breast cancer. Conduction of further studies about breast cancer and establishment of a Breast Cancer Research Center in Erbil City are recommended.

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Introduction:-

Breast cancer formed 23% (1.38 million) of the annual total new cases of cancer and 14% (458,400) of the total cancer deaths in females worldwide during the year 2008 (Jemal A et al, 2010). According to Cancer Facts and Figures, only in the US, this estimation is 249,260 new cases and 40,890 deaths for 2016 (Cancer Facts and Figures, 2016). Studies indicated that the incidence rate of breast cancer among women in Kurdistan region of Iraq has grown in the last decades (Mulah Kareem S et al, 2015). Further studies in Iraq as whole reported that breast cancer is the most common type of cancer forming one third of the female cancers and that cause one quarter of female deaths from the disease. Within the last two decades, there has been an obvious increase in the incidence rates of breast cancer, which became one of the major threats to Iraqi female health (Iraqi Cancer Board, 2010 - International Agency for Research on Cancer, 2010 - Al-Alwan and Nada A.S, 2014). The World Health Organization (WHO) recommended early detection and adequate therapy for the purpose of offering a reduction in breast cancer mortality. Lack of early detection programs joined with inadequate diagnostic and treatment facilities are the leading causes to low survival rates in Iraq (WHO/EMRO, 2010). This study aimed to determine the incidence of breast cancer among the registered women in the hospitals and health centers of Erbil governorate and defining the most affected age groups and correlating the disease with certain variables as well.

Subjects and methods:-

Subjects:-

A retrospective study in a descriptive and analytic design based on findings from the statistical department of Erbil Directorate of Health. Erbil is the capital of Iraqi Kurdistan Region which is located on latitude 36.11 and longitude 42.2 and covering an area of about 60 km², while the governorate is covering about 17981 km² (UNICEF, 2000). The database was prepared by our research partner and used by specialized physicians in surgery who had interviewed 549 women with breast cancer from the period between 1st of January 2009 to 31st of December 2009. This was the most reliable sample representing the original population of Erbil governorate, due to the fact that immigration of a huge number of internal displaced people jointly with the refugees from the neighbor countries to the city had affected the original population size since 2014. The data was extracted from the case records including the socio-demographic characteristics of the patients who visited the hospitals and health centers of Erbil for the purpose of treatment and follow up.

Statistical analysis:-

Descriptive and inferential statistics were used through the Microsoft Access Database and the Statistical Package for Social Sciences (SPSS, Version 21). Bivariate correlations were used for data analysis. The P value of ≤ 0.05 was considered as statistically significant.

Results:-

Five hundred and forty nine females with breast cancer were studied. The mean (±SD) age of the studied women was 32.71 ± 10.64 years ranging from 13 to 73 years. This study revealed that the most registered age group by breast cancer was between 21 to 30 years old females who formed 201 (36.6%) of the study sample. But the peak incidence 37 (6.7%) of breast cancer was at the age 40 years. The lowest 5 (0.9%) registered age group was those women whose age was more than 60 years. There was a significant correlation between the ages of the registered cases and the frequency of the disease at $p = < 0.05$ and $r = - 0.485$ (Table 1). The marital status of the studied patients is shown in Table 2 which indicates that most 449 (81.8%) of them were married. The majority 465 (84.7%) of the patients were housewives as it is shown in Table 3. More than one third 40 (7.21%) of the patients were cigarette smokers (Table 4). The distribution of the breast cancer patients' parity can be seen in the Table 5 which shows that nearly one third 193 (35.2%) of the patients were nulliparous females who formed the highest percentage of the affected females by breast cancer. There was no significant correlation between parity and the frequency of the breast cancer patients ($p = 0.528$). Another finding can be noted in table 5 is the least number [3 (0.5%), 1

(0.2%)] of affected women by breast cancer who were in the groups of Para 13 and 15 respectively. One quarter 142 (25.88%) of the patients were using contraceptive pills (Table 6). Two thirds 66 (12.05%) of the patients stated the presence of breast cancer in their family histories (Table 7). More than one quarter 151 (27.51%) of the study sample had breastfed their children (Table 8).

Discussion:-

Breast cancer has been known to mankind since ancient times. It has been noted by Egyptians before 3500 years. Galen in A.D. 200 suggested that some tumors were more dangerous than others. At that time, surgical intervention was avoided due to the invasion characteristic of cancer. In 1680, French physician Francois de la BoeSylvius used chemical process that transformed lymphatic fluids from acidic to acrid. Paris physician Claude-DeshaisGendron in 1730s rejected the systemic theory of Galen as well suggesting development of cancer from mixed nerve and glandular tissue with lymph vessels. In 1713 Bernardino Ramazzini's correlated the high frequency of breast cancer among nuns with lack of sex as Ramazzini believed that reproductive organs, including the breast may decay and develop cancers due to avoidance of regular sexual activity. But Friedrich Hoffman of Prussia had related the cause of breast cancer to lymphatic blockage due to the fact that breast cancer occurs even among sexually active women. Other theories included curdled milk by Giovanni Morgagni, breast puss filled inflammations by Johanes de Gorter, depressive mental disorders by Claude-Nicolas Le Cat from Rouen, childlessness by Lorenz Heister, and other theories such as sedentary lifestyle. The New York physician William Halstead developed radical mastectomy jointly with the removal of axillary nodes, and chest muscles for prevention of cancer spread. In 1895, Scottish surgeon George Beatson discovered reduction of the tumor by removal of the ovaries which produce estrogen that help the tumor growth leading to reduced tumor size. Since estrogen is produced by the adrenal gland, in 1952, Charles Huggins performed adrenalectomy to cut estrogen from the tumor. Rolf Lefft and Herbert Olivecrona had removed the pituitary gland as another site of estrogen production stimulation. In 1955, George Crile and Bernard Fisher suggested the cancer spread and metastasis respectively. In 1976, Fisher published had used simpler breast-conserving surgery followed by radiation or chemotherapy. He noted the effectiveness of the latter procedure as radical mastectomy. In 1995, less than 10 percent of breast cancer-inflicted women had a mastectomy. Hormone treatments, surgeries and biological therapies are considered as the novel therapies. Development of mammography was a revolution in early detection of the cancers. Finally, scientists isolated the responsible genes for breast cancer: BRCA 1, BRCA 2 and ATM (Mandal A, 2016).

According to our study the incidence of breast cancer was 37.95 per 100,000 women after analysis of data regarding the number of registered cases and women population in Erbil Governorate. This finding comes in coincide with that of developing countries which had been estimated at less than 40 per 100,000 in most of the developing regions. Breast cancer incidence is different from region to region which was 66.4 and 27.3 per 100,000 women in developed and less developed regions respectively. This incidence was lower (26 per 100,000 women) in African Region, South East Asia Region and West Pacific Region reaching to 62.7 per 100,000 women in Europe Region. The age standardized incidence was greater than 80 per 100,000 in developed regions excluding Japan. The World Health Organization (WHO) Eastern Mediterranean Office, 2009 predicted a largest increase in cancer incidence among the WHO regions in the next 15 years including the Eastern Mediterranean Region where breast cancer is reported as the commonest type of female malignancy in almost all national cancer registries (USAID and Iraqi Ministry of Health, 2013). The total annual age standardized incidence for breast cancer among Sulaimaniyah Kurds was 40.5/100,000 women according to a study done by Majid R et al, 2012 which had been held on registered cases during 2008 to 2010. Suleimaniyah is another province in the region which is 204 km far from Erbil. Another finding of our current study is the significant correlation of the patients' ages with number of cases and the highest incidence of breast cancer 201 (36.6%) in the registered cases at the age group of 21 to 30 years. This means that the breast cancer incidence in this age group was 77.88 per 100,000. Unfortunately, many studies indicated bad prognosis of the disease among females aging ≤30 years. In a clinicopathological study by Yao Y et al, 2015 which compared the disease prognosis of patients aged ≤30 years with patients aged between 31 to 50 years, a greater chance of endocrine-unresponsive tumor and poor prognosis had been found among patients at the age ≤30 years. Although many studies agreed that breast cancer is more common in older age females due to the aging process as result of the cell mutations in the body. This aging process leads to incapability genetic damage repairmen (Breastcancer.org, 2016), but the high incidence of the disease among 21 to 30 years in this study may be related to many factors such as environmental factors, hormonal factors like having fewer children or using birth control pills, hormone replacement therapy including the synthetic hormones such as parabens which are chemicals with estrogen-like properties, and estrogen is one of the hormones involved in the development of breast cancer. The

parabens are widely used in personal care products like shampoo, lotion, deodorant, shaving gel and cosmetics. These dangerous chemicals have been found in breast cancer tissues at concentrations up to 1 million times higher than the estrogen (estradiol) levels naturally found in human breast tissue (Harvey PW and Everett DJ, 2012). Propylparaben is another chemical substance which had been detected in the highest concentration in the axillary area where deodorants are most used and breast cancer prevalence is at its highest. Exposure to chemical substances may arise in the womb as well. Milk is considered as another risk factor containing Recombinant Bovine Growth Hormone (RBGH), which is used for stimulation of milk production and banned in many European countries. It contains increased levels of insulin growth factor-1 (IGF-1) that regulates cell growth, cell division, and the ability of cancer cells to spread having potent growth-stimulating effects in human breast tissue, especially in the presence of estradiol (a form of estrogen). Growth factors stimulate the transformation and growth of breast cancer cells. Infants and children exposed to high IGF-1 develop health problems later in life, such as breast enlargement, and breast cancer in adulthood. Toxic substances, radiation, nutritional deficiencies, inflammation insult younger generations. Breast cancer being common among young females is mentioned by Rebecca et al (2013) who concluded the increase in the incidence of the disease in the United States between 1976 and 2009 for women aged 25 to 39 years, without a corresponding increase in older women (Johnson R et al, 2013). In another study in Sulaimaniyah governorate on the registered cases from 2011 to 2013, the estimated peak incidence (79.3 / 100,000 women) was at the age group 45–49 years old women (Molah Karim S et al, 2015). While, the peak incidence 37 (6.7%) in our study was at the age 40 years. Interpretation of this finding indicates the breast cancer specific age incidence among the 40 years women which was 5.24 / 100,000 women. This result is near to the age standardized incidence of the disease which is 6.59 / 100,000 for females in the age group 40 to 44 years according to WHO adjustment and 8.1 / 100,000 according to a study which was done by Majid R. et al in Suleimaniyagovernorate (Majid R et al, 2012). According to the current study, the low percentage of the patients with breast cancer was divorced women, widowed, and single, while the majority of them were married. Many studies consider marriage as a positive status for breast cancer survivors because the mortality rate among married patients is lower than that of single patients. Intimacy of partnership will help such patients to increase their immunity against disease. In another hand, many breast cancer women survive in their disease but their marriage will not survive. Being a breast cancer patient, a wife, and a mother at the same time is difficult. Fear for rejection and no longer being attractive are other problems of the patients. Some partners keep closer and some keep far from each other are different sexual behaviors which are experiences by the breast cancer survivor wives and their husbands (Harmer V, 2011). This study revealed that the majority of the breast cancer patients were housewives. This finding may be attributed to the fact that obesity is more common among housewives than other women. In a study on 373 age matched control patients in Italy by Talamini R et al, 1984, occupation was considered as a breast cancer risk among the housewives and non manual workers like teachers and clerical workers showed higher relative risks than those who work in agriculture. Although only 40 breast cancer patients out of the 549 patients of our study were cigarette smokers, but recent studies showed the link of heavy smoking over a long time to a higher risk of breast cancer specially among women who started smoking earlier to having their first child. The 2014 US Surgeon General's report on smoking concluded that there is not sufficient evidence that smoking increases the risk of breast cancer, but other studies have shown the mainstream and secondhand smoke chemicals had been found in the rodents' breast milk. This finding is another reason to avoid secondhand smoke (American cancer society, 2016). Pierce J. et al, 2013 had raised three conclusions which included the significant association of lifetime cigarette smoking with poor prognosis, the increased risks of disease recurrence among dose dependent smokers, and increased mortality. Although there was not a significant correlation between the parity of the study sample and the frequency of the breast cancer patients, but the highest percentage of the patients were nulliparousfemales. Many studies are in coincide with our finding such as Russa J et al, 2005 who agreed that there is an association between parity and lowered lifetime breast cancer risk related to the changes in differentiation of breast epithelium as a protective mechanism. They also had identified a significant gene expression signature that was upregulated in breast tissues of parous compared to nulliparous healthy women. Meanwhile, parity increases breast cancer risk transiently following pregnancy (Lambe M et al, 1994). About one quarter of the studied patients in this research had used contraceptive pills. Beaber E et al, 2014 studied 1,102 American women (20-49 years) during 1990 to 2009 depending on the electronic pharmacy records. They discovered an association between using oral contraceptive use and breast cancer risk. Oral contraceptive use was associated with an increased breast cancer risk relative to never or former use. This was stronger for estrogen receptor–positive than estrogen receptor–negative. Recent use of oral contraceptives involving high-dose estrogen, ethynodiol diacetate, or triphasic dosing with an average of 0.75 mg of norethindrone was associated with particularly elevated risks. But other types, including low-dose estrogen oral contraceptives, were not associated with the breast cancer risk. Women witha strong family history of breast cancer or past breast biopsies showing abnormal cells and having in their family an abnormal breast cancer gene must avoid using hormonal contraceptives

in order to prevent themselves from breast cancer (Breastcancer.org, 2014). Family history in addition to hormonal and environmental causes is considered as one of the important risk factors of breast cancer. In a study by Tazitte A et al, 2009 on 570 Moroccan breast cancer women, presence of family history had been found among 18.4% of breast cancer patients. The result of our study showed the presence of family history in 12.05% of the breast cancer patients. Weiss M et al, 2016 studied the presence of abnormal BRCA1 or BRCA2 gene which had 60% risk among diagnosed patients with breast cancer during the lifetime. The mentioned genes are found in 5-10% of the breast cancer cases in US. The latter study also found that the BRCA1 gene risk was 65% to age 70 and 90% to age 80. While, BRCA2 gene risk was 45% to age 70 and 41% to age 80 for breast cancer. This risk is lower among the gene carriers for ovarian cancer. Unfortunately only about one quarter of our study sample had been breastfed their babies. In a study by a Collaborative Group on Hormonal Factors in Breast Cancer in 30 countries from 47 epidemiological studies on 50,302 women with invasive breast cancer, 2002 the group reached to an interpretation that "The longer women breast feed the more they are protected against breast cancer". They also concluded that the high incidence of breast cancer in the developed countries is contributed to the short lifetime breastfeeding of the women.

Conclusions and Recommendations:-

Breast cancer incidence was higher among the registered young females than older ages with exception to the age 40 which recorded the highest incidence of the disease. The disease was very rare among Para 13 and 15 women. Being housewife, cigarette smoking, nulliparity, using oral contraceptive pills, and presence of breast cancer in the family history among can be considered as risk factors for breast cancer. Conduction of further studies about the incidence, risk factors, and survival and mortality rates among women with breast cancer is necessary. Control of case registration in both governmental and private health facilities jointly with health education about the risk factors of the disease are recommended.

Appendices:-

Table 1:-Distribution of breast cancer by age groups.

Age	**F**	**%**
≤ 20	62	11.3
21 - 30	201	36.6
31 - 40	163	29.7
41 - 50	95	17.3
51 - 60	23	4.2
> 60	5	0.9
Total	**549**	**100**

p = < 0.05 r = - 0.485

Table 2:-Distribution of the patients by their marital status.

Marital status	**F**	**%**
Single	78	14.2
Married	449	81.8
Widow	18	3.3
Divorced	4	0.7
Total	**549**	**100**

Table 3:-Distribution of the study sample by occupation.

Occupation	**F**	**%**
Housewife	465	84.7
Clerk	8	1.5
Teacher	16	2.9
Governmental staff	33	6.0
Student	21	3.8
Self employer	1	0.2
Biologist	1	0.2
Journalist	1	0.2

Nurse	2	0.4
Immigrant	1	0.2
Total	**549**	**100**

Table 4:-Distribution of the patients by smoking habit.

Smoking	**F**	**%**
Yes	40	7.21
No	509	92.79
Total	549	100

Table 5:-Distribution of breast cancer patients by parity.

Parity	**F**	**%**
Nullipara	193	35.2
1	27	4.9
2	51	9.3
3	42	7.7
4	41	7.5
5	27	4.9
6	30	5.5
7	29	5.3
8	33	6
9	32	5.8
10	21	3.8
11	13	2.4
12	6	1.1
13	3	0.5
15	1	0.2
Total	**549**	**100**

$P = < 0.05$ $r = - 0.815$

Table 6:-Usage of contraceptive pills by the patients.

Contraceptive pills	**F**	**%**
Yes	142	25.88
No	407	74.12
Total	549	100

Table7:-The patients' family history of breast cancer.

Family history of breast cancer	**F**	**%**
Negative	483	87.95
Positive	66	12.05
Total	549	100

Table 8:-Distribution of breast cancer by breast feeding.

Breast feeding	**F**	**%**
Yes	151	27.51
No	398	72.49
Total	549	100

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