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RESEARCH ARTICLE

CORRELATION BETWEEN THE HISTOLOGICAL GRADING AND SIZE OF BREAST CANCER WITH THE AXILLARY LYMPH NODE INVOLVEMENT, A CONTINUOUS RETROSPECTIVE AND PROSPECTIVE STUDY

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ABSTRACT

This is a continuous retrospective and prospective study which was planned and performed in Saddam Teaching Hospital in Najaf city for the period from the first of January 2001 to the thirtieth of August 2002 to study the correlation between the histological grading of breast cancer cells with the ipsilateral A.L.N involvement in relation to the size of the cancer to have an idea about the pattern and aggressiveness of the breast cancer in this city, with a note to the age and sex of the patient and the residence whether rural or urban. Breast cancer cases represent 34% of breast surgery in this hospital during the period of study. The commonest age groups was the 5th decade 36.9% followed by the 4th decade, 23% Urban cases more than rural area cases. (I.D.C) 81.5% and (l.LC) 18.5%. The histological grading grade ll came first 70.8% grade IlI, 20% and grade L.9.2%. ALN involvement 100% in grade Ill. 65.2% in grade l and 33.3% in grade I. Breast cancer size 2-5cm represents 63% of the cases, tumour size more than 5cm represent 30% and those with size less than 2cm 6.3%.

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INTRODUCTION

Carcinoma of the breast is the most common site specific cancer and the leading cause of death from cancer in women for female 40-44yeas of age. Breast cancer accounts for 32% of all female cancers and is responsible for 19% of cancer related death in women. Approximately 180.200 invasive breast cancer were expected to be diagnosed i n the United States in 1997. Approximately 43000 women will die because of the tumour (Kirby, 1999). The probability of women in the United States developing breast cancer was estimated as 1 in 8 in 1996 (Parker *et al.,* 1997). Worldwide breast carcinoma is an epidemiologic problem. England and Wales have the highest national age adjusted mortality for Breast cancer (27.7 per 100.000 population). The United State (22 cases per 100.000 population). Women living in less industrialized nation tend to have lower rates of breast cancer than those living in industrialized countries but Japan appears to be exceptional (Brinton *et al.,* 1993). Breast cancer is the commonest type of malignancy among women. Each year there are approximately 3 0.000 new cases and l6.000 deaths from the disease in United Kingdom. This figure compares with an annual total of cancer death of 75.000 and death from diseases in women of 340.000 breast cancer is uncommon under the age of 35 years and rare under the age of 20 years. Its incidence continues to rise with age (Robin, 1998).

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Male breast cancer accounts for less than 1% of all cancer and 0.1% of all deaths from cancer in men. The peak incidence at 60 years of age. It is usually ductal carcinoma. Which present at a more advanced stage and seems to carry a less favorable prognosis than its female counterpart. The majority of cancers (75-95% present as painless, firm. Sub areolar lumps). Other signs and symptoms include gynecomastia, breast tenderness. changes in areola, serous or bloody nipple discharge or inversion and skin erythema or ulceration (Memon, 1997). Pathological review: Breast cancer is an adenocarcinoma arising from epithelial lining ducts and acini. Cancer arise in the terminal duct lobular unit and are ductal and lobular type. Both ductal and lobular cancer may be invasive (infiltrating) or non invasive (non infiltrating) or insitue. Only invasive cancers metastasize.

Types of invasive cancers:

- Duct cancers represent 80°% of all invasive cancer.
- Lobular cancer 5-10% of breast cancer.
- Carcinoma in situ. It is non invasive cancer of the breast confined to ducts and acini which not penetrated the basement membrane of the epithelial cell layers (Al-Fallouji, 1998).
- Invasive ductal carcinoma (no special type) include the majority of carcinoma a 70-80°%, most of these cancers exhibit a marked increase in dense fibrous tissue stroma giving the tumor a hard consistency (scirrhous carcinoma).

- Invasive lobular carcinoma 5-10% of breast cancer. bilateral in 20% multicenteric within the same breast. Diffusely invasive pattern that make both primary tumor and metastases difficult to detect either by physical examination or by radiological studies, more frequently metastasize to C.S.F serosal surface ovary uterus and bone marrow compared with other subtype.
- Medullary carcinoma 1-5% of all mammary carcinoma in younger than average women. Have slightly better prognosis than duct carcinoma of no special type.
- Colloid (mucinous) carcinoma: unusual variant 1-6% of all carcinoma tend to occur in older women and grow slowly during the course of many years. Lymph node metastasis less than 20% of patients.
- Tubular carcinoma 2% of all breast cancer in younger age group in late 40 year. Multifocal within one breast in 10-56% of cases or bilateral in 9-38%.Axillary Lymph node metastasis occur in less than 10% of cases except in cases of multifocal disease has excellent prognosis.
- Invasive papillary carcinoma less than 1% of all invasive cancers. Papillary architecture is more commonly seen in DCIS. The clinical presentation is similar to that of carcinoma of no special type but the overall prognosis is better (Ramzi *et al.,* 1962).

Tumor grading: Grading is according to modification on the Bloom and Richardson grading scale where three parameter are scored on the basis of l-3.

Grade I ⟶ well differentiated
Grade II ⟶ moderately differentiated
Grade Il ⟶ poorly differentiated

The three parameters that are assessed are:

Tubule formation, cellular pleomorphism and number of mitosis (Bloom *et al.,* 1962). The most important risk factors for breast cancer are the patients age. gender and a family history of breast cancer immediate relative (sisters, mothers, daughters). The adjusted incidence of breast cancer increases with age. Breast cancer does occur in males but the disease is far more common in women. Other important risk factor are history of breast cancer obesity. Nulliprity, alcohol all appears to increase risk slightly.

Staging: The American Joint Committee on cancer staging divided the clinical Stages as follows:-

Stage 0: DCIS or LCIS (5 year survival rate 92%).

Stage I: invasive carcinoma 2cm or less in size (including carcinoma in situe with micro invasion) without nodal involvement and no distant metastasis. (5year survival rate 87%).

Stage II: invasive carcinoma 5cm or less in size with involved but mobile axillary lymph nodes and no distant metastases or a tumor greater than 5 cm without nodal involvement or distant metastases (5 year survival rate 75%).

Stage III: Breast cancer greater than 5cm in size with fixed axillary or any breast cancer with involvement of ipsilateral internal mammary L.N lymph nodes. Or any breast cancer with skin involvement. Pectoral or chest wall fixation. Edema or clinical inflammatory carcinoma it distant metastasis are absent (5 year survival rate 46°%).

Stage IV: Any formal breast cancer with distant metastases (including ipsilateral supraclavicular lymph nodes (5 year survival rate 13%) (AJCC cancer staging Manual, 1977).

PATIENTS AND METHODS

This is a continuous retrospective and prospective study for 20 months during which period all cases of breast cancer operated upon in Najaf City were included in this study. The parameters included are the histological types of the cancer with its grading, the size of the cancer and the ipsilateral L.N involvement status. The correlation between these parameters were studied and the P-value of each was calculated, also notes to the relation of breast cancer With the age of the patients and residence were studied.

RESULTS

During the 20 months period of the study the number of breast cancer cases in mastectomies patients was 65 cases. The total number of operations done on the breast in general in this hospital was I90 during the same period therefore the incidence of breast cancer in this hospital is 34.2%. Among the 65 cases of breast cancers recorded. 2 cases were male patients. 3.07% of breast cancer and 63 cases of breast cancers were females 96.3% as shown in Table (I). All of them were single breast involvement. Regarding the age incidence of breast cancer cases, the commonest age involved by breast cancer was 5th decade 39.9%, the 2th most common age was the 4th decade 23% and the 3rd age group was the 6th decade 16.9%. The youngest age was 19 years. And the oldest patient was 80 years old as shown in Table (1). Regarding the residence, number of breast cancer cases in urban region was 47 cases 73% and number of cases in rural region was 18 cases 27% as shown in pie graph I. Regarding the histological type of breast cancer cases in this hospital. The commonest type of breast cancer was infiltrative duct carcinoma. 53 cases 81.5% and the I.L.C were 12 cases 18.5%. The highest specific histological type was the No special type (scirrhous) 39 females+2 males (total 4I cases) 63.07%. The infiltrative lobular carcinoma (I.L.C) came 2nd 12 cases 18.5%. The medullary and colloid cancer came 3rd 4 cases for each 6.1 % as shown in Table (II). Among the 65 cases of breast cancer recorded 45 cases has L.N involvement +ve69.2% and 20 cases were –ve 30.8%, 37 cases 69.8% of infiltrative ductal carcinoma had +ve axillary L.N Involvement, and 16 cases 30.2% had -ve A.L.N. While 8 cases 66.6% of Infiltrative lobular carcinoma had +ve. Axillary L.N involvement and 4 cases 33.3% had -ve Axillary L.N involvement as shown in Table (lII). The relation between the histological grade and axillary L.N involvement is shown in Table (IV) were we see that 6 patients with grade I breast cancer 9.2% of these 2 cases with L.N +ve 33.3% and 4 cases with L.N -ve 66.6%. In grade Il 46 cases 70.8% of these 30 cases 65.2% with L.N-ve and 16 cases 34.8% had –ve axillary L.N involvement. While in grade III breast cancer which were 13 cases all of them had +ve axillary L.N involvement by cancer i.e 100% involvement. Regarding the size of the breast cancer with its relation to axillary L.N and histological grade is shown in Table V the size of the breast cancer as classified by American Joint Committee on Cancer Staging into 3 types which are less than 2cm. 2-5cm and finally more than 5cm.4cases 6.2% of the 65

Table l. Age and sex distribution of cases with breast cancer

Age	Female	%	Male	%	total	%
11-20 y	1	1.5%	0	0	1	1.5%
21-30 y	5	7.69%	0	0	5	7.69%
31-40 y	15	23%	0	0	15	23%
41-50 y	24	36%	2	3.07%	26	39.9%
51-60 y	11	16.9%	0	0	11	16.9%
61-70 y	6	9.2%	0	0	6	9.2%
71-80 y	1	1.5%	0	0	1	1.5%
total	63	96.9%	2	3.07%	65	100%

Table II. Distribution in relation to histological type of breast cancer cases

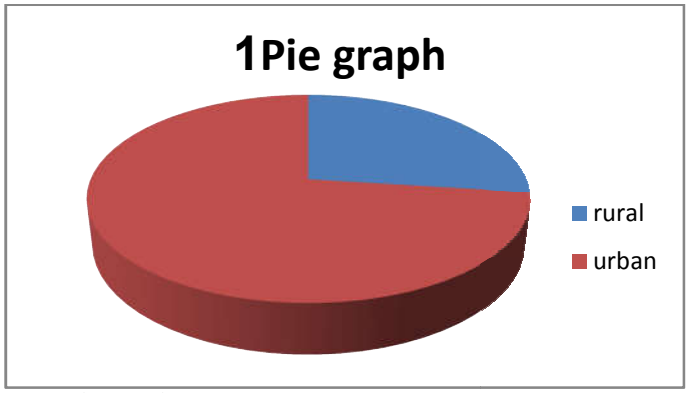
Histology	Female	%	Male	%	total	%
1/I.D.C						
N.S.T	39	60%	2	3.07%	41	63.7%
Medullary	4	6.1%	0	0	4	6.1%
Colloid	4	6.1%	0	0	4	6.1%
Papillary	2	3.07%	0	0	2	3.07%
Comedo	2	3.07%	0	0	2	3.07%
2/I.L.C	12	18.46%	0	0	12	18.46%
Total	63	96.9%	2	3.07%	65	100%

Table III. Histology with lymph nodes metasteses

Histology	L.N+ve	%	L.N-ve	%	total	%
I.D.C	37	69.8%	16	30.2%	53	81.5%
I.L.C	8	66.6%	4	33.3%	12	18.5%
Total	45	69.2%	20	30.8%	65	100%
P.value			<0.05			

Table IV. Grading with lymph nods metasteses

Grade	L.N+ve	%	L.N-ve	%	total	%
I	2	33.5%	4	66.6%	6	9.2%
II	30	65.2%	16	34.8%	46	70.8%
III	13	100%	0	0	13	20%
Total	45	69.2%	20	30.8%	65	100%
P.value			P<0.05			



27% rural; 73% urban

Table V. The relation between tumor size L.N involvement and grading

Size	L.N involvement									Grade
Tumor size	+ve	%	-ve	%	I	%	II	%	III	%
Less than 2cm	1	25%	3	75%	1	25%	3	75%	0	0
2-5 cm	27	65.8%	14	34.2%	5	12.2%	30	73.2%	6	14.5%
More than 5 cm	17	85%	3	15%	0	0	13	65%	7	35%
Total	45	69.2%	20	30.8%	6	9.2%	46	70.8%	3	20%
P. value			P<0.05		P. value					P>0.05

Table VI. Relation between morphological types of invasive breast cancer. lymph node Involvement

Type	Frequency	With L.N involvement %
Ductal with predictive fibrosis	78	60
Lobular	9	60
Medullar	4	44
Comedo	5	32
Colloid	3	32
Papillary	1	17

cases their Size was less than 2cm of these one with L.N +ve 25% and 3 cases 75% with L.N –ve. While regarding the grade. 1 case 25% grade 1. And 3 cases 75%grade II. No grade III. In tumor size 2-5 cm, 27 cases 65.8% with axillary L.N +ve and 14 cases 31.2% with L.N –ve and out of these 5 cases 12.2% was grade I. 30 cases 73.2% was grade Il and 6 cases 14.6% was grade lll. In the tumor size more than 5cm,(20 cases 30.7%) of those 17 cases 85% with L.N +ve and 3 cases 15% with L.N-ve while regarding the grade 13 cases 65% was grade II and 7 cases 35% grade III. No grade I.

DISCUSSION

The cancer incidence in breast surgery in this hospital was 34%. i.e. one third of breast operations are for carcinoma and this indicates increased incidence. 2 cases out of 65 were male breast cancer 3.07% which is a high incidence among males in our city, while male breast cancer represent less than 1% of all breast cancer as stated by Mc. Graw-Hill 1999 and Rüsell R.C.G 2000 (Rusell *et al.,* 2000). Carcinoma arising in the male breasts is a rare occurrence compared with breast cancer in females Risk factors are similar to those in women which are residency in western country, first degree relative with breast cancer cases, age, infertility, obesity. exposure to exogenous estrogen prior begin breast disease and exposure to ionizing radiation. Decreased testicular function like in congenital Klinefilter Syndrome is also a risk factor (Kirby, 1997; Rusell and Williams, 2000). We can add also the types of nutrition that people consume under embargo circumstances and the degree of the stress that people exposed to.The highest age group incidence in our study was the 5th decade. 39.9% and the 2nd is the 4th decade 23%. While the highest incidence of breast cancer was in the 4th decade in NAJIAF as seen in the result of Assad. Al-Janabi 1997 while our result is comparable with the result of Iraqi Cancer Registry 1992, 1994, 1995, 1997 and Zhang study. 1997, Al-Fallouji 1998; Kerby *et al.* 1999 in which the same decade (5th decade) has the higher incidence. The second common age group was the 4th decade in our study. While the international figures showed 6th decade as the 2nd common and this indicates a trend breast cancer in our country involving younger age group patients. A.L.N involvement in grade Ill which indicates a pattern of breast cancer in this city, (more aggressive). This indicates that the higher cellular differentiation i.e. less malignant cellular changes. the less lymphatic involvement and the lower cellular changes had more aggressive cancer as we go lower in the cellular differentiation. P value statistically significant. When we compare the size of the breast cancer with ALN involvement we can see that in cancer less than 2 cm, 25% ALN –ve. In cancer size 2-5cm 65.8% ALN +ve in cancer size more than 5cm,85% ALN involvement which indicate the larger the size of the cancer the more ALN +ve and this is similar to M. Shahid study 2000 and Al Asheeri 1999 and we had P value significance <0.05 in our study. From this we can see that majority of breast cancer cases presented to the surgeon are of size2 -5cm then patient with size >5cm and the least are patients with tumor size less than 2cm which indicate that the patients are not consulting the surgeon at early stage of the disease. This probably because of the less education of patients regarding the importance of early detection of breast cancer, and programs like self examination program and early consultation in simple changes in the breast and partly because of some cultural and social believes that operations on the breast will produce cancer in the breast as present in our rural areas. Therefore they present late and this has its reflection on

the line of treatment and adjuvant therapy availability because of embargo. And finally this is going to be reflected on the 5 years survival which is definitely lower than the international figures and this should be studied in another separate study. If we compare the size of the breast cancer with histological grading we can notice that cancer less than 2cm are in the favorable group in grade I and grade II and non in grade III while patients with tumor size 2-5 cm majority are in grade II and III and less in grade I, finally cancers more than 5cm in size are of less favorable group which is grade II. III and none in grade I. From this we can notice that the larger the tumors the higher the histological grade which makes the cancer less favorable regarding surgical treatment and adjuvant therapy. This probably related to the duplication time of the cancer and the time that it needs to reach such size. This finding is approximately similar to what is shown in Siddiqui study 2000, Koscienly *et al.* 1984 and Nemoto *et al.* 1980. Regarding the size of the tumor in our study less than 2cm 6.3%, size 2-5cm 63% and size more than 5cm 30.7% while in AL Asheer study approximately similar result 15.4% less than 2cm,52% in. tumor size of 2-5cm and tumor size more than 5cm 19.7°% by which we can notice that small size cancer in our study is less which also indicates latent presentation or misdiagnosis by the consulted doctors also if we notice in Siddiqui study 2000 the same finding i.e. late presentation in this study tumor less than 2cm 20%. a tumor 's size more than 2cm 80% and patients with ALN involvement in tumor' s size more than 2cm is relatively similar to Siddiqui's 2000 study. in our study 67.6% and70% in Siddiqui 2000.

Conclusion

1. Carcinoma of the breast is the most common cancer in females in Iraq according to the National Cancer Registry for the years 1992,1994,1996.and this reflects a major public health problem. The findings are alarming. We suggest an urgent need to improve women's awareness of breast cancer.
2. Breast cancer cases represent 34% of total breast surgical disease for the same period done in this hospital and this is an important percent which reflect the need for increased emphasis on early detection by clinical and mammographic method.
3. In our study the commonest age group was the 5th decade followed by the 4^{th}, this is similar to the international figures as the 5^{th} decade is commonest but the 2^{nd} is the 6^{th} decade. This finding plus the incidence of cancer in young patients like the 2^{nd} decade indicate a new trend which involves younger age groups in breast cancer. Of course we have increased risk factors including the ionized radiation after the American Bombardment by the depleted uranium missiles and this risk needs a special study to emphasize.
4. Regarding the histological type of breast cancer in our study the IDC higher than I.L.C we have one difference in that the I.L.C percentage is higher in our study than the international figures which is replaced by the medullary cancer.
5. Regarding the histological grading of breast cancer. Grade ll comes first followed by grade III and the least grade I if we compare it to the A.LN involvement according to the grade we can tind that grade Ill had the highest A.L.N involvement and grade Il came 2nd and the least one is grade I and this indicates that the lower the degree of cellular differentiation i.e. (higher grade), the more A.LN involvement which is similar to international figures which indicate that the majority of our cancer cases are of lower favorable group regarding surgical management and survival.
6. Regarding the size of the tumor majority of cases came with cancer size 2-5 cm followed by size more than 5cm the least the size less than 2cm means that the majority of the cases presents late and this is reflected on the surgical management and the survival rate of the patient.
7. The study reinforces the urgent need for improved screening technique for early detection and for an aggressive health education campaign, to increase the awareness of women in Iraq about the potential risk of breast cancer and early detection by regular testing and self-examination program.
8. Regarding the relation between the size of the cancer and the A.L.N involvement. The larger the size of the cancer the higher the A.L.N involvement and this is similar to the international figure.
9. Regarding the relation between the size of the breast cancer and the grade we found that the larger the size the higher the grade which is similar to the international figure and this deserves study by its own.

Abbreviations

I.D.C: Invasive Ductal carcinoma,
I.L.N: Invasive lobular carcinoma
A.L.N: Axillary lymph node,
+ve: Positive
-ve: Negative,
DCIS: Ductal carcinoma insitu
C.S.F: Cerebrospinal fluid,
N.S.T: No special type
cm: Centimeter

REFERENCES

AJCC cancer staging Manual, 1997. Philadelphia Lippincot-Raven, P171-180.

Al-Asheeri N. *et al.* 1990. Breast Cancer Patients characteristic and Survival analysis at Sulaymania Medical Complex. Bahrain, Vol,5 Issue 3, P.430-39.

Al-Fallouji, M.A.R. 1998. Post graduate surgery 2nd ed, P.613-307.

Assad al-Janabi, 1997. Prevalence of malignant tomors in Najaf a clinic pathological study 430 cases in Saddam Teaching Hospital. *Al-kufa Journal,* Vol. I N2, P. 25.29.

Bloom HJG. and Richardson WW. *et al.* 1962. Comparison and untreated and treated cases according to histological grade and malignane, *British medicine Journal,* 5299:213.

Brinton BA. JW. *et al.* 1993. Estrogen replacement therapy and breast cancer risk. Epidemiological Revise 15:256.

Ciccarone, M. 1994. Diagnostic evaluation of breast nodule Minerva-Gynecol, 46(11):P.635-42.

Kirby I. Bland, Mechael Sichwart 12 SI (cd) principles of surgery ed. 7. New York Me Graw-Hill 199 p. 554.

Koscienly, S. *et al.* 1994. Breast cancer relationship between the size of the primary tumor and the probability of metastasized dissemination. *Br. J. Cancer,* 49: 709.

Majeed, A.M.A. 1988. The Frequency of Breast cancer in the north part of Iraq (Ninevah). *J. fact. Med. Baghdad,* (302) 169-73.

Mc Divitt RW. *et al.* 1968. Tumors of the breast. in Atlas of Tumor Pathology, series 2 Fascicle 2, Washington DC. Armed Forces Institute of Pathology.

Memon, M.A., J.H. Donane, 1997. Male Breast Cancer British, *Journal of Surgery,* 84P.433-434.

Morris, A. Pomier, RF., Schmidt, W.A. 1998. Accurate evaluation of palpable beast masses by the triple test score. *Arch-surgery,* 123(9):930-4.

Nemoto T. *et al.* Management and Survival of female breast cancer Result of national surgery by The American College Surgeons, Cancer 45:2917.

Parker SL. and Tong T *et al.* 1997. Cancer statistics 1997 cancer 47: 14.

Ramzi. S. Corton. Kumor and Collins.

Result of Iraqi Cancer Registry 1992-1 194. 1995-1997.

Robin CN Williamson, Bruce P. Waxman, 1998. Scott An aid to clinical surgery 6th ed., P. 210.

Rosen PP. and Oberman HA. 1993. Tumours of the mammary gland, 3rd series. Fascicle 7 Washington. DC. Armed Forces Institute of Pathology.

Rusell R.C.G. Williams N.S. 2000. The Breast in Bailey and Love's Short Practice of Surgery, 23 ed, London, p.I.

Shahid Siddiqui M. *et al.* 2001. Faculty of Health Sciences. Breast Carcinoma in Pakistan Female Morphological Study of 272 cases. *Journal of Medical Association,* 286 (11) P.30-2.

Sherif, Fadil Abood Al-Alawehi, 2000. Analysis of Malingnant toumors in Patients attending the oncology unit at Merhan Teaching Hospital in Babylon. *Kufa Med. J.,* Vol. 3No I. P. 123-25.

Zhabg, C., Yu, X., Haung, S. 1997. Study on Measures to increase Diagnosis accuracy os FANC of breast masses. Chung-Hua. Ping-Li-Hsuch-Tsa-Chih, 26(6): P,3334-6.

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