

A study of the correlation between the histopathological grading and size of breast cancer with the axillary lymph node involvement

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Date Submitted: 10.7.2010

Date Accepted: 30.11.2010

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Abstract

Background: breast cancer In Iraq is the commonest tumor affecting females accounting for more than 18% in 2007 of registered female cancers with increase incidence in young women.

Aims: the study aims to outline the correlation between histopathological grading of breast cancer cells with the ipsilateral A.L.N involvement in relation to the size of cancer.

Patients & methods: A continuous prospective study where by almost all mastectomized patient for breast cancer in Al- Yarmouk Teaching Hospital were included from January 2008 to January 2011, revision to all histopathological reports in the histopathological department was done, tables were made and the P value was calculated.

Results: Breast cancer cases represent 28.1% of breast surgery in this Hospital during the period of study. The commonest age group 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 (I.L.C) 18.5%.

Regarding The histological grading grade II came first 70.8% grade III 20% and grade (I) 9.2%, A.L.N involvement 100% in grade (III), 65.2% In grade (II) and 33.3% in grade I.

Breast cancer size 2-5 cm represent 63% of The cases, tumor size more than 5 cm represent 30% and those with size less than 2 cm 6.3%.

Conclusions: Breast cancer cases represent 28.1% of total breast surgical disease for the same period of time 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 or U/S study.

Key Words: breast cancer, histopathological grade, axillary lymph node involvement

INTRODUCTION

Carcinoma of the breast is the most common site specific cancer and is the leading cause of death of cancer of women 40-44 years of age. Breast cancer accounts for 33% of all female cancers and is responsible for 20% of cancer related death in women. Approximately 211, 300 invasive breast cancers were expected to be diagnosed in the United States in 2003. Approximately 39800 Women will die because of the tumor.^[1]

The probability of women in the United States developing breast Cancer was estimated as 1 in 3 in 1996.^[2] Worldwide breast carcinoma is an epidemiologic problem. England and Wales have the highest national age adjusted mortality for breast cancer (27.7 per 100000 population), and in The United State (22 cases per 100000 population).

Women living in less industrialized nations tend to have lower rates of breast cancer than those living in high

industrialized countries but Japan appears to be exceptional.^[3]

Breast cancer is the commonest type of malignancy among women. Each year there are approximately 30000 newcases and 16000 deaths from the disease in United Kingdom. This figure compares with anannual total of cancer death of 75.000 and death from diseases in women of 340000, 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.^[4]

Male breast cancer accounts for less than 1% of all cancer and 0.1% of all deaths from cancer in men. The peak incidence is at 60 year 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.^[1]

The majority of cancers (75-95%) present as painless, firm, subareolar lumps. Other signs and symptoms include gynaecomastia breast tenderness, changes in areola, serous or bloody nipple discharge or inversion and skin erythema or ulceration.^[5]

Pathological review:

Breast cancer is an adenocarcinoma arising from epithelial lining ducts and acini. Cancer arise in the terminal duct lobular unit are divided into ductal and lobular type. Both ductal and lobular cancer may be invasive (infiltrating) or noninvasive (non-infiltrating) or in situe. Only invasive cancers metastasize.^[6]

Histopathological types of breast cancer^[7]

1. Invasive ductal carcinoma:-include the majority of carcinoma **70-80%**. Most of these cancers exhibit a marked increase in dense fibrous tissue stroma giving the tumor a hard consistency (scirrhous carcinoma).

2. Invasive lobular carcinoma:- 5-10% of breast cancer is bilateral in 20%, multicentric within the same breast. Diffusely invasive pattern make both primary tumor and metastases difficult to detect either by physical examination or by radiological studies more frequently metastasize to C.S.F, ovary, uterus and bone marrow compared with other subtype.

3. Medullary carcinoma:-1-5% of all mammary carcinoma in younger than average women. It has slightly better prognosis than duct carcinoma of no special type.

4. Colloid (mucinous) carcinoma:- unusual variant 1-6% of all carcinoma tend to occur in older women and grow the course of many years. Lymph node metastasis is less than 20% of patients.

5. Tubular carcinoma:- 2% of all breast cancer in younger age group and in late 5th decade. It is within one breast 10-56% of cases or bilateral in 9-38%. Axillary Lymph node metastasis occurs in less than 10% of cases except in cases of multifocal disease has excellent prognosis.

6. 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.

Tumour grading: Grading is according to modification on the scarff-Bloom and Richardson grading scale where three parameter are scored on the basis of 1-3.

Grade I ►well differentiated

Grade II ►moderately differentiated

Grade III ►poorly differentiated

Scarff-bloom Richardson grading been in use since 1950 and is the grading system of the world health organization modification by Elston and Ellis introduced Nottingham combined histological grading (NCHG)has resulted in widely accepted reproducible grading system.^[8]

Nottingham prognostic Index (NPI)^[9]

Is well established and widely used method of predicting survival of operable primary breast carcinoma.Three factors; tumor size(S), histological grade (G) and L.Ninvolvement (L)

by tumor cell used for calculation of NPI score.

Tumor size was measured in cm, the scoring of histological grade calculated was grade I=1, grade II=2, and grade III=3, if no lymph node involved by the tumor the score calculated was 1, if 1-3 lymph node involved by tumor cells the score calculated was 2, and if >3 L.N involved by tumor cells the score calculated was 3.

The NPI score was calculated by $G+L+(S*0.2)$.

If NPI score is 2.0-2.4 ----- 5 year survival rate 93%

If NPI score is 2.5-3.4 ----- 5 year survival are 85%

If NPI score is 3.5-5.4 ----- 5 year survival are 70%

If NPI score is >5.4 ----- 5 year survival are 50 %

The most important risk factors for breast cancer are the patient's age, gender and family history of breast cancer in 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 factors are history of breast cancer, obesity, Nulliparity, alcohol, smoking all appears to increase risk slightly.^[10]

Staging:

The American Joint Committee^[11] on cancer staging divided the clinical stages as the following:-

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

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

Stage II :- invasive carcinoma 5 cm or less in size with involved but mobile axillary lymph nodes and no distant metastases or (5 year survival rate 75%).

Stage III :- Breast cancer greater than 5 cm in size with fixed axillary or any breast cancer with involvement of ipsilateral internal mammary lymph nodes, or any breast cancer with skin involvement, Pectoral or chest wall fixation, edema or clinical inflammatory Carcinoma if 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%).

PATIENTS AND METHODS

This is a continuous prospective study for 36 months (from Jan.2008 to Jan. 2011) during this period almost all cases of breast cancer operated upon in Al-Yarmouk teaching hospital 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 was studied and the P-value of each was calculated, also notes to the relation of breast cancer with the age and sex of the patients and residence were studied, and finally a conclusion was written at the end of the discussion.

A correlation between our study and other regional and international studies was done, and statistical significance of the tables was calculated.

RESULTS

During the 36 months period of the study the number of breast cancer cases in mastectomized patients was 130. The total number of operations done on breasts in general in this hospital was 462 during the same period therefore the incidence of breast cancer in this hospital is 28.1% of total breast surgery.

Among the 130 cases of breast cancers recorded, 4 (3.07%) cases were male patients, of breast cancer cases and 126 (96.93%) cases of breast cancers were females as shown in Table 1. 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 (40%) the second most common age was the 4th decade (23.09%) and the third age group was the 6th decade (16.93%). The youngest age was 19 years, and the oldest patient was 80 years old, as shown in Table 1.

Table 1. Age and sex distribution of cases with breast cancer.

Age (yr)	Female (%)	Male (%)	Total (%)
11-20	2 (1.53)	0 (0)	2 (1.53)
21-30	10 (7.69)	0 (0)	10 (7.69)
31-40	30 (23.1)	0 (0)	30 (23.1)
41-50	48 (36.9)	4 (3.07)	52(40)
51-60	22 (16.93)	0 (0)	22 (16.93)
61-70	12 (9.23)	0 (0)	12 (9.23)
71-80	2 (1.53)	0 (0)	2 (1.53)
Total	126 (96.9)	4 (3.07)	130 (100)

Regarding the residence, number of breast cancer cases in urban region was 94 cases (72.3%) and number of cases in rural region was 36 cases (27.7%) as shown in figure 1.

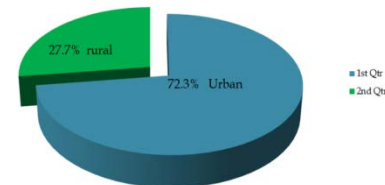


Figure 1. Rural and urban distribution.

Regarding the histopathological type of breast cancer cases in this hospital. The commonest type of breast cancer was infiltrative duct carcinoma. 106 cases (81.53%) and the I.L.C were 24 cases (18.46%). The highest specific histopathological type was the scirrhous type (no special type) 78 females+4males total 82 cases (63.07%). The infiltrative lobular carcinoma (I.L.C) came 2nd, 24 cases (18.46%).

The medullary and colloid cancer came third 8 cases (6.16%) for each, as shown in Table 2.

Among the 130 cases of breast cancers recorded 90 (69.23%) cases had +ve ipsilateral L.N involvement and

40(30.77%) cases were -ve, 74 cases (69.81%) of infiltrative ductal carcinoma had +ve axillary L.N involvement, and 32cases (30.19%) had -ve A.L.N, while 16cases (66.66%) of Infiltrative lobular carcinoma had +ve axillary L.N involvement and 8 cases (33.34%) had -ve Axillary L.N involvement as shown in Table 3.

The relation between the histological grade and the axillary L.N involvement is shown in Table 4 where we see that 12 (9.23%) patient with grade (I) breast cancer. of these 4 (33.34%) cases with L.N +ve and 8 (66.66%) cases with L.N -ve.

In grade (II) 92 cases (70.77%) of these 60 cases (65.22%) with L.N+ve and 32cases (34.78%)had -ve Axillary L.N involvement. in grade (III) breast cancer which were 26 cases (100%) cases had +ve Axillary L.N involvement by cancer.

Regarding the size of breast cancer with its relation to axillary L.N and histopathological grade is shown in Table 5.

8 cases (6.16%) of the 130 cases their size was less than 2 cm of these 2 (25%) with L.N +ve and 6 cases (75%) with L.N. -ve While regarding the grade, 2 case (25%) grade (I). and 6 cases (75%) grade (II). No grade (III).

In tumor size 2-5 cm, 54 cases (65.8%) with axillary L.N +ve and 28 cases (34.2%) with -ve L.N.

Regarding the grade, 10 cases (12.2%) was grade (I), 60 cases (73.2%) was grade (II) and 12cases (14.6%) was grade (III).

In tumor size more than 5 cm, 40 cases (30.77%) of these 34 Cases (85%) with L.N +ve and 6 cases (15%) with L.N -ve , while Regarding the grade, 26 cases (65%) was grade (II) and 14 cases (35%) was Grade (III). No grade (I).

Table 2. Distribution in relation to histological type of breast cancer cases.

Histology	Female (%)	Male (%)	Total (%)
1/I.D.C	102 (78.46)	4 (3.07)	106 (81.5)
N.S.T. (Scirrhus)	78 (60)	4 (3.07)	82 (63.1)
Medullary	8 (6.16)	0 (0)	8 (6.2)
Colloid	4 (3.07)	0 (0)	8 (6.2)
Papillary	4 (3.07)	0 (0)	4 (3.07)
Comedo	4 (3.07)	0 (0)	4 (3.07)
2/ I.L.C	24 (18.46)	0 (0)	24 (18.5)
Total	126 (96.93)	4 (3.07)	130 (100)

Table 3. The relation between histopathological type of breast cancer and the A.L.N involvement.

Histology	Lymph node + ve	Lymph node - ve	Total
I.D.C	74 (69.8)	32 (30.2)	106 (81.5)
I.L.C	16 (66.7)	8 (33.3)	24 (18.5)
Total	90 (69.3)	40 (30.8)	130 (100)
P Value	< 0.05		

Table 4. The relation between histopathological grade and lymph node involvement.

Grade	Lymph Node + ve	Lymph Node - ve	Total
I	4 (33.3)	8 (66.7)	12 (9.3)
II	60 (65.2)	32 (34.8)	92 (70.8)
III	26 (100)	0 (0)	26 (20)
Total	90	40 (30.8)	130 (100)
P Value	< 0.05		

Table 5. The relation between tumor size, L.N involvement and grading.

Tumor Size	Lymph Node involvement		Grade		
	Positive	Negative	I	II	III
< 2 cm	2 (25)	6 (75)	2 (25)	6 (75)	0 (0)
2-5 cm	54 (65.8)	28 (34.2)	10 (12.2)	60 (73.2)	73.2 (12)
> 5 cm	34 (85)	6 (15)	0 (0)	26 (65)	14 (35)
Total	90 (69.3)	40 (30.8)	12 (9.2)	92 (70.8)	26 (20)
P Value	< 0.05		> 0.05		

DISCUSSION

The incidence of breast cancer in Al-Yarmouk teaching hospital is 28.1%. I.e. nearly one third of breast operations were for carcinoma and this indicates high incidence.

4 cases out of 130 were male breast cancer 3.07% which is a high incidence among males in our hospital, while male breast cancer represent less than 1% of all breast cancer as slated by McGraw-Hill 2004^[1] and Norman S. 2008.^[12]

The Commest age incidence was the 5th decade, 40% and the 2nd was the 4th decade 23%, While the result of Assad. Al-Janabi1997 (local study)^[13] show the highest incidence of breast cancer was in the 4th decade, while our result is comparable with the result of Iraqi Cancer Registry 1994, 1995, 1997, 2004^[14] and Zhabg study 199^[15], Al-Fallouji 1998^[6] and Kerby I. bland 2004^[1] in which the same decade (5th decade) has the highest incidence. The second common age group was the 4th decade in our study, while the international figures showed the 6th decade as the 2nd common age group and this indicates a new trend of breast cancer in our country involving younger age group patients. We see now a days cases with breast cancer at a younger age group i.e 2nd and 3rd decade and this can be explained by the increased risk factors.

In our study we found that people living in cities have higher incidence than people living in rural areas, and this is comparable with international papers that people in USA and western European developed countries has a higher incidence than people living in developing countries and in the cities than rural area as shown by Robin CN 1998^[4]. And Morris- A 1998.^[16]

Regarding the histopathological types of breast cancer in this hospital showed I.D.C was the commonest 81.53% with all its types scirrhus, medullary, Colloid, papillary and comedo which is approximately similar to Abrektsen study^[17] and I.L.C came 2nd in both studies as shown In Table 4 but I.L.C 18.5% while in Abrektsen study 6.3%.

Regarding the ipsilateral A.L.N involvement were +ve in 69.8% in I.D.C which is higher than I.L.C 60.6%. Therefore, the I.D.C had higher A.L.N involvement than I.L.C as

compared to Abrektsen 2010^[17] and Robin CN. Williamson 1998^[4] in which the I.D.C and I.L.C. had the same percentage of A.L.N involvement.

I.D.C frequently involved in the lymphatic and perineural space which is readily evident while in I.L.C the diffusely invasive pattern that can make both primary tumors and metastasis difficult to detect either by physical examination or radiological studies.^[4]

Regarding the histological grading, 12 cases 9.23% of grade (I) 92 cases 70.77% of grade (II) and 26 cases 20% grade (III). The +ve ALN involvement 33.34% in grade (I), 65.22% in grade (II) and 100% ALN involvement in grade (III) While in a study done in Pakistan; the +ve A.L.N involvement was 6.11% of grade(I), 65% of grade (II) and 24% of grade (III) M.ShahidSiddiqi 2001,^[18] We can notice in our study we have higher incidence of A.L.N involvement in grade (III) .

This indicates that the higher cellular differentiation i.e. less malignant cellular changes, the less lymphatic involvement and the lower cellular differentiation 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 the +ve ALN involvement was in cancer less than 2 cm ---- 25%, In 2-5 cm tumor-----65.8% and in more than 5 cm tumor---- 85% ALN involvement, so there is a linear correlation between size of tumor and ALN involvement^[19] and this is similar to M. Shahid study 2001^[18], and N. AlAsheeri 1999^[20] 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 size 2-5 cm then patient with size >5 cm and the least are patients with tumor size less than 2 cm, while in western papers reported 2 cm tumor in most cases,^[21] and in Pakistaian study Ashok Kumartanwani,^[22] tumor more than 5 cm most common, which indicate that the patients are not consulting the surgeon at early stage of the disease in eastern countries. 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 protocols. 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 2 cm is 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 5 cm 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 histopathological 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 M-shahid Siddiqui study 2000.^[18] Kosciely et al.; 1994^[23] and Nemoto et al. 1980.^[24]

Regarding the size of the tumor in our study less than 2 cm 6.3%, size 2-5 cm. 63% and size more than 5 cm 30.7% while in N. Al Asheeri study,^[20] had approximately similar result 15.4% less than 2 cm. 52% in tumor size of 2-5 cm and tumor size more than 5 cm, 19.7% by which we can notice that small size cancer in our study is less which also indicates late presentation or misdiagnosis by the consulted doctors also if we notice in Siddiqui study 2000^[18] the same finding i.e. (late presentation) in this study tumor less than 2 cm, 20% and in 2-5 cm tumor, 80% also in this study the ALN involvement in tumor's size more than 2-5 cm is relatively similar to M-shahid Siddiqui's 2001 study, in our study was 67.6% and 70% in Siddiqui 2000 study.^[18]

Conclusion:

1. Breast cancer cases represent 28.1% of total breast surgical disease for the same period of time done in this hospital and this is an important percentage which reflects the need for increased emphasis on early detection by clinical and mammographic method or U/S study.
2. The 5th decade is commonest followed by the 4th decade. This finding plus the incidence of cancer in young patients like the 3rd decade indicate a new trend which involves younger age groups by breast cancer, in this hospital. It reflects the community.
3. Regarding the histological type of breast cancer in our study the I.D.C 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 are replaced by the medullary cancer.

4. The majority of our cancer cases are of lower favorable group and the majority of them present late and this is reflected on surgical management and survival rate of the patient.

Recommendation:

1. The study reinforces the urgent need for improved screening techniques for early detection and for an extensive health education campaign to increase the awareness of women in Iraq about the potential risks of breast cancer and early detection by regular testing and self-examination program.
2. We found that the larger the size of the tumor the higher the grade and this deserves a study by its own.

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