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## PROGNOSTIC FACTORS OF MALE BREAST CANCER

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### ABSTRACT

**Objectives:** This study is designed to study the clinico-epidemiological features of male breast cancer and to identify prognostic factors that may affect the overall survival and disease free survival.

**Methods:** During the period 1988-1995, 39 cases of male breast cancer were treated and followed up in Surgical Oncology Unit and Clinical Oncology and Nuclear Medicine Dept., Mansoura University Hospital. Detailed review of their clinical records was carried out which included: patients' characteristics, staging investigations, surgical treatment, histopathological data, postoperative treatment, and date and disease status at last follow up.

**Results:** The median age was 53 years (range: 25 to 83 years). Majority of cases presented with breast lump (87%), invasive duct carcinoma (95%), grade II histology (61%), T<sub>2</sub>-tumor (56%), and axillary lymph node involvement (71%). The median survival was 36.8 months, while the median disease free survival (DFS) was 22.8 months. By univariate analysis (log rank test) presence of metastases was the only adverse prognostic factor affecting overall survival ( $P < 0.05$ ), while for DFS, presence of metastases ( $P = 0.000$ ), axillary lymph node involvement ( $P < 0.05$ ), postoperative radiotherapy treatment ( $P < 0.01$ ) and tumor size ( $P < 0.01$ ) were significant prognostic factors. By multivariate analysis (Cox regression), post-operative treatment, presence of metastases and axillary lymph node involvement remained significant prognostic factors affecting DFS.

**Conclusions:** Male breast cancer is a rare disease. Treatment results are affected by the small number of patients studied and the short duration of follow up. National cancer registry with analysis of large number of cases may enable better analysis and drawing guidelines for management.

### INTRODUCTION

Male breast cancer is a rare disease as it accounts for less than 1% of all cases of breast cancer. Knowledge relevant to many aspects of the disease, including prognostic factors is still limited. Information is based largely on retrospective analysis of data and case reports. Treatment has been guided largely by knowledge gained from treatment of women whose greater numbers permit controlled therapeutic trials.<sup>(1)</sup>

The aim of the present study is to study the clinico-epidemiological features of male breast cancer and to identify prognostic factors that may affect the overall survival and disease free survival.

### METHODS

The records of male breast cancer patients attending Surgical Oncology Unit, and Clinical Oncology and Nuclear Medicine Dept., Mansoura University Hospital (MUH) during the period 1988-1995 were reviewed. Median duration of follow up was 27.05 months (range: 2.97 to 80.97 months).

Data reviewed included: age of patient, presenting signs and symptoms, staging investigations, type of surgical treatment, histopathological data, and post operative treatment. All cases had complete blood picture, LFT, serum creatinine, chest X-ray, Abdominal Ultrasound, and skeletal survey (or bone scan).

Review of histopathological data included: tumor size (T), histological type, tumor grade, number of lymph nodes involved and presence of perinodal infiltration.

TNM staging system was adopted.<sup>(2)</sup> Duration of overall survival (OVS) was calculated from date of diagnosis (biopsy) to date of last follow up or death of the patient. Duration of disease free survival (DFS) was calculated from date of starting treatment to date of relapse or progression of the disease.<sup>(3)</sup>

### Statistical Analysis:

All statistical tests were done through a computerized statistical program (SPSS/PC for Windows version 6.13). The overall and disease free survivals were analyzed using the life table method. The log-rank test and COX-regression test were used to determine prognostic factors through univariate and multivariate analyses respectively.

### RESULTS

During the period 1988-1995, 39 cases of male breast cancer were treated and followed up in Surgical Oncology Unit and Clinical Oncology and Nuclear Medicine Dept., MUH.

The patient's characteristics are shown in Table I. The mean age was 55 years and median age was 53 years (range: 25 years to 83 years). Breast mass was the most common presenting symptoms in 28 cases (72%). Skin changes (including eczema, discharge from nipple, and/or ulceration) were the presenting symptoms in 5 cases (13%), while remaining 6 cases presented with both breast mass and skin changes (15%). Pain was associated symptom in 4 cases (10%).

Metastatic work up at presentation revealed 7 cases (18%) with metastases, in the bones in 4 cases (10%), in the lung in one case and in both bone and

**Table II:** Pathological data of 39 cases of male breast cancer.

	No. = 39	%
<b>- Histological type :</b>		
Infiltrating duct carcinoma	37	95
Poorly differentiated carcinoma	2	5
<b>Tumor Grade (G) :</b>		
GI	5	13
GII	24	61
GIII	10	26
<b>Tumor Size (T) :</b>		
T <sub>1</sub>	22	56
T <sub>2</sub>	3	8
T <sub>4</sub>	14	36
<b>Axillary lymph node (LN)status :</b>		
Negative	6	15
Positive	28	72
≤ 3 LN	10	26
> 3 LN	9	23
> 3 LN with perinodal infiltration	9	23
Not assessed	5	13
Skin involvement	12	31
Chest wall fixation :	4	10

**Table III:** Univariate analysis of prognostic factors affecting OVS (log-rank test).

Factor	Statistics	df	Significance P-value
1- Presence of metastases	3.98	1	0.0461
2- Tumor grade	2.39	2	0.3026
3- Chest wall fixation	0.79	1	0.373
4- Lymph node status	6.60	3	0.086
5- Skin involvement	1.90	1	0.1684
6- Type of surgery	6.56	3	0.0873
7- PO treatment	10.20	5	0.0697
8- Tumor size (T)	3.73	2	0.1804

**Table IV:** Univariate analysis of prognostic factors affecting DFS (log-rank test).

Factor	Statistics	df	Significance P-value
1- Presence of metastases	20.27	1	0.000
2- Tumor grade	4.65	2	0.0979
3- Chest wall fixation	1.58	1	0.2082
4- Lymph node status	10.03	3	0.0184
5- Skin involvement	2.36	1	0.1244
6- Type of surgery	4.62	3	0.2017
7- PO treatment	14.27	5	0.014
8- Tumor size (T)	10.04	2	0.0066

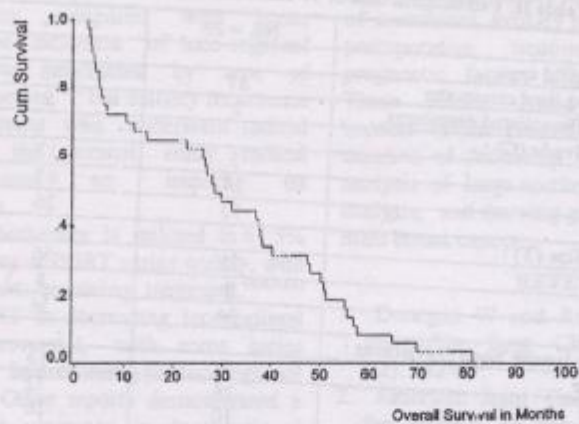


Fig.1: Overall Survival in Months of 39 cases of Male Breast Cancer.

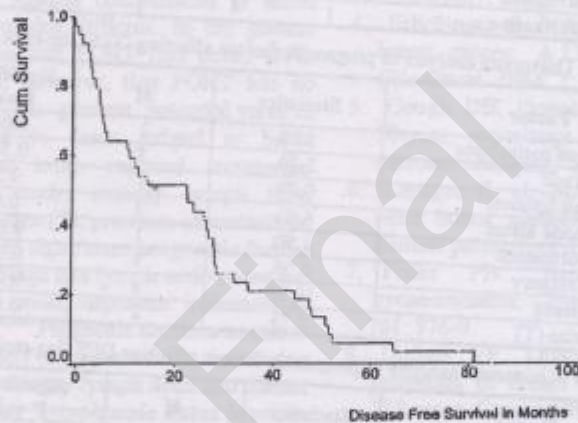


Fig.2: Disease free survival in months of 39 cases of male breast cancer.

#### DISCUSSION

Only 39 male patients with breast cancer were registered during the period of the study, 8 years. Male breast cancer is an infrequent disease as it accounts for less than 1% of all cases of breast cancer.<sup>(1)</sup> In NCI registry, Egypt, male breast cancer was ranked as number 10 in male malignancies with only 65 cases (3.8% of all breast cancers) registered during the period 1985-1989.<sup>(3)</sup>

The mean age of presentation is usually above 60 years, with a range of age of mid - 20s to early 90s.<sup>(4,6)</sup> In this series, patients were affected at younger age, may be due to relative small number of patients. Bilharziasis is an endemic disease in Egypt, associated with hyperestrogenemia with gynecomastia in males.<sup>(7)</sup>

The clinical presentation of our cases is similar to that reported in the literature. Male breast cancer mainly presents with breast lump (79-98%) followed by nipple retraction and/or discharge (11-57%), axillary adenopathy (40-45%), chest wall fixation

(3-17%) and breast pain in 16%.<sup>(5,6,8,9,10)</sup>

The initial therapy of disease localized to the breast and axillary nodes is mastectomy with axillary dissection.<sup>(4,8,9,11)</sup> Whereas radical mastectomy was the procedure most often utilized in early series,<sup>(12,13)</sup> less radical procedures often combined with radiation therapy such as modified radical or simple mastectomy are common in recent series.<sup>(8,10)</sup>

In this series, radical mastectomy was performed in 70% of patients, modified radical mastectomy in 10% and simple mastectomy in 20%. *Gough et al*,<sup>(5)</sup> reviewed the surgical procedures of male breast cancer over 50 years, 1933-1983. The surgical procedure from 1933 to 1958 was radical mastectomy in 82% of the patients, modified radical mastectomy in 2%, simple mastectomy in 14% and lumpectomy in 2%, and from 1959-1983, these frequencies were 12%, 63%, 11% and 12% respectively. In support of less radical procedures, a number of series have not shown significant

differences in survival of patients who underwent radical mastectomy compared with lesser procedure.<sup>(5,11,13)</sup> The incidence of loco-regional recurrence rate was unaffected by type of mastectomy in one series,<sup>(14)</sup> but axillary recurrence was lowest in patients who underwent radical mastectomy.<sup>(11)</sup> In the present study, radical mastectomy showed no impact on survival or recurrence.

Postoperative radiotherapy is utilized in 61.5% of our patients. The use of PORT varies widely, with 5% to 80% of patients receiving treatment.<sup>(4,8,9,11)</sup> The value of PORT in decreasing locoregional recurrence is controversial, with some series showing no efficacy in decreasing the locoregional recurrence rate.<sup>(5,11)</sup> Other reports demonstrated a statistical significant decrease in loco-regional recurrence.<sup>(4,6)</sup> This controversy may be due to relative small number of each series and to the use of different techniques and radiation dose over the past four decades making comparisons of series from dissimilar decades difficult. In the present series, patients who had PORT had better DFS. There is agreement, however, that PORT has no survival benefit.<sup>(4-6)</sup> The greatest potential value of radiation therapy is in cases judged to be at substantial risk for local- regional recurrence.

In the present study, axillary lymph node involvement, tumors size (T), presence of metastases and PO treatment were significant prognostic factors affecting survival. Stage and lymph node status has been reported to be most important indicators in male breast cancer.<sup>(4,6,8)</sup> Prognosis declines as tumor size increases, largely because of the increasing probability of both axillary lymph node and distant metastases.<sup>(6,9)</sup> Axillary lymph node status provides the single most useful indicator of prognosis. Ten-year corrected survival fell from 55% in males with No status to 22% in those with N<sub>1</sub> or N<sub>2</sub> status.<sup>(6)</sup> Again Guinee et al.,<sup>(8)</sup> reported the prognostic importance of the number of histologically positive axillary lymph nodes. The survival rates at 5-years were 90%, 73% and 55% for patients with negative nodes, one to three positive nodes, and four or more positive nodes respectively.

#### Summary And Conclusions:

The clinical presentation of the present series is similar to that reported in the literature. The median overall and disease free survival were 36.8 months and 22.8 months respectively. By univariate analysis, presence of metastases, axillary lymph node involvement, tumor size, and postoperative treatment were significant prognostic factors

affecting survival. By multivariate analysis, presence of metastases, axillary lymph node involvement, and postoperative treatment remained significant prognostic factors affecting disease free survival. These results should be interpreted cautiously because of the patient small number and the short duration of follow up. National cancer registry with analysis of large number of cases may enable better analysis, and drawing guidelines for management of male breast cancer.

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### العوامل النذرية لسرطان الثدي بالذكور

**مقدمة البحث:** يمثل هذا البحث دراسة إبترجاعية لعدد ٣٩ حالة سرطان ثدى فى الذكور تم علاجها ومتابعتها بوحدة جراحة الأورام وقسم علاج الأورام والطب النووى بمستشفى المنصورة الجامعى فى الفترة من ١٩٨٨ إلى ١٩٩٥ .

**الهدف من البحث:** هو دراسة الخواص الوبائية الإكلينيكية والتعرف على العوامل التكهنية لهذا المرض .  
**طرق البحث والنتائج:** وكان متوسط العمر لهؤلاء المرضى ٥٣ عاما (من ٢٥ إلى ٨٣ عاما) أشتكى معظمهم من وجود تورم فى الثدي . وقد عولج هؤلاء المرضى جراحيا بالإستئصال الجذرى للثدى (٧٠% من الحالات) إضافة إلى طرق الإستئصال الأخرى فى باقى الحالات ثم العلاج الإشعاعى بعد الجراحة فى ٦٢% من الحالات .  
وقد تشابهت الخواص الوبائية الإكلينيكية فى هذه الدراسة مع الدراسات المنشورة الأخرى لهذا المرض وبلغ متوسط فترة الإعاشة الكلية ٣٦,٨ شهرا والإعاشة بدون إرتجاع مرضى ٢٢,٨ شهرا . وشملت العوامل التكهنية - ذات الدلالة الإحصائية- التى تتحكم فى فترة الإعاشة وجود إنتشار للورم - وجود ثانويات فى الغدد الليمفاوية تحت الأبط - العلاج المكمل بعد الجراحة .

**الإستنتاج:** يجب النظر إلى هذه النتائج بإحتياط الواجب نظرا لقله عدد الحالات وعدم إنتظامهم فى المتابعة النورية . لذا فإن وجود تسجيل قومى لحالات سرطان الثدي فى الرجال يمكن أن يودى إلى دراسة وتحليل عدد كبير من هؤلاء المرضى وتحديد السياسة العلاجية المثلى لهذا الورم .