

Epidemiological and Histological Profile of Breast Cancer in the Ghrab Chrarda Bni Hsein Region, Morocco

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ABSTRACT

Introduction

Breast cancer is the most common cancer, accounting for 38.9% of all cancers diagnosed, it is also the most fatal among Moroccan women. The aims of this study were to draw up an epidemiological profile of breast cancer and to establish the link between patient characteristics and the histological types of cancer observed.

Methods

This was a retrospective study including 877 patients with histologically confirmed breast cancer. The study was conducted at the Reproductive Health Reference Center in the province of Kénitra (Morocco). It covered the period 2013 - 2018.

Results

The median age of patients at diagnosis was 50 years (Q1-Q3: 42 - 58 years). Most patients were aged 40 years or older (84.04%) and married (67.32%). They were nulliparous in 18.61% of cases. The average number of live children (LVC) was 3.5 LVC (Q1-Q3: 2 - 5 LVC). Approximately 10.22% of patients had a family history of invasive carcinoma (96.58%). The median tumour size was 25 mm (Q1 - Q3: 20 - 36 mm). The predominant histological type was invasive ductal carcinoma. The most common Scarff-Bloom-Richardson (SBR) grade was SBR II (63.64%). High histological grade correlated with large tumour size. Histological type showed a significant association with time to consultation ($p < 0.05$) and age at first pregnancy ($p < 0.05$).

Conclusion

All the contextual factors need to be taken into account to improve the assessment of the risk of developing breast cancer, and even of dying from it. Research, awareness-raising and ongoing education are essential if we are to develop more effective prevention strategies and treatments.

Keywords

Breast cancer ; Reproduction ; History ; Histological type ; Morocco

INTRODUCTION

Breast cancer continues to attract increasing attention and interest from clinicians and researchers because of its growing morbidity and high mortality. According to the World Health Organisation, breast cancer is the second leading cause of death worldwide. It affected 2.3 million women and caused 685,000 deaths in 2020¹. In Africa, the breast cancer mortality rate (19.4%) is the highest in the world, making this disease a serious public health problem in the majority of African countries². In Morocco, breast cancer is the most common cancer among women, accounting for 38.9% of all cancers

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diagnosed. Around 56.4 new cases of breast cancer are reported every year for every 100,000 women. It is also the leading cause of cancer-related death among Moroccan women³.

Morocco has introduced a national public health policy to prevent and treat cancer, including breast cancer. The two national plans for cancer prevention and control (2010-2019) and (2020-2029) include four clearly defined strategic areas: prevention, early detection, diagnosis and treatment, and palliative care^{4,5}.

The diagnosis of breast cancer, which is essentially histological, is based on radiological examination^{6,7}. When an abnormality is detected during a clinical examination, mammography or breast ultrasound, a biopsy is carried out to obtain a sample of tissue in order to search for the specific characteristics of the cancer⁸.

Breast cancer is a clinically heterogeneous disease and it is generally accepted that the different clinical course of patients with histologically similar tumours is due to molecular differences between the cancers.⁹ Therefore, knowledge of the particularities of each histological type will lead to an individualised and better therapeutic approach¹⁰. To date, no study of breast cancer has been carried out in the Gharb-Chrarda-Beni Hssen region (according to the 1st administrative division of Morocco). In the present study, we described the study population, and investigated possible associations between socio-demographic characteristics, reproductive characteristics, and histological features of breast cancer in patients at the Reproductive Health Reference Centre in the study region.

METHODS

We conducted a retrospective study of 877 patients with histologically confirmed breast cancer (all histological types combined). The study took place at the Reproductive Health Reference Center in Kenitra, the capital of the study region, over a six-year period from 2013 to 2018.

The data were collected after examining the patients' files, using a data processing form. Files containing no anatomopathological report were excluded. Ethical rules were respected.

The variables studied were sociodemographic (age of diagnosis, area, origin and family situation), reproductive (gestational age, parity, age of first

pregnancy and menopause) and cancer-related (time to diagnosis, family history of breast cancer, grade and histological type of cancer, tumour location and size). The age groups are determined by 3 classes : young women

< 40 years old¹¹, the target age group for the national program for the early detection of breast and cervical cancers (40-69 years)¹² and older women ≥ 70 years of age¹³.

SPSS version 21.0 was used to analyse the data. Frequencies and quartiles were calculated, since the quantitative variables were not normally distributed. Frequencies were compared using Pearson's Chi-square test (in the case of violation of the application condition, Yates' correction or Fisher's exact test). For quantitative variables, we used the z-score for two independent groups and the Kruskal-Wallis test for more than two independent groups. Simple logistic regression was used to identify possible associations. The significance level was set at

1.05 for all statistical analyses.

RESULTS

Patient profile

The median age at diagnosis was 50 years (Q1-Q3: 42-58 years). They were 40 years or older in 84.04% of diagnosed cases. About two-thirds of the patients were from urban areas (64.56%). Married women were the most frequently diagnosed (67.32%). Nulliparous women accounted for 18.61% of those diagnosed. The median number of live children was 3.5 EV (Q1-Q3: 2 - 5 EV). The majority of women with cancer (75.63%) had had their first pregnancy before the age of 30. The median age at first pregnancy was 23 years (Q1-Q3: 18 - 29 years). Family history was present in only 10.22% of cases, 42.17% of which were on the patient's sister's side. Approximately 97% of cases involved invasive carcinoma. Tumours were present in the left breast in 49.94% of cases. The cancer was bilateral in 3.19 cases. Invasive carcinomas were in the majority (96.58%), with a predominance of invasive ductal carcinoma (IDC) (88.03%). Non-invasive cancers accounted for a small proportion (2.73%), and were represented by ductal carcinoma in situ (DCIS) in 2.05% of cases. Other histological types were observed at low frequencies (less than 1%) (Table 1). The smallest tumour size was 5 mm, the largest 165 mm. The median tumour size was

25 mm (Q1 - Q3: 20 - 36 mm). The distribution of SBR (Scarff-Bloom-Richardson) histological grade was as follows: SBR I in 23.41% of patients, SBR II in 63.64% of patients and SBR III in 12.95% of patients.

Table 1. Distribution of different histological types of breast cancer according to infiltration

Histological type of breast cancer		n (%)
	Infiltrating ductal carcinoma	772 (88.03)
	Infiltrating lobular carcinoma	29 (3.31)
	Mucinous carcinoma	14 (1.60)
	Non-specific invasive carcinoma	8 (0.91)
	Medullary carcinoma	6 (0.68)
Invasive cancer	Mixed cancer	6 (0.68)
	Infiltrating tubular carcinoma	5 (0.57)
	Infiltrating metaplastic carcinoma	3 (0.34)
	Infiltrating cribriform carcinoma	2 (0.23)
	Infiltrating micropapillary carcinoma	1 (0.11)
	Poorly differentiated adenocarcinoma	1 (0.11)
	Ductal carcinoma in situ	18 (2.05)
Non-invasive cancer	Papillary carcinoma in situ	5 (0.57)
	Cribriform carcinoma	1 (0.11)
	Phyllodes tumour	2 (0.23)
	Squamous cell carcinoma	1 (0.11)
Other types	Bowen's disease	1 (0.11)
	Paget's disease	1 (0.11)
	Myxoid sarcoma	1 (0.11)
Total		877 (100.00)

n (%): number of cases (percentage).

Variations linked to the histological type of breast cancer

The choice of treatment and the patient's vital prognosis may vary according to the histological type and grade of the breast cancer. We reclassified the carcinomas into invasive and non-invasive cancers, to rebalance the groups formed and limit false conclusions. Analysis

of time to diagnosis and age at first pregnancy by histological type showed that the two patient cohorts were distributed differently ($p < 0.01$ and $p < 0.05$, respectively). The other co-variables showed no significant difference (Table 2). According to the regression analysis, the histological type of breast cancer was associated with time to diagnosis ($p < 0.01$) and age at first pregnancy ($p < 0.05$), with a risk not exceeding 7%.

Table 2. Distribution of quantitative characteristics according to histological type of breast cancer

Features	Histological type of breast cancer		z (p-value)
	Invasive cancer (Q2 (Q1-Q3))	Non-invasive cancer (Q2 (Q1-Q3))	
Time to diagnosis (n=761)	8.00 (6.00-14.00)	22.00 (7.75-98.25)	-3.27 (0.001)
Median age at diagnosis (n=877)	50.00 (42.00-58.00)	49.50 (42.25-56.50)	-0.08 (0.933)
Number of pregnancies (n=648)	4 (2-6)	4 (2-5)	-0.30 (0.763)
Number of parity (n=632)	3 (2-5)	4 (1.5-5)	-0.17 (0.868)
Age at menopause (n=267)	51.00 (48.00-53.00)	50.50 (49.00-51.00)	-0.42 (0.676)
Age at first pregnancy (n=595)	22.00 (18.00-29.00)	27.00 (20.75-32.50)	-2.06 (0.039)
Tumor size (n=780)	25.00 (20.00-36.00)	28.00 (20.50-38.25)	-0.33 (0.739)

Q1, Q2 and Q3: quartiles; z: z-score; p-value: statistical significance

Comparison of frequencies showed differences with age at first pregnancy (between before and after 30 years) and histological grade of SBR ($p < 0.05$). Invasive cancer was more common in patients who became pregnant before the age of 30 years. The majority of invasive cancers (511 cases) were intermediate histological grade SBR II (Table 3).

Table 3. Distribution of qualitative characteristics according to histological type of breast cancer

Histological type of breast cancer			
Features	Invasive cancer (n (%))	Non-invasive cancer (n (%))	χ^2 (p-value)
Age groups (n=877)			
< 40 years	135 (96,43)	5 (3,57)	
40 - 69 years	650 (97,16)	19 (2,84)	0,45 (0,825)
≥ 70 years	66 (97,06)	2 (2,94)	
Areas (n=872)			
Urban	547 (97,16)	16 (2,84)	0,11 (0,743)
Rural	299 (96,76)	10 (3,24)	
Family situation (n=811)			
Single	93 (97,89)	2 (2,11)	
Married	531 (97,25)	15 (2,75)	0,80 (0,833)
Divorced	56 (96,55)	2 (3,45)	
Widow	108 (96,43)	4 (3,57)	
Parity (n=795)			
Nulliparous	144 (97,30)	4 (2,70)	0,00 (1,000)
Multipare	628 (97,06)	19 (2,94)	
Origin (n=872)			
Kenitra	559 (97,05)	17 (2,95)	
Sidi Kacem	153 (98,71)	2 (1,29)	3,31 (0,207)
Sidi Slimane	134 (95,04)	7 (4,96)	
Menopause (n=727)			
Yes	374 (97,65)	9 (2,35)	1,26 (0,261)
No	331 (96,22)	13 (3,78)	
Age group of first pregnancy (n=595)			
After 30 years	136 (93,79)	9 (6,21)	
Before 30 years	441 (98,00)	9 (2,00)	6,62 (0,010)
Family history (n=812)			
Yes	81 (97,59)	2 (2,41)	0,10 (0,757)
No	707 (96,98)	22 (3,02)	

Histological type of breast cancer			
Features	Invasive cancer (n (%))	Non-invasive cancer (n (%))	χ^2 (p-value)
Breast affected (n=877)			
Two breasts	27 (96,43)	1 (3,57)	0,04 (0,847)
One breast	824 (97,06)	25 (2,94)	
Histological grade (n=803)			
Grade 1	185 (98,40)	3 (1,60)	
Grade 2	511 (100,00)	0	6,82 (0,027)
Grade 3	104 (100,00)	0	

χ^2 : the statistic is calculated using the chi-square test if the application condition is met (if not, using the Yates correction or Fisher's exact test); p-value: the statistical significance.

Variations related to histological grade SBR of breast cancer

We found that higher histological grade was associated with larger tumour size. From grade I to grade III, tumour size increased. The difference was highly significant ($p < 0.001$). The other co-variables showed no difference between the three histological grades of breast cancer (Table 4).

DISCUSSION

Breast cancer is a complex disease with wide variations in clinical presentation and prognosis [14]. Among the many factors that influence the development and characteristics of breast cancer, age has been identified as a key factor¹⁵. In our study, 84.04% of patients were women over 40 years of age, which is consistent with epidemiological data reported in other studies (82.3%)¹⁶ and (67.21%)¹⁷. Similarly, studies have found that breast cancer is more aggressive in young women¹⁸. However, in our series, the study of the relationship between age and type of breast cancer showed no significant association (p of 0.825), which is not consistent with what has been reported in several previous studies^{19,20}. Patients' family situation and type of breast cancer were not significantly associated ($p=0.833$). This result is similar to the study by Foxcroft et al²¹.

Table 4. Distribution of quantitative characteristics according to histological grade of breast cancer

Features	Histological grade of breast cancer			H (p-value)
	SBR I (Q2 (Q1-Q3))	SBR II (Q2 (Q1-Q3))	SBR III (Q2 (Q1-Q3))	
Diagnosis delay (n=707)	7 (6-13)	7 (6-14)	8 (6-15)	1,84 (0,399)
Age (n=803)	50 (42-59)	50 (43-58)	50 (41-57,75)	0,65 (0,724)
Number of pregnancies (n=597)	4 (3-6)	4 (2-6)	4 (3-6)	1,22 (0,544)
Number of parities (n=584)	4 (2-5)	3 (2-5)	3,5 (2-5)	2,28 (0,319)
Age at menopause (n=252)	50 (47-53,5)	50,29 (48-53)	51,5 (49-55)	1,99 (0,370)
Age at 1 st pregnancy (n=544)	21 (17,5-26,5)	23 (18-30)	22,5 (18-29)	5,38 (0,068)
Tumour size (n=726)	22 (18-30)	26 (20-37,25)	30 (22-43)	22,36 (0,000)

H: Kruskal Wallis test statistic; p-value: statistical significance

The analysis also revealed that 64.91% of patients lived in urban areas, 73.75% of whom had histological grade SBR II or SBR III. Patient origin showed differences between histological grades. The difference was highly significant ($p < 0.01$). The other variables showed no statistically significant difference in histological grade (Table 5).

Table 5. Distribution of qualitative characteristics according to histological grade of breast cancer

Features	Histological grade of breast cancer			χ^2 (p-value)
	SBR I (n (%))	SBR II (n (%))	SBR III (n (%))	
Age groups (n=803)				
< 40 years old	31 (23,85)	79 (60,77)	20 (15,38)	2,98 (0,561)
40 - 69 years old	138 (22,66)	396 (65,02)	75 (12,32)	
≥ 70 years	19 (29,69)	36 (56,25)	9 (14,06)	
Family situation (n=749)				
Single	23 (25,56)	55 (61,11)	12 (13,33)	3,52 (0,741)
Married	120 (23,81)	326 (64,68)	58 (11,51)	
Divorced	13 (25,00)	29 (55,77)	10 (19,23)	
Widow	27 (26,21)	62 (60,19)	14 (13,59)	
Multiparity (n=735)				
Nulliparous	32 (23,02)	92 (66,19)	15 (10,79)	0,63 (0,730)
Multipare	147 (24,66)	374 (62,75)	75 (12,58)	
Area (n=798)				
Urban	136 (26,25)	308 (59,46)	74 (14,29)	12,00 (0,002)
Rural	50 (17,86)	201 (71,79)	29 (10,36)	

Features	Histological grade of breast cancer			χ^2 (p-value)
	SBR I (n (%))	SBR II (n (%))	SBR III (n (%))	
Origin (n=798)				
Kenitra	123 (23,70)	321 (61,85)	75 (14,45)	5,88 (0,208)
Sidi Kacem	28 (19,31)	100 (68,97)	17 (11,72)	
Sidi Slimane	35 (26,12)	88 (65,67)	11 (8,21)	
Menopause (n=671)				
Yes	78 (21,73)	237 (66,02)	44 (12,26)	5,01 (0,082)
No	89 (28,53)	181 (58,01)	42 (13,46)	
Menopause age group (n=252)				
50 years and under	29 (23,02)	86 (68,25)	11 (8,73)	1,11 (0,573)
Over 50 years	26 (20,63)	84 (66,67)	16 (12,70)	
Age group of 1st pregnancy (n=544)				
Before 30 years	113 (27,23)	247 (59,52)	55 (13,25)	4,78 (0,092)
After 30 years	24 (18,60)	90 (69,77)	15 (11,63)	
Family history (n=745)				
Yes	22 (28,21)	47 (60,26)	9 (11,54)	0,73 (0,695)
No	159 (23,84)	425 (63,72)	83 (12,44)	
Breast affected (n=803)				
Two breasts	4 (16,67)	16 (66,67)	4 (16,67)	0,78 (0,677)
One breast	184 (23,62)	495 (63,54)	100 (12,84)	

χ^2 : Chi-square test statistic; p-value: statistical significance

In Algeria and Libya, researchers found a significant association between delay in diagnosis and stage of disease ($p = 0.031$ ²² and $p < 0.0001$ ²³, respectively), which was confirmed by our study ($p = 0.001$). Although some results do not show a statistically significant association, the majority of studies emphasise the importance of reducing delays in management for patient survival²⁴.

We found that 18.61% of the women included in this study were nulliparous. In a Tunisian study, Frikha demonstrated the negative impact of nulliparity on breast cancer²⁵. It is also known that the risk of breast cancer increases with age at the time of the first pregnancy. Women who have had at least one full-term pregnancy have an average 25% lower risk of breast cancer than women who have never had children.¹⁵ There seems to be a positive correlation between the number of children and the level of protection against breast

cancer, although 79.4% of the cases in our population were multiparous women (79.4%). In addition, a woman who gives birth to her first child after the age of 30 has a higher risk than a woman who has never given birth. Our study found a significant association ($p = 0.010$) between the age of first pregnancy and the histological type of breast cancer.

A family history of breast cancer, especially in a mother, sister or daughter, increases the risk of breast cancer by an estimated two to three times²⁵. Thirty-five patients, or 43.20% of cases with one of the infiltrating histological types, reported that their sister had breast cancer. Similarly, according to the study by Krainer M et al²⁶, 40% of patients with an invasive histological type reported that their sister had breast cancer. However, we found no significant correlation ($p = 0.695$) between breast cancer type and family history of breast cancer. This result is not consistent with the results of the study

by Jmor et al ($p=0.002$) [27].

According to our study, half of the patients diagnosed had cancer in the left breast and 3.19% in both breasts. These results indicate a relatively even distribution of breast cancer between the two sides of the breast. There is also an increased risk of developing a second primary cancer in the contralateral breast. Previous studies have shown that this risk is approximately five to seven times higher than the risk of developing a first primary breast cancer in the contralateral breast.²⁸

Our analysis showed a significant correlation between tumour size and histological type of breast cancer ($p=0.000$). These results support the idea that tumour size is crucial for classifying and understanding breast cancer. A larger tumour is generally associated with a more advanced stage of the disease and the potential to spread to other tissues or organs²⁹. This correlation between tumour size and histological type (invasive versus non-invasive carcinoma) is consistent with previous studies by^{30,31}. These studies have also highlighted the importance of tumour size in predicting the stage and prognosis of breast cancer. A 1 cm breast cancer is cured in 90% of cases, but when it reaches 10 cm the cure rate is less than 10%. Our study confirms that invasive ductal carcinoma is the predominant histological type, representing a significant proportion of 88% of the cases studied, which corroborates the results of the study reported by³².

We found that Scarff-Bloom-Richardson (SBR) grades II and III were present in 615 cases, representing over three quarters of the sample. Our results showed a significant correlation between SBR grade and breast cancer type ($p = 0.027$), which is consistent with recent studies suggesting a strong significant correlation between breast cancer type and SBR grade^{16,33}. Thus, SBR grade may be an important indicator of breast cancer type and aggressiveness.

Place of residence is an important socio-demographic factor influencing delay in breast cancer diagnosis due to inequalities in health care³⁴. Our study showed that 64.91% of patients lived in urban areas, 73.75% of whom had histological grade SBR II or SBR III. We can explain these observations by the effect of urban lifestyle, which may increase women's susceptibility to breast cancer and late stage breast cancer, as shown by the significant association found in our study ($p=0.002$). Women living in urban areas are twice as likely to develop breast cancer as those living in rural areas^{35,36}.

Given the diversity of histological types of breast cancer, accurate identification of these types is essential for appropriate clinical management. The results reported by this study may contribute to a better understanding of the disease in the population studied and to the development of more targeted prevention, screening and treatment strategies. A longitudinal study would be useful to corroborate our findings, to cover the subject comprehensively, and possibly to investigate existing cause-effect relationships.

CONCLUSION

The histological type of breast cancer, in addition to specific epidemiological characteristics, helps to determine the prognosis of this disease. Breast tumours can be divided into invasive and non-invasive cancers according to their severity. Each type has unique characteristics in terms of tumour growth, ability to metastasise and response to treatment. Characteristics associated with the histological type and/or grade of breast cancer may influence the development of different types of breast cancer. Understanding the histological type and epidemiological characteristics of each patient is essential for personalising treatment, developing an appropriate treatment plan and making more accurate prognostic predictions.

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