Research Article

Cancer Control
Volume 31: 1–8

DOI: 10.1177/10732748241300655
journals.sagepub.com/home/ccx
Sage

Immunohistochemical-Based Molecular Subtypes of Female Breast Cancer: A Retrospective Cross-Sectional Study at Cheikh Khalifa Hospital in Casablanca, Morocco

Bouaddi Oumnia, DMD[1,2], Diaby Maladho, MD[1], Gordon Amanda, Msc[3], Kaikani Wafaa, MD[4], Guessous Fadila, PhD[5], Chahboune Mohamed, MD[6], Adil Najdi, MD[7], AL Bouzidi Abderrahmane, MD[8], Nejjari Chakib, PhD[9,10], Ismaili Nabil, MD[4], and Khalis Mohamed, PhD[1,2,11]

Abstract

Introduction: Breast cancer is a major public health concern worldwide and the most prevalent form of cancer in Morocco. This study aimed to describe the histological and immunohistochemical profiles of breast cancer in women admitted to Cheikh Khalifa Hospital in Casablanca, Morocco.

Methods: This is a retrospective cross-sectional study. All histologically confirmed female breast cancer cases diagnosed between January 2017 and May 2021 at the Cheikh Khalifa University Hospital were included in the study. Data were collected from patient electronic medical records. Using an electronic sheet, information was collected about the socio-demographic characteristics of the patients, clinical features, histopathology, molecular characteristics, treatment received, and progression.

Results: Invasive carcinoma of no special type was the most common type of cancer accounting for 90.7% of all cases. The majority of the tumors (56.1%) were grade II tumors. About 42.1% of tumors were lymph node-positive and only 13.4% developed distant metastasis. Immunohistochemical data revealed that 57.9% of the tumors in this study were hormone receptor-positive (ER+ and PR+), 74.4% were estrogen receptor-positive (ER+), 58.5% were progesterone receptor positive (PR+), and 18.9% were HER2 positive (HER2+). The most common molecular subtype was Luminal A-like (43.9%). A statistically significant difference was found in histological grades across the four molecular subtypes ($P < 0.001$).

[1]Mohammed VI International School of Public Health, Mohammed VI University of Sciences and Health, Casablanca, Morocco
[2]Department of Public Health and Clinical Research, Mohammed VI Center for Research and Innovation, Rabat, Morocco
[3]University of Minnesota School of Public Health, Minneapolis, MN, USA
[4]Department of Oncology, Faculty of Medicine, Mohammed VI University of Sciences and Health, Casablanca, Morocco
[5]Faculty of Medicine, Mohammed VI University of Sciences and Health, Casablanca, Morocco
[6]Laboratory of Sciences and Health Technologies, Higher Institute of Health Sciences, Hassan First University of Settat, Settat, Morocco
[7]Department of Epidemiology, Faculty of Medicine and Pharmacy, Tangier, Morocco
[8]Laboratory of Pathological Anatomy, Cheikh Khalifa International University Hospital, Mohammed VI University of Sciences and Health, Casablanca, Morocco
[9]Faculty of Medicine, Euromed Research Center, Euromed University of Fez (UEMF), Fez, Morocco
[10]Faculty of Medicine, Sidi Mohamed Ben Abdellah University, Fez, Morocco
[11]Higher Institute of Nursing Professions and Health Techniques, Rabat, Ministry of Health and Social Protection, Rabat, Morocco

Corresponding Author:
Khalis Mohamed, Department of Public Health and Clinical Research, Mohammed VI Center for Research and Innovation, Rabat, Morocco. Rue Mohamed Al Jazouli, Madinat Al Irfane, Rabat 10112, Morocco.
Email: mkhalis@um6ss.ma

Conclusions: Our findings should be used to guide breast cancer management policies in Morocco. Larger cohort studies are needed to determine the specificity of the breast cancer profile in Morocco as well as the epidemiological risk factors specific to every subtype.

Keywords
Morocco, breast cancer, molecular subtypes, immunohistochemistry, cancer epidemiology

Received January 10, 2024. Received revised October 13, 2024. Accepted for publication October 28, 2024.

Introduction

Breast cancer is a major public health concern worldwide, accounting for 11.7% of all cancers, all sites combined, and for 24.5% of female cancers in 2020. This type of cancer is the most prevalent in most countries of the world. In North Africa, the gross incidence rate of breast cancer was estimated at 49.9 per 100,000 inhabitants, with a mortality rate of 18.2 per 100,000 inhabitants in 2020.[1] In Morocco, breast cancer was the most prevalent type of cancer (20.1%) in 2022, regardless of gender and age. In the same year, 12 756 new cases, all female, were recorded, accounting for 38.8% of the total cancer incidence.[2] Breast cancer has been shown to have major repercussions on the physical and mental well-being and the quality of life of its patient population. Studies in Morocco have reported that breast cancer patients experience anxiety, depression and body image dissatisfaction.[3] Additionally, the incidence of chronic pain at 3 months after surgery was estimated at 38.6%.[4]

Considering its heterogeneous nature, breast cancer diagnosis and treatment remain a major challenge in oncology and medical care as a whole. Indeed, breast tumors can present enormous variations in terms of clinical features as well as in their response to treatment. Several classifications (clinical, histopathological and molecular) have been established to allow for a more precise identification of the most aggressive subgroups and assist oncologists in adopting an appropriate therapeutic approach.[5,6] In 2017, the revision of the eighth edition of the American Joint Commission of Cancer (AJCC) TNM (primary tumor, lymph node and metastasis) staging system for breast cancer was conducted by a multidisciplinary team of breast cancer experts.[7,8] Thus, the need to incorporate histological and immunohistochemical factors such as histological grade, hormone receptor expression (estrogen and progesterone), and human epidermal growth factor 2 (HER2) expression into the classification system, was recognized by the expert panel.[7-9] Five molecular subtypes of breast cancer have been identified. The first subtype is Luminal A (estrogen receptor-positive [ER+] and/or progesterone receptor-positive [PR+] and HER2-negative [HER2-]). This subtype tends to have low proliferation rates and a good prognosis. Luminal B tumors are also ER+ and/or PR + but can be either HER2-positive or HER2-negative. Luminal B tumors generally have higher proliferation rates and a worse prognosis compared to Luminal A. Luminal breast cancer tumors account for the majority of all breast cancer cases in Western countries. The HER2-enriched subtype is ER-, PR-, and HER2-positive (defined as HER2 [3+] by IHC or confirmed by FISH if HER2 is [2+]). Triple-negative breast cancer (TNBC) is ER, PR-, and HER2-negative. This subtype is aggressive and is often associated with a worse prognosis. Finally, unclassified tumors are negative for all three markers, including HER2, as well as HER1 and cytokeratin (CK) 5/6.[7,10-12] Of these subtypes, hormone receptor positive tumors are likely to respond to hormonal therapy and often yield good results in terms of disease progression, whereas the prognosis is poor and with increased recurrence when the HER2 gene is amplified in invasive tumors.[13-16] Furthermore, it has been shown that diagnosis of breast cancer at an early stage ensures a much more effective and less burdensome therapeutic management and would thus allow an improvement of the overall prognosis.[5] Independently of the molecular classification described above, invasive breast cancers are classified into various histological types based on cytological characteristics and proliferation patterns. Based on the most recent classification by WHO, these include but are not limited to, invasive lobular carcinoma, mucinous carcinoma, cribriform carcinoma, invasive micropapillary carcinoma, and tubular carcinoma.[17] Tumors that do not fall into these specific categories are often classified as invasive breast cancer of no special type (NST).[18]

In Morocco, some advances have been made in breast cancer screening, diagnosis and treatment thanks to the National Cancer Control Plan which entered into force in 2010. This plan has spurred the organization of nationwide awareness campaigns and educational activities in the month of October, by the Morocco Ministry of Health (MoH) and its civil society partners. The latest estimates showed that nearly 3 million eligible women were screened in 2015 and 2016 according to an evaluation conducted by the International Agency for Research on Cancer (IARC).[19] Additionally, specialized publicly funded breast cancer care units were established in Rabat and Casablanca in 2013. A recent situational analysis of the patterns of care (POC) in the two centers - conducted by the IARC in collaboration with the MoH and Lalla Salma Foundation for Prevention and Treatment of Cancer - showed a significant increase in the proportion of patients presenting with a pathologically confirmed diagnosis, signaling major improvement in referral pathways between

2013 and 2017. However, this analysis also raised the issue of the lack of immunohistochemistry facilities which poses a barrier to the provision of comprehensive and tailored breast cancer care.[12] IHC plays a significant role in the estimation of prognosis and the prediction of treatment response.[20] Unfortunately, very few studies among breast cancer patients in Morocco have explored the immunohistochemical and histological characteristics of breast cancer tumors. Therefore, the aim of the retrospective study is to describe the immunohistochemical and histological profile of breast cancer tumors among Moroccan female breast cancer patients admitted to the Department of Oncology at Cheikh Khalifa University Hospital in Casablanca, Morocco. Additionally, this study aims to compare the four molecular subtypes across age, menopausal status, grade, severity and disease progression. Our findings would improve the level of knowledge on the local clinical epidemiology of breast cancer and should be used to guide public health investments and the development of new research hypotheses.

Materials and Methods

Study Design

This was a descriptive retrospective cross-sectional study of breast cancer cases in women admitted to the Oncology Department of the Cheikh Khalifa Hospital in Casablanca, Morocco, between January 2017 to May 2021.

Study Population

All histologically confirmed female breast cancer cases diagnosed between January 2017 and May 2021 were included in the study. The exclusion criteria were the absence of histology-supported diagnosis and cases with untraceable or incomplete records. Cases where the breast tumors were caused by another metastatic cancer and non-invasive forms were also excluded.

Data Collection

Data were collected from patient medical records, pathology reports and admission records. An electronic data sheet was used to collect information on each breast cancer case. This information sheet collected information about sociodemographic characteristics of the patients (e.g. personal identifiers, age at diagnosis, place of residence, menopausal status, medical insurance or social security,), clinical features (tumor size, lymph-node status, metastasis status [TNM]), histopathology, molecular characteristics (IHC marker status), treatment received (chemotherapy, radiotherapy, hormonal therapy, combination of therapies) and disease progression. Interpretations and diagnoses were not done by the same pathologist. For disease progression, we considered the latest available status.

Classification of Molecular Subtypes of Breast Cancer Using Immunohistochemical (IHC) Data. Based on the results of the IHC marker status, the tumors were classified into four molecular subtypes defined as follows: (i) Luminal A-like: ER-positive, PR-positive, HER2-negative, Ki-67 < 14%; (ii) Luminal B-like: ER-positive, HER2-negative, and at least one of the following: Ki-67 ≥ 14%, PR <20%; (iii) ER-positive, HER2-positive, any Ki-67, any PR; (iv) HER2: ER-negative, PR-negative, HER2-positive when the IHC (3+) or FISH amplified when cases were equivocal (2+) in the IHC; (v) Triple negative: ER-negative, PR-negative, HER2-negative. HER2 was considered positive in the IHC result if HER2 (3+) or in the FISH result if HER2 (2+).

Statistical Analysis

The data were collected, cleaned and coded in Excel, then analyzed using SPSS version 21 software. Qualitative variables were presented in numbers and percentages, while the quantitative variables were presented in means and standard deviations. A bivariate analysis was performed using the Chi-square test for categorical variables. Small *P*-values were two-tailed and the significance level was set at 0.05.

Ethical Considerations

The study protocol was approved by the Ethics Committee of the Faculty of Medicine and Pharmacy in Tangier (Ref 10/2022). Data were collected anonymously and confidentiality was guaranteed by limited access to the database. This study was conducted upon approval from the hospital's medical management as well as the heads of the involved departments. Individual patient consent was not required as only anonymized data were handled. This study was reported in accordance with the reporting guidelines for observational studies.[21]

Results

A total of 281 cases of female breast cancer were documented in the medical records of the Department of Oncology at the Cheick Khalifa University Hospital in Casablanca between January 2017 and May 2021. Of these, 117 cases were excluded due to the lack of available data on IHC and TNM. Therefore, only 164 breast cancer cases were analyzed in this study.

Table 1 shows the sociodemographic, clinical, histological, and molecular characteristics, as well as the treatment and progression of the breast cancer cases in our study. The mean age at diagnosis was 54.3 ± 12.3 years and the majority of patients (94.4%) lived in urban areas. Invasive carcinoma of no special type was the most common histological type accounting for 90.7% of all cases, followed by invasive lobular carcinoma (5.5%), mucinous carcinoma (2.4%), and papillary carcinoma (0.6%) and tubular carcinoma (0.6%). The size of

Table 1. Characteristics of the Study Population.

Characteristics	Distribution n (%)
Age at diagnosis	
Average (years±SD)	54.3 ± 12.3
Median (years)	54
Place of residence	
Urban	150 (94.4)
Rural	9 (5.6)
Missing	5
Histological type	
Invasive carcinoma of no special type	146 (90.7)
Invasive lobular carcinoma	9 (5.6)
Mucinous carcinoma	4 (2.4)
Papillary carcinoma	1 (0.6)
Tubular carcinoma	1 (0.6)
Tumor size	
<2 cm	56 (34.1)
2.0-5.0 cm	88 (53.6)
>5 cm	20 (12.2)
Histological grade SBR	
I	7 (4.4)
II	92 (57.5)
III	61 (38.1)
Missing	4
Lymph node status	
N0	57 (45.2)
N+ (N1, N2 and N3)	69 (54.8)
Missing	38
Metastasis status	
M0	96 (81.3)
M+	22 (18.6)
Missing	46
Tumor stage	
I	39 (23.8)
II	67 (40.8)
III	37 (22.6)
IV	21 (12.8)
IHC marker status	
ER+	122 (74.4)
PR+	96 (58.5)
HER2+	31 (18.9)
Type of treatment received	
Chemotherapy	83 (68.6)
Combination of therapies	28 (23.1)
Radiotherapy	8 (6.6)
Hormonal therapy	2 (1.6)
Missing	43
Social security coverage	
Not covered	73 (44.5)
Covered	91 (55.5)

*SD = Standard deviation.

the tumors was greater than or equal to 2 in 65.9% of cases. Regarding the Scarff-Bloom-Richardson (SBR) grading score, the majority (57.5%) were grade II tumors, 38.1% were grade III and only a small minority (4.4%) were grade I tumors. Among patients with a known lymph node status, about 54.8% were lymph-node positive, and among those with a known metastatic status, only 18.6% developed distant metastases. IHC data revealed that 74.4% of the tumors were estrogen receptor positive (ER+), 58.5% were progesterone receptor positive (PR+) and 18.9% were HER2 positive (HER2+). Of the 121 cases for which treatment was determined, 68.6% received chemotherapy, 23.1% received a combination of therapies, 6.6% received radiotherapy, and 1.6% received hormonal therapy. Patients with HER2 + Breast Cancer received Trastuzumab. Over half of the patients (55.5%) had social security coverage while 44.5% paid for their own treatment.

Table 2 shows the distribution of molecular subtypes based on the results of IHC. The most common subtype was Luminal A-like (43.9%), followed by Luminal B-like (30.5%), Triple Negative (15.2%), and HER2 (10.4%). Regarding menopausal status, the majority of Luminal B-like (86%) and Triple Negative (84%) cases were observed in post-menopausal patients. However, this difference was not statistically significant. ($P = 0.825$). Regarding tumor size, HER2 tumors were the largest (2.00 cm ± 0.6), followed by Triple Negative (1.88 cm ± 0.5), Luminal A-like (1.79 cm ± 0.7) and Luminal B-like (1.64 cm ± 0.6). However, this difference was not statistically significant ($P = 0.177$). Grade III was majorly observed in Triple Negative (72%) and HER2 (41.2%) subtypes compared to other subtypes. The differences observed were statistically significant ($P < 0.001$). Regarding disease progression, the Luminal B-like subtype showed the highest level of metastasis and/or recurrence (37.5%) compared to other subtypes. Overall, only 3 cases showing recurrence were associated with in situ carcinoma. Positive disease outcomes were observed in all molecular subtypes, with a high occurrence in the case of HER2 (73.3%) followed by Luminal A-like (68.6%). However, the differences observed in disease progression across molecular subtypes were not statistically significant ($P = 0.913$).

Discussion

The aim of this study was to describe the immunohistochemical and histological profile of breast cancer in female patients admitted to the Department of Oncology in the Cheikh Khalifa University Hospital in Casablanca. The main findings of this study were that the most common histological type was Invasive carcinoma of no special type and the most common molecular subtype were the Luminal A-like and B-like subtypes. Furthermore, statistically significant differences were found histological grade across the four molecular subtypes.

The majority of patients in our study were aged 54 years old on average at the time of diagnosis. Furthermore, most of patients lived in urban areas. Similar results were reported in a South African study where the mean age of female patients presenting with breast cancer was 56.2 ± 14.4, however, in this

Table 2. Characteristics of Molecular Subtypes of Breast Cancer at Cheikh Khalifa Hospital From January 2017 to May 2021 (N = 164).

Variables	Luminal A-like n (%)	Luminal B-like n (%)	HER2-like n (%)	Triple Negative n (%)	*P*-Value
Percentage of subtypes	72 (43.9)	50 (30.5)	17 (10.4)	25 (15.2)	
Average (years ± SD[a])	57±13.5	53±11.6	48±10.2	54±10.8	0.056
Menopausal status					
Premenopause	13 (18.1)	7 (14)	4 (23.5)	4 (16)	0.825
Post-menopause	59 (81.9)	43 (86)	13 (76.5)	21 (84)	
Histological type					
Invasive carcinoma of no special type or lobular carcinoma	69 (88.9)	48 (96)	14 (82.4)	24 (96)	0.144
Other (mucinous/ Papillary/Tubular)	3 (4.2)	2 (4)	3 (17.6)	1 (4)	
Tumor size (T)					
T1 tumor ≤ 2.0	27 (37.5)	21 (42)	3 (17.6)	5 (20)	0.177
T2 tumor ≥ 2.0 but ≤ 5.0	33 (45.8)	26 (52)	11 (64.7)	18 (72)	
T3 tumor ≥ 5.0	12 (16.7)	3 (6)	3 (17.6)	2 (8)	
Histological grade SBR					
I or II	51 (73.9)	31 (63.3)	10 (58.8)	7 (28)	<0.001
III	18 (26.1)	18 (36.7)	7 (41.2)	18 (72)	
ND[b]	3	1			
Status of vascular emboli					
Negative	35 (66)	30 (73.2)	13 (81.3)	9 (69.2)	0.671
Positive	18 (34)	11 (26.8)	3 (18.8)	4 (30.8)	
ND[b]	19	9	4	9	
N0	26 (36.1)	17 (34)	6 (35.3)	8 (32)	0.994
N+ (N1, N2 and N3)	30 (41.7)	20 (40)	8 (47.1)	11 (44)	
Nx	16 (22.2)	13 (26)	3 (17.6)	6 (24)	
Metastasis status					
M0	43 (59.7)	26 (52)	9 (52.9)	18 (72)	0.591
M+	8 (11.1)	8 (16)	4 (23.5)	2 (8)	
Mx	21 (29.2)	16 (32)	4 (23.5)	5 (20)	
Tumor stage					
I	19 (26.4)	14 (28)	3 (17.6)	3 (12)	0.513
II	29 (40.3)	20 (40.0)	5 (29.4)	13 (52)	
III	17 (23.6)	8 (16)	5 (29.4)	7 (28)	
IV	7 (9.7)	8 (16)	4 (23.5)	2 (8)	
Disease progression					
NSTR	24 (68.6)	15 (62.5)	11 (73.3)	6 (66.7)	0.913
Reccurence and/or metastasis	11 (31.4)	9 (37.5)	4 (26.7)	3 (33.3)	
ND[b]	37	26	2	16	

[a]SD = Standard deviation.
[b]ND = Not Determined.

study, the patients lived predominantly in urban areas. Contrasting results were reported in Eastern and Northern Morocco where the mean age at the time of diagnosis was 48.7 ± 11.4 years (range 19-105) and 45 years (range 18-80) respectively.[13,22] This may be explained by the fact that in these parts of Morocco the population is relatively young compared to other regions of the country.[13,22] In some Western countries, breast cancer also occurs at an older age.[23] The association between older age and the risk of breast cancer has been well-documented. In fact, there is a 3% increase in the risk of developing breast cancer at age 50. Interestingly, previous studies also found a relationship between particular molecular subtypes and patients' age. Triple Negative subtype has been shown to occur more commonly in individuals under age 40 and Luminal A-like subtype is often diagnosed in individuals aged 70 and older.[18,24] In this study, Luminal cancers represented the majority of cases (74.4%) which is consistent with existing literature. Similar to our findings, one retrospective study in DRC also found that Luminal A-like and Luminal B-like subtypes were the most common, 44.74% and 40.53% respectively.[25] In fact, it is estimated that Luminal breast cancer accounts for 70%–80% of breast cancer diagnoses.[26] Additionally, HER2 tumors are the second most common breast cancers followed and triple negative

cancers.[26] This is inconsistent with our findings where Triple Negative tumors were more common than HER2-like tumors, which may be due to the relatively younger age of the study sample. However, the Triple Negative breast cancer presents 15% of total breast cases in this study which is consistent with other Moroccan studies (16.5% and 17.5%) as well as the global prevalence (10%–17%).[27]

In this study, invasive carcinoma of no special type was the most predominant histological type, which is consistent with the literature. Invasive lobular carcinoma was the second most common histological type in our study (5.5%) which is higher than the prevalence reported in South Africa (3.7%)[24] and in a Moroccan city, Fez (4.7%).[13] Our findings are supported by most studies which indicate that the two most prevalent histologic types of invasive breast cancer are ductal carcinoma followed by lobular carcinoma.[28-30] The presence or absence of ductal carcinoma in situ is an important factor that influences tumor recurrence and behavior. Therefore, future research should consider including data on the presence of ductal carcinoma in situ associated with invasive carcinomas to provide a more comprehensive understanding of tumor recurrence and behavior.

In this study, we found a high percentage of tumors with a histological grade SBR II (56.1%) followed by grade III (37.2%) which is similar to the findings in Fez, 56.7% and 39.4% for grade II and III respectively.[13] In the eastern region of the country, the highest histological grade reported was grade II (70.4%).[22]

Another alarming finding in this study is that only over half of patients had medical coverage. A recent evaluation of the patterns of care (POC) in breast cancer conducted by the IARC showed a staggering increase in the proportion of Moroccans patients insured, from 33.8% in 2012 to 90.2% 2017.[12] This remarkable leap is linked to the implementation and scale up of the state-funded insurance scheme Régime d'Assistance Médicale (RAMed).[12] Innovative health financing mechanisms are needed to mitigate incurring financial hardship, this is especially relevant in the case of breast cancer where follow-up is detrimental to preventing relapse and detecting recurrent tumors at an early stage. Additionally, it is estimated that 20% of the world population will be 65 or older by 2030. This trend combined with the technological advances in screening, treatment and diagnosis would result in increasing numbers of breast cancer patients, diagnosed at an early stage, thus, requiring long-term care.[31]

In the West, the majority of breast tumors are <2 cm, which may be explained with early detection and diagnosis.[23] However, in this study, the average tumor size was greater than or equal to 2 cm in 65.9% of cases. This is lower than compared to the numbers reported in studies in Fez, Eastern and Northern eastern Morocco, where the average size of breast cancer tumors was 3.6 cm ± 2.6, 3.5 ± 1.96 and 3.7 cm respectively.[13,22,32] Lymph-node positive tumors were observed in less than half of cases in this study, and only 13.4% of patients had distant metastasis. Eastern and North-Eastern Morocco, the frequency of lymph-node positive tumors was higher 64.8% and 29.3% with distant metastases,[22] 53% and 17.5% with distant metastases, respectively.[32] This may be linked to a delay in follow-up consultations during the progression of the disease as well as the lack of medical coverage, the scarcity of mammography screening programs and lack of awareness among women especially in rural areas.[22,32]

The IHC staining in our study revealed that 74.4% of the tumors were ER+, 58.5% were PR+ and 18.9% were HER2+. Similarly, the study in Fez' revealed that 72% of the tumors were hormone receptor positive (54.7% ER+, 66% PR+, 26% HER2+).[13] In Eastern Morocco, 64.2% of tumors were ER+ and 66.5% were PR+.[22] Hormone receptor status has important implications for the prognosis and management of breast cancer. In fact, hormone receptor-positive tumors generally have a favorable prognosis and are amenable to endocrine therapy.[13,22,32] Furthermore, molecular testing is particularly of high clinical importance in the case of Triple Negative subtype which is more aggressive and often has poor prognosis. In one Moroccan study at the National Institute of Oncology in Rabat, the overall survival rate of patients presenting with Triple Negative breast cancer was 76,5%[33] which consistent with the literature (78.5 % (95 % CI 73.8; 83.3).[34] This poor survival rate further makes the case for targeted interventions aimed at increasing early detection and improving therapeutic outcomes.

This study has some limitations. First, this is single-center study conducted in a special care unit and the potential confounding effects linked to the center cannot be excluded. Furthermore, the presence of comorbidities was not documented. In addition, interpretations and diagnoses were not done by the same pathologist which may introduce some variability. Third, we were not able to extend the study period as originally planned over a long period which did not allow us to have a very large sample. Lastly, some difficulties were encountered in completing certain variables due to the absence of data.

Conclusions

This study described the histological and immunohistochemical profile of breast cancer among the Moroccan patient population. Based on our findings, it would appear that breast tumors in Morocco are predominantly Luminal-like with differences between the four subtypes with regards to histological grade. Our findings must be used to guide breast cancer management policies in Morocco. Larger cohort studies are needed to determine the specificity of breast cancer profile in Morocco as well as the epidemiological risk factors specific to every subtype. This will help guide the development of targeted diagnosis and treatment practices, thereby improving clinical outcomes.

Acknowledgments

We would like to thank all personnel in the Department of Oncology and the Laboratory of Pathological Anatomy at Cheikh Khalifa University Hospital in Casablanca, Morocco.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Ethical Statement

Ethical Approval

Ethical approval for this study was obtained from the Ethics Committee of the Faculty of Medicine and Pharmacy in Tangier (Ref 10/2022). This study adhered to the ethical principles of the Helsinki Declaration in its design and implementation. All research procedures were conducted in accordance with the ethical guidelines outlined in the Helsinki Declaration.

Informed Consent

This study was conducted using retrospective data from patient records. Individual patient consent was not required for this type of research as it involved anonymized data.

ORCID iD

Bouaddi Oumnia https://orcid.org/0000-0001-9114-6889

Data Availability Statement

Data will be made available on request.

References

1. GLOBOCAN. Cancer data. Accessed June 5, 2022.https://gco.iarc.fr/today/home
2. The Global Cancer Observatory (GCO) 2022. International Agency for Research on Cancer, Lyon, France. Available at https://gco.iarc.fr/en
3. el kherchi O, Aquil A, el khoudri N, et al. Anxiety and depression comorbidities in Moroccan patients with breast cancer. *Front Psychiatr*. 2021;11:584907. doi:10.3389/FPSYT.2020.584907/PDF
4. Motiaa Y, Ghannam A. Chronic pain assessment and management during post-treatment follow up should be considered as a high value quality indicator for specialist breast cancer center. *Breast*. 2021;60:308. doi:10.1016/J.BREAST.2021.09.001
5. Schnitt SJ. Classification and prognosis of invasive breast cancer: from morphology to molecular taxonomy. *Mod Pathol*. 2010;23:S60-S64. doi:10.1038/modpathol.2010.33
6. Ihemelandu CU, Leffall LD, Dewitty RL, et al. Molecular breast cancer subtypes in premenopausal and postmenopausal african-American women: age-specific prevalence and survival. *J Surg Res*. 2007;143(1):109-118. doi:10.1016/j.jss.2007.03.085
7. Giuliano AE, Connolly JL, Edge SB, et al. Breast Cancer-Major changes in the American Joint Committee on Cancer eighth edition cancer staging manual. *CA Cancer J Clin*. 2017;67(4):290-303. doi:10.3322/caac.21393
8. Biswal A, Erler J, Qari O, et al. The effect of the new eighth edition breast cancer staging system on 100 consecutive patients. *J Clin Med Res*. 2019;11(6):407-414. doi:10.14740/jocmr3803
9. Amin MB, Edge SB, Greene FL, et al. American Joint committee on cancer (AJCC). In: *AJCC Cancer Staging Manual*. Philadelphia: Lippincott-Raven; 2017. https://link.springer.com/book/9783319406176. Accessed 5 June 2022.
10. Franchet C, Duprez-Paumier R, Lacroix-Triki M. Luminal breast cancer and the contribution of intrinsic molecular classifications: how to identify luminal A and B tumors in 2015? *Bull Cancer*. 2015;102(6):S34-S46. doi:10.1016/S0007-4551(15)31216-9
11. Wirapati P, Sotiriou C, Kunkel S, et al. Meta-analysis of gene expression profiles in breast cancer: toward a unified understanding of breast cancer subtyping and prognosis signatures. *Breast Cancer Res*. 2008;10(4):R65. doi:10.1186/bcr2124
12. Mrabti H, Sauvaget C, Benider A, et al. Patterns of care of breast cancer patients in Morocco - a study of variations in patient profile, tumour characteristics and standard of care over a decade. *Breast*. 2021;59:193-202. doi:10.1016/J.BREAST.2021.07.009
13. Abbass F, Bennis S, Znati K, et al. Epidemiological and biologic profile of breast cancer in Fez-Boulemane, Morocco. *East Mediterr Health J*. 2011;17(12):930-936. doi:10.26719/2011.17.12.930
14. Osborne CK, Yochmowitz MG, Knight WA, McGuire WL. The value of estrogen and progesterone receptors in the treatment of breast cancer. *Cancer*. 1980;46(12 S):2884-2888.
15. Clark GM, McGuire WL. Steroid receptors and other prognostic factors in primary breast cancer. *Semin Oncol*. 1988;15(-2 SUPPL. 1):20-25.
16. Ross JS, Gray GS. Targeted therapy for cancer: the HER-2/neu and Herceptin™ story. *Clin Leader Manag Rev*. 2003;17(6):499-505.
17. Cserni G. Histological type and typing of breast carcinomas and the WHO classification changes over time. *Pathologica*. 2020;112(1):25-41. doi:10.32074/1591-951X-1-20
18. Łukasiewicz S, Czeczelewski M, Forma A, Baj J, Sitarz R, Stanisławek A. Breast cancer—epidemiology, risk factors, classification, prognostic markers, and current treatment strategies—an updated review. *Cancers*. 2021;13(17):4287. doi:10.3390/CANCERS13174287
19. Basu P, Selmouni F, Belakhel L, et al. Breast cancer screening program in Morocco: status of implementation, organization and performance. *Int J Cancer*. 2018;143(12):3273-3280. doi:10.1002/IJC.31749
20. Zaha DC. Significance of immunohistochemistry in breast cancer. *World J Clin Oncol*. 2014;5(3):382-392. doi:10.5306/WJCO.V5.I3.382
21. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE)

statement: guidelines for reporting observational studies. *J Clin Epidemiol*. 2008;61(4):344-349. doi:10.1016/J.JCLINEPI.2007.11.008

22. Elidrissi Errahhali M, Elidrissi Errahhali M, Ouarzane M, el Harroudi T, Afqir S, Bellaoui M. First report on molecular breast cancer subtypes and their clinico-pathological characteristics in Eastern Morocco: series of 2260 cases. *BMC Wom Health*. 2017;17(1):3. doi:10.1186/s12905-016-0361-z
23. Blamey RW, Hornmark-Stenstam B, Ball G, et al. Oncopool - a European database for 16,944 cases of breast cancer. *Eur J Cancer*. 2010;46(1):56-71. doi:10.1016/j.ejca.2009.09.009
24. Kakudji BK, Mwila PK, Burger JR, du Plessis JM. Epidemiological, clinical and diagnostic profile of breast cancer patients treated at Potchefstroom regional hospital, South Africa, 2012-2018: an open-cohort study. *Pan Afr Med J*. 2020;36:9. doi:10.11604/pamj.2020.36.9.21180
25. Maseb'A Mwang Sulu S, Batalansi DB, Sulu AMS, et al. Immunohistochemical features of breast cancer seen in women in kinshasa, democratic republic of the Congo: a six-year retrospective study. *Int J Breast Cancer*. 2022;2022:8860947. doi:10.1155/2022/8860947
26. Perou CM, Sørlie T, Eisen MB, et al. Molecular portraits of human breast tumours. *Nature*. 2000;406(6797):747-752. doi:10.1038/35021093
27. Slaoui M, Razine R, Ibrahimi A, Attaleb M, Mzibri ME, Amrani M. Breast cancer in Morocco: a literature review. *Asian Pac J Cancer Prev APJCP*. 2014;15(3):1067-1074. doi:10.7314/APJCP.2014.15.3.1067
28. Sharma GN, Dave R, Sanadya J, Sharma P, Sharma KK. Various types and management of breast cancer: an overview. *J Adv Pharm Technol Res*. 2010;1(2):109-126.
29. Weigelt B, Geyer FC, Reis-Filho JS. Histological types of breast cancer: how special are they? *Mol Oncol*. 2010;4(3):192-208. doi:10.1016/j.molonc.2010.04.004
30. Cosar R, Sut N, Topaloglu S, et al. Classifying invasive lobular carcinoma as special type breast cancer may be reducing its treatment success: a comparison of survival among invasive lobular carcinoma, invasive ductal carcinoma, and no-lobular special type breast cancer. *PLoS One*. 2023;18(7):e0283445. doi:10.1371/JOURNAL.PONE.0283445
31. McGuire A, Brown JAL, Malone C, McLaughlin R, Kerin MJ. Effects of age on the detection and management of breast cancer. *Cancers*. 2015;7(2):908-929. doi:10.3390/CANCERS7020815
32. Bennis S, Abbass F, Akasbi Y, et al. Prevalence of molecular subtypes and prognosis of invasive breast cancer in north-east of Morocco: retrospective study. *BMC Res Notes*. 2012;5:436. doi:10.1186/1756-0500-5-436
33. Rais G, Raissouni S, Aitelhaj M, et al. Triple negative breast cancer in Moroccan women: clinicopathological and therapeutic study at the National Institute of Oncology. *BMC Wom Health*. 2012;12:35. doi:10.1186/1472-6874-12-35
34. Hennigs A, Riedel F, Gondos A, et al. Prognosis of breast cancer molecular subtypes in routine clinical care: a large prospective cohort study. *BMC Cancer*. 2016;16(1):734. doi:10.1186/S12885-016-2766-3