

Molecular Subtypes among Patients with Breast Cancer

Lucy Navsaria, MBBCh BAO* Fatema Adel Ali, MBBCh BAO*
Rohit Goswamy, MBBCh BAO* Ghufuran Jassim, MD**
Zainab Abdul Razzak Ebrahim, MD***

Objective: To evaluate the estrogen receptor (ER), progesterone receptor (PR) and HER-2 receptor expression in breast cancer patients.

Design: A Retrospective Study.

Setting: Oncology Department, King Hamad University Hospital, Bahrain.

Method: All women with a confirmed diagnosis of breast cancer via biopsy from 2010 to 2016 were reviewed. The following were documented: age, type, and stage of cancer.

Result: Eighty-nine patients were included in the study. A total of one hundred and two patients were diagnosed with breast cancer based on biopsy results; thirteen patients were excluded due to the unknown stage and/or grade. The mean age was 53.9 years. The majority of cases were infiltrating ductal carcinoma (IDC), 82 (92%). The most common molecular subtype detected in the study was Luminal B (ER+, PR+, HER2+), 29 (32.6%) of the study population. Nine (10%) had an unknown grade, and 8 (8.9%) had unknown stage were excluded from the analysis.

Conclusion: Many patients were lost to follow-up. More effort is needed to reduce the proportion of unknown stages and grades of breast cancer cases. Further research is advised to evaluate the prognosis of breast cancer patients in Bahrain due to the high incidence in the Gulf Cooperation Council (GCC).

Bahrain Med Bull 2018; 40(1): 35 - 37

Breast cancer is the most common cancer among women worldwide with an estimated 1.67 million new cancer cases diagnosed in 2012¹. It is the most prevalent type of cancer and the leading cause of death among women in Bahrain². Bahrain has the highest incidence of breast cancer in the GCC countries³.

While breast cancer is considered the most common cancer in females in all Gulf countries, data reveals that Bahrain has the highest incidence, as well as the highest age-standardized incidence (ASR) compared to other Gulf counties with a value of 46.8 per 100,000 cases⁴.

The most common type of breast cancer found among Bahraini women is infiltrating ductal carcinoma, which is similar to that reported in all GCC countries³. That, compared to the five-year survival rates of other countries, found Bahrain to lie midway between the lowest rate (45%) among developing countries and the highest rate (89%) among developed countries³.

The quality of life of Bahraini women is diminished as a result of breast cancer; therefore, further research in the area is an urgent need^{5,6}.

Breast cancer pathological and clinical heterogeneity and presentations make predicting the prognosis of breast cancer a challenge. Several advances have been made to predict the prognosis of the different subtypes of breast cancer. The analysis of hormonal receptor status has been widely used to evaluate the prognosis and individualize the treatment for breast cancer patients.

Hormonal receptors are protein molecules attached to cells. Breast cells contain different types of hormonal receptors including estrogen (ER), progesterone (PR) and human epidermal growth factor receptor 2 (HER-2). They are found in normal and breast cancer cells. These receptors support the growth of the breast cancer cells. Breast cancers that express estrogen, progesterone or HER2 receptors are referred to as estrogen receptor positive (ER+), progesterone receptor positive (PR+) and HER2+ respectively⁷.

There are four molecular subtypes of breast cancer: Luminal A, Luminal B, HER-2 enriched, triple negative. These subtypes are based on the genes expressed by the cancer cells. Luminal A breast cancers are ER+, PR+, HER2-. These cancers tend to be low grade and usually have the best prognosis. Luminal B

* Medical Student
** Senior Lecturer in Family Medicine
Royal College of Surgeons in Ireland – Medical University Bahrain
*** Consultant Oncologist
Oncology Center
King Hamad University Hospital
The Kingdom of Bahrain
E-mail: zeinab.alhaddad@khuh.org.bh

breast cancers known as triple positive, are ER+, PR+, HER2+ and have a slightly worse prognosis than Luminal A. HER2 enriched breast cancers are ER-, PR-, HER2+. These grow faster and have a poorer prognosis than Luminal cancers, but are often successfully treated with therapies targeted at the HER2 protein. Triple Negative (basal-like) breast cancers are ER-, PR-, HER2; this subtype is frequently seen in younger age groups and often associated with BRCA1 gene. Pathology, stages, grades, and metastasis were then determined for each subtype.

The TNM staging system follows the American Joint Committee on Cancer (AJCC) depending on the tumor size, number of lymph nodes involvement and presence or absence of metastatic disease⁸. Tumors can be classified into three grades: well-differentiated (Grade I), moderately differentiated (Grade II) and poorly differentiated (Grade III)⁹.

The aim of this study is to evaluate the estrogen receptor, progesterone receptor and HER-2 receptor expression in breast cancer patients.

METHOD

Eighty-nine women diagnosed with breast cancer from 2010 to 2016 were reviewed. All cases underwent immunohistochemistry testing to determine hormonal receptor status. In addition, relevant pathological and clinical variables were included: grade, stage, family history and metastasis. ER and PR positivity were determined in the laboratory by a staining intensity score of greater than or equal to 3.

Data collection was achieved by convenience sampling with medical record review. Electronic patient records (I-SEHA, HOPE) were used to collect histopathology reports.

SPSS (IBM version 22) was used to analyze the data. SPSS was used to analyze the most common molecular subtype of breast cancer amongst patients.

RESULT

Eighty-nine patients diagnosed with breast cancer from 2010 to 2016 were included in this study. Thirteen were excluded due to the unknown stage and/or grade. The mean age was 53.9 years. Twenty-nine (32.6%) had luminal B molecular subtype. Eighty-two (92%) were infiltrating ductal carcinoma; both breasts were equally affected. In this study, 15 (16.9%) cases were found to be positive for metastatic disease; 2 (2.2%) did not fit into any of the subtypes. Ten (11%) patients had bone metastasis. Metastasis was common in Luminal A subtype.

Twenty-nine patients (32.6%) had luminal B subtype cancer. Twenty-one (23.6%) patients had infiltrative ductal carcinoma (IDC), equally distributed between left and right breasts. Forty-nine (55%) patients had grade II (moderately differentiated). Twelve (13.5%) patients had T1N1M0 and T1N0M0, six each. Four (4.5%) had metastatic disease in luminal B.

Twenty-two (24.7%) patients had luminal A subtype breast cancer. Eight (8.9%) patients had right breast IDC. Forty-nine (55%) patients had grade II and four (4.5%) patients had

T1N0M0. Metastatic disease was present in 5 (5.6%) patients of this subgroup.

Sixteen (18%) patients had triple negative breast cancer; seven (7.9%) patients had left breast IDC. In this group, 8 (8.9%) patients had grade III and five (5.6%) patients had T2N0M0. Metastatic disease was seen in 2 (2.2%) patients of this subgroup.

Twelve (13.5%) patients had HER-2 enriched. Seven (7.9%) patients had left breast IDC. Forty-nine (55%) patients had grade II and four (4.5%) patients had T2N0M0. Metastatic disease was found in 2 (2.2%) patients of this group.

Table 1 (A): Clinical Data

Grade	Total No. (89)
I	9 (10%)
II	49 (55%)
III	28 (31.5%)
IV	3 (3.4%)
TOTAL	89 (100%)

Table 1 (B): Clinical Data

	Total No. (89)	Percentage (%)
ER, PR		
neg	29	32.6%
pos	60	67.4%
TOTAL	89	100%
HER-2		
neg	40	44.9%
pos	49	55.1%
TOTAL	89	100%
Molecular Subtype		
Luminal B (ER, PR, HER-2 +)	29	32.6%
Triple Negative (ER, PR, HER-2 -)	16	18%
Luminal A (ER+, PR+, HER-2 -)	22	24.7%
HER2 Enriched (ER-, PR-, HER-2 +)	12	13.4%
Other Subtype (ER+, PR-, HER2+)	10	11.2%
TOTAL	89	100%

DISCUSSION

In this study of hormonal status amongst breast cancer patients in KHUH, we demonstrate that 32.6% of cases were Luminal B - (ER+, PR+, HER2+). However, worldwide Luminal A is found to be most commonly detected¹⁰. In addition, the most common breast cancer type was found to be IDC 92%. This data is comparable to prior observations published by Sultan Taboos University in 2015 which stated IDC to be most common subtype amongst Bahraini and GCC females³. Further analysis is needed to evaluate the approach to screening,

diagnosis, and management of breast cancer patients in KHUH and Bahrain in order to implement a more organized approach to breast cancer care. In our study, 12.7% patients were found to have an unknown grade or stage and were thus not included in our dataset. This is in comparison to prior data, which also found significant proportions of unknown stages and grade³. Further research is needed to evaluate why patients are being lost due to unknown stage or grade, and significant effort is needed in order to reduce this.

CONCLUSION

The results of this study are applicable largely to the women in Bahrain and the GCC. The number of patients lost to follow up decreases the validity of said results. A more systematic approach to the screening, diagnosis, and management of breast cancer needs to be adopted in Bahrain. An organized system for the collection and categorization of breast cancer cases in Bahrain will standardize what is currently a relatively disorganized system. That would pave the way to future research and advancing the management of breast cancer in Bahrain and the GCC.

Author Contribution: All authors share equal effort contribution towards (1) substantial contributions to conception and design, acquisition, analysis and interpretation of data; (2) drafting the article and revising it critically for important intellectual content; and (3) final approval of the manuscript version to be published. Yes.

Potential Conflicts of Interest: None.

Competing Interest: None.

Sponsorship: None.

Acceptance Date: 7 February 2018.

Ethical Approval: Approved by the Research and Ethics Committee, King Hamad University Hospital, Bahrain.

REFERENCES

1. Ferlay J, Soerjomataram I, Dikshit R, et al. Cancer Incidence and Mortality Worldwide: Sources, Methods and Major Patterns in GLOBOCAN 2012. *Int J Cancer* 2015; 136(5): E359-86.
2. Al-Madouj A, Eldali A, Al-Zahrani A, et al. Ten-Year Cancer Incidence among Nationals of the GCC States 1998–2007. Saudi Arabia: Gulf Center for Cancer Control and Prevention, 2011; 16-9.
3. Hamadeh RR, Abulfatih NM, Fekri MA, et al. Epidemiology of Breast Cancer among Bahraini Women. *Sultan Qaboos Univ Med J* 2014; 14(2): e176–e182.
4. Alsayyad J, Hamadeh R. Cancer Incidence among the Bahraini Population: A Five-Year (1998-2002) Experience. *Hematology/Oncology and Stem Cell Therapy* 2008; 1(3):175-82.
5. AlZaman AS, Mughal SA, AlZaman YS, et al. Correlation between Hormone Receptor Status and Age, and Its Prognostic Implications in Breast Cancer Patients in Bahrain. *Saudi Med J* 2016; 37(1): 37–42.
6. Jassim GA, Whitford DL. Understanding the Experiences and Quality of Life Issues of Bahraini Women with Breast Cancer. *Soc Sci Med* 2014; 107:189-95.
7. Smith RA, Cokkinides V, von Eschenbach AC, et al. American Cancer Society Guidelines for the Early Detection of Cancer. *CA Cancer J Clin* 2002; 52(1):8-22.
8. AJCC Cancer Staging System. American Joint Committee on Cancer. <https://cancerstaging.org/Pages/default.aspx>. Accessed in February 2018.
9. Breast Cancer Care. Cancer Size and Grade. <https://www.breastcancercare.org.uk/information-support/facing-breast-cancer/ Diagnosed-breast-cancer/diagnosis/cancer-size-grade>. Accessed in February 2018.
10. American Cancer Society. Breast Cancer Facts & Figures 2015-2016. Atlanta: American Cancer Society, Inc, 2015.