Outcomes and Clinicolopathological Features of Breast Cancer in HBOC

Mussadique Ali Jhattial[1], Manzoor Khan[2],Syed Shahmeer Raza[3*], Umair Ahmad[4], Naila Sheikh[5], Haris Manan[6], Dur E Shehwar Ali[7]

[1, 2, 4] Clinical Fellow-Dept. of Medical Oncology, Shaukat Khanum Memorial Cancer Hospital and Research Center, Lahore.

[3*] **Syed Shahmeer Raza (Corresponding Author), MBBS, M. Phil**
EMAIL: shamir.raza@gmail.com
Phone Number: 03059006082
Lecturer, Department of Physiology, Khyber Medical College/Teaching Hospital, Peshawar, Pakistan.

[5] Consultant-Dept. of Nuclear Medicine, Anmol Hospital, Lahore.

[6] Khyber Medical College/Teaching Hospital, Peshawar, Pakistan.

[7] Assistant Professor, Department of Physiology, Khyber College of Dentistry, Peshawar, Pakistan.

ABSTRACT

Background: Breast cancer is one of the leading causse of mortality and morbidity in women.Recent studies have unearthed an interesting correlation between these two types of cancers particularly with regards to genetic alterations. Hereditary breast and ovarian cancer syndrome (HBOC) is caused by pathogenic variants in BRCA and other cancer related genes.

Objectives: To evaluate the outcomes and clinicopathological features of breast cancer in HBOC.

Methodology: This Retrospective Cohort study was performed in the Department of Medical Oncology at SKMCH&RC, Lahore, Pakistan from January 1st 2020 to 31st December 2020. Forty-Two patients diagnosed with HBOC were included from the hospital medical records after analyzing hospital records for the last 25 years.Twenty-FivePatient's out of these were 1st primary breast cancer. All information was recorded using proforma and analysed on IBM SPSS for MacBook, Version 26.0.

Results: Upon diagnosis of ovarian cancer, the most common tumor types (tumor histopathology) was found to be: Invasive Ductal Carcinoma (in 25 patients with 1st primary breast cancer in those with HBOC). Whereas diagnosis of breast cancer followed by ovarian cancer, the most common tumor types (tumor histopathology) were found to be: Invasive Ductal Carcinoma (in 15 patients with 2nd primary breast cancer in those with HBOC). This was followed by Invasive Lobular Carcinoma (2 patients with 2nd primary breast cancer in those with HBOC). 10 out of the 17 were Premenopausal and the rest 15 were postmenopausal.

Conclusion: Treating HBOC is a physician's dilemma. Although further functional analyses are necessary to better characterize the contribution of those variants to the genetic mutations, these

findings would improve the risk estimation and clinical follow-up of patients with HBOC clinical suspicion. Timely diagnosis and histopathology of the tumour type is of utmost importance in any cancer particularly in treatment of Breast cancer.

Key Words: ECOG Performance Score; Invasive Ductal Carcinoma; Invasive Lobular Carcinoma; Histopathology

INTRODUCTION

Breast cancer is the most common cancer in women. According to the World Health Organization (WHO), the number of new cases of breast cancer in 2018 exceeded 2 millionaccounting for 11.6% of all new cases of cancer in both men and women. Studies on hereditary breast and ovarian cancer (HBOC) involve not only determining the predisposition to developing cancer, but also considering the current treatment for breast cancer, prevention of next cancer, risk diagnosis, and adoption of protective measures for relatives. [1]

BRCA1/2 is the most frequent cause of high penetrance among HBOCs and affects all ethnic groups and races. The frequency of BRCA1/2 pathogenic variants in the general population, excluding Ashkenazi Jews, has been estimated to be one in 400–500.[2,3] Among all patients with breast cancer the BRCA1/2 mutation retention rate was 4.2–6.1%. [4,5,6,7,8]

We carried out thisretrospective study to evaluate the outcomes and clinicopathological features of breast cancer in HBOC.

METHODOLOGY

This Retrospective Cohort study was performed in the Department of Medical Oncology at SKMCH&RC, Lahore, Pakistan from January 1st 2020 to 31st December 2020. Forty-Two patients diagnosed with HBOC were included from the hospital medical records after analyzing hospital records for the last 25 years.

Twenty-Five Patient's out of these were 1st primary breast cancer.Patient's ECOG Performance Status, Menopausal Status, type of Breast tumor on 1st Primary and 2nd Primary tumor were studied and analyzed.

All information was recorded using proforma and analysed on SPSS software (version 26.0; SPSS, Chicago, IL, USA). Data was presented as Tables.Medical Record were searched and 42 patients with both primary breast cancer and primary ovarian cancer were included. Out of these, 25 patients with Ovarian cancer following Breast cancer were selected.

RESULTS

Upon diagnosis of breast cancer (1st primary breast cancer in those with HBOC), 10 out of the 17 were Premenopausal and the rest 15 were postmenopausal.

Table. 1

Initial Diagnosis (Breast Cancer) N=25	
Premenopausal	**Postmenopausal**
10	15

Table. 1 showing pre-menopausal and post-menopausal status of patients with 1st primary breast cancer in those with HBOC

Upon diagnosis of ovarian cancer, the most common tumor types (tumor histopathology) was found to be: Invasive Ductal Carcinoma (in 25 patients with 1st primary breast cancer in those with HBOC). **Table. 2**

Initial Diagnosis (Breast Cancer) N=25	
IDC	**Invasive Lobular**
25	0

Table. 2 showing Histopathology of Ca Breast (1st Primary Breast Ca)

Upon diagnosis of breast cancer followed by ovarian cancer, the most common tumor types (tumor histopathology) were found to be: Invasive Ductal Carcinoma (in 15 patients with 2nd primary breast cancer in those with HBOC). This was followed by Invasive Lobular Carcinoma (2 patients with 2nd primary breast cancer in those with HBOC). **Table. 3**

Initial Diagnosis (Ovarian Cancer) N=17	
IDC	**Invasive Lobular**
15	2

Table. 3 showing Histopathology of Ca Breast (2nd Primary Breast Ca)

Eastern Cooperative Oncology Group (ECOG) Performance Status of the patients is an estimate of measuring how the disease impacts a patient's daily living abilities (known to physicians and researchers as a patient's performance status). It describes a patient's level of functioning in terms of their ability to care for themself, daily activity, and physical ability (walking, working, etc.).[9]Most of the patients (16) had a score of 1-2 (able to perform daily activities) with an ECOG score of 5 (Dead) in 7 patients.

Initial Diagnosis (Breast Cancer) N=25	
Score 1	8
Score 2	8
Score 3	1
Score 4	1
Score 5	7

Table. 4 showing ECOG Performance status of patients with 1st Primary Breast Cancer

DISCUSSION

This is important to mention that not much scientific evidence or literature exists in the databases which had evaluated the Histopathological features of patients with ovarian cancer as a subset of HBOC. In this we carried out a retrospective study to evaluate the clinicopathological profile of ovarian cancer in HBOC.

The type of Breast cancer and it being 1st or 2nd primary has an important role in the management. In our study when the diagnosis is breast cancer the most common tumor types (tumor histopathology) was found to be: Invasive Ductal Carcinoma (in 25 patients with 1st primary breast cancer in those with HBOC). When the diagnosis is ovarian cancer, the most common tumor types (tumor histopathology) were found to be: Invasive Ductal Carcinoma (in 15 patients with 2nd primary breast cancer in those with HBOC). This was followed by Invasive Lobular Carcinoma (2 patients with 2nd primary breast cancer in those with HBOC).

Morphologically, BRCA1-associated breast carcinomas are most commonly a high-grade invasive ductal carcinoma of no special type. [9,10] In contrast to *BRCA1*-associated breast cancers, *BRCA2*-associated tumors are very similar to sporadically-occurring "luminal-type" tumors. [11]

For risk reduction, bilateral mastectomy is recommended for all BRCA1/2 mutation carriers.[12]From a pathological perspective, BRCA1 and BRCA2-associated breast tumours have been shown to differ on both morphological and molecular levels. Furthermore, BRCA1-associated tumours tend to be more difficult to visualize on mammographic studies compared to BRCA2-associated tumours which more commonly present with microcalcifications and/or isolated ductal carcinoma in situ. [13]

CONCLUSION

Treating HBOC is a physician's dilemma. Although further functional analyses are necessary to better characterize the contribution of those variants to the genetic mutations, these findings would improve the risk estimation and clinical follow-up of patients with HBOC clinical suspicion. Timely diagnosis and histopathology of the tumour type is of utmost importance in any cancer particularly in treatment of Breast cancer.

REFERENCES

1. Global Cancer Observatory. International Agency for Research on Cancer; WHO. https://gco.iarc.fr/

2. Anglian Breast Cancer Study Group. Prevalence and penetrance of BRCA1 and BRCA2 mutations in a population-based series ofbreast cancer cases. Br J Cancer. 2000;83:1301–8.

3. Whittemore AS, Gong G, John EM, McGuire V, Li FP, Ostrow KL, et al. Prevalence of BRCA1 mutation carriers among U.S. non-Hispanic Whites. Cancer Epidemiol Biomarkers Prev. 2004;13:2078–83.

4. King MC, Marks JH, Mandell JB, New York Breast Cancer Study Group. Breast and ovarian cancer risks due to inherited mutations in BRCA1 and BRCA2. Science. 2003;302:643–6.

5. Momozawa Y, Iwasaki Y, Parsons MT, Kamatani Y, Takahashi A, Tamura C, et al. Germline pathogenic variants of 11 breast cancer genes in 7,051 Japanese patients and 11,241 controls. Nat Commun. 2018;9:4083.

6. Sun J, Meng H, Yao L, Lv M, Bai J, Zhang J, et al. Germline mutations in cancer susceptibility genes in a large series of unselected breast cancer patients. Clin Cancer Res. 2017;23:6113–9.

7. Wen WX, Allen J, Lai KN, Mariapun S, Hasan SN, Ng PS, et al. Inherited mutations in BRCA1 and BRCA2 in an unselected multiethnic cohort of Asian patients with breast cancer and healthy controls from Malaysia. J Med Genet. 2018;55:97–103.

8. Karnofsky D, Burchenal J, The clinical evaluation of chemotherapeutic agents in cancer. In: MacLeod C, ed. Evaluation of Chemotherapeutic Agents. New York, NY: Columbia University Press; 1949:191–205.

9. Pedersen L, Holck S, Mouridsen HT, Schødt T, Zedeler K. Prognostic comparison of three classifications for medullary carcinoma of the breast. Histopathology. (1999) 34:175–8.

10. Ridolfi RL, Rosen PP, Port A, Kinne D, Miké V. Medullary carcinoma of the breast: a clinicopathologic study with 10 year follow-up. Cancer. (1977) 40:1365–85

11. Perou CM, Sørlie T, Eisen MB, van de Rijn M, Jeffrey SS, Rees CA, et al. Molecular portraits of human breast tumours. Nature. (2000) 406:747–52

12. NCCN Guidelines. National Comprehensive Cancer Network Web Site. (2020)

13. Krammer J, Pinker-Domenig K, Robson ME, Gonen M, Bernard-Davila B, Morris EA, et al. Breast cancer detection and tumor characteristics in BRCA1 and BRCA2 mutation carriers. Breast Cancer Res Treat. (2017) 163:565–71. 10.1007/s10549-017-4198-4