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Evaluation of Clinicolopathological Profile of Ovarian Cancer in HBOC

Manzoor Khan[1], Umair Ahmad[2], Syed Shahmeer Raza[3*], Mussadique Ali Jhattial[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: Ovarian cancer is a major cause of mortality and morbidity in women.A correlation between breast and ovarian cancer has been documented in recent studies particularly with regards to genetic alterations. This correlation is referred to as Hereditary breast and ovarian cancer syndrome (HBOC).

Objectives: To evaluate the clinicopathological profile of ovarian 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.Seventeen Patient's out of these were 1st primary ovarian 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) were found to be: Papillary Cystadenocarcinoma (5 patients with 1st primary ovarian cancer in those with HBOC). This was followed by Papillary Carcinoma (3 patients with 1st primary ovarian cancer in those with HBOC). Whereas diagnosis of ovarian cancer followed by breast cancer, the most common tumor types (tumor histopathology) were found to be: Serous Carcinoma (8 patients with 2nd primary ovarian cancer in those with HBOC). This was followed by Papillary Carcinoma and Poorly Differentiated Ovarian Carcinoma (4 patients each with 2nd primary ovarian cancer in those with HBOC). 5 out of the 17 were Premenopausal and the rest 12 were postmenopausal.

Conclusion: Timely diagnosis and histopathology of the tumour type is of utmost importance in any cancer particularly in treatment of Ovarian cancer, especially when the sword of HBOC hangs on the

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physician's mind. HBOC diagnosis on time could prevent 2nd primary tumour and thereby decrease mortality and morbidity.

Key Words: Hereditary Breast and Ovarian Cancer Syndrome; Premenopausal; Papillary Carcinoma; Cystadenocarcinoma

INTRODUCTION

Hereditary breast and ovarian cancer (HBOC) syndrome is characterized by an autosomal-dominant inheritance pattern with increased risk of early-onset breast cancer (BC) and ovarian cancer (OC) in multiple family members.[1,2] HBOC syndrome is associated with 50% to 85% lifetime risk of BC and 15% to 30% risk of OC in women.[3,4]

Mutations in BRCA1 and BRCA2 are commonly implicated in HBOC.[5]The prevalence of germline mutations; their relative frequencies in high, moderate, and low-penetrance genes; and their founder status all vary with geography and ethnicity. Pathogenic genetic mutation is estimated to occur in 10% to 15% of all patients with BC, with BRCA1 and BRCA2 accounting for 40% to 50% of pathogenic/likely pathogenic mutations.[6,7]

Leveraging the recent developments in the management of HBOC, more than 32 international guidelines published between 2010 and 2018 provide recommendations for genetic counselling and screening, preventive or risk reduction approaches, and systemic management of BRCA-mutated BC and OC, but all these guidelines cater to issues of Western patients.[8]We carried out a retrospective study to evaluate the clinicopathological profile of ovarian 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.

Seventeen Patient's out of these were 1st primary ovarian cancer. Patient's Menopausal Status, ECOG Performance Status, type of Ovarian 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, 17 patients with breast cancer following Ovarian cancer were selected.

RESULTS

Upon diagnosis of ovarian cancer (1st primary ovarian cancer in those with HBOC), 5 out of the 17 were Premenopausal and the rest 12 were postmenopausal. **Table. 1**

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Initial Diagnosis (Ovarian Cancer) N=17	
Premenopausal	**Postmenopausal**
5	12

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

Upon diagnosis of ovarian cancer, the most common tumor types (tumor histopathology) were found to be: Papillary Cystadenocarcinoma (5 patients with 1st primary ovarian cancer in those with HBOC). This was followed by Papillary Carcinoma (3 patients with 1st primary ovarian cancer in those with HBOC). **Table. 2**

Initial Diagnosis (Ovarian Cancer) N=17	
Adenocarcinoma	1
SerousCarcinoma	2
Poorly Differentiated Endometroid Carcinoma	2
Papillary Cystadenocarcinoma	5
Papillary Carcinoma	3
Differentiated Serous Papillary Carcinoma	
Clear Cell Carcinoma	2
Granulosa Cell Tumor	2

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

Upon diagnosis of ovarian cancer followed by breast cancer, the most common tumor types (tumor histopathology) were found to be: Serous Carcinoma (8 patients with 2nd primary ovarian cancer in those with HBOC). This was followed by Papillary Carcinoma and Poorly Differentiated Ovarian Carcinoma (4 patients each with 2nd primary ovarian cancer in those with HBOC). **Table. 3**

Initial Diagnosis (Breast Cancer) N=25	
Adenocarcinoma	2
Endometroid	2
Serous Carcinoma	8
Poorly Differentiated Ovarian Carcinoma	4
Papillary Cystadenocarcinoma	3
Papillary Carcinoma	4

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Differentiated Serous Papillary Carcinoma	2

Table. 3 showing Histopathology of Ovarian Ca (2nd Primary Ovarian 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 (11) had a score of 1-2 (able to perform daily activities) with an ECOG score of 5 (Dead) in 4 patients.

Initial Diagnosis (Ovarian Cancer) N=17	
Score 1	6
Score 2	5
Score 3	1
Score 4	1
Score 5	4

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

HBOC syndrome is the inherited tendency to develop breast, ovarian and other cancers and believed to be transmitted by mutations in the specific genes. Clinical characteristics, including the type of tumour and age at occurrence as well as family history, predict the prevalence of BRCA germline mutations. We have identified the types of tumours in both 1st primary and 2nd primary ovarian cancer.

A number of clinicians usually take into account the age of the youngest breast cancer patient and the number of ovarian cancer cases in a family as well as pathological diagnosis. Up to 80% of the HBOC cases are due to mutations in BRCA1 or BRCA2 genes. Both BRCA1 and BRCA2 mutations are scattered throughout the whole coding exons.[10]

The hallmark histopathologic diagnosis of HBOC-related tubo-ovarian cancer due to BRCA mutations is that of high-grade serous carcinoma and the frequency of BRCA1 and BRCA2 germline mutations increases to approximately 25% in patients diagnosed with these neoplasms. [11,12,13,14,15,16] In addition to high-grade serous carcinoma, other ovarian tumor histotypes including those with endometrioid, mucinous and clear cell differentiationhave also been described to varying degrees in BRCA-associated cohorts.

In our study when the 1st Primary tumor is ovarian cancer, the most common tumor types (tumor histopathology) were found to be: Papillary Cystadenocarcinoma (5 patients with 1st primary ovarian cancer in those with HBOC). This was followed by Papillary Carcinoma (3 patients with 1st primary ovarian cancer in those with HBOC). However when Ovarian cancer is the 2nd primary tumor, the most common tumor types (tumor histopathology) were found to be: Serous Carcinoma (8 patients with 2nd primary ovarian cancer in those with HBOC). This was followed by Papillary Carcinoma and Poorly Differentiated Ovarian Carcinoma (4 patients each with 2nd primary ovarian cancer in those with HBOC).

CONCLUSION

Timely diagnosis and histopathology of the tumour type is of utmost importance in any cancer particularly in treatment of Ovarian cancer, especially when the sword of HBOC hangs on the physician's mind. HBOC diagnosis on time could prevent 2nd primary tumour and thereby decrease mortality and morbidity.

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