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ORIGINAL ARTICLE

Outcomes of Hereditary Breast-Ovarian Cancer Syndrome: A single center experience

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ABSTRACT

Aim: To assess the survival and progression patterns of Hereditary Breast and Ovarian Cancer (HBOC) at our hospital.
Methods: We did retrospective cohort study of thirty patients presenting with hereditary breast ovarian and cancer diagnosed and treated at Shaukat Khanum Memorial Cancer Hospital and Research Center (SKMCH&RC), Lahore, Pakistan from 1994 to 2012. Patient's demographics, clinical and histopathology data was obtained from cancer registry department of SKMCH&RC hospital. Chi-square test and independent sample T-test were used to analyze the data to find the association between variables i.e. age, comorbidities, BMI and progression free survival.
Result: All patients except two received chemotherapy and surgery as per guidelines. Of the thirty patients, thirteen patients had shown progression free survival (PFS) out of which one patient died whereas progression of disease was observed in seventeen patients of HBOC out of which six patients were expired. Comorbidities and family history of cancer did not show statistically significant results for the mortality ($P > 0.05$). Metastasis and presence of ascites indicated statistically significant influence on PFS having P value < 0.05. CA-125 at presentation, chemotherapy usage and adjuvant therapy did not show significant impact on PFS ($P > 0.05$).
Conclusion: Seven cases of diagnosed HBOC died. We identified that there were 43.33% cases of diagnosed HOBC who met progression free survival and rest developed the progression. Metastasis and presence of ascites showed significant impact for the progression of disease.
Keywords: Progression free survival (PFS), BRCA mutation; Hereditary Breast and Ovarian cancer (HBOC).

INTRODUCTION

Majority of women with breast or ovarian malignancy have sporadic disease[1]. HBOC is a clinical syndrome leading to an increased predisposition to breast and/or ovarian cancer. The proportion of HBOC is 10-15% of total cancer cases, principally secondary to germline mutations in high penetrance BRCA1 and BRCA2 genes[2].

Out of the patients who develop breast cancer, about 5 to 10% of breast cancer and 13–15% of ovarian cancer patients are hereditary and nearly 25% are linked to HBOC syndrome, due to aberrations in the BRCA1 and BRCA2 (DNA repair genes).
A recent prevalence study conducted in Pakistan revealed that one out of every four patients of hereditary breast-ovarian cancer, one out of every five patients of male breast cancer, and one out of every eight patients of early onset breast cancer are secondary to BRCA1 and BRCA2 mutations[3]. The survival of breast cancer is not dependent on BRCA gene mutations, whereas survival of ovarian cancer seems to be better for BRCA carriers as compared to those who are not[4].

There is scarce literature on survival of HBOC with one study quoting more severe breast and ovarian cancer phenotypes and a worse overall prognosis when compared to women with sporadic tumors.

The objectives of our study were to look in to clinical characteristics of disease and their impact on outcomes.

MATERIALS AND METHODS

After approval from Institutional Ethical Review committee, the current research was conducted in SKMCH&RC. All patients who presented with hereditary breast and ovarian cancer from 1994 to 2012 were included. Thirty patients diagnosed with hereditary breast ovarian cancer were analyzed. Patient's baseline characteristics including age, comorbidities and BMI were recorded. None of the patient underwent BRCA1/2 gene test due to limited resources. Details of therapy including surgical procedure was obtained.

Statistical Analysis: For statistical analysis SPSS was used. Chi square test or Fisher's exact test (when necessary) were used for categorical variable. Statistical significance was defined as a two-tailed p-value 0.05. Approval for study was taken from our Institutional Review Board (IRB).

RESULTS

The demographic and clinical characteristics of patients having hereditary breast ovarian cancer patients were presented in Table. 1. The mean age at diagnosis of breast cancer was 48.40 years while the mean age at diagnosis of ovarian cancer was 47.80 years. The mean BMI of all female patients was 28.31 kg/m². Twenty percent patients had multiple comorbidities, 27% had one comorbidity and 53% had none. Twenty-seven percent patients had family history of cancer. None of the demographic factors posed a significant impact on overall survival of patients with hereditary breast and ovarian cancer as evident of the p values shown in Table 1.

Table 2. presents the statistical relationship between the clinical characteristics and outcomes. Mean duration between both the diseases was 6.93 years. By using independent t-test, mean duration between diagnosis of breast cancer and ovarian cancer was 6.93 years with no statistically significant effect on the overall response. The mean CA-125 value was 1790 with no statistically significant effect on the overall response. Development of metastases (66.7% cases) posed a statistically significant impact on overall response ($p= 0.001$ using chi-square test). Development of ascites (56.7% cases; $p = 0.001$ using chi-square test) also impacted overall response with statistical significance. Adjuvant chemotherapy and number of chemotherapy cycles did not have a significant impact on overall response

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Table 1

Variable	Categories	Total = N (%)	Alive	Death	P-value
Age at Breast Cancer (Years)	Mean ± SD	48.40± 12.74 (30)	48.74± 13.12 (23)	47.29± 10.61 (7)	0.80
Age at Ovarian Cancer (Years)	Mean ± SD	47.80± 12.02 (30)	48.83± 12.61 (23)	44.43± 9.86 (7)	0.40
Body Mass Index	Mean ± SD	28.31 ± 5.56 (30)	28.46 + 5.64 (23)	27.81 + 5.69 (7)	0.79
Comorbid	Nil	16 (53.3)	12 (52.2)	4 (57.1)	0.91
	Single	8 (26.7)	6 (26.1)	2 (28.6)	
	Multiple	6 (20)	5 (21.7)	1 (14.3)	
Family History	Yes	8 (26.7)	6 (26.1)	2 (28.6)	0.89
	No	22 (73.3)	17 (73.9)	5 (71.4)	

Table 2

Variable	Categories	Total = N (%)	Complete Response	No complete Response	P-value
Duration between breast & ovarian cancer	Mean ± SD	6.93± 2.70 (30)	7.69± 2.87 (13)	6.35± 2.50 (17)	0.18
CA-125	Mean ± SE	1790.48±577.64 (30)	860.42± 311.26 (13)	2501.71± 820.5 (17)	0.11
Metastasis	Yes	20 (66.7)	4 (30.8)	16 (94.1)	0.001*
	No	10 (33.3)	9 (69.2)	1 (5.9)	
Ascites	Yes	17 (56.7)	3 (23.1)	14 (82.4)	0.001*
	No	13 (43.3)	10 (76.9)	3 (17.6)	
Chemotherapy	Yes	28 (93.3)	12 (92.3)	16 (94.1)	0.84
	No	2 (6.4)	1 (7.7)	1 (5.9)	
Chemotherapy Cycle	Mean ± SD	5.57± 2.14 (30)	5.46± 1.94 (13)	5.65± 2.34 (17)	0.82
Adjuvant Therapy	Yes	20 (66.7)	10 (76.9)	10 (58.8)	0.28
	No	10 (33.3)	3 (23.1)	7 (41.2)	

DISCUSSION

Ovarian and breast cancer are separate clinical conditions; however, recently a correlation between both the cancers have been seen with regard to epigenetic and genetic variations. This study provides a perspective depending upon demographic, clinical and histopathological characteristics of patients having hereditary breast and ovarian cancer and survival outcomes. However, there still is scarce data on associations of clinical features and outcomes of concurrent or metachronous breast and ovarian cancers.

In our study, there was no significant difference in mean age at diagnosis of breast or ovarian cancer. The mean age at onset of breast cancer in our patient population was similar as compared to published literature, however ovarian cancer was diagnosed at a relatively younger age[5]. Chemotherapy was used in all except two patients. Almost half of patient population had comorbid medical conditions; (single 26.7% and multiple 20%) and family history was found in patients of hereditary breast/ovarian cancer. We could not check BRCA1/2 gene mutations for any patient due to limited resources. Claes K, et al recognized many variants of unknown clinical significance except some true pathogenic mutations in combination with a family history, an early average age of female breast cancer diagnosis, and the presence of a relative with ovarian cancer or multiple primary breast cancers[6].

Association of CA-125 was found to be contrary to BRCA 1/2 gene mutations. Our study rules out significant impact of CA-125 levels for overall response. Values of CA-125 at presentation did not show significant influence on overall survival (p=0.11) as compared to previous study conducted by Zorn KK et al showed that increase in CA-125 level was associated with an increase in hazard for disease progression (p<0.001), this could however be defined by ethnic variation[7].

Two thirds of our patients (66.67%) had metastatic disease at presentation. Metastatic disease showed significant impact (p=0.001) on progression of disease. Seventeen (56.7%) patients had ascites at the time of presentation while 13 patients (43.3%) had no ascites. Presence of ascites had a significant association (p=0.001) on progression. Zinvadinovic R et al described in their research that the presence of ascites is associated with ovarian cancer furthermore it showed key role for the progression of disease[8]. Ascitic fluid is also the main cause of the spread of ovarian cancer and the occurrence of peritoneal and abdominal metastasis[9].

Latifi A et al and Rafehi S et al indicated that ascites stimulates tumor cell growth and also generate resistance in tumor cell for chemotherapy[10,11]. Slack-Davis JK, et al also highlighted in their work that presence of ascites is responsible for recurrence. Recurrence rate was observed as 29% without ascites while with ascites recurrence rate was observed increased as 59%[12].

Contrary to published literature, our study showed a poor responsiveness to adjuvant chemotherapy. Adjuvant platinum based chemotherapy, especially in patients with underlying germline BRCA mutations has been proved to have better overall treatment outcomes[13].

CONCLUSION

Our study is limited with a small number of patients reported from a resource constrained setup. Further studies with larger dataset are required to shade light on clinical characteristics and outcomes of Hereditary Breast and Ovarian Cancer Syndrome.

Conflict of interest: Nil

REFERENCES

1. Foulkes WD, Narod SA. Hereditary breast and ovarian cancer: epidemiology, genetics, screening and predictive testing. *Clin Invest Med*. 1995;18(6):473-483.
2. Yoshida R. Hereditary breast and ovarian cancer (HBOC): review of its molecular characteristics, screening, treatment, and prognosis. *Breast Cancer*. 2021;28(6):1167-1180. doi:10.1007/s12282-020-01148-2
3. Rashid MU, Muhammad N, Bajwa S, et al. High prevalence and predominance of BRCA1 germline mutations in Pakistani triple-negative breast cancer patients. *BMC Cancer*. 2016;16(1):673. Published 2016 Aug 23. doi:10.1186/s12885-016-2698-y
4. Zhu Y, Wu J, Zhang C, et al. BRCA mutations and survival in breast cancer: an updated systematic review and meta-analysis. *Oncotarget*. 2016;7(43):70113-70127. doi:10.18632/oncotarget.12158
5. Chen C, Xu Y, Huang X, et al. Clinical characteristics and survival outcomes of patients with both primary breast cancer and primary ovarian cancer. *Medicine (Baltimore)*. 2020;99(32):e21560. doi:10.1097/MD.0000000000021560
6. Claes E, Evers-Kiebooms G, Denayer L, et al. Predictive genetic testing for hereditary breast and ovarian cancer: psychological distress and illness representations 1 year following disclosure. *J Genet Couns*. 2005;14(5):349-363. doi:10.1007/s10897-005-1371-4
7. Zorn KK, Tian C, McGuire WP, et al. The prognostic value of pretreatment CA 125 in patients with advanced ovarian carcinoma: a Gynecologic Oncology Group study. *Cancer*. 2009;115(5):1028-1035. doi:10.1002/cncr.24084
8. Živadinović, Radomir et al. "Ascitic Fluid in Ovarian Carcinoma – From Pathophysiology to the Treatment". Ascites - Physiopathology, Treatment, Complications and Prognosis, edited by Luis Rodrigo, IntechOpen, 2017. 10.5772/intechopen.70476.
9. Ahmed N, Stenvers KL. Getting to know ovarian cancer ascites: opportunities for targeted therapy-based translational research. *Front Oncol*. 2013;3:256. Published 2013 Sep 25. doi:10.3389/fonc.2013.00256
10. Latifi A, Luwor RB, Bilandzic M, et al. Isolation and characterization of tumor cells from the ascites of ovarian cancer patients: molecular phenotype of chemoresistant ovarian tumors. *PLoS One*. 2012;7(10):e46858.
11. Rafehi S, Ramos Valdes Y, Bertrand M, et al. TGFβ signaling regulates epithelial-mesenchymal plasticity in ovarian cancer ascites-derived spheroids. *Endocr Relat Cancer*. 2016;23(3):147-159. doi:10.1530/ERC-15-0383
12. Slack-Davis JK, Atkins KA, Harrer C, Hershey ED, Conaway M. Vascular cell adhesion molecule-1 is a regulator of ovarian cancer peritoneal metastasis [published correction appears in Cancer Res. 2009 Mar 15;69(6):2694]. *Cancer Res*. 2009;69(4):1469-1476. doi:10.1158/0008-5472.CAN-08-2678
13. Long KC, Kauff ND. Hereditary ovarian cancer: recent molecular insights and their impact on screening strategies. *Curr Opin Oncol*. 2011;23(5):526-530. doi:10.1097/CCO.0b013e3283499da9