Germ-line *BRCA1* and *BRCA2* gene mutation among epithelial ovarian / primary peritoneal cancer at King Faisal Specialist Hospital & Research Center

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Introduction

- Ovarian cancer is the seventh most common cancer in women worldwide and the second most common gynecologic malignancy.
- Saudi Arabia has a similar trend of ovarian cancer. (1)
- Ovarian cancer is usually fatal, and it is the eighth most common cause of cancer death in women worldwide.(2)
- *BRCA1* or *BRCA2* gene germ-line mutation is one of the risk factors for ovarian cancer accounting for the majority of hereditary ovarian cancers. (3),(4)
- Women with *BRCA* gene mutation have a greatly increased risk of ovarian and breast cancer. (5)
- Until now there is no data in Saudi Arabia neither about mortality rate nor about incidence of *BRCA* gene mutation among Saudi women with epithelial ovarian/ primary peritoneal cancer.

Objective

- This is a retrospective cohort study conducted in the oncology center at King Faisal Specialist Hospital and Research Center :
- To determine the prevalence and the type of *BRCA1* and *BRCA2* gene mutation among patients who have been diagnosed with epithelial ovarian or primary peritoneal cancer.
 - To look at the tumor risk factors (including histologic type, stage and grade of the tumor) in these patients.
 - To look at the patient's personal history risk factors including history of breast cancer and family history risk factors including history of breast cancer, ovarian cancer and to explore the correlation with *BRCA* gene mutation.

Method

- Sixty seven patients were included in the study.
- The presence of germ-line *BRCA1* and *BRCA2* mutation among them was obtained.
- A detailed information was collected on patients' characteristics emphasizing on personal, family risk factors and tumor characteristics, and the main primary treatment given.
- Continuous variables have been summarized using median and rages and compared using Mann-Whitney test.
- Categorical variables have been summarized using frequencies and percentages and compared using Chi-squared test.
- Association between *BRCA* mutation and proposed risk factors has been evaluated using Logistic regression. P-value less than 0.05 was considered statistically significant.
- Statistical analysis has been done using SPSS (version 20).

Results

- Twenty six patients with mutation were identified (twenty four in *BRCA1* and two in *BRCA2*) representing (38.1%). (Figure 1)
- The number of Saudi patients with *BRCA* gene mutation were 24 with a percentage of (92.3%).
- The median age at diagnosis was 51 year old with a range of (17-75).
- Six of mutation-positive patients (23%) had a previous history of breast cancer and six (23%) had a family history of breast or ovarian cancer as shown in (Table 1).
- All patients with *BRCA* gene mutation were of serous histology and of high grade.
- Twenty-two patients (84.6%) have high Ca 125 at diagnosis and nineteen (73.0%) presented at advanced stage as shown in (Figures 2 and 3).
- Most of the patients (53.8%) had interval de-bulking surgery while (46.2%) had upfront surgery. Two out of 26 patients had Heated Intra-Peritoneal Chemotherapy . (Table 2 and 3).

Table 1 Patients characteristics (personal and family risks factors)

Baseline characteristic	Estimate
Age at diagnosis (Median / Range)	51 (17-75) year
Saudi Nationality	24 patients (92.3%)
Previous History of Breast ca	6 patients (23%)
Family History of Breast or ovarian ca	6 patients (23%)
Total No of patients	26 patients

Figure 2: Level of ca 125 at presentation

Figure 1: Type of BRCA gene mutation

Figure 3: Stage of the disease at diagnosis stage

Table 2 Type of Surgical treatment

Surgery type	No of patient /Percentage
Upfront surgery	12 (46.2%)
Interval debulking	14 (53.8%)
Total	26 patients

Table 3 Type of chemotherapy given

Type of chemotherapy	No of patient /Percentage
Adjuvant	10 (38.4%)
Neo-adjuvant	14 (53.8%)
Heated Intraperitoneal	2 (7.7%)
Total	26 patients

Discussion

- The frequency of *BRCA* gene mutation was high among our patients (38.1%) which is almost reaching the same frequency found in Ashkenazi Jewish (41.1%) who has the highest prevalence of gene mutation in USA.
- As compared to international reference, the presence of *BRCA1* mutation accounted for higher proportion of patients (92.3%) compared to *BRCA2* mutation (7.7%).
- The lower median age of ovarian cancer in Saudi Arabia (51 year old) can be explained by the high percentage of patients with *BRCA* gene mutation.
- Only (23%) of our patients with *BRCA* gene mutation had positive family history and a similar proportion had a personal history. There is no significant association between *BRCA* gene mutation and family/ personal risk factors.
- All patients with *BRCA* mutation were of serous histology and of high grade. The same findings were also obtained in studies done earlier.
- Twenty-two (84.6%) of *BRCA* gene mutation patients had high Ca 125 at diagnosis and nineteen (73.0%) presented at advanced stage; reason why most of them (53.8%) had interval de-bulking surgery.

Conclusion

- The frequency of *BRCA* gene mutation was high among our patients (38.1%).
- The lower median age of ovarian cancer in Saudi Arabia (51 year old) can be explained by the high percentage of patients with *BRCA* gene mutation.
- Only (23%) of our patients with *BRCA* gene mutation had a positive family history.

References

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