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ORIGINAL ARTICLE

Retrospective Study

# Low testing rates and high *BRCA* prevalence: Poly (ADP-ribose) polymerase inhibitor use in Middle East *BRCA*/homologous recombination deficiency-positive cancer patients

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## Abstract

***BACKGROUND***

Poly (ADP-ribose) polymerase inhibitors (PARPis) are approved as first-line therapies for breast cancer gene (*BRCA*)-positive, human epidermal growth factor receptor 2-negative locally advanced or metastatic breast cancer. They are also effective for new and recurrent ovarian cancers that are *BRCA*- or homologous recombination deficiency (HRD)-positive. However, data on these mutations and PARPi use in the Middle East are limited.

***AIM***

To assess *BRCA*/HRD prevalence and PARPi use in patients in the Middle East with breast/ovarian cancer.

***METHODS***

This was a single-center retrospective study of 57 of 472 breast cancer patients

tested for *BRCA* mutations, and 25 of 65 ovarian cancer patients tested for HRD. These adult patients participated in at least four visits to the oncology service at our center between August 2021 and May 2023. Data were summarized using descriptive statistics and compared using counts and percentages. Response to treatment was assessed using Response Evaluation Criteria in Solid Tumors criteria.

***RESULTS***

Among the 472 breast cancer patients, 12.1% underwent *BRCA* testing, and 38.5% of 65 ovarian cancer patients received HRD testing. Pathogenic mutations were found in 25.6% of the tested patients: 26.3% breast cancers had germline *BRCA* (*gBRCA*) mutations and 24.0% ovarian cancers showed HRD. Notably, 40.0% of *gBRCA*-positive breast cancers and 66.0% of HRD-positive ovarian cancers were Middle Eastern and Asian patients, respectively. PARPi treatment was used in 5 (33.3%) *gBRCA*-positive breast cancer patients as first-line therapy ($n$ = 1; 7-months progression-free), for maintenance ($n$ = 2; > 15-months progression-free), or at later stages due to compliance issues ($n$ = 2). Four patients (66.6%) with HRD-positive ovarian cancer received PARPi and all remained progression-free.

***CONCLUSION***

Lower testing rates but higher *BRCA* mutations in breast cancer were found. Ethnicity reflected United Arab Emirates demographics, with breast cancer in Middle Eastern and ovarian cancer in Asian patients.

**Key Words:** Homologous recombination repair; *BRCA1*; *BRCA2*; Homologous recombination deficiency; Ovarian cancer; Breast cancer; Poly (ADP-ribose) polymerase inhibitors; Olaparib; DNA double-strand breaks



**Core Tip:** Following National Comprehensive Cancer Network guidelines, breast cancer patients were tested for *BRCA1/2* mutations, while ovarian cancer patients underwent homologous recombination defect testing. These mutations can be targeted with poly (ADP-ribose) polymerase inhibitor (PARPi) therapy, a form of precision medicine. In this single-center study, we analyzed the proportion of breast and ovarian cancer patients tested for mutations, demographics and disease characteristics of tested patients, and PARPi therapy outcomes. This first-of-its-kind study in the Middle East offers insights into targeted therapy use, contributing to knowledge on PARPis for breast and ovarian cancers.

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## INTRODUCTION

Poly (ADP-ribose) polymerase (PARP) is a protein responsible for fixing single-stranded breaks. Proteins translated from other pathways, such as homologous recombination repair (HRR) genes, repair the double-strand breaks (DSBs) in DNA and help to maintain genomic stability[1]. *BRCA1/2* are the most identifiable and actionable genes of the HRR pathway. There is an increased risk of breast (45%-72%) and ovarian (39%-44%) cancers in patients or carriers with *BRCA1* and/or *BRCA2* pathogenic variants compared to the general population[2]. PARP inhibition using drugs called PARP inhibitors (PARPis) leads single-stranded breaks to become DSBs. While normal cells can repair the DSBs because of a normal HRR pathway, cancer cells with these genes mutated cannot repair DSBs, leading to the accumulation of defects and selective cancer cell death.

### Breast cancer

The prevalence of *BRCA* mutations ranges widely from 1.8% to 36.9%, depending on whether the tested subjects were selected and the country from which they were reported[3,4]. Nearly 20% of *BRCA* mutated breast cancers are triple-negative breast cancer (TNBC) and have a bad prognosis[5,6]. TNBC with these mutations occur at a younger age, are high grade and highly aggressive, have a worse prognosis, and respond well to platinum-based chemotherapy with or without PARPi[7]. Patients with or carriers of these mutations have higher chances of a second cancer in the opposite breast, ovary, pancreas, and prostate[8]. Olaparib is a PARPi approved for locally advanced or metastatic human epidermal growth factor receptor 2 (HER2)-negative breast cancer[9,10].

### Ovarian cancer

The homologous recombination deficiency (HRD) test, which not only tests mutations of HRR pathway genes but also overall deficiency in this pathway, is preferred in ovarian cancer[11]. Ovarian cancers with HRD tend to occur at a young

age, have a higher incidence of high-grade serous ovarian cancer (HGSOC), and respond well to standard platinum-based chemotherapy and PARPi[12-14]. Olaparib is approved as maintenance therapy after primary chemotherapy in germline *BRCA* (*gBRCA*) or somatic *BRCA* mutated patients who achieved complete response (CR) or stable disease (SD). Along with olaparib, niraparib and rucaparib are approved for recurrent ovarian cancer, but the specific indications depend on the *BRCA* or HRD status (SOLO-1, NOVA and ARIEL3) trials[14-16]. Moreover, the field of PARPi use in ovarian cancer is rapidly evolving, and new indications are emerging.

According to 2018 World Health Organization cancer statistics for the United Arab Emirates (UAE), breast cancer was the most common malignancy, accounting for 22.4% of diagnoses[17]. Studies in Gulf countries like UAE, Oman, and Kuwait have reported a 2%-8% prevalence of BRCA1/BRCA2 somatic variants in ovarian cancer[18]. Additionally, the prevalence of *gBRCA* mutations was found to be 10.2% in breast cancer and 30.7% in ovarian cancer in the region[19].

The aim of this study was to uncover the prevalence of *gBRCA* mutations in breast cancer and HRD in ovarian cancer. Beyond mere prevalence, the study compared the characteristics of patients with and without these pathogenic mutations within the tested breast and ovarian cancer groups. Finally, to assess the potential treatment implications of these findings, the study reported the proportion of patients who received PARPi therapy and their response to this targeted treatment. This study not only seeks to illuminate the selected DSB repair gene mutations in the region but also pave the way for understanding targeted treatment strategies.

## MATERIALS AND METHODS

### Study design

This single-center, retrospective study delves into the genetics of breast and ovarian cancer patients tested from August 2021 to May 2023 (22 months).

### Genetic testing

Genetic susceptibility testing adhered to current clinical practice: *BRCA1/2* analysis for breast cancer and full HRD assessment (including gene mutations and functional testing of HRR pathway) for ovarian cancer. We tested for these through ISO 15189-certified labs (Invitae, Genotypos, and Myriad) due to in-house limitations.

### Patients

All patients were at least 18-years-old and participated in four or more clinic visits within the study period to ensure sufficient clinical workup for the included cancers.

### National Comprehensive Cancer Network criteria

Our analysis focused on the 82 patients who underwent *BRCA* or HRD testing. Resource limitations prevented us from definitively determining testing rates across the entire patient population (including the 455 patients who were not tested). Detailed National Comprehensive Cancer Network criteria were reported only in tested cancer patients (breast cancer: young age, family history of cancer, TNBC, advanced HER2-negative breast cancer and history of first primary cancer; ovarian cancer: all epithelial histological types and recurrent cancers).

### Data collection

Prior ethics approval was secured. Data on demographics, diagnoses, mutations, treatment response (Response Evaluation Criteria in Solid Tumors criteria), disease-free interval, progression-free interval, and other clinical details were sourced from electronic medical records and oncologist/radiology reports.

### Statistical analyses

We employed descriptive statistics (*e.g.*, central tendency, dispersion, frequency distributions) and compared percentages to identify patterns, trends, and group differences using Datatab software[20]. The sample size calculation was not determined, as the objective of this study was descriptive. Similarly, statistical methods for hypothesis testing were not employed due to the descriptive nature of the analysis.

## RESULTS

### Proportion of breast and ovarian cancer patients tested

Of the 472 breast cancer patients, 12.1% ($n$ = 57) received *BRCA* testing, and 38.5% ($n$ = 25) of the 65 ovarian cancer patients underwent HRD testing. The distribution of ethnicity differed between the two cancer groups. UAE nationals were the largest ethnic group among breast cancer patients (45.3% or 214), followed by Middle Eastern (25.0%, 118/472), Asian (16.7%, 79/472), and African (10.4%, 49/472). Similarly, UAE nationals were the predominant group for ovarian cancer patients (33.8%, 22/65), followed by Asian (29.2%, 19/65), Middle Eastern (24.6%, 16/65), and African (7.6%, 5/65).

### Mutation status and testing criteria

Among the 82 patients who underwent testing, 21 (25.6%) had pathogenic mutations identified. Among the tested breast cancer patients, testing criteria were as follows: 68.4% (39/57 patients) were young (age < 50 years), 15.8% (9/57 patients) had a family history of cancer, 7.0% (4/57 patients) had a history of recurrence or another primary cancer, and 8.8% (5/57 patients) had TNBC. All 25 tested ovarian cancer patients had single or mixed epithelial histology. PARPis were utilized in 42.8% of the patients with pathogenic mutations.

### Breast cancer: BRCA mutation analysis and patient characteristics

Among the 57 breast cancer cases tested for *gBRCA* mutations, 15 (26.3%) harbored pathogenic mutations. Of these, 10 (17.7%) involved *gBRCA1* mutations, while the remaining 5 (8.7%) were associated with *gBRCA2* as shown in Figure 1. Four cases had *BRCA2* variants of unknown significance (VUS). The median age at time of diagnosis was 42.1 years in the *BRCA* mutated group *vs* 45.3 years in the non-mutated group. Patients from the Middle East, excluding UAE nationals, were the highest in both groups. UAE national patients were the second highest (33.3%) in the mutated group and the third (19%) in the non-mutated group, as shown in Figure 2. Family history of cancer (53.3% in the mutated group *vs* 38.1% in the non-mutated group) and a history of a first-degree relative having cancer (53.3% in the mutated group *vs* 21.3% in the non-mutated group) were more prevalent in the mutated group. Additionally, Eastern Cooperative Oncology Group performance status (ECOG PS) was distributed differently between the groups, with 86.7% of mutated patients and 95.2% of non-mutated patients having a score of 0, while 13.3% and 4.8% had a score of 1, respectively. The mutated group also showed a higher median grade of breast cancer (3 *vs* 2). Both groups were similar in cancer staging, wherein stage 2 was most common followed by stages 3 and 4. Both groups had invasive ductal carcinoma as the most common histological type (80% in the mutated group *vs* 83.3% in the non-mutated group), followed by invasive lobular carcinoma (6.6% *vs* 9.5%). The distribution of molecular subtypes also differed slightly, namely TNBC (20% *vs* 19%), hormone-positive (HR+)/HER2-negative (40% *vs* 35.7%), and HR+/HER2-positive (20% *vs* 14.3%), as detailed in Table 1.

Notably, the response rates to chemotherapy were similar between the groups, with CR being 40% in the mutated group *vs* 45.2% in the non-mutated group, SD being 40% in the mutated group *vs* 19% in the non-mutated group, partial response (PR) being 0% in the mutated group *vs* 7.2% in the non-mutated group, and progressive disease being 20% in the mutated group *vs* 28.6% in the non-mutated group, as shown in Figure 3.

Within the mutated group ($n$ = 15), 5 patients (33.3%) received PARPi. Of these, 1 patient with advanced disease received PARPi as first-line therapy and progressed after 7 months, the other patient with advanced disease presented to us after progression on ribociclib plus letrazole and could receive PARPi for 5 months only. The other 3 patients received PARPi after adjuvant or neoadjuvant chemotherapy and 2 achieved CR to chemotherapy and were disease-free for more than 15 months on olaparib. Unfortunately, 1 patient progressed on two lines of chemotherapy and could take PARPi for 40 days only. Detailed outcomes are presented in Table 2.

### Ovarian cancer: HRD analysis and patient characteristics

Among the 25 ovarian cancer cases, 6 (24.0%) harbored HRD, comprising 2 (8.0%) somatic *BRCA1* and 1 (4.0%) somatic *BRCA2*. The remaining 19 (76.0%) cases were HRD-negative, as shown in Figure 1. The median age at time of diagnosis was slightly higher in the mutated group (56.5 years) compared to the non-mutated group (52.5 years). In terms of ethnicity, Asians formed the majority of the mutated group at 66.6%, followed by UAE nationals and patients from other Middle Eastern countries, both at 16.7% each. The non-mutated group displayed a different distribution, with Asians comprising 36.8%, followed by Middle Easterners at 31.6%, UAE nationals at 21%, and Africans at 10.6%, as detailed in Figure 2. The mutated group reported no such history, whereas 26.3% of the non-mutated group had a positive family history. Both groups were predominantly composed of patients with good PS (ECOG 0: 83.3% *vs* 89.4%). Serous adenocarcinoma was the most prevalent histological type in both groups (83.3% in the mutated and 47.3% in the non-mutated), followed by mixed type (0% and 26.3%, respectively). Notably, the majority in both groups presented with advanced-stage (stages 3 and 4) and high-grade (grade 4) ovarian cancer. Additionally, most patients in the mutated group underwent interval debulking surgery (66.7% and 26.4%, respectively), as detailed in Table 3.

Overall treatment response to chemotherapy was more favorable in the mutated group, with a 50% CR rate compared to 15.7% in the non-mutated group. SD was also achieved by 16.7% of mutated patients *vs* 42.1% of non-mutated patients, while progressive disease rates were lower in the mutated group (16.7%) compared to the non-mutated group (31.6%) as shown in Figure 3. Among the patients with mutated ovarian cancer who received maintenance PARPi, 3 (75%) achieved disease-free status, while the remaining patient (25%) showed no evidence of disease progression. Notably, all patients remained on PARPi at study completion, as shown in Table 2. No deaths were reported in the mutated group, compared to 10.5% (2 patients) in the non-mutated group, as shown in Figure 3.

### Recurrence or first primary malignancies

Among the 82 patients who underwent testing, 12 (14.6%) had a history of cancer. Notably, 4 (33.3%) of these patients harbored *gBRCA*- or HRD-positive mutations, while the remaining 8 (66.6%) had no identifiable mutations. Within the *gBRCA* group, 2 (16.7%) had recurrence of breast cancer, and in the HRD-positive group, 1 (16.7%) had recurrence of ovarian cancer. Additionally, 1 HRD-positive ovarian cancer patient had a history of another first primary, thyroid cancer. Among the unmutated group, 4 (50%) had recurrence of breast cancer, 1 (12.5%) had recurrent ovarian cancer, and 3 (37.5%) had different first primary cancer.

**Table 1 Demographics and clinical characteristics of germline *BRCA*-positive and *BRCA*-negative breast cancer**

| *gBRCA*[1] | Positive | Negative |
|---|---|---|
| Total, *n* (%) | 15 (26.3) | 42 (73.7) |
| Age in yr at diagnosis, mean ± SD | 42.1 ± 11 | 45.3 ± 8.7 |
| Positive family history, *n* (%) | 8 (53.3) | 16 (38.1) |
| First-degree relative, *n* (%) | 8 (53.3) | 9 (21.3) |
| Non-first-degree relatives, *n* (%) | 4 (26.6) | 11 (26.1) |
| H/o IVF & Rx, *n* (%) | 0 | 0 |
| H/o hormone Rx, *n* (%) | 1 (6.6) | 4 (9.5) |
| ECOG PS at diagnosis[2], *n* (%) | | |
| 0 | 13 (86.7) | 40 (95.2) |
| 1 | 2 (12.3) | 2 (4.8) |
| Histology at diagnosis, *n* (%) | | |
| Invasive ductal carcinoma | 12 (80) | 35 (83.3) |
| Invasive lobular carcinoma | 1 (6.6) | 4 (9.5) |
| Grade at diagnosis, mean ± SD | 3 ± 0.6 | 2 ± 0.7 |
| Stage at diagnosis, *n* (%) | | |
| 1 | 1 (6.6) | 0 |
| 2 | 7 (46.6) | 21 (50) |
| 3 | 4 (26.6) | 13 (31) |
| 4 | 3 (20) | 8 (19) |
| Categories[3], *n* (%) | | |
| HER2-positive | 4 (26.6) | 12 (28.7) |
| Triple-negative | 3 (20) | 8 (19.0) |
| HR-positive and HER2-negative | 6 (40) | 15 (35.7) |
| HR-positive and HER2-positive | 3 (20) | 6 (14.3) |

[1]Includes *BRCA1* and *BRCA2*.
[2]Eastern Cooperative Oncology Group Performance Status.
[3]Categories of breast cancer having prognostic significance.
ECOG PS: Eastern Cooperative Oncology Group Performance Status; HER2: Human epidermal growth factor receptor 2; HR: Homologous recombination; IVF: *In vitro* fertilization; Rx: Medical prescription.

## DISCUSSION

Our study, the first of its kind in the Middle East, investigated the genetic testing rates in cancer patients, prevalence of *gBRCA* mutations in tested breast cancer patients and HRD in tested ovarian cancer patients. We further compared the demographics, disease characteristics, and response to chemotherapy of these cancers with and without these mutations. Additionally, we analyzed the proportion of patients receiving PARPi therapy and their respective response outcomes. Notably, our cohort comprised 82 tested patients of 537 and 21 (25.6%) harbored pathogenic mutations, exceeding the previously reported rate[21]. Interestingly, 9 (11%) patients carried VUS, falling within the lower range of reported frequencies (0%-44%)[22]. These findings reflect the well-established role of *BRCA* and other HRR genes in these cancers [2].

*BRCA*/HRD testing rates were 12% (57 of 472 patients) for breast cancer and 38.4% (25 of 65 patients) for ovarian cancer. These rates are modestly lower than the figures of 14.2% and 43% reported elsewhere respectively[23,24]. However, it is important to acknowledge limitations in our data. Due to limited resources, we lacked information on the eligibility criteria for the untested patients ($n$ = 455). This absence makes it challenging to determine the exact proportion of eligible patients who may not have received testing.

### *Breast cancer*

The prevalence of pathogenic *gBRCA* mutations in breast cancer patients tested in our study was 26.3%, more than two

**Table 2 Clinical outcomes of poly (ADP-ribose) polymerase inhibitor therapy in *BRCA* gene-positive breast cancer and homologous recombination deficiency-positive ovarian cancer patients**

| Cancer type | Patient | Stage | Response change to PARPi | Duration of PARPi | PARPi status at end of study |
|---|---|---|---|---|---|
| *BRCA*+ breast cancer, 5/15 (33.3%) | 1 | II | CR–DF | 13 months+ | On Rx |
| | 2[1] | II | PR–PR | 40 days | Stopped |
| | 3 | III | CR–DF | 17 months+ | On Rx |
| | 4 | IV | PR–PR | 5 months | Stopped |
| | 5[2] | IV | PR | 7 months | Stopped |
| HRD+ ovarian cancer, 4/6 (66.6%) | 1 | III | PR–DF | 15 months+ | On Rx |
| | 2 | IV | CR–DF | 13 months+ | On Rx |
| | 3 | IV | SD–PRF | 20 months+ | On Rx |
| | 4 | IV | CR–DF | 25 months+ | On Rx |

[1]Received three cycles of neoadjuvant chemotherapy and then lost to follow-up and received poly (ADP-ribose) polymerase inhibitor in the advanced stage.
[2]Received olaparib as first line. + indicates the status of still receiving poly (ADP-ribose) polymerase inhibitor at the time of data collection/study end.
CR: Complete remission, DF: Disease-free; HRD: Homologous recombination deficiency; PR: Partial response; PRF: Progression-free; SD: Stable disease.

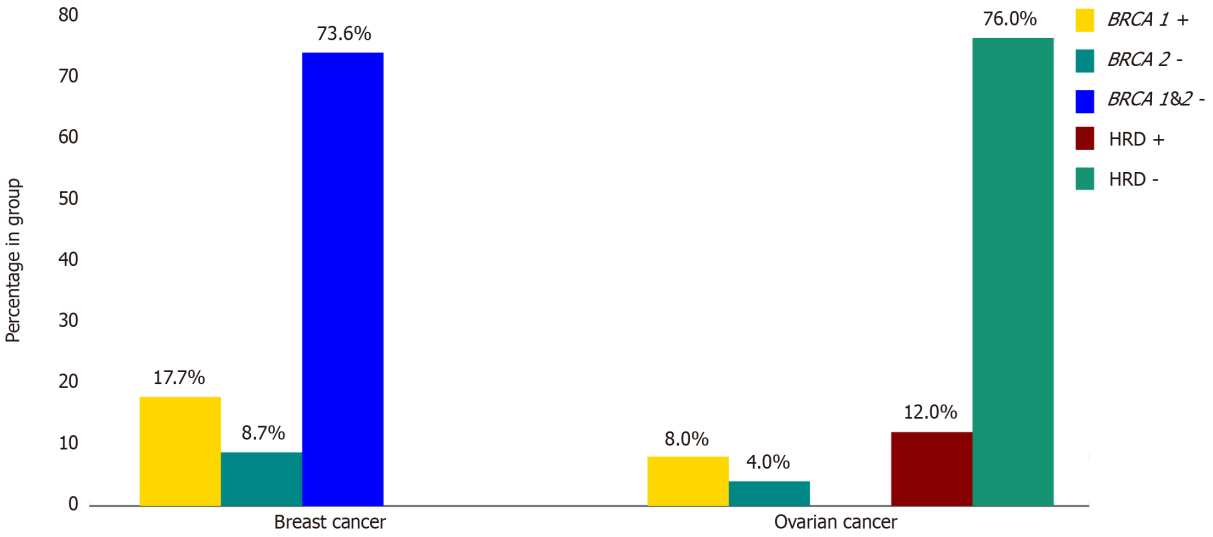


**Figure 1 Distribution of breast cancer gene mutations and homologous recombination deficiency in breast and ovarian cancers.** Among breast cancer patients, 17.7% (10/57) harbored pathogenic mutations in germline *BRCA1* (*gBRCA1*), while 8.7% (5/57) had mutations in *gBRCA2*. In the ovarian cancer group, 8% (2/25) of patients had *gBRCA1* mutations, 4% (1/25) had *gBRCA2* mutations, and 12% (3/25) had homologous recombination deficiency.

times the 12% reported in a large, multicenter study involving 2733 women[25]. *BRCA* testing is commonly recommended for women diagnosed with breast cancer at a young age, and the lower median age in our cohort aligns with this practice[25]. Moreover the median age of 45.3 years in the non-mutated group aligns with a review confirming the median age of breast cancer in UAE is 48 years[26]. While Figure 2 shows that UAE nationals formed the largest group among tested breast cancer patients, followed by Middle Eastern patients, this is not consistent with the overall demographics of the UAE, as reported elsewhere[27]. This trend is also observed in the overall breast cancer patients within our cohort. Consistent with previous reports of higher histological grade at presentation in *gBRCA*-mutated breast cancers, our study found a significantly higher proportion of high-grade tumors in the mutated group compared to the non-mutated group[28]. The good PS (low ECOG PS) observed in both groups, reflecting their young age, aligns with the reported literature. The proportion of HR-positive cases was slightly lower in both the mutated group (40%) and the non-mutated group (35.7%), which falls within the range observed in a large study (44% HR-positive with 1236 patients)[8, 29]. Overall, the *BRCA* mutated and non-mutated breast cancer groups appeared similar, although the significance of these values could not be calculated due to limitations in statistical analysis.

**Table 3 Demographic and clinical characteristics of homologous recombination deficiency-positive and -negative ovarian cancer**

| Characteristic | HRD-positive | HRD-negative |
|---|---|---|
| Total, *n* (%) | 6 (24) | 19 (76) |
| Age years at diagnosis, mean ± SD | 56.5 ± 11 | 52.5 ± 13 |
| Positive family history, *n* (%) | 0 | 5 (26.3) |
| ECOG PS at diagnosis, *n* (%) | | |
| 0 | 5 (83.3) | 17 (89.4) |
| 1 | 1 (16.7) | 1 (5.3) |
| 2 | 0 | 1 (5.3) |
| Histology, *n* (%) | | |
| Serous | 5 (83.3) | 9 (47.3) |
| Endometrioid/mucinous/clear cell | 1 (16.7) | 5 (26.3) |
| Mixed | 0 | 5 (26.3) |
| Grade of cancer, mean ± SD | 4 ± 0 | 4 ± 0.9 |
| Stage of cancer, *n* (%) | | |
| 1 | 1 (16.7) | 2 (10.5) |
| 2 | 0 | 0 |
| 3 | 2 (33.3) | 11 (58) |
| 4 | 3 (50) | 6 (31.5) |
| Surgical Rx, *n* (%) | 6 (100) | 17 (89.5) |
| Primary | 2 (33.3) | 12 (63.1) |
| Interval | 4 (66.7) | 5 (26.4) |

Of the 6 homologous recombination deficiency-positive cases, 3 had somatic *BRCA* gene mutations. ECOG PS: Eastern Cooperative Oncology Group Performance Status; HRD: Homologous recombination deficiency; Rx: Medical prescription.

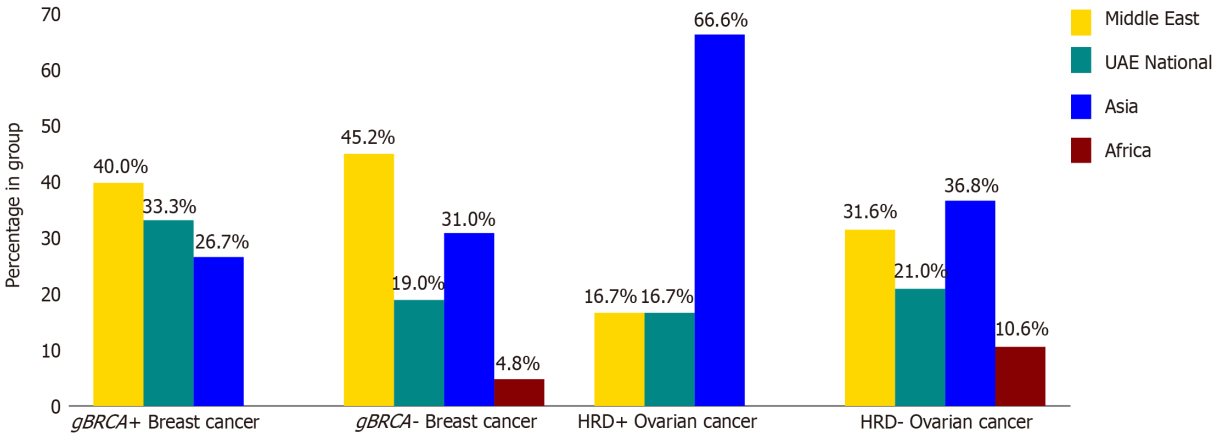


**Figure 2 Breast and ovarian cancer distribution based on mutation status and ethnicity.** A higher percentage of breast cancer (*n* = 57), both germline *BRCA* (*gBRCA*)-positive and *gBRCA*-negative, was found in Middle Eastern patients excluding United Arab Emirates nationals. Conversely, a higher percentage of ovarian cancer (*n* = 25), both homologous recombination deficiency HRD-positive and HRD-negative, was found in Asian patients.

Response to chemotherapy, 80% of *gBRCA*-mutated patients and 64.2% in the non-mutated group achieved either complete or PR or SD to chemotherapy, as shown in Figure 3.

This negligible difference in outcomes in the mutated group compared to the non-mutated group aligns with findings from the previous reports that suggested no significant difference in response rates[9]. Of the 33% (*n* = 5) of *gBRCA*-positive patients who received PARPi therapy, 4 (80%) had TNBC, while the remaining 1 (20%) was HR+/HER2-negative, as shown in Table 2. Interestingly, the response to PARPi in 3 out of 5 patients was in line with that reported in

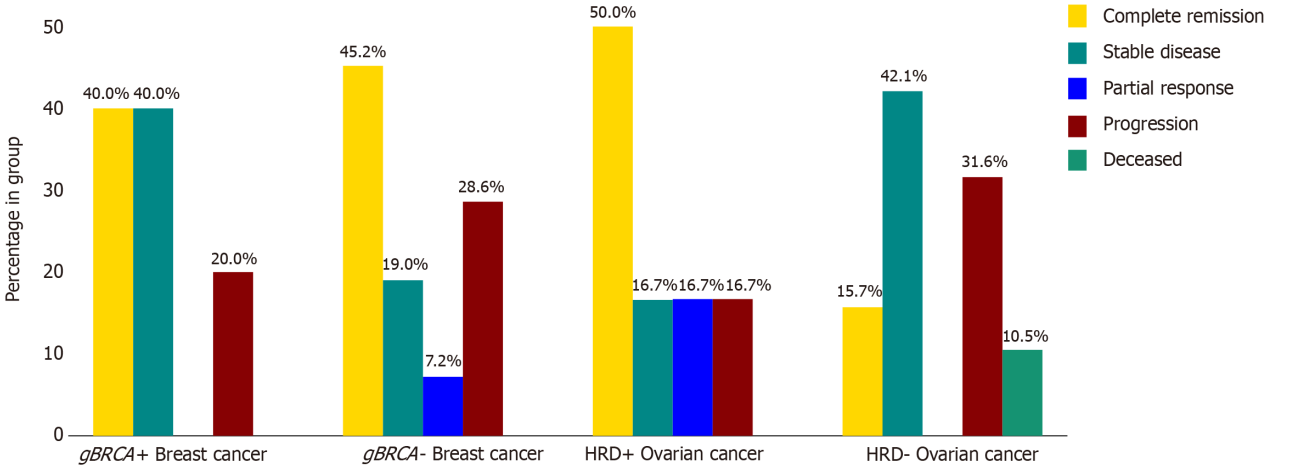


**Figure 3 Response status to chemotherapy of breast and ovarian cancers with and without mutations.** Homologous recombination-deficient (HRD) ovarian cancer (*n* = 6) had a higher percentage of complete remission (3/6) than cancer not HRD (3/19). While germline *BRCA* gene non-mutated breast cancer (*n* = 42) patients showed a slightly higher complete response rate (19/42), the overall treatment response remained similar in both mutated and non-mutated groups.

the OlympiAD and OlympiA trials. These 3 patients received PARPi/olaparib after neoadjuvant or adjuvant chemotherapy; among them 2 patients remained progression free even after 15 months as in OlympiA trial[30]. Unfortunately, the other patient, who took olaparib for 40 days, presented in advanced stage after she had refused chemotherapy and had been lost to follow up. One patient received PARPi as first line for advanced disease progressed after 7 months similar to the duration that reported in the OlympiAD trial, whereas other advanced stage patients did receive PARPi for 5 months but as second line[9]. Our findings suggest that PARPi therapy is used in approximately one-third of patients with *BRCA*-positive cancer. Interestingly, patients who received PARPi treatment according to established guidelines from major clinical trials seemed to experience better outcomes compared to those who did not receive treatment as per the guidelines.

### *Ovarian cancer*

Our study revealed a 24% prevalence of HRD-positive ovarian cancers, which is in the 20%-25% range observed in similar studies from this region, and studies from North America and China[11,19,31]. The HRD-positive group had a higher median age (56.5 years) compared to the negative group (52.5 years), both of which fall within the 52-60 years range[11]. As shown in Figure 2, Asians were the majority among the tested ovarian cancer patients. This is consistent with the overall demographics of the UAE, where Asians comprise 71% of the population[27,32]. Additionally, Asians were the second-highest ethnicity among all ovarian cancer patients in our cohort, following UAE nationals. Both groups demonstrated similar proportions of patients with good ECOG performance scores, and neither group reported a positive history of family cancer. However, as shown in Table 3, the HRD-positive group displayed a significantly higher prevalence of HGSOC and advanced-stage cancer, reflecting a trend consistent with the reported literature. Most patients had advanced ovarian cancer, and their response to primary treatment was consistent with the expected course of the disease[13,14]. Overall, the HRD-positive and HRD-negative ovarian cancer groups were not similar and were in line with the earlier reports. The significance (*P* values) of these comparative values could not be calculated due to limitations in statistical analysis.

HRD-positive ovarian cancers have been shown to have better overall survival and platinum responsiveness, a trend observed in our cohort where 83.3% of patients with mutations achieved CR or SD, compared to only 57.8% of those without mutations. Notably, the proportion of patients experiencing progressive disease was 50% lower in the HRD-positive group compared to the non-mutated group, as shown in Figure 3[11,33]. We acknowledge that, due to the short duration of study, the majority of newly diagnosed patients may not have yet reached the point of relapse, which is typically 3 years.

Among HRD-positive patients, 66.6% received PARPi therapy as maintenance; among those, 3 patients (75%) remained disease-free and 1 patient (25%) remained progression-free. All of those who received olaparib remained progression-free at the end of study, in line with the trials that led to the approval of PARPi/olaparib alone or with bevacizumab[14,34]. Overall, our findings regarding prevalence, disease characteristics, and treatment response in HRD-positive ovarian cancer align with the existing literature.

### *Second primary malignancies*

Among the 15 *gBRCA*-positive breast cancer patients, 2 (13.3%) had a recurrence of breast cancer, while 2 (33.2%) of the 6 HRD-positive ovarian cancer patients had a recurrence of ovarian cancer. These recurrence rates or history of having first primary cancer in a mutation-positive group fall within the range reported in a large multicenter study[29].

## CONCLUSION

Our study identified a higher-than-reported prevalence of *BRCA* mutations (26.3%) in the tested breast cancer patients. HRD positivity rates in ovarian cancer patients were at the upper end of the reported range. Testing rates for *BRCA* in overall breast cancer patients and HRD in ovarian cancer patients, however, remained low. While UAE nationals formed the majority of patients with both cancers in our cohort, the ethnic distribution of tested patients differed. Specifically, Middle Eastern patients dominated the positive *BRCA* mutation and testing group for breast cancer, while Asian patients formed the majority in the positive HRD and testing group for ovarian cancer. This pattern likely reflects the broader demographics of the UAE population, where Asians are the predominant ethnicity.

While most of our findings on disease characteristics (including triple-negative status, histological types, grades, and stages) and treatment responses to chemotherapy and PARPi aligned with published data, the limited sample size restricts definitive conclusions about statistical significance. Larger studies are necessary to confirm our observations and explore potentially unexpected trends, such as the observed ethnic distribution and the high prevalence of *BRCA* positivity in breast cancer patients.

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## FOOTNOTES

**Author contributions:** Syed N contributed to the conceptualization of the study, design of the methodology, formal analysis of the data, and original drafting of the manuscript as well as review and editing of the successive versions; Chintakuntlawar AV contributed to the design of the methodology, formal analysis of the data, review and editing of the successive versions of the manuscript, and supervision of the overall project; Vilasini D provided resources for the study and contributed to the review and editing of the successive versions of the manuscript; Al Salami AM, Al Hasan R, Uttam Chandani K and Chandani AU provided resources for the study; Afrooz I contributed to the original drafting of the manuscript as well as review and editing of the successive versions, provided resources for the study, and performed supervision of the overall project; Chehal A contributed to the conceptualization of the study and design of the methodology, provided resources for the study, and participated in the review and editing of the successive versions and to the supervision of the overall project.

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