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PREVALENCE OF BRCA GENE MUTATION IN EPITHELIAL OVARIAN CANCER PATIENTS IN ODISHA: A SINGLE TERTIARY CARE CENTRE-BASED CROSS-SECTIONAL ANALYTICAL STUDY

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ABSTRACT

Background: Epithelial ovarian cancer (EOC) accounts for nearly 90% of ovarian malignancies and remains the leading cause of mortality among gynecologic cancers. Approximately 10–15% of cases are hereditary and are mainly associated with germline mutations in the BRCA1 and BRCA2 genes. These genes play a crucial role in DNA repair through homologous recombination, and mutations significantly increase the lifetime risk of ovarian and breast cancers. Determining the prevalence of BRCA mutations in regional populations is important for guiding targeted therapy and genetic counseling.

Objective: To determine the prevalence of BRCA1 and BRCA2 gene mutations among patients with epithelial ovarian cancer in a tertiary cancer care center in Odisha.

Methods: This cross-sectional analytical study included patients with histopathologically confirmed epithelial ovarian cancer, primary peritoneal carcinoma, or fallopian tube carcinoma. After obtaining written informed consent, demographic data, family history, clinical details, and histopathological findings were recorded. Germline mutation testing was performed using blood samples, and somatic mutation testing was conducted using tumor tissue samples. Next Generation Sequencing (NGS) technology was used for genetic analysis in collaboration with inDNA Life Sciences. The prevalence of BRCA mutations was calculated and patients were categorized as BRCA-positive or BRCA-negative.

Results: A total of 566 patients were studied over a period of 1 year and 7 months. The mean age of patients was 47 years (range 20–65 years). BRCA mutations were detected in 64 patients (11.3%). Among these, 41 patients (7.24%) had BRCA1 mutations and 23 patients (4.06%) had BRCA2 mutations. Of the mutation-positive patients, 11 had a family history of breast or ovarian cancer. High-grade serous ovarian carcinoma was the most common histological subtype observed.

Conclusion: The prevalence of BRCA mutations in epithelial ovarian cancer patients in our institution was 11.3%, with BRCA1 mutations being more frequent than BRCA2 mutations. Identification of BRCA mutations has important implications for targeted therapy with PARP inhibitors and for genetic counseling of family members.

KEYWORDS: BRCA1, BRCA2, epithelial ovarian cancer, germline mutation, PARP inhibitors, genetic screening

INTRODUCTION

Ovarian cancer is one of the most aggressive gynecologic malignancies and remains a major cause of cancer-related mortality among women worldwide. Among the various histological types, epithelial ovarian cancer (EOC) accounts for approximately 90% of ovarian malignancies. Due to its nonspecific symptoms and late presentation, most patients are diagnosed at advanced stages, resulting in poor overall survival. A proportion of ovarian cancers arise due to inherited genetic predisposition. Approximately 10–15% of epithelial ovarian cancers are hereditary and are primarily associated with mutations in the BRCA1 and BRCA2 genes. [1,2] These genes function as tumor suppressor genes involved in DNA damage repair through the homologous recombination pathway. Mutations in these genes impair DNA repair mechanisms, leading to genomic instability and increased susceptibility to malignancies. The association between hereditary cancer and familial clustering was first described in the nineteenth century when Paul Broca documented a high incidence of breast cancer in his wife's family. Later advances in molecular genetics identified the BRCA1 gene on chromosome 17q21 in 1994 and the BRCA2 gene on chromosome 13q12 in 1995.[3,4] BRCA1 and BRCA2 proteins play important roles in maintaining genomic stability. BRCA1 is primarily involved in DNA damage response, cell-cycle regulation, and repair of double-strand DNA breaks. BRCA2 plays a critical role in homologous recombination by facilitating RAD51-mediated DNA repair. Defects in these genes lead to defective DNA repair pathways, which predispose individuals to the development of breast and ovarian cancers.[5,6] Women carrying BRCA1 mutations have an estimated lifetime risk of ovarian cancer of approximately 39–46%, whereas BRCA2 mutation carriers have a lifetime risk of approximately 10–

27%. [7]These risks are significantly higher compared with the general population lifetime risk of ovarian cancer, which is approximately 1–2%. The prevalence of BRCA mutations varies widely depending on geographic location, ethnicity, and histological subtype of ovarian cancer. The highest prevalence is observed in high-grade serous ovarian carcinoma, where mutation rates may reach up to 20–25%. [8] In contrast, lower mutation frequencies are reported in endometrioid, mucinous, and clear cell carcinomas.

Studies conducted in India have reported BRCA mutation prevalence ranging from 12% to 30% among ovarian cancer patients.[9] However, there is limited data regarding the prevalence of these mutations in eastern India, particularly in the state of Odisha.

Identification of BRCA mutations has important clinical implications. Tumors with BRCA mutations often show increased sensitivity to platinum-based chemotherapy[10]. More importantly, the discovery of PARP inhibitors has revolutionized the treatment of ovarian cancer. These targeted therapies exploit the concept of synthetic lethality in tumors with defective homologous recombination repair.[11-13]

In addition to therapeutic implications, BRCA testing provides an opportunity for genetic counseling and preventive interventions among family members. Risk-reducing surgeries such as prophylactic salpingo-oophorectomy and enhanced breast cancer screening strategies can significantly reduce cancer incidence in high-risk individuals.[14]

Therefore, the present study was conducted to determine the prevalence of BRCA1 and BRCA2 gene mutations in patients with epithelial ovarian cancer treated at a tertiary care center in Odisha.

MATERIALS AND METHODS

Study Design

This study was designed as a cross-sectional analytical study conducted in the Department of Gynecologic Oncology at a tertiary care center in Odisha.

Study Period

The study was conducted over a period of 1 year and 7 months.

Study Population

Patients diagnosed with epithelial ovarian cancer, primary peritoneal carcinoma, or fallopian tube carcinoma during the study period were included in the study.

Sample Size

A total of 566 patients meeting the eligibility criteria were included.

Inclusion Criteria

Patients were included if they met the following criteria:

- Histopathologically confirmed epithelial ovarian cancer
- Primary peritoneal carcinoma
- Fallopian tube carcinoma
- Provided written informed consent for participation in the study

Exclusion Criteria

Patients were excluded if they:

- Did not provide written informed consent
- Had non-epithelial ovarian malignancies

Data Collection

After obtaining written informed consent, relevant clinical and demographic data were collected. Information recorded included patient age, family history of breast or ovarian cancer, medical and surgical history, stage of disease, histopathological subtype, and tumor grade. These data were recorded in electronic case report forms.

Radiological Evaluation

Radiological investigations included contrast-enhanced computed tomography (CECT) of the abdomen and pelvis and high-resolution computed tomography (HRCT) of the thorax to determine the extent of disease and staging.

Genetic Testing

Genetic testing was performed to identify germline and somatic BRCA mutations.

Germline mutation analysis was performed using peripheral blood samples. Tumor tissue samples were used for detecting somatic mutations. Genetic testing was conducted using Next Generation Sequencing (NGS) technology in collaboration with inDNA Life Sciences. The testing was provided free of cost to patients.

Counseling and Follow-Up

Patients identified with germline BRCA mutations were counseled regarding cancer risk and preventive strategies. Family members were encouraged to undergo genetic testing so that appropriate risk-reduction strategies could be implemented. All BRCA-positive patients were advised to undergo regular breast cancer screening through mammography.

Statistical Analysis
The prevalence of BRCA mutations was calculated using descriptive statistics. Patients were categorized into BRCA-positive and BRCA-negative groups for analysis.

RESULTS
A total of 566 patients with epithelial ovarian cancer were included in the study during the study period of 1 year and 7 months.

Age Distribution
The mean age of the patients was 47 years, with an age range of 20 to 65 years.

Prevalence of BRCA Mutations
Among the 566 patients included in the study, 64 patients (11.3%) were found to have BRCA gene mutations.
Among the mutation-positive patients:

- 41 patients (7.24%) had BRCA1 mutations
- 23 patients (4.06%) had BRCA2 mutations

Thus, BRCA1 mutations accounted for approximately 64% of mutation-positive cases, while BRCA2 mutations accounted for approximately 36%.

TABLE 1: DISTRIBUTION OF BRCA GENE MUTATIONS(BRCA MUTATION STATUS)

VARIANT	BRCA 1 mutation (41)	BRCA 2 mutation (23)
Pathogenic	27	14
Likely Pathogenic (L.P)	8	5
Variant of Uncertain Significance (VUS)	6	4

FIGURE 1: DISTRIBUTION OF BRCA MUTATIONS AMONG PATIENTS

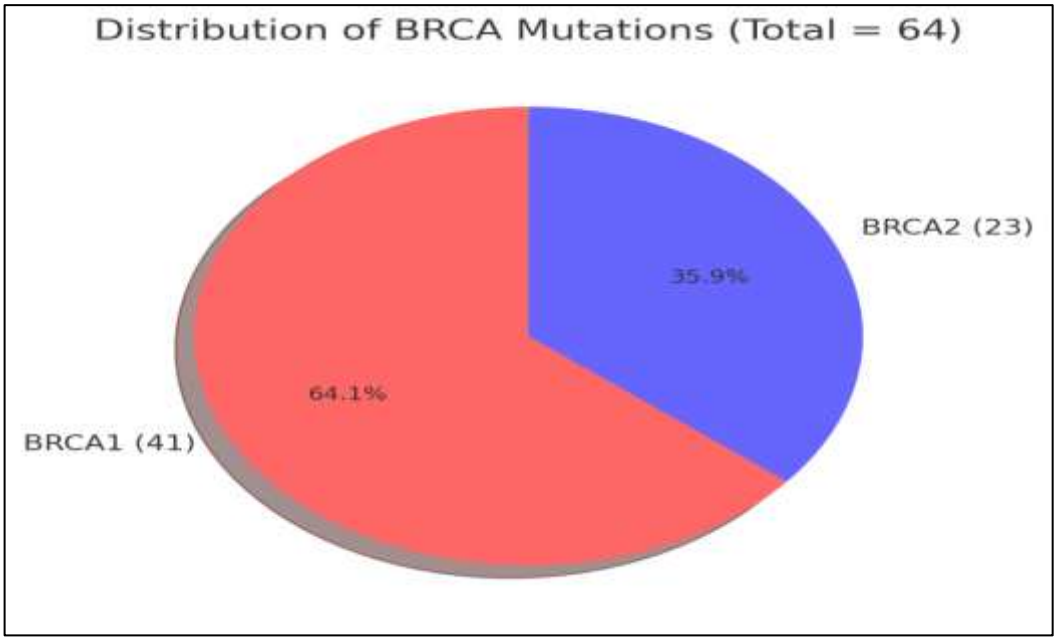
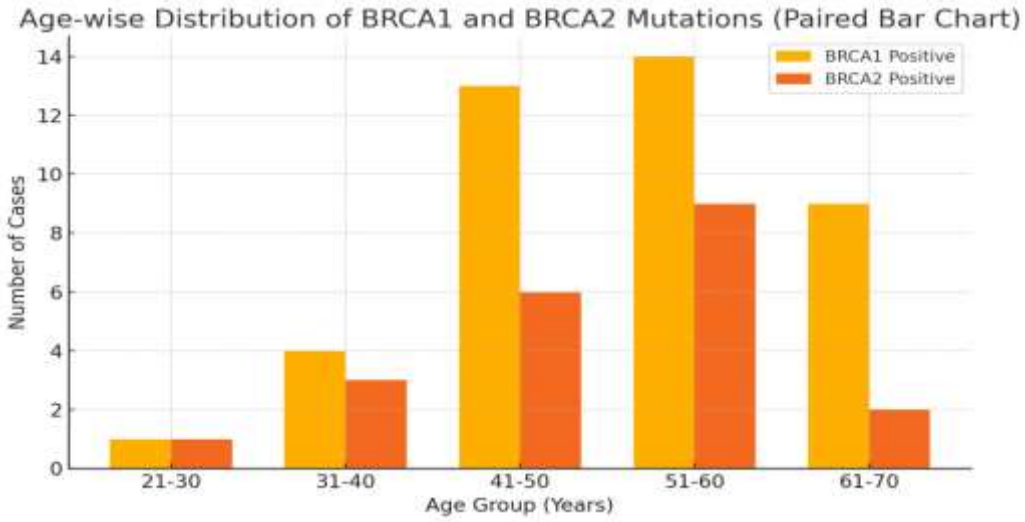


Figure legend: Distribution of BRCA gene mutations among epithelial ovarian cancer patients showing predominance of BRCA1 mutations

- BRCA1 mutation – 64%
- BRCA2 mutation – 36%

FIG 2: AGE WISE DISTRIBUTION OF BRCA MUTATIONS



Family History

Among the 64 patients who tested positive for BRCA mutations, 11 patients reported a positive family history of breast or ovarian cancer.

TABLE 2: FAMILY HISTORY AMONG BRCA MUTATION POSITIVE PATIENTS

Parameter	**Number of Patients**
BRCA mutation positive patients	64
Patients with positive family history	11
Patients without family history	53

Histopathological Distribution

The histopathological distribution of cases was as follows:

- High-grade serous ovarian carcinoma (HGSOC): 470 cases
- Endometrioid carcinoma: 58 cases
- Low-grade serous ovarian carcinoma (LGSOC): 17 cases
- Mucinous carcinoma: 21 cases

High-grade serous ovarian carcinoma constituted the majority of cases and demonstrated the strongest association with BRCA mutations.

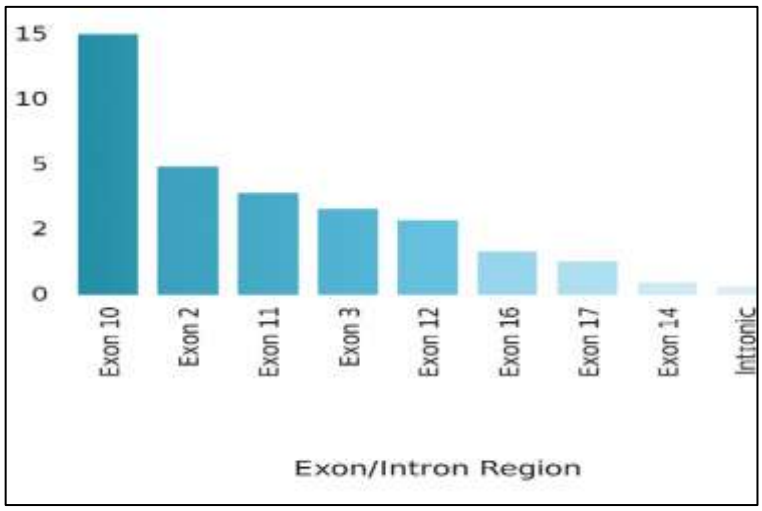
TABLE 3: HISTOPATHOLOGICAL DISTRIBUTION OF EPITHELIAL OVARIAN CANCER

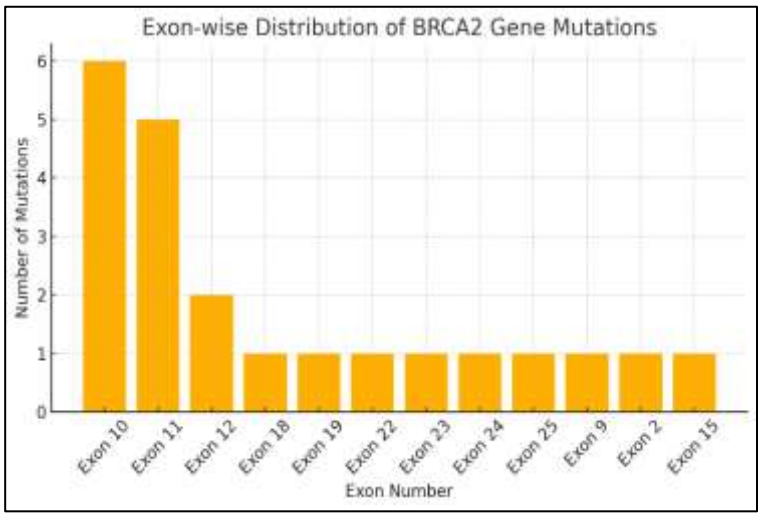
Histologic Subtype	**BRCA1 Positive (n)**
High-grade serous carcinoma (HGSOC)	**38**
Endometrioid carcinoma	**2**
HGSOC + Carcinoma breast	**1**
Low-grade serous carcinoma (LGSOC)	**0**
Mucinous carcinoma	**0**

Exon Distribution

Exon-wise analysis of BRCA1 and BRCA2 mutations revealed heterogeneous distribution across different exons of both genes.

FIG3: EXONWISE DISTRIBUTION OF BRCA GENE MUTATION





DISCUSSION

Hereditary ovarian cancer accounts for a significant proportion of epithelial ovarian malignancies, with BRCA1 and BRCA2 mutations being the most important genetic determinants. Identification of these mutations has profound implications for personalized therapy, targeted treatment strategies, and preventive interventions among high-risk individuals.

In the present study, the prevalence of BRCA mutations among epithelial ovarian cancer patients was found to be **11.3%**, which is consistent with the prevalence reported in international literature, where BRCA mutations account for approximately **8–13% of ovarian cancer cases**.[1,8] This finding supports the importance of routine genetic testing in ovarian cancer patients to identify individuals who may benefit from targeted therapies.

BRCA1 mutations were more common than BRCA2 mutations in this study, accounting for approximately **64% of mutation-positive cases**, while BRCA2 mutations accounted for **36%**. This predominance of BRCA1 mutations is consistent with previous studies, which have demonstrated that BRCA1 mutations contribute to the majority of hereditary ovarian cancers. [2,7]The higher frequency of BRCA1 mutations may be related to the greater penetrance and earlier onset of disease associated with BRCA1 gene alterations.

The mean age of patients in this study was **47 years**, which is relatively younger compared with Western populations where the median age at diagnosis of ovarian cancer is typically above 60 years. Similar observations have been reported in other Indian studies, suggesting that ovarian cancer may occur at a younger age in the Indian population.[9] This difference may be influenced by genetic, environmental, and socioeconomic factors.

Another important observation in the present study was that only **11 out of 64 BRCA mutation-positive patients reported a positive family history** of breast or ovarian cancer. This highlights a critical limitation of relying solely on family history to identify individuals at risk of hereditary cancer syndromes. Many patients carrying pathogenic mutations may not have a strong family history due to small family size, incomplete penetrance, or lack of awareness of cancer history in relatives. Therefore, universal or broader BRCA testing strategies may be more effective in identifying mutation carriers.

The majority of cases in this study were **high-grade serous ovarian carcinoma (HGSOC)**, which accounted for 470 cases. High-grade serous carcinoma is known to be strongly associated with BRCA mutations and defects in homologous recombination repair pathways. This subtype is characterized by aggressive clinical behavior but also demonstrates improved response to platinum-based chemotherapy due to underlying DNA repair defects.[11-13]

The identification of BRCA mutations has significant therapeutic implications. Tumors harboring BRCA mutations show increased sensitivity to platinum-based chemotherapy and respond favorably to **Poly (ADP-ribose) polymerase (PARP) inhibitors**, which have emerged as a major advancement in ovarian cancer treatment. PARP inhibitors exploit the concept of synthetic lethality by targeting cancer cells with defective homologous recombination repair mechanisms. Clinical trials have demonstrated improved progression-free survival among BRCA-mutated ovarian cancer patients receiving PARP inhibitor therapy.

Beyond therapeutic benefits, genetic testing also provides opportunities for cancer prevention in family members. Relatives of patients with BRCA mutations can undergo genetic testing to identify carriers of pathogenic variants. Individuals identified as mutation carriers may benefit from risk-reducing strategies such as **risk-reducing salpingo-oophorectomy, prophylactic mastectomy, and enhanced breast cancer screening through mammography and MRI**. These preventive measures can significantly reduce cancer incidence and improve long-term outcomes in high-risk populations.[14]

The present study also demonstrates the feasibility of integrating genetic testing into routine oncological practice, particularly when collaborative programs are available to reduce financial barriers for patients. Providing genetic testing free of cost can significantly improve access to personalized cancer care in resource-limited settings.

However, certain limitations should be acknowledged. This study was conducted at a single tertiary care center, and therefore the findings may not be fully representative of the entire population of Odisha or eastern India. Additionally, long-term survival outcomes and treatment responses were not evaluated as part of this study.

Future multicenter studies involving larger patient populations and long-term follow-up are required to better understand the regional prevalence of BRCA mutations and their impact on treatment outcomes in ovarian cancer patients.

CONCLUSION

This study demonstrated that the prevalence of BRCA mutations among epithelial ovarian cancer patients in our tertiary care center in Odisha was 11.3%. BRCA1 mutations were more frequently observed than BRCA2 mutations.

Identification of BRCA mutations plays a crucial role in guiding targeted therapy with PARP inhibitors and enables genetic counseling for family members at risk. Routine BRCA testing in patients with epithelial ovarian cancer may improve personalized treatment strategies and facilitate preventive interventions for high-risk individuals.

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