fortune Journals

Research Article

JOURNAL OF WOMENS HEALTH AND DEVELOPMENT

ISSN: 2644-2884

Current Understanding of the Epidemiology and Clinical Implications of BRCA1 and BRCA2 Mutations for Epithelial Ovarian Cancer

Jannatul Ferdous[1], Jakanta Faika[2], Muhammad Mobarock Hossain[3], Moniruzzaman Khan[4], Mohuwa Parvin[5], Kashfia Binte Quasem[6], Mahira Zehreen Khan[7], Moktadir Mobarock Monsur Hossain[8]

Abstract

Background: BRCA1 and BRCA2 gene mutations are critical genetic factors associated with an increased risk of developing epithelial ovarian cancer (EOC). Understanding the epidemiology and clinical implications of these mutations is essential for effective risk assessment, treatment planning, and patient management.

Objectives: To assess the clinical implications of BRCA1 and BRCA2 mutations on the prognosis and treatment outcomes of epithelial ovarian cancer patients.

Methods: This retrospective study was conducted at BSMMU and Lab Aid Cancer Hospital & Super Speciality Center, Department of Gynecological Oncology, from April 2020 to September 2023, including 130 patients diagnosed with epithelial ovarian cancer. All patients underwent genetic testing to identify BRCA1 and BRCA2 mutations.Clinical data, including patient demographics, family history, tumor characteristics, and treatment outcomes, were collected from medical records. Statistical analyses of the results were be obtained by using window-based Microsoft Excel and Statistical Packages for Social Sciences (SPSS-24).

Results: Of the 130 patients, 90 patients were belonged in group of BRCA1 and 40 were in group of BRCA2. Patients with BRCA mutations had a younger median age at diagnosis and were more likely to have a family history of breast or ovarian cancer. BRCA mutation carriers showed a better response to platinum-based chemotherapy, with a higher overall survival rate compared to non-carriers. However, these patients also exhibited a higher risk of developing secondary malignancies, emphasizing the need for ongoing surveillance and tailored treatment strategies.

Conclusion: The presence of BRCA1 and BRCA2 mutations in epithelial ovarian cancer patients has significant clinical implications, influencing treatment response and long-term outcomes. The study highlights the importance of genetic testing for BRCA mutations in the management of ovarian cancer, particularly in identifying patients who may benefit from targeted therapies and personalized care. Further research is warranted to optimize treatment protocols and improve survival rates in this high-risk population.

Keywords: Epidemiology; Clinical implication; BRCA1; BRCA2mutation; Epithelial ovarian cancer

Introduction

Germline mutations in the tumor suppressor genes BRCA1 (NCBI Entrez Gene 672) and BRCA2 (NCBI Entrez Gene 675) are the strongest known

Affiliation:

[1]Professor, Department of Gynecological Oncology, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka, Bangladesh

[2]Medical Officer, Department of Gynecological Oncology, Mugda Medical College and Hospital

[3]Assistant Professor, Department of Cardiology, Uttara Adhunik Medical College Hospital, Dhaka, Bangladesh

[4]Professor, Department of Physical Medicine and Rehabilitation, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka, Bangladesh

[5]Resident, Department of Gynecological Oncology, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka, Bangladesh

[6]Resident, Department of Gynecological Oncology, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka, Bangladesh

[7]Level A Student, Scholastica, Dhaka, Bangladesh.

[8]Double major in Molecular Biology Immunology and Disease and Neuroscience, University of Toronto, 27 King's College Cir, Toronto, ON M5S 1A1, Canada.

***Corresponding Author**
Jannatul Ferdous, Professor, Department of Gynecological Oncology, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka, Bangladesh.

Citation: Jannatul Ferdous, Jakanta Faika, Muhammad Mobarock Hossain, Moniruzzaman Khan, Mohuwa Parvin, Kashfia Binte Quasem, Mahira Zehreen Khan, Moktadir Mobarock Monsur Hossain. Current Understanding of the Epidemiology and Clinical Implications of BRCA1 and BRCA2 Mutations for Epithelial Ovarian Cancer. Journal of Women's Health and Development. 7 (2024): 104-109.

Received: October 08, 2024
Accepted: October 14, 2024
Published: October 29, 2024

Ferdous J, et al., J Women's Health Dev 2024
DOI:10.26502/fjwhd.2644-288400126

genetic risk factors for breast and epithelial ovarian cancer (EOC), occurring in 6% to 15% of women with EOC. [1,2] BRCA1 is involved in DNA repair, cell cycle checkpoint control, chromatin remodeling, transcriptional regulation, and mitosis, whereas BRCA2 plays a key role in homologous recombination. [3] Clinical characteristics of EOCs in BRCA1/2 carriers differ from those in noncarriers. BRCA1-related illness is more likely to have a serous histology, be high grade, and progress to an advanced stage. [4] There is less evidence available for BRCA2-related EOC due to their lower frequency and EOC penetrance compared to BRCA1, although a similar pattern is frequently described [5]. Germ-line mutations in the BRCA1 or BRCA2 genes significantly increase the risk of developing ovarian cancer over one's life. The prevalence of highly penetrant germ-line BRCA mutations in most populations is less than 0.5%, with the striking exception of Ashkenazi Jews. [6,7] Identifying BRCA mutation carriers is a significant achievement since these women can consider prophylactic oophorectomy and other ways to reducing ovarian cancer mortality; yet, because BRCA mutations are rare, the overall impact on mortality will unavoidably be minimal [8].

BRCA1 and 2 were found in families with multiple early onset breast or ovarian cancers. It is predicted that high penetrance mutations in these genes cause approximately 10% of ovarian cancers. [9] However, research comparing the prevalence of ovarian cancer in identical and fraternal twins found that 22% of cases are heritable. [10] Although other unknown high penetrance genes may exist, there may be weakly penetrant functional genetic polymorphisms that contribute to the burden of ovarian cancers categorized as "sporadic" due to the absence of other cases in a pedigree. Because BRCA1 and BRCA2 mutations significantly increase ovarian cancer risk, polymorphisms in these genes are reasonable candidates for identifying low penetrance susceptibility alleles. N372H is the only amino acid-changing polymorphism in the BRCA2 gene with a rare allele frequency of more than 6%, and HH homozygotes had a higher risk of breast cancer, according to a major case-control study. [11] An Australian study later observed that homozygosity for the H allele was related with an elevated risk of both breast and ovarian cancer. [12]

Methodology

This retrospective study was conducted at BSMMU and Lab Aid Cancer Hospital & Super Speciality Center, Department of Gynecological Oncology, from April 2020 to September 2023, including 130 patients diagnosed with epithelial ovarian cancer. All patients underwent genetic testing to identify BRCA1 and BRCA2 mutations. Clinical data, including patient demographics, family history, tumor characteristics, and treatment outcomes, were collected from medical records. The prevalence of BRCA mutations was determined, and their impact on treatment response, particularly to platinum-based chemotherapy, as well as overall survival rates, was analyzed. Statistical analyses were performed to evaluate the correlation between BRCA status and clinical outcomes, with a focus on identifying significant predictors of prognosis and treatment efficacy.

Results

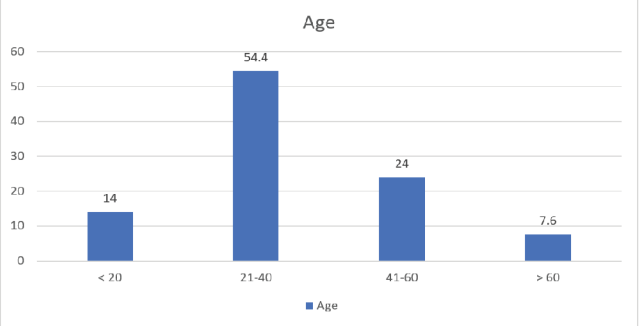

Figure 1: Age distribution of the patients (n=130).

Figure I show, age distribution of the patients, age between <20 - >60 years. It observed that, <20 patients were 14%, 21-40 patients were 54.4%, 41-60 patients were 4% and >60 were 7.6%.

Table 1: Distribution of the study population according to characteristics. (n=130).

Characteristics	BRCA1 (n=90)	BRCA2 (n=40)
Diagnosis to study entry	2	2
median (IQR), mo	(0-18)	(0-17)
Follow-up	61	69
median (IQR), mo	(18-66)	(21-75)
Year of EOC diagnosis	2021	2022
median (range)	(2020-2023)	(2020-2023)
Deaths within 4 y of EOC	25	12
diagnosis, No. (%)	-19.3	-9.23

Table 2: Distribution of the study population according to Histology. (n=130).

Histology	BRCA1 (n=90)	BRCA2 (n=40)	*P* Value
Serous	78 (86.6%)	28 (70%)	0.18
Mucinous	9 (10%)	0 (0%)	0.31
Endometroid	86 (95.55%)	24 (60%)	0.14
Clear cell	15 (16.66%)	6 (15%)	0.38
Other	10 (1.11%)	5 (12.5%)	
Carcinoma, not otherwise specified	80 (88.88%)	18 (45%)	
Missing	75 (83.33%)	38 (95%)	

Citation: Jannatul Ferdous, Jakanta Faika, Muhammad Mobarock Hossain, Moniruzzaman Khan, Mohuwa Parvin, Kashfia Binte Quasem, Mahira Zehreen Khan, Moktadir Mobarock Monsur Hossain. Current Understanding of the Epidemiology and Clinical Implications of BRCA1 and BRCA2 Mutations for Epithelial Ovarian Cancer. Journal of Women's Health and Development. 7 (2024): 104-109.

Ferdous J, et al., J Women's Health Dev 2024
DOI:10.26502/fjwhd.2644-288400126

Table I shows characteristics status of the study population, it was observed that, according to diagnosis to study entry, the median was 0-18 in BRCA1 and 0-17 in BRCA2. And according to follow-up, the median was 18-66 in BRCA1 and 21-75 in BRCA2. According to deaths within 4 y of EOC diagnosis, 19.3 in BRCA1 and 9.23 in BRCA2.

Table II shows the study population according to histology, it was observed that, the serous was 86.6% in BRCA1 and 70% in BRCA2. And according to Endometroid 95.55% was in BRCA1 and 60% in BRCA2. According to Carcinoma, not otherwise specified, 88.88% was in BRCA1 and 45% in BRCA2. The difference was not statistically significant (p>0.05) between two groups.

Table 3: Distribution of the study population according to Grade. (n=130).

Grade	BRCA1 (n=90)	BRCA2 (n=40)	*P* Value
Well differentiated	22 (24.44%)	12 (30%)	
Poorly differentiated	82 (91.11%)	28 (70%)	0.37
Undifferentiated	66 (73.33%)	24 (60%)	
Missing	52 (57.77%)	26 (65%)	

Table III shows the study population according to grade, it was observed that, the well differentiated was 24.44% in BRCA1 and 30% in BRCA2. And according to poorly differentiated 91.11% was in BRCA1 and 70% in BRCA2. According to Undifferentiated, 73.33% was in BRCA1 and 60% in BRCA2. The difference was not statistically significant (p>0.05) between two groups.

Table IV shows the study population according to stage (FIGO), it was observed that, the stage I was 93.33% in BRCA1 and 55% in BRCA2. And according to stage II, 78.88% was in BRCA1 and 32.50% in BRCA2. According to stage III, 77.77% was in BRCA1 and 90% in BRCA2. The difference was not statistically significant (p>0.05) between two groups.

Table 4: Distribution of the study population according to Stage (FIGO). (n=130).

Stage (FIGO)	BRCA1 (n=90)	BRCA2 (n=40)	*P* Value
I	84 (93.33%)	22 (55%)	
II	71 (78.88%)	13 (32.50%)	
III	70 (77.77%)	36 (90%)	0.007
IV	87 (96.66%)	27 (67.50%)	
Missing	83 (92.22%)	22 (55%)	

Table 5: Effect of BRCA1/2 Mutations on All-Cause Mortality in Adjusted Models Stratified by Selected Subgroups.

Subgroups	BRCA1 (n=90)	BRCA2 (n=40)	*P* Value
Stage			
Localized	61 (67.77%)	22 (55%)	0.51
Advanced	68 (75.55%)	34 (85%)	0.01
Grade			
Well differentiated	82 (91.11%)	35 (87.50%)	0.03
Poorly undifferentiated	67 (74.44%)	28 (70%)	0.01
Histology			
Nonserous	27 (30%)	37 (92.50%)	0.75
Serous	61 (67.77%)	17 (42.50%)	0.01
High-grade serous	59 (65.55%)	31 (77.50%)	0.01
Breast cancer before or during study period			
No	73 (81.11%)	25 (62.50%)	0.08
Yes	55 (61.11%)	33 (82.50%)	0.42

Table V shows the effect of BRCA1/2 mutations on all-cause mortality in adjusted models stratified by selected subgroups. It was observed that, according to stage, localized and advanced were 67.77% and 75.55% in BRCA1 and 55% and 85% in BRCA2 respectively. And well differentiated and poorly undifferentiated were 91.11% and 74.44% in BRCA1 and 87.50% and 70% in BRCA2 respectively.

Discussion

This cross-sectional study was carried out in the Department of Gynecological Oncology, Bangabandhu Sheikh Mujib Medical University, Dhaka. During April 2020 to September 2023 of study period, total 130 samples were included in this study, among them 90 patients were in group BRCA1 and 40 were in group BRCA2. Only ovarian cancer has a genetic proportion more than 10% among the most frequent cancers in adults. [13] Risch discovered that 11.7% of 515 unselected women with invasive ovarian cancer in Ontario had a BRCA1 or BRCA2 mutation, 7% for BRCA1 and 4% for BRCA2. Women with BRCA1 mutations were diagnosed at an average age of 51.2 years, compared to 57.5 years for those with BRCA2 mutations. BRCA1 mutations accounted for 83% of all mutations detected in women under the age of 50, while BRCA2 mutations accounted for 60% of those diagnosed after the age of 60. Jewish women are far more likely to have mutations. Moslehi discovered that 41% of Jewish women with ovarian cancer had one of three common founder mutations, including the majority of those diagnosed between the ages of 40 and 60. [14] Modan discovered a mutation in 29% of 40 Jewish women diagnosed with ovarian cancer in Israel [15]. There are various hypotheses about the

Ferdous J, et al., J Women's Health Dev 2024
DOI:10.26502/fjwhd.2644-288400126

histologic origin of ovarian carcinoma. Most people assume that ovarian malignancies develop in the ovary's epithelial component, however it is unclear whether they originate in the single-cell layer of surface epithelium or in architectural aberrations of the surface epithelium. The latter include surface epithelial-lined clefts and cortical inclusion cysts. These are thought to be the result of wound repair following ovulation, tissue remodeling caused by pregnancy or aging, paraovarian adhesions, or the dynamic interplay between the surface epithelium and the underlying stroma.

Our findings show that individuals with EOC with germline BRCA1 and BRCA2 mutations have a better chance of survival, with BRCA2 carriers having the best prognosis. BRCA1 carriers developed EOC at a younger age than BRCA2 carriers, which is consistent with the age-related pen-etrances for BRCA1 versus BRCA2 carriers. The pathological characteristics of BRCA1- and BRCA2-related malignancies are similar; however, they differ from tumors in noncarriers. In contrast, breast cancer exhibits significant variations between BRCA1- and BRCA2-associated illness. [16] BRCA1 and BRCA2 mutations appeared to have similar effects on survival in patients with both localized and advanced-stage cancers, as well as serous and nonserous tumors. The lack of a survival advantage for BRCA1 and BRCA2 mutation carriers with low grade disease suggests that disruptions of the BRCA1/2 pathways may not be as important in the etiology of these tumors, which supports previous evidence of etiologic heterogeneity between high and low-grade serous carcinomas [17]. Several research groups have now investigated whether morphologic changes to the ovarian surface epithelium are more common in women with ovarian cancer or those who are at high genetic risk for ovarian cancer than in healthy controls. [19] However, these types of modifications are ubiquitous; it has not been established that they occur at a higher frequency than expected in cancer-prone ovaries, and these investigations have yielded few insights as to the tumor's origins. Another idea suggests that ovarian carcinomas develop in the secondary Mullerian system, including rete ovarii, paraovarian or paratubal cysts, endosalpingiosis, endometriosis, or endomucinosis, which are found within or near the ovary. [20] As a result, if these tumors develop from the ovarian epithelium, a metaplastic process must occur during ovarian carcinogenesis. Some ovarian cancers develop within endometriosis implants. [21] Some believe that the lower risk of ovarian cancer after tubal ligation indicates that ovarian cancers may be metastatic fallopian tube cancers [22]. If surgical prophylaxis is to be the cornerstone of ovarian cancer prevention, women must be provided with the best possible treatment to alleviate acute menopausal symptoms and prevent the chronic effects of estrogen deprivation. A young woman having surgical menopause should have her bone mineral density and lipid profile checked. It is unclear whether hormone replacement therapy raises the risk of breast cancer in BRCA mutation carriers. If the woman has had a bilateral mastectomy and has no prior history of breast cancer, hormone replacement treatment is a reasonable option. There is currently no consensus on the use of hormone replacement treatment for women who have intact breasts. When using hormone replacement treatment, it's best to avoid using progesterone. Several studies have found that the progesterone component considerably increases the risk of developing breast cancer. [23] Most doctors are reluctant to administer estrogen to high-risk women, therefore alternatives must be sought. The management of surgical menopause should be customized and tailored to the woman's specific concerns and symptoms [24].

The most significant advantage and disadvantage of our study is that it is based on a heterogeneous population; these data were gathered from studies including different ethnic groups, using various mutation screening approaches and case ascertainment. By including a wide range of studies, we were able to obtain a big enough sample size to effectively address the issue of heterogeneity in the survival effect across BRCA1 and BRCA2 carriers. Differences in study design and population may restrict the specificity of the conclusions reached. Furthermore, varying levels of misclassification of BRCA status and other variables of interest may have influenced our estimations to the null.

Limitations of the study

The present study was conducted in a very short period due to time constraints and funding limitations. The small sample size was also a limitation of the present study.

Conclusion

BRCA1 and BRCA2 mutations are major genetic contributors to hereditary ovarian cancer, specifically epithelial ovarian cancer (EOC), which is the most common histological subtype of ovarian cancer. Unaffected women who are determined to have a mutation are at a higher risk of ovarian cancer. Prophylactic oophorectomy eliminates the majority of the risk, although the probability of primary peritoneal cancer remains. The fallopian tubes must be completely removed since they can be the source of primary cancers. Prior to oophorectomy, tubal ligation and oral contraception can minimize the incidence of ovarian cancer. BRCA1 and BRCA2 mutations play a critical role in both the epidemiology and treatment of epithelial ovarian cancer, with significant implications for cancer risk, management, and targeted therapies. Genetic testing and precision medicine approaches continue to evolve, offering hope for better outcomes for patients with BRCA-associated ovarian cancer.

Recommendation

This study can serve as a pilot to much larger research involving multiple centers that can provide a nationwide picture, validate regression models proposed in this study for

Citation: Jannatul Ferdous, Jakanta Faika, Muhammad Mobarock Hossain, Moniruzzaman Khan, Mohuwa Parvin, Kashfia Binte Quasem, Mahira Zehreen Khan, Moktadir Mobarock Monsur Hossain. Current Understanding of the Epidemiology and Clinical Implications of BRCA1 and BRCA2 Mutations for Epithelial Ovarian Cancer. Journal of Women's Health and Development. 7 (2024): 104-109.

future use and emphasize points to ensure better management and adherence.

Acknowledgements

The wide range of disciplines involved in a study defining the current understanding of the epidemiology and clinical implications of BRCA1 and BRCA2 mutations for epithelial ovarian cancer research means that editors need much assistance from referees in the evaluation of papers submitted for publication. I would also like to be grateful to my colleagues and family who supported me and offered deep insight into the study.

Reference

1. Zhang S, Royer R, Li S, et al. Frequencies of BRCA1 and BRCA2 mutations among 1,342 unselected patients with invasive ovarian cancer. Gynecologic oncology 121 (2011): 353-357.
2. Pal T, Permuth-Wey J, Betts JA, et al. BRCA1 and BRCA2 mutations account for a large proportion of ovarian carcinoma cases. Cancer: Interdisciplinary International Journal of the American Cancer Society 104 (2005): 2807-2816.
3. O'Donovan PJ, Livingston DM. BRCA1 and BRCA2: breast/ovarian cancer susceptibility gene products and participants in DNA double-strand break repair. Carcinogenesis 31 (2010): 961-967.
4. Lakhani SR, Manek S, Penault-Llorca F, et al. Pathology of ovarian cancers in BRCA1 and BRCA2 carriers. Clinical Cancer Research 10 (2004): 2473-2481.
5. Cass I, Baldwin RL, Varkey T, et al. Improved survival in women with BRCA-associated ovarian carcinoma. Cancer: Interdisciplinary International Journal of the American Cancer Society 97 (2003): 2187-2195.
6. Whittemore AS, Gong G, Itnyre J. Prevalence and contribution of BRCA1 mutations in breast cancer and ovarian cancer: results from three US population-based case-control studies of ovarian cancer. American journal of human genetics 60 (1997): 496.
7. Szabo CI, King MC. Population genetics of BRCA1 and BRCA2. American journal of human genetics. 1997 May;60(5):1013.
8. Eisen A, Rebbeck TR, Wood WC, et al. Prophylactic surgery in women with a hereditary predisposition to breast and ovarian cancer. Journal of Clinical Oncology 18 (2000): 1980-1995.
9. Frank TS, Manley SA, Olopade OI, et al. Sequence analysis of BRCA1 and BRCA2: correlation of mutations with family history and ovarian cancer risk. Journal of Clinical Oncology 16 (1998): 2417-2425.
10. Lichtenstein P, Holm NV, Verkasalo PK, et al. Environmental and heritable factors in the causation of cancer—analyses of cohorts of twins from Sweden, Denmark, and Finland. New England journal of medicine 343 (2000): 78-85.
11. Healey CS, Dunning AM, Dawn Teare M, et al. A common variant in BRCA2 is associated with both breast cancer risk and prenatal viability. Nature genetics 26 (2000): 362-364.
12. Auranen A, Spurdle AB, Chen X, et al. BRCA2 Arg372Hispolymorphism and epithelial ovarian cancer risk. International journal of cancer 103 (2003): 427-430.
13. Risch HA, McLaughlin JR, Cole DE, et al. Prevalence and penetrance of germline BRCA1 and BRCA2 mutations in a population series of 649 women with ovarian cancer. The American Journal of Human Genetics 68 (2001): 700-710.
14. Moslehi R, Chu W, Karlan B, et al. BRCA1 and BRCA2 mutation analysis of 208 Ashkenazi Jewish women with ovarian cancer. The American Journal of Human Genetics 66 (2000): 1259-1272.
15. Lu KH, Garber JE, Cramer DW, et al. Occult ovarian tumors in women with BRCA1 or BRCA2 mutations undergoing prophylactic oophorectomy. Journal of clinical oncology 18 (2000): 2728-2732.
16. Lakhani SR, Van De Vijver MJ, Jacquemier J, et al. The pathology of familial breast cancer: predictive value of immunohistochemical markers estrogen receptor, progesterone receptor, HER-2, and p53 in patients with mutations in BRCA1 and BRCA2. Journal of clinical oncology 20 (2002): 2310-2318.
17. Singer G, Stöhr R, Cope L, et al. Patterns of p53 mutations separate ovarian serous borderline tumors and low-and high-grade carcinomas and provide support for a new model of ovarian carcinogenesis: a mutational analysis with immunohistochemical correlation. The American journal of surgical pathology 29 (2005): 218-224.
18. Yang D, Khan S, Sun Y, et al. Association of BRCA1 and BRCA2 mutations with survival, chemotherapy sensitivity, and gene mutator phenotype in patients with ovarian cancer. Jama 306 (2011): 1557-1565.
19. Tresserra F, Grases PJ, Labastida R, et al. Histological features of the contralateral ovary in patients with unilateral ovarian cancer: a case control study. Gynecologic Oncology 71 (1998): 437-441.
20. Dubeau L. The cell of origin of ovarian epithelial tumours. The lancet oncology 9 (2008): 1191-1197.
21. Chapman WB. Developments in the pathology of ovarian tumours. Current Opinion in Obstetrics and Gynecology 13 (2001): 53-59.

Ferdous J, et al., J Women's Health Dev 2024
DOI:10.26502/fjwhd.2644-288400126

22. Narod S. Tubal ligation and risk of ovarian cancer. The Lancet 358 (2001): 844.

23. Ross RK, Paganini-Hill A, Wan PC, et al. Effect of hormone replacement therapy on breast cancer risk: estrogen versus estrogen plus progestin. Journal of the National Cancer Institute 92 (2000): 328-332.

24. Schairer C, Lubin J, Troisi R, et al. Menopausal estrogen and estrogen-progestin replacement therapy and breast cancer risk. Jama 283 (2000): 485-491.

Citation: Jannatul Ferdous, Jakanta Faika, Muhammad Mobarock Hossain, Moniruzzaman Khan, Mohuwa Parvin, Kashfia Binte Quasem, Mahira Zehreen Khan, Moktadir Mobarock Monsur Hossain. Current Understanding of the Epidemiology and Clinical Implications of BRCA1 and BRCA2 Mutations for Epithelial Ovarian Cancer. Journal of Women's Health and Development. 7 (2024): 104-109.