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BRCA1 Gene 5382insC Polymorphism and its Associated Risk Factor among Breast Cancer Patients in the University of Gondar Comprehensive Specialized and Felege Hiwot Referral Hospital, Northwest Ethiopia

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ABSTRACT

Background: Breast cancer is the most common cancer that causes death among women worldwide. In Ethiopia, though there has not been an adequate study, the incidence of new cases of breast cancer is currently increasing and has become one of the most common cancer types, causing high rates of morbidity and mortality. Mutation in the BRCA1 gene in 5832insC regions has been demonstrated as the most common genetic factor that increases the occurrence of breast cancer. Thus, this study aimed to detect the frequency of 5832insC gene polymorphism in the BRCA1 gene and its associated risk factors among breast cancer-positive patients visiting the study sites.

Materials and Methods: A cross-sectional study was conducted on 100 blood samples of females with breast cancer. Following genomic DNA isolation, PCR amplification was done using specific primer pairs for 5832insC BRCA1 regions. The amplified products were digested with restriction enzymes (HinfI) to detect 5382insC polymorphism.

Results: Based on the findings of this study, family history was the only variable that had a significant association (P = 0.001) with 5382insC mutation in the BRCA1 gene. On the other hand, alcohol consumption (P = 0.542), age (P = 0.376), and residence zone (P = 0.856) of the participant did not show any association for this mutation. The total frequency of 5382insC BRCA1 gene mutations in the study participants was found to be 6%.

Conclusion: The present study confirmed that 5382insC was the potential BRCA1 alterations that have been encountered in most breast cancer patients in the study area. The use of molecular techniques for early breast cancer detection is highly recommended to improve treatment efficiency and minimize the rate of mortality.

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List of Abbreviations and Acronyms
BP: Base Pair
BRCA: Breast Cancer Gene
BSE: Breast Self-Examination
CI: Confidence of Interval
CSA: Central Statistical Agency
DNA: Deoxy Ribonucleic Acid
EDTA: Ethylene diamine tetra acetic acid
GWAS: Genome-Wide Association Studies
KAP: Knowledge Attitude Practice
KB: Kilo Base
MIM: Molecular Interaction Map
NGS: Next-Generation Sequencing
OR: Odds Ratio
PALB: Partner And Localizer of BRCA
PCR: Polymerase Chain Reaction
RFLP: Restriction Fragment Length Polymorphism
SNP: Single Nucleotide Polymorphism
SSA: Sub-Saharan Africa
UV: Ultra Violet
WHO: World Health Organization
ML: Micro Litter

Introduction

Breast cancer is a condition when the breast's cells proliferate uncontrollably. At first, the malignant development is limited to the duct or lobule, where it usually presents with no symptoms and a little chance of spreading. These in situ tumors may eventually spread to the surrounding lymph nodes, breast tissue, and other bodily organs [1]. It is one of the most common types of cancer and contributes to high mortality among women [2]. Following lung cancer in women, breast cancer is the most frequent cancer [3]. A WHO study (2020) announced that 685,000 people died globally and 2.3 million women received a breast cancer diagnosis [4].

Sub-Saharan Africa (SSA) is facing an increasing incidence of breast cancer, a disease that is a major public health concern [5]. While breast cancer incidence is currently lower in SSA compared with high-income countries, mortality rates are disproportionately high, and incidence is increasing [6]. Even though well-organized data on the national prevalence picture is limited in Ethiopia, some research from various parts of the country has reported that the risk of new cases of breast cancer is currently growing, resulting in high rates of morbidity and mortality [2]. According to a population-based register data investigation, breast cancer is the most common illness in Ethiopia, accounting for 23% of all cancers and 33% of cancers in women. [7].

The chance of getting breast cancer can be increased by several factors, including sex, age, estrogen, family history, gene mutations, and an unhealthy lifestyle. [8]. Several studies have found that, among all the risks, the genetic component has a significant role in the development of breast cancer [9]. One of the main causes of breast cancer is mutations in tumor suppressor genes, namely breast cancer genes 1 and 2. They are the most common breast cancer-susceptible genes in clinical practice and play a great role in damaged DNA repair mechanisms.

Since the detection of BRCA1 and 2 about 20 years ago, linkage analysis has been used to identify other high-penetrance susceptibility genes [5]. The genes' locations were first discovered as linkage peaks on chromosomes 17q21 and 13q12 in investigations of just 23 and 15 families, respectively. Women carrying mutations in the BRCA1 and 2 genes will increase the risk of developing breast cancer in their lives, particularly at the age of 70 (45–85%) compared with the general population (12.5%) [10]. There are several forms of mutations reported in BRCA genes, such as frameshift mutations, which occur when either deletion or insertion of one or more nucleotides results in a missing or non-functional product [7]. Various studies in different parts of the world regarding the mutations of the BRAC1 and BRAC2 genes have come up with different results. In a study conducted by Jaure et al. (2015) [11], it was reported that these mutations in the BRAC1 gene increase the risk of breast cancer significantly in the Argentine population [12].

Different mutation regions have been reported in the BRCA1 gene that exceeds 600, which increases the risk of developing breast cancer. Among those mutation regions, 5382insC polymorphic in the BRCA1 gene is the most frequent, and this mutation is higher in Ashkenazi Jews [13]. These founder mutations are also found in several countries or ethnic groups, including Turkey, Canada, France, and several populations in Europe [14].

The most critical point for the best prognosis is to identify early-stage cancer cells. The gene mutations could serve as an early diagnosis of breast cancer, which will reduce mortality due to intervention [15]. Moreover, this gene detection technique using PCR is less expensive and less resource intensive and could serve as an early diagnostic means for breast cancer and also provide basic data regarding the frequency of 5382insC polymorphic among the study participants [13]. Thus, this study aimed to investigate the frequency of the 5382insC polymorphic region in the BRCA1 gene using the PCR-RFLP technique, which is a useful early diagnostic strategy for breast cancer in the study area.

Materials and Methods

Study Area

The study was conducted at selected hospitals in the Amhara region of northwest Ethiopia. The Amhara region comprises West Gojam, East Gojam, Bahir Dar City, South Gondar, and the Central, West, and North Gondar Zones. Each of these zones has hospitals situated in the capital of the respective zone. Out of the total area of the Amhara region (154,708.96 km2), the study area covers 146,705.14 km2. According to the 2015 census by the Central Statistics Agency, the total population of the Amhara region was 20,018,988. Of which the population within the study area sums up to 2,786,962 [16].

Study Design, Period and Population

A cross sectional study was conducted to determine the frequency of 5382insC polymorphism and its associated risk factor among breast cancer patients who visited the University of Gondar Comprehensive Specialized Hospital and Felege Hiwot Referral Hospital from November 2021 to June 2022. Physicians and laboratory technicians at each of the hospitals were responsible for taking blood samples and interviewing the patients with their consent. Individuals between the ages of 15 and 80 who visited those hospitals and were diagnosed with breast cancer were included. However, individuals who have other serious communicable and mental illnesses were not recruited for this study. The study laboratory procedure was carried out at the University of Gondar, Institute of Biotechnology, and molecular biology laboratory.

Sampling Technique and Sample Collection

A non-randomized purposive sampling technique was used for collecting blood samples from breast cancer patients. Based on the population density, a total of 100 blood samples were collected proportionally from each institution. 55 samples were gathered at the University of Gondar Comprehensive Specialized Hospital, designated as "D," and 45 samples were taken from Felege Hiwot Referral Hospital, represented as "B." Three milliliters of blood were collected using EDTA-coated cutaneous tubes from each study participant. The blood samples were transported to the University of Gondar molecular biology laboratory, Institute of Biotechnology. The socio-demographic data of all the participants was taken from the registration book based on parameters including age, sex, location, and alcohol consumption. All collected samples were tested and analyzed according to standard testing procedures.

Laboratory Protocol

DNA Extraction

Genomic DNA was isolated using the Gene EluteTM mammalian Genomic DNA Purification Kit (SIGMA-ALDRICH) according to the manufacturer's instructions. The quality of the gDNA was checked by nanodrop and gel electrophoresis (1.5%). The DNA was stored at -20 °C and used as a template for PCR.

PCR Amplification and Gel Electrophoresis

Forward primer 5'ATATGACGTGTCTGCTCCAC'3 and reverse primer 5'AGTCTTACAAAATGAAGCGG sequence were used to amplify the BRAC1 gene, which contains a 259-bp-sized 5382insC polymorphic region [17]. The PCR reaction contained: 2µl DNA, 4µl of 5X FIRPOL Master Mix Ready to Load (Solis Bio Dyne, Riia, Tartu, Estonia, and Europe), 0.5µl each forward and reverse primer, and 13µl dH2O with a total volume of 20µl. PCR was carried out using a TC-04 thermocycler. The PCR condition was as follows: initial denaturation at 95 °C for 5 min, followed by 30 cycles of denaturation at 94 °C for 1 min, annealing at 59 °C for 30 seconds, extension at 72 °C for 1 min, and final extension at 72 °C for 7 min. The PCR products were visualized using gel electrophoresis on 2% agarose gel in 1x TAE buffer (Blulux, India). The gels were stained with ethidium bromide and observed with a UV detector [18]. Moreover, the approximate molecular

sizes of the amplicons were determined using the molecular weight markers 100 and 50 bp DNA Ladder (HIMEDIA, Swastik Disha Business Park, Mumbai, India).

Restriction Fragment Length Polymorphism

Restriction enzyme (HinfI) was used to determine the single nucleotide polymorphism (SNP) according to the manufacturer's instructions (Merck, India), and DNA fragments were resolved by using 2% agarose under gel electrophoresis.

Data Analysis

The socio-demographic parameters, frequency, and associated risk factors were tabulated and recorded properly using SPSS version 23. Data like age at diagnosis, alcohol consumption, residence, and family history from the demographic data and the frequency of the 5382insC polymorphic region in the BRCA1 gene were analyzed using descriptive statistics. Based on the results from demographic parameters, the prevalence of breast cancer was tabulated and recorded. The association between the 5382insC polymorphism and risk factors for the study subject was analyzed using binary logistic regression and properly interpreted. The odds ratio and their related 95% confidence interval (CI) were calculated. A P value ≤ 0.05 was regarded as significant.

Results

Socio Demographic Parameter of Study Participants

The descriptive data presents the frequency and percentage of socio-demographic characteristics of breast cancer patients at the University of Gondar Comprehensive Specialized Hospital and Felege Hiwot Referral Hospital in Ethiopia during the years 2021–2022, as shown in Table 1.

Table 1: Demographic Characteristics of the Study Participants

Character		Frequency (n)	Percent (%)	Cumulative percent (%)
Age	< 30 year	8	8	8
	30-39 year	25	25	33
	40-49 year	38	38	71
	50-59	17	17	88
	≥60 year	12	12	100
Alcohol consumption	Yes	28	28	28
	No	72	72	100
Family history	Yes	17	17	17
	No	83	83	100
	South Gondar	11	11	11
	North Gondar	16	16	27
	Central Gondar	11	11	38
Residence Zone	Gondar city	16	16	54
	West Gojam	22	22	76
	East Gojam	14	14	90
	Bahir Dar city	10	10	100
Total		100	100	100

3.2. Detection of 5382insC polymorphic regions Using PCR-RFLP

The amplification process results in 259 bp-sized 5382insC polymorphic regions of the BRCA1 gene, which were visualized using a 2% agarose gel as shown in Figure 1.

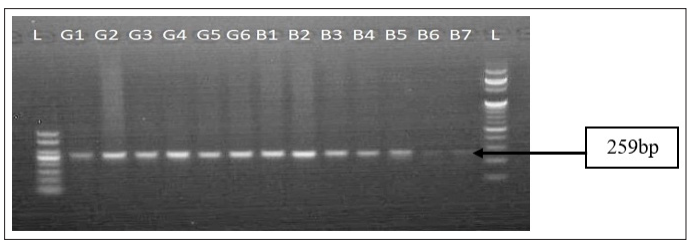

Figure 1: Agarose gel electrophoresis shows PCR amplification; lanes G1 to G6, followed by B1-B7: amplification bands of 259 bp; lane L: 50 bp and 100 bp size DNA markers, respectively

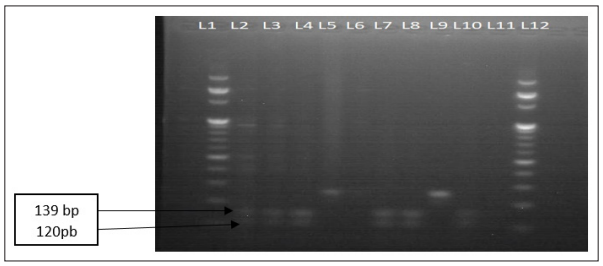

Figure 2: Representative agarose gel electrophoresis image of BRCA1 gene restriction digestion with HinfI, using 2% agarose. Based on the restriction result, lanes 5 and 9 represent the 5382insC undigested mutant allele; lanes 2, 3, 4, 7, 8, and 10 represent the wild-type allele, having 139 and 120 bp-sized products; Lanes 6 and 11: no template; L1: 50 bp-sized and L12: 100 bp-sized DNA markers, respectively.

Association between socio-demographic data and 5382insC polymorphism in BRCA1 gene

A chi-square test and binary logistic regression result indicated that study participants with a positive family history at diagnosis were significantly associated with the 5382insC mutation, as presented in Tables 2 and 3, respectively.

Table 2: The Association between Socio-Demographic Data and BRCA1 5382insC Polymorphism in the Study Participants

Variable	Category	Detection of 5382insC polymorphism		x^2 value	P (≤ 0.05)
		No	Yes		
Family history	No	81	2	11.159	0.001
	Yes	13	4		
Alcohol consumption	No	71	4	9.964	0.542
	Yes	23	2		
	South Gondar	10	1		
	North Gondar	16	0		
	Central Gondar	11	0		
Residence zone	Gondar city	15	1		
	West Gojam	20	2	2.600	0.856
	East Gojam	13	1		
	Bahirdar	9	1		
	<30 years	8	0		
Age groups	30-39 years	23	2		
	40-49 years	36	2	4.230	0.376
	50-59 years	17	0		
	≥60 years	10	2		

* The above data were the responses of the study participants for each variable, the frequency of 5382incCmutation for each category, the x2 value, and the p-value (P ≤ 0.05), in which the significant associations of variables with 5382insC mutation were determined.

Table 3: Binary Logistic Regression Analysis of Risk Factors and 5382insc Brca1 Gene Polymorphism in the Study Participants (Breast Cancer Patients)

Dependent variable	Variables	(β)	0R	95% confidence of interval		Sig. (p≤0.05)
Detection of BRCA15382insC polymorphism	Family history	0.246	1.27	1.130	1.362	0.000
	Alcohol	-.068	0.93	0.074	1.262	0.581
	<30 years	0.950	2.58	0.880	2.810	0.999
	30-39 years	0.833	2.30	0.863	2.929	0.436
	40-49 years	1.281	3.60	0.940	3.862	0.228
	50-59 years	0.957	2.60	0.871	2.938	0.890
	≥ 60 years	0[a]				
	S. Gondar	0.105	1.11	0.609	1.220	0.944
	N. Gondar	0.369	1.44	0.892	1.630	0.999
	C. Gondar	0.360	1.43	0.885	1.563	0.990
	Gondar city	0.511	1.66	0.982	3.403	0.729
	W. Gojam	0.105	1.11	0.103	2.631	0.935
	E. Gojam	0.368	1.44	0.531	3.267	0.804
	Bahir Dar city	0[a]				

* The above data (beta coefficient value (β), odd ratio, 95% confidence interval, followed by the significant value (p≤ 0.05)) were used to determine the potential risk factors of *the BRCA1* 5382insC mutant allele. "S. Gondar: South Gondar; N. Gondar: North Gondar; C. Gondar: Central Gondar; Gondar City; W. Gojam: West Gojam; E. Gojam: East Gojam; and Bahir Dar City" represents where the study participants are located. Where 0a was used as a reference during binary regression analysis of each age group and location.

Discussion

This study was conducted to determine the frequency of 5382insC polymorphism in the BRCA1 gene and its associated risk factor among 100 breast cancer patients visiting Bahir Dar Felege Hiwot and the University of Gondar Comprehensive Specialized Hospital from November 2021 to June 2022. Of the total participants, 28% were alcohol consumers, and 72% were not alcohol consumers. The majority of the study groups were within the age category of 40–49 years, with a mean age of 43.73 ± 9.980. The youngest and oldest age groups, which are<30 and ≥60, represent a minority group of cases with percentages of 8% and 12%, respectively. Concerning the family history of the study subject, most of the study participants did not have a family history with a frequency of 87%, and the rest had a family history with a total frequency of 13%.

In the present study, the overall frequency of 5382insC polymorphism polymorphisms in the BRCA1 gene mutation in the study participants was found to be 6%, similar to a study conducted in Ukraine 5.81% [19]. But the frequency of the BRCA1 5382insC mutation is variable among different populations: 2.5% to 7.1% in Ukraine [20], 1% in Pakistan [21], 5% in Egypt [22], and 7.60% in Eastern India [13]. This might be due to the impacts of socio-demographic factors and the number of study participants considered. Furthermore, this specific mutation in exon2 is the second most commonly observed BRCA1 mutation worldwide, found in Asian, American, African, and European populations [23]. It is also recognized as a founder mutation in Russian and Turkish populations [24]. Thus, this study revealed that the presence of the 5382insC polymorphism was detected in breast cancer patients within the research location.

A chi square test and binary logistic regression were conducted for all samples to analyze the association between risk factors and 5382insC polymorphism in the BRCA1 gene among breast cancer patients. Based on the analysis results of this finding, there has been a significant link between family history and 5382insC mutation. The likelihood of getting BRCA1 5382insC in the study participants with family history (OR: 1.27, P< 0.001) exceeded by 27% as compared to breast cancer patients with no family history. Likewise, a study in Egypt [18, 22] and in South India [25] showed that 5382insC mutation has a significant association with family history among breast cancer patients. Unlike the present findings, the studies in Ukraine [19], South India [26], and Eastern India [27] suggest that the BRCA1 5382insC gremlin mutation is frequent in breast cancer patients, irrespective of family history. The absence of the 5382insC polymorphism in breast cancer patients who have a family history of the disease suggests that there may be other types of harmful mutations and risk factors that could be responsible for the development of breast cancer.

In the present study, age did not show any significance in increasing the risk of 5382insC mutation, which was in line with the previous study conducted in East Iran [28]. The study in Ukraine [19] represents a frequency of occurrence of 5382insC 7/79 (8.9%) for individuals under age 40 and 2/114 (1.8%) for patients older than 40 years. Meanwhile, the study participant's geographic location was not shown to be substantially linked with an increased frequency of 5382insC polymorphism in the BRCA1 gene. However, other studies have reported that there is a significant difference in the frequency of 5382insC mutations across the country [18, 23]. Such variation might be due to the proximity of the locations in which the study participants were selected. There was no significant relationship between alcohol consumption and this type of mutation, comparable to previous studies in Western countries and France [29, 30].

Conclusion

In this study, the BRCA1 5382insC founder mutation was detected at 6% carrier frequency, which is comparable to worldwide frequencies. BRCA1 5382insC did not show any association with the increased age, alcohol consumption, or geographic location of the study participants. Interestingly, and in contrast to other reports, this study suggested a strong association between the occurrence of 5382insC mutation frequencies and the family history of breast cancer patients. Thus, based on the results of the present study, family history was the only probable risk factor for BRCA1 5382insC mutation-type breast cancer patients. Generally, cancer treatment centers can use the results of this study to develop rational healthcare strategies and formulate novel drugs, mainly for breast cancer patients. Moreover, additional research with a large sample size and assessment in different breast cancer-endemic areas of the Amhara region and other parts of the country is recommended.

Institutional Review Board Statement

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Review Board (or Ethics Committee) of the Institute of Biotechnology, University of Gondar (IOB/139/11/2022).

Data Availability Statement

The data is available upon request from the corresponding author.

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Authors Contributions

N.B; Conceptualization, Supervision, and Project administration: T.E, M.M, and Y.J; Methodology, Investigation, Software, Writing original draft.

Declaration of Interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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References

1. DeSantis CE, Bray F, Ferlay J, Lortet Tieulent J, Anderson BO, et al. (2015) International variation in female breast cancer incidence and mortality rates. Cancer epidemiology, biomarkers & prevention 24: 1495-1506.
2. Deressa BT, Cihoric N, Badra EV, Tsikkinis A, Rauch D (2019) Breast cancer care in northern Ethiopia–cross-sectional analysis. BMC cancer 19: 1-6.
3. Ginting SF, Syukur S, Ibrahim S,Tjong DH (2017) The Influence of Estradiol and HDL-Cholesterol Levels on Breast Cancer in Pre-menopause and Menopause Women and Its Correlation with BRCA1 Gene C61G Mutation. American Scientific Journal for Engineering Technology and Sciences (ASRJETS] 38: 250-257.
4. Berhane NZ, Chekol A, Seid (2023) Detecting the Frequency of c. 5946delT Pathogenic Variant in the BRCA2 Gene and Associated Risk Factors Among Breast Cancer Patients Visiting Felege Hiwot Referral Hospital and University of Gondar Comprehensive Specialized Hospital. Breast Cancer: Targets and Therapy 421-427.
5. Tsu VDJ, Jeronimo J, BO Anderson (2013) Why the time is right to tackle breast and cervical cancer in low-resource settings. Bulletin of the World Health Organization 91: 683-690.
6. Sighoko, D., et al., Breast cancer in pre-menopausal women in West Africa: analysis of temporal trends and evaluation of risk factors associated with reproductive life. The Breast, 2013. 22(5): p. 828-835.
7. Memirie ST, Habtemariam MK, Asefa M, Deressa BT, Abayneh G,et al. (2018) Estimates of cancer incidence in Ethiopia in 2015 using population-based registry data. Journal of Global Oncology 4: 1-11.
8. Majeed W, Aslam B, Javed I, Khaliq T, Muhammad F, et al. (2014) Breast cancer: major risk factors and recent developments in treatment. Asian Pacific Journal of Cancer Prevention 15: 3353-3358.
9. Michailidou K, Beesley J, Lindstrom S, Canisius S, Dennis J, et al. (2015) Genome-wide association analysis of more than 120,000 individuals identifies 15 new susceptibility loci for breast cancer. Nature Genetics 47: 373-380.
10. Kwong A (2016) Genetic testing for hereditary breast cancer in Asia—moving forward. Chinese Clinical Oncology.
11. Jaure O, Alonso EN, Braico DA, Nieto A, Orozco M, et al. (2015) BRCA1 polymorphism in breast cancer patients from Argentina. Oncology Letters 9: 845-850.
12. Chen S, Parmigiani G (2007) Meta-analysis of BRCA1 and BRCA2 penetrance. Journal of clinical oncology: official journal of the American Society of Clinical Oncology 25: 1329.
13. Chakraborty A, Banerjee D, Basak J, Mukhopadhyay A (2015) Absence of 185delAG and 6174delT mutations among breast cancer patients of eastern India. Asian Pacific Journal of Cancer Prevention 16: 7929-7933.
14. Anis A (2015) Mutations and cancer genesis highlights on BRCA1 and BRCA2 Genes. J Cancer Prev Curr Res 2: 00063.
15. Park JM, Yoon GS, Kim SM, Ahn SH (2003) Sonographic detection of multifocality in breast carcinoma. Journal of Clinical Ultrasound 31: 293-298.
16. Beyene A, Tamene H, Kebede F, Helmut K (2015) Current state and trends of access to sanitation in Ethiopia and the need to revise indicators to monitor progress in the Post-2015 era. BMC Public Health 15: 1-8.
17. Singh A, Pandey A, Tewari M, Pandey P, Pandey HP, et al. (2015) BRCA1 Gene's EXON 11 and breast carcinoma: A mutational hot spot for familial patients and prone to metastases in Northern India. J Clin Exp Pathol 5: 2161-06811000219.
18. Rizk MM, El etreby NM, El Attar LM, Elzyat EA, Saied MH (2022) A case-control study of BRCA1 founder mutations 185delAG and 5382insC in a cohort of Egyptian ovarian cancer patients using pyrosequencing technique. Egyptian Journal of Medical Human Genetics 23: 11.
19. Gorodetska I, Serga S, Levkovich N, Lahuta T, Ostapchenko L, et al. (2015)The frequency of BRCA1 founder mutation c. 5266dupC (5382insC) in breast cancer patients from Ukraine. Hereditary cancer in clinical practice 13: 1-3.
20. Kitsera N, Shparyk YV, Bilynskyy BT, Tryl OV, Mashalyga MS, et al. (2012) Analysis of mutations in the genes BCRA1/2 in patients with family/hereditary breast cancer which live in the Lviv region (Ukraine). Onkologiia 11: 44-9.
21. Rashid MU, Muhammad N, Naeemi H, Khan FA, Hassan M, et al. (2019) Spectrum and prevalence of BRCA1/2 germline mutations in Pakistani breast cancer patients: results from a large comprehensive study. Hereditary cancer in clinical practice 17: 1-13.
22. Mogahed SHG, Hamed YS, Moursy YEI, Saied MHM (2020) Analysis of heterozygous BRCA1 5382ins founder mutation in a cohort of Egyptian breast cancer female patients using the pyrosequencing technique. Asian Pacific Journal of Cancer Prevention: APJCP 21: 431.
23. Kharel S, Shrestha S, Yadav S, Shakya P, Baidya S, et al. (2022) BRCA1/BRCA2 mutation spectrum analysis in South Asia: a systematic review. Journal of International Medical Research 50: 03000605211070757.
24. Lang GT, Shi JX, Hu X, Zhang CH, Shan L, et al. (2017) The spectrum of BRCA mutations and characteristics of BRCA-associated breast cancers in China: Screening of 2,991 patients and 1,043 controls by next-generation sequencing. International journal of cancer 141: 129-142.
25. John AO, Singh A, Joel A, Yadav P, Thumaty DB, et al. (2022) BRCA1 and BRCA2 gene mutation spectrum and a high frequency of BRCA1 185delAG among breast and ovarian cancer patients from Southern India.
26. Rajagopal T, Seshachalam A, Jothi A, Rathnam KK, Talluri S, et al. (2022) Analysis of pathogenic variants in BRCA1 and BRCA2 genes using next-generation sequencing in women with triple-negative breast cancer from South India. Molecular Biology Reports 49: 3025-3032.
27. Chakraborty A, Mukhopadhyay A, Bhattacharyya D, Bose CK, Choudhuri K, et al. (2013) Frequency of 5382insC mutation of BRCA1 gene among breast cancer patients: an experience from Eastern India. Familial cancer 12: 489-495.
28. Khalili Tanha G, Sebzari A, Moodi M, Hajipoor F, Naseri M (2019) Mutations analysis of BRCA1 gene in patients with breast cancer in South Khorasan province, East Iran. Medical Journal of the Islamic Republic of Iran 33: 105.
29. Li H, Terry MB, Antoniou AC, Phillips KA, Kast K, et al. (2020) ConFab Investigators. Alcohol consumption, cigarette smoking, and risk of breast cancer for BRCA1 and BRCA2 mutation carriers: results from The BRCA1 and BRCA2 Cohort Consortium. Cancer Epidemiology, Biomarkers & Prevention 29: 368-378.
30. Lecarpentier J, Nogues C, Mouret Fourme E, Stoppa Lyonnet D, Lasset C, et al. (2011) Variation in breast cancer risk with mutation position, smoking, alcohol, and chest X-ray history, in the French National BRCA1/2 carrier cohort (GENEPSO). er research and treatment 130: 927-938.