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An psychological study on BRCA1 Gene Polymorphisms in Iraqi Breast Cancer Patients

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Abstract:
Background: Breast cancer and a few other malignancies are significantly more likely to develop in people who carry BRCA1 mutations, according to research. One of the most well-known tumor suppressor gene mutations is the 185delAG change in BRCA1. Resources and Techniques Examining the frequency of these BRCA1 mutations in familial and sporadic breast cancer cases in Iraq was the objective of a recent study. Participants in the study comprised 50 girls with sporadic breast cancer, 50 girls with a first-degree cousin who had the disease, and 50 girls in good health
In conclusion, the results of this investigation demonstrated that of the aforementioned founder mutations had been identified in the agencies analyzed. According to our research, breast cancer patients in Iraq have more frequent 185delAG mutations in BRCA1.

Keywords: An psychological study**;** BRCA1 , breast cancer , mutation

INTRODUCTION

Due to hereditary changes in the breast cancer susceptibility gene 1, women of specific ages and ethnic groups are more likely to develop breast and ovarian cancer (BRCA1). These clearly defined, highly penetrant genes exhibit loss-of-full characteristic germ line mutations in hereditary instances, and their expression is reduced in sporadic malignancies [2]. Hereditary factors account for roughly 5–10% of all incidences of breast cancer with an early onset. The 185del AG mutation in the breast cancer susceptibility gene 1 (BRCA1) is one of the most precisely identified mutations associated with an increased risk of breast cancer. (3) and (4) Modern research aims to investigate the clinico-pathological elements of breast tumors and to carry out genetic testing for the 185del AG gene. (5) The range of mutations in these genes varies throughout populations, with some exhibiting an excessive frequency of uncommon mutations [6]. Such changes usually result from a founder effect in isolated communities [7], and they might also be the cause of population-specific variations in the likelihood of getting the majority of malignancies (8).

METHOD AND MATERIALS

The Margan Hospital for Research in Applied and Experimental Medicine at the National University of Science once hosted the authors' study. The BRCA1 gene mutational screening in cases of breast and ovarian cancer, both hereditary and sporadic, was the main focus of this investigation. In order to search for the BRCA1 gene, all exonintron boundaries have been sequenced. In the past, the BRCA1 exon-intron boundaries were amplified by polymerase chain reaction (PCR) using oligonucleotide primers made from the gene's intronic regions.

Sampling and document gathering

In this experiment, 100 samples were protected, of which 50 were classified as routine samples and 50 as samples from patients who had breast cancer complaints (control group). The patients ranged in age from 26 to 70. Three to five milliliters of blood were drawn into vacutainer tubes with EDTA acting as the anticoagulant in order to extract the DNA and carry out the subsequent PCR analysis. After being transferred, the blood samples were stored at -20 °C in the Laboratory of Genetic Engineering Department of the Biotechnology Research Center until needed.

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DNA extraction

DNA genes were previously extracted using blooding and EDTA tubes from all things using a Mini Kit (FAVORGENE). The amount of pure (ng/ml) DNA that is eliminated has been calculated at 260 nm and 280 nm using a NanoDrop of spectrophotometer (OPTIZENn POP – Korea).(Ishraq and Rabab,2018)

Genotyping

White blood cells (WBCs) were utilized to extract genomic DNA using the (Favrogene) DNA extraction kit for both diabetes and management organizations. selected BRCA1 185delAG

Common ahead (P1) 5' ggttggcagcaatatgtgaa
Wild-type reverse (P2) 5' gctgacttaccagatgggactctc 335 bp
Mutant reverse (P3) 5' cccaaattaatacactcttgtcgtgacttaccagatgggacagta 354 bp

PCR-amplified with an annealing temperature of 55.3, and the PCR-ARMS technique was used for analysis. The thermo cycler was programmed to start with a denaturation step at 94 °C for 6 min (including polymerase activation); after this first step, 35 cycles were performed, each consisting of 30 seconds of primer denaturation at 94 °C, 30 seconds of primer annealing at 54 °C, 30 seconds of primer extension at 72 °C, and finally a 10-minute extension step at 72 °C. After electrophoresis on a 2% agarose gel at 5-8 V/cm (Rede safe) Statics, genomic DNA and PCR products were separated, assessed, and stained using a safe stain. The outcomes were evaluated statistically using Qi Square, the t test, and a one-way ANOVA with a 0.05 p cost. BRCA1 185delAG was chosen by the extraction toolkit.

Results AND DISCUSSION

Recent analysis results reveal that the DNA has (50-200)ng and righteousness (1.7-2.2), as shown in parent (1) Numerous studies have been made regarding its genotyping, and the BRCA1 gene used to be associated with risky development in higher examiners. It was once suggested that existing tests examine genotyping BRCA1 similarly to contaminated DNA because of these findings

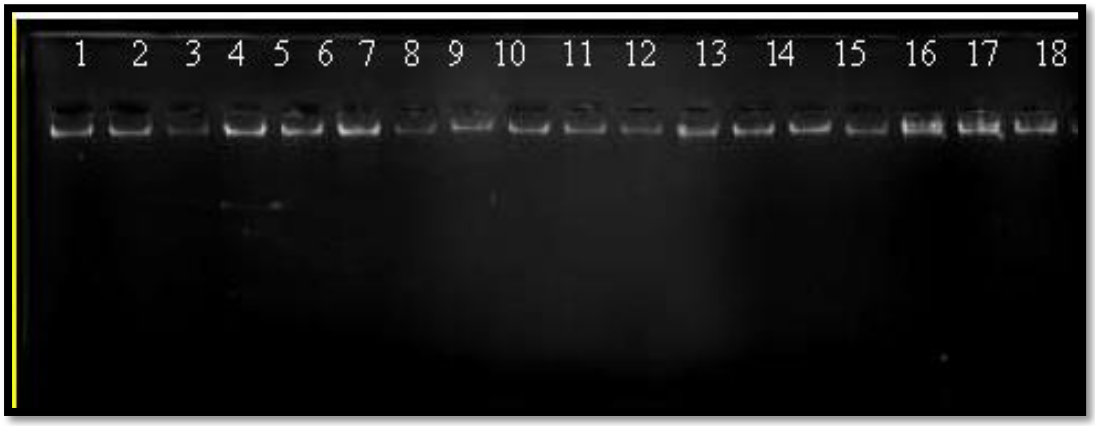

Figure 4-4 : Electrophoresis pattern of gnomic DNA extracted from blood samples of patients and healthy control groups. Lane 1 refers to genomic DNA from blood samples (1-10 patients & 11-18 control) ; Electrophoresis conditions, 1% agarose, red safe stained 5 Ml for 15 min on high (50 volt) &60 min on low.

A breast cancer-related fine polymorphism in the BRCA1 gene was discovered in the most recent research. This information was discovered regarding genotype and allele frequencies in the BRCA1 gene. The distribution of the BRCA1 gene's 185delAG mutation in control subjects and ovarian cancer patients is shown in Table 1. In controls, there were 52% WW, 32% WM, and 16% MM, and 18%, 46% WM, and 36% MM in cases. Comparing patients to controls, a higher frequency of heterozygotic mutan genotypes (WM) had been found. Before, there was a statistically significant difference in the allele frequency distribution between patients and controls (W v/s M: 2 P0.0001, OR 0.3640 95% CI 0.2027 to 0.6537)

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Table 1: Allelic frequencies and the distribution of the 185delAG mutation in patients and control subjects

Genotypes	Patients (N=50)		Control (N=50)	OR(95%CI)	P-value
BRCA1	W/W[a], n(%)	9(18%)	26 (52%)		
	W/ M, n(%)	23(46%)	16 (32%)	0.24 (0.08 - 0.64)	0.004*
	M /M, n(%)	18 (36%)	8 (16%)	0.15 (0.05 - 0.47)	< 0.001 *
Allele Frequency					
	W, n (%)	41 (0.41)	68 (0.68)	0.32 (0.18 - 0.58)	<0.001*
	M, n (%)	59 (0.53)	32 (0.32)		

WW-homozygous wild , WM-heterozygous, MM-homozygous mutant

P<0.005:OR =(95%Cl): [a] Reference

The results of these tests on Group A revealed that all nine DNA samples were homozygous (both alleles are normal) and that mutations had previously been found. The results of amplification using wild-type specific primers are depicted in Figure 1. (p1, p2) As a result of the presence of wild type alleles in these samples, 335bp ARMS PCR product was found in lanes 1WM, 2MM, 3WM, 4WT, 5 WT,6WM, 7WM, 6WM and 9WM,. The segment of 354bp was no longer detectable in the mutant kind lanes (2MT) since this mutation was not present in the samples.

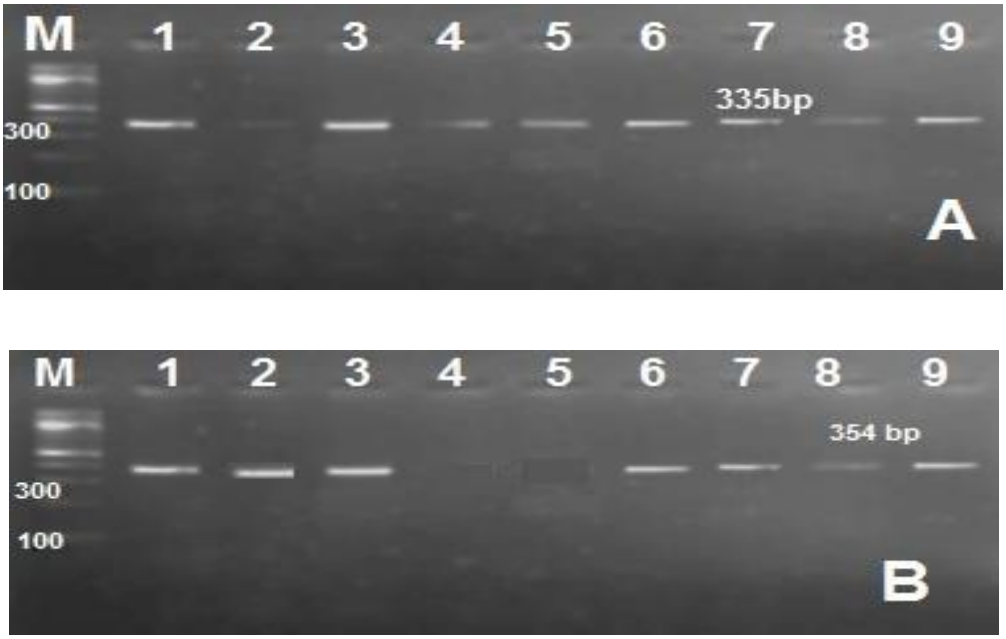

Fig. 1 Figure -1: Represents amplification Products of BRCA1 Exon 2; A: wild-type alleles with 335bp by wild-type specificprimers (p1, p2) with DNA samples in Group B: Mutant-type alleles with 354bp by mutan -type specificprimers (p1, p3) with DNA samples in Group A. On a 2% agarose gel, electrophoresis was carried out using 5-8 V/cm for two hours. There was a DNA molecular marker in Lane M. (1500-50 bp).

When first discovered, Ashkenazi Jews exhibited an abnormally high frequency of the mutation 185delAG (Friedman et al., 1995; Struewinget al., 1995). However, in our research for Group A (25–35) years, the 185delAG mutant was no longer found at this age. This conclusion was shared by (Trincado et al., 1999), who similarly missed the 185delAG mutation in fifty-five Chilean women who had breast cancer, 40 of whom had sporadic breast cancer and 15 of whom had a good family history. The focus of a lot of recent research has been on finding mutations in breast and ovarian cancer.

In general, breast cancer can develop at any age, but younger women are significantly less likely to develop the disease (Mathew et al., 2004).The results of these tests for the 185delAG mutation in Group B samples proved once more that out of 22 DNA samples, 22 were consistently homozygous, and no mutation was found in these samples.

The wild-type pieces are in lanes, as seen in Figure 2. (1WT, 2WT, 3WT, 4WT, 5WT). Due to the absence of mutations or mutant segments 354 bp in lanes 1MT, 2MT, 3MT, 4MT, and 5MT, mutant fragments are no longer present in these lanes.

The results of these trials were in agreement with searches that were recommended in China using (Ikeda et al., 2001; Zhiet al., 2002). These investigations also Japanese families no longer included the 185delAG mutation. However, it has been noted that in certain populations, the 185delAG mutation only occurs at certain frequency in families with breast and ovarian cancer (Mullineauxet al., 2003).

CONCLUSION

In general, breast cancer can develop at any age, but younger women are significantly less likely to develop the disease (Mathew et al., 2004).The results of these tests for Group B samples with 185delAG indicated once more that the range of samples from 22 DNA samples.The most prevalent and pervasive BRCA1 gene mutation in breast cancer is 185delAG. These founder mutations have been observed in several groups, according to numerous research. We investigated the potential application of the above stated Iraqi mutations using the ARMS-PCR method. The average age of all of our patients used to be under 45 years because aging significantly affects the likelihood of discovering a mutation. We found that none of the 50 healthy individuals, the 100 patients with sporadic breast cancer, the 50 patients with familial breast cancer, or any of the other patients had any of the three mutations. Our results agreed with past research on Iraqi women with breast cancer. The 185delAG founder mutation in the BRCA1 gene occurs at a low frequency identified in Iraqi women with breast cancer.

However, there is little knowledge on how these two susceptibility genes affect breast cancer globally. IraQ. reported a new mutation in the BRCA1 gene at codon 1534 (G to A). 6 The sample of mutations seen in the BRCA1 genes among Iraqis had previously been warned to be unusual from other populations. A thorough examination of the BRCA1 gene sequence may be required in Iraq, a nation with a diverse ethnic population, in order to pinpoint specific alterations.

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