

Polymorphism of Interleukin-1 β 511 Gene in Women with Breast Tumor in Babylon Province

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Abstract

Background: Interleukin-1 (IL-1) is a member of the cytokine family that is, crucial for initiating and regulating inflammatory and immune responses. **Objective:** It has been demonstrated that the pro-inflammatory cytokine interleukin-1 β (IL1 β 511) affects breast tumor susceptibility. Our study sought to determine whether the IL1 β 511 gene polymorphism and susceptibility to breast tumors are related. This association between the risk of breast tumors and the IL1 β 511 polymorphism has been established. **Materials and Methods:** The blood samples were collected from 50 healthy women and 100 nonhealthy ones. Following collection, DNA extraction was performed on the samples. Restrictions fragment polymorphism and polymerase chain reaction were used to analyze the IL-1 β 511 promoter primer. **Results:** According to our findings, all genetic models significantly associated common SNPs in IL-1 β 511 (rs16944) with breast tumor risk. IL-1 β 511 polymorphism significantly decreased breast tumor risk between patients and healthy—control (CT, CC, TT: OR 2.29, 0.43, 0.54 CI 95, *P* value: 0.02*, 0.01*, 0.54, respectively). **Conclusion:** The IL-1 β 511 (rs16944) polymorphisms were significantly associated with the risk of breast tumor.

Keywords: Breast tumors, genetic susceptibility, interleukin-1 β polymorphism genetic

INTRODUCTION

Breast soft tissue lesions typically provide a diagnostic challenge in daily practice. Their collective range of histopathological abnormalities can be roughly divided into benign and malignant tumor lesions. Breast cancer is the most common type of cancer in women.^[1] Breast carcinoma is the most common malignant tumor and is the second most common cause of carcinoma death in women, with more than 1.7 million cases occurring worldwide annually.^[2] In Iraq, breast cancer has remained the most common cancer affecting women and the most common cause of morbidity and mortality in Iraqi women,^[3] and the Breast MR imaging depicts more accurate dimensions of the tumor and its extensions than digital and sonomammography.^[4] Throughout 2016, 897 women died from that disease which is recorded as the first cause of cancer-related mortality among Iraqi females after bronchogenic cancer.^[5]

The synthesis and processing of IL-1 are tightly regulated and require two signals: the activation signal, which

activates inflammasome complexes and inflammatory caspases to cleave pro-IL-1 into mature IL-1, and the “priming” signal, which permits transcription of the IL-1 β gene.^[6] According to Schroder and Tschopp^[6] and Momiyama *et al.*,^[7] the interleukin-1 gene has three SNPs that may be functional: -31 (rs1143627, C>T), -511 (rs16944, C>T) in the promoter region, and +3954 (rs1143634, C>T) in exon 5. The three SNPs (rs16944, rs1143634, and rs1143627) in IL-1 and breast cancer risk have been the subject of numerous studies to date.^[8]

In addition to its function in inflammatory processes, IL-1 has also been thoroughly investigated in a number of cancers. Breast cancer tissue has been shown to express IL-1^[9] also a few more tumor tissues.^[10] In human breast

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Submission: 17-Aug-2023 **Accepted:** 16-Dec-2023 **Published:** 30-Apr-2026

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How to cite this article: Baram WNM, Abd FG. Polymorphism of interleukin-1 β 511 gene in women with breast tumor in Babylon province. *Med J Babylon* 2026;23:411-4.

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DOI:
10.4103/MJBL.MJBL_1218_23

Table 1: Demographic features of the participants in this study

Demographic features		Patients	Control
Number in each group		100	50
Age years	14–29	22 (23%)	18 (36%)
	30–45	45 (47%)	27 (54%)
	46–66	28 (30%)	5 (10%)
Types and numbers of breast cancer	Invasive ductal carcinoma	20	–
	Lobular carcinoma	15	–
	Fibrocystic change	20	–
Types and numbers of benign breast	Fibro adenoma	30	–
	Granulomatous	15	–
	Before surgery	–	–

cancer, it is produced and released by tumor cells, which induces pro-metastatic genes in an autocrine and paracrine manner.^[11] There is a link between IL-1 polymorphisms and an elevated risk of breast cancer, according to two recent studies.^[12,13] The purpose was to determine The IL-1-511 polymorphism and the risk of breast cancers have been linked, it has been found.

MATERIALS AND METHODS

Sample collection

From January 2021 to September 2021, the blood samples were collected from 100 women with breast tumors and 50 healthy women at AL-Hilla Teaching Hospital. The age of women in the current study ranged between 14 and 66 years old.

DNA extraction

The collected blood samples were subjected to DNA extraction, Genotyping Magna Pure LC was used to extract genomic DNA from 2 mL of peripheral blood leukocytes in accordance with the manufacturer's instructions (Roche, Germany).

IL-1 β 511 genotyping

Using PCR-RFLP (restriction fragment length polymorphism) techniques, all genotypes were determined. A forward primer 5'-TGGCATTGATCTGTTTCATC-3' and a reverse primer 5'-GTTAGGAATCTTCCCACTT-3'^[14] were used for IL-1 β 511 promoter polymorphism. Each patient's and the control group's DNA samples were amplified in a reaction volume of 50 containing 200 ng of DNA and 2.5 mmol/L magnesium chloride (MgCl). Taq DNA polymerase (2.5 U/ μ L), oligonucleotide primers (10 pmol each), and a mixture of deoxyribonucleotide triphosphates (d NTPs) are also included.

The PCR program was as follows: initial denaturation at 95°C followed by 35 cycles of (denaturation 95°C for 1 min, annealing at 54°C for 1 min, and extension at 74°C for 1 min), followed by final extension for 5 min. Then

the amplified products subjected to RFLP technique as follows.

PCR products digested with *A. val.* were added to the 108-bp PCR product, and the reaction mixture was then incubated at 37°C overnight. To distinguish different genotypes, 5–10 μ L of the digestion result was placed onto a 3% agarose gel electrophoresis and observed using a UV transilluminator.

Statistical analysis

The SPSS program (version 23 SPSS) was used for the statistical presentation and analysis of the current study. Statistical significance was defined as $P = 0.05$.

Ethical approval

The study was conducted in accordance with the Helsinki Declaration's ethical guidelines. The patient's verbal and written agreement was obtained before any samples were taken. The study protocol, subject data, and permission form were reviewed and approved in accordance with document M220106 (which has the number and date of January 17, 2022).

RESULTS

The results of the current investigation showed that the most prevalent age range was between 30 and 45 years old (47%). Most instances in all the samples included in this study were diagnosed as benign, accounting for 65% of all cases; the remaining 65% were suspected of being malignant. The present study shows that benign Fibro adenoma was the most common [Table 1].

IL-1 β -511 promoter primer genotyping PCR

Each case study's gene was amplified using particular primers. After Agarose gel electrophoresis using UV light, the results of the amplification showed that a 304 bp product was produced. The gel documentation system was then used to calculate the fragment's size, as illustrated in Figure 1.

Gel electrophoresis for samples from patients with breast cancers and control groups following *AvaI* digestion. TT homozygous (304bp), CT heterozygous (304, 190, and

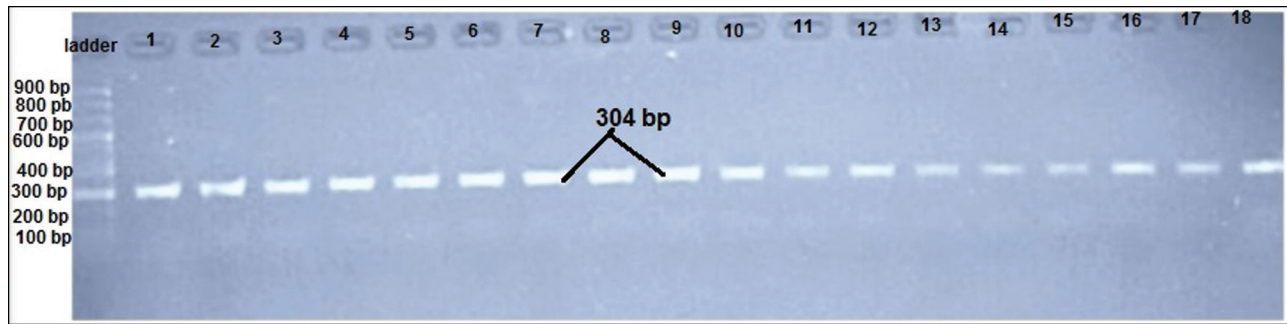


Figure 1: Electrophoresis pattern of PCR product of *IL-1 β -511* in the blood of patients, M: molecular DNA ladder, 1–18 PCR product, electrophoresis condition: agarose 1.5%, volt 85, for 1 h, ethidium bromide



Figure 2: PCR amplification patterns of *IL-1 β -511* digested with restriction enzyme *AvaI*. Lane M represents 1KB marker. lane (2) homozygous TT genotype 304bp, lane (1, 3, 4, 6, 7, 8, 10, 11) homozygous (CT) genotype (304, 190, and 114 bp), lane (5, 9, 12) heterozygous (CC) genotype (190 and 114 bp)

114bp), and CC homozygous (190 and 114bp) were the genotypes of the *IL-1-511* gene polymorphism with allele frequency between patients and healthy As shown in Figure 2.

Results from genotyping and allele frequency analyses show statistically significant differences and increased risk by odd ratio and *P* value in CC and CT between breast tumor patients and control groups but no significance of TT genotypes, as listed in Table 2.

DISCUSSION

The age range with the highest prevalence in our study was between 30 and 45 years old (47%). Sixty-five percent of the cases in all the samples examined for this study were benign, making up the majority of cases; the remaining 65% were believed to be malignant cases [Table 1]. The most common age range in our study (28.6%) was between 15 and 25 years, contrary to the study,^[15] which found that. The most frequent diagnosis in the current study's samples was cancer, which accounted for 24% of all diagnosed cases. Meanwhile, 5.5% of patients had malignancy suspicions. Benign Fibro adenoma was the most common type in the present study, which disagreed with study by Saadaat *et al.*^[16] that discovered fibroadenosis in 21% of patients,

followed by cyst in 16%, and fibroadenoma in 8% of instances. However, the result of this study agreed with the study of Cox *et al.*^[17] which determined that fibroadenoma (57.28%), fibroadenosis (16.43%), and determined pyogenic abscesses (7.51%) were the most common lesions.

The current study aims to investigate the impact of the *IL-1 β -511 C/T* SNP on the prevalence of breast tumors in Hilla women. With mounting evidence suggesting they play a role in tumor initiation, development, and metastasis, cytokines were thought to be closely linked to the pathophysiology of cancer.^[18] The relationship between cytokine gene polymorphisms and a variety of inflammatory and malignant disorders has been the subject of numerous investigations.^[19] Regarding rs16944, some research suggested that the rs16944 genotype decreased the risk of breast cancer, while others demonstrated the opposite findings. To determine the associations between three polymorphisms in the *IL-1* gene and the risk of breast cancer.^[20]

The results of the present investigation were at odds with those of a study by,^[21] who demonstrated that the polymorphisms rs16944 and rs1143634 did not exhibit any relationships with breast cancer risk. In light of this, we updated our previous meta-analysis to look into the relationships between three polymorphisms in the *IL-1* gene and the chance of

Table 2: Genotype of IL-1 β C31 T gene polymorphism with allele frequency in patients' blood and healthy

Genotype IL-1 β 511	Patients (blood)	Healthy	P value	Odd ratio	CI 95%
CT	55 (61%)	12 (24%)	0.02*	2.29	(1.13–4.67)
CC	20 (22%)	23 (47%)	0.01*	0.43	(0.22–0.87)
TT	15 (17%)	14 (29%)	0.13	0.54	(0.24–1.20)
Total	100	50			
Alleles frequency					
C	95 (0.48)	58 (0.58)			
T	85 (0.42)	83 (0.40)			

developing breast cancer.^[22] who demonstrated a substantial link between the rs16944 polymorphism and a higher risk of breast cancer in the Asian population. The present study was disagreed with the study^[23] which indicated that, overall, neither the -511 SNPs nor the +3954 SNPs are related to breast cancer risk, severity or survival. However, the present study agreed with the study^[24] revealing that functional polymorphisms in the IL-1 gene promoter may increase the risk of breast cancer, indicating a potential biological importance of these two polymorphisms.

CONCLUSION

The IL-1 511 (rs16944) polymorphisms were significantly associated with the risk of breast tumor.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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