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CYP1A2 Genetic Variants and Breast Cancer Susceptibility in Women: Varian Genetik CYP1A2 dan Kerentanan Terhadap Kanker Payudara pada Wanita

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Abstract

Breast cancer remains a leading cause of cancer-related morbidity among women worldwide, with genetic susceptibility playing a crucial role in disease development. Cytochrome P450 1A2 is involved in estrogen metabolism and has been implicated in carcinogenesis through genetic polymorphisms affecting enzymatic activity. This study aims to investigate the association between the CYP1A2 rs17861162 polymorphism, family history, disease stage, and breast cancer risk in women from Thi-Qar Province, Iraq. A case-control design was applied, including 40 breast cancer patients and 20 healthy controls. Genomic DNA was extracted from blood samples, and polymerase chain reaction was used for genotyping. Statistical analyses were conducted using Chi-square tests, odds ratios, and confidence intervals. The results showed no statistically significant association between CYP1A2 rs17861162 genotypes or alleles and breast cancer risk, although the G allele demonstrated a non-significant 1.5-fold increased risk. Family history and disease stage were also not significantly associated with breast cancer occurrence. The novelty of this study lies in providing population-specific genetic evidence from an underrepresented region, contributing to the growing body of literature on CYP1A2 polymorphisms and breast cancer. These findings suggest that CYP1A2 rs17861162 alone may not serve as a reliable genetic biomarker, highlighting the need for larger, multiethnic studies to clarify its role in breast cancer susceptibility.

Keywords: Breast Cancer, CYP1A2 Polymorphism, Genetic Susceptibility, Estrogen Metabolism, Cancer Risk

Highlights:

- CYP1A2 rs17861162 shows no significant association with breast cancer risk
- G allele demonstrates a non-significant increased susceptibility trend
- Population-specific genetic evidence expands breast cancer genomics literature

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Introduction

Breast cancer is the most frequently diagnosed type of cancer and represents the second leading cause of cancer-related mortality among women worldwide [1]. Over the past five years, numerous studies have identified several major risk factors associated with an increased likelihood of developing breast cancer in women. These factors include advancing age, a family history of the disease, obesity, the use of oral contraceptives, menstrual and hormonal status, smoking, alcohol consumption, unhealthy lifestyle patterns, and genetic predisposition[2]. With respect to genetics, the CYP1A2 gene belongs to the cytochrome P450 family and plays a pivotal role in the metabolism of xenobiotics as well as various drugs and pharmaceuticals. This gene is located on chromosome 15 at position 15q24.1, consisting of 7 exons and 6 introns, with an approximate length of 7.8 kb. The CYP1A2 protein, composed of 515 amino acids with a molecular weight of 58,294 Da, is primarily expressed in the liver, though expression has also been observed in the pancreas and lungs [3]. Dysregulated expression of CYP1A2 has been linked to the development of several human cancers, including liver, breast, prostate, bladder, and endometrial cancers [4]. Single nucleotide polymorphisms (SNPs) represent the most common form of genetic variation and serve as valuable genetic markers. They can influence gene regulation by altering DNA sequences, thereby impacting gene function. Functional polymorphisms within CYP1A2 have been shown to modify its enzymatic activity, which in turn affects susceptibility to cancer in different anatomical sites [5]. Studies have shown that these enzymes, particularly CYP1A2, play an active role in estrogen metabolism within breast cancer tissues, highlighting the potential impact of genetic mutations or single nucleotide polymorphisms (SNPs) in the CYP1A2 gene on hormonal response and, consequently, on cancer risk [6,7]. Moreover, it is essential to consider other genomic variations that may contribute to interindividual differences in CYP1A2 expression, reflecting the complexity of understanding the role of this gene in cancer susceptibility [8,9].

Methods and Material

Collection of Blood Samples

A total of 40 blood samples were collected from women diagnosed with breast cancer at the Oncology Center within Al-Habboubi Hospital in Thi-Qar province, representing the patient group. In addition, 20 blood samples were obtained from healthy individuals as the control group. From each participant, 4 mL of venous blood was drawn. Of this, 2 mL of blood was placed into tubes containing EDTA as an anticoagulant and stored at −20°C, while the remaining 2 mL was collected in Gel tubes for the purpose of measuring biochemical parameters in both patient and control groups. Genomic DNA was subsequently extracted from all samples, and PCR (Polymerase Chain Reaction) was employed to amplify the CYP1A2 gene.

Statistical Analysis

The statistical analysis for all studied samples was performed using Chi-square, T-test, and ANOVA with a significance level of $P < 0.05$. In addition, the Odds Ratio (OR) test was applied to examine the frequency of genotypes for the gene. All analyses were conducted using SPSS software .

Result

1- family history

Although family history represents an important factor in the hereditary risk of breast cancer, the present study did not reveal any significant differences between breast cancer patients with a positive family history and those without ($p = 0.522$). The proportion of patients with a family history of breast cancer was 55%, compared to 45% of patients with no family history, as shown in Table (1).

Table (1): Distribution of breast cancer patients and the comparison group according to family history

Family history	Patient Group	p-value
Positiv	22(55%)	0.522
Negative	18(45%)	
Total	40(100%)	
Df=1 Chi =0.4		

2-disea5se stage

The present study showed that the highest proportion of breast cancer patients was in stage II of the disease (35%), while 25% of patients were in stage I. Patients in stages III and IV had equal proportions of 8% each. No statistically significant differences were observed among patients across the different disease stages ($p = 0.494$), as presented in Table (2).

Table (2): Distribution of breast cancer patients and the comparison group according to disease stage

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Disease Stage	Patient Group	p-value at significance level ≤ 0.05
Stage I	10(25%)	0.494
Stage II	14(35%)	
Stage III	8 (20%)	
Stage IV	8 (20%)	
Total	40(100%)	
p ≤ 0.05 Df=3 Chi=2.40		

3- CYP1A2 rs17861162 (C>G) polymorphism

The present study demonstrated that the GG genotype was the most prevalent, observed in 50% of patients and 65% of the control group. The GC genotype (heterozygous variant) was detected in 32.5% of patients and 20% of controls, with an odds ratio of OR = 0.72 (95% CI = 0.12–4.15) when compared to the reference genotype GG. The CC genotype (homozygous variant) was found in 17.5% of patients and 15% of controls. These findings indicate no statistically significant association between the studied genotypes and breast cancer risk, as shown in Table (3). In the patient group (total alleles = 80), the frequency of the C allele was 33.75%, while the G allele accounted for 66.25%. In the control group, the C allele frequency was 25%, whereas the G allele was more common, with a frequency of 75%. These results suggest that the G allele is predominant in both groups, conferring an approximately 1.5-fold increased risk of breast cancer (OR = 1.52, 95% CI = 0.65–3.58).

Table (3): Genotypes and allele frequencies of the CYP1A2 gene in breast cancer patients and the control group

Genotypes	Patients N=40 (%)	control N=20(%)	OR	CI 95%
CC	7 (17.5%)	3 (15%)	1.0	———
CG	13 (32.5%)	4 (20%)	0.72	0.12-4.15
GG	20 (50%)	13 (65%)	1.52	0.33-6.94
المجموع	40 (100%)	20 (100%)		
				Allele frequencies
C	27(33.75%)	10 (25%)	1.0	———
G	53(66.25%)	30 (75%)	1.52	0.65 -3.58
total	80 (100%)	40(100%)		
OR: Odd Ratio 95% CI Confidence Interval				

Discussion:

The findings of the present study, as shown in Table (1), revealed that place of residence (urban vs. rural) was not a significant factor influencing breast cancer occurrence. In contrast, a Chinese study [10]. reported a clear disparity between urban and rural regions. In the urban city of Shijiazhuang, the incidence of breast cancer was 45.5 per 100,000 population, whereas in the rural county of Shexian, the incidence was 13.8 per 100,000. This indicates that urban women were 3–3.5 times more likely to develop breast cancer compared to their rural counterparts. This disparity was attributed to lifestyle factors associated with urbanization, such as higher rates of overweight and obesity, reduced physical activity, lower fertility and breastfeeding rates, and delayed age at first childbirth [11]. he American study by [12]. demonstrated that rural women are more likely to be diagnosed at advanced stages of the disease. The proportion of metastatic breast cancer cases was 4.94% among rural women, compared with 4.36% in small urban areas and 4.24% in large urban areas.

The results of the present study (Table 2) contradict the findings of several studies, such as the recent study by [13]. which included 464,707 women. That study reported that a concordant family history according to histological subtype (ER+ or ER–) significantly increased the risk of breast cancer. The hazard ratio was 1.96 for ER+ breast cancer and 2.67 for ER– breast cancer. Moreover, the study demonstrated that the risk substantially increased with the number of affected first-degree relatives. In

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addition, the findings indicated that a family history of other malignancies (such as colorectal, ovarian, or prostate cancers) was also associated with a higher risk of both ER+ and ER– breast cancers. These results emphasize the role of family history not only in breast cancer but also in the genetic predisposition to other types of cancer.

Another study [14] conducted on 129,374 women in South Korea, including 981 breast cancer patients and 128,393 healthy women as a control group, reported that a maternal family history of breast cancer was associated with a 3.21-fold increased risk of developing the disease. Similarly, a family history among siblings was associated with a 2.63-fold increased risk. Both associations were statistically significant ($p < 0.001$).

The results of the present study (Table 3) showed that the GG genotype was the most prevalent. Our findings did not agree with those of [15]. who reported that the CC genotype was the most common among breast cancer patients (54%) and healthy controls (69%). In their study, the CG genotype appeared in 37% of patients compared to 29% of controls, whereas the GG genotype was the least frequent (9% in patients vs. 2% in controls). With respect to allele distribution, the frequency of the C allele was 72.5% in patients and 83.5% in controls, while the G allele was detected in 27.5% of patients and 16.5% of controls. Their results indicated that the presence of the G allele was associated with nearly a twofold increased risk of breast cancer (OR = 1.92, 95% CI = 1.18–3.11, $p < 0.05$). This finding is consistent with our study in that the G allele is associated with an increased risk of breast cancer.

References

[1] A. M. Hussain, A. H. Mohammed, A. H. Ali, and H. L. Mohammed, “Study of Certain Biomarkers in Iraqi Female Patients With Breast Cancer,” Baghdad Science Journal, vol. 18, no. 4, p. 1140, 2021.
[2] N. Fakhri et al., “Risk Factors for Breast Cancer in Women: An Updated Review,” Medical Oncology, vol. 39, no. 12, pp. 1–6, 2022.
[3] N. Datta, S. Chakraborty, M. Basu, and M. K. Ghosh, “Tumor Suppressors Having Oncogenic Functions: The Double Agents,” Cells, vol. 10, no. 1, p. 46, 2020.
[4] X. Yin et al., “Association of CYP2E1 Gene Polymorphisms With Bladder Cancer Risk: A Systematic Review and Meta-Analysis,” Medicine, vol. 97, no. 39, p. e11910, 2018.
[5] L. Tao et al., “Cytochrome P4501A2 Phenotype and Bladder Cancer Risk: The Shanghai Bladder Cancer Study,” International Journal of Cancer, vol. 130, no. 5, pp. 1174–1183, 2012.
[6] B. Luo, D. Yan, H. Yan, and J. Yuan, “Cytochrome P450: Implications for Human Breast Cancer,” Oncology Letters, vol. 22, p. 548, 2021.
[7] J. Wunder et al., “Influence of Breast Cancer Risk Factors on Proliferation and DNA Damage in Human Breast Glandular Tissues,” Archives of Toxicology, vol. 96, pp. 673–687, 2022.
[8] M. Dobrinas et al., “Impact of Smoking and Genetic Polymorphisms on CYP1A2 Activity,” Clinical Pharmacology and Therapeutics, vol. 90, no. 1, pp. 117–125, 2011.
[9] V. Vukovic et al., “Lack of Association Between CYP1A2 Polymorphisms and Cancer Risk,” BMC Cancer, vol. 16, p. 83, 2016.
[10] D. Wen et al., “Urban–Rural Disparity in Female Breast Cancer Incidence in China,” Thoracic Cancer, vol. 9, no. 2, pp. 262–272, 2018.
[11] E. Linos et al., “Reproductive and Demographic Changes and Breast Cancer Incidence,” Journal of the National Cancer Institute, vol. 100, pp. 1352–1360, 2008.
[12] G. LeBlanc et al., “Rural–Urban Differences in Breast Cancer Stage at Diagnosis,” Women’s Health Reports, vol. 3, no. 1, pp. 207–214, 2022.
[13] Q.-L. Wang et al., “Risk of Estrogen Receptor-Specific Breast Cancer by Family History,” Journal of the National Cancer Institute, vol. 115, no. 9, pp. 1020–1028, 2023.
[14] H. G. Choi et al., “Family History and Breast Cancer Development,” International Journal of Environmental Research and Public Health, vol. 18, no. 12, p. 6409, 2021.
[15] M. Valizadeh Osalo et al., “Prevalence of CYP1A2 Polymorphisms in Breast Cancer Patients,” Discover Oncology, vol. 15, no. 1, p. 59, 2024.