Indonesian Journal on Health Science and Medicine

Vol. 2 No. 3 (2025): Desember
DOI: 10.21070/ijhsm.v2i3.342

IJHSM

Indonesian Journal on Health Science and Medicine

UNIVERSITAS MUHAMMADIYAH SIDOARJO

ISSN 3063-8186 (online), https://ijhsm.umsida.ac.id, published by Universitas Muhammadiyah Sidoarjo

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Table Of Contents

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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

Published date: 2025-12-12

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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).

Family history	Patient Group	p-value

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