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The Effect of the rs396991 Mutation in the FCGR3A Gene on Trastuzumab Effectiveness in Iraqi Women with HER2-Positive Breast Cancer

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Abstract

Background: Trastuzumab is a human monoclonal antibody, an anti-HER2 antibody that binds to the HER2 receptors and suppresses downstream signalling pathways of HER2-positive breast cancer. The genetic variant of the FCGR3A protein is the rs396991, which is a SNP in the FCGR3A gene, and the protein is a Fc gamma receptor.

Purpose: The overall objective of the study is to investigate the impact of the mutation of FCGR3A gene, which is the rs396991, on the efficacy of trastuzumab.

Methods: This is a cross-sectional observational study which involved 100 Iraqi women who are diagnosed with HER2-positive breast cancer, and receiving trastuzumab treatment. Genotyping of the SNP rs396991 SNP was done using AS-PCR. The response of treatment was determined by measuring serum levels of the tumor marker CA 15-3.

Results: The frequency of the studied cohort genotyping of the genotyped genotype of the exon deletion (rs396991) was 28 (wild type), 61 (heterozygous), and 11 (homozygous variant). The frequencies of genotypes were not in the Hardy-Weinberg equilibrium ($P < 0.0104$). Analyzing the levels of CA 15-3 no statistically significant differences were found among the rs396991 genotypes ($p = 0.431$). There was no significant relationship between CA 15-3 levels and disease and duration of treatment.

Conclusion: this study suggests that the genetic polymorphism of rs396991 in the FCGR3A gene variability is distributed among breast cancer patients. At the same time, there is no variation in the tumor marker level, indicating that there is no need to modify the prescription guideline for trastuzumab. Similarly, CA 15-3 levels were not associated with disease or treatment duration in this cohort. Further studies with larger sample sizes may fully elucidate the impact of this genetic variant on trastuzumab efficacy.

تأثير تعدد الأشكال الجيني rs396991 في جين FCGR3A على فعالية العلاج بالتراستوزوماب لدى النساء العراقيات المصابات بسرطان الثدي الإيجابي لمستقبلHER2

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الملخص

الخلفية:يُعد التراستوزوماب جسمًا مضادًا أحادي النسيلة مُؤنسنًا يستهدف مستقبل عامل نمو البشرة البشري الثاني (HER2) ويثبط مسارات الإشارة الخلوية اللاحقة في سرطان الثدي الإيجابي لمستقبل .HER2ويشفّر جين FCGR3Aمستقبل الغلوبولين المناعي جاما IIIA (FcγRIIIA)، الذي يؤدي دورًا رئيسيًا في السمية الخلوية المعتمدة على الأجسام المضادة(ADCC) ، وهي إحدى الآليات الأساسية لفعالية التراستوزوماب. ويُعد تعدد الأشكال الجيني أحادي النوكليوتيد rs396991 (SNP) في جين FCGR3Aمن المتغيرات الوراثية التي يُعتقد أنها قد تؤثر في الاستجابة العلاجية للتراستوزوماب.

الهدف:هدفت هذه الدراسة إلى تقييم العلاقة بين تعدد الأشكال الجيني rs396991في جين FCGR3Aوفعالية العلاج بالتراستوزوماب لدى النساء العراقيات المصابات بسرطان الثدي الإيجابي لمستقبل .HER2

المواد وطرائق العمل:أُجريت دراسة مقطعية رصدية شملت 100 امرأة عراقية مشخصة بسرطان الثدي الإيجابي لمستقبل HER2ويتلقين العلاج بالتراستوزوماب. أُجري تحديد النمط الجيني لتعدد الأشكال rs396991باستخدام تقنية تفاعل البوليميراز المتسلسل النوعي للأليل .(AS-PCR)وتم تقييم الاستجابة للعلاج من خلال قياس مستويات الواسم الورمي CA 15-3في مصل الدم.

النتائج:بلغت تكرارات الأنماط الجينية لتعدد الأشكال FCGR3A rs396991 28%للنمط الجيني البري، و 61%للنمط الجيني متغاير الزيجوت، و 11%للنمط الجيني متماثل الزيجوت المتحور. وقد أظهر توزيع الأنماط الجينية انحرافًا معنويًا عن اتزان هاردي–واينبرغ .(P = 0.0104)ولم تُظهر مستويات الواسم الورمي CA 15-3فروقًا ذات دلالة إحصائية بين الأنماط الجينية المختلفة .(P = 0.431) كما لم تُسجل أي علاقة معنوية بين مستويات CA 15-3وكلٍ من مدة الإصابة بالمرض أو مدة العلاج بالتراستوزوماب.

الاستنتاج:أظهر تعدد الأشكال الجيني rs396991في جين FCGR3Aتباينًا وراثيًا بين النساء العراقيات المصابات بسرطان الثدي الإيجابي لمستقبل HER2، إلا أنه لم يرتبط ارتباطًا معنويًا بمستويات الواسم الورمي CA 15-3، مما يشير إلى عدم وجود تأثير واضح لهذا التعدد الشكلي على الاستجابة للعلاج بالتراستوزوماب في هذه العينة. كذلك، لم ترتبط مستويات CA 15-3بمدة الإصابة بالمرض أو مدة العلاج. وتُوصى بإجراء دراسات مستقبلية أوسع حجمًا، مع تضمين مؤشرات سريرية إضافية للاستجابة العلاجية، لتوضيح الدور المحتمل لتعدد الأشكال الجيني FCGR3A rs396991في التنبؤ بفعالية العلاج بالتراستوزوماب.

1. Introduction

Breast cancer is the most common cancer among women globally, accounting for approximately 30% of all new cancer types in females. It is also the second leading cause of mortality in women, responsible for 15% of all cancer deaths (SN, AS, and MAA, 2022). A complex interplay of internal and external factors influences the development and occurrence of breast cancer. The prevalence of it is influenced by unhealthy lifestyle habits, environmental exposures, and social-psychological factors. Although genetic mutations and a family history explain 5 percent to 10 percent of breast cancer incidences, 20 percent to 30 percent of incidences are caused by factors that can be modified. (Obeagu & Obeagu, 2024). Breast cancer being the most commonly diagnosed cancer among women all over the world has superseded lung cancer as the most common cancer. It is estimated that more than two million new cases will be reported around the world. By 2020, 685,000 women died of breast cancer which is about 16 percent or one in every six deaths among all female cancer patients. (Arnold et al., 2022). (Like most other types of cancer, advanced age is one of the main predisposing factors of breast cancer among women. Reproductive hormones affect breast tissue depending on various modifiable factors such as protracted postmenopausal hormone therapy, obesity, and lack of exercise. Reproductive factors, including an early menarche, late menopause, nulliparity, giving birth after 30 years of age, and use of hormonal contraception, also put women at risk. Moreover, a known risk determinant is a personal or family history of breast cancer. (Osei-Afriyie et al., 2021).

Trastuzumab is a monoclonal antibody (mAb) that is humanised and was produced in the early to mid-1990s. It specifically interacts with the extracellular domain of the HER2 receptor and hence inhibits downstream signalling pathways. In 1998, the U.S. Food and Drug Administration (FDA) gave its approval to trastuzumab as an adjuvant therapy to use against HER2-positive breast cancer as a first-line therapy. (Najjar et al., 2022). The therapeutic effects of trastuzumab take place in a number of ways: Antibody-Dependent Cellular Cytotoxicity (ADCC)-Activation Trastuzumab-induced ADDC is the recruitment and activation of immune effecter cells, including Natural Killer (NK) cells, in response to the Fc region of the antibody complex used on tumor cells. Developments to improve NK cell operations, alteration of the antibody itself or by isolating certain proteins (e.g., caspase, CD112R, Histone deacetylase (HDAC)) can amplify ADDC. (Nami, Maadi, & Wang, 2018).

Trastuzumab has the ability to suppress the PI3K/Akt and MAPK signaling. This inhibition stops cell proliferation and growth causing cell cycle arrest. Trastuzumab is also reported to inhibit the dimerization of Her2, thus leading to the inhibition of Akt phosphorylation and the overall HER2 activity. (Claret & Vu, 2012).

Trastuzumab interferes with the cellular DNA repair process by inhibiting HER2 signaling pathways, which is one of the factors that affect its anti-tumor effect. (Li et al., 2023). Changes in the amino acid changes of the coding sequences caused by SNPs (single-nucleotide polymorphism), which are alterations to one base in a gene that occur at a considerable frequency (usually, above 1 percent) in a population, can cause change(s) in protein functions. The clinical importance of SNPs in the fcgr3a and fcgr2a genes is because they have been clinically proven to be associated with the response to therapeutic monoclonal antibodies. Identifying genetic markers that predict trastuzumab response is a promising area, with most pharmacogenomic research on trastuzumab focusing on Fc gamma receptor polymorphisms (Mellor et al., 2013). The polymorphisms of FCGR are changes in genes at the locus of coding the various FCGR proteins including FCGR1A, FCGR2A, FCGR2B, FCGR2C, FCGR3A and FCGR3B.Such changes include copy number variants (CNVs) and SNPs that have the capability to alter ligand binding properties. These polymorphisms can therefore modify the activity of the receptors, affect the level of expression of the receptors, and the intensity of immune responses, especially in the treatment of mAb-based therapy. (Twomey, George, and

Zhang, 2025). The FCGR3A gene is pivotal in antibody-dependent cell-mediated cytotoxicity (ADCC), and this is one of the most common mechanisms of trastuzumab action. The SNP in the FCGR3A that leads to the amino acid mutation position 158 is non-synonymous (rs396991) with the phenylalanine replaced by valine. This particular form can have a great influence on the binding affinity of the receptor to immunoglobulin G (IgG) and, hence, the efficacy of monoclonal antibody therapies such as trastuzumab. (Hertz, McLeod, and Hoskins, 2009b). This study aimed to Identifying genotype distribution of rs396991 (GG, GT, TT) in the study population. Measuring the serum levels of CA 15-3 across different rs396991 genotypes to assess the potential effect of this genetic variant on response to trastuzumab.

2. Patients, Materials, and Methods

2.1. Study Design and Participants

This cross-sectional observational study was conducted over one year, from August 2024 to August 2025. A total of 100 Iraqi women diagnosed with her2 positive type of breast cancer , who were undergoing trastuzumab as a monotherapy, were enrolled. Participants were recruited from several medical facilities across Iraq, including the Oncology Centre at the Imam Al-Hussien Centre for Haematology and Oncology, Imam Al-Hassan Al-Mujtaba Teaching Hospital in Karbala Governorate. Ethical approval for the study was obtained from the Scientific Committee of the College of Pharmacy, University of Kerbala. All participants provided informed consent after being thoroughly briefed on the study's objectives and design.

2.2. Sample Collection and Processing

1. 2ml of blood used for DNA extraction.

2. The remaining 3 mL of blood was centrifuged for about 10 minutes at a suitable speed (e.g., 3000 rpm). The biochemical levels of important parameters, such as CA 15-3, which aid in determining the effectiveness of trastuzumab.

2.3. Clinical Data Collection

Comprehensive information about the clinical profiles and cancer history of the participants was also collected. Their diagnosis date, weight, age, family history, number of birth contractions, use of contraception, breastfeeding or bottle feeding, type of surgery (mastectomy or breast-conserving), use of adjuvant therapies, HER-2 receptor status (weak or strong positive), cancer stage and grading, presence of other diseases, use of different medications, date of breast cancer treatment, date trastuzumab was started.

2.4. Genetic Analysis

For genetic analysis, the allele-specific PCR (AS-PCR) method was employed. This technique depends on the creation of primers that can distinguish between the target (wild-type) and mutant (variant) alleles.

2.4.1. Primer Design

Primer design obtained by previous research (Liu et al., 2019). As shown in Table1.

Table1: primer sequences by fcgr3a gene (rs396991) (Liu et al., 2019)

Primer Type	Primer Sequence (5'->3')	Primer Size (bp)
Reverse allele G	TACTTCTGCAGGGGGCTTG	19mer
Reverse allele T	TACTTCTGCAGGGGGCTTT	19mer
Forward allele	CAACTCAACTTCCCAGTGTGAT	22mer

2.4.2. PCR Mixture and Conditions

The pcr conditions employed in Table2 and Table3.

Table2: PCR Mixture for Genotyping of FCGR3A(G>T) (rs396991) Genetic Polymorphism

Components	Volumes (µl)
Forward primer	2
Reverse allele G	2
Reverse allele T	2
DNA template	3
Nuclease-free water	11
Pre-mix	5
Total	**25**

Table3: PCR Conditions for Genotyping of FCGR3A (G>T) (rs396991) Genetic Polymorphism

Steps	Temperature (°C)	Time (Minutes: Seconds)	Cycles
Initial denaturation	95	5:00	1
Denaturation	94	0:25	35
Annealing	58	0:25	
Extension	72	1:00	
Final extension	72	5:00	1

PCR products were analysed through 2% agarose gel electrophoresis, which revealed bands at 174 bp, as seen in Fig.1.

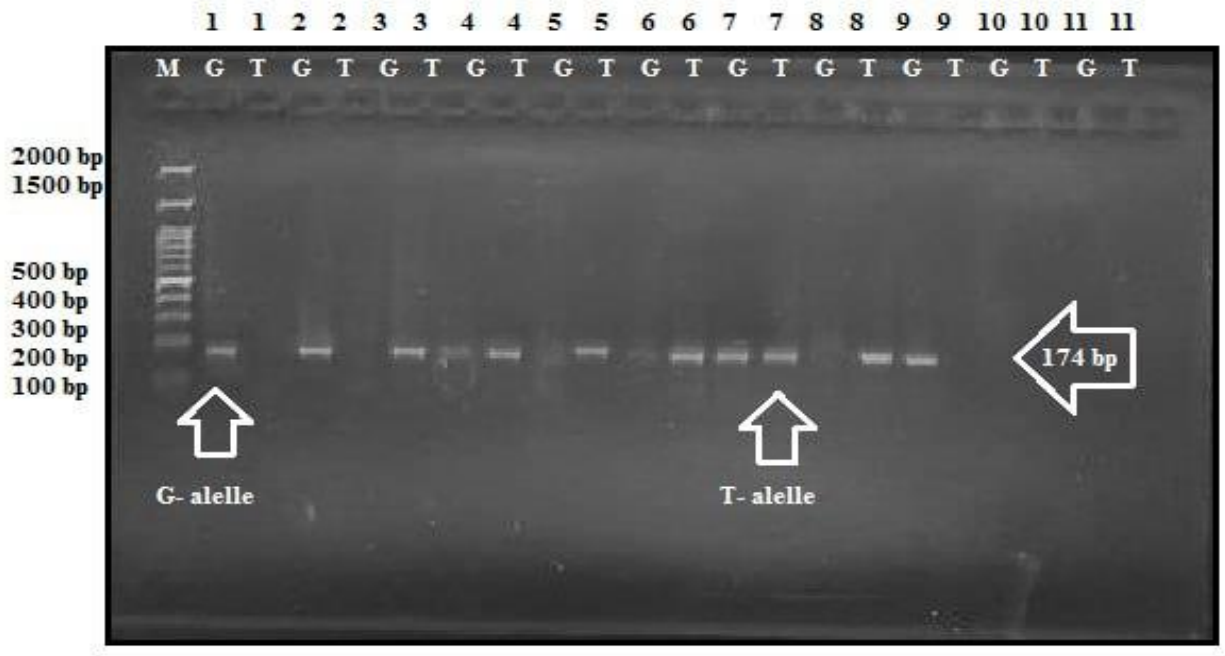

Figure1: Gel Electrophoresis Image Showed the rs396991 Variation, Line M is the DNA ladder, the Individual Samples are in lines 1-11. The band at 174 base pairs Indicates the T allele.

2.5 Biomarker Analysis

A chemical analyser was employed to determine the levels of CA 15-3 in the collected serum samples.

2.6. Statistical analysis

An independent t-test was used to compare continuous variables between two groups, and a one-way ANOVA test was used for comparisons among three or more groups. The Hardy-Weinberg equilibrium (HWE) was assessed using a chi-square (X^2) test. A p-value of < 0.05 was considered statistically significant. Results are presented as mean ± standard deviation (SD).

3. Results

3.1 Biomarkers According to Disease Duration

Fig.2. shows a comparison of CA 15-3 levels in patients categorised by disease duration (1-2 years vs. 3-5 years). The study included 100 patients, and an independent t-test was used to assess statistical significance.

Note: An Independent t-test was used (a significant p-value of less than 0.05). Results are presented as mean ± SD. The mean CA 15-3 levels were slightly higher in the 1–2-year disease duration group (17.17 ± 9.96 U/ml) compared to the 3–5-year group (16.38 ± 9.10 U/ml). However, the p-value of 0.790 indicates no statistically significant difference, suggesting that disease duration does not significantly influence CA 15-3 levels in this patient population.

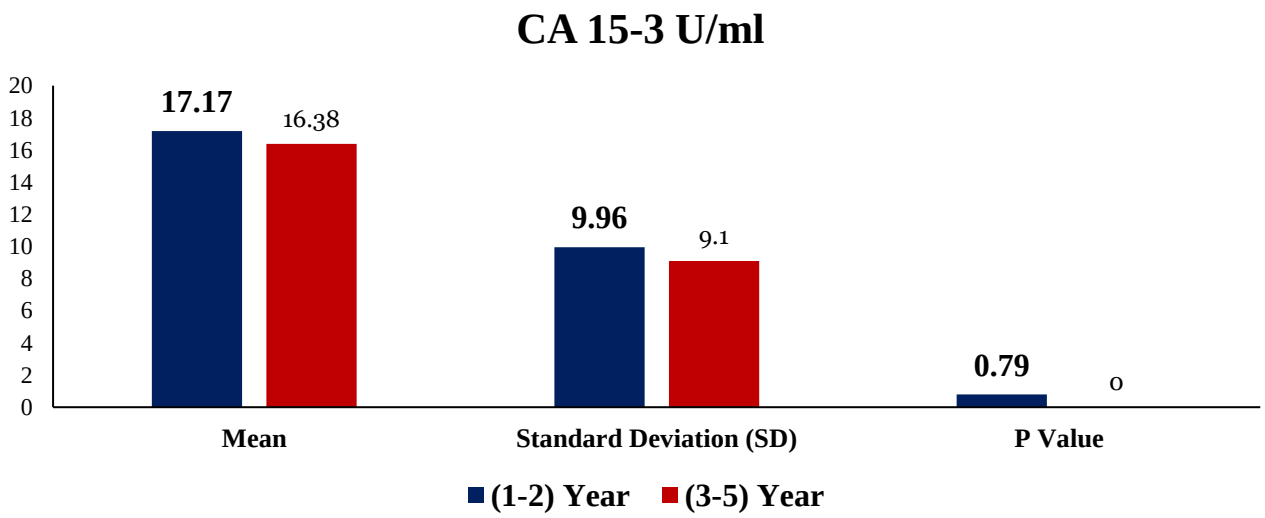

Figure2: Description of Biomarkers of The Studied Patients According To Duration Of Disease (Years). (N=100)

3.2 Biomarkers According to Treatment Duration

Fig.3 shows the analysis of CA 15-3 levels in relation to the duration of trastuzumab treatment. The data includes CA 15-3 measurements across two treatment duration groups: 3-10 months and 11-18 months. Mean values, standard deviations (SD), and p-values from an independent t-test are reported.

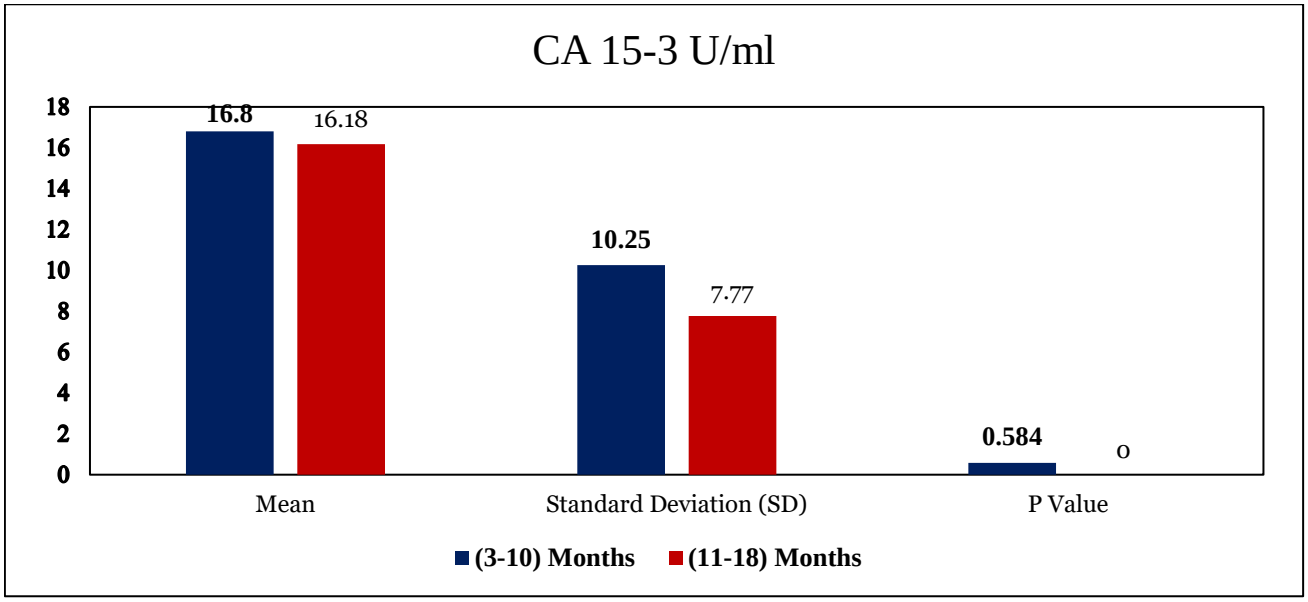

Figure3: Description of Biomarkers of the Studied Patients According to Duration of Treatment (months) (n=100).

Note: An Independent t-test (a significant p-value of less than 0.05). Results are presented as mean ± SD. The average CA 15-3 patients with 3-10 months treatment were 16.80 ± 10.25 U/ml and the patients with 11-18 months treatment were 18.18 ± 7.77 U/ml. The p-value of 0.584 reveals that there is no statistically significant difference between the levels of CA 15-3 of the two treatment duration groups, and hence it can be concluded that the duration of treatment has no significant effects on the level of CA 15-3 in this cohort.

3.3. Distribution of Genotypes

Fig.4 shows the frequency of the genotypes of the patient cohort of the rs396991 locus. The genotype of morbidity of the rs396991 polymorphism had 3 genotypes namely; GG (wild type) in 28% patients, GT (heterozygous), and TT (homozygous variant) in 61 and 11 percent patients respectively. The most dominant was the GT heterozygous genotype (61%), and the least common was the TT homozygous (11%). Wild-type GG genotype existed in 28% of the patients. Such a distribution can be an indicator of a balanced polymorphism in the population.

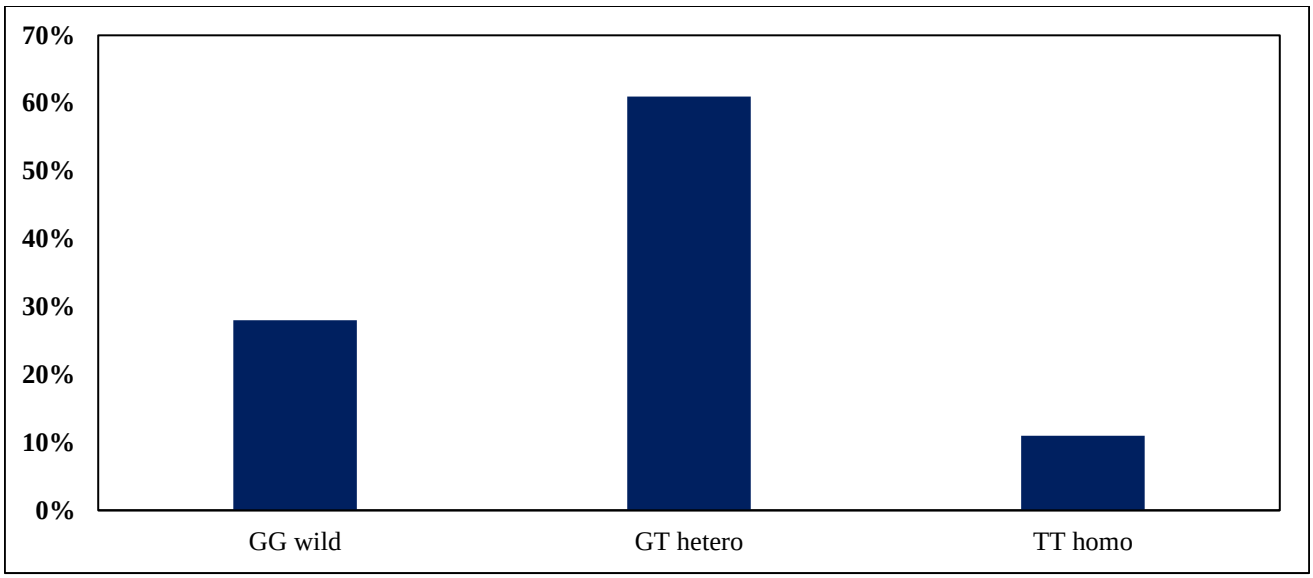

Figure4: Distribution of Gene Polymorphism, N=100

3.4. Laboratory Biomarker According to Genetic Variant rs396991

Table4 Description of laboratory biomarker of the studied patients according to genetic variant rs396991 (n=100). The mean levels of CA 15-3 were 15.13 ± 8.41 U/ml in the GG group, 18.03 ± 10.80 U/ml in the GT group, and 16.61 ± 6.73 U/ml in the TT group. The p-value of 0.431 indicates no statistically significant difference in CA 15-3 levels across the genotypes, suggesting that the rs396991 variant does not significantly influence CA 15-3 expression in this patient population.

Table4: Presents the Mean CA 15-3 Levels Categorised by The Rs396991 Genetic Variant (GG, GT, And TT Genotypes). A One-Way ANOVA Test Was Used for Comparison.

Parameter	GG	GT	TT	P Value
CA 15-3 U/ml	15.13 ± 8.41	18.03 ± 10.80	16.61 ± 6.73	0.431
Results are presented as mean ± standard deviation (SD).				

3.5 Hardy–Weinberg Equilibrium

Table5 Hardy–Weinberg equilibrium for rs396991 in patients. The observed genotype frequencies for rs396991 were GG: 28 (28%), GT: 61 (61%), and TT: 11 (11%). The expected genotype frequencies under HWE were calculated as GG: 34.22 (34.22%), GT: 48.55 (48.55%), and TT: 17.22 (17.22%). The allele frequencies were G allele: 117 (58.5%) and T allele: 83 (41.5%). A chi-square (X^2) test comparing observed and expected frequencies yielded $X^2 = 6.5693$ with a P-value = 0.0104. Since the p-value is less than 0.05, there is a statistically significant deviation from the Hardy-Weinberg equilibrium, suggesting that the observed genotype frequencies differ from what would be expected under random mating and the absence of evolutionary forces.

Table5: Shows the Observed and Expected Genotype Frequencies for rs396991, Along with The Results of The Hardy-Weinberg Equilibrium (HWE) Test.

Variable	Genotype	Observed	Expected	Percent	Alleles	Hardy–Weinberg Equilibrium X^2 Test
rs396991	GG wild	28	34.22	28%	G T	**X^2 = 6.5693, P < 0.0104**
	GT hetero	61	48.55	61%		
	TT homo	11	17.22	11%		
Total		100				
Note: The table summarizes the genotype distribution for rs396991 in patients, including observed and expected frequencies, percentages, and results of the Hardy–Weinberg equilibrium test.						

4. Discussion

Cancer Antigen 15-3 (CA 15-3) is a crucial biomarker in breast cancer management, particularly in monitoring the disease progression as well as determining treatment efficacy, particularly in metastasis disease. (Ryu et al., 2023).CA 15-3 is a glycoprotein synthesized by the MUC1 gene and released into the blood in case of cell degradation of the breast. (Fu & Li, 2016). Table4 shows that the difference in CA 15-3 levels between the patients of various durations of the disease (1-2 years and 3-5 years) was not statistically significant (p = 0.790). This implies that the duration of the illness does not affect CA 15-3 levels significantly. The fact that there is no direct correlation between the CA 15-3 level and the duration of the disease can be attributed to several reasons. Indicatively, the CA 15-3 is normally elevated in patients who have larger tumors or more advanced metastatic disease, particularly in the liver and the bones. Moreover, not every breast cancer will show CA 15-3, and some of the cancers, especially those at an early stage, might not release measurable amounts of the marker. (Nieder et al., 2017). The levels of CA 15-3 can also be used to inform the adjuvant treatment strategies because it could be an indicator of high potential recurrence risk. Thus, CA 15-3 is not an instrument that should be employed in the initial diagnosis but it is a useful tool to reflect the tumor burden, determine the outcomes of the patient, and make decisions about his or her treatment (Park et al., 2008). The length of treatment also affects the level of interpretation of CA 15-3, which is an important sign of determining the progress of the disease and how effective the treatment is in the breast cancer patient. The time of high CA 15-3 levels may dictate the need to change treatment as it can be the signs of metastasis or recurrence. Depending on the degree of breast cancer, the levels of CA 15-3 can vary and may be augmented with the enlargement of the tumor. In patients who have undergone chemotherapy, a temporary increase, or so-called flaring, of CA 15-3 (125 percent above baseline), which is linked to high risk of disease progression, was observed. It is important to interpret the initial increase in CA 15-3 levels during the first four to six weeks of new therapy carefully because it may be a false elevation. A subsequent decline in CA 15-3 levels could indicate that an early cancellation or change of chemotherapy regimen was unwarranted. Therefore, CA 15-3 is an important protein that can be used to monitor the treatment of breast cancer particularly at the advanced stage, and it also depends on the treatment regimen used and the clinical staging of the patient. Although usually a response to treatment, temporary increases are to be viewed with discretion. (Hasan, 2022). Previous studies have shown that in patients with non-metastatic breast cancer, serum CA 15-3 concentration significantly decreases from pre-operative to post-operative periods. However, these levels can significantly increase from pre-operative and post-operative periods to one year following follow-up. This suggests that serum CA 15-3 concentration can evaluate and monitor the effectiveness of breast cancer treatment in both metastatic and non-metastatic cases. An increase in the levels of CA 15-3 may indicate a radiographic recurrence before it can be detected and can indicate a low response rate to chemotherapy (Abdelfattah et al., 2024).The differences witnessed in the literature on CA 15-3 levels and their relationship with clinical-pathological variables (including nodal involvement, age, histological types, tumor volume, grade, stage, and ER/PR status) could be explained by differences in the populations under

study, the size of samples, and diagnostic procedures used on the tumor marker. (Zhao et al., 2021; Hameed, Al-Rayahi and Muhsin, 2022). The rs396991 is a single-nucleotide polymorphism (SNP) in FCGR3A gene, which expresses Fc gamma receptor IIIa (Fc 3 gamma receptor IIIa or CD16). This polymorphism, which results in an amino acid replacement of phenylalanine (F) with valine (V) (FCGR3A-V158F) is located at position number 158. The impact of this change on IgG receptor binding affinity of the receptor significantly influences the efficacy of various monoclonal antibody treatments including trastuzumab. (Paul et al., 2019). Trastuzumab is a monoclonal antibody targeting of her2 positive breast cancer, in which improved patients out come in both early and metastatic stages of breast cancer. by the ADCC mechanism. (Abdel-Wahed et al., 2024). Our analysis did not show any significant association of the CA 15-3 levels to the polymorphism of the rs396991. This is contrary to some of the past results. As an example, Gavin et al. (2017) had conducted a retrospective analysis on patients at the NSABP B-31 trial, which had reported that the FCGR3A-158 polymorphism was an indicator of trastuzumab efficacy. They noted that homozygous with phenylalanine (F/F genotype) had less benefit than those with F/V or V/V genotypes indicating that ADCC had a substantial effect on trastuzumab efficacy. Equally, a different study examined the correlation between the FCGR3A F/V gene polymorphism and the trastuzumab efficacy in patients with breast caner HER2 positive type . The genotype or allele frequencies did not show any significant difference between breast cancer patients and healthy controls, however, the response of trastuzumab therapy among the patient population showed a significant relationship with this polymorphism. Specifically, the V/V genotype was linked to overall survival and better response, with V allele carriers showing improved response. In contrast, the F/F genotype and F allele were more common among non responder patients . (Abdel-Wahed et al., 2024). Our study findings are also inconsistent with observations by Musolino et al. (2008), who investigated 54 Italian women with HER2 positive type of breast cancer which metastasis and were treated with trastuzumab and taxane. His study reported an improved response rate for patients who had the FCGR3A V/V genotype; furthermore, Tamura et al. (2011) studied a Japanese patients . Similarly, a significant relation was revealed between FCGR3A V/V genotype and response rate among both early and metastatic HER2 positive breast cancer patients . In contrast, our results align with other studies that did not find a significant association between FCGR3A polymorphisms and clinical outcomes. For example, Kim et al. (2012) and Hurvitz et al. (2012) didn't find any association between FCGR3A polymorphism and progression-free survival in their studies of patients given taxanes and trastuzumab. Their results indicated that such differences could not necessarily be material differences that could be observed in clinical outcomes because of the SNPs. The fact that our results and those of the prior studies are inconsistent may be due to a number of variables, such as the ethnic composition and population genetics of the samples, disparities in sample size, discrepancies in certain end points, which include CA15-3 levels as compared to clinical response or survival, and combinations of therapies administered to a patient. Our research relies on CA 15-3 as the first choice of biomarker of efficacy, whereas valuable information may not be able to sufficiently reflect the multivariate interaction between genetic factors and clinical response. Lastly, the seen departure of the Hardy Weinberg equilibrium ($p < 0.0104$) of the variant of the rs396991 in our patient group is also worth attention. Such hints at a variety of methodology or biological problems such as stratification of the population, non-random mating, selection pressure, or genotyping errors. These aspects might have hypothetical effects on the genotype frequencies and further correlation with clinical measures.

Conclusion

Our research paper discusses the prevalence of the fcgr3a gene rs396991 SNP among Iraqi women with HER2-positive breast cancer. We found no statistically significant association between the GG, GT, TT and CA15-3 levels and the genotype of the

same, which is the rs396991. Also, the CA15-3 levels did not show significant correlation with the length of the disease and the length of treatment in the patient group. Our analysis reveals that this SNP that can potentially lead to a higher efficacy of trastuzumab even in this particular population and this biomarker is not the presence of the SNP, rs396991. The fact that it does not follow the Hardy-Weinberg equilibrium indicates the possibility of the intricacies in the genetic composition of the population. More and more detailed research on larger sample sizes, varied populations and direct clinical outcome measures is needed to have a better understanding of the role of FCGR3A polymorphism in trastuzumab response in patients with HER2-positive breast cancer.

Conflicts of Interest

The authors declare no conflicts of interest.

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