

The Role of TP53 Genetic Mutation in Breast Cancer Pathogenesis

Role of TP53
Genetic Mutation
in Breast Cancer

Soura Alaa Hussein¹, Ahmed Mudher Al-Khaykanee² and Tiba A.H. Al-Rubaye³

ABSTRACT

Objective: To review the role of TP53 genetic mutations in breast cancer

Study Design: Case-control study

Place and Duration of Study: This study was conducted at the Marjan Teaching Hospital in Babylon, from 1st December 2023 to 30th June 2025.

Methods: This case-control was conducted at Marjan Teaching Hospital in Babylon and 200 subject were enrolled, 100 patients with breast cancer and 100 healthy undivided were recruited. Subjects were selected at after the extraction of DNA the genotype of rs17878362 C/T and rs1042522 G/C was done using TaqMan-based Real-time PCR technique.

Results: The significant was noted in cancer antigen 15-3 level between the two group where it was 45.22 ± 4.32 U/ml in cases and 22.24 ± 2.10 U/ml in control ($p=0.001$). as for the polymorphism rs17878362. There was a statically significant difference in the frequency of CC 29% and CT 58% genotypes as well as in T alleles between cases and control ($p=0.001$), also similar result were obtained for the polymorphism rs1042522 .the frequencies of GG 38%; GC 62% genotypes and C alleles were statistically significantly more in the cancer group ($P=0.001$). The highest risk was found for TT genotype of rs17878362 which had the OR equal to 3.11. Discrepancies from Hardy-Weinberg Equilibrium were detected in the cases of breast cancer group in both genetic polymorphism ($p=0.001$).

Conclusion: The strong correlation between TP53 gene polymorphism rs17878362 and rs1042522 and high cancer incidence. These variants seem to affect the function of TP53 protein in terms of programmed cell death, causing genomic instability which is associated with developing of tumors. Thus, they might serve as important markers for cancer predicant and treatment.

Key Words: Breast cancer, Polymorphism, TP53 Genetic Mutation.

Citation of article: Hussein SA, Al-Khaykanee AM, Al-Rubaye TAH. The Role of TP53 Genetic Mutation in Breast Cancer Pathogenesis. Med Forum 2026;37(9):62-66. doi:10.60110/medforum.370912.

INTRODUCTION

According to the WHO data, breast cancer (BC) is currently the leading cause of death and morbidity due to its high incidence in females. for instance, about 2.3million new cases of BC are expected in 2022 while the forecasts predict that in 2025, BC will comprise almost 30% of newly diagnosed cancer among females in developed regions¹. Although 5 years several rates for locally diagnosed BC are relatively high and exceed

90% the mortality to incidence ratio continues to be significantly high in underdeveloped countries due to late stage presentation of the disease². Epidemiological evidence indicates including the gradual increase in BC incidence among postmenopausal females and a considerable 1.4% yearly increase in cases of early-onset BC among those under fifty years old¹. Both trends are believed to be driven by complicated interaction between lifestyle factors, such as increased obesity and late childbearing and genetic predisposition³. It has also been forecasted that there will be around 3.2 million new BC cases per year in 2050 if current tendencies continue⁴. Today's clinical management of BC relies heavily on molecular subtypes characterized by the status of estrogen receptors, progesterone receptors, and human epidermal growth factor receptor2 (HER2) expression⁵. Two new terms HER2-low and HER2 ultralow were introduced into the BC classification system to make a wider range of patients eligible for the use of drugs formerly prescribed exclusively for HER2 positive patents⁶. The TP53 gene is situated at 17p13.1 location and is responsible for p53 protein production, which sever as a transcription activator in cellular processes following different stimuli^{7,8}. As a wild type p53 usually has low levels and is under control of the negative inhibitor of

¹. Assistant Professor, Department of Technical Nursing, Technical Institute-Baghdad, Middle Technical University, Iraq.

². Lecturer, General Directorate of Education of Babylon Governorate, Iraq.

³. Lecturer, Department of Animal Production Technique, Al-Furat Al-Awsat Technical University, College of Health & Medical Technology, Babylon, Iraq.

Correspondence: Ahmed Mudher Al-Khaykanee, Lecturer, General Directorate of Education of Babylon Governorate, Iraq.

Contact No: 009647811602922

Email: ahmedmudher14@gmail.com

Received: May, 2026

Reviewed: June-July, 2026

Accepted: August, 2026

the TP53 in case of any changes in genomic integrity or activation of oncogenes TP53 becomes stable and gets activated⁹. Activated TP53 associates with certain DNA response elements to activate 500 target genes and triggers either cell cycle arrest via P21 expression or repair processes or causes programmed cell death if damage cannot be repaired¹⁰. Differently from other tumor suppressor genes which are often subject to deletion more than 70% of TP53 alterations are missense motions in the region of DNA binding domain¹¹. The mutant forms of TP53 possess a gain of function.

METHODS

This case-control was conducted at Marjan Teaching Hospital in Babylon in the period from 1st December 2023 to 30th June 2025 letter No. FTU-1401/Approval/JSDJNEHU dated November 25, 2023 and 200 subject were enrolled, 100 patients with breast cancer and 100 healthy undivided were recruited. The diagnosis of the BC was done through ultrasound magnetic resonance imaging, mammography on biopsy together with confirmatory test the CA15-3 marker test. Four milliliters of peripheral blood were taken from each subject two milliliters of the blood where then used of genotype TP53 whereas the other two milliliters where use of CA15-3 analysis

Genomic DNA was executed using the pure link Genomic DNA Excretion Kit USA based on the protocol provide by the manufacturer Qiagen DNA sample where type using TaqMan genotyping assay kit with the applied biosystem 7500 real time PCR system (Foster City CA, USA) TaqMan probes with VIC and FAM fluorophore markers were used for the TP53C/T RS17878362 and G/C RS1042522 primer sequences respectively the reference sequences (gene bank NC-000017.11:7668421-7687490) is shown below:

TP53 C/T rs17878362

Forward (5→3): CTGGGGACCTGGAGGGCTG

Reverse (5→3): TCACCCAGCCCTCCAGGT

TP53 G/C rs1042522

Forward (5→3): TCCCCCTTGCCGTCCCAAGCA

Reverse (5-3): CTGGTGCAGGGGCCACGCGT

The component of the 25 µl reaction mixture includes 6.25 µl of water nucleus 3 1.25 µl of snip test and 12.5 µl of Tuchman Master mix the reaction was performed in individual PCR tube containing 5 µl of Genomic DNA template 10 mg on microliter and 5 µl of DNA free water as the negative control the solution was mixed on beer fairly centrifuge before the reaction sample were edited to the thermal cycle and amplified genotype was analyzed by the applied biosystem. The CA15-3 tumor marker analysis was done by employing the Cubase E411 machine Machine an equipment that is used in testing tumor marker. Statistical analysis was done using the SPSS-18. For the control group Hardy-Weinberg equilibrium was tested for the genotype

frequencies odds ratio OR and their 95% confidence intervals (CI) were stimulated by the Chi square testing the relationship between the risk of BC and the genotype of the SNP of TP53 gene RS17878362 and RS1042522. Also, linkage disequilibrium between the two SNPs was stimulated by Halo view A p-value of less than 0.005 was considered significant.

RESULTS

There was no significant in age and gender while significant in tumor marker CA15.3U/ml (Table 1). It can be observed from table two that there exists a highly significant genetic correlation P=0.001 between the study samples and particular mutations of TP53. in the case of RS17878362, the control sample displays the predominance of the CC genotype 72% while BC sample indicates a greater number of individuals with the CT genotype 58% as well as with the T allele. Similarly, it is evident that in the control sample GG genotype has the greatest frequency 62% while in BC sample it is the GC genotype 62% as well as C allele (Table 2).

Table No. 1: Demographic and laboratory results of patients and controls (n=200)

Group	Control (n=100)	Breast cancer (n=100)	P value
Age	55.22±6.32	56.44±3.33	2.32
CA15.3U/ml	22.24±2.1	45.22±4.32	0.001

Table No. 2: Frequency of genotypes and alleles for TP53C/T rs17878362 and G/C rs1042522

Variable	Control		Breast Cancer		X ²	P value
	No.	%	No.	%		
Genotypes TP53 Rs17878362						
CC	72	72.0	30	30.0	60.33	0.001
CT	20	20.0	58	58.0		0.001
TT	8	8.0	12	12.0		0.001
Alleles						
C	164	82.0	118	40.0	61.54	0.001
T	36	18.0	82	60.0		0.001
TP53 Rs1042522						
GG	62	62.0	25	25.0	52.41	0.001
GC	30	60.0	62	62.0		0.001
CC	8	8.0	13	13.0		0.0014
Alleles						
G	154	77.0	112	56.0	64.37	0.001
C	46	23.0	88	44.0		0.001

The statistical assessment shows that rs104522 is statistically significantly different from HWE and the BC cohort P=0.014, while the controller group is in

agreement with HWE $P = 0.07$. The rs17878362 SNP is found to be statically significantly different from HWE in both the case and control groups Case group $P = 0.003$, control group $P = 0.004$ the difference, mark with asterisks indicate that the observed frequency of alleles such as GG, GC, and CC may differ from the expected frequency in these populations (Table 3).

Table No. 3: Genotype frequencies observed and their agreement with the Hardy Weinberg Equilibrium

	Observed	Expected	χ^2	P value
TP53rs1042522				
Case (n = 100)				
GG	25	21.8	4.795	0.014
GC	62	52.2		
CC	13	28.0		
Control (n = 100)				
GG	62	53	2.68	0.07
GC	30	25.1		
CC	8	4		
TP53 rs17878362				
Case (n = 100)				
CC	30	26.0	5.153	0.003
CT	58	53.0		
TT	12	20.0		
Control (n = 100)				
CC	72	66.0	4.027	0.004
CT	20	24.0		
TT	8	5.0		

Table No. 4: Associations of TP53rs1042522 and TP53 rs17878362 polymorphisms

Genotype	OR (CI.95%)	P
TP53 rs1042522		
GG®	1	
GC	3.08 (1.99 – 6.87)	<0.001
CC	2.72 (0.63 – 8.04)	<0.001
GC+CC	2.03 (2.25-7.00)	<0.001
Alleles		
G®	1	
C	2.55 (1.78–5.03)	<0.001
TP53 rs17878362		
CC	1	
CT	2.92 (2.00 – 7.23)	<0.001
TT	3.11 (2.01 – 6.77)	<0.001
CT+TT	2.55 (2.43-5.77)	<0.001
Alleles		
C®	1	
T	2.88 (1.57–1.95)	<0.001

There is a strong correlation in statistics between the occurrence of mutations in TP53 RS1042522 and RS17878362 and an enhanced likelihood of developing BC with regard to R 1042522. It is clear that the presence of C allele and the genotype GG leads to an

increase in BC risk, with P value less than 0.001 Regarding RS 17878362, the risk of developing BC is higher for the genotype TT compared to the genotype CC, resulting in odds ratio of 3.11. It is worth noting that there is a clear tendency in the combined genotypes GG/CC and TT/CT toward an elevated susceptibility (Table 4).

DISCUSSION

Breast cancer continues to be the most prevalent form of cancer among women in the world and its occurrence is often associated with the development index of a particular country .in addition the discovery of biomarkers to facilitate early detection is a critical to reduce to reducing fatalities worldwide¹². Also known as the guardian of the genome the TP53 gene produces the TP53 protein that regulates essential functions such as DNA repair cell cycle arrest and programmed cell death or apoptosis TP53 mutations occur in the highest numbers among BC patients about 30-50% of BC harbor mutations in the TP53¹³. It has been reported that certain mutations within the TP53 protein may also have oncogenic benefits thus making therapy difficult and highlighting the requirement for TP53 based therapeutic approaches¹². The current study highlights the relationship between some specific TP53 polymorphisms and an increased risk of BC for instance the polymorphism RS17878362, involving a-16 base pair duplication in intron 3 shows a market change in the frequency of the genotypes in control (CC equal 72% to CT 58%)with the presence of the minor allele T being associated with a higher risk of disease development this results aligns with other meta-analysis in the identification of the minor allele of RS17878362 as a risk factor for developing BC moreover another polymorphism Rs 1042522 which is responsible for the Arg 72 pro substitution^{14,15}. The most common genotype in control is GG Arg 62%, but in BC patents the GC genotype and the C allele have significantly higher frequencies 62% it is possible that the latter can affect the ability of TP53 gene product to undergo apoptosis and environmental stimuli¹⁶.

The genotypes for two TP53 mutations, RS1042522 and RS17878362, were analyzed among BC patients and healthy controls based on the findings, the genotypes for the RS1042522 mutations are significantly out of equilibrium in the BC patients ($P = 0.014$) but not in the controls $P = 0.07$ the RS1042522 mutation is located at the codon 72 locus, which results in the arginine to proline amino acid change affecting the protein function of apoptosis cell cycle control¹⁶. There is a significant departure from Hardy Weinberg equilibrium for the Rs 17878362 allele in the BC and control groups ($p = 0.003, p = 0.004$ respectively). Another important point to be noted is that genetic polymorphism of the TP53 gene, which is located on the 17 P13.1 chromosome may lead to

inactivation of the protein and increased vulnerability to various cancers¹⁷. Particularly, this is the case for the 16 base pair repeat in the RS17878362, which alters mRNA processing decreases TP53¹⁸. The findings indicate that the non-random localization of alleles in the genes encoding tumor suppressors can become a significant marker of predisposition to cancer and genomic instability and high-risk groups.

There appears to be a statistically strong correlation between TP53 mutations and increased risk of BC more specifically, when analyzing the Rs1042522 mutations, patients processing the C allele or GC genotype have significantly increased chances of suffering from BC (P 0.001). The findings confirm the role of the Arg 72 pro mutation as an essential regulator in the process of cancer development through its influence on the degradation of TP53 protein. Bunked in turn, with regard to the RS17878362 mutation, the genotype with the highest risk is the uh TT one with the odds ratio being 3.11^{19,20}. Mutations in the pathways of tumor suppressors act as markers for assessing the risk of developing cancer. There is a common pattern among the genotypes (GC + CC and CT + TT) that shows an inclination towards the greater BC predisposition in this experiment.

This specific gene mutation shows a close link with the clinical result. Modern scientific literature between 2023 and 2025 support this claim by showing the role of TP53 mutations and promoting carcinogenesis¹⁶. Thus, it becomes imperative to recognize these high-risk genotypes for the development of customized approaches and cancer therapy.

CONCLUSION

The genotype rs17878362 and rs1042522 show a strong relationship with BC among the current Iraq samples specifically occurring that the T allele in the former or the C allele in the later wall raise the change of developing BC. The two genetic mutations probably affect the activity of the TP35 gene leading to increase genomic instability additionally significant difference from Hardy-Weinberg equilibrium toward the non-random distribution of this genetic mutation in connection with the occurrence of breast cancer finely dedicating such high-risk genetic profiles represents a useful tool in cancer genetic for early detection and targeted treatment.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Soura Alaa Hussein, Ahmed Mudher Al-Khaykanee
Drafting or Revising Critically:	Soura Alaa Hussein, Tiba A.H. Al-Rubaye
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

Conflict of Interest: The study has no conflict of interest to declare by any author.

Source of Funding: None

Ethical Approval: No. FTU-1401/Approval/ JSDJNEHU Dated 25.11.2023

REFERENCES

1. Freihat O, Sipos D, Kovacs A. Global burden and projections of breast cancer incidence and mortality to 2050: a comprehensive analysis of GLOBOCAN data. *Frontiers Public Health* 2025;13:1622954.
2. Roheel A, Khan A, Anwar F, Akbar Z, Akhtar MF, Khan I, et al Global epidemiology of breast cancer based on risk factors: a systematic review. *Frontiers Oncol* 2023; 13: 1240098.
3. Li L, Doppalapudi A, Escamilla J, Karithara A, Pham C, Phillip A, et al. Precision medicine and beyond: Evolving roles of targeted therapy, immunotherapy, and artificial intelligence in oncology. *INNOSC Theranostics Pharmacol Sci* 2025;43.
4. Khan AQ, Touseeq M, Rehman S, Tahir M, Ashfaq M, Jaffar E, et al. Advances in breast cancer diagnosis: a comprehensive review of imaging, biosensors, and emerging wearable technologies. *Frontiers Oncol* 2025;15:1587517.
5. Marouf SS. Molecular subtypes of breast cancer: distribution and prognostic implications. *Zanco J Med Sci* 2025;470-80.
6. Gurau AM, Mihalache D, Satala CB, Rață AM, Rebegea LF. HER2-low breast cancer: biological framework and determinants of HER2 Instability. *Medicina* 2026;62(2):304.
7. Brücher BL. The erosion of healthcare and scientific integrity: A growing concern. *J Healthcare Leadership* 2025; 23-43.
8. Wali AF, El-Tanani M, Talath S, Rabbani SA, Rangraze IR, Satyam SM, et al. Antibody - drug conjugates and beyond: next-generation targeted therapies for breast cancer. *Cancers* 2025;17(24): 3943.
9. Baliakas P, Soussi T. The TP53 tumor suppressor gene: From molecular biology to clinical investigations. *J Internal Med* 2025;298(2):78-96.
10. Flores-López LA, Enríquez-Flores S, García-Torres I, López-Velázquez G, Viedma-Rodríguez R, Ávalos-Rodríguez A, et al. Pancreatic β cell apoptosis in type 2 diabetes is related to post translational modifications of p53. *Molecular Med Reports* 2024;30(5): 1-16.
11. Du T, Jiang T, Li X, Rahaman MM, Grzegorzec M, Li C. Prediction of TP53 mutations across female reproductive system pan-cancers using deep multimodal PET/CT radiogenomics. *Frontiers Med* 2025;12:1608652.

12. McDaniel JM, Morrissey RL, Chau GP, Su X, Ruff ZV, et al. Multi-omics analysis identifies intrinsic Trp53 driven metastatic breast cancer subtypes. *bioRxiv* 2026;2026-02.
13. Marvalim C, Datta A, Lee SC. Role of p53 in breast cancer progression: An insight into p53 targeted therapy. *Theranostics* 2023;13(4):1421.
14. Morten BC, Chiu S, Oldmeadow C, Lubinski J, Scott RJ, Avery-Kiejda KA. The intron 3 16 bp duplication polymorphism of p53 (rs17878362) is not associated with increased risk of developing triple-negative breast cancer. *Breast Cancer Res Treatment* 2019; 173(3): 727-33.
15. Sagne C, Marcel V, Amadou A, Hainaut P, Olivier M, Hall J. A meta-analysis of cancer risk associated with the TP53 intron 3 duplication polymorphism (rs17878362): geographic and tumor-specific effects. *Cell Death Dis* 2013; 4(2): e492.
16. Zhang XQ, Bai XH, Zhang HZ, He XF. Association between the p53 polymorphisms and cervical cancer risk: an updated meta-analysis. *Frontiers Oncol* 2025; 15: 1461737.
17. Dawood HH, Mohammed RK. The association between single nucleotide polymorphisms rs1042522 and rs1642785 in the TP53 gene and acute myeloid leukemia in a sample of the Baghdad/Iraq population. *Baghdad Sci J* 2024; 21(3): 10.
18. Macedo JMB, Silva AL, Pinto AC, Landeira LFL, Portari EA, Santos-Rebouças CB, et al. TP53 and p21 (CDKN1A) polymorphisms and the risk of systemic lupus erythematosus. *Adva Rheumatol* 2023; 63(1): 43.
19. Alhadheq AM, Parine NR, Shaik JP, Alhadheq R, Alkahtani S, Aljarba NH, et al. Polymorphisms of TP53 gene and its association with colorectal cancer: A case-control investigation. *J King Saud Univ Sci* 2023;35(10):102936.
20. Barnoud T, Parris JL, Murphy ME. Common genetic variants in the TP53 pathway and their impact on cancer. *J Molecular Cell Biol* 2019; 11(7): 578-85.