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Association of TP53 rs1042522 Polymorphism with Clinicopathological Features of Breast Cancer in Patients from a Tertiary Care Center in Pakistan

Anum Sitai, Fouzia Shaikh, Rehan Imad, Ummiya Tahir, Zehra Ahmed

ABSTRACT

Objective: Breast cancer (BC) is the most common cancer among women worldwide and a leading cause of cancer-related mortality; Pakistan has one of the highest incidence rates in Asia, highlighting its significant public health burden. Mutations in a tumor suppressor gene TP53 have attracted much interest. Therefore, the aim of this study was to evaluate the association between clinicopathological characteristics of breast cancer patients and TP53 rs1042522 polymorphism.

Study Design & Setting: This cross-sectional study used non-probability consecutive sampling, including cases with adequate FFPE tissue and complete clinicopathological data. Collected variables comprised age at diagnosis, tumor laterality, histological type, tumor grade, pathological stage, and hormone receptor status, recorded according to standardized pathology reporting criteria. Genomic DNA was extracted from FFPE blocks using the Quick-DNA™ FFPE MiniPrep Kit, and DNA concentration and quality were assessed by spectrophotometry.

Methodology: Formalin-fixed paraffin-embedded (FFPE) tissue samples and clinical records of 48 histologically diagnosed breast carcinoma cases were analyzed. TP53 rs1042522 genotyping was performed using tetra-amplification refractory mutation system polymerase chain reaction (T-ARMS-PCR). Associations between genotypes and clinicopathological variables were analyzed using Chi-square.

Results: Total of 48 female breast cancer patients were included. Invasive ductal carcinoma was the predominant histological subtype. TP53 rs1042522 genotypes were variably distributed across tumor grades, stages, and hormone receptor status and the results showed no statistically significant association ($p > 0.05$).

Conclusion: Study concluded with statement that, TP53 rs1042522 polymorphism showed variable distribution without significant association with clinicopathological features, suggesting a descriptive rather than predictive role in this population.

Keywords: *Breast Neoplasms, TP53 Protein, Polymorphism, Genetic, Polymerase Chain Reaction, Receptor,*

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INTRODUCTION

Breast cancer (BC) is the most prevalent disease among women worldwide and a primary cause of cancer-related deaths. According to the Shaukat Khanum Memorial Cancer Hospital & Research Centre cancer registry, breast cancer was the most commonly diagnosed malignancy in Pakistan in 2021, with 1,699 reported cases.[1,2] According to GLOBOCAN 2022, data from the International Agency for Research on Cancer indicate that breast cancer is the most frequently diagnosed cancer worldwide, with approximately 2.3 million new cases (11.7% of all cancers) and a mortality rate of 6.9%, ranking it among the leading causes of cancer-related deaths globally.[3]

Despite the recent improvements in treatment modalities, the disease continues to pose a great burden mainly in the low- and middle-income nations. The key causes of death in Pakistan are delays in diagnosis, a need to identify them through screening programs, and disparities in access to specialized care.[4,5] Additionally, advanced-stage disease at presentation is a significant factor that adversely affects treatment options and clinical outcomes. These observations

demonstrate that the knowledge of the nature of the disease in the local population should be better.

Breast cancer is a biologically heterogeneous disease, consisting of a wide spectrum of histopathological and molecular features. The TP53 rs1042522 polymorphism results in an arginine-to-proline substitution at codon 72 of the p53 protein.[6] This polymorphism has been studied broadly in different Countries, yet its clinical significance remains controversial. From a clinicopathological perspective, tumor grade, stage at diagnosis, and hormone receptor status are key indicators routinely used in pathological practice, as they reflect tumor aggressiveness, disease progression, and biological behavior, which may be influenced by underlying genetic variations such as TP53 polymorphisms.[7] However, these parameters are themselves influenced by complex interactions between genetic susceptibility, tumor biology, environmental exposures, and healthcare access.[8]

Due to these functional differences, rs1042522 has been continuously investigated for its relationship with breast cancer diagnosis and clinicopathological features. However, results have been reported inconsistent. Recent genomic studies further highlight evolving molecular patterns influencing breast cancer development globally.[9] Therefore, the objectives of this study were:

1. To evaluate the clinicopathological characteristics of breast cancer patients.

2. To assess the association between TP53 rs1042522 polymorphism and clinicopathological features.

3. To determine the relationship between TP53 rs1042522 genotypes and hormone receptor status.

METHODOLOGY:

This cross-sectional study was conducted after obtaining ethical approval from the Ethical Review Committee of Ziauddin University (ERC Approval Code: 10550625AAPAT). The study was carried out from January 1, 2025, to November 2025**.** Archived clinical records and formalin-fixed paraffin-embedded (FFPE) breast carcinoma tissue blocks were retrieved from the Department of Pathology, Ziauddin Medical Hospital and Laboratory, while all molecular procedures were performed at the Molecular Diagnostics and Research Laboratory (MDRL-1), Ziauddin University. A Waiver Certificate was obtained, as the researcher conducted a retrospective review of archived records/reports**,** and no direct interaction with patients took place during this research. Written informed consent had already been obtained from the patients or their legal guardians at the time of initial specimen submission. All procedures were conducted in accordance with institutional ethical standards and the principles of the Declaration of Helsinki.

The sample size was calculated using a single-population proportion formula, based on a previously reported TP53 mutation frequency of 0.66 among breast cancer patients, with a 95% confidence interval (Z = 1.96) and a margin of error of 13.12%. A slightly higher margin of error was used due to the exploratory nature of the study, limited patient availability, and feasibility constraints in a single-center setting. Non-probability consecutive sampling was then applied to include all eligible cases during the study period. (Ahmed et al. 2023)[11] (Datkile et al. 2023)[12] In order to cover all the eligible cases during the study, non-probability consecutive sampling was used.

To achieve methodological rigor and reliability of molecular analysis, eligible cases that qualify to be included in this study were selected on predetermined inclusion and exclusion criteria.[1,2]

Criteria used in the inclusion of the patients were: female patients, who had a histologically verified primary breast carcinoma, included in the study period, as specified by the World Health Organization (WHO) Classification of Breast Tumors, which puts more emphasis on the standardization of histopathological diagnosis, necessary in reproducible oncologic research. The cases where formalin-fixed paraffin-embedded (FFPE) tissue blocks were sufficient were considered as only FFPE-specimens are considered a valid marker of retrospective molecular research and have been demonstrated to provide DNA of adequate quality to facilitate polymerase chain reaction-based genotyping when properly extracted. Moreover, age at diagnosis, tumor laterality, histological subtype, tumor grade, pathological stage and hormone receptor (ER, PR, HER2) status where necessary as comprehensive clinical annotation is necessary to establish meaningful genotype phenotype interaction in molecular epidemiology research.[3]

To provide the consistency and comparability of breast cancer research with international standards, tumor grading and staging were recorded based on internationally accepted systems, such as the Nottingham histologic grading system and the American Joint Committee on Cancer (AJCC) TNM staging guidelines. Cases were eliminated when FFPE tissue samples were of poor quality, there was extensive necrosis or lack of sufficient tumor content conversely because degraded or low yielding DNA would negatively affect the accuracy of genotyping and provide either false-negative or non-reproducible results. Incomplete medical or pathological records of the patients were not included as well to eliminate the chances of information bias and provide strong statistical analysis of clinicopathological associations. Cases that had recurring breast tumors and those with the previous history of any other malignancy were eliminated because both conditions might confound genetic changes not directly related to primary breast carcinogenesis and hence confound the TP53 polymorphism association analysis. These criteria are consistent with the methodological guidelines of retrospective molecular pathology and genetic association studies, which guarantee internal validity and the reduction

of possible sources of bias STROBE Statement.

Clinicopathological information was obtained from pathology archives and included age at diagnosis, tumor laterality, histological subtype, tumor grade, pathological stage, and hormone receptor status (ER, PR, HER2). For quality control in molecular analysis, each T-ARMS PCR run included a known positive control (previously confirmed genotype) and a negative control (no-template control) to ensure assay specificity and to detect contamination. Genotyping was determined based on the presence of allele-specific bands visualized on agarose gel electrophoresis, corresponding to homozygous (CC, GG) and heterozygous (CG) patterns. A subset of samples was re-amplified to confirm reproducibility of results.

The grading and staging of tumors were reported based on the current international histopathological criteria. FFPE mini-prep was performed on the genomic DNA of FFPE tissue with the Quick-DNATM FFPE MiniPrep Kit (Zymo Research, USA) and concentration and purity of the DNA were measured by spectrophotometer. TP53 rs1042522 (Arg 72 Pro) polymorphism was picked up to be analyzed because it is functionally relevant, the minor allele frequency is above 5 percent and has been reported to be relevant to breast cancer susceptibility.

Tetra-amplification refractory mutation system polymerase chain reaction was used to genotype. A 25 ìL of the reaction mixture was used and consisted of 1 ìL of forward and reverse outer primers (10 pmol/ ìL), 1 ìL of forward and reverse inner primers, 5 ìL of DNA template (approximately 40 ng), 12.5 ìL of PCR master mix, and 5.5 ìL of nuclease-free water. The PCR design was that of a first round denaturing at 95 o C, 35 cycles of 95 o C 30 seconds, 56 o C 1 minute, 72 o C 1 minute and finally, a final extension of 72 o C 10 minutes. Primer sequences were as follows: forward outer—CCTCAGGGCAACTGACCG; reverse outer -GAAGGGCAGGCCCACCAC; forward inner -GGTGCAGGGGCCACGC; reverse inner -CCAGAGGCTGCTCCCCC. These cycling conditions and primer sets agree with confirmed standards of using these primers to genotype the rs1042522.

Agarose Gel Electrophoresis: PCR products were resolved on a 2% agarose gel in 1× TBE buffer, stained with ethidium bromide. Samples and a DNA ladder were electrophoresed and visualized under UV light to detect *p53* gene bands.

All the data was combined and analyzed by use of SPSS version 27. Clinicopathological characteristics were summarized using descriptive statistics and Chi-square or Fisher exact tests were used to determine the association between the TP53 rs1042522 genotypes and the categorical variables with statistical significance was set at $p < 0.05$.

Frequencies and percentages were used to summarize categorical variables such as marital status, clinical stage, tumor grade, hormone receptor status (estrogen receptor, progesterone receptor, and HER2), and breast cancer subtype in the description of the distribution of clinicopathologic characteristics. The age at diagnosis, a quantitative variable, was evaluated at the first instance to be tested about normality with the use of the Shapiro–Wilk test. The relationship of categorical clinicopathological variables and gene mutation status was analyzed using the Chi-square test of independency. In cases where the assumptions of the Chi-square test were not fulfilled particularly, when the anticipated number of cells was less than five in over 20 percent of the cells, the Fisher's exact test was used, and this assured a validity in the results.

RESULTS

The demographic and clinicopathological characteristics of the study population are summarized in Table 1. The total number of breast cancer cases used in the analysis presented in Table 1 is 48 confirmed. The above Table summarizes the age, marital status, tumor features, and clinical characteristics of 48 breast cancer patients. Most patients were older than 50 years, had left-sided tumors, invasive ductal carcinoma, were married, and were diagnosed mainly at stage 2 with moderately differentiated tumors

Table2 shows how different TP53 rs1042522 genotypes (CC, CG, GG) are distributed across tumor characteristics in breast cancer patients. No significant association was found between TP53 genotypes and tumor laterality, site, grade, stage, or nodal status (all p-values > 0.05).

Table 3 presents the distribution of TP53 rs1042522 genotypes across different histological subtypes of breast cancer. Invasive ductal carcinoma was the most common subtype observed in the study population. Although CC and CG genotypes were more frequently observed than GG, no statistically significant association was found between TP53 rs1042522 genotype distribution and breast cancer subtype ($p = 0.244$). Table 4, when genotypes were grouped as CC+CG versus GG, the combined CC+CG group was more frequently observed in higher tumor grades and across tumor stages; however, these differences were not statistically significant ($p > 0.05$). Although the high-risk allele group (CG + CC) was more frequently observed across higher tumor grades and stages, no statistically significant association was found with tumor grade ($p = 0.082$), age group ($p = 0.285$), or tumor stage ($p = 0.949$). In Table 5 Hormone receptor positivity, particularly ER and PR, was more frequently observed across tumor grades, stages, and sites; however, no statistically significant association was identified between clinicopathological variables and ER, PR, or HER2 status.

The Figure 2 show that ER and PR positivity is highest in well-differentiated and early-stage tumors and decreases with higher grade and stage, while HER2 positivity increases in poorly differentiated and advanced tumors. Marker

expression also differs by tumor site, with ER and PR more common in upper quadrants.

Table 1: Demographic and clinicopathological characteristics of breast

Variable	Frequency	%
Age at diagnosis (years)		
30–40	8	16.7
41–50	8	16.7
51–60	12	25.0
61–70	7	14.6
=71	13	27.1
Tumor laterality		
Left	26	54.2
Right	22	45.8
Site		
Upper Quadrant	12	25.0
Lower Quadrant	6	12.5
Central	12	25.0
Inner	2	4.2
Not specified	16	33.3
Histological type		
Invasive ductal carcinoma (NST)	39	81.3
Micropapillary carcinoma	1	2.1
Mucinous carcinoma	2	4.2
Lobular carcinoma	3	6.3
Metaplastic carcinoma	1	2.1
Microcapillary carcinoma	1	2.1
Solid papillary carcinoma	1	2.1
Marital Status		
Married	45	93.8
Unmarried	3	6.3
Tumor grade		
Well differentiated	6	12.5
Moderately differentiated	27	56.3
Poorly differentiated	15	31.3
Tumor Stage		
Stage 1	6	12.5
Stage 2	28	58.3
Stage 3	10	20.8
Stage 4	4	8.3
Nodal Stage		
Nodal stage 1	11	22.9
Nodal stage 2	9	18.8
Nodal stage 3	5	10.4
Not applicable	23	47.9

DISCUSSION

The clinicopathological characteristics of Pakistani breast cancer patients and their distribution in relation to the TP53 rs1042522 polymorphism are described in this study.

The majority of tumors presented at intermediate-to-high grade and advanced pathological stages, which was consistent with national and regional data. Delays in diagnosis are common in Pakistan because of limited screening programs, social cultural obstacles to early health care seeking as well as the problem of access to diagnostic centers and health care centers.[10] Tumor grade, stage, and hormone receptor status did not significantly correlate with any of the TP53 rs1042522 genotypes (Arg72/Pro72) found in clinicopathological groups.[11,12,13] These findings are in line with international meta-analyses, which have reported inconsistent or null associations between this polymorphism and breast cancer characteristics, suggesting that rs1042522 alone is unlikely to serve as a reliable clinicopathological marker in this population. The absence of a significant correlation among our population implies that rs1042522 estimation will not be a significant clinicopathological parameter within Pakistani patients with breast cancer. Although functional differences between the Arg72 and Pro72 variants have been reported in laboratory studies, translating these findings into consistent clinical patterns has proven difficult.[13] Experimental studies showed that the variant of Pro72 was related to increased transcriptional activation and turnover of cell cycle.[14] This highlights that germline TP53 polymorphisms, including rs1042522, have limited predictive value compared to well-established clinical indicators such as hormone receptor status and molecular subtype classification[15]

Several large-scale meta-analysis such as Diakité B et al., 2020; Zhuo W et al., 2009; Afzaljavan F et al., 2019 have been observed to find the association between TP53 rs1042522 and breast cancer susceptibility along with finding the tumor characteristics, which obtained heterogeneous results. The clinical relevance of this polymorphism may be dependent on population.[16] Such variability highlights the importance of conducting mix and specific studies, especially in controlled populations where genetic epidemiological data remain limited.[17]

Further rs1042522, other TP53 polymorphisms and related genes have been investigated for their potential modificational effects on the risk of breast cancer and its outcomes.[18] Studies exploring the haplotype structures and gene-gene interactions suggest that the isolated assessment of a single polymorphism may under estimate the complexity of TP53-mediated tumorigenesis.[19] This may partially explain the lack of consistent associations observed in many clinicopathological studies, including our findings.[20]

Consequently, genetic effects that might be detectable in well-screened populations could be unmasked in such areas

Table 2: Association of TP53 rs1042522 genotypes with clinicopathological variables

Variable	CC n (%)	CG n (%)	GG n (%)	Total	p-value
Tumor laterality					
Left	10 (38.5)	8 (30.8)	8 (30.8)	**26**	**0.149***
Right	9 (40.9)	11 (50.0)	2 (9.1)	**22**	
Site					
Upper quadrant	5 (41.7)	5 (41.7)	2 (16.7)	**12**	
Lower quadrant	2 (33.3)	2 (33.3)	2 (33.3)	**6**	**0.915***
Central / retroareolar	4 (33.3)	4 (33.3)	4 (33.3)	**12**	
Inner quadrant	1 (50.0)	1 (50.0)	0 (0.0)	**2**	
Not specified	7 (43.8)	7 (43.8)	2 (12.5)	**16**	
Tumor grade					
Well -differentiated	2 (33.3)	1 (16.7)	3 (50.0)	**6**	**0.123***
Moderately differentiated	13 (48.1)	9 (33.3)	5 (18.5)	**27**	
Poorly differentiated	4 (26.7)	9 (60.0)	2 (13.3)	**15**	
Pathological stage					
Stage I	2 (33.3)	2 (33.3)	2 (33.3)	**6**	
Stage II	14 (50.0)	8 (28.6)	6 (21.4)	**28**	**0317***
Stage III	2 (20.0)	6 (60.0)	2 (20.0)	**10**	
Stage IV	1 (25.0)	3 (75.0)	0 (0.0)	**4**	
Nodal stage					
Not applicable	10 (43.5)	7 (30.4)	6 (26.1)	**23**	
Nodal stage I	4 (36.4)	4 (36.4)	3 (27.3)	**11**	**0.149***
Nodal stage II	4 (44.4)	4 (44.4)	1 (11.1)	**9**	
Nodal stage III	1 (20.0)	4 (80.0)	0 (0.0)	**5**	
Total	19 (39.6)	19 (39.6)	10 (20.8)	**48**	

***** CC two Cytosine bases, *****CG one Cytosine and one Guanine**. *** GG means two Guanine bases**.**

Table3: Breast cancer subtypes with TP53 rs1042522 genotypes (n = 48)

Breast cancer subtype	CC n (%)	CG n (%)	GG n (%)	Total n (%)
Invasive ductal carcinoma	16 (41.0)	15 (38.5)	8 (20.5)	39 (100)
Micropapillary carcinoma	0 (0.0)	1 (100.0)	0 (0.0)	1 (100)
Mucinous carcinoma	0 (0.0)	0 (0.0)	2 (100.0)	2 (100)
Lobular carcinoma	2 (66.7)	1 (33.3)	0 (0.0)	3 (100)
Metaplastic carcinoma	1 (100.0)	0 (0.0)	0 (0.0)	1 (100)
Microcapillary carcinoma	0 (0.0)	1 (100.0)	0 (0.0)	1 (100)
Solid papillary carcinoma	0 (0.0)	1 (100.0)	0 (0.0)	1 (100)
Total	**19 (39.6)**	**19 (39.6)**	**10 (20.8)**	**48 (100)**

where late-stage disease is predominant.[21]

As far as clinical perspective is concerned, hormone receptor status and molecular subtype classification have shown as more absolute predictors of prognosis and treatment response than individual germ line polymorphisms. Although TP53 alterations are frequent in breast cancer, particularly in high-grade and triple-negative tumors, germ line polymorphisms such as rs1042522 appear to have limited stand-alone predictive value in routine clinical practices, which supports the present study findings.[22]

Lastly, TP53 rs1042522 represents a biologically relevant polymorphism with demonstrable functional effects at the molecular level, its clinical impact appears to be dependent. The absence of strong associations in the present study supports the assertion that this polymorphism alone is unlikely to serve as a reliable clinicopathological marker in Pakistani breast cancer patients.

Despite its small sample size, single-center design, and absence of long-term clinical follow-up, this study provides valuable baseline information on TP53 rs1042522 polymorphism in Pakistani breast cancer patients. The results

Table 4: Clinicopathological features with TP53 rs1042522 risk allele groups (n = 48)

Clinicopathological feature	High-risk n (%)	Low-risk n (%)	Total	p-value
Tumor grade				
Well differentiated	3 (50.0)	3 (50.0)	6	**0.082**
Moderately differentiated	19 (70.4)	8 (29.6)	27	
Poorly differentiated	14 (93.3)	1 (6.7)	15	
Age group				
30–40	6 (75.0)	2 (25.0)	8	
41–50	4 (50.0)	4 (50.0)	8	**0.285**
51–60	9 (75.0)	3 (25.0)	12	
61–70	7 (100.0)	0 (0.0)	7	
>71	10 (76.9)	3 (23.1)	13	
Tumor stage				
Stage I	4 (66.7)	2 (33.3)	6	
Stage II	21 (75.0)	7 (25.0)	28	**0.949**
Stage III	8 (80.0)	2 (20.0)	10	
Stage IV	3 (75.0)	1 (25.0)	4	
Total	**36 (75.0)**	**12 (25.0)**	**48**	

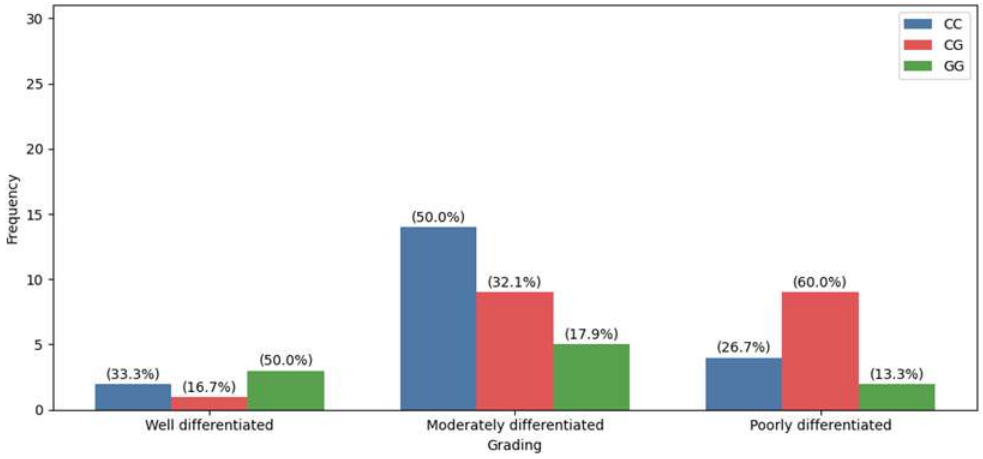
*High-risk = CG + CC | Low- risk = GG

Table 5: Association of clinicopathological variables with hormone receptor status (n = 15)

Variable	ER Positive n (%)	ER Negative n (%)	p-value	PR Positive n (%)	PR Negative n (%)	p-value	HER2 Positive n (%)	HER2 Negative n (%)	p-value
Tumor grade									
Well differentiated	1 (100.0)	0 (0.0)		1 (100.0)	0 (0.0)		0 (0.0)	1 (100.0)	
Moderately differentiated	6 (85.7)	1 (14.3)	0.700	5 (71.4)	2 (28.6)	0.700	1 (16.7)	5 (83.3)	0.823
Poorly differentiated	5 (71.4)	2 (28.6)		5 (71.4)	2 (28.6)		2 (40.0)	3 (60.0)	
Tumor stage									
Stage I	1 (100.0)	0 (0.0)		1 (100.0)	0 (0.0)		0 (0.0)	1 (100.0)	
Stage II	6 (85.7)	1 (14.3)	0.753	5 (71.4)	2 (28.6)	0.700	1 (16.7)	5 (83.3)	0.823
Stage III	5 (71.4)	2 (28.6)		5 (71.4)	2 (28.6)		2 (40.0)	3 (60.0)	
Tumor site									
Upper quadrant	11 (78.6)	3 (21.4)		11 (78.6)	3 (21.4)		3 (27.3)	8 (72.7)	
Lower quadrant	1 (100.0)	0 (0.0)	0.700	0 (0.0)	1 (100.0)	0.605	0 (0.0)	1 (100.0)	0.086
Total	**12 (80.0)**	**3 (20.0)**		**11 (73.3)**	**4 (26.7)**		**3 (20.0)**	**12 (80.0)**	

ER = Estrogen receptor, PR = Progesterone receptor, HER2 = Human epidermal growth factor receptor 2.

Figure 1: shows TP53 rs1042522 genotype distribution by tumor grade



emphasize the need for larger, multi-center studies that combine genomic profiling with long-term clinical data to better understand the role of TP53 variants and their potential impact on disease characteristics in this population.

Limitation of Study: The study is limited by its small sample size and single-center design, which may affect generalizability. The absence of a control group limits assessment of the association between TP53 rs1042522 polymorphism and disease susceptibility, and the modest sample size reduces statistical power to detect subtle associations. Allele frequency comparison with the general population and long-term clinical outcomes were not assessed. The relatively high frequency of "not specified" tumor sites reflect routine limitations of histopathology record documentation in retrospective studies, where quadrant details are not always consistently recorded in archived pathology reports. Although samples were collected from Ziauddin Hospital, a tertiary care center that receives patients from across Pakistan rather than only Karachi, Sampling patients from across Pakistan enhances population diversity, thereby increasing the relevance and applicability of the findings.

CONCLUSION

In conclusion, TP53 rs1042522 polymorphism showed variable distribution among breast cancer patients but was not significantly associated with clinicopathological characteristics in this study. These findings suggest that this polymorphism has limited clinical utility as a predictive marker in this population. Further large-scale, multicenter studies with comprehensive genetic profiling are recommended to better clarify its potential role in breast cancer.

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Authors Contribution:
Anum Sitai: data collection, statistical analysis and manuscript drafting
Fouzia Shaikh: supervised the study, critically revised the manuscript and approved the final version
Rehan Imad: conducted the molecular methodology and genotyping analysis
Ummiya Tahir: Conceived the study and provided all histopathological material and clinicopathological data
Zehra Ahmed: assisted in manuscript writing and literature review

REFERENCES:

1. Arnold M, Morgan E, Rumgay H, Mafra A, Singh D, Laversanne M, et al. Current and future burden of breast cancer: global statistics for 2020 and 2040. Breast. 2022; 66:15–23. DOI: https://doi.org/10.1016/j.breast.2022.08.010
2. Pink Ribbon Pakistan. The alarming rise of breast cancer deaths in Pakistan [Internet]. Karachi: Pink Ribbon Pakistan; 2024 [cited 2025 Dec 21]. Available from: https:// pinkribbon.org. pk/the-alarming-rise-of-breast-cancer-deaths-in-pakistan/
3. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71(3):209–249. DOI: https://doi.org/10.3322/caac.21660
4. Hanna TP, King WD, Thibodeau S, Jalink M, Paulin GA, Harvey-Jones E, et al. Mortality due to cancer treatment delay: systematic review and meta-analysis. BMJ. 2020;371:m4087. DOI: https://doi.org/10.1136/bmj.m4087
5. Harbeck N, Penault-Llorca F, Cortes J, Gnant M, Houssami N, Poortmans P, et al. Breast cancer. Nat Rev Dis Primers. 2019; 5:66. DOI: https://doi.org/10.1038/s41572-019-0111-2 \
6. Syeed N, Husain SA, Sameer AS, Abdullah S, Qadri Q, Siddiqi MA. TP53 R72P polymorphism in breast cancer patients of Kashmir. Asian Pac J Cancer Prev. 2011;12(3):621–625.
7. Blondeaux E, Arecco L, Punie K, Graffeo R, Toss A, De Angelis C, Trevisan L, Buzzatti G, Linn SC, Dubsky P, Cruellas M. Germline TP53 pathogenic variants and breast cancer: a narrative review. Cancer Treat Rev. 2023; 114:102522.
8. Nausheen H, Ahmed R, Khan S, Fatima S, et al. Clinicopathological characteristics of molecularly classified groups of invasive ductal breast carcinoma in Pakistani women. Pak J Med Dent. 2022;11(2):3–8.
9. Sandoval RL, Bottosso M, Tianyu L, Polidorio N, Bychkovsky BL, Verret B, Gennari A, Cahill S, Achatz MI, Caron O, Imbert-Bouteille M. TP53-associated early breast cancer: new observations from a large cohort. JNCI: Journal of the National Cancer Institute. 2024 Aug;116(8):1246-54.
10. World Health Organization. WHO classification of tumours of the breast. 5th ed. Lyon: International Agency for Research on Cancer; 2019.
11. Bonin S, Hlubek F, Benhattar J, Denkert C, Dietel M, Fernandez PL, et al. Multicentre validation study of acids extraction from FFPE tissues. Virchows Arch. 2010;457(3):309–17
12. Bass BP, Engel KB, Greytak SR, Moore HM. A review of preanalytical factors affecting molecular, protein, and histopathological analysis of FFPE tissue: how well do you know your specimen? Arch Pathol Lab Med. 2014;138(11):1520–30. doi:10.5858/arpa.2013-0691-RA.
13. Afzaljavan F, Alizadeh E, Ghaderian SMH, Akbari MT. TP53 codon 72 polymorphism (rs1042522) and breast cancer risk: case-control study and meta-analysis. Sci Rep. 2019; 9:12776. doi: https://10.1038/s41598-019-49120-1
14. Syeed N, Husain SA, Sameer AS, Abdullah S, Qadri Q, Siddiqi MA. TP53 R72P polymorphism in breast cancer patients of Kashmir. Asian Pac J Cancer Prev. 2011;12(3):621–625.
15. Nausheen H, Ahmed R, Khan S, Fatima S, et al. Clinicopathological characteristics of molecularly classified groups of invasive ductal breast carcinoma in Pakistani women. Pak J Med Dent. 2022;11(2):3–8.

16. Wu D, Zhang Z, Chu H, Li H, Wang M, Zhang Z. Intron 3 sixteen base pair duplication polymorphism of TP53 contributes to breast cancer susceptibility. PLoS One. 2013;8(4): e61662. doi: https://10.1371/journal.pone.0061662

17. Wu D, Zhang Z, Chu H, Li H, Wang M, Zhang Z. Intron 3 sixteen base pair duplication polymorphism of TP53 contributes to breast cancer susceptibility. PLoS One. 2013;8(4): e61662. doi: https://10.1371/journal.pone.0061662

18. Icen-Taskin I, Calik M, Ates O. TP53 rs1042522 polymorphism and early-onset breast cancer risk in Turkish women. J Res Med Sci. 2020; 25:25. doi: https://10.4103/jrms.JRMS_652_19

19. Cheng H, Ma B, Huang W, Wang X, Wang Y. Combined effects of MDM2 SNP309 and TP53 R72P polymorphisms on breast cancer risk. Mol Biol Rep. 2012;39(10):9781–9788. doi: https://10.1007/s11033-012-1842-4

20. Shahbandi A, Nguyen HD, Jackson JG. TP53 mutations and outcomes in breast cancer: reading beyond the headlines. Trends Cancer. 2020;6(2):98–110. doi: https://10.1016/j.trecan.2019.11.007

21. Grote I, Bartels S, Kandt L, Bollmann L, Christgen H, Gronewold M, et al. TP53 mutations are associated with primary endocrine resistance in luminal early breast cancer. Cancer Med. 2021;10(23):8581–8594. doi: https://10.1002/cam4.4361

22. Shahbandi A, Nguyen HD, Jackson JG. TP53 mutations and outcomes in breast cancer: reading beyond the headlines. Trends Cancer. 2020;6(2):98–110. doi: https://10.1016/j.trecan.2019.11.007