ASSOCIATION OF THE CHEK2 1100DELC GENETIC VARIANT WITH IMMUNOHISTOCHEMICAL MARKERS IN BREAST CANCER.

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ABSTRACT

The CHEK2 gene plays a crucial role in cell cycle checkpoint control mechanisms that respond to DNA damage. This study investigated the association between the CHEK2 1100delC polymorphism and immunohistochemical markers (ER, PR, Her2/neu, Ki67) in breast cancer (BC). The findings suggest that the CHEK2 1100delC polymorphism with the C/G genotype may increase the likelihood of association with higher proliferation levels, as indicated by Ki67 expression..

Introduction: Among the 200 patients constituting the main study group, 196 (98%) carried the normal *CHEK2* 1100delC C/C genotype, while 4 (2%) had the C/G heterozygous genotype; no cases with the homozygous mutant G/G genotype were detected. Among the 196 *C/C* genotype carriers, estrogen receptor (ER) expression was positive in 62.2% and negative in 37.8% of cases, indicating correspondingly effective and ineffective responses to hormone therapy. In the four patients with the *C/G* genotype, ER expression was evenly distributed (50% positive, 50% negative), suggesting no significant advantage in hormone therapy responsiveness. A similar trend was observed for the progesterone receptor (PR) marker: 57.6% of *C/C* genotype carriers showed positive results and 42.4% negative, whereas in *C/G* carriers, the ratio was 50% to 50%. Analysis of the Her2/neu marker revealed positive results in 28.1% and negative in 71.9% of *C/C* carriers, while among *C/G* carriers, the respective rates were 25% and 75%. Based on these findings, targeted therapy was found to be effective in 28.1% of *C/C* and 25% of *C/G* genotype carriers.

A more pronounced difference was observed for the Ki67 marker. Among the 196 patients with the *C/C* genotype, 83.7% showed a high proliferation index (>15%), while 16.3% had a low index (<15%). Among *C/G* carriers, these values were 75% and 25%, respectively. This finding indicates a potential biological association between the *C/G* genotype and higher proliferative activity. Statistical analyses demonstrated that for ER (*C/C*: 62.2%; *C/G*: 50%; OR = 1.65; RR = 1.24), PR (*C/C*: 57.7%; *C/G*: 50%; OR = 1.36; RR = 1.15), and Her2/neu (*C/C*: 28.1%; *C/G*: 25%; OR = 1.17; RR = 1.12), no significant differences were found between genotypes. However, for Ki67, the odds ratio (OR = 1.71) and relative risk (RR = 1.12) did not exclude the possibility of an increased proliferative index associated with the *C/G* genotype (Table 1).

Table 1.

Association of the *chek2* 1100delc polymorphism with immunohistochemical markers (ER, PR, Her2/neu, Ki67).

genotype	n	ER		PR		Her2/neu		Ki67	
		+	-	+	-	+	-	>15%	<15%
C/C	196	122 (62,2%)	74 (37,8%)	113 (57,6%)	83 (42,4%)	55 (28,1%)	141 (71,9%)	164 (83,7%)	32 (16,3%)
C/G	4	2 (50%)	2 (50%)	2 (50	2 (50%)	1 (25%)	3 (75%)	3 (75%)	1 (25%)
total	200	124 (62,2%)	76 (38,2%)	115 (57,5%)	85 (42,5%)	56 (28%)	144 (72%)	167 (83,5%)	33 (16,5%)

Note: "+" indicates a positive result; "–" indicates a negative result. For Ki67, values >15% are considered positive, and values <15% are considered negative. The homozygous G/G genotype of the CHEK2 1100delC polymorphism was not detected in either the main or control groups.

Conclusion: The obtained results suggest that the heterozygous *C/G* state of the *CHEK2* 1100delC polymorphism may increase the likelihood of association with the level of proliferation (Ki67). This indicates that *CHEK2* genetic variants may serve as important molecular factors influencing the clinical course of breast cancer.