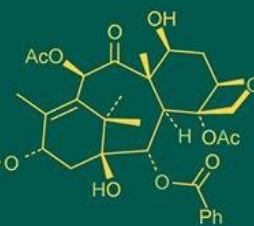
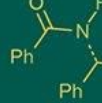
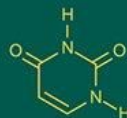
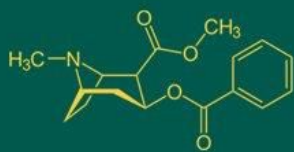


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The relationship between Survivin rs9904341 gene and its association with breast cancer risk

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Abstract

Background Several studies have shown an association between the The human survivin gene and lung, colon, breast, prostate, bladder, breast, kidney, pancreas, and stomach cancers. The main objective of this study was to find the relationship between genetic polymorphisms G/C of the coronary artery disease gene and the risk of breast cancer .**Method** The study included 60 samples and was divided into a control group and a group of patients with breast cancer before starting treatment. The samples were collected from Imam Al-Sadiq Hospital in Babylon Governorate, Oncology Department. All cases were diagnosed using local biopsy and magnetic resonance imaging. **Result** In the survivor gene, the prevalence of the G/C polymorphism of rs9904341 was found to be statistically significant across the studied samples, with the GG genotype being more prevalent in the control group, and the genotype considered a risk factor for breast cancer being the most prevalent G/C genotype. **Conclusion** The present study showed that Breast cancer is linked to the G/C polymorphism in Survivin rs9904341.

Keywords: Survivin gen , breast cancer, polymorphism of rs9904341

1. Introduction

The most common cancer to be diagnosed is breast cancer, which is a very diverse disease ^[1]. Breast cancer risk and development are linked to the combined effects of genetic predisposition and environmental variables, including being overweight, not exercising, drinking alcohol, using hormone replacement therapy, and having menstrual cycles ^[2].

Genetic factors are responsible for five to ten percent of breast cancer cases other causes include unregulated female hormones, bad lifestyle choices, and poor eating habits ^[3,4]. Breast cancer risk factors include Obesity-causing metabolic diseases, diabetes, hypertension, postmenopausal obesity, and hyperglycemia ^[5]. The risk of BC may be decreased by lowering obesity and other modifiable variables. even while inherited concerns cannot be avoided. Changes in the gut microbiota are intimately linked to obesity ^[6].

It has been discovered that the human survivin gene is essential for the development of cancer because it speeds up the buildup of genetic changes, inhibits both extrinsic and intrinsic apoptotic pathways, and makes treatment more sensitive ^[7]. This gene is rarely expressed in malignant tissues compared to healthy adult tissues ^[8]. Because of its role in preventing apoptosis, survivin mutation may alter survivin expression, which is essential for the development and metastasis of cancer, ^[9,10]. There are several mutations in the survivin gene. Numerous studies have connected survivin mutations to cancer susceptibility in different cultures including the missense variations rs9904341 in the promoter of exon 5 and rs1042489 in the 3' untranslated, region ^[11]. Tumors, colorectal cancer, ovarian cancer, laryngeal cancer, renal cell carcinoma, stomach cancer, breast cancer, and esophageal cancer are among the tumors, for which survivin overexpression has been linked to a bad prognosis ^[12-13]. We hypothesize that breast cancer is most likely linked to the survivin gene.

2. Materials and Methods

This study included 60 samples and was distributed as follows: The first group included 30 samples from healthy adults. The second group included 30 samples from women with breast cancer before starting treatment. The samples were collected from Imam Al-Sadiq Hospital in Babylon Governorate, Oncology Department, from 2022 to 2025.

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All cases were diagnosed using local biopsy and magnetic resonance imaging. Information was provided freely by the people involved in the study.

2.1. Laboratory investigation

Measurement of biochemical profile, activities was determined using Monarch-240 - Clinical Chemistry Analyzer Fully Automate And using kits from the company biorex Complete blood picture (CBC) was determined using SYSMEX JAPAN Fully Automated 3-part Cell Counter XP300 (Japanese) And using kits from the company SYSMEX, Regular testing for biochemical profile and CBC

2.2. SNP assay of Survivin rs9904341 and DNA extraction

Each participant had a 4 ml venous blood sample extracted into an EDTA vial. Using the phenol/chloroform technique, genomic DNA was extracted. A restriction fragment length polymorphism in a polymerase chain reaction to find the survivin promoter -32 G/C polymorphism, PCR-RFLP was employed. 0.1 mM dNTPs, 5 ml of 10× polymerase buffer, and 50 ng of genomic DNA 21 mol/l of forward primer (5'-GTTCTTTGAAAGGCAGTCGAG-3') and. reverse, primer

(5'-GCCAGTT CTTGAATGGTAGAG-3'), and Invitrogen, San Diego, California, provided 1.5 U of Taq polymerase in the 50 ml volume used for the PCR experiment. 35 cycles of denaturation at 95°C for 30 seconds, annealing at 58°C for 90 seconds, extension at 72°C for 90 seconds, and finalization using the PCR software were performed after an initial denaturation at 95°C for 5 minutes.

2.3. Statically analysis

The X2 test was used to compare the observed and expected genotypes of controls and to assess Hardy-Weinberg equilibrium. The association between the G/C polymorphism of the coronary artery disease gene and its association with breast cancer was investigated using the X2 test. The tests were also used for clinical analyses when compared with the control group if p value is ≤ 0.05 , it is considered statistically significant

3. Results

Two groups of sixty women participated in our study. thirty women in good health were in the first and Thirty women with breast cancer were in the second group

Table 1: Comparison of the age, hematological, and biochemical profiles of BC patients and controls.

Studied variable Mean $\pm$ SD.	Control n = 30	BC n = 30	p-value
Age(years)	56.86 $\pm$ 11.12	57.96 $\pm$ 11.56	0.37
WBCs (x 10 ³ /μl)	7.51 $\pm$ 0.22	4.98 $\pm$ 1.43	<0.001*
Hb (gm/dl)	12.43 $\pm$ 2.32	7.96 $\pm$ 1.23	<0.001*
Platelets (x 10 ³ / μl)	266.9 $\pm$ 24.55	97.3 $\pm$ 23.47	<0.001*
P.C.V (%)	90.23 $\pm$ 7.27	68.56 $\pm$ 7.43	<0.001*
ALT(IU/L)	14.35 $\pm$ 6.31	15.6 $\pm$ 4.67	0.27
Albumin (gm/dl)	4.43 $\pm$ 1.03	4.7 $\pm$ 0.77	0.43
T. protein (gm/dl)	7.66 $\pm$ 1.01	7.55 $\pm$ 1.22	0.32

This table show that there is significant decreases in Platelets, WBCs, Hb and P.C.V in BC compeer with control

group .while non-significant was dedicated between the two group regarding Age, T. protein, Albumin and ALT.

Table 2: Comparing the genotypes and alleles of the groups under study Distribution of surviving rs9904341 frequencies.

Genotypes and alleles	Control		Case		X ²	P
	%	NO	%	NO		
GG	65%	20	10	33.3%	0.62	0.001*
GC	6	20%	14	46.7%	0.45	0.001*
CC	4	15%	6	20%	0.35	0.001*
Alleles						
G ^R						
C	19	31.8%	60%	35	0.23	0.001*

In the survivor gene, the prevalence of the G/C polymorphism of rs9904341 was found to be statistically significant across the studied samples, with the GG

genotype being more prevalent in the control group, and the genotype considered a risk factor for breast cancer being the most prevalent G/C genotype

Table 3: Associations of surviving rs9904341 polymorphism with BC

XRCC1 rs139599857		
Genotype	OR (CI.95%)	P
GC	1.55 (1.23 - 2.21)	<0.001*
CC	4.22 (1.54 - 3.22)	<0.001*
GC+CC	3.23 (3.34-5.42)	<0.001*
Allele		
G [@]	1	
C	1.24 (0.75 - 2.66)	<0.001*

OR: Odds ratio for case vs control

Women carrying the C allele had an increased risk of breast cancer as shown by the values of [OR = 1.24 (0.75 - 2.66), $p < 0.00$] while the G allele was a strong factor against breast cancer while the G/C [OR (CI.95%) 1.55 (1.23 - 2.21), $p < 0.001$] C/C [OR (CI.95%) 4.22 (1.54 - 3.22), $p < 0.001$] genetic variants were significantly associated with the risk of BC.

4. Desiccation

Breast cancer is one of the most common malignant tumors among women in the world shows a wide range of molecular alterations, cellular makeup, responsiveness to treatment, and clinical results.^[14] In the UK, BC accounts for 15% of all new cancer cases annually, making it the most prevalent malignancy. By 2035, this is expected to increase by 2%^[15]. Over 80% of breast cancer diagnoses occur in women over 50, and the incidence rises with age, disproportionately affecting women. With 685 000 deaths globally in 2020, breast cancer is the primary cause of cancer-related mortality^[16].

Survivin belongs to the family of proteins that block apoptosis. Multiple pro mitotic and anti-apoptotic actions are displayed by Survivin, and these distinct roles appear to be brought about by variations in the molecule's subcellular location, phosphorylation, and acetylation.^[17] Over expression of survivin has been reported in many cancer lung colon breast prostate bladder breast renal pancreas and gastric cancer^[18].

Chronic disease anemia may be the cause of the reduced PCV of instances. If the cancer is ulcerating, as shown by reduced MCV, MCH, and MCHC compared to the controls, the anemia may be hemorrhagic and linked to iron shortage. In most situations, nutritional anemia observed in cancer patients might also be linked to anorexia. Erythropoiesis suppression may be linked to breast cancer metastases to the bone marrow. Red blood cell hemolysis (anemia) may be linked to infection in fungal cancers^[19].

In our current study, the survivin gene was rs9904341, and the genotype considered a risk factor for breast cancer was the most prevalent G/C genotype.

^[20, 21] Survivin appears to be overexpressed in nearly all human malignancies, according to recent reports^[22, 23]. As a result, it is frequently regarded as a malignancy diagnosis and prognostic sign. Because of the intricacy of its regulation, the processes underlying survivin repression in cancers remain unknown. It was discovered that the TP53 protein regulates survivin expression at the transcriptional level by either interfering with E2F-1^[24-25]. The alteration in survivin expression is associated with a polymorphism in the G/C rs9904341 CDE/CHR region^[26, 27].

5 .Conclusion

The present study showed that the Survivin rs9904341 G/C polymorphism is associated with breast cancer, but more studies, more samples, and different regions are needed to evaluate this association

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Conflict of Interest

The author reports no conflicts of interest in this work.

6. References

1. Martin AM, Weber BL. Genetic and hormonal risk factors in breast cancer. *Journal of the National Cancer Institute*. 2000;92(14):1126-1135.
2. Weiderpass E, Meo M, Vainio H. Risk factors for breast cancer, including occupational exposures. *Safety and Health at Work*. 2011;2(1):1-8.
3. Larsen MJ, Thomassen M, Gerdes AM, Kruse TA. Hereditary breast cancer: clinical, pathological and molecular characteristics. *Breast Cancer: Basic and Clinical Research*. 2014;8:BCBCR-S18715.
4. Taha Z, Eltom SE. The role of diet and lifestyle in women with breast cancer: an update review of related research in the Middle East. *BioResearch Open Access*. 2018;7(1):73-80.
5. Mili N, Paschou SA, Goulis DG, Dimopoulos MA, Lambrinoudaki I, Psaltopoulou T. Obesity, metabolic syndrome, and cancer: pathophysiological and therapeutic associations. *Endocrine*. 2021;1-20.
6. Híjová E. Synbiotic supplements in the prevention of obesity and obesity-related diseases. *Metabolites*. 2022;12(4):313.
7. Khosravi-Far R, White E, Melet A, Song K, Bucur O, Jagani Z, *et al*. Apoptotic pathways in tumor progression and therapy. *Programmed Cell Death in Cancer Progression and Therapy*. 2008;47-79.
8. Cheung CHA, Huang CC, Tsai FY, Lee JYC, Cheng SM, Chang YC, *et al*. Survivin-biology and potential as a therapeutic target in oncology. *OncoTargets and Therapy*. 2013;1453-1462.
9. Zhang LQ, Wang J, Jiang F, Xu L, Liu FY, Yin R. Prognostic value of survivin in patients with non-small cell lung carcinoma: a systematic review with meta-analysis. *PLoS One*. 2012;7(3):e34100.
10. Aynaci E, Coskunpinar E, Eren A, Kum O, Oltulu YM, Akkaya N, *et al*. Association between survivin gene promoter-31G/C and -644C/T polymorphisms and non-small cell lung cancer. *Genetics and Molecular Research*. 2013;12(3):3975-3982.
11. Guo G, Zhang Q, Yu Z, Li J, Ding Z, Li J, *et al*. Correlation between survivin genetic polymorphisms and lung cancer susceptibility. *International Journal of Clinical and Experimental Pathology*. 2015;8(6):7426.
12. Zhang S, Zhang C, Song Y, Zhang J, Xu J. Prognostic role of survivin in patients with glioma. *Medicine*. 2018;97(17):e0571.
13. Sørli T, Tibshirani R, Parker J, Hastie T, Marron JS, Nobel A, *et al*. Repeated observation of breast tumor subtypes in independent gene expression data sets. *Proceedings of the National Academy of Sciences*. 2003;100(14):8418-8423.
14. Katsura C, Ogunmwonyi I, Kankam HK, Saha S. Breast cancer: presentation, investigation and management. *British Journal of Hospital Medicine*. 2022;83(2):1-7.
15. World Health Organization. WHO consultation to adapt influenza sentinel surveillance systems to include COVID-19 virological surveillance: virtual meeting, 6-8 October 2020. World Health Organization. 2022.
16. Cheung KJ, Gabrielson E, Werb Z, Ewald AJ. Collective invasion in breast cancer requires a conserved basal epithelial program. *Cell*. 2013;155(7):1639-1651.

17. Mobahat M, Narendran A, Riabowol K. Survivin as a preferential target for cancer therapy. *International Journal of Molecular Sciences*. 2014;15(2):2494-2516.
18. Akinbami A, Popoola A, Adediran A, Dosunmu A, Oshinaike O, Adebola P, *et al.* Full blood count pattern of pre-chemotherapy breast cancer patients in Lagos, Nigeria. *Caspian Journal of Internal Medicine*. 2013;4(1):574.
19. Li F, Ambrosini G, Chu EY, Plescia J, Tognin S, Marchisio PC, *et al.* Control of apoptosis and mitotic spindle checkpoint by survivin. *Nature*. 1998;396(6711):580-584.
20. Altieri DC. The molecular basis and potential role of survivin in cancer diagnosis and therapy. *Trends in Molecular Medicine*. 2001;7(12):542-547.
21. Ambrosini G, Adida C, Altieri DC. A novel anti-apoptosis gene, survivin, expressed in cancer and lymphoma. *Nature Medicine*. 1997;3(8):917-921.
22. Fukuda S, Pelus LM. Survivin, a cancer target with an emerging role in normal adult tissues. *Molecular Cancer Therapeutics*. 2006;5(5):1087-1098.
23. Hoffman WH, Biade S, Zilfou JT, Chen J, Murphy M. Transcriptional repression of the anti-apoptotic survivin gene by wild type p53. *Journal of Biological Chemistry*. 2002;277(5):3247-3257.
24. Mityaev MV, Kopantzev EP, Buzdin AA, Vinogradova TV, Sverdlov ED. Functional significance of a putative sp1 transcription factor binding site in the survivin gene promoter. *Biochemistry (Moscow)*. 2008;73:1183-1191.
25. Xu Y, Fang F, Ludewig G, Jones G, Jones D. A mutation found in the promoter region of the human survivin gene is correlated to overexpression of survivin in cancer cells. *DNA and Cell Biology*. 2004;23(7):419-429.
26. Borbély A, Murvai M, Szarka K, Kónya J, Gergely L, Hernádi Z, *et al.* Survivin promoter polymorphism and cervical carcinogenesis. *Journal of Clinical Pathology*. 2007;60(3):303-306.