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Polymorphism detection of catalase-21A\T (rs 7943316) gene in chronic myeloid leukemia patients infected with human herpes virus-7

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Abstract:

BACKGROUND: Chronic myeloid leukemia (CML) is a type of cancer that originates in hematopoietic stem cells, particularly those that develop into myeloid cells. A key feature of CML is the Philadelphia (Ph) chromosome, which is produced by a reciprocal translocation between chromosome 9 and chromosome 22 (designated as t [9;22]). This chromosomal change results in the creation of the BCR-ABL1 fusion gene. Several genetic association studies have analyzed the link between the catalase (CAT) C262T variant and different cancers, but the findings remain controversial.

OBJECTIVE: This study was aimed to determine the association between CAT-21A\T (rs 7943316) gene polymorphism and the percentage of human herps virus-7 (HHV-7) in patients with CML.

PATIENTS AND METHODS: A case–control study included 120 CML blood specimens enrolled in the current research, including 40 newly diagnosed CML patients and 80 treated CML patients, as well as 50 blood specimens collected from persons as the control group. Sequencing was used to identify the CAT-21A\T (rs 7943316) gene polymorphism and HHV-7 DNA using conventional polymerase chain reaction (PCR).

RESULTS: The current study included 40 newly diagnosed CML patients with a mean age of 48 ± 12.7 years and 80 treated CML patients with a mean age of 50 ± 10.53 years, whereas the mean age of the 50 controls was 50 ± 12.95 years. PCR testing for HHV-7 revealed positive results in 6 (15%) of newly diagnosed CML patients and in 19 (23.8%) of those treated for CML. In contrast, one person in the control group was infected by HHV-7. The difference in frequency of genotype distribution of the polymorphism between newly diagnosed, treated patients with CML and control groups was statistically significant. There was no correlation between CAT-21A\T (rs 7943316) polymorphism and HHV-7 infection. New recording for CAT-21A\T (rs 7943316) polymorphism in gene bank NCBI and American bank.

CONCLUSION: HHV-7 acts as a cofactor in pathogenesis as well as the development biology of CML in Iraqi patients. Polymorphism of CAT-21A\T (rs 7943316) may play a role as a risky factor in the pathogenesis of idiopathic CML.

Keywords:

Catalase-21A\T (rs 7943316), chronic myeloid leukemia, gene, human herps virus-7, polymerase chain reaction, sequencing

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Introduction

Chronic myeloid leukemia (CML) is a blood cancer that develops due to a genetic abnormality known as reciprocal chromosomal translocation, specifically t (9;22) (q 34; q11). This translocation leads to the formation of an abnormal oncogene called BCR-ABL, which is responsible for the development of the disease.[1] Neoplastic cells tend to develop various genetic

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defects as time passes, leading to the advancement of the disease.[2] There is a suggestion that the likelihood of developing cancer and the way the body processes cancer-causing substances are linked to variations in detoxification enzymes. These enzymes are crucial for removing toxic substances from the body and safeguarding cells against cancer by breaking down activated cancer-causing substances through hydrolysis, reduction, and/or oxidation.[3-5]

Catalase (CAT), frequently referred to as CAT is an exceptionally potent antioxidant enzyme due to its remarkable turnover rate and widespread presence in virtually all species that engage in aerobic respiration.[6] The CAT gene located on the short arm of chromosome 11 in position 13 encodes CAT production. Three polymorphisms in the promoter region of the CAT have been identified: -21A/T (rs7943316), C-262T (rs1001179), and C-844T (rs769214). Moreover, -21A/T and C-262T polymorphisms are significantly associated with the activity of CAT promoter.[7]

The gene polymorphism in the promoter region of the CAT-21A/T (rs7943316) gene can modify the binding affinity of transcription factors. Research has demonstrated that this polymorphism variation in the promoter region has an impact on the binding of transcriptional factors. Consequently, this results in alterations in the process of transcribing and subsequently expressing the CAT gene.[8] Recently many studies have identified a link between the CAT-C262T polymorphism and the likelihood of developing different diseases, these include hepatocellular carcinoma (HCC),[9] prostate cancer,[10] invasive cervical cancer,[11] endometriosis,[12] ulcerative colitis,[13] and other similar conditions. Nevertheless, there was no substantial correlation discovered between the CAT C262T polymorphism and vulnerability to myeloid leukemia.[14,15]

Human herpes virus (HHV)–6 and HHV–7 are two closely related viruses that are classified into the roseola virus genus under the Beta herpes virinae subfamily. A large proportion of adults are seropositive for both viruses.[16] HHV6 and HHV7 are associated with numerous lymphoproliferative malignancies, including pediatric lymphoma, Hodgkin's lymphoma, non-Hodgkin's lymphoma, basal cell carcinoma, glioma, and acute leukemia.[17] This in HHV-7 could infect each primary CD4+ T cell and the SupT1 lymphoblastoid T-cell line fiction promotes the development of cancer by causing an accumulation of cells in the G2/M phase of the cell cycle, polyploidy, and an increase in cell size. HHV-7 infection induces activation of cdc in infected cells, leading to inhibition of cytotoxic T-cell function and modulation of the immune response.[18] The purpose of the study is to determine the association between CAT-21A\T (rs 7943316**)** gene polymorphism and the percentage of HHV-7 in patients with CML.

Patients and Methods

This study involved 120 individuals diagnosed with CML. Diagnosis and follow-up were based on complete blood count, blood film examination, bone marrow, and identification of BCR-ABL gene mutation. Forty of these patients were newly diagnosed, whereas the remaining 80 were already undergoing treatment, and 50 apparently healthy individual was also included as a control group. All participants, both patients and controls, were recruited from the National Center of Hematology at as well as general hospitals in Baghdad and Middle Euphrates provinces Iraq.

Genotyping for CAT rs7943316 research involved isolating DNA from blood samples using the complete DNA extraction kit provided by Intron firm in Korea. The DNA that was obtained was subsequently preserved at a temperature of –20°C until it was ready for utilization. Detection of CAT rs7943316 gene polymorphism using specific primers (IDT/Korea) designed with NCBI Primer-BLAS.

F: CAT-F: CTCCTGGGTATCTCCGGTCT.

R: CAT-R: AAAAGTCCGTCTGCACCGAA.

Product size: 4776 bp

polymerase chain reaction (PCR) amplification was performed using a standard thermal cycler (Biometra Germany). A volume of 2 µl of template DNA was supplied to PCR master mix tubes followed by the addition of 1 µl each of forward and reverse primers to the same PCR master mix tubes. A volume of 25 µl of distilled water was added to the PCR-premixed tubes using conventional PCR.

Thermal cycle conditions

The amplification of the target regions of CAT rs7943316 polymorphism was performed using primers, according to mentioned conditions in Table 1. Annealing

Table 1: Age and sex distribution between patients with chronic myeloid leukemia groups and control groups

Parameters	Patients (*n*=120)		Controls (*n*=50)	*P*
	Newly diagnosis (*n*=40)	Treated (*n*=80)		
Age±SD	48±12.7	50±10.53	50±12.95	0.52
Sex, *n* (%)				
Male	23 (57.5)	44 (55)	28 (56)	0.4
Female	17 (42.5)	36 (45)	22 (44)	
Ratio	1:3	1:2	1:3	

SD=Standard deviation

temperature provided by manufacture instruction (IDT/Korea).

The PCR protocol for the CAT rs7943316 gene involves an initial denaturation step at 95°C for 5 min, followed by 29 cycles of denaturation at 95°C for 1 min, annealing at 58°C for 1 min, and extension at 72°C for 2 min. A final extension step at 72°C for 5 min is performed after the cycles are completed.

After then, the PCR products were sent to Macrogene\ Korea to investigate the presence of genetic variation within CAT rs7943316 gene.

Polymerase chain reaction analysis for human herps virus-7

The viral genome was extracted from whole blood samples using a blood and tissue kit in accordance with the instructions provided by the manufacturer (Intron/Korea). The DNA that was obtained was preserved at a temperature of −20°C until it was ready for utilization using conventional PCR.

HHV-7 (300 bp) primer sequences (IDT/Korea) were designed using NCBI Primer-BLAST.

The outer primers were:

F: 5-AGTTCCAGCACTGCAATCG-3.

R: 5-CACAAAAGCGTCGCTATCAA-3.

Thermal conditions for HHV-7 detection were illustrated in Table 2, annealing temperature provided by manufacture instruction (IDT/Korea).

The PCR protocol for the HHV-7/DNA detection involves an initial denaturation step at 95°C for 2 min, followed by 29 cycles of denaturation at 95°C for 30 s, annealing at 56°C for 50 s, and extension at 72°C for 5 min. A final extension step at 72°C for 5 min is performed after the cycles are completed.

Ethical approval

Ethical permission was obtained for this study from review ethical committee of National Center of Hematology with reference number nch-erc-2-1 in 15/12/2022, according to the ethical principles derived from the Declaration of Helsinki. Before obtaining a sample,.All patients gave their written informed consent.

Statistical analysis

The statistical analysis was conducted using the software package SPSS IBM Corp., Released 2021. IBM SPSS Statistics for Windows, Version 26.0. (IBM Corp., Armonk, NY, USA). Demographic data were characterized using descriptive statistics, mean, percentage, ratio, and *t*-test. Estimated $P < 0.05$ were considered significant.

Results

Age and sex distribution among groups

The mean age of newly diagnosed and treated CML patients was 48 ± 12.7 years and 50 ± 10.53; respectively, whereas the mean age of the control group was 50 ± 12.95 years. Nonsignificant differences were matching with the control group (0.52).

The sex ratio among newly diagnosed group and the treated group was 1.3 and 1.2, respectively. While the sex ratio among the control group was 1.3, no significant differences in sex between patients and controls ($P = 0.4$) as illustrated in Table 1.

Genotyping of catalase rs7943316 polymorphism among studied groups

The CAT rs7943316 polymorphism frequency among newly diagnosed and treated CML patients according to AT; AA and TT were 53.3%; 26.7% and 20%, and 42.5%; 40% and 17.5%, respectively, whereas, the CAT rs7943316 polymorphism distribution in the control group according to AT; AA and TT were 24%, 56% and 20%, respectively. The difference in frequency of genotype distribution of the polymorphism among patients (newly diagnosed and treated CML patients)

Table 2: Genotyping of CAT rs7943316 (rs743572) in newly diagnosed and treated chronic myeloid leukemia patients and AHC groups

Zygosity status	Newly diagnosis, *n* (%)	Treated, *n* (%)	Controls, *n* (%)	Position in PCR fragment	OR (95%)	SNP type	Significant
AT	21 (53.3)	34 (42.5%	12 (24)	475	1.78 (0.38–3.33)	Missense variant	0.04
AA	11 (26.7)	32 (40)	28 (56)		1.83 (0.42–3.11)		0.047
TT	8 (20)	14 (17.5)	10 (20)				0.58
Totals	40	80	50				
Allele							
K							
T	55	56	48		2.76 (0.55–2.756)		0.049
A	45	44	52				

OR=Odds ratio, SNP=Single nucleotide polymorphisms, PCR=Polymerase chain reaction

and control group was statistically significant as shown in Table 2.

We have a new CAT rs7943316 recording in GENE BANK and NCBI. LC771091; LC771092; LC771093; LC771094.

Detection of human herps virus-7 genome by conventional polymerase chain reaction

The percentage of DNA-HHV-7 in newly diagnosed and treated CML patients was 6 (15%) and 19 (23.8%), respectively. While only 1 (2%) positive DNA-HHV-7 in Control specimens [Figure 1 and Table 3]. The statistical analysis of the differences between newly diagnosis and treated CML as well as control groups was significant ($P = 0.04$).

Table 4 presents data on the association between the CAT rs7943316 polymorphism and HHV-7 infection among CML patients. The polymorphism has three genotypes: AA, TA, and TT. Of the 60 individuals with the AA genotype, 13 tested positive for HHV-7 and 47 tested negative. For the TA genotype, 11 out of 40 were positive, and 29 were negative. Finally, for the TT genotype, only 1 out of 20 individuals tested positive, whereas 19 were negative. A Chi-square test was conducted to assess the statistical significance of this association, yielding a $P = 0.146$. This P value indicates that there is no significant association between the CATrs7943316 polymorphism and HHV-7 infection.

Spearman's Rho statistical tests to analyze the relationship between age, sex, human herps virus-7-DNA-polymerase chain reaction, and catalase rs7943316 single nucleotide polymorphism in patients with chronic myeloid leukemia

No significant correlation between CAT rs7943316 single nucleotide polymorphism (SNP) and HHV-7-DNA in patients with CML ($r = 0.078$; $P = 0.398$).

In addition, a significant correlation was found between SNP of CAT rs7943316 according to the age of the patients who have CML ($r = 0.322$, $P = 0.03$).

The current study did not reveal significant correlations between sex and the CAT rs7943316 SNP ($r = 0.677$, $P = 0.08$) or between HHV-7 and age ($r = 0.799$, $P = 0.08$) Conversely, a statistically significant correlation was identified between HHV-7-DNA levels and sex in CML patients ($r = 0.325$, $P = 0.048$), as depicted in Table 5.

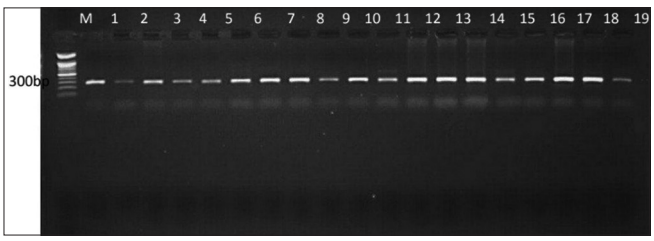

Figure 1: The electrophoresis pattern of human herps virus-7 (HHV-7) DNA (300bp) detection in chronic myeloid leukemia patients and control groups. Lane 1 - lane 19 refers to HHV-7 DNA samples; Electrophoresis conditions, 1% agarose, 75 V, 20 mA for 1 h (5 μl in each well), stained with red safe solution

Discussion

The CAT enzyme can regulate the oxidative stress by breaking down hydrogen peroxide. However, polymorphisms in the promoter region of the CAT gene may reduce gene expression leading to lower enzyme activity and an elevation in oxidative stress.[19]

This study investigated the CAT-21A/T (rs7943316) gene polymorphism across multiple states, the frequencies of the CAT rs7943316 polymorphism among newly diagnosed and treated CML patients were 53.3%, 26.7%, and 20% for AT, AA, and TT variants, respectively, in the newly diagnosed group and 42.5%, 40%, and 17.5% in the treated group, whereas the CAT rs7943316 polymorphism distribution for AT, AA, and TT variants in the control group was 24%, 56%, and 20%, respectively. Various research has been conducted, showing that CAT gene promoter polymorphisms play

Table 3: Results of human herps virus-7-DNA in specimens among studied groups

HHV-7 Genome	Newly diagnosis CML, *n* (%)	Treated CML, *n* (%)	Controls, *n* (%)	*P*
Positive	6 (15)	19 (23.8)	1 (2)	0.04
Negative	34 (85)	61 (76.2)	49 (98)	0.03
Total	40 (100)	80 (100)	50 (100)	

CML=Chronic myeloid leukemia, HHV-7=Human herps virus-7

Table 4: Association between the CAT rs7943316 polymorphism and human herps virus-7 infection among chronic myeloid leukemia patients

HHV-7	CAT rs7943316 polymorphism			*P*
	AA	TA	TT	
Positive	13	11	1	0.146
Negative	47	29	19	
Total	60	40	20	

HHV-7=Human herps virus-7

Table 5: Spearman's rho statistical testing of age, sex, human herps virus-7-DNA-PCR and CAT rs7943316 single nucleotide polymorphisms to evaluate the studied markers in patients with chronic myeloid leukemia

Spearman's rho	Age	CAT rs7943316	HHV-7-DNA	Sex
CAT rs7943316				
r	0.322	1	0.078	0.677
P	0.03		0.398	0.08
HHV-7-DNA				
r	0.799	0.078	1	0.325
P	0.08	0.398		0.048

HHV-7=Human herps virus-7

a significant role in disease resistance, particularly in metabolic disorders.[20,21]

The CAT-21A/T variant, which alerts gene expression patterns,[22] and the CAT-262C/T variant, which reduces CAT enzyme activity,[23] have the potential to disrupt the detoxification of reactive oxygen species (ROS) and elevate oxidative stress levels. This, in turn, can lead to oxidative DNA damage and raise the risk of developing certain diseases.[24]

The stratified genotyping analysis, including several confounding variables, indicated that the occurrence of the homozygous variation AT genotype was more prevalent in individuals who did not respond to treatment (53.3%). Liu and his colleagues found that there was a higher risk of cancer when using the recessive model and homozygote model.[25] This suggests that the presence of the variation T allele, which has reduced CAT activity and consequently higher amounts of ROS, may be involved in causing genomic instability and elevating the risk of developing cancer.[26] Prior research found no significant links between the risk of gastric cancer, colorectal cancer, and HCC with ROS.[27]

Tefik *et al*.[28] found that the frequency of the TT genotype in healthy individuals in Istanbul is 10.2%. This is slightly more than the frequencies of our genotypes. In addition, the prevalence of persons with the TT genotype was 9% in the Swedish population[23] and 6% in the German population,[29] both of which were healthy. The distribution of genotypes in our control group is comparable to that observed in this case. Nevertheless, there were no individuals in a Chinese community who were both healthy and had the TT genotype.[30] Certain SNPs in the CAT gene lead to alterations in the amino acids at specific locations within the gene. The CAT C262T polymorphism is a SNP located in the promoter region.[10] Multiple investigations were conducted to examine the relationship between CAT genotype and the danger of developing cancer.[31,32] An analysis that combines and evaluates data from five case–control studies, involving 3865 cases and 28,224 controls, the studies found that C262T polymorphism was associated with an increased risk of prostate cancer (OR = 1.094, 95% CI: 1.015–1.178, $P = 0.018$).[10]

According to the current study, the percentage of HHV-7/DNA in newly diagnosed and treated CML patients was 6 (15%) and 19 (23.8%), respectively. While only 1 (2%) positive DNA-HHV-7 in control specimens [Figure 1 and Table 3].

HHV-6 and HHV-7 are viruses that primarily infect lymphocytes. These viruses frequently spread during the first few months of infancy. HHV-7 usually infects over 90% of individuals by the age of 6 years by the oral salivary route. This infection can lead to a condition called roseola infantum, characterized by high fever and seizures.[16]

The result of this study, the CAT rs7943316 polymorphism has three genotypes: AA, TA, and TT. Of the 60 CML patients with the AA genotype, 13 tested positive for HHV-7 and 47 tested negative. For the TA genotype, 11 out of 40 were positive, and 29 were negative. Finally, for the TT genotype, only 1 out of 20 individuals tested positive, whereas 19 were negative. A Chi-square test was conducted to assess the statistical significance of this association, yielding a $P = 0.146$. Furthermore, there was no significant correlation between CML patients HHV-7 positive and CAT rs7943316 ($r = 0.078$, $P = 0.398$).

Typically, HHV-7 virus forms an inactive infection in many cellular places, such as lymphocytes, salivary glands, and the central nervous system.[33] This virus is primarily infecting CD4+ T lymphocytes and SupT1 lymphoblastoid T-cells.[17] A recent review in the *Journal of Virology* outlines the clinical aspects and pathogenesis of HHV-7, highlighting its potential role in various diseases, including hematological conditions.[34]

The current study result is not compatible with studies which are illustrated the herpesvirus family includes HSV, CMV, varicella zoster virus, HHV, and Epstein–Barr virus, which are all DNA viruses implicated on the redox of state of host cells and can effect on the immune system.[35] While not specific to HHV-7, research has shown that oxidative stress plays a significant role in cancer biology. The CAT gene is crucial for managing oxidative stress, and its expression can be influenced by viral infections. Understanding how HHV-7 might affect oxidative stress pathways could provide insights into its role in hematological malignancies.[36]

Conclusion

This study suggests that HHV-7 may contribute to the development and progression of CML in Iraqi patients. While the CAT-21A/T polymorphism (rs7943316) might increase the risk of developing idiopathic CML, it does not seem to be linked to HHV-7 infection.

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Conflicts of interest
There are no conflicts of interest.

References

1. Sampaio MM, Santos ML, Marques HS, Gonçalves VL, Araújo GR, Lopes LW, *et al.* Chronic myeloid leukemia-from the Philadelphia

chromosome to specific target drugs: A literature review. World J Clin Oncol 2021;12:69-94.
2. Jenkins T, Gouge J. Nrf2 in cancer, detoxifying enzymes and cell death programs. Antioxidants (Basel) 2021;10:1030.
3. Miller MC 3rd, Mohrenweiser HW, Bell DA. Genetic variability in susceptibility and response to toxicants. Toxicol Lett 2001;120:269-80.
4. Wolf AB, Caselli RJ, Reiman EM, Valla J. APOE and neuroenergetics: An emerging paradigm in Alzheimer's disease. Neurobiol Aging 2013;34:1007-17.
5. Yang IA, Fong KM, Zimmerman PV, Holgate ST, Holloway JW. Genetic susceptibility to the respiratory effects of air pollution. Thorax 2008;63:555-63.
6. Nandi A, Yan LJ, Jana CK, Das N. Role of catalase in oxidative stress- and age-associated degenerative diseases. Oxid Med Cell Longev 2019;2019:9613090.
7. Nawab SN, Zehra S, Fawwad A, Azhar A. A study on catalase gene promoter polymorphism -21 A/T (rs7943316) in healthy Pakistani population. Pak J Med Sci 2017;33:1521-4.
8. Saify K, Saadat I, Saadat M. Influence of A-21T and C-262T genetic polymorphisms at the promoter region of the catalase (CAT) on gene expression. Environ Health Prev Med 2016;21:382-6.
9. Elkhamy M, Badra G, Sakr MA, Abdel Aziz AA, Lotfy M. The association between catalase gene rs1001179 and rs769217 polymorphisms and the hepatocellular carcinoma risk in Egyptian patients. Egypt Acad J Biolog Sci 2022;14:475-87.
10. Hu J, Feng F, Zhu S, Sun L, Li G, Jiang N, *et al.* Catalase C-262T polymorphism and risk of prostate cancer: Evidence from meta-analysis. Gene 2015;558:265-70.
11. Castaldo SA, da Silva AP, Matos A, Inácio Â, Bicho M, Medeiros R, *et al.* The role of CYBA (p22phox) and catalase genetic polymorphisms and their possible epistatic interaction in cervical cancer. Tumour Biol 2015;36:909-14.
12. Zarafshan SS, Salehi Z, Salahi E, Sabet EE, Shabanipour S, Zahiri Z. Polymorphism of catalase gene (CAT C-262T) in women with endometriosis. J Obstet Gynaecol 2015;35:269-71.
13. Khodayari S, Salehi Z, Fakhrieh Asl S, Aminian K, Mirzaei Gisomi N, Torabi Dalivandan S. Catalase gene C-262T polymorphism: Importance in ulcerative colitis. J Gastroenterol Hepatol 2013;28:819-22.
14. Bănescu C, Trifa AP, Voidăzan S, Moldovan VG, Macarie I, Benedek Lazar E, *et al.* CAT, GPX1, MnSOD, GSTM1, GSTT1, and GSTP1 genetic polymorphisms in chronic myeloid leukemia: A case-control study. Oxid Med Cell Longev 2014;2014:875861.
15. Bănescu C, Iancu M, Trifa AP, Cândea M, Benedek Lazar E, Moldovan VG, *et al.* From six gene polymorphisms of the antioxidant system, only GPX Pro198Leu and GSTP1 Ile105Val modulate the risk of acute myeloid leukemia. Oxid Med Cell Longev 2016;2016:2536705.
16. Tesini BL, Caserta MT. Human Herpesviruses: Human Herpesvirus 6. Viral Infections of Humans: Epidemiology and Control. New York, NY: Springer US; 2023. p. 1-26.
17. Alibek K, Baiken Y, Kakpenova A, Mussabekova A, Zhussupbekova S, Akan M, *et al.* Implication of human herpesviruses in oncogenesis through immune evasion and supression. Infect Agent Cancer 2014;9:3.
18. Sausen DG, Reed KM, Bhutta MS, Gallo ES, Borenstein R. Evasion of the host immune response by betaherpesviruses. Int J Mol Sci 2021;22:7503.
19. Eras N, Türkoz G, Tombak A, Tiftik N, Yalin S, Berkoz M, *et al.* An investigation of the relation between catalase C262T gene polymorphism and catalase enzyme activity in leukemia patients. Arch Med Sci 2019;17:928-33.
20. LeBlanc JG, del Carmen S, Miyoshi A, Azevedo V, Sesma F, Langella P, *et al.* Use of superoxide dismutase and catalase producing lactic acid bacteria in TNBS induced Crohn's disease in mice. J Biotechnol 2011;151:287-93.
21. Alemany-Cosme E, Sáez-González E, Moret I, Mateos B, Iborra M, Nos P, *et al.* Oxidative stress in the pathogenesis of Crohn's disease and the interconnection with immunological response, microbiota, external environmental factors, and epigenetics. Antioxidants (Basel) 2021;10:64.
22. Lourdhu Mary A, Nithya K, Isabel W, Angeline T. Prevalence of catalase (-21 A/T) gene variant in South Indian (Tamil) population. Biomed Res Int 2014;2014:894237.
23. Forsberg L, Lyrenäs L, de Faire U, Morgenstern R. A common functional C-T substitution polymorphism in the promoter region of the human catalase gene influences transcription factor binding, reporter gene transcription and is correlated to blood catalase levels. Free Radic Biol Med 2001;30:500-5.
24. Chistiakov DA, Zotova EV, Savost'anov KV, Bursa TR, Galeev IV, Strokov IA, *et al.* The 262T>C promoter polymorphism of the catalase gene is associated with diabetic neuropathy in type 1 diabetic Russian patients. Diabetes Metab 2006;32:63-8.
25. Liu K, Liu X, Wang M, Wang X, Kang H, Lin S, *et al.* Two common functional catalase gene polymorphisms (rs1001179 and rs794316) and cancer susceptibility: Evidence from 14,942 cancer cases and 43,285 controls. Oncotarget 2016;7:62954-65.
26. Anwar S, Alrumaihi F, Sarwar T, Babiker AY, Khan AA, Prabhu SV, *et al.* Exploring therapeutic potential of catalase: Strategies in disease prevention and management. Biomolecules 2024;14:697.
27. Jardim SR, de Souza LM, de Souza HS. The rise of gastrointestinal cancers as a global phenomenon: Unhealthy behavior or progress? Int J Environ Res Public Health 2023;20:3640.
28. Tefik T, Kucukgergin C, Sanli O, Oktar T, Seckin S, Ozsoy C. Manganese superoxide dismutase Ile58Thr, catalase C-262T and myeloperoxidase G-463A gene polymorphisms in patients with prostate cancer: Relation to advanced and metastatic disease. BJU Int 2013;112:E406-14.
29. Zarbock R, Hendig D, Szliska C, Kleesiek K, Götting C. Pseudoxanthoma elasticum: Genetic variations in antioxidant genes are risk factors for early disease onset. Clin Chem 2007;53:1734-40.
30. Mak JC, Ho SP, Yu WC, Choo KL, Chu CM, Yew WW, *et al.* Polymorphisms and functional activity in superoxide dismutase and catalase genes in smokers with COPD. Eur Respir J 2007;30:684-90.
31. Shen Y, Li D, Tian P, Shen K, Zhu J, Feng M, *et al.* The catalase C-262T gene polymorphism and cancer risk: A systematic review and meta-analysis. Medicine (Baltimore) 2015;94:e679.
32. Quick SK, Shields PG, Nie J, Platek ME, McCann SE, Hutson AD, *et al.* Effect modification by catalase genotype suggests a role for oxidative stress in the association of hormone replacement therapy with postmenopausal breast cancer risk. Cancer Epidemiol Biomarkers Prev 2008;17:1082-7.
33. Meyding-Lamadé U, Strank C. Herpesvirus infections of the central nervous system in immunocompromised patients. Ther Adv Neurol Disord 2012;5:279-96.
34. Verbeek R, Vandekerckhove L, Van Cleemput J. Update on human herpesvirus 7 pathogenesis and clinical aspects as a roadmap for future research. J Virol 2024;98:e0043724.
35. Zhang K, Huang Q, Li X, Zhao Z, Hong C, Sun Z, *et al.* The cGAS-STING pathway in viral infections: A promising link between inflammation, oxidative stress and autophagy. Front Immunol 2024;15:1352479.
36. Camini FC, da Silva Caetano CC, Almeida LT, de Brito Magalhães CL. Implications of oxidative stress on viral pathogenesis. Arch Virol 2017;162:907-17.