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Association between CTLA4-658C>T polymorphism and colorectal cancer in Medan, Indonesia

IMELDA REY[1, *], DARMADI DARMADI[1]

[1] Department of Internal Medicine, Faculty of Medicine, Universitas Sumatera Utara, Indonesia

Abstract

Background: Colorectal cancer (CRC) is a global health concern, including in Indonesia. Genetic factors, particularly those affecting immune regulation and tumor immune evasion, contribute significantly to CRC pathogenesis The cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) gene, which encodes an immune checkpoint receptor, influences T-cell activation and immune response. Certain CTLA4 gene polymorphism has been associated with altered immune function and increased risk of CRC.

Objectives: This study aims to explore the potential role of CTLA4-658C>T as a genetic marker for CRC susceptibility.

Methods: This case-control study included 60 colorectal cancer (CRC) patients and 60 non-CRC patients from January 2023 to December 2024 at Universitas Sumatera Utara Hospital and its network hospitals. CRC patients aged 18 years or older were included in the case group, while patients with non-CRC findings after colonoscopy served as controls. Patients with systemic diseases (e.g., diabetes, heart or kidney failure, other cancers) were excluded. Data on demographics and CRC characteristics were collected from medical records. Participants were interviewed to complete missing data and provided blood samples for CTLA4-658C>T polymorphism analysis.

Results: The CTLA4-658T>C polymorphism was significantly associated with colorectal cancer (CRC). Individuals with the CC+CT genotype had a 2.69-fold higher risk of developing CRC than those with the TT genotype (p=0.022). Additionally, carriers of the C allele had a 2.26-fold higher risk of CRC than those with the T allele (p=0.015).

Conclusion: These findings suggest that CTLA4-658C>T may serve as a potential genetic marker for CRC susceptibility, highlighting the role of immune regulation in CRC development.

Keywords: Colorectal Neoplasms, CTLA-4 Antigen, Polymorphism, Single Nucleotide, Genetic Predisposition to Disease, Risk Factors.

What is new? What is important?

This research is important because colorectal cancer (CRC) remains a major public health issue in Indonesia, yet genetic factors contributing to its development are not well studied in the local population. The CTLA-4 gene, which plays a crucial role in immune regulation and tumor immune evasion, has been linked to CRC risk in various populations. However, genetic susceptibility can vary across ethnic groups, necessitating population-specific studies. By identifying the CTLA4-658C>T polymorphism as a potential genetic marker for CRC, this study provides critical insights into the role of immune regulation in cancer development. Understanding these genetic associations may help refine CRC screening strategies, allowing for earlier detection and targeted prevention efforts. Moreover, the findings contribute to precision medicine approaches, paving the way for individualized risk assessment and potential immunotherapy advancements tailored to the Indonesian population.

INTRODUCTION

Colorectal cancer (CRC) is a significant global health concern, ranking as the third most commonly diagnosed cancer worldwide, with approximately 1.9 million new cases in 2022. CRC is the fourth most prevalent malignancy in Indonesia, with an estimated 80,000 new cases in 2022. [1,4] Several key risk factors are associated with CRC, including age, body mass index, family history of malignancy, smoking, and alcohol consumption. [3,4] Overweight and obese individuals had a significantly higher risk of developing CRC and adenomas, with an odds ratio (OR) of 10.968 (95% CI: 2.33–51.55). Additionally, a family history of other cancers was found to increase the risk of CRC and adenomas, with an OR of 18.800 (95% CI: 5.13–68.85).[5]

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The significance of family history in CRC encompasses genetic and shared environmental influences. Individuals with a family history of CRC have a 2 to 4 times higher risk compared to those without such a history. This increased risk is attributed to the inheritance of pathogenic gene variants transmitted across generations, underscoring the role of genetics in colorectal carcinogenesis.[2] A prominent example is mutations in the APC gene, which play a significant role in CRC carcinogenesis. Approximately 30%–70% of sporadic adenomas and CRCs exhibit mutations in the APC gene, leading to the synthesis of a truncated protein. Another critical mutation involves the MUTYH gene associated with base excision repair. Individuals with a single, mutated copy of MUTYH exhibit a genetic signature indicative of additional mutations and a defective base excision repair pathway, contributing to CRC development. [6]

Cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) is an immune checkpoint receptor crucial in regulating T-cell activation and maintaining immune tolerance. In colorectal cancer (CRC), CTLA-4 expression has been studied to understand its potential as a diagnostic marker. Previous studies evaluated the expression of CTLA-4 in colon cancer tissues using immunohistochemistry, which found that CTLA-4 expression was frequently observed in colon cancer tissues, suggesting a role in modulating the tumor microenvironment. This expression pattern indicates that CTLA-4 may contribute to immune evasion mechanisms in CRC by modulating T-cell responses within the tumor. The findings from this study highlight the potential of CTLA-4 as a diagnostic marker in colon cancers. However, its significance should be evaluated and compared to known risk factors such as alcohol intake and smoking history.[3,4] Assessing the independent value of CTLA-4 expression could aid in understanding the immune landscape of CRC and may have implications for developing targeted immunotherapies to enhance anti-tumor immunity.[7]

The CTLA-4 gene contains a single nucleotide polymorphism (SNP) known as rs11571317, located at position -658 in the promoter region, where cytosine (C) is replaced by thymine (T). This SNP, or CTLA-4 -658C>T, has been studied for its potential association with colorectal cancer (CRC) susceptibility. Akhtar *et al.* investigated the variant allele frequency of the CTLA-4 rs11571317 (-658 C/T) polymorphism in the Saudi population and compared it with other ethnic groups. The study suggests that the CTLA-4 -658C>T polymorphism may influence individual susceptibility to CRC.[8] However, genetic variations can significantly differ across populations due to ethnic and environmental factors, underscoring the need to explore this polymorphism. This study aims to explore the potential role of CTLA4-658C>T as a genetic marker for CRC susceptibility in North Sumatra, Indonesia, which may contribute to personalized medicine approaches and improved CRC screening programs in the region

MATERIAL AND METHODS

This case-control study, conducted at Universitas Sumatera Utara Hospital and its affiliated network hospitals from January 2023 to December 2024, involved 60 colorectal cancer (CRC) patients and 60 non-CRC patients.

INCLUSION AND EXCLUSION CRITERIA

The inclusion criteria for the CRC group were adult patients (aged 18 years or older) diagnosed with colorectal cancer. Patients who underwent the colonoscopy procedure but without a CRC diagnosis were categorized as the control group. Patients with systemic diseases such as type 2 diabetes, coronary heart disease, kidney failure, heart failure, or other malignancies were excluded from both the case and control groups as such may alter CTLA-4 -658C>T levels.

To minimize confounding, the control group was frequency-matched to the case group based on three key demographic factors: age (within a ±5-year range), sex, and ethnicity (Batak versus non-Batak). This matching strategy ensured baseline comparability between groups for major CRC risk factors.

DATA COLLECTION

Demographic and clinical characteristics were collected from medical records. Baseline characteristics include gender, age, ethnicity, smoking history, and alcohol consumption. Smoking history was determined by the average number of cigarettes smoked per day (in the sticks) and the number of years of smoking. Smoking intensity was categorized as light (0–199 sticks), moderate (200–599 sticks), or heavy (>600 sticks). Alcohol consumption was quantified by multiplying the average amount of alcohol consumed per day (in grams) by the duration of alcohol consumption (in years). The categories for alcohol consumption

were never, light (<24 grams/year), moderate, and heavy (>24 grams/year). One standard drink was defined as containing 10 grams of ethanol, equivalent to 285–330 mL of beer, 30 mL of whiskey, or 120 mL of wine.

CTLA-4 -658C>T POLYMORPHISM ANALYSIS

Blood samples were collected for genetic analysis of the CTLA-4 -658T>C polymorphism. DNA extraction was performed using the spin column method with a high-purity PCR template preparation kit (Roche Applied Science). Genotyping was carried out using TaqMan SNP Genotyping Assay for CTLA-4 -658C>T (Applied Biosystems). The primers used were forward primer: 5′- GCTTTTCTTTGGACCTTCTTCA-3′ and reverse primer: 5′ –TCACAAGAAATAAACTGAAAA TAG CC-3′.

PCR amplification was performed using the TaqMan GTXpress Master Mix (Applied Biosystems) on a C1000 Thermal Cycler CFX96 Real-Time System (Bio-Rad) with the following protocol: 10 minutes of enzyme activation at 95°C, followed by 40 cycles of denaturation at 92°C for 15 seconds and annealing/extension at 60°C for 1 minute.

STATISTICAL ANALYSIS

Data analysis was performed using chi-square tests and binomial logistic regression. Statistical significance was set at $p<0.05$, and all analyses were conducted using SPSS version 26.

ETHICAL CLEARANCE

This study was approved by the Research Ethics Committee of Universitas Sumatera Utara (approval no. 741/KEPK/USU/2023). Written informed consent was obtained from all participants.

RESULTS

The study included 120 participants with a mean age of 54.78 ± 9.83 years. Of the participants, 66 (55%) were male and 54 (45%) were female. Regarding ethnicity, 74 participants (61.7%) were of Batak ethnicity, while 46 participants (38.3%) belonged to other ethnic groups. For smoking history, 43 participants (35.8%) had a moderate to severe smoking history, whereas 77 participants (64.2%) had no or mild smoking exposure. In terms of alcohol consumption, 23 participants (19.2%) reported moderate to severe alcohol intake, while 97 participants (80.8%) had no or mild alcohol consumption. Analysis of the CTLA-4 -658T>C polymorphism showed that the majority of participants carried the TT genotype (89 participants, 74.2%), followed by the CC genotype (16 participants, 13.3%) and the CT genotype (15 participants, 12.5%). The baseline characteristics of the study are summarized in Table 1.

Table 1

Baseline Characteristics

Variables	n = 120
Gender	
Male	66 (55%)
Female	54 (45%)
Age (years)	54.78 ± 9.83
Ethnic	
Batak	74 (61.7%)
Others	46 (38.3%)
Smoking history	
Moderate to Severe	43 (35.8%)
No to mild	77 (64.2%)
Alcohol consumption	
Moderate to Severe	23 (19.2%)
No to mild	97 (80.8%)
CTLA-4 -658T>C polymorphism, n (%)	
CC	16 (13.3%)
CT	15 (12.5%)
TT	89 (74.2%)

Table 2 presents the tumor location and histological differentiation of colorectal cancer (CRC) in 60 patients. Regarding tumor location, the majority of cases were found in the rectum (26 cases, 43.3%), followed by the distal colon (18 cases, 30%), and the proximal colon (16 cases, 26.7%).

For histological differentiation, 27 cases (45%) exhibited poor differentiation, making it the most common category. Meanwhile, 17 cases (28.3%) were well-differentiated, and 16 (26.7%) were moderately differentiated. These findings suggest that rectal cancer was the most frequent CRC location in this cohort, and that a significant proportion of tumors exhibited poor differentiation, potentially indicating a more aggressive disease course.

Table 3 presents the association between baseline demographic characteristics and the presence of colorectal cancer. Among the analyzed variables, age and alcohol history showed statistically significant associations with colorectal cancer occurrence. A higher proportion of colorectal cancer cases occurred among males (63.3%) compared to females (36.7%), although the difference was not statistically significant ($p = 0.067$). Individuals older than 55 years had a significantly higher likelihood of colorectal cancer ($p = 0.003$), with an odds ratio (OR) of 3 (95% CI: 1.42–6.28), indicating a strong association between older age and colorectal cancer. The Batak ethnic group had a slightly higher proportion of colorectal cancer cases (65%) compared to other ethnicities (35%); however, this difference was not statistically significant ($p = 0.453$, OR = 1.33, 95% CI: 0.63–2.78). Moderate to severe smokers had a higher proportion of colorectal cancer cases (40%) than those with no or mild smoking history (60%), but this association was not statistically significant ($p = 0.341$, OR = 1.44, 95% CI: 0.68–3.05). Moderate to severe alcohol consumption was significantly associated with colorectal cancer (26.7% vs. 11.7% in the control group, $p = 0.037$), with an OR of 2.75 (95% CI: 1.04–7.29), suggesting an increased risk of colorectal cancer in individuals with higher alcohol consumption. These findings highlight age and alcohol consumption as potential risk factors for colorectal cancer, whereas gender, ethnicity, and smoking history did not show significant associations.

Table 2

Location and Histological Differentiation of CRC

Variables	n = 60
Location	
Proximal colon	16 (26.7%)
Distal colon	18 (30%)
Rectum	26 (43.3%)
Histological differentiation	
Well-differentiated	17 (28.3%)
Moderate differentiated	16 (26.7%)
Poor differentiated	27 (45%)

Table 4 presents the association between CTLA-4 -658C>T polymorphism and colorectal cancer. The analysis shows that specific genotypic and allelic variations are significantly associated with colorectal cancer risk. The TT genotype was the most prevalent among colorectal cancer patients (65%), compared to 83.3% in the control group. The CC genotype had the lowest prevalence (16.7% in cases vs. 10% in controls), while CT was found in 18.3% of cases and 6.7% of controls. However, the association between individual genotypes and colorectal cancer was not statistically significant ($p = 0.060$). The comparison between CC+CT versus TT showed a significant association with colorectal cancer ($p = 0.022$), with an odds ratio (OR) of 2.69 (95% CI: 1.14–6.37), indicating that individuals carrying at least one C allele had a higher risk of developing colorectal cancer. The

CC versus CT+TT comparison did not show statistical significance (p = 0.283, OR = 1.8, 95% CI: 0.61–5.32), suggesting that at least one T allele did not significantly alter the risk. The T allele was more frequent in both groups but had a higher proportion among colorectal cancer cases. The C allele was significantly associated with an increased risk of colorectal cancer (p = 0.015), with an OR of 2.26 (95% CI: 1.16–4.41). These findings suggest that the presence of the C allele (either in CC or CT genotypes) may contribute to an increased risk of colorectal cancer.

Table 3

Association between baseline demographic and colorectal carcinoma

Variables	Colorectal cancer, n(%)		P	OR (CI 95%)
	Yes	No		
Gender				
Male	38 (63,3)	28 (46,7)	0.067	1,97 (0,95-4,1)
Female	22 (36,7)	32 (53,3)		
Age				
> 55 years old	37 (61.7)	21 (35)	0.003*	3 (1.42-6.28)
< 55 years old	23 (38.3)	39 (65)		
Ethnicity				
Batak	39 (65)	35 (58.3)	0.453	1.33 (0.63-2.78)
Other	21 (35)	25 (41.7)		
Smoking history				
Moderate + Severe	24 (40)	19 (31.7)	0.341	1.44 (0.68-3.05)
No + Mild	36 (60)	41 (68.3)		
Alcohol history				
Moderate + Severe	16 (26.7)	7 (11.7)	0.037*	2.75 (1.04-7.29)
No + Mild	44 (73.3)	53 (88.3)		

*p<0.05, **p<0.01

Table 4

The association between CTLA-4 -658C>T polymorphism and colorectal carcinoma

CTLA-4-658C>T Polymorphism	Colorectal Cancer Yes n (%)	No n (%)	p	OR (CI 95%)
CC	10 (16.7)	6 (10)	0.060	NA
CT	11 (18.3)	4 (6.7)		
TT	39 (65)	50 (83.3)		
CC+CT	21 (35)	10 (16.7)	0.022*	2.69 (1.14-6.37)
TT	39 (65)	50 (83.3)		
CC	10 (16.7)	6 (10)	0.283	1.8 (0.61-5.32)
CT+TT	50 (83.3)	54 (90)		
C Allele	31 (25.8)	16 (13.3)	0.015*	2.26 (1.16 – 4.41)
T Allele	89 (74.2)	104 (86.7)		

*p<0.05

Table 5 presents the results of a multivariate logistic regression analysis identifying independent risk factors for colorectal cancer. Three variables – age, moderate to severe alcohol consumption, and the presence of the CTLA-4 -658C>T allele C polymorphism – showed statistically significant associations with colorectal cancer. Older age was significantly associated with an increased risk of colorectal cancer (p = 0.002), with an odds ratio (OR) of 3.487 (95% CI: 1.13–5.66), suggesting that individuals in the older age group had more than three times the risk compared to younger individuals. Individuals with moderate to severe alcohol intake had a significantly higher likelihood of colorectal cancer (p = 0.018), with an OR of 3.420 (95% CI: 1.07–4.92), indicating that alcohol consumption plays a role in increasing colorectal cancer risk. The presence of the C allele in the CTLA-4 -658C>T polymorphism was also significantly associated with colorectal cancer risk (p = 0.039), with an OR of 2.310 (95% CI: 1.04–4.62), indicating that individuals carrying this allele had more than twice the risk of developing colorectal cancer. These findings suggest that older age, significant alcohol consumption, and genetic susceptibility (via CTLA-4 polymorphism) are independent risk factors for colorectal cancer.

Table 5

Multivariate analysis of factors associated with colorectal cancer

Variable	B	P	OR (CI 95%)
Age	1.249	0.002*	3.487 (1.13-5.66)
Moderate-severe alcohol consumption	1.240	0.018*	3,420 (1.07-4.92)
CTLA-4 -658C>T allele C polymorphism			
Constant	1.144	0.039*	2,310 (1.04-4.62)
	-6.347		

*p<0.05

DISCUSSION

This study aimed to investigate the potential role of the CTLA-4 -658C>T polymorphism as a genetic marker for colorectal cancer (CRC) susceptibility. Our findings indicate that individuals carrying at least one C allele (CC or CT genotypes) have a significantly increased risk of developing CRC compared to those with the TT genotype. Specifically, the presence of the C allele was associated with more than twice the risk of CRC (OR = 2,31, 95% CI: 1.04–4.62). Our findings are consistent with previous studies suggesting that CTLA-4 polymorphisms may influence susceptibility to CRC. Notably, previous studies investigating the CTLA-4 -658C>T polymorphism in other populations have yielded findings consistent with our results. Akhtar et al. reported that the -658C>T variant was significantly associated with increased CRC susceptibility in the Saudi population, supporting the role of this promoter polymorphism in colorectal carcinogenesis.[8] Similarly, Al-Harbi *et al.* demonstrated a significant association between CTLA-4 polymorphisms, including -658C>T, and CRC risk among Saudi patients, further reinforcing these observations.[13] In contrast, studies in Chinese populations have shown weaker or inconsistent associations between CTLA-4 polymorphisms and CRC risk. This variability may be attributed to differences in allele frequencies, genetic background, or environmental exposures influencing immune regulation and cancer susceptibility.[17] These inter-population discrepancies emphasize the importance of population-specific genetic studies and validate the need for regional genetic risk profiling. For instance, a meta-analysis demonstrated that the rs231775 polymorphism is associated with an increased predisposition to colorectal and pancreatic cancers. Similarly, a case-control study involving 1,003 CRC patients and 1,303 cancer-free controls investigated several CTLA-4 tagging polymorphisms, including rs231775. The study identified a significant association between the rs231775 G>A polymorphism and increased CRC risk, particularly under the homozygous model (adjusted OR = 1.40, 95% CI: 1.05–1.87, p = 0.022).

[9] A comprehensive meta-analysis encompassing 87 case-control studies with 29,464 cancer cases and 35,858 controls examined the rs231775 polymorphism in the CTLA-4 gene. The analysis revealed that this polymorphism is a risk factor for CRC, with individuals carrying the G allele exhibiting an increased risk (GA vs. AA: OR = 1.72, 95% CI = 1.13–2.60, p = 0.011).[10] Another meta-analysis focusing on the rs231775 polymorphism and CRC risk highlighted a significant association in Caucasian populations. The analysis demonstrated that individuals with the AG genotype had a higher risk of developing CRC than those with the AA genotype (OR = 1.22, 95% CI = 1.03–1.46). This suggests that the rs231775 polymorphism may be a risk factor for CRC, especially among Caucasians.[11] While our study focuses on the -658C>T polymorphism, these findings underline the significance of CTLA-4 genetic variations in CRC susceptibility.

The CTLA-4 -658C>T polymorphism is located within the promoter region of the CTLA-4 gene and is thought to influence transcriptional activity. Variations at this site may affect the binding affinity of transcription factors, potentially leading to altered CTLA-4 expression on T cells. Reduced CTLA-4 expression may impair negative regulation of T-cell activation, promoting a hyperactive immune response; conversely, increased CTLA-4 expression may enhance immune evasion by tumor cells. Functional studies have suggested that certain CTLA-4 promoter variants, including -658C>T, can modulate immune regulatory pathways and contribute to cancer susceptibility. [2,8]

The CTLA-4 gene encodes a protein that plays a crucial role in downregulating immune responses. Polymorphisms in this gene may alter its expression or function, potentially leading to impaired immune surveillance and increased cancer risk. For instance, the rs3087243 single nucleotide polymorphism (SNP) has been associated with colorectal cancer (CRC) susceptibility and prognosis in Swedish patients, suggesting it could serve as a prognostic marker for CRC.[12] Similarly, the rs231775 polymorphism has been linked to an increased risk of cervical cancer, with individuals carrying the AA genotype exhibiting a higher susceptibility.[13] Our observation that the C allele of the -658C>T polymorphism is associated with higher CRC risk suggests that this variant may contribute to a less effective immune response against emerging tumor cells.

In addition to genetic factors, our study identified older age and moderate to severe alcohol consumption as independent risk factors for CRC. These findings are consistent with established literature indicating that advancing age and significant alcohol intake are associated with increased CRC risk. The incidence of CRC increases markedly with age. Data suggests that individuals aged 65 years or older with a history of alcoholism have a significantly higher risk of developing CRC, with adjusted odds ratios (ORs) of 2.649 (95% CI: 2.497–2.811) compared to younger populations.[14] Alcohol intake has been consistently linked to an elevated risk of CRC. A meta-analysis reported that a 10-gram increase in daily alcohol consumption correlates with a 7% increase in CRC risk overall, with an 8% increase observed in men and a 4% increase in women.[15] Furthermore, heavy alcohol consumption during early adulthood (ages 18–22) has been associated with a higher risk of developing CRC later in life. Specifically, individuals consuming ≥15 grams of alcohol per day during early adulthood exhibited a multivariable hazard ratio (HR) of 1.28 (95% CI: 0.99–1.66) for CRC, compared to those consuming less than 1 gram per day.[16] The interplay between these environmental factors and genetic predispositions, such as CTLA-4 polymorphisms, warrants further investigation to elucidate their combined effect on CRC risk.

Several limitations should be considered when interpreting our findings. Despite achieving statistical significance, the relatively modest sample size (n = 120) may constrain the precision and reproducibility of the results. Smaller sample sizes inherently reduce the statistical power of association studies, thereby increasing the risk of spurious findings. Consequently, while these preliminary data are promising, larger multicenter studies are necessary to confirm the associations identified. Second, our study population was predominantly of Batak ethnicity (61.7%), which may limit the applicability of the findings to other ethnic groups. Genetic variations can affect populations differently; thus, studies involving diverse cohorts are necessary. Nonetheless, the study possesses several strengths. It provides valuable preliminary data on the role of CTLA-4 -658C>T in CRC risk within the Indonesian population, a group that remains underrepresented in genetic studies. This research highlights the importance of population-specific genetic markers, which could eventually contribute

to personalized screening and prevention strategies. Additionally, identifying genetic risk factors for CRC could aid in public health initiatives by refining screening guidelines for high-risk individuals and promoting early detection efforts.

While we identified associations between specific risk factors and CRC, the study's observational nature precludes establishing causality. Finally, we did not assess other potentially relevant CTLA-4 polymorphisms, such as rs231775 and rs3087243, which have been implicated in CRC risk in different studies.[17] Future research should consider a more comprehensive analysis of CTLA-4 genetic variations.

CONCLUSION

Our study suggests that the CTLA-4 -658C>T polymorphism, particularly the presence of the C allele, is associated with an increased risk of colorectal cancer. Alongside older age and significant alcohol consumption, this genetic variant may serve as a potential marker for CRC susceptibility. However, due to the study's limitations, further research with larger, more diverse populations and a broader assessment of CTLA-4 polymorphisms is necessary to validate these findings and fully elucidate the role of CTLA-4 in colorectal carcinogenesis.

Introducere: *Cancerul colorectal (CRC) reprezintă o problemă majoră de sănătate la nivel global, inclusiv în Indonezia. Factorii genetici, în special cei care afectează reglarea imunitară și evaziunea tumorală de la răspunsul imun, contribuie semnificativ la patogeneza CRC. Gena CTLA-4 (cytotoxic T-lymphocyte-associated protein 4), care codifică un receptor checkpoint imun, influențează activarea limfocitelor T și răspunsul imun. Anumite polimorfisme ale genei CTLA4 au fost asociate cu o funcție imună modificată și cu un risc crescut de apariție a CRC.*

Obiective: *Studiul își propune să investigheze rolul potențial al polimorfismului CTLA4-658C>T ca marker genetic pentru susceptibilitatea la cancer colorectal.*

Metode: *Acest studiu de tip caz-martor a inclus 60 de pacienți cu cancer colorectal (CRC) și 60 de pacienți fără CRC, între ianuarie 2023 și decembrie 2024, în cadrul Spitalului Universității Sumatera Utara și în spitalele afiliate. Pacienții cu CRC, cu vârsta de 18 ani sau mai mult, au fost incluși în grupul de cazuri, iar pacienții fără leziuni CRC confirmate prin colonoscopie au constituit grupul de control. Au fost excluși pacienții cu boli sistemice (de exemplu, diabet, insuficiență cardiacă sau renală, alte tipuri de cancer). Datele demografice și caracteristicile CRC au fost colectate din dosarele medicale. Participanții au fost intervievați pentru completarea datelor lipsă și au furnizat probe de sânge pentru analiza polimorfismului CTLA4-658C>T.*

Rezultate: *Polimorfismul CTLA4-658T>C a fost semnificativ asociat cu cancerul colorectal. Indivizii cu genotipul CC+CT au avut un risc de 2,69 ori mai mare de a dezvolta CRC comparativ cu cei cu genotipul TT (p=0,022). De asemenea, purtătorii alelei C au prezentat un risc de 2,26 ori mai mare de CRC comparativ cu cei cu alela T (p=0,015).*

Concluzie: *Aceste rezultate sugerează că polimorfismul CTLA4-658C>T ar putea reprezenta un marker genetic potențial pentru susceptibilitatea la cancer colorectal, subliniind rolul reglării imunitare în dezvoltarea CRC.*

Correspondence to: Imelda Rey, M.D, Jl. Dr. Mansyur No.5, Padang Bulan, Kec. Medan Baru, Kota Medan, Sumatera Utara 20155
Email: imeldareyusu@gmail.com; imelda.rey@usu.ac.id

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