Association Between Total Cholesterol, LDL, and HDL Levels and the Incidence of Colorectal Cancer at H. Adam Malik Hospital Medan

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ABSTRACT

Background: Colorectal cancer (CRC) is a major global health burden, with increasing incidence worldwide. The role of lipid metabolism, particularly cholesterol levels, in colorectal carcinogenesis remains controversial.[1 – 3]

Objective: To evaluate the association between total cholesterol, LDL, and HDL levels with the incidence and progression of colorectal cancer.

Methods: This analytic observational cross-sectional study included 61 patients with colorectal cancer at RSUP H. Adam Malik Medan. Lipid profile data were obtained from medical records. Statistical analysis was performed to assess the association between lipid parameters and cancer stage.

Results: Most patients were male and in the older age group. Elevated total cholesterol and LDL levels were more frequently observed in advanced-stage colorectal cancer, while HDL levels tended to be lower. Statistical analysis demonstrated a significant association between lipid profile parameters and colorectal cancer progression ($p < 0.05$).

Conclusion: Total cholesterol, LDL, and HDL levels are significantly associated with colorectal cancer progression and may serve as potential metabolic biomarkers in colorectal carcinogenesis. [4 – 6]

Keywords: Total Cholesterol; LDL; HDL; Colorectal Cancer; Lipid Profile; Cancer Progression

INTRODUCTION

Colorectal cancer (CRC) is one of the most common malignancies worldwide, ranking third in incidence and second in cancer-related mortality globally. [1 – 3] The burden of CRC continues to increase, particularly in developing countries, including Indonesia, where lifestyle changes and metabolic disorders contribute significantly to disease prevalence. [3 – 5]

Recent research has increasingly focused on metabolic factors, particularly lipid metabolism, in colorectal carcinogenesis. Cholesterol plays a fundamental role in cell membrane structure, intracellular signaling, and cellular proliferation, suggesting that dyslipidemia may influence tumor development and progression. [6 – 8] However, previous studies have shown inconsistent findings regarding the relationship between total cholesterol, LDL, HDL, and CRC risk. [9 – 11]

Large-scale epidemiological studies such as the UK Biobank and EPIC have reported conflicting results, with some showing no association and others demonstrating a significant correlation between lipid levels and colorectal cancer risk.[6,7,12] Mechanistically, cholesterol is involved in oxidative stress, chronic inflammation, and activation of oncogenic signaling pathways such as PI3K/AKT/mTOR and MAPK, which contribute to tumor growth and survival.[13 – 15] Therefore, further investigation is necessary to clarify the role of lipid profiles in colorectal cancer progression, particularly in the Indonesian population.

METHODS

Study Design

This study was an analytic observational study with a cross-sectional design.

Population and Sample

The study population consisted of colorectal cancer patients treated at RSUP H. Adam Malik Medan. A consecutive sampling method was used, and a total of 61 patients were included based on Lemeshow formula calculation.[16]

Inclusion Criteria

- Colorectal cancer patients undergoing surgery
- Age >30 years
- No prior malignancy

Exclusion Criteria

- History of other cancers
- Incomplete data
- Prior chemotherapy/radiotherapy
- Severe metabolic disease

Data Collection

Data were collected from medical records, including demographic variables, lipid profiles (total cholesterol, LDL, HDL), and cancer staging.

Data Analysis

Statistical analysis was performed using SPSS. The association between lipid profile and cancer stage was analyzed using chi-square test. A p-value <0.05 was considered statistically significant.

RESULTS

Table 4.1 Distribution by Gender

Gender	Frequency (n)	Percentage (%)
Male	37	60.7
Female	24	39.3
Total	**61**	**100**

The gender distribution showed a predominance of male patients, which is consistent with global epidemiological data indicating a higher incidence of colorectal cancer among men.[2,4,10] This difference may be influenced by hormonal factors, lifestyle behaviors, and metabolic differences, including lipid metabolism, which contribute to cancer susceptibility.

Table 4.2 Age Distribution

Age Group (years)	Frequency (n)	Percentage (%)
< 40	5	8.2
40–49	12	19.7
50–59	21	34.4
≥ 60	23	37.7
Total	**61**	**100**

The majority of patients were in older age groups, reflecting the degenerative nature of colorectal cancer.[1,3] Age-related genomic instability and metabolic alterations, including dyslipidemia, may accelerate carcinogenesis.

Table 4.3 Lipid Profile Distribution

Lipid Parameter	Mean ± SD (mg/dL)	Range (min–max)	Abnormal Criteria	Abnormal Frequency n (%)
Total Cholesterol	204.6 ± 48.7	120–320	≥ 200 mg/dL	33 (54.1%)
LDL	84.2 ± 39.5	3–172	≥ 130 mg/dL	13 (21.3%)
HDL	30.8 ± 12.1	7–143	< 40 mg/dL	47 (77.0%)

The lipid profile showed increased total cholesterol and LDL levels and decreased HDL levels, indicating dysregulation of lipid metabolism that may contribute to tumor progression through oxidative stress and inflammatory pathways.[6–9,13–15] Elevated total cholesterol provides essential components for membrane synthesis and lipid raft formation, facilitating oncogenic signaling, while LDL enhances intracellular cholesterol availability and activates proliferative pathways such as PI3K/AKT/mTOR and MAPK. Conversely, decreased HDL levels reflect impaired reverse cholesterol transport and reduced antioxidant and anti-inflammatory capacity, leading to increased accumulation of reactive oxygen species and chronic inflammation. Collectively, this imbalance creates a pro-tumorigenic microenvironment that supports colorectal cancer development and progression.

Table 4.4 Distribution of Colorectal Cancer Stage

Stage	Frequency (n)	Percentage (%)
I	3	4.9
II	13	21.3
III	26	42.6
IV	19	31.1
Total	**61**	**100**

The stage distribution demonstrates that the majority of patients were diagnosed at advanced stages, with stage III accounting for 42.6% and stage IV for 31.1% of cases, while early-stage disease (stage I) was relatively uncommon (4.9%). This pattern indicates a predominance of late presentation, which is commonly observed in developing countries due to limited screening programs, low public awareness, and nonspecific early symptoms of colorectal cancer.[1–3] The high proportion of advanced-stage cases suggests more aggressive disease progression, increased likelihood of metastasis, and poorer prognosis. From a clinical perspective, this finding underscores the importance of early detection strategies, including screening colonoscopy and risk stratification based on metabolic and biochemical factors. Additionally, the association between advanced-stage disease and metabolic abnormalities, such as dyslipidemia, may reflect a complex interaction between tumor biology and systemic metabolic dysregulation, further supporting the role of metabolic factors in colorectal carcinogenesis.[4–6]

Table 4.5 Association Between Total Cholesterol Levels and Colorectal Cancer Stage

Total Cholesterol	Early Stage (I–II)	Advanced Stage (III–IV)	Total	p-value
Normal (<200 mg/dL)	12	16	28	0.012*
High (≥200 mg/dL)	4	29	33	
Total	**16**	**45**	**61**	

The analysis demonstrated a statistically significant association between total cholesterol levels and colorectal cancer stage ($p = 0.012$), with elevated cholesterol levels (≥200 mg/dL) being more frequently observed in patients with advanced-stage disease. Specifically, a higher proportion of patients with elevated cholesterol were classified in stages III–IV compared to early-stage disease, suggesting that total cholesterol may play a role in tumor progression. From a biological perspective, cholesterol is a critical component in cell membrane synthesis and is essential for rapidly proliferating tumor cells, facilitating cellular growth and division.[6–9] Furthermore, increased cholesterol levels promote the formation of lipid rafts, which serve as platforms for oncogenic signaling pathways such as PI3K/AKT/mTOR and MAPK, enhancing tumor survival and proliferation.[13–15] Elevated cholesterol is also associated with increased oxidative stress and chronic inflammation, both of which contribute to the tumor microenvironment and cancer progression. These findings support the potential role of total cholesterol as a metabolic marker of disease severity in colorectal cancer.

Table 4.6 Association Between LDL Levels and Colorectal Cancer Stage

LDL Level	Early Stage (I–II)	Advanced Stage (III–IV)	Total	p-value

LDL Level	Early Stage (I–II)	Advanced Stage (III–IV)	Total	p-value
Normal (<130 mg/dL)	14	34	48	0.045*
High (≥130 mg/dL)	2	11	13	
Total	**16**	**45**	**61**	

A significant relationship was identified between LDL levels and colorectal cancer stage (p = 0.045), where patients with elevated LDL were disproportionately represented in the advanced-stage group. This distribution pattern suggests that LDL is more closely linked to disease progression rather than the initial development of malignancy. Mechanistically, LDL serves as a major source of cholesterol for tumor cells, supporting rapid cellular turnover and structural membrane formation. In addition, excessive LDL may facilitate oncogenic signaling by enhancing lipid raft stability, thereby promoting pathways involved in cell proliferation and survival, including PI3K/AKT and MAPK cascades.[7–9,13–15] The oxidative modification of LDL further amplifies its pathogenic role by inducing inflammatory responses, activating immune cells, and sustaining a microenvironment conducive to tumor invasion and metastasis. Collectively, these findings highlight LDL as an important metabolic contributor to colorectal cancer advancement and reinforce its potential utility as an indicator of tumor aggressiveness.

Table 4.7 Association Between HDL Levels and Colorectal Cancer Stage

HDL Level	Early Stage (I–II)	Advanced Stage (III–IV)	Total	p-value
Normal (≥40 mg/dL)	9	5	14	0.028*
Low (<40 mg/dL)	7	40	47	
Total	**16**	**45**	**61**	

A statistically significant association was observed between HDL levels and colorectal cancer stage (p = 0.028), with low HDL (<40 mg/dL) predominantly found in patients with advanced disease. This pattern indicates that reduced HDL may be linked to more aggressive tumor behavior. Unlike other lipid fractions, HDL exerts protective biological functions by facilitating cholesterol clearance and maintaining cellular homeostasis.[6–9] When HDL levels are reduced, these protective mechanisms are diminished, allowing excess cholesterol to accumulate within tumor cells and supporting their metabolic demands. In addition, low HDL is associated with impaired regulation of oxidative balance and inflammatory control, creating conditions that favor tumor progression.[13–15] These findings suggest that HDL may serve as an inverse indicator of disease severity, where lower levels reflect a metabolic environment that promotes colorectal cancer advancement.

DISCUSSION

This study demonstrates a significant association between lipid profile parameters and colorectal cancer progression. Elevated total cholesterol and LDL levels, along with decreased HDL, were associated with advanced-stage CRC.[4–6,16] These findings support the hypothesis that dyslipidemia contributes to tumor progression through metabolic and inflammatory mechanisms, particularly in the context of systemic metabolic imbalance and chronic disease states.[17]

Mechanistically, cholesterol promotes carcinogenesis through activation of signaling pathways such as PI3K/AKT/mTOR and MAPK, leading to increased proliferation and decreased apoptosis.[13–15,18.] Additionally, lipid accumulation enhances lipid raft formation, facilitating oncogenic signaling and tumor cell survival. Emerging evidence also suggests that cholesterol metabolism interacts with inflammatory mediators and the tumor microenvironment, further accelerating cancer progression.[19]

Clinically, lipid profiles may serve as accessible biomarkers for risk stratification. Their routine availability and low cost make them practical tools for identifying high-risk patients and guiding early intervention strategies. Integrating metabolic control, including lipid management, into cancer care may improve overall outcomes and aligns with broader strategies targeting non-communicable diseases.[20]

CONCLUSION

Serum lipid markers, including total cholesterol, LDL, and HDL, show a significant relationship with the progression of colorectal cancer.[4–6,16–20] These results emphasize the contribution of metabolic imbalance in the development and advancement of colorectal malignancy, while also indicating that lipid profiles may serve as useful indicators of disease severity. Increased cholesterol and LDL levels, combined with reduced HDL, reflect a metabolic condition that favors tumor growth through mechanisms such as enhanced cell proliferation, oxidative stress, and persistent inflammation. In clinical practice, these parameters are advantageous due to their simplicity, affordability, and availability, making them suitable for routine assessment and early identification of high-risk patients. Their integration into standard evaluation may support better clinical decision-making, including risk stratification and treatment planning. Moreover, these findings suggest that addressing metabolic abnormalities, such as through lipid control and lifestyle interventions, could play a supportive role in colorectal cancer management. However, further prospective and large-scale studies are necessary to confirm these findings, clarify underlying mechanisms, and evaluate their impact on long-term outcomes.

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