The Association Between Diabetes Mellitus and the Incidence of Colorectal Cancer at H. Adam Malik General Hospital, Medan

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Abstract

Introduction: Colorectal cancer is one of the leading cancers in terms of incidence and mortality worldwide, including in Indonesia. Type 2 diabetes mellitus (T2DM) is increasingly recognized as a significant risk factor for the development of colorectal cancer, with underlying mechanisms involving insulin resistance, hyperinsulinemia, impaired glucose metabolism, and chronic inflammation that promote malignant transformation. While international epidemiological studies have demonstrated an increased risk of colorectal cancer among patients with T2DM, local data in Indonesia, particularly in Medan, remain limited.
Objective: This study aimed to analyze the association between type 2 diabetes mellitus and the incidence of colorectal cancer, as well as to assess the relationship between glycemic parameters (random blood glucose, fasting blood glucose, 2-hour postprandial glucose, and HbA1c) and the progression of colorectal cancer at RSUP H. Adam Malik Medan.
Methods: This was an analytical observational study with a cross-sectional design, involving 61 colorectal cancer patients treated at the digestive surgery division of RSUP H. Adam Malik Medan from March to June 2025. Data were collected through consecutive sampling and included demographic characteristics (age, gender), history of T2DM, laboratory results for random blood glucose, fasting blood glucose, 2-hour postprandial glucose, HbA1c, and cancer stage. Statistical analysis used the chi-square test to evaluate the association between T2DM and glycemic parameters with the incidence and progression of colorectal cancer.
Results: Most colorectal cancer patients were male, with the largest age group being 50–69 years. Of all patients, 37.7% had a history of type 2 diabetes mellitus. There was a statistically significant association between T2DM and the incidence of colorectal cancer ($p=0.042$). Furthermore, high glycemic parameters—random blood glucose $\geqslant$200 mg/dL, fasting blood glucose $\geqslant$126 mg/dL, 2-hour postprandial glucose $\geqslant$200 mg/dL, and HbA1c $\geqslant$6.5%—were significantly more common in patients with advanced-stage colorectal cancer compared to early-stage cases ($p<0.05$ for all parameters). The majority of patients had adenocarcinoma as the histopathological type.
Conclusion: Type 2 diabetes mellitus is a significant risk factor for the incidence of colorectal cancer. Poor glycemic control is associated with the progression of colorectal cancer. Most colorectal cancer patients were male and aged 50–69 years, with adenocarcinoma as the most common histopathological type. These findings highlight the importance of optimal metabolic control in diabetic patients to reduce the risk and progression of colorectal cancer.
Keywords: Type 2 diabetes mellitus, Colorectal Cancer Glycemic parameters, Cancer progression.

1. INTRODUCTION

Colorectal cancer remains a significant global health concern due to its high incidence and mortality rates. In 2014, there were an estimated 3.5 million cases of colorectal cancer worldwide, with 1.4 million new

cases reported in 2012. The highest burden was observed in Europe, accounting for 32 percent of cases, followed by Asia at 19.3 percent, and North America at 11.6 percent. The disease resulted in approximately 694,000 deaths globally, with a case fatality rate of 20 percent. The five-year survival rates for colorectal cancer have shown improvements over time, with reported rates of 65 percent in the United States, 64 percent in Canada, and 50 percent in Australia during the period from 1980 to 1988, increasing significantly by 2017.[1]

In Indonesia, colorectal cancer was the fourth most commonly diagnosed cancer in 2018, with 30,017 reported cases, representing 8.6 percent of all cancers. The incidence was higher among males at 11.9 percent, compared to 5.8 percent in females. Male individuals were found to have a greater risk across all age groups. Regional variations were observed, with the Special Region of Yogyakarta recording the highest prevalence at 4.9 per thousand, while West Nusa Tenggara had the lowest prevalence at 0.9 per thousand. In North Sumatra, prevalence increased from 1.0 percent in 2013 to 1.6 percent in 2018, indicating a growing public health burden.[2]

Colorectal cancer is a multifactorial disease influenced by both modifiable and non-modifiable risk factors. Modifiable risk factors include obesity, dietary habits, sedentary lifestyle, alcohol consumption, smoking, and diabetes mellitus. Non-modifiable risk factors encompass increasing age, male gender, a positive family history of colorectal malignancy, and the presence of colorectal polyps. Among these, the contribution of metabolic disorders, particularly diabetes mellitus, to colorectal carcinogenesis has garnered increasing research interest in recent years.[3]

Numerous studies have reported a significant association between diabetes mellitus and the risk of developing colorectal cancer, particularly in individuals with type 2 diabetes mellitus. A large-scale meta-analysis that included over 2.5 million individuals from 15 studies demonstrated that diabetes mellitus is associated with a 30 percent increased risk of colorectal cancer. Furthermore, patients with diabetes mellitus have been found to exhibit significantly higher colorectal cancer-specific mortality, with a reported hazard ratio of 1.41 and a 95 percent confidence interval ranging from 1.18 to 1.70.[4,5]

The pathophysiological mechanisms linking diabetes mellitus and colorectal cancer are believed to be complex and interconnected. Shared risk factors such as obesity, poor dietary intake, and physical inactivity contribute to the increased prevalence of both diseases. Additionally, insulin resistance and hyperinsulinemia, commonly seen in type 2 diabetes, are thought to promote tumor development through the mitogenic effects of insulin and insulin-like growth factors, which enhance cellular proliferation and inhibit apoptosis in colorectal epithelial cells.[6]

Emerging evidence has also pointed to the potential protective effects of metformin in reducing cancer risk among diabetic patients. Metformin, a first-line antidiabetic agent, has been shown to exert antineoplastic properties beyond its glucose-lowering effect. It improves insulin sensitivity and glycemic control, while also inhibiting the proliferation of colorectal cancer cells through the activation of AMP-activated protein kinase and suppression of mTOR signaling pathways, thereby potentially reducing cancer progression.[7]

Despite the increasing volume of global data on the relationship between diabetes mellitus and colorectal cancer, region-specific studies remain limited, particularly in low- and middle-income countries such as Indonesia. Considering the rising prevalence of both diabetes and colorectal cancer in North Sumatra, especially in Medan, local epidemiological data are needed to improve clinical awareness, risk stratification, and the implementation of targeted preventive strategies.

Therefore, the objective of this study is to evaluate the association between diabetes mellitus and the incidence of colorectal cancer among patients treated at RSUP H. Adam Malik Medan. In addition to assessing demographic characteristics and clinical profiles, this study also aims to explore the relationship between glucose metabolism parameters, including random blood glucose, fasting plasma glucose, two-hour postprandial glucose, and hemoglobin A1c levels, with the progression of colorectal cancer, in order to provide scientific evidence for future preventive and therapeutic strategies.

2. METHODS

2.1. Methods

This study was designed as an analytical observational investigation using a cross-sectional approach to examine the association between type 2 diabetes mellitus and the incidence of colorectal cancer. The research was conducted in the Division of Digestive Surgery at RSUP H. Adam Malik Medan over a four-month period from March to June 2025. Ethical clearance was obtained from the Health Research Ethics Committee of the Faculty of Medicine, Universitas Sumatera Utara. All patients provided written informed consent prior to their inclusion in the study.

2.2. Population

The study population included patients diagnosed with colorectal cancer, with or without a history of diabetes mellitus, who sought treatment at RSUP H. Adam Malik Medan. Sampling was performed using a non-probability consecutive sampling technique. The sample size was calculated using the Lemeshow formula, with the following parameters: $Z\alpha = 1.96$, $P = 0.2$ (prevalence of diabetes in the control population), $Q = 0.8$, and a margin of error (d) of 0.1. Based on these calculations, the final sample size was determined to be 61 subjects.

Inclusion criteria for the study were patients aged over 30 years, diagnosed histopathologically with colorectal cancer, able to communicate effectively, and who had not previously received chemotherapy or radiotherapy. Participants were required to consent to surgical therapy and provide written informed consent. Exclusion criteria included patients with a history of other primary cancers, chronic illnesses that affect glucose metabolism (e.g., advanced chronic kidney disease, liver cirrhosis, uncontrolled thyroid disease), endocrine disorders such as Cushing's syndrome or acromegaly, type 1 or gestational diabetes, and those using medications significantly influencing blood glucose levels such as corticosteroids, immunosuppressants, or psychotropics. Incomplete medical records, particularly those lacking data on diabetes status or tumor staging, were also grounds for exclusion.

The operational definition of colorectal cancer was histopathologically confirmed malignant epithelial tumors located in the colon or rectum, based on WHO histological classification. Type 2 diabetes mellitus was defined by clinical history and laboratory parameters: random plasma glucose $\geq$ 200 mg/dL, fasting plasma glucose $\geq$ 126 mg/dL, 2-hour postprandial glucose $\geq$ 200 mg/dL, or HbA1c $\geq$ 6.5%. Glucose levels were measured via the hexokinase method, and HbA1c was assessed using the immunoturbidimetric method. Blood samples were processed using the Architect c6000 autoanalyzer following centrifugation at 5000 rpm for approximately 5 minutes. All laboratory measurements were performed at the hospital's clinical pathology laboratory.

2.3. Ethical Compliance

This research already followed the ethical standard that had bee granted by each institution according to Helsinki Declaration. This study was also reviewed by Ethical Committee for Health Research Universitas Sumatera Utara as the Institutional Research.

2.4. Statistical Analysis

The Data were collected through interviews, medical record reviews, and laboratory test results documented in structured questionnaires. Univariate analysis was conducted to describe demographic and

clinical characteristics. Categorical variables were presented as frequencies and percentages, while continuous variables were expressed as means and standard deviations. Bivariate analyses were conducted using the Chi-square test or Fisher's exact test for variables not meeting the assumptions of Chi-square. Statistical significance was set at $p < 0.05$. All analyses were performed using SPSS statistical software.

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3. RESULTS

This observational analytic study with a cross-sectional design was conducted to evaluate the association between type 2 diabetes mellitus and the incidence of colorectal cancer in patients at the Digestive Surgery Division of RSUP H. Adam Malik Medan from March to June 2025. A total of 61 subjects diagnosed with colorectal cancer were included in the study. Data collection involved demographic characteristics, glycemic profiles, and staging of colorectal cancer to assess the relationship between diabetes status and cancer progression.

The demographic profile of the subjects is shown in Table 1. The majority of the subjects were male (54.1%), while females comprised 45.9% of the sample. The age group with the highest proportion of colorectal cancer patients was 50–59 years (34.4%), followed by those aged 60–69 years (27.9%). These findings suggest that colorectal cancer predominantly affects individuals in the middle-aged to elderly population. Male predominance in the sample may also reflect a higher risk or detection rate in this demographic.

Table 1 Distribution of Subjects by Age and Gender

Variable	Frequency	Percentage (%)
Gender		
Male	33	54.1
Female	28	45.9
Age (years)		
30–39	5	8.2
40–49	11	18.0
50–59	21	34.4
60–69	17	27.9
≥70	7	11.5
Total	**61**	**100.0**

Table 2. Association Between Type 2 Diabetes Mellitus and Colorectal Cancer

Variable	Frequency	Percentage (%)	p-value
T2DM (+)	23	37.7	
T2DM (-)	38	62.3	0.042
Total	**61**	**100.0**	

A statistically significant association was observed between the presence of type 2 diabetes mellitus and the incidence of colorectal cancer ($p = 0.042$), as presented in Table 2. Among the 61 subjects, 23 individuals (37.7%) had a confirmed history of type 2 diabetes, while 38 individuals (62.3%) did not. The chi-square test confirmed that the presence of diabetes mellitus was significantly correlated with the incidence of

colorectal cancer in this patient population.

Table 3. Association Between Glycemic Markers and Colorectal Cancer Staging

Variable	Early Stage	Advanced Stage	Total	p-value
GDS <200	18	19	37	
GDS ≥200	6	18	24	0.031
GDP <126	15	12	27	
GDP ≥126	9	25	34	0.016
G2PP <200	17	13	30	
G2PP ≥200	7	24	31	0.020
HbA1c <6.5%	14	11	25	
HbA1c ≥6.5%	10	26	36	0.008
Total	**24**	**37**	**61**	

Further analysis explored the relationship between glycemic parameters and the stage of colorectal cancer. As shown in Table 3, subjects with elevated random blood glucose levels (GDS ≥200 mg/dL) were more frequently found in the advanced stage group compared to those with GDS <200 mg/dL ($p = 0.031$). A similar trend was observed for fasting blood glucose (GDP), with 25 of 34 patients with GDP ≥126 mg/dL presenting with advanced-stage cancer ($p = 0.016$). These findings indicate that poor glycemic control, as evidenced by hyperglycemia, may be associated with more severe cancer progression.

Moreover, postprandial blood glucose (G2PP) and HbA1c levels were significantly associated with cancer staging. Patients with G2PP ≥200 mg/dL were more likely to be in advanced stages of colorectal cancer ($p = 0.020$). In addition, 72.2% of patients with HbA1c ≥6.5% were in the advanced-stage group, compared to only 44.0% in those with HbA1c <6.5%, with a statistically significant p-value of 0.008. These findings underscore the potential role of chronic hyperglycemia and suboptimal glycemic control in the progression of colorectal cancer.

4. DISCUSSION

This study demonstrated that most colorectal cancer patients at RSUP H. Adam Malik Medan were aged between 50 and 69 years and predominantly male. These demographic patterns are consistent with global epidemiological data, as highlighted in the GLOBOCAN report, which indicates that colorectal cancer incidence rises markedly after the age of 50. Moreover, the higher prevalence in males aligns with findings by Rawla et al. (2019), who reported that men are at greater risk for colorectal cancer, likely due to hormonal influences, higher rates of tobacco and alcohol use, and dietary patterns rich in red and processed meats. These demographic trends underscore the importance of age and sex as critical factors in colorectal cancer epidemiology, particularly in Indonesia.[8,9]

In this study, 37.7% of colorectal cancer patients had a history of type 2 diabetes mellitus (T2DM), and the association between T2DM and colorectal cancer incidence was statistically significant ($p = 0.042$). This finding supports existing evidence from large-scale meta-analyses, including that of Yuhara et al. (2011), who analyzed data from over 2.5 million individuals and found a 27% increased risk of colorectal cancer among diabetic patients (RR = 1.27; 95% CI: 1.21–1.34). Similarly, Larsson et al. (2005) identified a 30% elevated risk. These associations are biologically plausible given the underlying mechanisms in T2DM, particularly hyperinsulinemia and insulin resistance, which promote cell proliferation and inhibit apoptosis via insulin and

IGF-1 signaling pathways.[10-12]

Despite these robust associations, conflicting results have been reported. For instance, a prospective study by Limburg et al. (2006) in the United States did not observe a significant increase in colorectal cancer risk after adjusting for body mass index (BMI) and physical activity. Such discrepancies may arise from variations in population genetics, diabetes duration and control, or methodological differences in exposure and outcome assessment. Nonetheless, the present study contributes additional support for a potential link between T2DM and colorectal carcinogenesis in the Indonesian population.[13]

Beyond diabetes status, this study also explored glycemic parameters—random blood glucose (RBG), fasting blood glucose (FBG), 2-hour postprandial glucose (2h-PPG), and HbA1c—and their relationship with colorectal cancer progression. Notably, patients with RBG ≥200 mg/dL were more frequently diagnosed at advanced stages (III–IV), with statistical significance ($p = 0.031$). This aligns with findings from Stattin et al. (2007), who proposed that hyperglycemia may contribute to cancer initiation and progression by inducing oxidative stress, NF-κB pathway activation, and chronic inflammation, all of which foster a tumor-promoting microenvironment.[14]

Fasting blood glucose also exhibited a significant association with disease severity, where patients with FBG ≥126 mg/dL were more likely to present with advanced-stage disease ($p = 0.016$). He et al. (2014), in a large Chinese cohort, similarly reported that elevated FBG independently increased colorectal cancer risk after controlling for potential confounders such as age, BMI, and smoking status. These findings suggest that poor fasting glycemic control may be a predictive marker of colorectal cancer progression.[15]

Postprandial glycemia, measured by 2h-PPG, also demonstrated a significant relationship with disease stage ($p = 0.020$). Goto et al. (2004) concluded in a Japanese cohort study that 2h-PPG was a stronger predictor of gastrointestinal cancer risk than FBG, likely because postprandial hyperglycemia reflects broader disturbances in glucose metabolism and exaggerated glycemic responses to dietary intake. This underscores the importance of monitoring 2h-PPG in diabetic and prediabetic populations at risk for malignancy.[16]

HbA1c, a marker of long-term glycemic control, was significantly higher among patients with advanced-stage colorectal cancer ($p = 0.008$). This observation is consistent with meta-analytic data by Xu et al. (2016), which showed that each 1% increment in HbA1c was associated with a 22% increased risk of colorectal cancer. Tsilidis et al. (2015) also reported that elevated HbA1c levels were associated with both increased incidence and mortality from colorectal cancer. These associations are mechanistically linked to the accumulation of advanced glycation end-products (AGEs), oxidative DNA damage, and activation of proliferative signaling cascades such as PI3K/AKT/mTOR, all of which drive oncogenesis.[17.18]

However, not all studies confirm a strong relationship between HbA1c and cancer progression. Research in Northern European cohorts, such as that by Pearson-Stuttard et al. (2016), found that this association diminished after adjusting for variables like diabetes duration, medication use, and metabolic status. This suggests that while HbA1c is a valuable marker of long-term glycemic exposure, its role as an independent oncogenic factor may be influenced by broader metabolic and therapeutic contexts. Nonetheless, in the present study, HbA1c levels showed a significant correlation with disease progression, reinforcing the importance of glycemic control in cancer management.[19]

From a pathophysiological perspective, the link between hyperglycemia and colorectal cancer can be explained by several mechanisms. Elevated glucose stimulates insulin and IGF-1 production, which enhances cellular proliferation and suppresses apoptosis, creating a tumor-favorable environment. Chronic hyperglycemia also increases the formation of reactive oxygen species (ROS) and AGEs, which can induce genetic mutations and impair cellular repair mechanisms. Moreover, systemic inflammation and immune dysfunction in diabetic patients further reduce the body's ability to suppress tumor growth.[20,21]

The clinical implications of these findings are considerable. Glycemic parameters may serve as prognostic indicators of colorectal cancer severity and could be integrated into risk stratification tools. Additionally, early glycemic intervention may alter the course of malignancy, as suggested by studies evaluating metformin, an insulin-sensitizing agent. Zhang et al. (2013) demonstrated that metformin use was associated

with reduced cancer incidence and improved survival in diabetic patients with colorectal cancer, suggesting a potential protective role mediated by improved metabolic control.[22]

Despite the strengths of this study, including the use of standardized laboratory criteria and histopathological confirmation, several limitations must be acknowledged. The cross-sectional design precludes causal inference, and the relatively small sample size may limit generalizability. Furthermore, confounding factors such as duration of diabetes, nutritional status, physical activity, and antidiabetic treatments were not comprehensively assessed. These variables may influence both glycemic control and cancer progression and warrant further investigation.

Additionally, the lack of longitudinal follow-up limits the ability to assess survival outcomes or temporal changes in glycemic status. Future studies employing cohort or case-control designs with larger sample sizes and multivariate analyses are recommended to validate and expand upon these findings. Incorporating molecular markers and tumor genotyping may also elucidate the biological pathways linking hyperglycemia to carcinogenesis.

Nonetheless, the present study provides important evidence of the association between poor glycemic control and advanced colorectal cancer in an Indonesian tertiary referral center. It underscores the need for integrated metabolic and oncologic care in patients with diabetes, particularly given the rising prevalence of both conditions in Southeast Asia. Clinicians should be vigilant in screening diabetic patients for early signs of colorectal neoplasia, especially those with persistently elevated glucose levels or suboptimal HbA1c control. Incorporating routine colonoscopy in high-risk diabetic populations may facilitate earlier diagnosis and improve prognosis.

This study confirms a statistically significant association between type 2 diabetes mellitus and the incidence of colorectal cancer. Furthermore, elevated glycemic parameters including RBG, FBG, 2h-PPG, and HbA1c were correlated with more advanced stages of cancer. These findings support the integration of glycemic management into colorectal cancer prevention and treatment strategies. Future research should focus on prospective studies and intervention trials to assess the benefits of metabolic control on colorectal cancer outcomes.

5. CONCLUSION

This study concludes that colorectal cancer is more commonly found in male patients and those aged 50–69 years. A significant association was identified between type 2 diabetes mellitus and the occurrence of colorectal cancer, indicating a possible metabolic contribution to cancer development. Additionally, elevated glycemic parameters such as random blood glucose, fasting glucose, two-hour postprandial glucose, and HbA1c were significantly related to more advanced cancer stages.

These findings emphasize the importance of glycemic control in patients at risk for colorectal cancer, especially among diabetics over 50 years old. Incorporating glycemic markers in cancer risk assessments may improve early detection and management strategies. Future research should explore causal relationships using larger, longitudinal studies, and integrated screening programs are recommended for high-risk diabetic populations.

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Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this article. Neither financial relationships nor personal affiliations have influenced the design, execution, or reporting of the research. All contributions were made in accordance with academic integrity and institutional ethics.

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