

RESEARCH ARTICLE

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Perioperative Thrombocytosis as a Predictor of Long-Term Survival in Colorectal Cancer Patients: A Retrospective Cohort Study

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Abstract

Background: Colorectal cancer (CRC) is one of the leading causes of cancer-related death globally. Thrombocytosis, or increased platelet count, has been identified as a poor prognostic factor in various cancers, including CRC. This study aimed to investigate the relationship between preoperative and postoperative thrombocytosis and the survival rate of CRC patients. **Methods:** This retrospective cohort study enrolled 160 CRC patients who underwent surgery. Clinical data on preoperative and postoperative platelet counts, as well as survival rates, were collected from medical records. Thrombocytosis was defined as platelet levels exceeding $400 \times 10^9/L$. Survival analysis was performed using the Kaplan-Meier method, and relationships between variables were assessed with the Chi-squared test. **Results:** A total of 54 (33.7%) of patients experienced preoperative thrombocytosis and 23.1% experienced postoperative thrombocytosis. The 5-year cumulative survival rate of 160 CRC patients was 27.83 ± 16.97 months, with a mortality rate of 92.5%. There was a significant relationship between thrombocytosis and cancer stage ($p=0.001$) and tumor location ($p=0.003$), where patients with thrombocytosis were more likely to present with late-stage tumors and tumors of the rectum. Kaplan-Meier analysis showed that patients with thrombocytosis, especially those with postoperative thrombocytosis, had a significantly lower survival rate than patients without thrombocytosis. **Conclusion:** Thrombocytosis, particularly after surgery, is an important predictor of poor prognosis in CRC patients. Monitoring and managing thrombocytosis should be considered in efforts to improve patient survival.

Keywords: Surgical Procedures- thrombocytosis- prognosis- survival rate- colorectal Neoplasms

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Introduction

Colorectal cancer (CRC) is the second leading cause of cancer-related death worldwide. In 2020, it was estimated that more than 1.9 million new cases of CRC and over 930,000 CRC-related deaths occurred globally [1]. According to GLOBOCAN 2020 data, CRC was the fourth most common cancer in Indonesia (8.6%), following breast, cervical, and lung cancers. In 2020, there were 396,914 new CRC cases and 234,411 deaths [2]. At Dr. Wahidin Sudirohusodo Hospital, 293 CRC patients reportedly underwent treatment in the Digestive Surgery Division [3]. The highest survival rates for CRC cases (more than 65%) have been reported in Australia, South Korea, and Israel, while India reported the worst prognosis [4]. In Taiwan, the 5-year survival rates for patients with stage I, II, III, and IV CRC were 91.20%,

82.20%, 63.20%, and 21.70%, respectively [5]. In Makassar, Eastern Indonesia, the overall 5-year survival rate for CRC is 36.5% [6].

Increased platelet counts, a condition known as thrombocytosis, play important roles in cancer progression and metastasis. When cancer cells detach from a primary tumor and enter the bloodstream, platelets are among the first cells to elicit an immunological response. However, cancer cells can exploit platelets to evade the endogenous immune system [7]. Studies have shown that thrombocytosis at the time of CRC diagnosis is associated with tumor invasion, metastasis, and poorer survival outcomes [8]. Increased platelet counts after CRC surgery were also found to be associated with poor prognosis. Thus, postoperative thrombocytosis is a demonstrated prognostic factor for CRC patient survival, underscoring the predictive power of thrombocytosis [9].

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Despite the known prognostic role of thrombocytosis in CRC, there remains a need for detailed regional data, particularly in Eastern Indonesia, where specific survival rates have been reported. Furthermore, a comprehensive analysis investigating the combined and comparative impact of both preoperative and postoperative thrombocytosis on CRC patient survival within this specific population is currently limited in the literature. Therefore, herein, we investigated the relationship between preoperative and postoperative thrombocytosis and CRC patient survival in Eastern Indonesia.

Materials and Methods

Setting

This study was conducted at Dr. Wahidin Sudirohusodo Hospital, Makassar, Indonesia.

Study Design and Participants

This retrospective cohort study enrolled 160 CRC patients who underwent surgery at our institution, between January and December 2018. The patients were followed for at least five years.

Inclusion criteria for participants were a histopathological diagnosis of CRC, having undergone surgery, and having complete data pertaining to demographics, tumor location, and preoperative and postoperative platelet counts available in their medical records. Patients with chronic inflammation, infection, a history of platelet transfusion, thrombocytopenia, and/or other malignancies or hematological disorders were excluded from the study. Tumor staging was based on the American Joint Committee on Cancer (AJCC) 2017 classification [10, 11]. Histopathological grading of tumors was performed in accordance with World Health Organization recommendations [12, 13].

Instrument

Data were collected retrospectively using a standardized data collection sheet. This instrument facilitated the extraction of comprehensive demographic, clinical, and laboratory examination data from patient medical records. The items included demographic data (sex and age), tumor characteristics (tumor location and cancer stage), histopathological data (histopathological type and grade), laboratory data (preoperative and postoperative platelet counts), treatment history (chemotherapy history), and survival data.

Data Collection

Clinical data, including preoperative and postoperative platelet counts, as well as survival rates, were systematically collected from medical records. Platelet counts were measured before surgery (preoperative platelet count) and at least 21 days after surgery (postoperative platelet count). This specific timing for postoperative platelet count measurement was chosen to minimize the influence of acute, transient thrombocytosis often observed immediately after surgery due to acute surgical stress, inflammation, and tissue injury.

Thrombocytosis is characterized by platelet levels

exceeding $400 \times 10^9/L$ [14]. Patient survival was measured from the date of surgery until death or the end of the study period.

Data Analysis

The Chi-squared test was used to evaluate the relationship between thrombocytosis and clinical variables such as sex, age, tumor location, cancer stage, histopathological type, histopathological grade, and chemotherapy history. The Kaplan-Meier method was used to compare survival rates between patients with and without thrombocytosis, both preoperatively and postoperatively. Data analysis was carried out using SPSS version 27 (IBM Corp.).

Ethical Considerations

The study was approved by the Research Ethics Committee of the Faculty of Medicine Universitas Hasanuddin, Makassar, Indonesia, with protocol number: UH24090712 on October 9, 2024. The researchers ensured that participants' data were anonymized or maintained with confidentiality, that the rights or interests of participants were not invaded, and that informed consent was obtained from all individual participants.

Results

Patient Characteristics

This study enrolled 160 CRC patients (Table 1); males and females comprised 60% and 40% of the study population, respectively. Most patients (52.5%) were aged 40–60 years, with an average age of 54.13 years. Most tumors were located in the rectum (58.1%) and diagnosed at stage IV (43.8%) or stage III (33.8%). Based on histopathology, 85% of patients had adenocarcinoma, with the majority of tumors categorized as moderate grade (75%). A total of 80% of patients received chemotherapy.

A total of 54 (33.7%) of patients experienced preoperative thrombocytosis, while 23.1% experienced postoperative thrombocytosis. The average cumulative 5-year survival rate of 160 CRC patients was 27.83 months, with a mortality rate of 92.5%; only 7.5% of patients survived after 5 years.

The Relationship Between Pre/Postoperative Thrombocytosis and Non-Thrombocytosis

Based on an analysis comparing patients with preoperative thrombocytosis and non-thrombocytosis (Table 2), we found that sex and age were not significantly associated with CRC patient thrombocytosis status. In the preoperative thrombocytosis group, there were more males (61.1%) than females, and the predominant age group in both categories was 40–60 years. However, tumor location and cancer stage were significantly associated with thrombocytosis status. Tumors in the rectum were more frequently found in patients with preoperative thrombocytosis ($p=0.003$), and stage IV tumors were more prevalent in the preoperative thrombocytosis group ($p=0.001$). On the other hand, histopathology, grade, and chemotherapy history were not significantly associated with thrombocytosis status. Overall, these results suggest

Table 1. Demographic and Clinical Characteristics of Colorectal Cancer Patients

Variable	n	%
Sex		
Male	96	60
Female	64	40
Age (years)	54.13 ± 12.74	
<40	23	14.4
40–60	84	52.5
>60	53	33.1
Tumor location		
Ascending colon	21	13.1
Transverse colon	15	9.4
Descending colon	11	6.9
Sigmoid colon	20	12.5
Rectum	93	58.1
Tumor stage		
Stage I	9	5.6
Stage II	27	16.9
Stage III	54	33.8
Stage IV	70	43.8
Histopathological type		
Adenocarcinoma	136	85
Mucinous	18	11.3
Signet ring cell	4	2.5
Squamous cell	2	1.3
Histopathological grade		
Low	32	20
Moderate	120	75
High	8	5
Chemotherapy history		
Yes	128	80
No	32	20
Platelet Counts		
Preoperative (109/L)		
>400,000	54	33.7
≤400,000	106	66.3
Postoperative (109/L)		
>400,000	37	23.1
≤400,000	123	76.9
5-year survival rate (months)	27.83 ± 16.97	
Deceased	148	92.5
Alive	12	7.5

that tumor location and cancer stage are significantly associated with preoperative thrombocytosis, while other variables do not show significant associations.

Based on an analysis comparing patients with postoperative thrombocytosis and non-thrombocytosis (Table 2), sex and age were not significantly associated with postoperative thrombocytosis. Most patients with postoperative thrombocytosis were male and aged between 40 and 60 years. However, tumor location and cancer stage

were significantly associated with thrombocytosis status. Tumors in the rectum were more frequently found in patients with postoperative thrombocytosis, and stage IV tumors predominated in this group ($p=0.003$). On the other hand, histopathology, tumor grade, and chemotherapy history did not show significant relationships with thrombocytosis status. Overall, tumor location and cancer stage were significantly associated with postoperative thrombocytosis, while other variables did not show significant effects.

Survival Rate Analysis Based on Thrombocytosis Status

Figure 1A shows that patients with non-thrombocytosis had better survival rates than patients with thrombocytosis, both preoperative and postoperative. We observed significant differences in overall survival (OS) among the three groups, suggesting that thrombocytosis negatively affects the OS of CRC patients. Figure 1B shows that non-thrombocytosis patients had higher OS than patients with preoperative thrombocytosis patients, indicating that preoperative thrombocytosis significantly reduces OS.

Figure 1C demonstrates that patients with postoperative thrombocytosis had lower OS than non-thrombocytosis patients, demonstrating the negative impact of postoperative thrombocytosis on OS. Finally, Figure 1D shows that the OS of patients with preoperative thrombocytosis did not differ from that of patients with postoperative thrombocytosis. This indicates that both preoperative and postoperative thrombocytosis have similar effects on prognosis.

Discussion

In this study, no significant relationship was found between sex and thrombocytosis status. This result is consistent with the findings of Josa et al., who demonstrated that although thrombocytosis is more prevalent in males, especially those with advanced-stage cancer, this difference does not significantly impact overall prognosis [9]. A similar finding was reported by Bailey et al., who stated that although males tend to experience thrombocytosis more often, its effect on survival rate is not significant [14]. Thus, sex does not appear to be a key factor influencing the prognosis of CRC patients who experience thrombocytosis.

Additionally, there was no significant difference in thrombocytosis status based on age. Thrombocytosis was more prevalent in elderly patients, particularly those with advanced-stage cancer; however, age was not a primary factor that influenced CRC patient prognosis. Sasaki et al. reported that advanced age does not affect the survival rate of patients with thrombocytosis [15]. This finding is also supported by Baranyai et al., who found that although age may influence the risk of CRC complications, it does not have a significant impact on survival rate [8].

Tumor location was found to be associated with thrombocytosis, particularly in patients with distal tumors such as those in the rectum, which are more likely to trigger stronger inflammatory responses. A study by Xia et al. supports this result, in that distal tumor locations often cause thrombocytosis, thereby affecting patient prognosis

Table 2. Incidence of Preoperative and Postoperative Thrombocytosis

Variable	Pre-operative thrombo-cytosis n (%)	Non-thrombo- cytosis n (%)	p- value	Post-operative thrombo-cytosis n (%)	Non- thrombo- cytosis n (%)	p- value
Sex						
Male	33 (61.1)	63 (59.4)	0.378	23 (62.2)	73 (59.3)	0.595
Female	21 (38.9)	43 (40.6)		14 (37.8)	50 (40.7)	
Age (years)						
<40	10 (18.5)	13 (12.3)	0.417	9 (24.3)	13 (10.6)	0.639
40–60	27 (50.0)	54 (50.9)		14 (37.8)	67 (54.5)	
>60	17 (31.5)	39 (36.8)		14 (37.8)	43 (35)	
Tumor location						
Ascending colon	13 (24.1)	8 (7.5)	0.003	7 (18.9)	14 (11.4)	0.034
Transverse colon	7 (13.0)	8 (7.5)		3 (8.1)	12 (9.8)	
Descending colon	6 (11.1)	5 (4.7)		5 (13.5)	6 (4.9)	
Sigmoid colon	3 (5.6)	17 (16.0)		1 (2.7)	20 (16.3)	
Rectum	25 (46.3)	68 (64.2)		21 (56.8)	71 (57.7)	
Stage						
I	1 (1.9)	8 (7.5)	0.001	1 (2.7)	8 (6.5)	0.003
II	4 (7.4)	23 (21.7)		4 (10.8)	23 (18.7)	
III	10 (18.5)	44 (41.5)		6 (16.2)	48 (39.0)	
IV	39 (72.2)	31 (29.2)		26 (70.3)	44 (35.8)	
Histopathology						
Adenocarcinoma	45 (83.3)	93 (87.7)	0.414	31 (83.8)	107 (87.0)	0.829
Mucinous	7 (13.0)	9 (8.5)		4 (10.8)	12 (9.8)	
Squamous cell	1 (1.9)	3 (2.8)		1 (2.7)	1 (0.8)	
Signet ring cell	1 (1.9)	1 (0.9)		1 (2.7)	3 (2.4)	
Grade						
Low	10 (18.5)	22 (20.8)	0.209	8 (21.6)	24 (19.5)	0.566
Moderate	39 (72.2)	81 (76.4)		26 (70.3)	94 (76.4)	
High	5 (9.3)	4 (2.8)		3 (8.1)	5 (4.1)	
Chemotherapy history						
Yes	36 (66.7)	84 (79.2)	0.137	25 (67.6)	75 (61.0)	0.241
No	18 (33.3)	22 (20.8)		12 (32.4)	48 (39.0)	

[16]. However, different findings were reported by Yu et al., who reported that although thrombocytosis is more common in distal tumors, it does not significantly affect survival rates [17]. These differences suggest that while tumor location may influence thrombocytosis, its effect on prognosis requires further investigation.

Cancer stage is an important factor that significantly affects the survival rates of patients with thrombocytosis. This study found that thrombocytosis is particularly associated with late-stage CRC (stages III and IV), which significantly decreases patients' overall survival. Josa et al. demonstrated that thrombocytosis in advanced stages increases the risk of metastasis and worsens prognosis [9]. Additionally, studies by Sasaki et al. and Voutsadakis also support these findings, in that advanced-stage cancer patients with thrombocytosis have a higher risk of metastasis and lower survival rates [15, 18].

No significant relationship was found between histopathological type and thrombocytosis status. Certain

histopathological subtypes, such as adenocarcinoma, did not significantly impact prognosis in patients with thrombocytosis. Previous studies have found that histopathological type does not significantly affect the survival rates of CRC patients with thrombocytosis, although mucinous tumors have a higher risk of thrombocytosis [16, 19].

Histopathological grade was also not significantly associated with thrombocytosis status. A study by Väyrynen et al. reported that lower tumor grades may trigger thrombocytosis; however, thrombocytosis impact on prognosis has not been consistent across studies [20]. Josa et al. also reported that high-grade tumors increase the risk of metastasis and reduce overall survival, but this relationship has not been consistently reported in the literature [9].

Chemotherapy history was not found to significantly affect thrombocytosis status. Studies by Sasaki et al. and Voutsadakis reported that chemotherapy does not directly

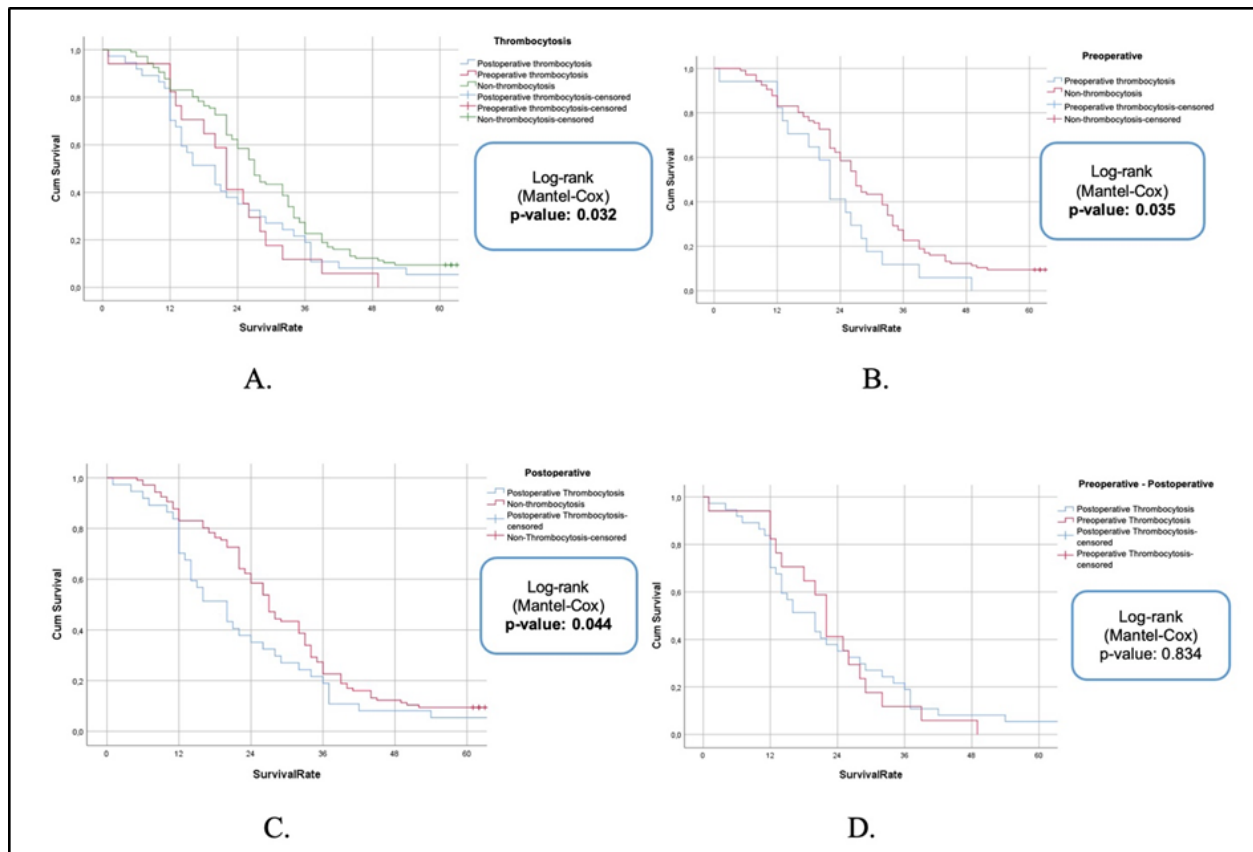


Figure 1. Kaplan-Meier Survival Rates Comparing Patients with A. thrombocytosis vs. non-thrombocytosis; B. preoperative thrombocytosis vs. non-thrombocytosis; C. postoperative thrombocytosis vs. non-thrombocytosis; D. preoperative thrombocytosis vs. postoperative thrombocytosis.

trigger thrombocytosis; instead, thrombocytosis is more likely to be triggered by the body's response to the tumor itself [15, 18]. A study by Bailey et al. supported this finding, showing that thrombocytosis is more likely to be caused by interactions between the tumor and the immune system rather than direct effects of chemotherapy [14].

Both preoperative and postoperative thrombocytosis negatively impact patient survival rates. Although no significant differences were found between preoperative and postoperative thrombocytosis, both were associated with reduced overall CRC patient survival. Sasaki et al. [15] showed that both thrombocytosis conditions carry the same risk for patient prognosis, particularly among those with advanced-stage cancer. Baranyai et al. also reported that the cumulative effects of thrombocytosis before and after surgery worsen patient prognosis, particularly in those with tumors that are difficult to treat post-surgery [8].

The strength of this study lies in its comprehensive analysis of the relationship between preoperative and postoperative thrombocytosis and the survival rates of CRC patients. It provides valuable insights into clinical management and treatment strategies by identifying a significant impact of thrombocytosis on patient survival. Additionally, the study identified associations among thrombocytosis, cancer stage, and tumor location, adding further depth to our findings.

The present study has several limitations that warrant

consideration. Firstly, while a sample size of 160 CRC patients provided valuable insights for initial analysis, it may lack the statistical power necessary to generalize findings across broader and more diverse populations. This relatively modest sample size could impact the external validity of our conclusions. Secondly, the retrospective design of this study inherently introduces potential biases and confounding factors that could influence the results. Such designs rely on existing medical records, which may not always contain all desired information or could be subject to variations in data collection practices. This highlights the need for validation with prospective studies to confirm our findings.

Additionally, while patients with overt chronic inflammation, active infection, a history of platelet transfusion, thrombocytopenia, and/or other malignancies or hematological disorders were excluded to refine our focus on thrombocytosis in CRC, our analysis does not adequately address the potential confounding effects of more subtle systemic inflammatory responses or other specific hematological parameters (beyond platelet counts) on survival and thrombocytosis. The retrospective nature of the study limited our ability to collect detailed data on such variables (e.g., C-reactive protein, specific cytokine levels) to adjust for them in our statistical models. These unmeasured factors could potentially influence both thrombocytosis and survival outcomes, thereby representing an unaddressed confounding variable. This

limitation restricts the direct applicability of our findings to real-world clinical settings where such comorbidities are common, and further limits our ability to definitively isolate the independent effect of thrombocytosis from that of broader inflammatory or hematological responses that may coexist.

Finally, this study does not explore the specific mechanisms underlying the relationship between thrombocytosis and cancer progression. Furthermore, the influence of other treatment histories, such as chemotherapy or radiotherapy, on thrombocytosis requires further exploration to better understand the underlying mechanism of this relationship.

Clinical Implications and Future Directions

Our findings hold several important implications for the clinical management of CRC patients. Firstly, the consistent association between postoperative thrombocytosis and poorer survival rates highlights the importance of routine platelet count monitoring in the post-surgical period. Postoperative thrombocytosis, easily assessed through a standard complete blood count, serves as an accessible and cost-effective prognostic marker. This suggests that patients who develop or maintain thrombocytosis after CRC surgery may represent a high-risk group warranting closer surveillance, more intensive follow-up, or consideration for more aggressive adjuvant therapeutic strategies, subject to further validation.

Secondly, while our study reinforces the prognostic value of thrombocytosis, it also opens avenues for future research. Larger, multicenter prospective studies are essential to validate these findings in diverse patient populations and overcome the inherent limitations of retrospective designs. Such studies should also aim to systematically collect and adjust for potential confounding variables, including detailed systemic inflammatory markers (e.g., C-reactive protein, cytokine profiles) and other hematological parameters that may influence both thrombocytosis and survival.

Furthermore, future research should delve deeper into the underlying biological mechanisms by which thrombocytosis contributes to CRC progression, metastasis, and reduced survival. Investigating the role of platelet-derived factors and their interactions with tumor cells could pave the way for novel therapeutic targets. Finally, studies exploring the effectiveness of antiplatelet therapies or other interventions aimed at normalizing platelet counts in improving survival outcomes for CRC patients with persistent thrombocytosis are warranted. Understanding the interplay of various treatment modalities (e.g., specific chemotherapy regimens, radiotherapy) with thrombocytosis development and its prognostic impact will also be crucial for developing more targeted and personalized therapeutic strategies.

In conclusion, this study shows that thrombocytosis, especially after surgery, is a significant predictor of decreased CRC patient survival. High postoperative platelet counts are associated with lower survival rates, particularly in patients with advanced-stage cancer or rectal tumors. Monitoring thrombocytosis should be an important component of CRC patient clinical

management as a step toward estimating prognosis and establishing more optimal treatment strategies. Further research is needed to better understand the relationship between thrombocytosis and the underlying inflammatory mechanisms driving cancer progression.

Author Contribution Statement

Conceptualization: ATS, ES, SS, AA, FH, RM, and MF; Data curation: ATS, ES, AA, and FH; Formal analysis: ATS, ES, AA, and FH; Funding acquisition: ATS; Investigation: ATS, ES, AA, FH, and MF; Methodology: ES, SS, AA, FH, and RM; Project administration: ATS, AA, and MF; Resources: ATS and MF; Validation: ATS, AA, and FH; Visualization: MF; Writing – original draft: ATS, ES, and SS; Writing – review & editing: ES, SS, AA, FH, RM, and MF; All authors read and approved the final manuscript.

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Competing interests

No competing interests were reported.

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