

ORIGINAL RESEARCH

Maternal-Fetal Medicine

Spinal anesthesia-related complications and associated risk factors among women undergoing cesarean delivery in a resource-limited maternity hospital in Sudan

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Abstract

Background: Spinal anesthesia (SA) is widely used for cesarean delivery (CD) due to its safety and efficacy; however, it is not free of complications. In resource-limited settings where anesthetic care is often delivered by non-physician providers, SA-related adverse outcomes may be underestimated or underreported. This study aimed to determine the prevalence and risk factors of SA-related complications among women undergoing CD at Dongola Maternity Hospital in Northern Sudan.

Methods: A prospective observational study was conducted at Dongola Maternity Hospital between March and August 2021. A total of 384 women who underwent CD under SA were selected by convenience sampling. Data were

collected using structured questionnaires, patient interviews, and chart reviews. Participants were followed intraoperatively, at discharge, and two weeks postoperatively. Descriptive statistics, Chi-square tests, and binary logistic regression were performed using SPSS version 24. A p-value < 0.05 was considered statistically significant.

Results: Of the 384 women included, 57 (14.8%) experienced one or more SA-related complications. The most frequent complications were nausea (8.6%), post-dural puncture headache (6.3%), suspected post-spinal meningitis (3.1%), hypotension (1.3%), and transient neurological symptoms (0.8%). Two maternal deaths (0.5%) occurred following SA and were considered possibly related to anesthesia-related complications. Logistic regression identified the following independent

predictors: preterm gestational age (AOR=3.48; 95% CI: 1.42–8.54), category 2 (AOR=5.59) and category 3 (AOR=2.34) urgency of CD, crystalloid co-loading (AOR=2.25), and fluid volume >2 liters (AOR=3.81). A history of prior SA complications showed a marginal association (AOR=2.51; $p=0.090$).

Conclusion: SA-related complications are not uncommon and can be severe in resource-limited settings. Preterm delivery, surgical urgency, and

fluid management practices significantly increase risk. Improved infection prevention practices, standardized procedural protocols, and enhanced training for anesthesia providers may reduce complication rates.

Keywords: Cesarean Section; Meningitis; Anesthesia, Spinal; Headache, Post-Dural Puncture; Obstetric Surgical Procedures; Sudan

Introduction

The global rate of cesarean delivery (CD) has risen significantly over recent decades. According to the World Health Organization (WHO), approximately 21% of all births were delivered via cesarean section in 2021, with projections estimating an increase to nearly 29% by 2030 (1). This growing reliance on surgical delivery necessitates safe, effective, and context-appropriate anesthesia techniques to ensure optimal maternal and neonatal outcomes (2).

Spinal anesthesia (SA) is the preferred anesthetic technique for most cesarean deliveries because of its rapid onset, reliability, and favorable maternal and neonatal outcomes (3, 4). It also avoids complications associated with GA, such as difficult airway management and risk of aspiration (5). However, SA is not without risks. Although generally considered safe, it may lead to a range of complications, from common side effects like hypotension, post-dural puncture headache (PDPH), and nausea, to more serious adverse events such as post-spinal meningitis, transient neurological symptoms, and rarely maternal death (6).

In resource-limited settings such as Sudan, the use of SA for cesarean delivery has expanded significantly in recent years. At Dongola Maternity Hospital (DMH), located in Northern Sudan, there has been a marked shift since 2008 from GA to SA as the primary anesthetic technique for CD following the global shift (7). Despite this shift, anesthetic services at DMH are primarily delivered by anesthesia technicians, with no anesthesiologists or specialist oversight, raising concerns about standardization, complication management, and overall safety (8,9).

While international literature has extensively documented SA-related complications (3), studies in Sudan are scarce, particularly in public hospitals outside the capital. Most available data

come from audits or observational reports, offering limited insight into risk factors and clinical outcomes within the local healthcare system (8,9). Moreover, there is a lack of evidence addressing how factors such as urgency of surgery, fluid management, and patient characteristics affect complication rates in such contexts. Therefore, this study aimed to assess the frequency and types of spinal anesthesia-related complications and to identify the associated risk factors among women undergoing cesarean delivery at Dongola Maternity Hospital. The findings may inform improvements in obstetric anesthesia practice and maternal safety in comparable resource-limited settings.

Methods

Study design and setting

This was a descriptive cross-sectional study conducted at Dongola Maternity Hospital (DMH), the central maternity hospital in Northern State, Sudan. The hospital is located in the state capital, Dongola, and provides comprehensive maternity services, including a nursery unit. The institution is staffed by consultants, registrars, and house officers, with anesthesia services primarily delivered by anesthesia technicians (non-physician anesthesia providers). No anesthesiologists or anesthesia specialists were available during the study period. As all spinal anesthesia procedures during the study period were performed exclusively by anesthesia technicians without anesthesiologist supervision, provider cadre was uniform across participants and therefore not included as a confounding variable in the regression analysis.

Study population

The study was conducted over a six-month period. All women who underwent cesarean delivery (elective or emergency) under spinal anesthesia at DMH during this time were eligible for inclusion. Women who underwent cesarean delivery under other forms of anesthesia (e.g., gen-

eral or epidural), or those who declined participation, were excluded.

Sample size calculation and sampling technique

The sample size was calculated using the formula for a known population size, Yamane's formula ($N = 1205$ cesarean deliveries performed under spinal anesthesia during the study period), assuming a 95% confidence level ($Z = 1.96$), 50% expected prevalence ($P = 0.5$), and 5% margin of error ($e = 0.05$). This yielded a minimum required sample of 293 participants. To account for increased variance due to non-probability sampling (convenience sampling), a design effect of 1.2 was applied, resulting in an adjusted sample of 352. Allowing for a 9% non-response rate, the final sample size was further increased to 384 participants were enrolled.

Spinal anesthesia procedures

All spinal anesthesia procedures were performed by anesthesia technicians. The standard protocol included: Injection of 2–3 mL of 0.5% hyperbaric bupivacaine into the subarachnoid space. Use of a Quincke spinal needle, typically 25G. Prophylactic administration of 30 mg diluted ephedrine intravenously post-spinal. Left uterine displacement was performed in the supine position to reduce aortocaval compression.

Data collection and collection

Data were collected using a pre-designed structured questionnaire and review of medical records. Each participant was followed: Intraoperatively by direct observation and symptom inquiry, at discharge (on postoperative day 3), and two weeks postoperatively by follow-up phone call.

Definition of complications

Hypotension was defined as systolic blood pressure ≤ 90 mm Hg or a reduction of at least 20% from baseline.

Post-dural puncture headache (PDPH): Headache within 5 days of SA, worsened by upright posture and relieved by lying down.

Post-spinal meningitis (PSM): Headache, fever, neck stiffness, and/or altered mental status following SA.

Transient neurological symptoms: Self-limited lower back pain radiating to the lower limbs within 24 hours, resolving within 48 hours.

Maternal death: Any maternal mortality directly related to spinal anesthesia complications.

Classification of cesarean urgency

Surgical urgency was classified according to the National Institute of Health and Care Excellence (NICE) guidelines:

1. Category 1: Immediate threat to life of woman or fetus.
2. Category 2: Maternal or fetal compromise not immediately life-threatening.
3. Category 3: No immediate maternal or fetal compromise but early delivery required.
4. Category 4: Elective procedure.

Data analysis

Data were entered and analyzed using SPSS version 24. Descriptive statistics were used to summarize patient characteristics and complication rates. The Chi-square test was used to assess associations between categorical variables. Binary logistic regression was used to identify independent predictors of spinal anesthesia-related complications. Variables entered into the logistic regression model were selected based on clinical relevance and statistical significance in univariate analysis ($p < 0.20$). These included gestational age, urgency category of cesarean delivery, timing of fluid administration, volume of crystalloid infused, and previous history of spinal anesthesia-related complications. Sociodemographic variables (age, parity, education) and comorbidities were evaluated but were not retained in the final model due to lack of association. A p -value < 0.05 was considered statistically significant. All statistical tests were two-tailed.

Ethical consideration

Ethical approval was obtained from the Ministry of Health, Northern State of Sudan – Research Ethics Committee (Ref ID: NSMH/22/A). Written permission was granted by the hospital administration. Informed verbal and written consent were obtained from each participant. Data confidentiality was maintained, and all participants who developed complications were managed according to standard clinical protocols.

Results

A total of 384 women who underwent cesarean delivery under spinal anesthesia were included. The mean age was 28.6 ± 5.9 years (range 15–48). Most participants were housewives (87.2%), had completed primary or secondary education (64.1%), and were multiparous (68%). The majority were at term gestation (93.2%), with singleton pregnancies (95.8%). No statistically

significant associations were found between spinal anesthesia-related complications and age ($p=0.478$), occupation ($p=0.820$), education level ($p=0.776$), or parity ($p=0.635$). However, preterm gestational age (24 to <37 weeks) was significantly associated with complications ($p=0.003$) (Table 1).

Table 1: Sociodemographic and obstetric characteristics of participants and their association with spinal anesthesia-related complications at Dongola Maternity Hospital

Variables	Total	Complications		P-value
	N (%)	Yes n (%)	No n (%)	
Age group				
<25 years	135 (35.2)	16 (4.2)	119 (31)	0.478
25 - 35 years	200 (52.1)	33 (8.6)	167 (51.1)	
>35 years	49 (12.8)	8 (2.1)	41 (10.7)	
Occupation				
Housewife	335 (87.2)	48 (12.5)	287 (74.7)	0.820
Laborer	3 (0.8)	0 (0)	3 (0.8)	
Employed	36 (9.4)	7 (1.8)	29 (7.6)	
Student	6 (1.6)	1 (0.3)	5 (1.3)	
Other	4 (1.0)	1 (0.3)	3 (0.8)	
Education level				
Illiterate	21 (5.5)	2 (0.5)	19 (4.9)	0.776
Primary	126 (32.8)	22 (5.7)	104 (27.1)	
Secondary	120 (31.3)	17 (4.4)	103 (26.8)	
University	114 (29.7)	16 (4.2)	98 (25.5)	
Postgraduate	3 (0.8)	0 (0)	3 (0.8)	
Parity				
Primigravida	91 (23.7)	13 (3.4)	78 (20.3)	0.635
Multipara	261 (68)	37 (9.6)	224 (58.3)	
Grand multipara	29 (7.6)	6 (1.6)	23 (6)	
Great grand multi-para	3 (0.8)	1 (0.3)	2 (0.5)	
Gestational age				
24 - <37 weeks	26 (6.8)	9 (2.3)	17 (4.4)	0.003
37 – 42 weeks	358 (93.2)	48 (12.5)	310 (80.7)	
Number of fetuses				
Single	368 (95.8)	54 (14.1)	314 (81.8)	0.658
Twin	14 (3.6)	3 (0.8)	11 (2.9)	
Triple or more	2 (0.5)	0 (0)	2 (0.5)	

The majority of cesarean deliveries were elective (category 4, 76.3%), with repeated cesarean scar

(67.2%) being the most common indication. Urgency of surgery was significantly associated with complications ($p<0.001$), while CS indication and comorbidities were not ($p=0.808$ and $p=0.470$, respectively). Although elective cesarean deliveries constituted the majority of cases, complications were disproportionately higher among the smaller subgroup of preterm and urgent procedures. A previous history of spinal anesthesia-related complications was significantly associated with current complications ($p=0.035$) (Table 2).

Table 2: Clinical and surgical variables in relation to spinal anesthesia-related complications at Dongola Maternity Hospital

Variables	Total	Complications		P-value
	N (%)	Yes n (%)	No n (%)	
Urgency				
Category 1	11 (2.9)	2 (0.5)	9 (2.8)	0.000
Category 2	34 (8.9)	13 (3.4)	21 (5.5)	
Category 3	46 (12)	10 (2.6)	36 (9.4)	
Category 4	293 (76.3)	32 (8.3)	261 (68)	
Cesarean delivery indications				
Repeated scar	258 (67.2)	40 (10.4)	218 (56.8)	0.808
Failure to progress	8 (2.1)	2 (0.5)	6 (1.6)	
Fetal distress	12 (3.1)	2 (0.5)	10 (2.6)	
Malpresentation	6 (1.6)	1 (0.3)	5 (1.3)	
Preeclampsia and eclampsia	17 (4.4)	3 (0.8)	14 (3.6)	
Antepartum hemorrhage	4 (1)	0 (0)	4 (1.0)	
Failed induction	9 (2.3)	1 (0.3)	8 (2.0)	
Assisted conception	8 (2.1)	0 (0)	8 (2.1)	
Postdatism	5 (1.3)	1 (0.3)	4 (1.0)	
Fetal macrosomia	5 (1.3)	0 (0)	5 (1.3)	
Maternal request	14 (3.6)	0 (0)	14 (3.6)	
Other	38 (9.9)	7 (1.8)	31 (8.1)	
Comorbidity				
None	342 (89.1)	49 (12.8)	293 (76.3)	0.470
Hypertension	14 (3.6)	3 (0.8)	11 (2.9)	
Asthma	4 (1)	2 (1)	2 (1)	
Epilepsy	1 (0.3)	0 (0)	1 (0.3)	
Thyroid disorder	5 (1.3)	1 (0.3)	4 (1)	
Diabetes mellitus	16 (4.2)	2 (0.5)	14 (3.6)	
Other	2 (0.5)	0 (0)	2 (0.5)	
History of SA complications (4.9%)				
Headache	12 (3.1)	4 (1.0)	8 (2.1)	0.362
Hypotension	3 (0.8)	0 (0)	3 (0.8)	
Nausea and vomiting	4 (1)	2 (0.5)	2 (0.5)	

Spinal anesthesia was administered using 25G Quincke needles in most cases (82.6%), with one puncture attempt achieved in 66.4%. Stylet replacement before needle removal was practiced in 74.2%. Regarding fluid administration, 50.3% received crystalloid preload, 40.4% received coload, and 9.4% received both. Most patients (96.6%) received 1–2 liters of fluid, while 3.4% received >2 liters. A significant association was found between complications and timing of fluid administration ($p=0.027$), volume infused ($p=0.015$), and previous SA-related complications ($p=0.035$). Other procedural factors, such as needle size, number of puncture attempts, and stylet replacement, were not statistically significant (Table 3).

Table 3: Procedural and anesthetic factors associated with spinal anesthesia-related complications at Dongola Maternity Hospital

Hospital		Total	Complications		P-value
Variables		N (%)	Yes n (%)	No n (%)	
Timing					
Preload		193 (50.3)	20 (5.2)	173 (45.1)	0.027
Coload		155 (40.4)	32 (8.3)	123 (32)	
Both		36 (9.4)	5 (1.3)	31 (8.1)	
volume					
1-2 L		371 (96.6)	52 (13.5)	319 (83.1)	0.015
>2 L		13 (3.4)	5 (1.3)	8 (2.1)	
Needle size (Quincke)					
24 G		67 (17.4)	14 (3.6)	53 (13.8)	0.125
25 G		317 (82.6)	43 (11.2)	274 (71.4)	
Puncture attempts					
One attempt		255 (66.4)	33 (8.6)	222 (57.8)	0.123
Two attempts		100 (26.0)	21 (5.5)	79 (20.5)	
3 or more attempts		29 (7.6)	3 (0.8)	26 (6.8)	
Stylet replacement					
Done		285 (74.2)	39 (10.2)	246 (64.0)	0.278
Not done		99 (25.8)	18 (4.7)	81 (21.1)	
Previous history of SA complications					
Yes		19 (4.9)	6 (1.5)	13 (3.4)	0.035
No		365 (95.1)	51 (13.3)	314 (81.8)	

Multivariate binary logistic regression analysis was conducted to identify independent predictors of spinal anesthesia-related complications in cesarean deliveries. After adjusting for confounding variables, five factors were found to be significantly associated with higher odds of complications. Preterm gestational age (24–<37 weeks) was significantly associated with increased risk of complications, with an adjusted odds ratio (AOR) of 3.48 (95% CI: 1.42–8.54; $p=0.006$), indicating that preterm parturients were over three times more likely to experience complications compared to those at term (37–42 weeks). Regarding the urgency of cesarean delivery, patients in category 2 (maternal or fetal compromise not immediately life-threatening) had over five-fold increased odds of complications (AOR = 5.59; 95% CI: 2.37–13.20; $p < 0.001$) compared to those undergoing elective procedures (category 4). Similarly, patients in category 3 (no immediate compromise but early delivery needed) had a more than two-fold increased risk (AOR = 2.34; 95% CI: 1.04–5.25; $p=0.038$). The timing of fluid administration was also a significant factor. Women who received crystalloid co-load were more than twice as likely to experience complications compared to those who received preload (AOR = 2.25; 95% CI: 1.20–5.25; $p=0.011$). Additionally, patients who received more than 2 liters of crystalloid had significantly higher odds of complications compared to those who received 1–2 liters (AOR = 3.81; 95% CI: 1.15–12.62; $p=0.028$). A previous history of spinal anesthesia-related complications showed a trend toward increased risk (AOR = 2.51; 95% CI: 0.87–7.32), although this was not statistically significant ($p=0.090$) (Table 4).

Discussion

This study assessed the frequency and risk factors of spinal anesthesia (SA)-related complications among women undergoing cesarean delivery at Dongola Maternity Hospital in Northern Sudan. The findings highlight a complication rate of 14.8%, with the most common adverse events being nausea (8.6%), post-dural puncture headache (PDPH, 6.3%), suspected post-spinal meningitis (PSM, 3.1%), hypotension (1.3%), transient neurological symptoms (0.8%), and maternal death (0.5%). These findings are consistent with international studies (10), though some complications such as PSM and maternal death deserve particular attention in the context of a resource-limited setting.

Table 4: Logistic regression analysis of risk factors associated with spinal anesthesia-related complications at Dongola Maternity Hospital

Variables	Total N (%)	OR (95% CI)	P. value	AOR (95% CI)	P-value
GA					
24 - <37 weeks	26 (6.8)	3.42 (1.44-8.12)	0.005	3.48 (1.42-8.54)	0.006
37 – 42 weeks	358 (93.2)	Reference	Reference	Reference	Reference
Urgency					
Category 1	11 (2.9)	1.81 (0.38-8.76)	0.46	2.09 (0.14- 10.55)	0.372
Category 2	34 (8.9)	5.05 (2.31-11.05)	<0.001	5.59 (2.37-13.20)	<0.001
Category 3	45 (11.7)	2.27 (1.03-4.99)	0.043	2.34 (1.04-5.25)	0.038
Category 4	293 (76.3)	Reference	Reference	Reference	Reference
Timing					
Pre-load	193 (50.3)	Reference	Reference	Reference	Reference
Co-load	155 (40.4)	2.25 (1.23-4.12)	0.009	2.25 (1.20-5.25)	0.011
Both	36 (9.4)	1.40 (0.49-3.99)	0.535	1.44 (0.47-4.41)	0.522
Volume					
1 - 2 litres	371 (96.6)	Reference	Reference	Reference	Reference
>2 litres	13 (3.4)	3.83 (1.21-12.17)	0.023	3.81 (1.15-12.62)	0.028
Previous history of SA complication					
Yes	19 (4.9)	2.84 (1.03- 7.81)	0.043	2.51 (0.87- 7.32)	0.090
No	365 (95.1)	Reference	Reference	Reference	Reference

The incidence of PDPH (6.3%) in this study was lower than that reported in Omdurman Maternity Hospital, Sudan (47.7%) (8), but similar to a Jordanian study (6.3%) (11). Other studies from Ethiopia and Nigeria reported higher PDPH rates ranging from 15.8% to 23.5% (12,13). This variability may be due to differences in needle size, technique, or diagnostic thresholds. In our setting, the use of 25G Quincke needles and routine stylet reinsertion may have contributed, although this study was not designed to evaluate procedural determinants of PDPH. Hypotension, one of the most anticipated complications of SA, was observed in only 1.3% of patients, which is markedly lower than rates reported in both local and international literature (9,15–17). The low incidence may reflect the effectiveness of routine measures practiced at DMH, including crystalloid pre-loading or co-loading, prophylactic ephedrine use, and left uterine displacement. However, studies suggest that while these interventions reduce hypotension, they may not eliminate it entirely (18–23).

Post-spinal meningitis (PSM) was suspected in 3.1% of patients, which is significantly higher

than published estimates ranging from 0% to 0.04% (24). Twelve cases of PSM were reported over a four-week period, with clinical features including headache, fever, neck stiffness, and altered mental status. Although the exact etiology could not be confirmed due to the lack of CSF analysis and culture, the temporal clustering and lack of similar community cases raise suspicion of chemical meningitis, potentially linked to a change in antiseptic agents. The temporal clustering suggested a potential procedural or antiseptic-related factor; however, the absence of microbiologic confirmation precludes definitive conclusion regarding etiology. Following its withdrawal, no further cases were recorded. This outbreak underscores the need for stringent aseptic protocols, proper antiseptic selection, and the presence of infection control committees in all operating theatres, especially where non-physician providers deliver anesthesia. Two maternal deaths (0.5%) occurred due to suspected SA-related complications. This figure, though seemingly small, is unacceptably high when extrapolated to national obstetric mortality rates. These events further warrant further investiga-

tion because causal attribution could be conclusively established.

Regression analysis identified five significant predictors of SA complications: preterm gestational age (<37 weeks), urgency of cesarean (categories 2 and 3), crystalloid co-loading, infusion of >2 liters of fluid, and previous history of SA complications. Preterm parturients were over three times more likely to develop complications (AOR 3.48; $p = 0.006$). This may be attributed to altered CSF dynamics, reduced uterine size, or heightened drug sensitivity (26,27). However, data specific to the preterm population and SA are limited, and further investigation is warranted.

While most cesarean deliveries in this cohort were elective, this reflects the overall service profile of the hospital rather than risk distribution. Preterm gestations and urgent cesarean categories, although less frequent, carried significantly higher odds of spinal anesthesia-related complications. This suggests that risk is concentrated within specific clinical subgroups rather than evenly distributed across procedure types. Furthermore, urgent cesareans (category 2 and 3) were also associated with higher complication rates. This may be due to heightened stress, inadequate preparation time, and more hemodynamically unstable patients. This finding is consistent with clinical logic, although prior studies have not always found significant associations between urgency and SA complications (28).

Regarding fluid management, co-loading and administration of >2 liters of crystalloids were both associated with increased complications. While fluid administration is standard practice to prevent hypotension, excessive volume may paradoxically contribute to morbidity through fluid overload or dilutional effects. Moreover, current evidence favors vasopressors like phenylephrine over large-volume crystalloid administration (21,22). Our findings support revisiting institutional protocols for fluid management during SA. A previous history of SA-related complications showed a trend toward significance ($p = 0.090$), highlighting the importance of preoperative risk assessment and documentation of anesthesia history.

Study strengths and limitations

This study provides one of the first in-depth analyses of SA complications in a Sudanese mater-

nity hospital, offering valuable insights into anesthesia safety in resource-limited settings. However, several limitations must be acknowledged. The absence of anesthesiologists represents a system-level limitation that may influence complication rates; however, because this exposure was constant for all participants, it could not be evaluated analytically as a confounder. Because participants were enrolled through convenience sampling, selection bias cannot be excluded, and associations identified through regression analysis should be interpreted cautiously. The diagnosis of post-spinal meningitis was based solely on clinical criteria because cerebrospinal fluid analysis and microbiological confirmation were unavailable. The absence of anesthesiologist supervision may have affected procedural quality but also reflects the reality in many rural or peripheral centers in Sudan. The single-center design may limit generalizability to other settings. Outcome ascertainment relied partly on patient-reported symptoms during telephone follow-up, introducing potential recall bias.

Conclusion

This study highlights a significant burden of spinal anesthesia-related complications among women undergoing cesarean delivery at Dongola Maternity Hospital, with a complication rate of 14.8% and notable occurrences of post-dural puncture headache, nausea, post-spinal meningitis, and even maternal deaths. Key risk factors include preterm gestational age, increased urgency of surgery, large fluid volumes (>2 liters), co-loading strategies, and a previous history of anesthesia-related complications. These findings underscore the urgent need for enhanced perioperative protocols, better risk stratification, and improved training for non-physician anesthesia providers in resource-limited settings. The unexpectedly high rate of post-spinal meningitis raises serious concerns about infection control practices and highlights the critical role of aseptic technique and proper antiseptic selection. Future research should focus on prospective, multi-center studies to validate these findings and explore tailored interventions aimed at improving safety and outcomes of spinal anesthesia in obstetric care, particularly in low- and middle-income countries.

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Conflicts of interest

The authors have no conflicts of interest to declare.

Author contributions

All authors contributed to the conceptualization and intellectual development of the research. M.S. was responsible for data collection and initial data organization. M.M. and M.M.A. analyzed the data and M.O., M.E., and T.S.M.S. participated in manuscript drafting, critical review, and final editing. All authors read and approved the final version of the manuscript.

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Data availability

All data generated or analyzed during this study are included in this article, and additional details or raw data are available from the corresponding author upon reasonable request.

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