

Efficacy and safety of carbon dioxide versus room-air insufflation in pediatric colonoscopy: a randomized controlled trial

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Background: Adequately powered studies in children are scarce and there are reports on the risk of carbon dioxide (CO₂) retention after colonoscopy.

Purpose: This study investigated the efficacy and safety of CO₂ insufflation in children undergoing colonoscopy.

Methods: This prospective randomized clinical trial was conducted at a tertiary care hospital between March 2023 and July 2024. We recruited 200 consecutive children (age, 5–18 years; n=100 in each arm) who underwent colonoscopy under conscious sedation. Patients were randomized to receive CO₂ or room air using a random number table. The primary outcome measure was postprocedural pain assessed by using a visual analogue scale (VAS). Secondary outcome measures included time to reach the cecum, total procedure duration, abdominal distension, and end-tidal (ET) CO₂ level. Complications were recorded.

Results: Pain scores at 2 and 4 hours postprocedure were significantly lower in the CO₂ versus room-air group (1.12 vs. 1.66, $P=0.001$ at 2 hours and 0.37 vs. 0.61, $P=0.002$ at 4 hours). The time to reach the cecum was significantly higher in the CO₂ group (39.6 vs. 26.6 min, $P=0.01$). A greater proportion of children in the room-air group (29% vs. 19%, $P=0.04$) reported significant pain (VAS score, ≥ 3). The subgroup analysis revealed a significantly longer time to reach the cecum and total procedure duration in the CO₂ group among first-year trainees. ET-CO₂ levels were significantly higher in the CO₂ group (36 [interquartile range, 35–37] mmHg vs. 34 [interquartile range, 32–35] mmHg, $P=0.001$), but none developed any signs of CO₂ retention. No significant intergroup differences were noted in abdominal girth, bloating sensation, analgesic requirements, or procedure-related complications.

Conclusions: CO₂ insufflation is safer and makes the procedure less painful but slower than room-air insufflation, especially in first-year trainees, without an increased risk of retention.

Key words: Pediatric colonoscopy, Carbon dioxide, Air insufflation, Abdominal pain

Key message

CO₂ insufflation has been used instead of air insufflation to reduce postprocedure pain and discomfort in adults; however, adequately powered studies in children are scarce. This randomized controlled trial of 200 children showed that CO₂ insufflation reduces postprocedure pain and discomfort during pediatric colonoscopy with no signs of CO₂ retention. CO₂ insufflation is safe and causes less pain in children.

Introduction

Adequate distension and visualization of gastrointestinal lumen is essential during colonoscopy.¹⁾ Traditionally room-air has been used for insufflation during all endoscopic procedures. Carbon dioxide (CO₂) insufflation during colonoscopy has been studied since 1950's in adults.²⁾ The initial purpose of CO₂ use was to reduce the explosive potential with room-air use during electrocauterization for polypectomy. Subsequent studies showed that CO₂ causes less postprocedural abdominal pain, decreased time taken to reach cecum and cecal intubation rate³⁾ and increased patient satisfaction.⁴⁾ Beneficial effect of CO₂ has been attributed to its rapid diffusion across intestine which is 160 times more rapid than nitrogen (78% of room-air) and 13 times more rapid than oxygen (21% of room-air) resulting in reduced bowel distension following the procedure.⁵⁾ Concerns regarding the safety of using CO₂ were raised but despite elevations reported in end-tidal carbon dioxide (ET-CO₂) levels, no significant adverse respiratory compromise has been reported so far.⁶⁾ Numerous studies have shown

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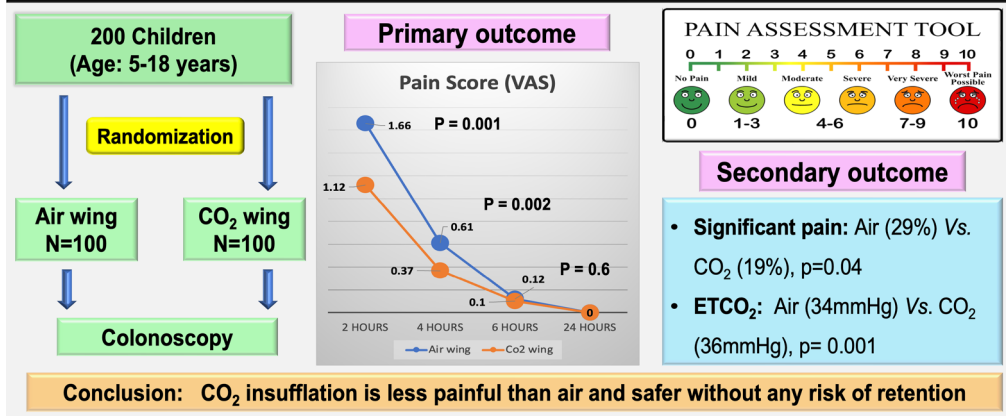
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Graphical abstract. VAS, visual analogue scale; ET, end-tidal.

the safety and efficacy of CO₂ insufflation as compared to room-air insufflation in adults during colonoscopy.^{7,8)} A few published reports in children compared CO₂ and room-air insufflation during colonoscopy, however, all are underpowered. The aim of our study was to find out whether CO₂ insufflation is safe and reduces the postprocedural pain and discomfort when compared with room-air insufflation in children undergoing colonoscopy.

Methods

The study was a prospective randomized controlled clinical trial. Children of age 6 years to 18 years who underwent colonoscopy in the department of Pediatric Gastroenterology at Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, India between March 2023 and July 2024 were recruited. Children with neurological abnormalities and unable to complete visual analogue scale (VAS), chronic lung diseases, previous colectomy, prior participation in the study were excluded from the study. Written informed consent was obtained from either parents before participation in the study. The study was approved by the Institutional ethical committee and the study was registered with the Clinical Trial Registry of India (CTRI/2023/03/050641).

1. Endoscopic procedure/randomization/blinding

All patients underwent full bowel preparation with Poly Ethylene Glycol electrolyte solution 3350 powder (PEGLEC, Tablets India Ltd., India) as per standard protocol at our institution. Stratified block randomization was done using computer generated random number table. The study subjects were blinded to the insufflation gas used. The colonoscopies were performed by pediatric gastroentero-

logy consultants or pediatric gastroenterology trainees from our institute who were categorized as first year, second year and third-year trainees for the purpose of subgroup analysis. Colonoscopies were performed by using Olympus Video System, Olympus Exera-III PCF-Q180AL. For CO₂ insufflation, the Olympus UCR CO₂ Regulation insufflator unit was used. Room-air insufflation was performed using an ordinary air inlet system.

2. Sedation and monitoring

Procedural sedation in all children was administered by combination of injection midazolam and ketamine. ET-CO₂ was measured by capnograph (Nellcor OxiMax N-85, Covidian Corp., Israel) throughout the procedure and was monitored by a dedicated nursing staff. The baseline levels of ET-CO₂ before sedation and the peak level of ET-CO₂ during the procedure were recorded.

3. Patient assessment

Demographic parameters such as age, sex, body mass index, and history of prior colonoscopy, physician performing the procedure, indication for colonoscopy were recorded in a proforma. Details of the colonoscopic examination including time to reach the cecum, total duration of the procedure, quality of bowel preparation as per modified Aronchick scale,⁹⁾ and any additional procedures such as biopsies or polypectomies performed were also recorded.

The patient's abdominal pain was assessed using a 10-point VAS, ranging from 'no pain' indicated by 0 points to 'worst pain ever' indicated by 10 points. Children were asked to score their level of pain at the following intervals: before colonoscopy, 2, 4, 6, and 24 hours after the procedure. Significant pain was defined as level 3 or higher. Need of additional rescue pain medications after the procedure

and postprocedure complications, if any, were recorded. All patients had undergone abdominal examination before the discharge and was given standard instructions regarding diet, activity, medication, and follow-up schedule and contact information at the time of discharge from the hospital. The pain scores before discharge were acquired directly from the children at the given time points, and pain scores at 24 hours after the procedure were acquired over the telephone. Abdominal girth was measured before the procedure and immediately after the colonoscopy was completed. Measurements were made with a measuring tape at the level of the umbilicus.

4. Statistical analysis

Statistical analysis was performed by using IBM SPSS Statistics ver. 25.0 (IBM Co., USA). Normality testing was done using the Kolmogorov-Smirnov test. Data were expressed as median (interquartile range [IQR]) for skewed variables and mean standard deviation for normally distributed variables. Mann-Whitney tests or *t* tests for continuous variables and chi-square tests or Fisher exact tests for categorical variables were used to compare between both intervention groups. Univariate analysis was performed using chi-square test and odds ratio (OR), 95% confidence interval (CI) was calculated. Multivariable logistic

regression model was used for the primary outcome (postprocedure pain). Covariates used for the models were age, gender, time to reach the cecum as a binary predictor with threshold of 30 minutes and duration of procedure as a binary predictor with threshold of 45 minutes, and consultant versus trainees, procedure versus no procedures. *P* value<0.05 was considered statistically significant.

Results

A total 200 children were randomly assigned to insufflation of either room-air or CO₂ during colonoscopy (100 children in each arm). Study design (CONSORT [Consolidated Standards of Reporting Trials] flow chart) is shown in Fig. 1. Patient's demographic data are shown in Table 1. The patient population consisted of 126 boys (62.4%) and 74 girls (36.6%), with a median (IQR) age of 12 (9–16) years. The most common indications for colonoscopy were; surveillance for inflammatory bowel disease. No significant differences were observed between the 2 groups with respect to baseline characteristics. Highlights of the results are shown in graphical abstract.

1. Primary outcome

The primary outcome of this study was to compare post procedural pain using VAS (Table 2). Median (IQR) abdominal pain scores 2 and 4 hours after the procedure were significantly lower in the CO₂ group as compared with the room-air group (CO₂: 1.12 [1–2] vs. room-air: 1.66 [1–2], *P*=0.001 at 2 hours and (CO₂: 0.37 [0–1] vs. room air: 0.61 [0–1], *P*=0.002 at 4h respectively]. Pain score at 6 hours after

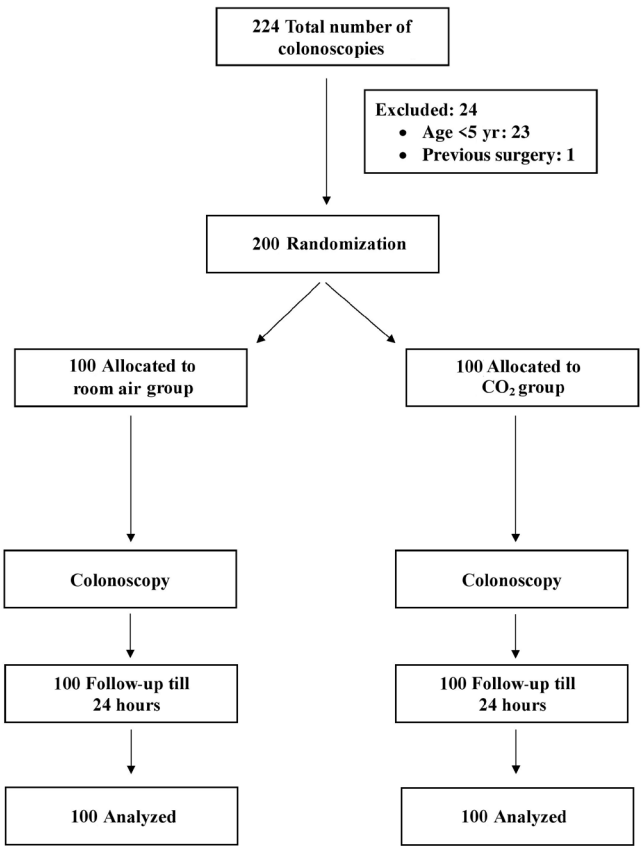


Fig. 1. Study design: CONSORT (Consolidated Standards of Reporting Trials) flow chart.

Table 1. Baseline characteristics of children undergoing colonoscopy in room-air versus CO₂ insufflation groups

Characteristic	Air (n=100)	CO ₂ (n=100)	<i>P</i> value
Age (yr)	12.3±4.06	11.9±3.93	0.526
Sex, male:female	29:21	31:19	0.442
Colonoscopist			0.760
1st year trainee	23 (23)	21 (21)	
2nd year trainee	34 (34)	37 (37)	
3rd year trainee	15 (15)	18 (18)	
Consultant	28 (28)	24 (24)	
Bowel preparation			1.00
Good	98 (98)	98 (98)	
Inadequate	2 (2)	2 (2)	
Procedures			0.584
Biopsies	64 (64)	68 (68)	
Polypectomy	23 (23)	19 (19)	
None	13 (13)	13 (13)	
Indication			0.78
Functional	19 (19)	17 (17)	
Nonfunctional	81 (81)	83 (83)	

Values are presented as mean±standard deviation or number (%).

the procedure was not significant different between the 2 groups (0.1 [0–0.25] vs. 0.12 [0–0.25], $P=0.6$) and none had pain at 24 hours after the procedure. We also found that significant pain (VAS ≥ 3) is more with room-air group (29%) as compared with CO₂ group (19%) ($P=0.04$). Multivariate logistic regression analyses (Table 3) found that abdominal pain was significantly lower in patients after CO₂ versus room-air insufflation (OR, 3.302; 95% CI, 1.075–10.146; $P=0.037$). No significance in relation to pain were observed with male versus female (OR, 1.041; 95% CI, 0.363–2.986; $P=0.941$), time to reach the cecum over 30 minutes (OR, 2.912; 95% CI, 0.971–8.737; $P=0.056$), duration of the procedure over 45 minutes (OR, 3.593; 95% CI, 0.893–14.462; $P=0.072$), consultant vs. trainee (OR, 0.417; 95% CI, 0.089–1.961; $P=0.268$) and additional procedure vs. no additional procedure (OR, 1.097; 95% CI, 0.221–5.439; $P=0.910$).

Table 2. Primary and secondary outcome variables among children undergoing colonoscopy using room-air versus CO₂ insufflation

Parameter	Room-air (n=100)	CO ₂ (n=100)	P value
Pain score (VAS)			
2 Hours	1.66 (1–2)	1.12 (1–2)	0.001
4 Hours	0.61 (0–1)	0.37 (0–1)	0.002
6 Hours	0.12 (0–0.25)	0.1 (0–0.25)	0.60
24 Hours	0 (0–0)	0 (0–0)	-
Significant pain (VAS ≥ 3)	29 (29)	19 (19)	0.04
No pain (VAS 0)	24 (24)	28 (28)	0.081
Time to reach cecum (min)	26.6 (20–35)	39.6 (35–45)	0.01
Total duration of procedure (min)	47.7 (40–55)	51.2 (40–55)	0.21
ET-CO ₂ (mmHg)	34 (32–35)	36 (35–37)	0.001
Abdominal girth increased from baseline (cm)	3.8 (2–4.5)	3.4 (2.5–4)	0.678
Bloating sensation	12 (12)	9 (9)	0.494
Postprocedure events	1 (1)	1 (1)	1.00
Analgesic requirement			
Midazolam (mg/kg)	0.27 (0.2–0.36)	0.25 (0.19–0.32)	0.232
Ketamine (mg/kg)	2.4 (1.7–3.1)	2.5 (1.7–3.2)	0.66

Values are presented as median (interquartile range) or number (%).

VAS, visual analogue scale; ET, end-tidal.

VAS scores ranged from 0 (no pain) to 10 (worst pain ever).

Boldface indicates a statistically significant difference with $P<0.05$.

2. Secondary outcomes

Median time to reach the cecum was significantly higher in CO₂ group as compared to room-air group (CO₂: 39.6 [IQR, 35–45] minutes vs. room-air: 26.6 [IQR: 20–35] minutes, $P=0.01$). No difference in duration of the procedure was observed (CO₂: 51.2 [IQR: 35–45] minutes vs. room air: 47.7 [IQR: 40–45] minutes, $P=0.21$). No significant increase in abdominal girth from baseline between both groups (room air: 3.8 [IQR: 2–4.5] cm vs. CO₂: 3.4 [IQR: 2.5–4] cm, $P=0.678$). Need for rescue pain medication following the procedure was there in 3 children (3%) in room-air group as compared to 2 children (2%) in CO₂ group ($P=0.66$). Bloating sensation was reported by 12 children (12%) in room-air group as compared to 9 children (9%) in CO₂ group ($P=0.494$). Iatrogenic colonoscopic perforation occurred in 1 each in both groups which were managed conservatively. Maximum ET-CO₂ values measured during the procedure were higher in the CO₂ group as compared with the room-air group (CO₂: 36 [IQR, 35–37] mmHg vs. room air: 34 [IQR, 32–35] mmHg, $P=0.001$). No clinical signs of other adverse events or impaired ventilation was, however, observed during the procedure or postprocedure during the observation period.

3. Subgroup analysis

We obtained information about the colonoscopist to make sure that there were no advantages for one group

Table 4. Subgroup analysis of colonoscopist training level with respect to time to reach the cecum and procedure duration

Parameter	Air	CO ₂	P value
Time to reach cecum (min)			
1st year trainee	29.8 (20–35)	37.8 (35–45)	0.04
2nd year trainee	29 (20–35)	28 (25–35)	0.671
3rd year trainee	23.1 (16–27)	27.92 (20–35)	0.117
Consultant	24.2 (20–35)	26.6 (20–35)	0.394
Duration of procedure (min)			
1st year trainee	51.8 (43–57)	57.8 (55–62)	0.03
2nd year trainee	48.4 (44–55)	50.1 (40–57)	0.394
3rd year trainee	45.2 (40–56)	49 (40–55)	0.310
Consultant	43.5 (40–50)	49.6 (42–55)	0.083

Values are presented as median (interquartile range).

Table 3. Multivariate model of primary outcome postprocedure pain after CO₂ versus room-air insufflation in pediatric colonoscopy

Parameter	Univariate analysis			Multivariate analysis		
	OR	95% CI	P value	OR	95% CI	P value
Air vs. CO ₂	0.386	0.131–1.140	0.04	3.302	1.075–10.146	0.037
Male vs. female	0.825	0.300–2.200	0.709	1.041	0.363–2.986	0.941
Time to reach cecum, >30 min vs. ≤ 30 min	0.607	0.221–1.665	0.328	2.912	0.971–8.737	0.056
Total duration of procedure, >45 min vs. ≤ 45 min	0.418	0.116–1.510	0.172	3.593	0.893–14.462	0.072
Trainee vs. consultant	2.820	0.600–12.700	0.162	0.417	0.089–1.961	0.268
Additional procedure vs. no procedure	1.025	0.219–4.700	0.975	1.097	0.221–5.439	0.910

OR, odds ratio; CI, confidence interval.

Boldface indicates a statistically significant difference with $P<0.05$.

over the other (Table 4). There was no difference in allocation of colonoscopy with respect to year of training or consultants in room-air or CO₂ groups. First year trainees performed 44 colonoscopies (23 room-air, 21 CO₂), second year trainees performed 71 colonoscopies (34 room-air, 37 CO₂), and third-year trainees performed 33 colonoscopies (15 room-air, 18 CO₂) and consultants performed 52 colonoscopies (28 room-air, 24 CO₂) ($P=0.760$). The median time to reach the cecum was higher in CO₂ group when performed by first year trainees (CO₂: 37.8 [IQR, 35-45] minutes vs. room air: 29.8 [IQR, 20-35] minutes, $P=0.04$). No difference in time to reach the cecum was observed between room-air and CO₂ group when performed by second year or third-year trainees or consultants. Similarly, the median total duration of the procedure was higher in CO₂ group when performed by first year trainees (CO₂: 57.8 [IQR, 55-62] minutes vs. room air: 51.8 [IQR, 43-57] minutes, $P=0.03$). No difference in the duration of procedure was observed between room-air and CO₂ group when performed by second year or third-year trainees or consultants.

Discussion

This prospective, randomized, single-blind study in children undergoing colonoscopy with conscious sedation showed statistically significant change between postprocedure pain in children insufflated with CO₂ versus room-air. On multivariate analysis, we found reduced rate of postprocedural pain with CO₂ insufflation. To our knowledge, this is the first pediatric study to show a significant relationship with increased time to reach the cecum with CO₂ as compared to room-air. Subsequently, we also did subgroup analysis to find the duration of the procedure which revealed significantly longer time to reach the cecum and total duration of the procedure with CO₂ insufflation when done by first year trainees as compared to more competent endoscopists. The possible explanation for the same could be because of rapid diffusion of CO₂ across the intestinal wall as compared to room-air causing early collapse and reduced visualization of the lumen. Various studies have reported the advantages of CO₂ use in colonoscopy in reducing the postprocedure pain but none had reported increased duration of the procedure with CO₂ insufflation during colonoscopy. Our study had demonstrated significant increase in duration of procedure with CO₂ especially in beginners' hands. These findings may need to be considered especially in training institutes during initial colonoscopy training.

Previously, Bretthauer et al.,⁴ in a study of 230 adult patients reported that the use of CO₂ in patients who

underwent flexible sigmoidoscopy was associated with decreased post procedural pain up to 6 hours after examination. In another study of 103 patients reported by the same group, CO₂ insufflation was associated with decreased postprocedure pain compared with room-air at 1, 3, and 6 hours after colonoscopy.⁶ A meta-analysis performed on 21 randomized control trials comprising 3,607 adult patients concluded that CO₂ insufflation during colonoscopy in adults decreases postoperative pain over room-air insufflation.⁷ In those studies, insufflation with CO₂ did not prolong the procedure or lengthen the time to reach the cecum and proved to be safe in all patients. In another study of 35 adult patients by Saito et al.¹⁰ reported reduced patient pain postprocedure with CO₂ insufflation in potentially difficult cases when performed by less experienced colonoscopist. Other studies in adults have also demonstrated the significant differences in postprocedural pain between room-air and CO₂.¹¹⁻²¹

Very few studies have investigated the effects of CO₂ insufflation in children. Homan et al.²² in a study of 76 children, reported a significantly higher proportion of children were pain free after colonoscopy in the CO₂ group compared with the room-air group. In our study, we found that significant pain (VAS $\geq$ 3) was more with room-air group as compared to CO₂ group. Thornhill et al.²³ in a study of 40 children reported no significant increase in ET-CO₂ between groups in the pediatric population and significantly high pain scores following room-air compared with those receiving CO₂ insufflation. Dike et al.²⁴ in a study of 178 children who underwent esophago gastro duodenoscopy [EGD] (n=88) and colonoscopy with or without EGD, reported sustained elevation in ET-CO₂ (>50 mmHg elevation for >5 minutes) in 2 of the children who underwent colonoscopy with CO₂ insufflation but no significant respiratory events occurred. Our findings revealed significantly high ET-CO₂ levels in CO₂ group as compared to room-air group but no clinical signs of other adverse events or impaired ventilation was observed during the procedure or postprocedure and CO₂ insufflation was well tolerated in all patients in our study. In addition, various studies reported the benefits of permissive or therapeutic hypercapnia in increasing tissue perfusion, reduce barotrauma, infection risk even in preterm babies.²⁵⁻²⁸ Dharmaraj et al.²⁹ in a study of 100 children reported significant pain when duration of the procedure extend beyond 30 minutes in multivariate analysis. But our observation revealed no significant difference in pain with relation to the duration of the procedure.

Our study highlights the advantage of using CO₂ insufflation in reducing postprocedure pain and discomfort in children undergoing colonoscopy. Regarding the disadvantage of CO₂ insufflation, beginners might have technical

difficulties in negotiation of the scope through the flexures, possibly related to the rapid diffusion of CO₂ across the intestinal wall causing luminal collapse. However, we observed that this difficulty has been seen only in the early learning phase. Additionally, the availability of CO₂ source is a matter of concern. Additional randomized controlled trials with CO₂ insufflation in children for procedures like upper gastrointestinal endoscopy, endoscopic retrograde cholangio pancreatography is a potential area of research.

The present study has some limitations. Firstly, we did not measure the volume of gas used for insufflation during colonoscopy. Another limitation was that level of CO₂ was not measured by performing arterial blood gases; however, this does not seem to be appropriate, given that the children would have to undergo multiple arterial punctures during and after the procedure. We could not do double blinding due to logistic reason (CO₂ cylinder and connections are easily visible to endoscopist).

In conclusions, the use of CO₂ insufflation during colonoscopy makes the procedure less painful. CO₂ insufflation was well tolerated by all study participants. Use of CO₂ also makes the procedure longer especially during the initial learning phase which might be considered during the colonoscopy training.

Footnotes

Conflicts of interest: No potential conflict of interest relevant to this article was reported.

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Author contribution: Conceptualization: AA, UP, AS, MSS; Data curation: AA, UP, AS, MSS; Formal analysis: AA, UP; Funding acquisition: Not applicable; Methodology: AA,

UP, AS, MSS; Project administration: AA, UP, AS, MSS; Visualization: AA, UP; Writing-original draft: AA; Writing-review & editing: AA, UP, AS, MSS

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