The Turkish Journal of Pediatrics 2024; 66: 556-566
https://doi.org/10.24953/turkjpediatr.2024.4830

Original Article

Sedation - analgesia - muscle relaxant - withdrawal and delirium practices in pediatric intensive care units in Türkiye

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ABSTRACT

Background. Pain and sedation management is an integral part of pediatric intensive care practice. Sedoanalgesia management must be balanced in order to optimize comfort and avoid complications. In order to achieve this balance, sedoanalgesia management needs to be clarified in pediatric intensive care units (PICU). With this study, we aimed to investigate sedation, analgesia, withdrawal and delirium practices, pharmacologic agent preferences, and current experiences and practices in scoring systems in PICUs in Türkiye.

Method. A questionnaire consisting of 57 questions was sent via e-mail to the 'Pediatric Intensive Care and Emergency' group, which includes all intensive care specialists, subspecialty students and lecturers in Türkiye.

Results. Our study involved 36 pediatric intensive care physicians working in PICUs in Türkiye. Among the PICU specialists who participated in the study, 83.3% stated that they performed routine assessments of sedation efficacy. While dexmedetomidine was the most commonly used sedative agent in patients undergoing noninvasive mechanical ventilation, benzodiazepines were the most preferred pharmacologic agent for sedation during mechanical ventilation. Of the pediatric intensivists who participated in the study, 94.4% stated that they performed routine pain assessments in their units. Of the PICU specialists who participated in the study, 69.4% stated that muscle relaxants were most commonly used to prevent patient-ventilator incompatibility during mechanical ventilation. Of the participants, 88.8% made withdrawal assessments when discontinuing sedo-analgesic agents. Delirium assessment was routinely performed by 58.3% of the participants.

Conclusions. This study showed that the practices in sedoanalgesia management in PICUs in Türkiye are in parallel with recommendations of the sedation guideline. Despite the increased sensitivity in sedoanalgesia management, awareness in the management of delirium and withdrawal syndrome is not at the desired level. Therefore, there is a need to develop guidelines, raise awareness and increase training on these issues in our Türkiye.

Key words: pediatric intensive care, sedation, analgesia.

Optimal sedation-analgesia management is one of the most important issues in pediatric intensive care units (PICU). Underlying disease, unfamiliar environments, noise and crowd, disruption of the day-night cycle, separation from parents, mechanical ventilation (MV), repetitive invasive interventions are factors that cause fear, stress, anxiety and pain in children who are being monitored in the PICU.[1] Pain and sedation management is an integral part

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Received 10th Jun 2024, revised 26th Aug 2024, accepted 12th Sep 2024.

of PICU practice. Sedoanalgesia management must be performed with a balance, to ensure optimal comfort and avoid complications. While inadequate sedation may cause unnecessary psychological and physical stress as well as accidental extubation, excessive sedation may lead to prolonged MV, prolonged stay in the PICU, iatrogenic withdrawal syndrome and delirium.[2,3] To date, only a few international and national clinical practice guidelines for the management of pain and sedation in children have been published.[4,5] Therefore, the need for studies on sedoanalgesia management in PICUs still remains.

With this study, we aimed to investigate sedation, analgesia, withdrawal and delirium practices, pharmacologic agent preferences, and current experiences and practices in scoring systems in PICUs in Türkiye.

Materials and Methods

Our study was announced by sending e-mails to the 'Pediatric Intensive Care and Emergency' group, which includes all intensive care specialists, subspecialty students and lecturers in Türkiye. The e-mail included a link to the survey titled "Approaches to Sedation-Analgesia-Muscle Relaxant-Withdrawal and Delirium Practices in the PICU" consisting of 57 questions. Pediatric intensive care specialists, subspecialty students receiving training in this field and faculty members providing education were invited to the study. After the announcement of the study, four weeks were given to participate in the survey. At the end of the period, the responses received were saved in a Microsoft Excel 2018 file. The study was approved by Çukurova University Faculty of Medicine Ethics Committee (13-10-2023).

Survey content

The survey consisted of 57 questions about general information, sedation, analgesia, muscle relaxants, withdrawal syndrome and delirium, environmental arrangements and early mobilization. In the first part of the survey, there were descriptive questions including age, title, affiliation, and years of service. In the second part, there were common questions such as whether assessment scales related to sedation, analgesia, withdrawal and delirium were used, who performed the assessment, how often it was performed, and what was the most commonly used scale (with the statement that more than one option can be chosen). In addition, there were questions about the most common and primary sedative agent used in patients receiving high-flow nasal oxygen, patients undergoing noninvasive MV, intubated patients, and the most common and primary analgesic agent used in short-term medical interventions, trauma patients, postoperative surgical patients and postoperative cardiac surgery patients. There were questions about whether muscle relaxants were used, usage indications, whether brain activity measures electroencephalography (EEG), bispectral index (BIS) are used to assess patient wakefulness in units administering muscle relaxants, application methods related to early mobilization, participation of parents in treatment in the PICU, and the clinical approach to patients who develop delirium and withdrawal (with the statement that more than one option can be chosen).

Statistical analysis

Only descriptive statistics were analyzed. Categorical variables were expressed as percentages (%) and continuous variables were calculated as the mean and standard deviation. Microsoft Excel 2018 was used to analyze the data.

Results

General characteristics

Thirty-six pediatric intensive care physicians working in PICUs in Türkiye participated in our study. Of the physicians who completed the questionnaire, 28 (77.7%) were 40 years of age or older. Seventeen (47.2%) physicians had been working in intensive care for 10 years

or more. Of the physicians who participated in the study, 11 (30.6%) were professors, 11 (30.6%) were subspecialists, six (16.7%) were assistant professors, five (13.9%) were associate professors, and three (8.3%) were subspecialty students.

Sedation practices in PICU

Thirteen (36.1%) of the PICU specialists who participated in the study stated that they used a written sedation protocol for patients on MV. While dexmedetomidine was the most commonly used sedative agent in patients undergoing noninvasive MV, benzodiazepines were the most preferred pharmacologic agents for sedation during MV. In case of inadequate sedation, 29 (80.6%) participants preferred ketamine, 24 (66.7%) dexmedetomidine, 12 (33.3%) chloralhydrate, 4 (11.1%) propofol, and 1 (2.8%) thiopental. Daily waking up in sedated patients was reported to be done by 14 (38.9%) of the participants, while 15 (41%) of the participants reported that it was done according to the clinical condition of the patient. Routine assessment of sedation efficacy during MV follow-up was performed by 30 (83.3%) of the participants. The characteristics of the assessment of sedation efficacy (the frequency, the scales used, and who performed the assessment) are given in Table I.

Analgesic agent applications in PICU

Thirty-four (94.4%) of the pediatric intensivists who participated in the study stated that they performed routine pain assessments in their units. For pain assessment, 27 (75%) of the participants did not use a written protocol. Table II presents the characteristics of the pain assessment, including the scales used, the person conducting the assessment, and the frequency of the assessment. While fentanyl was the most frequently preferred opiate as analgesic, ketamine was the most commonly used agent in short-term interventions (catheter insertion, performing biopsy, lumbar puncture, thoracic tube insertion, etc.) in extubated patients. The most preferred analgesic agents in various clinical situations (in patients with high-flow nasal cannula due to respiratory failure, in post-operative pediatric surgery patients, in trauma patients, in patients who underwent postoperative cardiac surgery) are listed in Table III.

Muscle relaxant applications in PICU

It was reported that the PICU specialists who participated in the study most frequently used muscle relaxants during MV to prevent patient-mechanical ventilation asyncrony (69.4%). While 34 (94.4%) of PICU specialists frequently

Table I. Practices related to the assessment of sedation efficacy in pediatric intensive care units.

		N	%
Practitioner performing sedation assessment	Nurse	27	74.3
	Doctor	9	25.7
Frequency of sedation efficacy assessment	Once in every 2 hours	6	17.1
	Once in every 4 hours	11	31.4
	Once in every 6 hours	4	11.4
	Once in every 8 hours	5	14.3
	Once in every 12 hours	6	17.1
	Once in every 24 hours	3	8.6
Scales used in the assessment of sedation efficacy	COMFORT	13	39.4
	COMFORT Behavior (COMFORT-B)	13	39.4
	Ramsey Sedation Scale (RAS)	11	33.3
	State Behavioral Scale (SBS)	6	18.2
	The Brussels Sedation Assessment Scale	4	12.1
	Richmond Agitation and Sedation Scale (RASS)	3	9.1

Table II. Practices related to pain assessment in pediatric intensive care units.

		N (35)	%
Practitioner performing the pain assessment	Nurse	26	77.1
	Doctor	9	29.9
Frequency of pain efficacy assessment	Once in every 2 hours	4	11.8
	Once in every 4 hours	11	32.4
	Once in every 6 hours	9	26.5
	Once in every 8 hours	3	8.8
	Once in every 12 hours	4	11.8
	Once in every 24 hours	3	8.8
Scales used in the assessment of pain efficacy in patients aged 6 years and older	Wong-Baker Faces Scale	13	41.9
	Visual Analog Scale (VAS)	12	38.7
	FLACC (Face, Legs, Activity, Cry, Consolability)	11	35.5
	COMFORT-B	10	32.3
	Numerical Rating Scales	2	6.5
	Multidimensional Assessment Pain Scale (MAPS)	1	3.2
Scales used in the assessment of pain efficacy in patients aged 6 years and younger	Wong-Baker Faces Scale	17	50
	FLACC (Face, Legs, Activity, Cry, Consolability)	13	38.2
	Visual Analog Scale (VAS)	10	29.4
	COMFORT-B	10	29.4
	Numerical rating scales	1	2.9

Table III. The most commonly preferred analgesic agents in various clinical situations.

		n	%
Post-operative pediatric surgery patients	Acetaminophen	29	80.6
	Opiate	26	72.2
	Dexmedetomidine	10	27.8
	Ibuprofen	4	11.1
	Ketamine	1	2.8
	Other non-steroidal anti-inflammatory agents	1	2.8
In trauma patients	Opiate	31	86.1
	Acetaminophen	26	72.2
	Dexmedetomidine	7	19.4
	Ketamine	4	11.1
	Ibuprofen	2	5.6
	Other non-steroidal anti-inflammatory agents	1	2.8
In post-operative cardiac surgery patients	Opiate	27	75
	Dexmedetomidine	23	63.9
	Acetaminophen	20	55.6
	Ketamine	6	16.7
	Ibuprofen	1	2.8
	Other non-steroidal anti-inflammatory agents	1	2.8
High-flow nasal cannula in the PICU due to respiratory failure.	Dexmedetomidine	21	58.3
	Ketamine	12	33.3
	Midazolam	2	5.6
	No agent	1	2.8

preferred rocuronium as muscle relaxant, 13 (36.1%) stated that they preferred vecuronium. Two (5.6%) of the participants used muscle relaxants as intermittent infusion, 8 (22.2%) as continuous infusion, and 26 (72.2%) as intermittent or continuous infusion depending on the situation. All participants applied eye closure and lubricant to prevent corneal abrasions in patients to whom they applied muscle relaxants. To assess the depth of sedation in patients receiving muscle relaxants, 17 (47.2%) of the participants used BIS monitoring instead of approved clinical scoring tools.

Withdrawal and delirium practices in PICU

Thirty-two (88.8%) of the participants were making withdrawal assessments when discontinuing sedo-analgesic agents. Table IV presents practices related to withdrawal assessment, including who performs the assessment, the scales used, and the frequency of assessment. The PICU specialists who participated in the study stated that they applied the following strategies to patients with withdrawal symptoms: 23 (63.9%) increasing the dose of benzodiazepines and opiates, 8 (22.2%) ensuring frequent oral feeding, 22 (61.1%) bringing the family with the patient, 8 (22.2%) making the patient listen to music, 11 (30.6%) allowing the appropriate age group to use a television, tablet, telephone, 23 (63.9%) changing medication or adding new medication. Sixteen of the participants (16.7%) used phenobarbital, 29 (80.6%) dexmedetomidine, and thirteen (36.1%) chloralhydrate as drugs to help them with withdrawal.

Delirium assessment was being routinely performed by 21 (58.3%) of the participants. Practices regarding the assessment of delirium (who performed the assessment, the scales used, the frequency of assessment) are presented in Table V. Thirty (83.3%) of the participants were practicing environmental optimization to prevent the development of delirium. While haloperidol among the pharmacologic agents administered in patients with delirium was preferred by 30 (83.3%) participants, melatonin was preferred by 7 (19.4%), risperidone by 9 (25%), olanzapine by 4 (11.1%), quetiapine by 4 (11.1%), benzodiazepine by 1 (2.8%) participant. Thirty (83.3%) of the participants practiced early mobilization to prevent the development of delirium.

Methods applied for environment optimization in PICU

The following were the practices performed by PICU specialists to provide patients with a day-night cycle and improve patients' sleep quality: 32 (88.9%) participants reduced lights at night, 10 (27.8%) participants used eye patches and 3 (8.3%) participants used earplugs in appropriate patients during sleep, 29 (80.6%) participants reduced invasive procedures in the evening and at night. All of the study participants stated that they did not allow parents to be present during invasive procedures such as central

Table IV. Practices related to withdrawal assessment in pediatric intensive care units.

		n	%
Practitioner conducting the withdrawal assessment	Doctor	29	90.6
	Nurse	3	9.4
Frequency of withdrawal assessment	Once in every 4 hours	12	37.5
	Once in every 6 hours	7	21.9
	Once in every 8 hours	4	12.5
	Once in every 12 hours	9	28.1
Scales used in the assessment of withdrawal	Withdrawal Assessment Tool version-1 (WAT-1)	19	65.5
	Sedation Withdrawal Score (SWS)	5	17.2
	Opioid and Benzodiazepine Withdrawal Score (OBWS)	3	10.3
	Sophia Observation withdrawal Symptoms Scale (SOS)	1	3.4

Table V. Practices related to delirium assessment in pediatric intensive care units.

		N (35)	%
Practitioner performing the delirium assessment	Doctor	15	71.4
	Nurse	6	28.6
Frequency of delirium assessment	Once in every 8 hours	8	38
	Once in every 12 hours	6	28.6
	Once in every 24 hours	7	33.4
Scales used in the assessment of delirium	CAP-D (Cornell Assessment of Pediatric Delirium)	13	61.9
	pCAM-ICU (Pediatric Confusion Assessment Method-ICU) or psCAM-ICU Preschool	7	33.3
	Pediatric Anesthesia Emergence Delirium Scale (PAED)	2	9.5
	Confusion Assessment Method-ICU	1	4.8

venous catheterization, endotracheal intubation and chest tube placement. PICU specialists reported that they implemented the following practices regarding parents: 21 (58.4%) allowed the parents to be with the patient at certain times during the day, 7 (19.4%) allowed the parents to be with the patient in the unit for 24 hours, 11 (30.6%) allowed the parents to be near the patient in an isolated room for 24 hours, 13 (36.1%) allowed the parents to be with the patient for a certain period of time only on visiting days. Participants stated their concerns about the impact of parents on patient care were as follows: 20 (55.6%) delay in intervening in a sudden and unexpected negative situation, 15 (41.6%) create risk of infection, 32 (88.9%) stated that parents would overreact to negative situations.

Discussion

Assessment of pain and agitation in children is an ongoing challenge for PICU specialists. Therefore, the need for standardization has emerged to ensure an adequate level of sedation.[6] Over the past two decades, reports of the use of nurse-dependent sedation protocols have increased.[7-10] Although there are studies showing that applying a protocol in sedation decreases the duration of stay on the MV, there are also studies showing the contrary.[11,12] In our study, most of the participants (63.9%) stated that they did not use a written sedation protocol for patients on MV but performed routine assessments of sedation efficacy (83.3%). Similarly, we observed a high rate of pain assessment (94.4%) but a low use of a written protocol (25%). In a recent survey involving 215 PICUs from twenty-seven European countries, 71% reported using protocols for analgesia-sedation management. Daily assessment for pain (81%) and sedation (87%) was reported by most PICUs using the preferred validated FLACC scale (54%) and COMFORT Behavior (COMFORT-B) scale (48%), respectively. Both analgesia and sedation were mostly monitored by nurses.[13] In a survey study conducted in the United States, it was reported that most of the participants had a written sedation protocol and used scoring systems to evaluate sedation analgesia and the most common scoring tool used was the COMFORT score.[14] A survey conducted with 27 PICUs in Türkiye and published in 2020 reported that only 9 (33.3%) and 13 (48.1%) centers had a written protocol for analgesia and sedation, respectively. It was found that sedation efficacy was routinely evaluated in all PICUs and COMFORT (55.5%) and Ramsay (37%) sedation scales were the most commonly used scales for this purpose. The most commonly used rating scales for analgesia were reported to be the Wong-Baker FACES pain rating scale (51.8%) and the COMFORT behavior scale (44.4%). It was observed that nurses frequently made these assessments.[15] When our study is compared with these studies covering Europe, America and our country, it was observed that sedation and

analgesia assessment is routinely performed in our country, but the rate of written protocol implementation remains low compared to European and American countries, similar to the study[15] conducted in our country in 2020. This situation can be explained by the low number of trained personnel serving in PICUs compared to the pediatric population of our country and the excessive workload.

Similar to previous studies conducted in other countries, midazolam and fentanyl were found to be the most commonly used sedoanalgesic agents in intubated patients in PICUs in our country.[16-18] In cases of inadequate sedation, ketamine and then dexmedetomidine were the most commonly used agents. In retrospective and prospective studies of ketamine, it has shown good efficacy and a favorable safety profile in the short term, but data on long-term outcomes are not clear.[19,20] The conducted studies found that dexmedetomidine has similar sedation efficacy to benzodiazepine and reduces the need for opiates in PICU patients.[21-23] Studies have also shown that it reduces tachyarrhythmia and shortens the duration of MV exposure in postoperative cardiac surgery patients.[24] Benzodiazepine alone is a risk factor for delirium development.[25] For these reasons, dexmedetomidine is recommended in the first place in the guidelines for sedation in postoperative cardiac surgery patients hospitalized in the ICU and intubated patients hospitalized for other indications.[4] In the literature, its use has been described as a single agent with a continuous infusion in patients using noninvasive MV and as an adjuvant agent given simultaneously with benzodiazepines and opiates for sedation in patients undergoing postoperative cardiac surgery.[5] In our country, dexmedetomidine use ranks first in patients who are followed up with noninvasive MV and high-flow nasal cannula. In cases of inadequate sedation, it is often used after ketamine. Its use as first choice in intubated patients is low, which is consistent with the literature.[26,27]

In a survey study conducted in Canada, morphine was the most common analgesic agent used in intubated patients in PICUs, while acetaminophen and ibuprofen were the most commonly used adjuvant analgesics.[28] In our study, while opiates were the most commonly used analgesic agent in postoperative surgery patients, trauma patients and patients who underwent postoperative cardiac surgery, it was seen that the rates of acetaminophen and dexmedetomidine use were also high in these patient groups. In a survey involving anesthesiologists and emergency physicians except PICU specialists in the United States, the most commonly used sedoanalgesic agents were propofol, ketamine and fentanyl, respectively, in short-term procedures in extubated patients.[29] In our country, the preference of PICU specialists was ketamine, similar to the study conducted in 2020.[15]

Daily sedation interruption is one approach developed to avoid the negative effects of excessive sedation. Research demonstrates that daily sedation interruption decreases the duration of hospital stays and the number of days spent on MV in the adult population.[30] In a study comparing patients receiving daily sedation interruption with sick children receiving continuous sedation, daily sedation interruption led to improved clinical outcomes, including shorter MV and PICU stays.[31] In a survey conducted in Argentina, the rate of daily sedation interruption was 4%, whereas in our study, it was 38.9%.[26]

In our study, muscle relaxants were the most commonly used in intubated patients to prevent patient-mechanical ventilator asynchrony. The muscle relaxant of choice is often rocuronium. In the study by Twite et al. it was observed that the use of muscle relaxants could be preferred by 69% with similar indications, the rate of muscle relaxant use was 30%, the most commonly used agent was vecuronium, and hemodynamic findings (51.7%) were most frequently used as a sedation assessment tool in patients using muscle relaxants.[14] In a European centered study, it was observed that rocuronium was mostly preferred, the depth of sedation was mostly monitored through

hemodynamic findings (75%) in patients using muscle relaxants and the use of BIS (32%) was low.[13] The BIS monitor has been well validated in the pediatric anesthesiology literature for titrating depth of anesthesia in children and its use in PICUs is promising.[32,33] In our study, we observed that approximately half of the participants used BIS monitoring to assess the depth of sedation in patients receiving muscle relaxants. We observed an increase in the use of BIS monitors compared to previous years in our country, which was also higher than studies conducted in other countries.

Several prospective observational studies in PICUs have shown that delirium is frequently seen.[34] The biggest problem in PICUs today is the recognition of delirium. Assessment scales have been developed for this purpose. According to an international survey in 2014, 71% of PICU do not monitor delirium and the Pediatric Confusion Assessment Method (pCAM-ICU) is the only scale used in delirium assessment.[35] In a survey study conducted in Japan, it was observed that delirium was assessed at a rate of 21%, and the most frequently used scale was pCAM-ICU.[27] In our study, it was seen that delirium assessment increased compared to the past and the most commonly used assessment scale was the Cornell Assessment of Pediatric Delirium. Despite limited data, implementing environmental modifications, such as maintaining day/night cycles and ensuring healthy sleep conditions at night may affect the incidence and severity of delirium in children.[4] In our study, it was also found that environmental changes were frequently used to prevent the development of delirium. The use of atypical antipsychotic agents is preferred in resistant and severe delirium.[4] Although it was not asked in which condition it was used, the most frequently used medical agents were found to be haloperidol, risperidone and melatonin, respectively.

Prolonged and high dose sedoanalgesic use may lead to iatrogenic withdrawal syndrome.[36] There are some validated and reliable assessment tools for pediatric withdrawal syndrome. Studies have shown that the Withdrawal Assessment Tool version-1 (WAT-1) scale is effective for the assessment of withdrawal and its use has also been recommended by the sedation guide.[4,37,38] In our study, withdrawal assessment was performed by 88.8% of the participants and the most frequently used scale was WAT-1. There is no solid evidence on the prevention and management of withdrawal syndrome in critically ill children.The most current recommendation is to discontinue opiates and benzodiazepines in accordance with the protocol and to perform opiate and benzodiazepine replacement therapy when withdrawal symptoms occur.[5] In our study, it was observed that the most commonly used approach in patients with withdrawal was to increase the dose of the medication or to add new medication which is mostly dexmedetomidine and chloralhydrate. In addition to these, we observed that common approaches included allowing the patient's family to be present and encouraging them to listen to music.

To prevent stress and facilitate sleep in the PICU, it is important to promote an environment with adequate light and sound. Non-pharmacological comfort measures and sleep promotion are recommended by both adult and pediatric clinic guidelines[4,27] In our country, methods such as reducing lights at night, using eye patches for suitable patients, reducing blood collection and invasive interventions have been applied for this purpose. Parents are increasingly actively involved in decisions about children hospitalized in the PICU. It has been emphasized and suggested that parental involvement is important to make pediatric patients comfortable in an unfamiliar environment and to reduce anxiety and stress of parents, but there are limited studies on this subject.[4,5] All participants stated that they did not allow parents to be present by the patient during invasive interventions in our country. Only 19.4% of the PICU specialists allow the parents to stay with the patient permanently. This situation may be attributed to personnel and space limitations in our country, but we

believe that the primary cause is the violence patients' relatives inflict on healthcare workers. In fact, our study revealed that the most prevalent worry about parents' involvement in patient care was their tendency to overreact to potential negative circumstances and postpone intervention due to familial reactions.

Limitations

The number of participants in the study was low considering the number of physicians working in the field of PICU in our country. However, since almost half of the physicians who participated in the study have been working in the PICU for more than 10 years and 61.1% of them were lecturers, we think that they adequately reflect sedation analgesia, withdrawal and delirium practices in PICUs in our country.

Conclusion

This is the second survey study conducted on the management of sedation and analgesia in PICUs within Türkiye. This second survey revealed the implementation of practices similar to those in other countries in recent years. Although protocol usage rate related to sedation-analgesia remained low, it was found that the usage rate of assessment scales increased, and the assessment scale utilization and the sedoanalgesic agents used in various clinical scenarios were performed in parallel with the recommendations of the sedation guides. While awareness of delirium and withdrawal assessment has increased, it has not yet reached the desired level. Therefore, there is a need to develop guidelines, raise awareness, and increase training on these issues in our country.

Ethical approval

The study was approved by the local ethics committee of Çukurova University Faculty of Medicine (Date: October 13, 2023; number: 137).

Author contribution

The authors confirm contributions to the paper as follows: Study conception and design: EK, DY, AK, UA, GB; data collection: EK, DY, AK, UA, GB; analysis and interpretation of results: EK, DY; draft manuscript preparation: EK, DY All authors reviewed the results and approved the final version of the manuscript.

Source of funding

The authors declare the study received no funding.

Conflict of interest

The authors declare that there is no conflict of interest.

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