DOI https://doi.org/10.47310/jpms202514S0143



# Adverse Events Associated with Sedation and General Anesthesia in Pediatric Dentistry: A Systematic Review

## Hanadi Abdullah Alwafi<sup>1\*</sup>

Department of Pediatric and Prevention Dentistry, General Dentistry Program, Batterjee Medical College, 21442 Jeddah, Saudi Arabia

Author Designation: 'Consultant Pediatric Dentist

\*Corresponding author: Hanadi Abdullah Alwafi (e-mail: hanadi.alwafi@bmc.edu.sa).

 $@2025 \ the \ Author(s). \ This is an open access article \ distributed under \ the terms of the Creative Commons \ Attribution \ License \ (http://creativecommons.org/licenses/by/4.0$ 

**Abstract Background and Objectives:** A systematic review investigated adverse event frequencies and types occurring during pediatric dental sedation and general anesthesia administration to children using different medications through multiple delivery methods. **Methods:** A complete database search based on PRISMA guidelines spanned from 2015 until 2024. The initial screening process yielded 211 articles which was reduced to 20 studies comprising three RCTs and seventeen cross-sectional types. The evaluation of bias risk applied the ROBINS-E along with RoB 2.0 assessment tools. **Results:** Twenty studies were assessed for the research with 13 featuring data about GA and 7 providing data about PDS. The sedative agents commonly selected for sedation included propofol, sevoflurane, ketamine and midazolam. Data showed a wide range of adverse event incidence between 8% to 47.5% that included agitation at 47.5% and postoperative pain reaching 90% and nausea affecting 19.6% and laryngospasm that rose up to 36.8%. Cognitive and financially speaking office-based sedation proved better than treating patients with GA. **Conclusion:** Successful reduction of adverse events depends on selecting suitable patients followed by personalized sedation methods and continuous intraoperative alongside postoperative surveillance. Professional sedation guidelines along with specialized pediatric dental sedation training demonstrably need implementation according to this research.

Key Words Adverse events, Conscious sedation, Dental treatment, General anesthesia, Pediatric dental sedation

## **INTRODUCTION**

Procedural sedation and analgesia (PSA) are commonly used for unpleasant or possibly distressing procedures in pediatric patients. In the previous decade, PSA has maintained consistency in the established rules and monitoring activities [1,2]. Furthermore, efforts have been made to standardize the reporting of Adverse Events (AEs) [3]. Despite advancements in monitoring and treatment choice, no medicine for PSA is entirely 'safe' and 'free of risk' [4,5]. The behaviour and developmental phases of a child distinguish PSA in children from that of adults. Children require larger doses of drugs according to their body weight, even when identical medications are frequently used in the adult population [6]. Often, a greater degree of sedation is required to conduct a procedure on a child than on an adult [7]. Children possess an intrinsic habitus that predisposes them to AEs. Their occiput is greater in size, complicating airway placement. They possess a fairly large tongue and upper airway soft tissue that may obstruct their airway. A child's airway has increased resistance owing to its funnel-like

glottis. They possess an elevated metabolic demand, leading to the rapid onset of hypercarbia and hypoxia following apnoea [8-10]. All of these issues contribute to the difficulty in administering PSA prudently in pediatric patients [11].

Multiple patient management approaches have been utilized during intricate dental treatment, encompassing behavioural interventions, oral sedatives, inhaled nitrous oxide and General Anesthesia (GA) [12,13]. Despite its prevalent application, minimal or moderate Pediatric Dental Sedation (PDS), such as the administration of oral sedatives and nitrous oxide, remains unreliable. GA is more effective; nonetheless, it is intrusive and carries a greater risk. Deep sedation administered by nonanesthesiologist professionals for various non-invasive and semiinvasive treatments in children has demonstrated safety, efficacy and cost-effectiveness [13,14].

The utilization of drug combinations, comparisons to a single agent and/or the use of various administration routes have taken up a large portion of the current PSA literature. We performed a systematic study to ascertain the occurrence of AEs during PDS or GA in children, considering the frequency of

occurrences linked to specific medicines and various drug combinations. It is anticipated that the findings of the review may furnish valuable insights for healthcare professionals during PDS/GA for a particular patient, risk sharing, collaborative decision-making and informed consent procedures [11].

The physiological and anatomical features of children make their response to sedation and anesthesia demonstrate major variations compared to adult patients. Children show elevated risk of adverse medical events including airway obstruction and hypoxia because they have big heads compared to their small airways and fast oxygen usage and unripe metabolic processes. Accurate dose calculation requirements pair with elevated procedural sedation observation intensity because of the physiological distinctions between children and adults.

The sedation medications midazolam and ketamine show different effects on pediatric patients due to age-related developmental changes and forcing healthcare providers to administer more drug based on body weight. The human development and drug pharmacological properties between children and adults support conducting a specialized systematic review only investigating pediatric sedation risks combined with safety protocols. This review aimed to both analyze recorded adverse events in Pediatric Dental Sedation (PDS) and General Anesthesia (GA) and evaluate sedation protocol safety while identifying particular combinations and procedural aspects which increase risk levels.

### MATERI ALS AND METHODS

## **Study protocol**

The review complied with the standards set by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) regarding the choice of study, data synthesizing and final result presentation [15].

#### **Focused Question**

The research question was "What are the documented adverse effects associated with PDS and GA during pediatric dental treatment?"

#### **Sources of Information and Search Techniques**

We performed an extensive search on PubMed, Scopus and Google Scholar to identify research articles published from January 2015 to August 2024 that evaluated data on AEs associated with PDS and GA during dental procedures. Following a comprehensive review of the existing literature, the subsequent amalgamation of Medical Subject Headings (MeSH) terms were employed: ("Pediatric dental sedation" OR "Oral sedation" OR "General anesthesia" OR "Office-based anesthesia" OR "Procedural sedation and analgesia" OR "Deep sedation") AND "Ketamine" ("Propofol" OR "Sevoflurane" OR OR "Midazolam" OR "Nitrous oxide" OR "Fentanyl" OR "Isoflurane" OR "Meperidine" OR "Hydroxyzine" OR "Dexmedetomidine") AND ("Adverse events" OR "Postanesthesia outcome" OR "Nausea" OR "Vomiting" OR "Agitation" OR "Emergence delirium" OR "Anxiety" OR "Sleepiness" OR "Bradycardia" OR "Laryngospasm" OR "Oxygen desaturation" OR "Respiratory depression" OR "Hypoxia"). A thorough review of the citations from the selected investigation was performed to uncover articles unavailable from electronic databases. Two reviewers performed an unbiased search and assessed the records based on the criteria of the review.

## **Eligibility criteria**

The review utilized the PEO inclusion criteria (population, exposure and outcome).

## Population

Original research studies, encompassing randomized controlled trials (RCTs), observational or cross-sectional studies, wherein PDS or GA conducted on children were included (exclusively studies with individuals under 18 years of age).

## Exposure

Studies on PDS or GA conducted in the dental office or emergency department by emergency service providers, emergency medicine residents, pediatricians, anesthetists and/or specialized practice practitioners (nurse practitioners or dental assistants). Any drug, administered solely or in combination through any form of administration (intravenous, intramuscular injection, inhalational, intranasal, or oral), was addressed.

## Outcome

Studies on subsequent postanesthesia events or PDS outcomes encompassed: agitation, breathing difficulties, aspiration, bradycardia, positive pressure ventilation, hypotension, hypoxia, intubation, laryngospasm, myoclonus, vomiting and oral airway insertion.

We eliminated systematic reviews, narrative reviews, survey questionnaires, case reports, case series, editorial commentaries, cadaver studies, pilot trials and expert comments. Articles that did not emphasize the relevant information or were not in English were excluded. We acknowledge that excluding non-English studies may have led to the omission of valuable data. However, this decision was made to ensure accuracy and consistency in interpretation.

#### **Selection of Studies**

Articles that did not adhere to the guidelines were discarded. Two independent evaluators individually examined the titles and abstracts and selected full-text articles of the research study. In the absence of unanimity, a third reviewer was solicited to render a conclusion and all three evaluators reached a unanimous agreement. To minimize interpretation bias, two reviewers independently screened and extracted data from the selected studies. In cases of disagreement, a third expert reviewer was consulted and consensus was reached through discussion.

## **Data Extraction**

A systematic data collection method was utilized to get information including the primary author and journal, publication year, study location, research design, sample size, mean age, type of medication used, procedure employed, reported AEs and study conclusions.

## **Evaluation of Evidence Quality of the Studies**

The cross-sectional studies were evaluated using the risk of bias (RoB) in non-randomized exposure studies (ROBINS-E) was categorized as low, with some concerns, high and very high [16]. The instrument assesses confounding bias, exposure measurement bias, selection bias, post-exposure intervention bias, missing data bias, outcome evaluation bias and selective reporting bias. The overall RoB for each study was classified as follows: Upon fulfillment of all criteria, a low RoB was conferred. The study raises concern if at least one domain exhibits an issue although no domains are classified as having a high or very high RoB. A domain exhibiting a high RoB without significant risk or notable concerns results in an overall assessment of high RoB. If any of the domains exhibit a significantly high RoB, the entire assessment is said to be very high.

The RoB for RCTs was evaluated as low, with some concerns, or high, based on an assessment of research quality following the criteria established by the Cochrane Handbook for Systematic Reviews of Interventions. The categories covered in RoB 2.0 include all types of bias recognized to affect the results of RCTs. These biases include randomization bias, planned intervention bias, missing data bias, measurement of outcomes bias and bias in the selection of reported results [17].

#### RESULTS

Figure 1 illustrates the sequential study selection process. After a comprehensive database search and manual review, 211 studies fulfilled the inclusion criteria. Following the elimination of 54 unsuitable papers, 149 articles underwent evaluation for title and abstract assessment. Following assessments, 49 electronic database research and three manual search investigations were reviewed for full-text publications. Thirty-two items were rejected for failing to fulfill the standards. This systematic analysis included 17 cross-sectional studies [18-30,33,35-37] and three randomised controlled trials [31,32,34] (Table 1). A total of

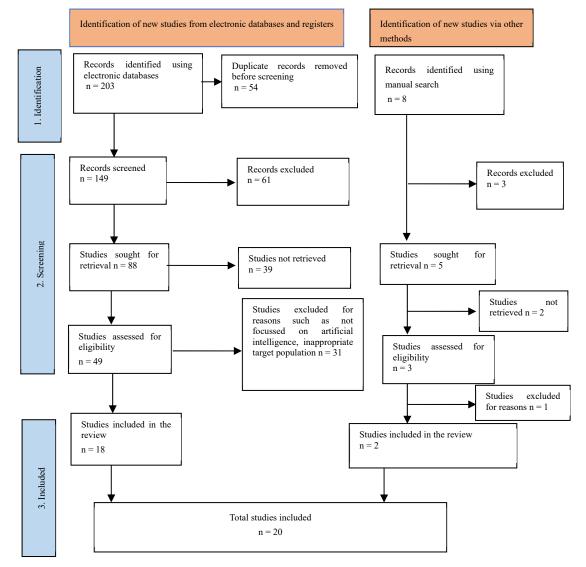


Figure 1: PRISMA (2020) flow chart of the reviewed studies

Table 1: Descriptive summary of the reviewed studies	summary of the	reviewed studies						
Author-Year	Country	Study design	Sampl e size	Age (Mean/medi an/range)	Medication used	Procedure used	Reported AEs	Study inference
Hill <i>et al</i> [18]	Netherlands	Natural experiment	25872	2 to 18 years with the ASA classification s I and II	Propofol	PPSA	Unclear	After the updated 2017 guideline was implemented, there was a substantial decrease in AEs, emphasizing the significance of adherence to evidence- based protocols in out-of-dental offices
Gandhi <i>et al</i> [19]	NSA	Cross-sectional	175	2-17	Intramuscular ketamine followed by intravenous propofol	DS	Airway and breathing category: 36.84% Sedation quality (dizzy patient and sustained a head laceration after a fall): 47.37% Allergy: 15.79%	In outpatient dentistry clinics, 1 in 12 paediatric DS cases have minor or serious AEs.
Radacsi <i>et al.</i> [20]	Hungary	Cross-sectional observational	103	5.07 ± 2.55	Midazolam syrup (preoperative), and Sevoflurane	GA using the Wong-Baker FACES Pain Rating Scale.	Pain: 38% (preoperative), 66% (postoperative)	Pain throughout the week after paediatric dental procedures under GA corresponds with intervention length, indicating the necessity for an established therapeutic strategy.
Wu <i>et al</i> [21]	China	Cross-sectional	342	2.8-16.1 (ASA I and II)	Intravenous Propofol	SQ	Minor complications: 13.7% Choking/cough during treatment: 10.2% Tachycardia: 1.5% Hypoxemia: 7.3%	The incidence of respiratory depression was increased as the duration of treatment increased, and complications during treatment were closely associated with coughing.
Rajab <i>et al.</i> [22]	Jordan	Prospective observational	150	5.5 (ASA I)	Fentanyl, rocuronium, and Isoflurane intravenously.	GA	92% experienced at least one postoperative morbidity on day 1. Dental pain: 81.3%, sleepiness: 70%, and poor appetite: 46.7%	Postoperative motbidity was predicted by gender; age, and procedure time.
Zouaidi <i>et al.</i> [23]	USA	Retrospective	351 (690 PDS)	7.4 (ASA I/II)	Oral (nependine, hydroxyzine, meperidine, midazolam, and diazepam) and intramuscular (ketamine, and midazolam) sedations	SO4	Agitation: 47.5% Emesis: 1.3% Respiratory: 0.7% Cardiovascular: 0.6%	Agitation caused sedation failures in several sedated children.
Ferrazanno <i>et al.</i> [24]	Italy	Prospective	109	8.36±3.68	Propofol	Non-Operating Room Anesthesia	Intraoperative side effects: 33.3%. Postoperative side effects: 6.4% (pain: crying: fever; vomiting: headache; drowsiness; excitability; imitability; inability to eat; and requiring medical care)	Intravenous Propofol sedation in NORA functions well for uncooperative paediatric outpatient treatment.
Ghafournia <i>et al.</i> [25]	lran	Cross-sectional observational	72	3.32±1.14 (ASA I)	midazolam and propofol intravenously	GA	Attachment to parents, dental pain, and inability to eat normal and excessive crying	With the exception of excessive sobbing, which endured a substantial decrease after 48 hours, all psychological issues experienced an insignificant reduction by the second day.
Zhang <i>et al.</i> [26]	China	Prospective	369	4.38±0.77	Sevoflurane inhalation followed by intravenous cisatracurium, propofol, and sulfentaryl	GA	Postoperative pain (62.70%), followed by weariness, agitation, masticatory problems, drowsiness, oral bleeding, coughing, fever, sore throat, nausea, constipation, epistaxis, vomiting, excitement, and diarrhea.	Reduced dental treatment duration may lessen postoperative pain and fatigue. Adequate nutritional status may prevent postoperative fever.

Almaz et al. [28] Turkey							Transient desaturation: 1.8% Hypersalivation: 0.6%	proves safe and efficacious in managing pediatric oro-dental trauma situations, with 10.2% mild risk outcomes documented.
	key	Observational	133	4.3±1.4	Intravenous propofol or sevoflurane or a combination	GA	Dental pain and bleeding, nausea, coughing, sore throat, fever, vomiting, inability to eat, sleepiness, drowsiness, and psychological changes	The postoperative issues that resulted from dental procedures under GA were typically moderate and restricted to the first day following the dental procedure.
Bartella <i>et al.</i> [29] Gern	Germany	Retrospective	220	5.9	MM	GA	Vomiting, ventilator problems, prolonged hospitalizations	GA for pediatric dental care is safe and routine in terms of perioperative care and complications.
Hu et al. [30] China		Prospective observational		3.34±1.66 (ASA I/II)	WN	GA	Dental pain and bleeding	Dental pain was frequently experienced than bleeding following dental procedures under GA and was linked to the number of teeth treated.
Keles <i>et al.</i> [31] Turkey	key	Prospective RCT	70	4.6±1.1 (ASA I/II)	Sevoflurane	GA	Postoperative nausea and vomiting, laryngeal pain, Dental pain, Dysphonia	Children undergoing full-mouth dental rehabilitation under GA were more at ease postoperatively with laryngeal mask airway than nasotracheal intubation.
[32] Turkey	key	Prospective RCT	116	Sevoflurane group: 4.89±1.32 Propofol group: 4.67±1.39 (ASA I/II)	Sevoflurane or Propofol intravenous anesthesia	GA	Pediatric Anesthesia Emergence Delirium scores, Face, Legs, Activity, Cry, Consolability scale	Propofol intravenous anaesthesia minimised postoperative discomfort and did not affect extubation or time for recuperation.
Keles <i>et al.</i> [33] Turkey	key	Retrospective	06	4.6±1.7 (ASA I)	Propofol, fentanyl, rocuronium, sevoflurane	GA	Postoperative pain using Wong- Baker FACES score: 90%	Compared to dental fillings, pulpotomy patients exhibited increased postoperative pain levels and needed more rescue analgesics.
Somri <i>et al.</i> [34] Israel	el	Prospective RCT	100	5-7	Midazolam	PDS	Respiratory AE: SMM group: 20% PTS+SMM group: 44%	After administering 0.75mg/kg midazolam and oxygen, PTS was determined to be advantageous for the identification of respiratory adverse events during PDS.
	ana	Cross-sectional	7041	4.7±2.9	MM	GA	Predischarge laryngospasm: 0.5% Postdischarge nausea: 5% Vomiting: 3.26%	Results indicate office-based anaesthesia safety.
Huang et al. [36] USA	A	Prospective	51	5.8	One of the following regimens: morphine or meperidine, chloral hydrate, benzodiazepine, midazolam or diazepam, and/or hydroxyzine HCl	Oral sedation	Sleepiness: 60.1% Nausea: 19.6% Vomiting: 10.1% Fever: 7%	The child needed close supervision until baseline condition was restored, which took a few hours to the next morning.
Wong <i>et al.</i> [37] Canada	lada	Prospective	33	(IVI VSA I/II)	WN	GA	Postoperative pain	Wong <i>et al.</i> [37] Canada Prospective 33 (ASA I/II) NM GA Postoperative pain The Faces Pain Scale-Revised and Parents' Postoperative Pain Measure determine the postoperative pain in children   A Not et al. A Astoperative pain Parents' Postoperative Pain Measure determine the postoperative Pain in children   A A Astoperative pain Astoperative pain Astoperative pain in children   A A Astoperative pain Astoperative pain

13 studies focused on pediatric dental care under GA, whereas seven studies were on PDS. Propofol was utilized in the majority of the reviewed studies, followed by sevoflurane, midazolam and ketamine. Where available, adverse events were categorized into mild (e.g., nausea, sleepiness), moderate (e.g., vomiting, transient desaturation) and severe (e.g., laryngospasm, bradycardia). Agitation was reported in up to 47.5% of cases, while respiratory complications such as oxygen desaturation occurred in 1.8% to 13.7% depending on the sedation method and monitoring technique.

The natural experiment conducted by Hill *et al.* [18] aimed to evaluate the effect of revised guidelines on the incidence of AEs during Paediatric Procedural Sedation and Analgesia in 12 Dutch dental clinics, utilizing data from an anesthesia complication database. The results indicated a notable protective impact linked to the adoption of the revised guidelines, leading to a statistically significant decrease in the incidence of AEs. The likelihood of encountering AEs diminished by 25% after the guideline update compared to the preceding period. Additionally, significant diversity in the incidence of AEs was noted among the nine clinics, suggesting the possible existence of a cluster phenomenon within these clinical environments. This highlights the necessity of accounting for clinic-specific variables when assessing the influence of clinical guidelines [18].

Gandhi et al. [19] employed a sedative protocol consisting of intramuscular ketamine followed by intravenous propofol in all patients studied. Among the 175 deep sedation (DS) cases, 24 AEs were identified in 19 patients. Among the 24 AEs, 19 AEs in 15 patients were considered associated with the sedation treatment. Consequently, during the 3-year trial period, it was ascertained that 8.6% of patients encountered an AE associated with profound sedation. Among the 19 recorded AEs, 36.84% comprised laryngospasm or oxygen desaturation that required intervention. The interventions encompassed the necessity for a nasopharyngeal tube, a bag-valve mask, or pharmacological measures including the administration of propofol. Nearly all the recorded AEs were reported in patients aged 9 years or younger [19]. Wu et al. [21] similarly reported that the predominant consequence under deep intravenous propofol sedation was a reduction in oxygen saturation in outpatient dental procedures with recalcitrant youngsters. Most of the AEs documented by Zouaidi et al. [23] were observed during oral sedation. 68% of AEs were recorded during oral sedation, 21.4% were during parenteral sedation and 10.7% during nitrous oxide sedation. Of the AEs detected during oral sedation, 58% of them occurred with the use of Midazolam, either alone or in combination [23]. Postdischarge somnolence, nausea and emesis were common problems after oral sedation [36].

The most significant conclusion regarding the comparison of particular monitoring techniques between the two patient groups is that the majority of respiratory AEs were identified with the addition of the pretracheal stethoscope (PTS) to the conventional monitoring techniques. This may indicate the ability of PTS auscultation to identify respiratory AEs during PDS with midazolam and oxygen, in the presence of an anaesthetist, before they

become visually or electronically detectable [34]. Around 11% AEs were observed with the most prevalent being emesis (9.0%), followed by transitory desaturation (1.8%) and hypersalivation (0.6%) after injectable ketamine sedation delivered by emergency department physicians for dental treatment of oro-dental injuries [27].

Rajab et al. [22] identified prevalent postoperative symptoms in children after dental procedures under GA at an educational facility and investigated factors potentially associated with postoperative morbidity to assess their impact on the morbidity of pediatric patients. On the first postoperative day, the majority of patients suffered at least one morbidity indication or symptom and by the third day, most of them had subsided. In contrast to the other symptoms, diminished appetite was observed on all days, including the seventh day. The persistence of oral pain till Day 7 may elucidate the cause of the diminished appetite [22]. Radacsi et al. [20] reported that postoperative pain was substantially more prevalent and acute than baseline pain. Wong et al. [37] proposed that prophylactic analgesics be administered intraoperatively to enable a transition to oral analgesics, such as children's ibuprofen or acetaminophen, for home use. Moreover, the findings indicate that postoperative guidelines should prioritize continuous doses for a minimum of 2 days rather than endorsing "as-needed for pain" dosing [37]. Propofol in non-operating room anesthesia showed efficacy with few AEs, as described by Ferrazzano et al. [24].

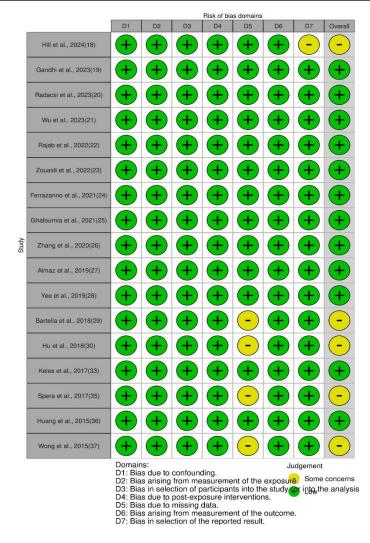
Keles *et al.* [33] found varying degrees of postoperative discomfort in 90% of all patients. Patients who received primary molar pulpotomies exhibited higher postoperative pain levels (moderate to severe) at 49%, compared to 13% in those receiving standard restorative treatment, irrespective of the number of procedures conducted. Rescue analgesia was administered based on postoperative pain levels; however, no local anesthesia was applied intraoperatively in any of the patients [33]. Ghafournia *et al.* [25] indicated that the predominant psychological issue was parental attachment (70.7%), succeeded by excessive sobbing (56.9%). The predominant non-psychological consequence on the first and second postoperative days was oro-dental pain [25].

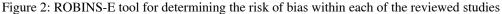
#### Assessment of the Quality of the Examined Studies

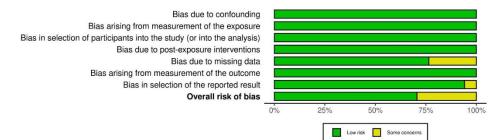
The ROBIN-E assessment technique classified 12 research as having low RoB [19-28,33,36], whereas five studies [18,29, 30,35,37] were identified as having some concerns regarding risk. Figure 2 and 3 depict the risk of bias within and among the reviewed studies, respectively. The use of the RoB 2.0 approach revealed that all three RCTs [31,32,34] had a low RoB. Figure 4 encapsulates information from the RCTs of the reviewed studies. Figure 5 illustrates the RoB across the trials.

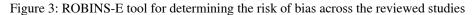
#### DISCUSSION

This review aimed to consolidate existing data to present incidence rates of AEs in pediatric dental care under GA or PDS. Furthermore, our objective was to concentrate on the past decade of data to elucidate current treatment patterns and monitoring procedures for PDS/GA. No pediatric fatalities









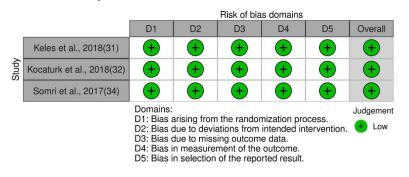


Figure 4: ROB 2.0 tool for determining the risk of bias within each of the reviewed RCTs

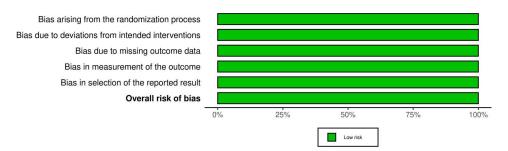


Figure 5: ROB 2.0 tool for determining the risk of bias across the reviewed RCTs

were reported in the reviewed studies conducted over the past decade. In 1983, three pediatric fatalities occurred in the same dentistry practice as a result of a combination of drugs administered for dental treatments. The fatalities prompted the formulation of the inaugural sedation guidelines issued by the American Academy of Paediatrics (AAP) in 1985 [38]. In 2001, a study detailed a newborn who experienced an overdose of demerol, phenergan and thorazine in the emergency department, resulting in cardiac arrest, from which the infant ultimately recovered [39]. Pediatric sedation safety trends now require healthcare providers to use capnography together with pulse oximetry and pretracheal auscultation as essential monitoring technologies. Professional dental training needs to emphasize the identification of respiratory symptoms at their earliest stages and proper airway emergency response techniques. Age- and weight-interactive procedures should have priority in clinical guidance along with comprehensive patient risk assessments and necessary parental consent procedures.

In recent years, the incidence of pediatric procedures necessitating PSA has markedly risen, along with claims of AEs. While GA is typically considered safe in a hospital environment, it is widely acknowledged that it should be minimized whenever feasible due to heightened risks of complications, the necessity for highly qualified staff and specialized equipment and its associated costs. Employing DS for pediatric dental procedures is an alternative approach. Despite the publication of numerous guidelines, there exists a lack of consensus on which pharmaceuticals can be properly provided in a non-specialist environment. Sury et al. [40] have shown that oral sedation with chloral hydrate or benzodiazepines, administered under the care of specialized nurses, is both effective and safe for diagnostic imaging. Nonetheless, the efficacy of regimens suitable for painful treatments seems to be inadequately established [41,42].

The PDS has been effectively performed utilizing several pharmacological protocols. In the present review, the predominant sedation procedures employed by pediatric dentists at present are propofol, sevoflurane, ketamine and midazolam, either administered alone or in combination. In-office sedation is more cost-effective and more secure than conscious sedation and GA [19,35]. Other strategies comprise dexmedetomidine hydrochloride, an adrenergic agonist, meperidine, hydroxyzine and chloral hydrate, all of which exert inhibitory effects on the cerebral hemisphere of

the central nervous system, along with general anesthesia [14]. All drugs utilized for PSA are intended to diminish awareness, which may consequently impair control regions in the brain, leading to agitation. Furthermore, preprocedural agitation has been markedly correlated with recovery agitation [43]. Medication selection and patient predilection are critical elements in the decision-making process for PSA [11]. Agitation was observed in 47.5% of children receiving PSA, with 34.1% of these instances leading to a recorded cessation of dental treatment. This was most commonly observed with nitrous oxide sedation [23]. Likewise, midazolam has a longstanding history of inducing 'paradoxical reactions' or agitation. The pathway is believed to result from the suppression of cortical restraint areas and reduced serotonin, which may trigger aggressive conduct [44]. A comprehensive review indicated that the occurrences of agitation for ketamine/midazolam and ketamine/propofol were comparable, at 6% and 4%, respectively [11].

Propofol facilitates swift recovery, rendering it an optimal agent for minor procedures conducted outside of operating rooms. Bradycardia has been identified as a potential AE of propofol, whether delivered independently or in conjunction with opioids. AEs include temporary hypotension and respiratory depression that is dosedependent [14]. Ketamine was the most commonly utilized drug for PSA. Ketamine is distinctive as a dissociative drug, diverging from the dose-dependent sedation continuum of minimal, moderate, deep and global anesthesia [45]. Endtidal carbon dioxide monitoring has demonstrated the ability to identify apnoea and hypoventilation before the onset of hypoxia [46]. The 2006 AAP recommendations advocated using capnography, but both the American College of Emergency Physicians (ACEP) and the American Society of Anaesthesiologists (ASA) have endorsed its routine application during all PSAs conducted [1,2]. While vomiting is not a grave side effect, it induces worry for patients and their relatives. This must be considered while acquiring informed consent and engaging families and patients in collaborative decision-making. Laryngospasm was predominantly managed with a bag-valve mask with positive pressure ventilation. In a previous study reporting the highest prevalence of laryngospasm, 69% of patients experiencing laryngospasm were administered injectable ketamine [39]. However, laryngospasm can also manifest with other PSA medicines [11,35,47].

Various factors, including variations in the study population, characterizations of respiratory AEs and the inclusion of intravenous ketamine in other investigations, may explain the minor variances in incidence rates. The predominant cause of these respiratory AEs was oxygen desaturation. Oxygen desaturation is classified as a moderate respiratory AE when SpO<sub>2</sub> ranges from 75% to 90% due to its temporary nature and the ease of reversal with straightforward interventions such as airway repositioning, suctioning and supplemental oxygen administration [3]. The threshold for oxygen desaturation, determined by noninvasive SpO<sub>2</sub> testing, differs between institutions. The World Health Organisation recommendations for pediatric oxygen therapy advise initiating treatment when SpO<sub>2</sub> falls below 90% to avert tissue hypoxia and below 94% in the presence of comorbidities that impair oxygen delivery [48,49].

The postoperative period is frequently worsened by the onset of delirium and postoperative nausea and vomiting [32,36]. Consequently, dual antiemetic prophylaxis is justified. 5HT3 antagonists, including 0.15 mg/kg of ondansetron and 0.1-0.2 mg/kg of dexamethasone, significantly diminish the risk of postoperative nausea and vomiting compared to monotherapy [50]. Effective monitoring of children during sedation is essential for identifying minor physiological alterations that may precede severe outcomes. The multifaceted character of the AEs in this study underscores the various components of care that dentists must be aware of to guarantee patient safety. Dosages of local anesthetics and sedative drugs should be regularly established based on weight to reduce the danger of overdosing toxicity reactions. The recommended dosage of local anesthetics should be reduced when administered alongside any CNS-depressant sedatives. Dental practitioners who give sedative medications to children for dental treatment must adhere to the monitoring standards established by the American Academy of Paediatric Dentistry sedation guidelines. As the treating dentist is most likely to be the initial responder during an adverse event, both the dentist and staff must be equipped to diagnose and initiate treatment for such emergencies. Mortality resulting from PSA in the emergency department is infrequent; meticulous oversight by clinicians possessing the requisite abilities to manage deeper sedation levels is crucial for the safe administration of PSA. Meticulous attention to all details, regardless of their insignificance and strict adherence to the AAPD sedation guidelines are essential to guarantee the safest environment for the administration of drugs to children in the dental office [11,51].

Our systematic review may have numerous potential shortcomings. The primary restriction is the inconsistency in the definitions of the outcomes presented in the research. The absence of standardization in the reporting of outcomes by the original research may have influenced the estimations. Diversity among participants, the kinds or timing of outcome assessments and the nature of the intervention can lead to considerable statistical heterogeneity, erroneous summary implications, misleading outcomes and incorrect decisionmaking. The depth of sedation used depends heavily on the difficulty of dental procedures that patients must undergo. Long invasive procedures need deep sedation and general anesthesia for treatment yet these high-risk methods can generate additional adverse effects. The availability of trained anesthetists together with emergency preparedness systems strongly decreases the occurrence and intensity of such events. A number of restrictions affect this review analysis. The differences in definitions along with measurement methods for adverse events among selected studies prevented the conduct of a meta-analysis. A lack of English-language restrictions during selection excluded potentially valuable data from different countries. Special needs children were excluded from the research which makes it hard to extend the study findings beyond pediatric populations who did not have special needs. Real-world incidence of adverse events tends to be underestimated because the research exclusively relied on published data sources.

## CONCLUSION

Risk minimization needs an evidence-based comprehensive approach for pediatric dental procedures that need sedation because of rising patient demand. Preoperative evaluations should be thorough and drug selection must match patient profiles and healthcare providers should maintain readiness to respond to complications. All dental practitioners need specialized training about emergency response in sedation cases while following established monitoring protocols. The majority of pediatric procedures succeed when performed as outpatient procedures but children with intricate medical histories generally need hospital admission. Pediatric dental care outcomes together with caregiver trust increase when dental professionals explain potential risks and safety requirements to parents and guardians.

#### **Ethical Considerations**

As this is a systematic review utilizing previously published data, no direct ethical approval was required. Nevertheless, the review adheres to principles of ethical research, including respect for data privacy and accurate reporting. Pediatric patients represent a vulnerable population and their safety remains central to the recommendations drawn from this study.

## REFERENCES

- Coté, Charles J. *et al.* "Guidelines for monitoring and management of pediatric patients before, during, and after sedation for diagnostic and therapeutic procedures." *Pediatrics*, vol. 143, no. 6, June 2019. https://pubmed.ncbi.nlm.nih.gov/31138666/.
- [2] Godwin, Steven A. et al. "Clinical policy: procedural sedation and analgesia in the emergency department." Annals of Emergency Medicine, vol. 63, no. 2, 2014, pp. 247-258. https://www. annemergmed.com/article/S0196-0644(13)01489-3/abstract.
- [3] Mason, K.P. *et al.* "Adverse event reporting tool to standardize the reporting and tracking of adverse events during procedural sedation: a consensus document from the World SIVA International Sedation Task Force." *British Journal of Anaesthesia*, vol. 108, no. 1, January 2012, pp. 13-20. https://academic.oup.com/bja/article-abstract/108/ 1/13/234237.

- [4] Cravero, Joseph P. *et al.* "The incidence and nature of adverse events during pediatric sedation/anesthesia with propofol for procedures outside the operating room: a report from the Pediatric Sedation Research Consortium." *Anesthesia & Analgesia*, vol. 108, no. 3, March 2009, pp. 795-804.
- [5] Coté, Charles J. *et al.* "Adverse sedation events in pediatrics: analysis of medications used for sedation." *Pediatrics,* vol. 106, no. 4, October 2000, pp. 633-644. https://publications. aap.org/pediatrics/article-abstract/106/4/633/65823/Adverse-Sedation-Events-in-Pediatrics-Analysis-of.
- [6] Sahyoun, Cyril and Baruch Krauss. "Clinical implications of pharmacokinetics and pharmacodynamics of procedural sedation agents in children." *Current Opinion in Pediatrics*, vol. 24, no. 2, April 2012, pp. 225-232. https://journals.lww.com/ co-pediatrics/abstract/2012/04000/clinical\_implications\_of\_ pharmacokinetics\_and.15.aspx.
- [7] Krauss, Baruch and Steven M. Green. "Procedural sedation and analgesia in children." *The Lancet*, vol. 367, no. 9512, March 2006, pp. 766-780. https://www.thelancet.com/journals/lancet/ article/PIIS0140-6736(06)68230-5/abstract.
- [8] Marcus, Carole L. "Developmental pattern of hypercapnic and hypoxic ventilatory responses from childhood to adulthood." *Journal of Applied Physiology*, vol. 76, no. 1, January 1994, pp. 314-320. https://journals.physiology.org/ doi/abs/10.1152/jappl.1994.76.1.314.
- [9] Pacheco, Garrett S. and Angelique Ferayorni. "Pediatric procedural sedation and analgesia." *Emergency Medicine Clinics*, vol. 31, no. 3, August 2013, pp. 831-852. https://www. emed.theclinics.com/article/S0733-8627(13)00039-4/abstract.
- [10] Adewale, Lola. "Anatomy and assessment of the pediatric airway." *Pediatric Anesthesia*, vol. 19, no. 1, July 2009, pp. 1-8. https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1460-9592.2009.03012.x.
- [11] Bellolio, M. Fernanda *et al.* "Incidence of adverse events in paediatric procedural sedation in the emergency department: a systematic review and meta-analysis." *BMJ Open*, vol. 6, no. 6, 2016. https://bmjopen.bmj.com/content/6/6/e011384.short.
- [12] Morley, K. R. and A. Milnes. "Pediatric patients in dental practice: behaviour management for the 1990s." *Ontario Dentist*, vol. 69, no. 8, October 1992, pp. 35-36. https://europe pmc.org/article/med/1287504.
- [13] Patel, Kalpesh N. *et al.* "Pediatric procedural sedation by a dedicated nonanesthesiology pediatric sedation service using propofol." *Pediatric Emergency Care*, vol. 25, no. 3, March 2009, pp. 133-138. https://journals.lww.com/pec-online/full text/2009/03000/ pediatric\_procedural\_sedation\_by\_a\_dedicated.1.aspx.
- [14] Ahmed, Suhael et al. "Evaluation of safety of using sedative anesthesia in pediatric dentistry: a systematic review." Journal of Research in Medical and Dental Science, vol. 10, no. 9, 2022, pp. 166-172. https://www.jrmds.in/articles/evaluationof-the-safety-of-using-sedative-anesthesia-in-pediatric-dentistrya-systematic-review.pdf.
- [15] Page, Matthew J. et al. "The PRISMA 2020 statement: an updated guideline for reporting systematic reviews." Systematic Reviews, vol. 10, no. 1, March 2021. https://pubmed.ncbi.nlm.nih. gov/33781348/.

- [16] Higgins, Julian P.T. et al. "A tool to assess risk of bias in non-randomized follow-up studies of exposure effects (ROBINS-E)." Environment International, vol. 186, April 2024. https://www.sciencedirect.com/science/article/pii/ S0160412024001880.
- [17] Higgins, Julian P.T. "Chapter 8: Assessing risk of bias in a randomized trial." Systematic Reviews of Interventions, edited by Higgins J.P.T., UK, The Cochrane Collaboration, 2019, pp. 205-228. https://onlinelibrary.wiley.com/doi/abs/10.1002/978 1119536604.ch8.
- [18] Hill, Jonah M. *et al.* "Pediatric sedation in Dutch dental clinics: The influence of guideline modifications on adverse events." *Dentistry Journal*, vol. 12, no. 3, March 2024. https://www.mdpi.com/2304-6767/12/3/66.
- [19] Gandhi, Henal Alpesh *et al.* "Assessing the safety of deep sedation in outpatient pediatric oral health care." *The Journal* of the American Dental Association, vol. 154, no. 11, November 2023, pp. 975-983. https://www.sciencedirect.com/ science/article/pii/S0002817723004622.
- [20] Radacsi, A. et al. "Pain-related complaints of paediatric patients after dental treatment under general anaesthesia." European Journal of Paediatric Dentistry, vol. 24, no. 1, February 2023, pp. 61-68. https://europepmc.org/ article/med/36853211.
- [21] Wu, Xiaoran *et al.* "Safety of deep intravenous propofol sedation in the dental treatment of children in the outpatient department." *Journal of Dental Sciences*, vol. 18, no. 3, July 2023, pp. 1073-1078. https://www.sciencedirect.com/science/ article/pii/S1991790222002975.
- [22] Rajab, Lamis D. *et al.* "Postoperative morbidity of dental paediatric patients treated under general anaesthesia at a university hospital: An observational study." *International Journal of Dentistry*, vol. 1, 2022. https://onlinelibrary.wiley. com/doi/abs/10.1155/2022/9606010.
- [23] Zouaidi, Kawtar *et al.* "An observational retrospective study of adverse events and behavioral outcomes during pediatric dental sedation." *Pediatric Dentistry*, vol. 44, no. 3, 2022, pp. 174-180. https://www.ingentaconnect.com/content/aapd/pd/2022/ 00000044/0000003/art00003.
- [24] Ferrazzano, Gianmaria Fabrizio *et al.* "Effectiveness and safety of intravenous sedation with propofol in non-operating room anesthesia (NORA) for dental treatment in uncooperative paediatric patients." *Children*, vol. 8, no. 8, July 2021. https://www.mdpi.com/2227-9067/8/8/648.
- [25] Ghafournia, Maryam *et al.* "Complications after dental rehabilitation under general anesthesia in Isfahan during February to May 2016." *Dental Research Journal*, vol. 18, no. 1, 2021. https://journals.lww.com/derj/fulltext/2021/ 18000/complications\_after\_dental\_rehabilitation\_under.53. aspx.
- [26] Zhang, Qiong et al. "Postoperative complications in Chinese children following dental general anesthesia: A cross-sectional study." Medicine, vol. 99, no. 45, November 2020. https://journals.lww.com/md-journal/ fulltext/2020/11060/Postoperative\_complications\_in\_Chi nese\_children.58.aspx.

- [27] Yee, Ruixiang *et al.* "Safety and effectiveness of intramuscular ketamine sedation in the management of children with orodental trauma in a paediatric emergency department." *Dental Traumatology*, vol. 36, no. 1, June 2019, pp. 19-24. https:// onlinelibrary.wiley.com/doi/abs/10.1111/edt.12497.
- [28] Almaz, Merve Erkmen *et al.* "Postoperative morbidity in pediatric patients following dental treatment under general anesthesia." *European Oral Research*, vol. 53, no. 3, October 2019, pp. 113-118. https://dergipark.org.tr/en/pub/eor/issue/ 58126/807497.
- [29] Bartella, A.K. *et al.* "The safety of paediatric dentistry procedures under general anaesthesia. A five-year experience of a tertiary care center." *European Journal of Paediatric Dentistry*, vol. 19, no. 1, 2018, pp. 44-48. https://europepmc. org/article/med/29569453.
- [30] Hu, Yu-Hsuan *et al.* "Postoperative dental morbidity in children following dental treatment under general anesthesia." *BMC Oral Health*, vol. 18, May 2018. https://link. springer.com/article/10.1186/s12903-018-0545-z.
- [31] Keles, Sultan and Ozlem Kocaturk. "Postoperative discomfort and emergence delirium in children undergoing dental rehabilitation under general anesthesia: comparison of nasal tracheal intubation and laryngeal mask airway." *Journal of Pain Research*, vol. 11, January 2018, pp. 103-110. https://www.tandfonline.com/doi/full/10.2147/JPR.S153637.
- [32] Kocaturk, Ozlem and Sultan Keles. "Recovery characteristics of total intravenous anesthesia with propofol versus sevoflurane anesthesia: a prospective randomized clinical trial." *Journal of Pain Research*, vol. 11, July 2018, pp. 1289-1295. https://www.tandf online.com/doi/full/10.2147/JPR.S164106.
- [33] Keles, Sultan and Ozlem Kocaturk. "Immediate postoperative pain and recovery time after pulpotomy performed under general anaesthesia in young children." *Pain Research and Management*, vol. 1, June 2017. https://onlinelibrary.wiley. com/doi/full/10.1155/2017/9781501.
- [34] Somri, Mostafa et al. "Detection of respiratory adverse events in pediatric dental patients sedated with 0.75 mg/Kg of Midazolam and Oxygen by continuous pretracheal auscultation: prospective randomized а controlled trial." Journal of Clinical Pediatric Dentistry, vol. 41, no. 2, 2017, pp. 154-160. https://meridian.allenpress.com/jcpd/ article-abstract/41/2/154/78374?\_\_cf\_chl\_rt\_tk=gtftjlk4wmM 4uFOr5mV0wpgF1KVXgfVPxxxGQPMy9r4-1744885548-1. 0.1.1-32emcG9w6zcFCM8na.i8XysU32ACvBiN1Noyqqunf NI.
- [35] Spera, Allison L. *et al.* "Office-based anesthesia: safety and outcomes in pediatric dental patients." *Anesthesia Progress*, vol. 64, no. 3, 2017. https://pmc.ncbi.nlm.nih.gov/ articles/PMC5579815/.
- [36] Huang, Annie and Thomas Tanbonliong. "Oral sedation postdischarge adverse events in pediatric dental patients." *Anesthesia Progress*, vol. 62, no. 3, 2015. https://pmc.ncbi.nlm.nih.gov/articles/ PMC4581021/.
- [37] Wong, Michelle *et al.* "Postoperative pain in children after dentistry under general anesthesia." *Anesthesia progress*, vol. 62, no. 4, 2015. https://pmc.ncbi.nlm.nih.gov/articles/PMC 4675339/.

- [38] Coté, Charles J. "Sedation protocols—why so many variations?." *Pediatrics*, vol. 94, no. 3, 1994, pp. 281-283. https://publications.aap.org/pediatrics/article-abstract/94/3/ 281/59023.
- [39] Brown, E ric T. "Iatrogenic cardiopulmonary arrest during pediatric sedation with meperidine, promethazine, and chlorpromazine." *Pediatric Emergency Care*, vol. 17, no. 5, October 2001, pp. 351-353. https://journals.lww.com/pec-online/fulltext/2001/10000/ Iatrogenic\_cardiopulmonary\_arrest\_during\_pediatric.8.as px.
- [40] Sury, M.R.J. et al. "Development of a nurse-led sedation service for paediatric magnetic resonance imaging." The Lancet, vol. 353, May 1999, pp. 1667-1671. https://www. thelancet.com/journals/lancet/article/PIIS0140-6736(98)0838 3-4/abstract.
- [41] Peña, Barbara M.G. and Baruch Krauss. "Adverse events of procedural sedation and analgesia in a pediatric emergency department." *Annals of emergency medicine*, vol. 34, no. 4, May 1999, pp. 483-491. https://www.sciencedirect.com/science/article/pii/S01960 6449980050X.
- [42] Green, Steven M. *et al.* "Intramuscular ketamine for pediatric sedation in the emergency department: safety profile in 1,022 cases." *Annals of emergency medicine*, vol. 31, no. 6, June 1998, pp. 688-697. https://www.sciencedirect.com/science/ article/pii/S0196064498702264.
- [43] Sherwin, Thomas S. *et al.* "Does adjunctive midazolam reduce recovery agitation after ketamine sedation for pediatric procedures? A randomized, double-blind, placebo-controlled trial." *Annals of emergency medicine*, vol. 35, no. 3, March 2000, pp. 229-238. https://www.sciencedirect.com/science/ article/abs/pii/S0196064400700734.
- [44] Mancuso, Carissa E. et al. "Paradoxical reactions to benzodiazepines: literature review and treatment options." *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy*, vol. 24, no. 9, January 2012, pp. 1177-1185. https://accpjournals.onlinelibrary.wiley.com/ doi/abs/10.1592/phco.24.13.1177.38089.
- [45] Green, S.M. and B. Krauss. "Ketamine is a safe, effective, and appropriate technique for emergency department paediatric procedural sedation." *Emergency MedicineJournal*, vol. 21, no. 3, May 2004, pp. 271-272. https://pubmed.ncbi.nlm.nih. gov/15107359/.
- [46] Deitch, Kenneth et al. "Does end tidal CO2 monitoring during emergency department procedural sedation and analgesia with propofol decrease the incidence of hypoxic events? A randomized, controlled trial." Annals of emergency medicine, vol. 55, no. 3, March 2010, pp. 258-264. https://www.sciencedirect.com/science/article/pii/ S0196064409014292.
- [47] Babl, Franz E. et al. "Laryngospasm with apparent aspiration during sedation with nitrous oxide." Annals of Emergency Medicine, vol. 66, no. 5, November 2015, pp. 475-478. https://www.sciencedirect.com/science/article/abs/pii/S01960 64415003789.

- [48] Le Lee, Jia and Lai Peng Tham. "Incidence and predictors of respiratory adverse events in children undergoing procedural sedation with intramuscular ketamine in a paediatric emergency department." *Singapore Medical Journal*, vol. 63, no. 1, January 2022. https://pmc.ncbi.nlm.nih.gov/articles/ PMC9251216/.
- [49] World Health Organization. Oxygen therapy for children: a manual for health workers Oxygen therapy for children: a manual for health workers. 2016, https://pesquisa.bvsalud.org/ portal/resource/pt/who-204584.
- [50] Puri, Sunaakshi et al. "General Anesthesia for Dental Procedures in Children: A Comprehensive Review." Journal of Postgraduate Medicine, Education and Research, vol. 56, no. 1, 2022, pp. 29-33. https://jpmer.com/doi/JPMER/pdf/ 10.5005/jp-journals-10028-1555.
- [51] Chicka, Maggie C. et al. "Adverse events during pediatric dental anesthesia and sedation: a review of closed malpractice insurance claims." *Pediatric dentistry*, vol. 34, no. 3, June 2012, pp. 231-238. https://www.ingentaconnect.com/content/ aapd/pd/2012/00000034/00000003/art00008.