OPEN ACCESS

Saudi Journal of Medical and Pharmaceutical Sciences

Abbreviated Key Title: Saudi J Med Pharm Sci
ISSN 2413-4929 (Print) | ISSN 2413-4910 (Online)
Scholars Middle East Publishers, Dubai, United Arab Emirates
Journal homepage: https://saudijournals.com

Original Research Article **N/A**

Pharmacodynamics and Pharmacokinetics of Anesthesia in Obese Children: A Systematic Review

Omnya Khalid AlKhaliwi[1*], Hind Ali Bafaqih[2], Adnan Bakur AlKurdi[3], Abdulrahman Abdulwahed AlGarni[3]

[1]PICU Fellow, Prince Sultan Military Medical City, Riyadh, Saudi Arabia
[2]Head of PSMMC PICU, Head of Scientific Committee of Saudi Board, Pediatric Critical Care Fellowship, Vise President SCCS, Prince Sultan Military Medical City, Riyadh, Saudi Arabia
[3]PICU Consultant, Prince Sultan Military Medical City, Riyadh, Saudi Arabia

DOI: https://doi.org/10.36348/sjmps.2025.v11i07.029 | **Received:** 02.06.2025 | **Accepted:** 29.07.2025 | **Published:** 31.07.2025

***Corresponding author:** Omnya Khalid AlKhaliwi
PICU Fellow, Prince Sultan Military Medical City, Riyadh, Saudi Arabia

Abstract

Objectives: To investigate the existing literature on the pharmacokinetics (PK) and pharmacodynamic (PD) of anesthetic agents in obese children. ***Methods:*** A total of 419 pertinent publications were found after a comprehensive search across four databases. 26 full-text publications were examined after duplicates were eliminated using Rayyan QCRI and relevance was checked; five studies finally satisfied the requirements for inclusion. ***Results:*** We included five studies with a total of 10,570 children and less than half of them 4741 (44.8%) were females. Research on the PK of propofol in obese adolescents identified total body weight (TBW) as a key determinant of drug clearance, emphasizing the limitations of relying solely on clinical factors for dosing. Additionally, a study on fentanyl highlighted the importance of TBW for loading doses and LBW/ lean body weight (LBW) for maintenance dosing, while cautioning against the heightened susceptibility of severely obese patients to fentanyl's respiratory side effects, necessitating careful PD considerations. ***Conclusion:*** Anesthesia management in obese children requires addressing unique physiological and pharmacological challenges. This review emphasizes the importance of TBW in dosing strategies and the integration of LBW and IBW for maintenance regimens to minimize risks. While offering valuable insights, further research is needed to validate these findings and establish standardized protocols, ultimately enhancing safety and efficacy in anesthetic care for obese pediatric patients.

Keywords: Ventricular arrhythmias; ventricular tachycardia; Ventricular fibrillation; Saudi Arabia; Systematic review.

INTRODUCTION

Because the significance of the body composition's fat mass component is not recognized, total body weight dosing in obese children increases the risk of dose mistakes. There are few useful dose recommendations for obese children, despite the fact that it is known that fat mass may affect PK parameters like volume of distribution or clearance [1], that the effect of fat mass is drug-specific [1], that weight-based dosing contributes to dose inaccuracies, and that obesity influences disease processes [2,3]. Numerous body weight scales have been used to calculate dosage in obese people, including total body weight, body surface area, optimum body weight, lean body mass, modified body weight, body mass index, fat-free mass, and allometry [4]. Which measure is most appropriate for a certain child is frequently unclear, and it may vary depending on the stage of anesthesia (for example, total body weight for maintenance dose rate and lean body mass for propofol induction dosage) [5-7]. As a result, professional opinion tempers recommendations for any size scaler, assuming that a better understanding of PK will determine the dose in the obese child [3, 8, 9].

An estimated 60 million children are overweight or obese, and the prevalence of juvenile obesity rose from 4.2% in 1990 to 6.7% in 2010 and is expected to reach 9.1% by 2020 [10]. Obesity is predicted to contribute more than sixteen percent of health care spending by 2030 [11], as fat children often grow up to be obese adults [12].

Body weight is occasionally used as a straightforward indicator of adult obesity, but it is challenging to use weight alone to assess obesity in children and adolescents since, in addition to height

growth, body composition also varies quickly throughout this time. The dose [mg kg−1] and interval of a medicine are determined by two important PK factors. In SO children, the volume of distribution (Vd), which establishes a drug's loading dose, is frequently changed [13, 14].

Childhood obesity is increasingly becoming a global health concern and, with rising prevalence, creates unique challenges in medical management. This is especially true when it comes to anesthesia. The characteristic physiological and pharmacological changes that occur with obesity, like changes in fat distribution, cardiac output, and liver and renal functions, impact the PK and PD of anesthetic agents significantly. Despite these complexities, consolidated evidence is still lacking to guide clinicians in the tailoring of anesthetic strategies for obese pediatric patients. A systematic review will bridge this gap by synthesizing the available data and highlighting critical areas that need research and clinical application.

This systematic review analyzes the existing literature on the PD and PK of anesthetic agents in obese children to recognize the key alterations, clinical implications, and strategies that may potentially optimize anesthesia care in this population.

METHODS

Search Strategy

The PRISMA and GATHER criteria were followed for the systematic review. An overall search was conducted to identify relevant studies related to PD and PK of anesthetic agents in obese children. The following four electronic databases were used by the reviewers for searching: SCOPUS, Web of Science, Cochrane, and PubMed. We removed any duplicates and uploaded all the titles and abstracts we could find through electronic searches onto Rayyan. After that, all the study texts that met the inclusion criteria based on the abstract or title were collected for a full-text examination. Two reviewers independently evaluated the extracted papers' suitability and discussed any discrepancies.

Study Population—Selection

The PICO (Population, Intervention, Comparator, and Outcome) factors were implemented as inclusion criteria for our review: (i) Population: Obese children undergoing anesthesia for surgical or diagnostic procedures, (ii) Intervention: Administration of anesthetic agents, (iii) Comparison: Non-obese children receiving similar anesthetic interventions, (iv) Outcome: Implications in PD and PK.

Data Extraction

Data from studies that satisfied the inclusion requirements were extracted by two objective reviewers using a predetermined and uniform methodology. The following information was retrieved and recorded: (i) First author (ii) Year of publication, (iii) Study design, (iv) Country, (v) Sample size, (vi) Age, (vii) Gender, (viii) Anesthetic drug, (ix) BMI, (x) Main outcomes.

Quality Review

Since bias resulting from omitted factors is frequent in studies in this field, we used the ROBINS-I technique to assess the likelihood of bias since it enables a thorough examination of confounding. The ROBINS-I tool can be used for cohort designs where individuals exposed to different staffing levels are tracked over time and is designed to assess non-randomized studies. Each paper's risk of bias was evaluated independently by two reviewers, and any differences were settled by group discussion [15].

RESULTS

The specified search strategy yielded 419 publications **(Figure 1).** After removing duplicates (n = 211), 208 trials were evaluated based on title and abstract. Of these, 181 failed to satisfy eligibility criteria, leaving just 26 full-text articles for comprehensive review. A total of 5 satisfied the requirements for eligibility with evidence synthesis for analysis.

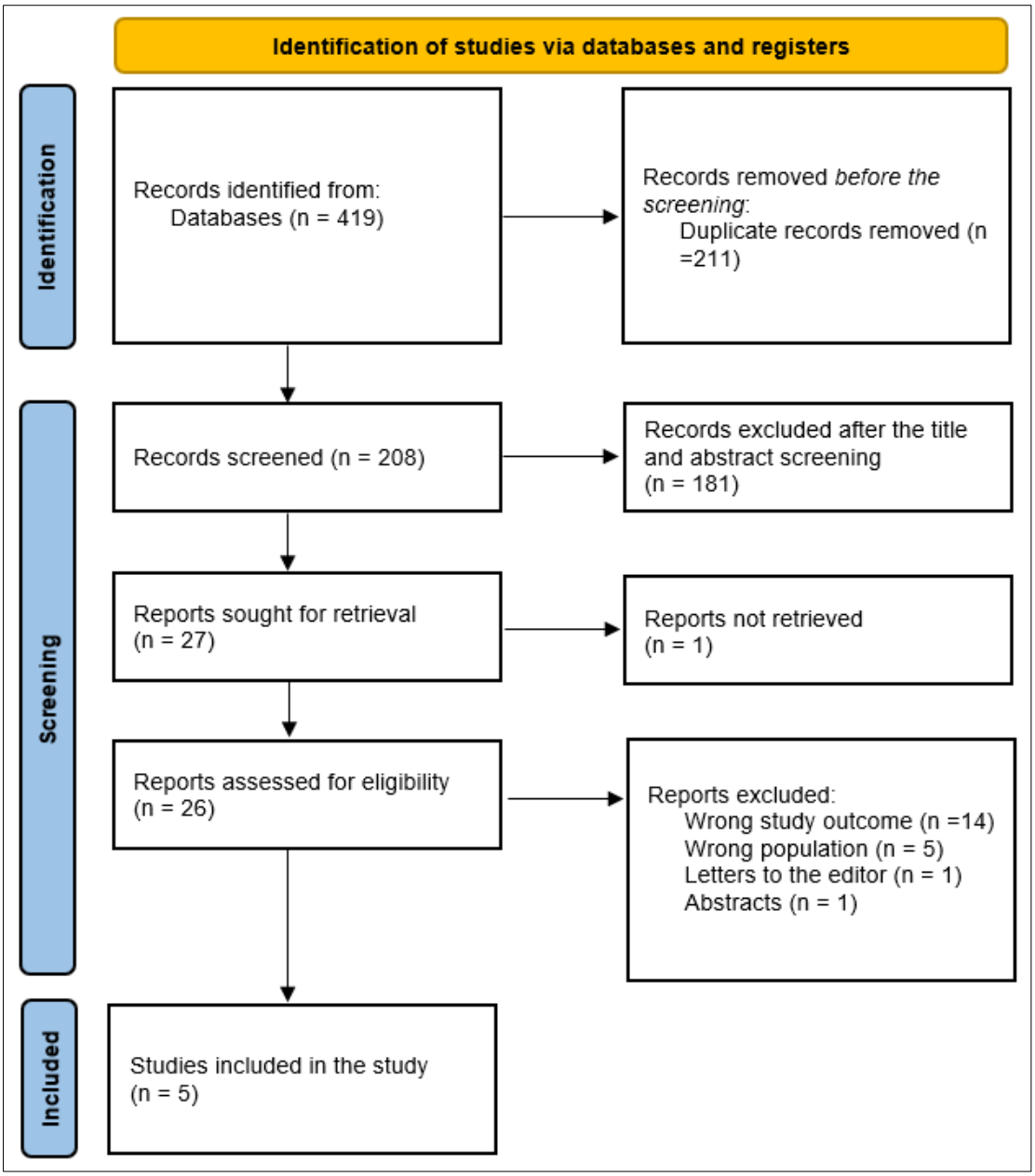

Figure 1: PRISMA flowchart [16]

Sociodemographic and clinical outcomes

We included five studies with a total of 10,570 children and less than half of them 4741 (44.8%) were females. Regarding study designs, four studies were prospective cohorts [18-21] and one was a prospective cohort [17]. The five studies were implemented in the USA. The earliest study was conducted in 2012 [20] and the latest in 2017 [21].

There is a possibility of overdose in obese children as a result of inappropriate dosing practices when using commonly administered anesthetic drugs. In this context, the study found that obese children had 3.5 times the possibility of being overdosed with morphine compared to non-obese children [17]. Three studies investigated the PK of propofol in obese adolescents [18-20]. Their observations showed that the TBBW was a major determinant of drug clearance and indicated the limitation of using solely clinical factors to guide dosing.

Another study pointed the concentration on fentanyl and drew attention to the role of TBW for loading doses while taking into consideration LBW and IBW for maintenance dosing. The study also warned of a great vulnerability in the severely obese patients to fentanyl's respiratory side effects, which pharmacodynamically requires great cautiousness during the dosing of this drug [21].

Table 1: Outcome measures of the included studies

Study ID	Study design	Country	Sociodemographic	Anesthetic drug	BMI (Kg/m^2)	Main outcomes
Burke *et al.,* 2014 [17]	Retrospective cohort	USA	N= 10,498 Mean age: 9.7 Females: 4695 (44.7%)	Midazolam, morphine, cisatracurium, neostigmine, and succinylcholine	39.8	Children who are obese may be at risk of receiving doses of routinely used anesthetic drugs that are higher than what is advised. Children in the obese group were 3.5 times more likely to have gotten an overdose from morphine than children in the control weight group.
Chidambaran *et al.,* 2013 [18]	Prospective cohort	USA	N= 20 Mean age: 15.8 Females: 12 (60%)	Propofol	45.8	The most important factor influencing clearance, according to PK study, was total body weight; no predictive variables for volume of distribution were found. Excessive depth of anesthesia may occur if TIVA and propofol are dosed using solely clinical factors.
Chidambaran *et al.,* 2015 [19]	Prospective cohort	USA	N= 26 Mean age: 15.7 Females: 16 (61.5%)	Propofol	48	This study suggest a dosage regimen for maintaining propofol anesthesia in severely obese adolescents utilizing TBW in an allometric curve with an exponent of 0.75 based on simulations based on the PK/PD model. It is worthwhile to do a prospective clinical investigation to confirm this dosage regimen.
Diepstraten *et al.,* 2012 [20]	Prospective cohort	USA	N= 20 Mean age: 16 Females: 12 (60%)	Propofol	46	TBW was found to be the most important factor influencing clearance in the population PK model for propofol in children and adolescents who

						were morbidly obese. Therefore, it is expected that the dosage of propofol for maintaining anesthesia in children and adolescents who are morbidly obese should be determined by TBW using an allometric function.
Vaughns *et al.,* 2017 [21]	Prospective cohort	USA	N= 6 Age range: 14-19 Females: 6 (100%)	Fentanyl	49.6	Fentanyl loading doses may be determined by TBW, with doses for maintenance based on LBW and IBW. It is important to note that patients who are clinically severely obese are more susceptible to fentanyl's respiratory side effects, and PD should be taken into account when dosing fentanyl.

Table 2: Risk of bias assessment using ROBINS-I

Study ID	Bias due to confounding	Bias in the selection of participants into	Bias in the classification of interventions	Bias due to deviations from the intended interval	Bias due to missing data	Bias in the measurement of outcomes	Bias in the selection of reported result	Overall bias
Burke *et al.,* 2014 [17]	Low	Mod	Low	Low	Low	Mod	Low	Low
Chidambaran *et al.,* 2013 [18]	Mod	Mod	Low	Mod	Low	Low	Low	Low
Chidambaran *et al.,* 2015 [19]	Mod	Low	Mod	Mod	Low	Low	Low	Moderate
Diepstraten *et al.,* 2012 [20]	Mod	Mod	Low	Mod	Low	Mod	Mod	Moderate
Vaughns *et al.,* 2017 [21]	Mod	Low	Mod	Mod	Low	Low	Low	Moderate

DISCUSSION

The PK and PD of anesthetic agents in obese children pose very important challenges due to the pathophysiological changes related to obesity. Findings from this systematic review indicate that TBW, being a principal covariate, is an essential variable for drug clearance and therefore dosing accuracy. Yet, unadjusted weight-based dosing usually leads to overdosing or underdosing with a subsequent potential for adverse effects or insufficient therapeutic effect. For example, weight-based dosing practices of anesthetic drugs, in particular morphine and propofol, illustrate the risks of excessive drug levels and inappropriate anesthesia depth when dosing is guided by purely clinical judgment without the integration of PK models.

In his review, Chidambaran *et al.,* reported that to maximize safe anesthetic management of these

difficult patients, a thorough grasp of the pathophysiological alterations linked to severe childhood obesity, as well as pertinent pharmacologic considerations, weight scalars, and dose guidelines for commonly used anesthetic medicines, is essential [22].

We again highlighted how individual dosing strategies become necessary, especially for a drug like fentanyl, wherein TBW becomes critical for calculating loading doses, and maintenance doses must be guided by LBW and ideal body weight to minimize respiratory side effects. These results underscore the necessity of introducing PD consideration into the dosing regimens in an attempt to protect such unique vulnerabilities in obese pediatric patients. Mortensen *et al.,* also found that because pediatric obesity is becoming more common, there is growing interest in anesthesia for obese children. Comorbidities that are significant to the management of anesthesia are present in many obese children. The PK of the majority of anesthetic drugs are affected by obesity. The dosage ought to be determined by TBW or LBW. Obese children are far more likely to experience problematic mask breathing, intraoperative oxygen desaturation, and airway blockage [23].

This systematic review highlighted the importance of an individualized dosing strategy of anesthetics in obese children. Total body weight was identified as the principal determinant of drug clearance in all studies, whereas LBW and IBW proved important for maintenance dosing. These findings suggest a role of weight-adjusted models in clinical practice to ensure safer and more effective drug administration. For instance, reliance on TBW for initial dosing and adjustment for maintenance based on LBW or IBW can reduce the chances of overdosing, underdosing, or other adverse side effects such as respiratory complications. These approaches point out the importance of PK models and that clinicians should not rely entirely on clinical judgment when making decisions on dosing.

LIMITATIONS

Although this review offers an enlightening overview, there are several limitations that have to be considered. Most of the available studies had small sample sizes, which may not allow the generalization of findings. Moreover, much of the data were from specific geographic regions, raising questions about the generalizability of the data on a worldwide pediatric population with obesity. Finally, although TBW was consistently identified as the key determinant of dosing, other physiological factors-such as fat distribution, hepatic and renal function, and comorbid disease states-were less uniformly evaluated. It further limits understanding of the long-term impact of anesthetic dosing strategies in this population due to a lack of longitudinal data.

Strengths

This review provides the first comprehensive analysis of the PK and PD of anesthetic agents in obese children. It therefore highlights, through the systematic synthesis of evidence across multiple anesthetic drugs, consistent patterns and key variables that influence dosing outcomes. The focus on both PK and PD factors provides a holistic understanding of the challenges and opportunities in optimizing anesthesia care for this vulnerable group. Further, emphasis on clinical applicability has ensured that the findings are directly relevant to practitioners seeking evidence-based solutions.

CONCLUSION

Anesthesia management in the obese child is uniquely different, with specific physiological and pharmacological challenges related to obesity that need to be addressed. This systematic review demonstrates the central role of TBW in guiding dosing strategies, while highlighting the importance of integrating LBW and IBW into maintenance regimens to mitigate risks. While the findings provide valuable guidance, further research is needed to validate these recommendations and develop standardized dosing protocols. The knowledge of the PK and PD processes is further expanded in this population, translating into safety and efficacy optimization in anesthetic care administration to obese pediatric patients.

REFERENCES

1. Greenblatt, D.J.; Bruno, C.D.; Harmatz, J.S.; Zhang, Q.; Chow, C.R. Drug Disposition in Subjects With Obesity: The Research Work of Darrell R. Abernethy. J. Clin. Pharmacol. 2022, 62, 1350–1363.
2. Matson, K.L.; Horton, E.R.; Capino, A.C. Medication Dosage in Overweight and Obese Children. J. Pediatr. Pharmacol. Ther. 2017, 22, 81–83.
3. Kendrick, J.G.; Carr, R.R.; Ensom, M.H. Pharmacokinetics and drug dosing in obese children. J. Pediatr. Pharmacol. Ther. 2010, 15, 94–109.
4. Anderson, B.J.; Holford, N.H. What is the best size predictor for dose in the obese child? Pediatr. Anesth. 2017, 27, 1176–1184.
5. Casati, A.; Putzu, M. Anesthesia in the obese patient: Pharmacokinetic considerations. J. Clin. Anesth. 2005, 17, 134–145.
6. Mulla, H.; Johnson, T.N. Dosing dilemmas in obese children. Arch. Dis. Child. Educ. Pract. Ed. 2010, 95, 112–117.
7. Mortensen, A.; Lenz, K.; Abildstrom, H.; Lauritsen, T.L. Anesthetizing the obese child. Paediatr. Anaesth. 2011, 21, 623–629.
8. Gaeta, F.; Conti, V.; Pepe, A.; Vajro, P.; Filippelli, A.; Mandato, C. Drug dosing in children with obesity: A narrative updated review. Ital. J. Pediatr. 2022, 48, 168.

9. Anderson, B.J.; Holford, N.H. Getting the dose right for obese children. Arch. Dis. Child. 2017, 102, 54–55.
10. de Onis M, Blossner M, Borghi E. Global prevalence and trends of overweight and obesity among preschool children. Am J Clin Nutr 2010;92(5):1257–64.
11. Biro FM, Wien M. Childhood obesity and adult morbidities. Am J Clin Nutr 2010; 91(5):1499S–505S.
12. Wang Y, Beydoun MA, Liang L, Caballero B, Kumanyika SK. Will all Americans become overweight or obese? Estimating the progression and cost of the US obesity epidemic. Obesity 2008;16(10):2323–30.
13. Jain R, *et al.,*Implications of obesity for drug therapy: limitations and challenges. Clin Pharmacol Ther 2011;90(1):77–89.
14. Mahmood I. Prediction of clearance and volume of distribution in the obese from normal weight subjects: an allometric approach. Clin Pharmacokinet 2012;51(8): 527–42.
15. Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, Henry D, Altman DG, Ansari MT, Boutron I, Carpenter JR. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. bmj. 2016 Oct 12;355.
16. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA, Prisma-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Systematic reviews. 2015 Dec;4:1-9.
17. Burke CN, Voepel-Lewis T, Wagner D, Lau I, Baldock A, Malviya S, Nafiu O. A retrospective description of anesthetic medication dosing in overweight and obese children. Pediatric Anesthesia. 2014 Aug;24(8):857-62.
18. Chidambaran V, Sadhasivam S, Diepstraten J, Esslinger H, Cox S, Schnell BM, Samuels P, Inge T, Vinks AA, Knibbe CA. Evaluation of propofol anesthesia in morbidly obese children and adolescents. BMC anesthesiology. 2013 Dec;13:1-9.
19. Chidambaran V, Venkatasubramanian R, Sadhasivam S, Esslinger H, Cox S, Diepstraten J, Fukuda T, Inge T, Knibbe CA, Vinks AA. Population pharmacokinetic–pharmacodynamic modeling and dosing simulation of propofol maintenance anesthesia in severely obese adolescents. Pediatric Anesthesia. 2015 Sep;25(9):911-23.
20. Diepstraten J, Chidambaran V, Sadhasivam S, Esslinger HR, Cox SL, Inge TH, Knibbe CA, Vinks AA. Propofol clearance in morbidly obese children and adolescents: influence of age and body size. Clinical pharmacokinetics. 2012 Aug;51:543-51.
21. Vaughns JD, Ziesenitz VC, Williams EF, Mushtaq A, Bachmann R, Skopp G, Weiss J, Mikus G, van den Anker JN. Use of fentanyl in adolescents with clinically severe obesity undergoing bariatric surgery: a pilot study. Pediatric Drugs. 2017 Jun;19:251-7.
22. Chidambaran V, Tewari A, Mahmoud M. Anesthetic and pharmacologic considerations in perioperative care of obese children. Journal of Clinical Anesthesia. 2018 Mar 1;45:39-50.
23. Mortensen A, Lenz K, Abildstrøm H, Lauritsen TL. Anesthetizing the obese child. Pediatric Anesthesia. 2011 Jun;21(6):623-9.