

PENELITIAN

Risk Factor That Influence The Occuring Of Cardiovascular Complications Post Anesthesia/Sedation Procedure In Pediatrics

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ABSTRACT

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Background: The morphology and physiology of neonates and children differ from those of adults. The most common complications encountered involve respiratory issues followed by cardiovascular problems. The predominant cardiovascular complications in the field of pediatric anesthesia are hemodynamic instability followed by cardiac arrest. Perioperative cardiovascular complications are closely related to a history of prematurity under the age of 1 year, ASA physical status ≥ 3 , concomitant cardiovascular or metabolic diseases, emergency surgeries, and surgical procedures. To date, few risk factors related to the cardiovascular system have been identified in pediatric anesthesia. **Objective:** To identify risk factors influencing the occurrence of post-anesthesia/sedation cardiovascular complications in pediatric patients at Dr. Sardjito Hospital, Yogyakarta. **Method:** The research design employed in this study was a prospective cohort observation of pediatric patients undergoing anesthesia or procedural sedation at Dr. Sardjito Hospital. Research subject data included demographic characteristics, ASA status, history of concomitant diseases, type of surgery, urgency level, and post-anesthesia complication occurrences. Data normality was tested using the Kolmogorov-Smirnov test, bivariate analysis was conducted using the Fisher test, variables with p-value < 0.25 underwent multivariate analysis using logistic regression for categorical data. The results were processed using SPSS version 23.00. **Results:** A total of 181 subjects were predominantly male patients aged > 5 years. Factors influencing post-anesthetic cardiovascular complications included ASA physical status ≥ 3 ($p=0.033$) OR 8.96 (95% CI 2.07 – 38.89), emergency procedures ($p=0.043$) OR 12.63 (95% CI 1.08 – 147.15), age > 5 years ($p=0.033$) OR 5.67 (95% CI 1.15 – 28.1), female gender ($p=0.001$) OR 7.85 (95% CI 2.23 – 27.71), and type of surgical procedure ($p=0.017$) OR 16.64 (95% CI 1.63 – 169.05). **Conclusion:** Age > 5 years, female gender, ASA physical status ≥ 3 , emergency procedures, and surgical procedures are risk factors associated with the occurrence of post-anesthetic/sedation cardiovascular complications in pediatric patients.

Keywords: pediatrics, anesthesia, sedation, cardiovascular complications

Introduction

The morphology and physiology of neonates and children differ from those of adults. These differences include anatomical variations in the size and shape of the airway, incomplete cardiac function, thicker skin, and others. Diseases and responses to various drugs also vary between adults and children within certain age ranges, including psychological conditions in children. These differences suggest that pediatric anesthesia procedures entail higher risks compared to those in adults, potentially leading to unforeseen incidents known as complications. Major complications of pediatric anesthesia procedures include cardiac arrest, brain damage, and death.

The most common complications during surgical anesthesia procedures primarily involve respiratory issues, followed by cardiovascular problems, medication-related issues, communication challenges, equipment-related issues, among others. Previous studies have highlighted the incidence and prevalence of complications during general anesthesia procedures in pediatric patients. A cohort study on pediatric anesthesia complications across 216 hospitals in 33 European countries reported an incidence rate of 5.2% for anesthesia-related complications, with respiratory complications at 3.1%, hemodynamic instability at 1.9%, and cardiac arrest at 0.03%. A case-control study on pediatric anesthesia complications in US hospitals indicated that 67.1% of complications were respiratory, while 10.8% were cardiovascular. Respiratory complications commonly included laryngospasm and bronchospasm, while cardiovascular complications mainly involved hemodynamic instability such as bradycardia, arrhythmia, and hypotension.

The number of pediatric anesthesia and

sedation procedures for minor diagnostic and therapeutic procedures performed outside the operating room has also increased. A study by Apostolidou et al. (2022) reported that the highest incidence of complications occurred in patients under 1 year old (14.9%). The overall complication rate was 6.5% (51 procedures), categorized as respiratory (4.2%) and hemodynamic (1%). The most common complications were apnea (1.7%), airway obstruction (1%), and bradycardia (0.1%). Serious adverse events occurred in 2.7% of cases, with hypotension, desaturation, hypersecretion, hypertension, and laryngospasm being the most frequent.

The cardiovascular system is the first organ system to form and function during the embryonic phase, including the heart. The majority of congenital cardiovascular abnormalities occur during the embryonic phase. At birth, several events occur, such as the closure of the ductus venosus, ductus arteriosus, and foramen ovale. The fetal and neonatal myocardium may have limited active tension in response to increased preload, but neonatal myocardium exhibits greater resting muscle stretch compared to adult myocardium. Normal vital signs vary between full-term and premature infants based on birth weight, as well as infants and children according to their respective ages. Structural and physiological abnormalities in the cardiovascular system also affect its development in children.

Given that the cardiovascular system in children is still developing, the risk factors for cardiovascular complications in children may differ from those in adults. Risk factors influencing perioperative complications in pediatric anesthesia include age, physical status (ASA classification), emergency surgery, and underlying diseases. Children under 1 year

old are at 4.5 times higher risk of perioperative death, decreasing with age by about 3% for each year increase. This is due to the incomplete development of organs in infants, especially premature babies, compared to older children. Clinical conditions indicating the urgency of surgery serve as better predictors of risk than the type of surgery. Several complex diseases in patients vulnerable to complications include burns, heart lesions, airway disorders, obstructive sleep apnea (OSA), neuromuscular diseases, and premature birth.

To date, few risk factors related to the cardiovascular system in pediatric anesthesia have been identified. Therefore, researchers are motivated to address this topic, especially through research at Dr. Sardjito Hospital in Yogyakarta, aiming to identify which risk factors can cause post-anesthesia complications in pediatric patients.

Method

This study is a prospective cohort study involving pediatric patients undergoing anesthesia procedures at Dr. Sardjito Hospital, Yogyakarta. It is part of the overarching research on Factors Influencing Major Complications Post-Anesthesia/Procedural Sedation in Pediatric Patients (Multicenter Study: Peri-Anesthetic Morbidity in Children in Asia - PEACH study) with ethical approval number KE/FK/1673/EC/2022. The data collected include occurrences of post-anesthesia/sedation cardiovascular complications, medical history, anesthesia procedures, and surgical interventions.

The research sample is drawn from the population of pediatric patients admitted to Dr. Sardjito Hospital after obtaining ethical clearance. Following the formula proposed by Riley et al. (2007), the required sample size is

determined to be 181 samples.

Numerical variable data will be presented as means and standard deviations, while nominal or categorical data will be presented as percentages. Normality tests for data distribution will be conducted using the Kolmogorov-Smirnov test, and bivariate analyses will employ Chi-square and Fisher tests for categorical data. Statistical significance is considered if $p < 0.25$ for multivariate analyses, and results are deemed significant if $p < 0.05$.

Multivariate analyses will be performed using logistic regression for categorical data. The incidence of complications will be determined in terms of frequency and percentage relative to the total observed sample.

Results

A total of 181 subjects were included in the study, with the majority falling into the surgical group comprising 132 (72.9%) subjects, while 49 (27.1%) belonged to the non-surgical group. The age category >5 years was the most prevalent in this study (45.9%), followed by 1-5 years at 38.7%, and <1 year at 15.5%. The majority of the research subjects were male (65.2%). ASA physical status ≥ 3 was observed in 14.9% of the subjects in this study. Additionally, 17.7% of subjects had a history of previous heart disease, and 19.9% had a history of premature birth. The most common type of surgery in this study was pediatric surgical operations (25.2%). In terms of urgency level, 2.8% of subjects fell into the emergency category, while 97.2% were categorized as elective procedures.

Bivariate analysis using the Fisher test was conducted due to the categorical nature of the data, and the Kolmogorov-Smirnov test indicated non-normal data distribution.

Table 1. Characteristics Demographics Subject Study

Variable		Median (minimum- maximum)	n	%
Age	<1 year		28	15.5
	1-5 years		70	38.7
	>5 years		83	45.9
Gender	Man		118	65.2
	Woman		63	34.8
TB (cm)*		104.5 (50-170)		
BB (kg)*		18 (3-64)		
ASA \geq3	Yes		27	14.9
	No		154	85.1
History of Prematurity	Yes		36	19.9
	No		145	80.1
Asthma	Yes		0	0
	No		181	100
OSA	Yes		9	5
	No		172	95
ISPA	Yes		16	8.8
	No		165	91.2
History of illness heart	Yes		32	17.7
	No		149	82.3
Abnormalities congenital	Yes		47	25.9
	No		134	74.1
Type procedure	Surgery		132	72.9
	Non surgical		49	27.1
Type of surgery	Pediatric Surgery		34	18.8
	Vascular Surgery		1	0.6
	Surgery eye		13	7.2
	Surgery mouth		8	4.4
	Oncology		1	0.6
	Orthopedics		19	10.5
	Surgery plastic		17	9.4
	Neurosurgery		9	5
	ENT		5	2.8
	Urology		25	13.8
Degrees urgency	Emergency		5	2.8
	Elective		176	97.2
Complications Anesthesia			18	9.9

in Cardiovascular		
Arrhythmia (Tachycardia)	3	1.7
Hypotension	6	3.3
Hypertension	0	0
Bleeding	15	8.3
Amount Bleeding (%EBV)*	0-156	

* served in the median and (minimum – maximum) because data distribution does not normal

Table 2. Analysis bivariate and multivariate factors _ risk to complicationscardiovascular

Risk Factors	Complications		Bivariate	Multivariate			
	Yes n (%)	No n (%)	p	p	OR	CI 95%	
Age	<1 year	3 (16.7)	26 (16)	0.116**			
	1-5 years	3 (16.7)	66 (40.5)		0.526	1.86	0.24 – 12.56
	>5 years	12 (66.7)	71 (43.6)		0.033 *	5.67	1.15 – 28.1
Gender _	Man _	7 (38.9)	111 (68.1)	0.014*			
	Woman	11 (61.1)	52 (31.9)		0.001 *	7.85	2.23 – 27.71
History of Prematurity	Yes	5 (27.8)	31 (19)	0.362			
	No	13 (72.2)	132 (81)				
ASA ≥3	Yes	6 (33.3)	21 (12.9)	0.033*	0.003 *	8.96	2.07 – 38.89
	No	12 (66.7)	142 (87.1)				
ISPA	Yes	1 (5.6)	15 (9.2)	1,000			
	No	17 (94.4)	148 (90.8)				
Degrees urgency	Emergency	3 (16.7)	2 (1,2)	0.007*	0.043 *	12.63	1.08 – 147.15
	Elective	15 (83.3)	161 (98.8)				
OSA	Yes	2 (11.1)	7 (4.3)	0.221**	0.09	6.06	0.75 – 48.5
	No	16 (88.9)	156 (95.7)				
History of illness heart	Yes	3 (16.7)	29 (17.8)	1,000			

	No	15 (83.3)	134 (82.2)				
Abnormalities congenital	Yes	4 (22.2)	37 (22.7)	1,000			
	No	14 (77.8)	126 (77.3)				
Type procedure	Surgery	17 (94.4)	115 (70.6)	0.046*	0.017	16.64	1.63 – 169.05
	Non Surgical	1 (5.6)	48 (29.4)		*		
Type of surgery	Pediatric	7 (41.2)	27 (23.5)	0.320			
	Surgery						
	Vascular Surgery	1 (5.9)	0 (0)				
	Surgery eye	0 (0)	13 (11.3)				
	Surgery mouth	0 (0)	8 (7)				
	Oncology	0 (0)	1 (0.9)				
	Orthopedics	3 (17.6)	16 (13.9)				
	Surgery plastic	2 (11.8)	15 (13)				
	Neurosurger	1 (5.9)	8 (7)				
	Y –						
	ENT	0 (0)	5 (4.3)				
	Urology	3 (17.6)	22 (19.1)				

*) significant $p < 0.05$, Fisher exact test

** variable with $p < 0.25$ in the analysis bivariate next with multivariate tests with regression testing logistics OR: Odds Ratio
CI 95%: Confidence Interval 95%

The bivariate analysis results in Table 6 showed that gender ($p=0.014$), ASA physical status ≥ 3 ($p=0.033$), urgency level ($p=0.007$), and procedure type ($p=0.046$) had an influence on the occurrence of cardiovascular complications.

Variables with p -values < 0.25 in the bivariate analysis were further analyzed using multivariate logistic regression. The results of the multivariate analysis indicated that ASA physical status ≥ 3 ($p=0.033$) with an odds ratio of 8.96 (95% CI 2.07 - 38.89) and urgency level (emergency procedures) with a p -value of 0.043

and odds ratio of 12.63 (95% CI 1.08 - 147.15) were significant risk factors. Age > 5 years also showed a p -value of 0.033 with an OR of 5.67 (95% CI 1.15 - 28.1), female gender with a p -value of 0.001 and OR of 7.85 (95% CI 2.23 - 27.71), as well as surgical procedure type with a p -value of 0.017 and OR of 16.64 (95% CI 1.63 - 169.05), significantly influenced cardiovascular complications. This implies that pediatric patients aged > 5 years, female gender, ASA physical status ≥ 3 , and urgency level (emergency procedures), as well as surgical procedures, are at higher risk of experiencing post- anesthesia cardiovascular

complications.

Discussion

This study aims to identify factors that influence cardiovascular complications in pediatric patients undergoing anesthesia/sedation at RSUP Dr. Sardjito. The research design used in this study was a prospective observational cohort study. Cardiovascular complications in this study occurred at 9.9% with the most types of cardiovascular complications occurring in the bleeding category at 8.3%, hypotension at 3.3%, arrhythmia (tachycardia) at 1.7%. This research is in line with research conducted in a prospective cohort study examining pediatric patients undergoing anesthesia. The risk factors that influence complications are infant age category, ASA 3 and 4 physical status, degree of urgency (emergency action). Cardiovascular complications were 13% with an incidence of hypotension of 38%⁸ APRICOT study proposed by Habre et al³ on 549 research subjects, Major risk factors that influence cardiovascular complications include age <1 year, ASA physical status, type of surgery, male gender, history of prematurity. The most common types of cardiovascular complications were hypotension 54.9%, arrhythmia 19.5% and bleeding 16%. This is different from previous research which showed that arrhythmias were the most frequent cardiovascular complication in pediatric patients, which may be due to the change in the use of inhalation anesthetics (halothane) to more modern inhalation anesthetics (sevoflurane)⁸

The results of the multivariate analysis showed that the risk factor variable was ASA physical status ≥ 3 ($p=0.033$) with an OR value of 8.96 (CI 95% 2.07 – 38.89) and the degree of urgency (emergency action) had a value of $p=0.043$ with an OR value amounted to 12.63

(CI 95% 1.08 – 147.15). Age > 5 years also obtained a p value = 0.033 with an OR of 5.67 (CI 95% 1.15 – 28.1), female gender with a value of $p = 0.001$ with an OR of 7.85 (CI 95% 2.23 – 27.71), as well as surgical procedures with a value of $p=0.017$ with OR 16.64 (CI 95% 1.63 – 169.05) have a significant effect on cardiovascular complications. This means that pediatric patients with these risk factors are at high risk of cardiovascular complications after anesthesia. The majority of subjects with ASA physical status ≥ 3 in this study had cyanotic congenital heart disease such as tetralogy of Fallot and acyanotic congenital heart disease with valve abnormalities. Other accompanying conditions in subjects with ASA physical status ≥ 3 are congenital abnormalities such as laryngomalacia, microcephaly with neurological disorders, and epidural bleeding conditions. In this study, 2 of 4 subjects (50%) were found to have a history of previous heart disease and a history of OSA in the surgical group who experienced cardiovascular complications. Patients with a high ASA physical status are known to be an individual risk factor for an increased incidence of perioperative complications, because at an ASA status ≥ 3 the condition of patients with severe systemic disease.^{9,10} Similar research conducted by Engelhardt et al 2018, in the APRICOT study in England, showed ASA physical status ≥ 3 has a 4.54 times higher risk compared with ASA physical status 1 and 2 (CI 95% 2.83-7.28; $p<0.001$) for the incidence of cardiovascular complications in pediatric patients undergoing anesthesia in the UK Comorbidities, as reflected by a high ASA score, are the strongest predictor of risk of cardiovascular complications including cardiac arrest and death, especially for children with congenital heart disease¹¹

The degree of urgency (emergency action) was also found to be a significant

variable in causing cardiovascular complications after anesthesia with an OR of 12.63 ($p=0.043$). These results are in line with research by Cronje et al which found that emergency surgery was a risk factor for cardiovascular complications in pediatric patients after sedation with an OR of 1.35 (1.02-1.78 CI 95%) ($p = 0.036$). Emergency surgery is a serious condition that can be life threatening, often triggering a stress response in the body, the hormone cortisol and other stress hormones can affect cardiovascular balance. Medical procedures in emergency surgery are actions that require careful assessment and careful anesthetic management because the patient is often in a vulnerable condition.¹²

Age >5 years in this study, is a risk factor that influences cardiovascular complications after anesthesia with an OR of 5.67 CI 95% 1.15 – 28.1 ($p=0.033$). This research is in line with previous research by Habre et al in 2017 which showed that the incidence of critical incidents in the respiratory and cardiac systems was much higher in children up to the age of 6 years, with the average age of those experiencing cardiovascular complications being 5.9 years. It is not clear why age was a significant risk factor in this study.

In this study, gender was a risk factor associated with the incidence of cardiovascular complications after anesthesia with an OR value of 7.85 CI 95% 2.23 – 27.71 ($p=0.001$). The highest incidence of cardiovascular complications in this study occurred in 11 girls (61.1%) compared to only 7 boys (38.9%). This is not in line with research conducted by Habre et al in 2017 in a large population that male subjects with a $p=0.0002$ RR value of 0.74 (CI 95%

0.64 – 0.87) experienced cardiovascular complications. Research that focuses on discussing gender variables that influence cardiovascular complications after anesthesia

in pediatrics is still rarely conducted. Several factors that may influence female gender in the context of post-anesthesia complications in children involve biological, hormonal conditions and response to medical care. Factors that can be considered such as differences in body weight and body composition between boys and girls can influence the distribution and metabolism of anesthetic drugs in the body. Some studies suggest that girls may have a higher stress response to medical situations than boys. Stress is defined as a stimulus that causes an imbalance in an organism that threatens homeostasis. When the human body faces stress such as injury or trauma, the hypothalamic-pituitary-adrenal (HPA) axis and sympathetic nervous system become active and various metabolic, endocrinological and immune system responses occur. Genetic factors and differences in the immune systems of boys and girls may contribute to the risk of post-anesthesia complications. Hormonal factors; The average age of menarche in girls is 10 -16 years.¹³ In this study, it was found that subjects aged ≥ 10 years (36.4%) were 4 out of 11 girls experiencing cardiovascular complications. In post-pubertal children, hormones in the body, such as estrogen, progesterone, and cortisol, can influence various aspects of the cardiovascular system, nervous system, and inflammatory response, all of which can impact how the body responds to anesthesia.

Obstructive Sleep Apnea (OSA) is a health problem that occurs in 1% – 6% of pediatric patients. The incidence will increase to 59% in children with obesity. OSA is a known risk factor for adverse perioperative complications including bronchospasm, laryngospasm, airway obstruction, pulmonary edema and desaturation. The risk of complications in the respiratory tract in OSA

patients increases to 20%.¹⁴ The OSA history variable in this study showed insignificant results, which is possible because this study examined the incidence of complications related to the cardiovascular system, while the incidence of complications related to the respiratory tract in this study was not assessed.

Many problems in the condition of babies with premature birth are found, such as temperature regulation disorders such as hypothermia, respiratory distress, bronchopulmonary dysplasia, apnea, closure of the arterial duct in premature babies with a gestational age of 30 weeks or more found at 96 hours after birth. However, in 70-80% of small premature babies, the ductus arteriosus often remains open, which can cause symptoms. The results obtained in this study, a history of prematurity is not a predictor/determinant of cardiovascular complications ($p=0.362$). In contrast to research by Habre et al which showed a history of prematurity at birth associated with cardiovascular complications with a p value <0.0001 which was possible because there were differences in the proportion of research subjects in the large population of 31,127 pediatric patients who received anesthesia. Another thing that is possible is that this study did not classify the gestational age at birth in subjects who had a history of premature birth, as it is known that babies born with a gestational age of <28 weeks (extremely premature infants) cause many problems that will increase the risk of morbidity and mortality to reached 70%.⁵ This is a limitation in this study, because it only assesses whether or not there is a history of premature birth.

Conclusion

Based on this study, age >5 years, female gender, ASA physical status ≥ 3 , urgency level (emergency procedures), and surgical

procedures are associated with the occurrence of post- anesthesia/sedation cardiovascular complications in pediatric patients.

Recommendations

Exploration with a larger sample size and a broader population across hospitals with different types is needed regarding the incidence of anesthesia complications. This would serve as a basis for creating a scoring system as predictors of anesthesia complications and risk management to avoid complications resulting from anesthesia procedures, especially in Indonesia, where research on anesthesia complications in pediatric patients is still lacking.

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