ASSESSMENT OF INCIDENCE OF ADVERSE EVENTS AND ASSOCIATED FACTORS IN PEDIATRICS OUT OF OPERATING ROOM PROCEDURAL SEDATION AT TIKUR ANBESA SPECIALIZED HOSPITAL, ADDIS ABABA IN 2022/2033.

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Educational Research and Ethical Standards

By
Addisu Bekele
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ASSESSMENT OF INCIDENCE OF ADVERSE EVENTS AND ASSOCIATED FACTORS IN PEDIATRICS OUT OF OPERATING ROOM PROCEDURAL SEDATION AT TIKUR ANBESA SPECIALIZED HOSPITAL, ADDIS ABABA IN 2022/2023

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APPROVED BY THE BOARD OF EXAMINATION

The thesis here, entitled " Assessment of incidence of adverse events and associated factors in pediatrics out of operating room procedural sedation in Tikur Anbesa specialized hospital, Addis Ababa, Ethiopia" is accepted in its present form by the board of examiners as partial fulfillment of the requirement for specialty certificate In Anesthesiology, critical Care and pain Medicine.

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STATEMENT OF DECLARATION

I hereby declare and affirm that this research is my own original work as a partial fulfillment of the requirements for the specialty certificate training in Anesthesiology. I have followed all the ethical considerations in the preparation, data collection, data analysis and completion of this research. All the sources of the materials used for this research and all people and institutions who gave support for this work are fully acknowledged. I affirm that I have cited and referenced all the sources used in this document.

There is no conflict of Interest.

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Name: _____ Signature _____Date _____

Acknowledgment

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Contents

Abbreviations and acronyms

AAU ---------- Addis Ababa University

AEs ---------- Adverse events

ASA ---------- American society of anesthesiologists

BMA----------Bone marrow aspiration

OR ----------Operating theatre

PPS----------Pediatrics procedural sedation

PSA---------- Procedural sedation &analgesia

SAEs----------Severe adverse events

SPSS---------- Statistical package for social sciences

TASH……Tikur Anbessa Specialized Hospital

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Summary

Background Procedural sedation and analgesia (PSA) describe the use of agents, such as sedatives and analgesics, to alleviate anxiety, pain, and fear during diagnostic and therapeutic procedures. Pediatric out of OR (operating theatre) procedural sedation is expanding throughout the world as well as in our setup. Children require sedation more often than adults and they are at the greatest risk of adverse events due to their physiology. Complications include hypoxia, vomiting, laryngospasm, and cardiac arrest. There is no single ideal sedative agent without risk. Despite the magnitude, there is no single study done in Ethiopia.

Objectives To assess the incidence of adverse events in pediatrics out of OR procedural sedation and associated risk factors in Tikur Anbessa specialized hospital.

Methods Institutional-based cross-sectional study design was in TASH (Tikur Anbessa specialized hospital) conducted from December 2022 – March 2023. The final sample size was 269. Simple convenient sampling technique was used as a sampling technique. Data was checked for completeness and then entered in to SPSS 26 software for analysis. Descriptive analysis was done for socio-demographic, surgery and anesthesia related characteristics of the study participants. Bivariate logistic regression was done for each predictor variable and outcome variable. Multivariable logistic regression was done for variables with P- value less than 0.25 and statistical significance P- value less than 0.05 was taken as a determinant factor.

Results Overall, the prevalence of adverse events in pediatrics out of OR procedural sedation was 9.2% (n=20). Respiratory adverse event was the most common adverse event occurring in 15 (6.9%) patients. the odds of developing respiratory adverse events is 10.27 times higher among patients who had moderate or severe malnutrition as compared to those who had normal nutritional status (AOR= 10.27;95%CI 3.21, 32.8; p<0.001.

Conclusion and recommendation Malnutrition is associated with the occurrence of respiratory adverse events in pediatrics out of OR procedural sedation. Careful evaluation and optimization of pediatric patients with malnutrition is necessary.

1. Introduction

1.1 Background

Procedural sedation and analgesia (PSA) describes the use of agents, such as sedatives and analgesics, to alleviate anxiety, pain, and fear during diagnostic and therapeutic procedures[1]. Given that children can suffer short- and long-term physical, physiological, and psychological effects from untreated pain, providing procedural pain and anxiety relief is essential in the care of children [1]. Procedural sedation and analgesia must include proper pain management. Procedure-related sedation aims to lessen a patient's fear, anxiety, and distress while limiting physical pain, and psychological trauma, preserving control of physiological parameters, and guaranteeing patient since insufficient pain control in the pediatric population has the potential to have long-lasting deleterious effects.[2] There are several levels of procedural sedation. It starts with light sedation, progresses to moderate and severe sedation, and culminates with the induction of general anesthesia[3]. To prevent accidental deeper levels of drowsiness, sedation should be thought of as a dose-dependent shift in the state of consciousness that should be adjusted based on the patient's response. Moderate to deep sedation is frequently used to facilitate diagnostic and therapeutic treatments; the patient or the operation determines the intended level of sedation needed. Unfortunately, no single safe sedative presently exists that meets all the requirements for becoming the ideal PSA modality.[2]

Commonly used drugs in our setup are ketamine, propofol and fentanyl either in combination or alone. Propofol, because of its pharmacological properties like quick onset and short duration of action, is the preferred sedation agent either alone or in combination with fentanyl or ketamine, allowing for rapid turnover of patients and optimal sedation[4]. Pediatric out of OR procedural sedation is expanding throughout the world. In our hospital it is being performed for BMA (bone marrow aspiration) , for oncologic radiotherapy, to facilitate radiologic imaging and in pediatrics emergency for different procedures by anesthetists and anesthesiology residents.

1.2 Statement of the problems

Sedation and anesthesia are more frequently used for pediatric patients than for adults. In addition, children need "deeper" sedation/anesthesia than adults do in order to create favorable "conditions" during a procedure. Most important, because of their physiology, children are at higher risk for respiratory depression and life-threatening hypoxia.[5] Sedation-related minor adverse events are complications during PPS, which are easily handled, and not expected to be associated with any squeal. Serious adverse events include aspiration, airway obstruction, laryngospasm, emergent airway interventions, cardiac arrest, and death.[4] Though Sedation is regarded as safe, it has been associated with serious adverse events (SAEs). The incidence of SAEs has been difficult to determine because of their infrequent occurrence and the lack of large, multicenter surveillance studies focused on systematic detection of adverse events [4].

1.3 Significance of the study

Although the risks and adverse outcomes of conventional operating room and ambulatory anesthesia are well delineated, the opposite is true for the field of out-of-operating room anesthesia. Studies in out-of-operating room locations have focused mainly on sedation regimens for specific procedures at specific sites, organizational prerequisites, and patient satisfaction, but little on sedation-related morbidity and mortality[6].

Since there is no single study done in this area in our setup, we aim to study the incidence of adverse events and associated risk factors in pediatrics out of OR procedural sedation. This study will be important to identify pattern of common complications encountered and risk factors in our setup so that we can optimize resources and outcomes. It will also be taken us a baseline for future studies in our set up.

2 .Literature review

In a multicenter retrospective analysis done in Cleveland from 2007 to 2011 published2015 20, 30 children under the age of 21 underwent procedural sedation out of operating theatre for esophagogastroduodenoscopy and colonoscopy. The prevalence of any adverse event was 4.8%, the most common being persistent desaturation. Age 5 years old or younger, ASA classification greater than or equal to 2, and coexisting medical conditions of obesity and lower airway disease were independent predictors of a higher adverse event.[7] Green et al. Published in 2009, a meta-analysis of articles from 1996 to 2008 across USA and Europe 8,282 emergency pediatric ketamine sedations, the overall incidence of airway and respiratory adverse events was 3.9%. independent predictors were age < 2 years, age 13 years or higher, high intravenous dosing (initial dose 2.5 mg/kg or total dose 5.0 mg/kg, co-administered anticholinergic and benzodiazepines[8]. Roback et al published in 2004 a retrospective study done from 1996 – 2003 in Colorado USA, comparison of common parentral drugs; a total of 2,500 pediatrics patients who were given parenteral sedation at the emergency department given by emergency physicians were enrolled. A total of 458 adverse events were observed in 426 patients (17%). Respiratory adverse events occurred as follows: ketamine alone, (6.1%); ketamine/midazolam, (10%); midazolam/fentanyl, (19.3%); midazolam alone, 15 patients (5.8%). Vomiting occurred as follows: ketamine alone, (10.1%); ketamine/midazolam, (5.4%); midazolam/fentanyl, (1.8%); midazolam alone, (0.8%)[9].

Another prospective, multicenter, observational cohort study was conducted in 6 pediatric emergency departments in Canada between July 10, 2010, and February 28, 2015. 6,760 Children 18 years or younger who received sedation for a painful emergency department procedure were enrolled in the study. The incidence of adverse events was 11.7%, Oxygen desaturation [5.6%]) and vomiting [5.2%]) were the most common of these adverse events. The combination of ketamine and fentanyl or ketamine and propofol had the greatest adverse events compared to ketamine alone[10].

CRAVERO et al. published 2006 a large multi-center prospective study on incidence and adverse events of pediatric out of operating theatre procedural sedation/anesthesia. In 26 institutions in Europe, Australia, the United States, and Canada a total of 30,037 patients enrolled. The overall incidence of adverse events was 5.3%. desaturation < 90% 15.7% ,

vomiting 4.7% excessive secretions 4.1% laryngospasm and stridor 0.4%, failed sedation 8.9% [5].

Single center prospective observational study on Independent risk factors for adverse events associated with Propofol-based pediatric sedation performed by anesthesiologists in the radiology suite in South Korea 2020; Among 2569 children < 18 years, 3.9% experienced respiratory problems related to the sedation. Cardiac and neurologic comorbidities, crying before sedation, a history of snoring or upper respiratory infection, and prolonged duration of sedation was independently associated with the occurrence of adverse respiratory events [11].

A prospective observational cohort study in Thailand, 2015 on incidence and risk factors for adverse events during anesthesiologist-led sedation or anesthesia for diagnostic Imaging in children 1,042 children < 15 years of age enrolled. Adverse events were recorded in 254 (24.4%, Adverse respiratory events occurred in 31 (3.0%), cardiovascular events in 7 (0.7%), sedation was prolonged in 165 (15.8%), there was one case of contrast allergy (0.01%), and there were 50 other minor complications (4.9%). Of the respiratory complications, there were 14 of airway obstruction (1.3%), 2 of apnea (0.2%), 14 of oxygen desaturation (1.3%), and one of laryngospasm (0.01%). Age < 1yr, ASA 2 or 3 were risk factors for respiratory complications[11].

Single center retrospective observational study done in Srilanka tertiary university teaching hospital in 2015 over 06 months, 249 children {median age of 22months}, procedural sedation given by pediatricians. Patients ASA classification was <3 and medications were IV midazolam, IV dexmedetomidine, and oral chloral hydrate. Serious adverse events were reported only in 3 patients (1.2%), oxygen desaturation requiring oxygen was 8.4%, and agitation/delirium 52 (20.9%)[4].

ROGERSON et al a single center retrospective observational study done in Indiana, published in 2016; analyzed 1976 patients ages 2 to 21 years old with oncologic diagnoses who underwent lumbar punctures and/or bone marrow aspirations.

Procedural sedation ketamine 0.5mg/kg followed by intermittent boluses of propofol administered. The results were children who were obese required less doses of propofol, and the incidence of adverse events was significantly higher in underweight children (Wt

for age <5%) 10.6%, while 4% in normal weight and obese children. The common adverse events were hypoxia, apnea , bradycardia, and hypotension[12].

Studies in Africa are scarce. A single-center prospective observational study was done in South Africa's Cape Town tertiary children's hospital in 2020. Over 3 months from all procedural out-of-theatre sedations performed, including ward patients and outpatient departments. All children <13 years of age were included. The reported incidence of airway obstruction was 4.9% (n=14/288), desaturation 4.2% (n=12/288), laryngospasm 0.3% (n=1/288) and nausea and vomiting 2.4% (n=7/288). Three cases required conversion to general anesthesia, and four cases were abandoned as a result of inadequate sedation[2].

3.0. Objectives

3.1. General objectives

- To assess the incidence of adverse events in pediatrics out of OR procedural sedation and associated factors in Tikur Anbessa specialized hospital in 2022/2023GC

3.2 specific objectives

- To study socio-demographic status and type of procedure done
- To determine the incidence of adverse events
- To determine associated risk factors

4.0 Method

4.1 Study design

A single-center prospective analytic cross-sectional survey

4.2 study area and period

The study was conducted at Tikur Anbessa specialized hospital (TASH). TASH is located in central part of Addis Ababa city, the capital of Ethiopia. Addis Ababa is found at 901'48" N, 380 44'24"E and 2355m above sea level. Addis Ababa has estimated population of 4.7 million by 2020 G.C TASH hospital is a tertiary hospital that gives services for referral cases from other specialized referral hospitals throughout the country.

Pediatrics procedural sedations are performed for bone marrow aspiration, radiology imaging, and oncology for radiotherapy services and pediatric emergency sedations for different procedures.

The study was conducted from December 2022 to March 2023.

4.3. Population

4. 3.1 source population

All pediatric patients who undergone procedural sedation at Tikur Anbessa hospital

4.3.2 Study population

All Pediatric patients who had undergone out-of-OR procedural sedation who fulfilled inclusion criteria during the study period at Tikur Anbessa hospital.

4.4 Inclusion and Exclusion criteria

4.4.1 Inclusion criteria

Pediatric patients age <18 years undergoing out of –OR procedural sedation during the study period

4.4.2 Exclusion criteria

Patients who had sedation in the Major operating theatre

4.5 sample size

A single population proportion formula was used to calculate the sample size (n) by considering the following statistical assumptions: the incidence of any adverse event for pediatrics out of operating room procedural sedation is (20%) which is taken from a study conducted in Cape town children's tertiary hospital (South Africa)[2] . Assuming a 95% confidence interval, 5% margin of error (d), and adding a 10% nonresponse rate

The formula for calculating the sample size (n) is:

$$N = \frac{z^2_{1-\frac{\alpha}{2}} \times p \times (1-p)}{d^2}$$

Where:

N= Initial estimated sample size

Z = Confidence level (alpha, α), 1.96

P = prevalence from previous study (20%),

d= marginal error (0.05)

N= (1.96)2* 0.2*0.8/ (0.05)2 = 245

Adding 10% non-respondent final sample size = 269

4.6 sampling method

Using a convenient sampling method, samples available during the study period were selected.

4.7 study variable

5.7.1 Dependent variable

Adverse events

4.7.2 Independent variable

Age, Sex, Type of procedure, ASA class, nutritional status, comorbidities, level of sedation, anesthetic medication used.

4.8 operational definition

Procedural sedation - the use of anxiolytic, sedative, hypnotic, analgesic, and/or dissociative medication(s) to attenuate anxiety, pain, and/or motion

Adverse events - Unexpected and undesirable response(s) to medication(s) and medical intervention used to facilitate procedural sedation and analgesia that threaten or cause patient injury or discomfort.

Sentinel AEs are the most serious and represent those critical enough to pose a real or major imminent risk of patient injury or death

Moderate AEs while not sentinel, are serious enough to endanger the patient if not promptly managed

Minor AEs encountered periodically in most sedation settings that pose little threat or danger of permanent harm to the patient, given appropriate sedation care provider skills and monitoring.

Respiratory adverse event - any episode of single/combination of coughing, breathe holding, hypoxemia, laryngospasm and bronchospasm.[13]

Oxygen desaturation- severe or prolonged (defined as any oxygen saturation, 75% or oxygen saturation, 90% for .60 s)

Intervention- measures performed with the intent of treating adverse event

Pediatrics - age < 18years

Upper airway obstruction – partial or complete obstruction responsive to repositioning or airway placement

Laryngospasm – partial /complete not responsive to airway repositioning or airway placement.

Paradoxical response - unanticipated restlessness or agitation in response to sedatives

Recovery agitation - abnormal patient affect or behaviors during the recovery phase that can include crying, agitation, delirium, dysphoria, hallucinations, or nightmares

Failed sedation - inability to attain suitable conditions to humanely perform the procedure

Prolonged recovery- failure to return to baseline clinical status within 2 hours.

Alteration in vital signs (bradycardia, tachycardia, hypotension, hypertension) is defined as a change of >25% from baseline.

Nutritional status -Indicator and cut-off value compared to the median of the WHO child growth standards.[14]

Moderately underweight - Weight-for-age < ‑ 2 SD and ⩾ ‑ 3 SD of the median

Severely underweight-Weight-for-age <–3 SD of the median

ASA Class – physical status to assess and communicate a patient's pre-anesthesia medical co-morbidities[15].

4.9 data collection, analysis and Interpretation

The data was collected using online Kobo toolbox questionnaire as well as hard copy questionnaire and cleaned and entered it to SPSS 26 26 version and Coded. Descriptive statistics including (percentage and frequency) and analytic statistics were used. Tables and

graphs were used for data presentation. Binary logistic regression was used to identify an association between the dependent and independent variables. Variables with a p-value < 0.25 on binary logistic regression analysis were subjected to logistic multivariable regression analysis. The variables which have an independent association with poor outcomes were identified and reported with OR, with 95% CI and a p-value less than 0.05.

4.12 Ethical issue

Ethical clearance and support letter was obtained from Addis Ababa University College of Health Science Institution of Review Board and submitted to Tikur Anbessa Comprehensive Specialized Hospital Chief Clinical and Academic Director Offices. Verbal informed consent was obtained from the participants after an explanation is given on the objective, procedure, potential risks and benefits of participating in the study and the right to withdraw from the study at any time throughout their interview.

5. Results

5.1 Socio-demographic data

A total of 218 cases were included in the cross sectional study, among which 120 (55%) were males and 98 (45%) females. The age of the participant's ranged from 6 months to 14 years of age with a mean age of 5.17±3.6 years. Among the study participants, majority 175 (80.3%) had normal nutritional status and the rest 32 (14.7%) and 11 (5%) had moderate and severe nutritional status, respectively. Almost half of the participants 106 (48.6%) were ASA class III, and the rest 92 (42.2%) and 20 (9.2%) were ASA class II & ASA class I, respectively. (Table 1)

Table 1Socio-Demographic and Clinical Data of Pediatrics Patients out of Operating Room Procedural Sedation at TASH, Addis Ababa, Ethiopia, 2023

Variable	Category	Frequency n	Percent %
Age - IQR (Median±SD)	6 month – 14 years, (5.17±3.6 years)		
Age categories	≤ 1 year	15	6.9
	1 to ≤5 year	121	55.5
	5 to ≤10 year	51	23.4
	>10 year	31	14.2
Sex	Female	98	45.0
	Male	120	55.0
Malnutrition	Normal	175	80.3
	Moderate	32	14.7
	severe	11	5.0
NPO status	<6 hrs.	25	11.5
	>6 hrs.	193	88.5
Comorbidity	Yes	197	90.4
	No	21	9.6
ASA classification	I	20	9.2
	II	92	42.2
	III	106	48.6

5.2 Primary Diagnosis

The most common primary diagnosis was Hematologic Malignancy with 96 (44%) of the study participant's, followed by Retinoblastoma 25 (11.5%), Wilms Tumor 22 (10.1%) and non-Hodgkin's lymphoma 21 (9.6%). (Table 2)

Table 2Description of Primary Diagnosis of Pediatrics Patients out of Operating Room Procedural Sedation at TASH, Addis Ababa, Ethiopia, 2023.

Diagnosis	Frequency	Percent
Brain tumor	12	5.5
Burkitt's lymphoma	1	0.5
Chronic Gastroenteritis	5	2.3
Congenital anemia	3	1.4
Esophageal Stricture	2	0.9
esophageal varices	1	0.5
Hematologic Malignancy	96	44.0
Hemophilia	1	0.5
Hodgkin's lymphoma	5	2.3
IGA nephropathy	1	0.5
Lymphoma	2	0.9
Neuroblastoma	4	1.8
Non-Hodgkin's lymphoma	21	9.6
Pulmonary Embolism	1	0.5
Prominent payer's patches	2	0.9
Rectal bleeding	1	0.5
Rectal polyp	2	0.9
Renal mass	2	0.9
Retinoblastoma	25	11.5
Rhabdomyosarcoma	2	0.9
Sarcoma	3	1.4
sliding hiatal hernia	1	0.5
Ulcerative Colitis	1	0.5
Upper GI bleeding	2	0.9
Wilms tumor	22	10.1
Coexisting medical conditions	CHD	3
	Down Syndrome	1
	URTI	1
	None	213

5.3. Description of Procedure Related Clinical Data and Types of Sedatives

Among the study participants, almost one-third of patients 141 (64.7%) underwent BMA/BMB procedure, followed by Radiotherapy 35 (16.1%), Tissue Biopsy 19 (8.7%) and Colonoscopy/Endoscopic 17 (7.8%). Majority of the procedures 159 (72.9%) took less than 30 min. Considering the level sedation, majority 146 (67%) had deep level of sedation, and the rest 63 (28.9%) and 9 (4.1%) were moderate and mild level. Whereas, in majority of the procedures 158 (72.5%) anesthesia was provided by Anesthetists BSc/MSc and in the rest 60 (27.5%) were by Resident/Attending. Among the study participants, the prevalence of ketofol use was 71.6% (n=156), while use of ketamine alone was 6.9% (n=15), propofol 10.6% (n=23), the combination of propofol and fentanyl citrate was 5.5% (n=12) and the combination of Fentanyl + Ketamine 4.6% (n=10). (Table 3)

Table 3: Description of Procedure Related Clinical Data and Types of Sedatives, Distribution of Respiratory Adverse Risk among Pediatrics Patients out of Operating Room Procedural Sedation at TASH, Addis Ababa, Ethiopia, 2023.

Variable	Category	Frequency n	Percent %	Respiratory Adverse Risk, n	
				Yes	No
Type of Procedure	BMA/BMB	141	64.7	9	132
	Colonoscopy/Endoscopic	17	7.8	1	16
	Radiotherapy	35	16.1	2	33
	Imaging	5	2.3	1	4
	Tissue Biopsy	19	8.7	2	17
	Circumcision	1	0.5	0	1
Duration of procedure	<30 min	159	72.9	11	148
	30-60 min	58	26.6	4	54
	>1 hr.	1	0.5	0	1
Sedation Level	Mild	9	4.1	0	9
	Moderate	146	67.0	9	137
	Deep	63	28.9	6	57
Anesthesia provider	Resident/Attending	60	27.5	6	54
	Anesthetist BSc/MSc	158	72.5	9	149
Type of Sedation Drugs	Ketofol	156	71.6	8	148
	Ketamine	15	6.9	2	13
	Propofol	23	10.6	3	20

Used	Fentanyl + Ketamine	10	4.6	1	9
	Propofol + Fentanyl	12	5.5	0	12
	Dexmedetomidine + Ketamine	1	0.5	1	0
	Ketofol + Fentanyl	1	0.5	0	1

5.4 Reported Adverse Events

Overall, the prevalence of adverse event was 9.2% (n=20). Respiratory adverse event was the most common adverse event occurring in 15 (6.9%) patients. Regarding the severity, moderate adverse events were seen in 15 (6.9%) cases, Oxygen desaturation (75-90%), <60 sec being the most common 3.7% (n=8), followed by Apnea, <60 sec 1.4% (n=3), laryngospasm 1.4% (n=3) and bradycardia, 0.5% (n=1). Sentinel adverse events observed only in one patient (0.5%). Whereas, Minimal Adverse Events occurred in 2.3% (n=5) of cases, of which Hyper salivation occurred in two patients, and Recovery agitation, Subclinical respiratory depression and vomiting in one patient each. (Table 4, Figure 1&2)

Table 4 Description of Reported Adverse Events in Pediatrics Patients out of Operating Room Procedural Sedation at TASH, Addis Ababa, Ethiopia, 2023

Variable		Frequency	Percent %
Any Adverse Event	Yes	20	9.2
	No	198	90.8
Respiratory Adverse Events	Yes	15	6.88
	No	203	93.1
Minimal Adverse Events	Hyper salivation	2	0.9
	Recovery agitation	1	0.5
	Subclinical respiratory depression	1	0.5
	Vomiting	1	0.5
	None	213	97.7
Moderate Adverse Events	Apnea, <60 sec	3	1.4
	Bradycardia	1	0.5
	Laryngospasm	3	1.4
	Oxygen desaturation (75-90%),<60 sec	8	3.7

	None	203	93.1
Sentinel Adverse Events	Severe Oxygen desaturation (<75%), >60 sec	1	0.5
	None	217	99.5

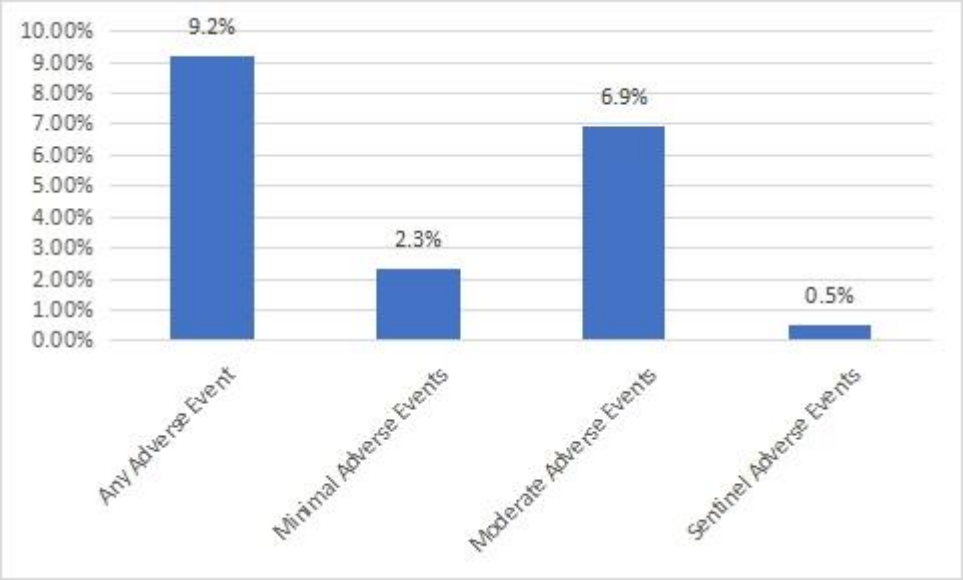

Figure 1Pattern of Adverse Events among Pediatrics Patients out of Operating Room Procedural Sedation at TASH, Addis Ababa, Ethiopia, 2023

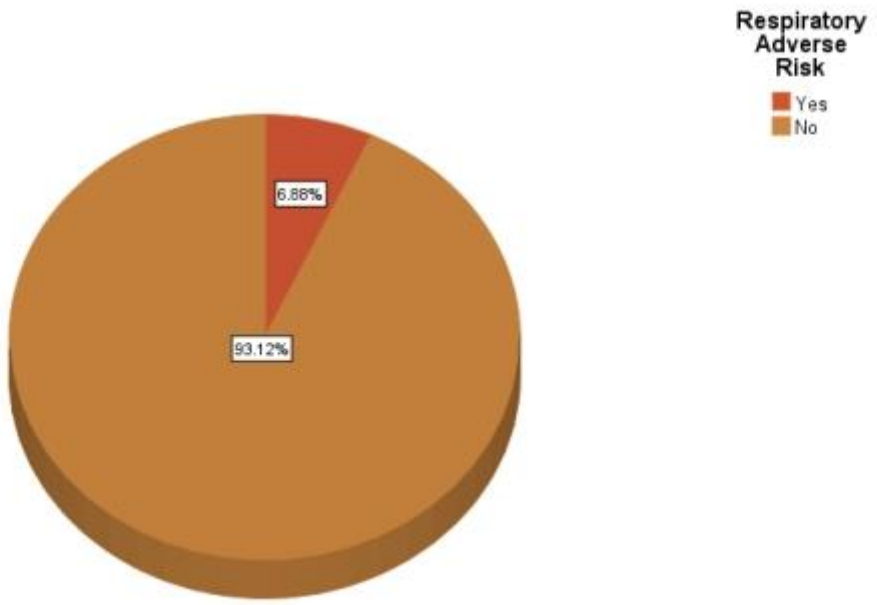

Figure 2Prevalence of Respiratory Adverse Events among Pediatrics Patients out of Operating Room Procedural Sedation at TASH, Addis Ababa, Ethiopia, 2023

5.5 Risk Factors Associated with Respiratory Adverse Event

The bivariate/univariate binary logistic regression analysis was performed on each independent variable with Respiratory Adverse Events. Finally, variable having p-value <=0.25 in at least one of the separate bivariate logistic regressions were selected, then included in the multivariable logistic regression analysis. Malnutrition, sedation level, type of procedure and ASA classification were included in the multivariable logistic regression. (Table 5)

The multivariable logistic regression analysis was performed on variables that have p value<= 0.25 in binary logistic regression, bivariate model.

After adjusting for other covariates, the odds of developing respiratory adverse events is 10.27 times higher among patients who had moderate or severe malnutrition as compared

to those who had normal nutritional status (AOR= 10.27;95%CI 3.21, 32.8; p<0.001). (Table 5)

Table 5Binary Logistic Regression Model: Factors Associated with Respiratory Adverse Effects in Pediatrics Patients out of Operating Room Procedural Sedation at TASH, Addis Ababa, Ethiopia, 2023

Variables		Respirator Adverse Effect		COR 95%CI	p-value	AOR 95%CI	p-value
		Yes	No				
Age (mean)	≤5 years	9(60%)	127(62.6%)	1.8(0.47,6.63)	0.4		
	>5 years	6(40%)	76(37.4%)	1			
Sex	Female	8(53.3%)	90(44.3%)	0.52(0.19,2.7)	0.62		
	Male	7(46.7%)	113(55.7%)	1			
Malnutrition	Normal	5(33.3%)	170(83.7%)	1			
	Moderate&Severe	10(66.7%)	33(16.3%)	11.6(3.45,38.7)	<0.001	10.27(3.21,32.8)	<0.001
Sedation Level	Mild&Moderate	9(60%)	146(71.9%)	2.32(0.54,9.91)	0.24	2.13(0.56,8.05)	0.26
	Deep	6(40%)	57(28.1%)	1			
Type of Procedure	BMA/BMB	9(60%)	132(65%)	3.6(0.61,21.5)	0.16	3.9(0.8,20.83)	0.10
	Others	6(40%)	71(35%)	1			
Duration of Procedure	<30 min	11(73.3%)	148(72.9%)	0.63(0.14,2.3)	0.56		
	≥30 min	4(26.7%)	55(27.1%)	1			
ASA	I&II	5(33.3%)	107(52.7%)	1			
	III	10(66.7%)	96(47.3%)	0.29(0.05,1.5)	0.14	0.26(0.06,1.21)	0.09

6. Discussion

The number of pediatric patients requiring procedural sedation is increasing. This study provides prospective overview of incidence & associated factors of adverse events encountered including respiratory events in pediatrics procedural sedation out of OR provided by anesthesiologists/residents/anesthetists. Sedation was successful in all patients included in the study.

In our study, the overall incidence of adverse event was 9.6 %(n=20) with respiratory adverse events being most common 6.9 %(n =15)this was consistent with studies in Canada and Srilanka, 11.6% and 8.4% respectively[10][4].

Almost in all studies the commonest adverse event observed is respiratory adverse event. This is In part due to children requirement of deeper level of sedation than adults in order for the procedure to be completed. Deeper level of sedation Leeds to apnea and Because of their higher metabolic demand, they are at greater risk of hypoxemia and hypercarbia during periods of apnea. [4], [5], [7], [9]–[11]

This study revealed higher incidence of adverse events (9.6%) as compared with studies done in south Korea (3.9%),Canada (5.3%), Biber (4.8%) across Europe, Green (3.9%)[16]–[18]. The possible explanation for this is, in our study almost half of patients (50%) were ASA class 3 and in their study majority of patients were ASA class 1 or 2 with better western setup.

In contrast to a study in Colorado and south Africa , our study revealed lower incidence of adverse events (9.6 % Vs 17%vs 20%)[2], [9].This may be due to the fact that majority of cases investigated study done in Colorado were emergency procedures and also sedation providers were Emergency physicians while in our study majority of cases were elective and underwent thorough pre-anesthetic evaluation and optimization. Additionally, in our study sedation providers were anesthesiology professionals (anesthesiologists/anesthesiology residents or anesthetists). Considering the study done in South Africa, the higher adverse events (20%) in their study may be due to higher prevalence of MRI sedations (50%) with major neurologic comorbidities.

In this study, moderate/severe malnutrition was significantly associated with the occurrence of respiratory adverse events (AOR=10.27, 95%CI (3.21, 32.8)). This is consistent with a Study done in INDIANA[12]. This association could be explained as first, malnourishment with a negative nitrogen balance can lead to respiratory muscle weakness. Such weakness may predispose to hypoventilation, hypoxia, and apnea during deep sedation. In addition most patients took propofol a lipophilic drug with low volume of distribution in these patients due to less adipose tissue, there will be more drug available in central compartment with greater Central nervous system effect leading to hypoventilation and hypoxia. However, in contrary to most studies association was not found for Age, ASA class and respiratory comorbidities.

Serious/sentinel adverse event was found in 1 patient (0.5%) which is the case in most of studies. There was no death or CPR or aspiration in our study. Though sentinel adverse event is rare, the patient is entitled to the same degree of vigilance and attention to the principles of safe practice, whether the procedure is undertaken in the office, surgery, a remote facility or operating theatre.

7. Strengths and Limitations

7.1 Strength

There are variations in the definition of adverse events but in this study we have used standardized definitions from world society federation of sedation

This study was also prospective study

We have tried to include different types of procedures

There is no similar study done our setting previously.

7.2 Limitations

The extra burden of data collection during duty hours may have contributed to our low capture rate of procedures done on Duty hours

Sample size was low due to cancelation of cases because of in availability of equipment's and patient factor and the radiotherapy machine was not functional for more than one month in the time of data collection

Single center study which makes generalization of the results questionable.

8. Conclusion and Recommendation

8.1 Conclusion

In this study the associated factor for occurrence of respiratory adverse events in pediatrics out of OR procedural sedation in the presence of confounding factor is malnutrition.

Although further multicenter researches are needed to better understand the factors causing adverse events in pediatrics out of OR sedation, the results of this study will be useful in recognizing malnourished patients who are at risk and optimize them before the procedure and cautious sedation and monitoring.

The reported incidence of these adverse events will direct targeted research and support the continued efforts of those who seek to encourage improved safety and reliability in the provision of pediatric procedural sedation.

8.2 Recommendation

Careful evaluation and optimization of pediatric patients with malnutrition is necessary

Further multicenter studies should be done to better understand the characteristics of factors associated with pediatrics out of OR sedation adverse events.

Ethiopian society of physician Anesthesiologists should continually monitor and advocate similar researches and try to develop local guidelines in line with the research findings.

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10. Annexes

10.1 Annex 1 subject information sheet

Addis Ababa University

School of medicine

Subject information sheet

Hello, my name is ----------, I am here on behalf of Dr. Addisu Bekele, a year three Resident in Anesthesiology Critical care and Pain Medicine, School of medicine, Addis Ababa University. He is conducting research on, Assessment of incidence of adverse events in out of OR pediatrics procedural sedation and associated factors at Addis Ababa University, college of health sciences, TASH". He has received permission from Addis Ababa University School of medicine and Tikur Anbessa Specialized Hospital officials to conduct the study.

You are selected to participate in this study because you got anesthesia service and anesthetic care for your operation within 24 hrs, your participation in this study will only be based on your willingness to participate. You have the right to choose not to take part in this study. If you are willing, you have the right to stop at any time or withdraw without giving any reason and you will not be subjected to any ill-treatment. There will be no direct benefit from participating in this study but in the future information gathered by this study will help policymakers, programmers, and researchers to give appropriate attention to issues of interest and design specific treatment options.

The information that you provide will be kept confidential by using only code numbers and locking the data. Only the members of the study team will have the access to the non-coded data and the data will not be used for purposes other than the study. Your willingness and active participation are very important for the success of this study.

If you need any further information or explanation regarding the study, you can have this address to contact.

Name: Dr. addisu bekele Tel- +251-921282066 Email-adebomb62@gmail.com

10.2 Annex 2 informed consent form

Consent Form

TITLE OF STUDY

Assessment of incidence of adverse events in out-of OR pediatrics procedural sedation and associated factors in TASH, Addis Ababa, Ethiopia,

PRIMARY RESEARCHER

Name –Dr. Addisu Bekele, Final year ACCPM resident
Primary Advisor- Dr Faiza Hulala Secondary advisor -Dr Yonathan Abebe.
Department - ACCPM
Address – Addis Ababa Phone – (+251) 921282066 Email – adebomb62@gmail.com

PROCEDURES

Cross-sectional study using semi-structured questionnaire and checklist by trained data collectors.

RISKS There is no anticipated risk to you if you participated in this study.

BENEFITS You will be contributing to the improvement of anesthesia services in the hospital and Ethiopia as a whole.

CONFIDENTIALITY

Every effort will be made by the researcher to preserve your confidentiality including the following by assigning code names/numbers for participants that will be used on all research notes and documents.

CONTACT INFORMATION

If you have questions at any time about this study, you may contact the researcher whose contact information is provided above.

VOLUNTARY PARTICIPATION

Your participation in this study is voluntary. If you decide to take part in this study, you will be asked to sign a consent form. After you sign the consent form, you are still free to withdraw.

CONSENT

I have read and understand the provided information and have had the opportunity to ask questions. I consent to take part in the research study "Assessment of incidence of adverse events in out of OR pediatrics procedural sedation and associated factors at Addis Ababa university college of health science, TASH Ethiopia"

Participant's Signature _____ Date _____

Researcher's Signature _____ Date _____

10.3 Annex 3: data collection checklist and questionnaire [1]

A) Demographic variables

Age _

Sex Male Female

Weight

Weight for Age

BMI for age

Height

ASA status

NPO status

Primary diagnosis

Comorbidities

B) Procedure

Type of procedure

Anesthesia provider

Duration of Procedure

C) Medication used

Primary ---------- dose---------

Adjunct

Level of Sedation

D) Adverse events

Minimal risk descriptors

- Vomiting / Retching
- Subclinical respriatory depression[a]
- Muscle rigidity, myoclonus
- Hypersalivation
- Paradoxical response[b]
- Recovery agitation[c]
- Prolonged recovery[d]

Minor risk descriptors

- Oxygen desaturation (75–90%) for <60 s
- Apnoea, not prolonged
- Airway obstruction
- Failed sedation[e]
- All ergic reaction without anaphylaxis
- Bradycardia[f]
- Tachycardia[f]
- Hypotension[f]
- Hypertension[f]
- Seizure

Sentinel risk descriptors

- Oxygren desaturation, severe (<75% at any time) or prolonged (<90% for >60 s)
- Apnoea, prolonged (>60 s)
- Cardiovascular collapse/ shock[g]
- Cardiac arrest/absent pulse

- Other, specify below

E) Interventions

Minimal risk

- No intervention performed

Administration of:

- Additional sedative(s)
- Antiemetic
- Antihistamine

Minor risk

- Airway repositioning
- Tactile stimulation

or the administration of:

- Supplemental oxygen, new or increased
- Antisialogogue

Moderate risk

- Bag valve mask-assisted ventilation
- Laryngeal mask airway
- Oral/nasal airway
- CPAP

or the administration of:

- Reversal agents
- Rapid i.v. fluids
- Anticonvulsant i.v.

Sentinel intervention

- Chest compressions
- Tracheal intubation

or the administration of:

- Neuromuscular block
- Pressor / epinephrine
- Atropine to treat bradycardia

- Other, specify below

E) Outcome of patients

Unplanned hospitalization/escalation of care

Pulmonary aspiration

Death

Other -------