TO COMPARE THE EFFECTIVENESS OF KETAMINE-PROPOFOL ADMIXTURE RATIOS (1:1 VS 2:1) ON SEDATION ADEQUACY IN PEDIATRIC PATIENTS UNDERGOING PROCEDURAL SEDATION AT BLACK LION HOSPITAL, ADDIS ABABA, ETHIOPIA FROM DECEMBER 1, 2024 – FEBRUARY 30 ,2025

BY: KASSAHUN ABEBAYEHU (ACCPMR YEAR 3)

THIS THESIS IS SUBMITTED TO ADDIS ABABA UNIVERSITY, SCHOOL OF MEDICINE, AS A PARTIAL REQUIREMENT FOR THE COMPLETION OF THE SPECIALTY CERTIFICATE IN ANESTHESIOLOGY, CRITICAL CARE, AND PAIN MEDICINE March: 2025

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Declaration of the investigator

In partial fulfillment of the requirements for the Specialty Certificate in Anesthesiology, Critical Care, and Pain Medicine, I, Dr. Kassahun Abebayehu, hereby declare that this thesis is my original work entitled Effectiveness of ketofol Ratios (1:1 and 2:1) on Sedation Adequacy, Airway Rescue Interventions, Additional Anesthetic Requirements, and Adverse Events in Pediatric Patients Undergoing Procedural Sedation at Black Lion Hospital, Addis Ababa, Ethiopia. The study was conducted between December 1, 2024, and February 30, 2025, as outlined in the methodology section of this thesis.

	Name of Investigator	Name of Advisors	
		Primary Advisor	Secondary Advisor
	Kassahun Abebayehu	Dr. Fetiya Aliferid	Dr. Tseganesh Berhanu
Title	MD, Year III Anesthesiology, Critical Care and Pain Medicine Resident	MD, MPH, Assistant professor of Anesthesiology, critical care and pain medicine	MD, Assistant professor of Anesthesiology, critical care and pain medicine
Institution	College of Health Sciences, Addis Ababa University	College of Health Sciences, Addis Ababa University	College of Health Sciences, Addis Ababa University
Email	Email- kassahuntobi293@gmail.com Tele- +251902722541	Email- falferidk2@gmail.com Tele- +251911305553	
Sign.	…….	…….	……

Department head Dr. Fetiya Alferid (MD) …….

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Abbreviations and Acronyms

ASA …… American society of anesthesiologists

BMA/B …….Bone marrow aspiration/ biopsy

CHS …….College of health sciences

CI…… Confidence interval

HR……..….Heart rate

Ketofol ……ketamine- propofol

MAP ……..Mean arterial pressure

RSS …….. Ramasy sedation scale

TASH……. Tikur Anbesa Specilized Hospital

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Summary

Background: Procedural sedation in children is a key component of safe and effective management during various diagnostic and therapeutic interventions. This study assessed effectiveness of 1:1 and 2:1 ketofol ratio for procedural sedation in children at Black Lion Hospital in Addis Ababa, Ethiopia. Knowing the effect of these ratios on sedation level, the need for rescue airway, additional anesthesia, recovery time and adverse events will help us to develop pediatric sedation local protocol.

Objective: To compare the effectiveness of ketofol ratios (1:1 & 2:1) on sedation adequacy, airway rescue interventions, requirement for additional anesthesia and adverse events in pediatric patients undergoing procedural sedation.

Methods: The study design was prospective observational cohort study in TASH with a sample size of 128 (group 1= group 2=64) ASA I,II and III age 1-12 years undergone procedural sedation. First participant was selected by a simple random sampling from the daily operation schedule, then every two patients (using a consecutive sampling technique) was included until the required sample size met. The observed data was documented on semi-structured anonymous questionnaire. The data was entered, coded, cleaned, and analyzed by SPSS 26 software. Normality of the data was checked by Kolmogorov-Smirnov test and analyzed with chi-square test with cross tabulation for categorical data and mean or medians values for numerical variables. p value < 0.05 at CI of 95% was used.

Result: All participants required additional bolus doses for maintenance except 3 cases in Group I and 30 (23%) of the participants received airway rescue intervention and from those 63.3% were from group I. For both 10 and 20 minutes of induction, majority of adequate sedation were seen in group II (p-value<0.05). Respiratory depression/apnea at any time during the procedure, 11 (8.6%), majority of them (81.8%) were from the group I. Majority of the signs of hallucination 19 (79.2 %) and vomiting 10 (83.3 %) during the procedure and recovery period were higher in group II.

Conclusion: ketofol 2:1 (group II) compared with ketofol 1:1 (group I) had adequate sedation level in 10 and 20 minutes, lower rescue airway interventions, bradycardia and respiratory depression/apnea but vomiting and hallucination were higher in group II as compared to group I

Chapter 1: Introduction

1.1.Background

Procedural sedation plays a vital role in pediatric healthcare, enabling the safe and effective completion of various medical interventions in children [1, 2]. Due to their distinct physiological and psychological characteristics, pediatric patients often experience anxiety, pain, and discomfort during invasive procedures, necessitating the use of sedation [3, 4]. Sedation facilitates patient cooperation, reduces distress, and enhances procedural success, ensuring a safer and more comfortable experience for the child [5].

Combining ketamine and propofol in varying ratios has emerged as a promising strategy to harness the benefits of both drugs while minimizing their individual limitations [7]. These ketamine-propofol mixtures are designed to create a synergistic effect that improves sedation quality, reduces required dosages, and lessens side effects [7, 8].

While several studies have examined the use of ketamine-propofol combinations in adults—showing improved sedation outcomes and fewer adverse effects—pediatric patients have unique physiological and pharmacological needs, making it necessary to conduct specific research in this population. Currently, there is limited data on the efficacy and safety of different ketamine-propofol ratios in children, particularly in resource-limited settings like Ethiopia.

This study aims to address the existing knowledge gap by evaluating the effectiveness and safety of two ketamine-propofol admixture ratios (1:1 and 2:1) for procedural sedation in children. Conducted as a pros pective cohort study at Black Lion Hospital in Addis Ababa—one of Ethiopia's largest healthcare institutions serving a diverse pediatric population—this research seeks to inform evidence-based sedation protocols and improve pediatric procedural care.

Given the hospital's broad pediatric case mix and the challenges posed by limited healthcare resources, identifying reliable and safe sedation methods is especially crucial. By examining the pharmacodynamic interactions between ketamine and propofol, this study will provide valuable insights into optimal sedation practices. The absence of well-established, evidence-

based protocols presents a risk, as current sedation approaches may not be adequately effective or safe. This research intends to contribute practical solutions to enhance sedation outcomes for children undergoing medical procedures.

1.2. Statement of the Problem

Pediatric procedural sedation presents unique challenges, as children often require medication to alleviate anxiety, pain, and discomfort during medical procedures. While ketamine and propofol are widely used for this purpose, there is no clear agreement on the optimal combination ratio for pediatric patients—especially in low-resource settings such as Ethiopia, and specifically at Black Lion Hospital, where approximately 80 children undergo procedural sedation each month.

At Black Lion Hospital, current sedation practices still largely follow general protocols that are not specifically tailored to the physiological characteristics of pediatric patients. This lack of adaptation may result in inadequate sedation, leaving children anxious, distressed, and at increased risk for procedural complications. Conversely, overly deep sedation can lead to serious adverse effects such as respiratory depression, cardiovascular instability, and delayed recovery—posing significant risks to patient safety and well-being.

1.3. Significance of the study

This study aims to generate valuable data for Improved sedation protocols that can lead to better management of anxiety and pain in children undergoing procedures, can contribute to minimizing risks associated with respiratory depression and other adverse effects commonly linked to sedative and can inform clinical best practices in Ethiopia.

Chapter 2. Literature Review

The combination of ketamine and propofol—commonly referred to as ketofol—has gained traction in clinical practice due to its balanced sedation profile. This admixture potentially offers effective sedation and analgesia while reducing the adverse effects typically associated with each drug when used alone. Early studies suggest that varying the mixing ratios of ketofol can influence sedation depth, hemodynamic stability, and recovery profiles, underlining the need for further investigation.

A prospective cohort study conducted at Tikur Anbessa Specialized Hospital, Addis Ababa University, Ethiopia, evaluated the effectiveness of ketofol in 1:2 versus 1:3 ratios for procedural sedation and analgesia in children undergoing bone marrow aspiration or biopsy. The study involved 64 patients in each group. While both groups achieved similar sedation levels (as measured by the Ramsay Sedation Scale), respiratory outcomes, and general postoperative adverse events, the 1:3 group required significantly more intraoperative analgesia (29.7%) compared to the 1:2 group (7.8%). The study concluded that the 1:2 ketofol ratio reduced the need for additional analgesics [9].

In a study conducted at the Department of Pediatric Dentistry, Gazi University, Ankara, Turkey, three ketofol ratios (1:1, 1:2, and 1:4) were compared in children undergoing dental procedures (n = 30 per group). Although there were no major differences in overall side effect incidence, Group 1 (1:1) had deeper sedation and more postoperative side effects, along with a greater need for additional dosing. Group 3 (1:4) had the shortest recovery time. Based on all measured parameters, the 1:2 mixture was identified as the most balanced and reliable option [11].

Another study from Shahid Sadoughi University and Tehran University of Medical Sciences, Iran, compared 1:2 and 1:3 ketofol mixtures in children undergoing lumbar puncture or bone marrow aspiration. While both groups maintained stable hemodynamics, adequate amnesia, and no respiratory depression, the 1:2 group experienced significantly more hallucinations and longer recovery times. The study recommended the 1:3 ratio due to its lower incidence of psychomimetic effects and faster recovery [12].

A randomized, double-blind controlled trial at Shahid Sadoughi University, Yazd, Iran, examined 1:3 and 1:5 ketofol ratios in 80 pediatric patients (ages 4–12) undergoing intrathecal chemotherapy injections. The study found a significantly shorter recovery time in the 1:5 group ($p = 0.001$), with all children maintaining SpO_2 levels >95%. It concluded that the 1:5 ratio was superior due to its faster recovery and lower heart rate [10].

Lastly, a randomized, double-blind study at Riyadh Armed Forces Hospital, Saudi Arabia, investigated 1:1 and 4:1 propofol-to-ketamine mixtures in 100 children undergoing procedural sedation. While both groups maintained stable hemodynamic parameters post-induction, Group I (1:1) had increased postoperative nausea, more psychomimetic effects, and longer discharge times compared to Group II (4:1). The study recommended using lower ketamine doses in ketofol mixtures to minimize side effects and expedite discharge [13].

Chapter 3. Objectives

3.1. General Objective

To compare the effectiveness of ketamine-propofol admixture ratios (1:1 & 2:1) on sedation adequacy, airway rescue interventions, requirement for additional anesthesia and adverse events in pediatric patients undergoing procedural sedation at Black Lion Hospital, Addis Ababa, Ethiopia from December 1, 2024 – February 30 ,2025.

3.2 Specific Objectives

To evaluate the adequacy of sedation in each admixture group from December 1, 2024 – February 30 ,2025

To assess airway rescue interventions and adverse events among the two ketamine- propofol admixture groups by oral airway insertion or jaw thurst application during the procedure from December 1, 2024 – February 30 ,2025

To assess mean duration of recovery and need for additional anesthesia requirement during the procedure based on patient responses among two ketamine- propofol admixture groups during the procedure from December 1, 2024 – February 30 ,2025

Chapter 4. Methods

4.1 Study Design

A hospital-based prospective observational cohort study was conducted to compare the effects of ketofol ratios (1:1 and 2:1) on procedural sedation outcomes in pediatric patients at Black Lion Hospital, Addis Ababa, Ethiopia, during the 2024/2025 period.

4.2 Study Setting and period

The study was conducted at Tikur Anbessa Specialized Hospital, a multi-specialty tertiary care and teaching hospital located in Addis Ababa, Ethiopia. Established in 1972, it currently serves as the country's primary referral center and teaching institution. The hospital is equipped with 17 functional operating theaters and operates alongside more than 11 other public hospitals in the city.

Procedural sedations for pediatric patients are carried out in a dedicated sedation room located within the pediatric oncology department. On average, approximately 224 pediatric patients undergo sedation procedures over a two-month period. These procedures include bone marrow aspiration/biopsy (BMA/B), ultrasound-guided core needle biopsy, lymph node biopsy, incisional biopsy, and other interventions requiring sedation.The study was conducted over a three-month period, from December 1, 2024 to February 30, 2025.

4.3 Source and Study population

Source population: The study involved pediatric patients who are scheduled for elective procedures requiring sedation

Study population: The study involved pediatric patients who are scheduled for elective procedures requiring sedation who fullfill the inclusion criteria

4.4. Operational definitions

- **Ketofol 1:1** (Group 1) -Ketamine 0.5 mg/kg and propofol 0.5 mg/kg combination.

- **Ketofol 2:1** (Group 2)- Ketamine 1 mg/kg and propofol 0.5 mg/kg combination.

- Ramsay sedation scale- will be assessed every 10 min. 3 times throughout the procedure by a score of 1-6 based on the clinical assessment of the level of sedation. RSS score of 4-6 is adequate sedation during the entire time of the procedure.

Sedation level	Score
Anxious , agitated, restless	1
Awake , but cooperative, tranquil, orientated	2
Responds to verbal commands only	3
Sleeping patients having brisk response loud noise or a glabella tap	4
Sleeping patients having sluggish response loud noise or a glabella tap	5
Sleeping patients having no response loud noise or a glabella tap	6

- **Post procedural adverse events –** described by bradycardia , desaturation , vomiting, respiratory depression/apnea and Hallucination.

-**Hypoxia**- saturation below 90% without oxygen or < 94% with oxygen

-**Bradycardia**- pulse rate reduction below normal range for age

-**Respiratory depression**- Respiratory rate below normal range for age

Age	Respiratory rate	Heart rate
1-3 years	20-30	70-110
3-6 years	20-25	65-110
6-12yrs	14-22	65-95

-**Apnea**- a brief period (20 seconds) when breathing stops.

- **Vomiting**-Expulsion of any stomach contents during the procedure and/or recovery period

- **Hallucination**- A child manifested by impaired consciousness, disorganized thinking, lack of purpose and inability to focus.

4.5. Inclusion criteria and Exclusion criteria

Inclusion criteria

Patients of ASA class I , II and III (for oncology pts without cardiorespiratory disease)

Age ranging from 1 to 12 years and

Undergoing procedural sedation with ketofol 1:1 or 2:1 combination was included in the study.

Exclusion criteria

Previous allergic reaction to Propofol and/or ketamine

Pre procedure desaturation

Significant comorbidities and ASA III patients with cardiorespiratory disease

Patients requiring pre procedure intubation

Patients having difficult airway to be done in sedation room and

Other ketofol combinations used for sedation and epileptic patients excluded from the study

4.6. Dependent and Independent variables

Dependent variables

Adequacy of sedation

Independent variables

Age, Sex, Weight, ASA Status, Total doses of study drugs used intraoperatively , Ketofol combination used (ketofol 1:1 Vs 2:1), intraoperative procedural adverse events, rescue airway intervention

4.7. Sample Size Determination

The sample size was determined using the formula for comparing two means with equal group sizes. Data from a previous study conducted in Iran, which compared ketofol ratios of 1:2

(Group I) and 1:3 (Group II), were used to estimate the required sample size. In that study, the mean Ramsay Sedation Scale (RSS) score was 4.17 with a standard deviation of 0.64 for Group I, and 3.87 with a standard deviation of 0.57 for Group II. These values correspond to Group I: $\mu_1 = 4.17$, $\sigma_1 = 0.64$ and Group II: $\mu_2 = 3.87$, $\sigma_2 = 0.57$

Assuming a significance level (α) of 0.05 and a power of 80% ($\beta = 0.20$), the calculated sample size was sufficient to detect a statistically significant difference

$$n_1 = n_2 = \frac{\left(z_{\alpha/2} + z_{\beta}\right)^2 \left(\sigma_1^2 + \sigma_2^2\right)}{\Delta^2}$$

$$n_1 = n_2 = \frac{(1.96 + 0.84)^2 \left(0.64^2 + 0.57^2\right)}{(4.17 - 3.87)^2} = n = 63.89 \approx 64 \quad (n_1 = 64 \;\&\; n_2 = 64)$$

where: n1 is sample size for Ketofol 1:1 n2 is sample size for Ketofol 1:2

A total of 128 patients enrolled for the study . (n1=n2= 64).

4.8. Sampling Procedure

Participants were randomly assigned to one of two ketofol admixture ratio groups (1:1 and 2:1) using the daily operating schedule as the sampling frame. The first participant each day was selected through simple random sampling using the lottery method. Subsequently, every second patient was enrolled alternately into the two groups. Participants were recruited using this alternating sampling technique until the target sample size was achieved. Physician residents or anesthetists working in the pediatric sedation room approached eligible patients and their families to obtain consent for participation.

4.9. Data analysis plan

The data were entered, coded, cleaned, and analyzed using SPSS version 26. Continuous numerical variables were described using means and standard deviations, whereas categorical variables were summarized as frequencies and percentages. A p-value less than 0.05 was regarded as statistically significant.

4.10.Data collection procedure

Anesthetists working in the pediatric sedation room approached eligible patients and their families to invite them to participate in the study. Data were collected by the assigned anesthetists using a structured questionnaire administered through an online Google Form. The completeness of the data was reviewed daily following the collection of questionnaire responses.

4.11. Dissemination plan

The study presented to Addis Abeba university, School of Medicine, department of Anesthesiology Critical care and Pain medicine

4.12. Ethical Considerations

Ethical approval was obtained from the Department of Anesthesiology, Critical Care, and Pain Medicine at Black Lion Hospital. Informed consent was secured from the parents or legal guardians of all participants prior to their inclusion in the study. All collected data were treated with strict confidentiality, and participants retained the right to withdraw from the study at any point without any repercussions.

Chapter 5. Result

5.1 Sociodemographic characteristics of the study participants

The majority of participants (57%) were between 4 and 10 years old, with a mean age of 5.34 years. Females accounted for 50.8% of the study population. Nearly 56% of the children were classified as ASA physical status class II, and 25.8% had a primary diagnosis of acute lymphoblastic leukemia (ALL). Bone marrow aspiration and/or biopsy (BMA/B) constituted 74.2% of the planned procedures.

Table 1: The sociodemographic characteristics -age and ASA classification of the study participants among patients undergoing procedural sedation in TASH from December 1, 2024 to February 30, 2025 (n=128)

Sociodemographic	Total (%)	Ketofol combination		p-value (chi square test)
		Group1 (1:1)	group 2(2:1)	
Age in years				0.69
1-3	40(31.2)	22(34.4)	18(28.1)	
4-10	73(57)	34(53.1)	39(60)	
Above 10	15(11.8)	8(12.5)	7(10.9)	
	128	64	64	
Sex				0.287
Male	63(49.2)	29(46)	34(54)	
Female	65(50.8)	35(53.8)	30(46,2)	
	128	64	64	
ASA classification				0.423
ASAI	38(29.7)	21(55.3)	17(44.3)	
ASAII	71(55.5)	36(50.7)	35(49.3)	
ASAIII	19(14.8)	7(36.8)	12(63.2)	
	128	64	64	

Table 2: The sociodemographic characteristics (Preoperative diagnosis and planned procedure) of the study participants among patients undergoing procedural sedation in TASH from December 1, 2024 to February 30, 2025 (n=128)

Preoperative diagnosis	Total	Ketofol combination		0.435
		Group1 (1:1)	group 2(2:1)	
ALL	33(25.8)	16 (48.5)	17(51.5)	
AML	10(7.8)	5	5	
Others a	85 (66.4)	43 (50.6)	42 (49.4)	
	128	64	64	
Planned procedure				0.327
BMA/B	95 (74.2)	47 (49.5)	48(50.5)	
BMA/B and lumbar puncture	6 (4.7)	1	5(83.3)	
bilateral BMA/B	6 (4.7)	4	2	
Bilateral BMA/B & LP	6 (4.7)	2	4	
Others b	15 (11.7)	10 (66.7)	5 (33.3)	

key: Others [a]- Aplastic anemia ,Bicytopenia, Burkit lymphoma, Dermatofibrosarcoma, Extraocular Retinoblastoma, hepatoblastoma, HL, HR ALL, Infantile leukemia, ITP, Neuroblastoma, NHL, Pancytopenia, Reactive lymphadenitis, Retinoblastoma, left eye retinoblastoma, Megaloblastic anemia, soft tissue sarcoma and SR ALL

Others b- BMA/B, lumbar puncture and CNB, BMB, CNB, CNB and lumbar puncture, IT-MTX, Lymph node Excisional biopsy, BMA/B and IT MTX, BMA/B & lumbar puncture and LN biopsy, lumbar puncture and BMA

5.2 The anesthesia management related characteristics of the study participants

A total of 23% of participants (n = 30) required intervention for airway rescue. Of these, 63.3% were from Group I and 36.7% from Group II. The mean duration of the procedure was 29.84 minutes in Group I and 30.23 minutes in Group II. However, a statistically significant difference was observed in the mean recovery time between the groups: 13.59 minutes for Group I and 16.25 minutes for Group II (p = 0.000).

Among the 19 participants in Group I who required airway intervention, 11 cases were managed with jaw thrust alone, while 8 cases required the insertion of an oral airway. In contrast, of the 11 participants in Group II who needed airway rescue, 6 were managed with jaw thrust, and 5 required oral airway insertion.

Table 3:The anesthesia management related characteristics of the study participants undergoing procedural sedation, in TASH from December 1, 2024 to February 30, 2025 (n=128):

Variable	Total (%)	Ketofol combination		p-value
		Group1 (1:1)	group 2(2:1)	
Rescue airways intervention given				0.077
Yes	30(23.4)	19(63.3)	11(36.7)	
No	98(76.6)	45(45.9)	53(54.1)	
	128	64	64	
Duration of procedure (mean ±SD)		29.84±8.18	30.23±6.28	0.905
<30 min	40(31.3)	20(50)	20(50)	
≥30 min	88(68.8)	44(50)	45(50)	
	128	64	64	
Duration to recovery form anesthesia from the procedure (Mean ±SD)		13.59±3.61	16.25±3.88	0.00
≤10 min	35 (27.3)	22(34.3)	13 (20.3)	
>10 min	93 (73.7)	42(65.7)	51(79.7)	
	128	64	64	

5.3 Maintenance dose related characteristics of the study participants

All participants in Group II required additional bolus doses for maintenance, whereas three cases in Group I did not require any additional bolus. These three cases involved intrathecal medication administration procedures, each lasting approximately five minutes. The median propofol dose administered was 60.0 ± 27.2 mg for Group I and 40.0 ± 14.4 mg for Group II, with a statistically significant difference between the groups (p = 0.000). Similarly, the median ketamine dose was 60 ± 26.0 mg in Group I and 80 ± 27.7 mg in Group II, also showing a statistically significant difference (p = 0.036).

Table 4: Maintenance dose related characteristics of the study participants undergoing procedural sedation, in TASH from December 1, 2024 to February 30, 2025 (n=128):

	Total (%)	Ketofol combination		p-value
		Group1 (1:1)	group 2 (2:1)	
Additional bolus drug given for maintenance of anesthesia				0.75
Yes	125(97.7)	61(48.8)	64(51.2)	
No	3(2.3)	3	0	
	128	64	64	
Total propfol dose given (mg) (Median ±SD)		60.0 ± 27.2	40.0 ± 14.4	0.000
<50 mg	51 (40.8)	10 (19.6)	41 (80.4)	
50-100 mg	61 (54.8)	38 (66.2)	23 (33.8)	
>100mg	13 (4.4)	13	0	
	125	61	64	
Total ketamine dose given (mg) (Median ± SD)		60 ± 26.0	80 ± 27.7	0.036
<50 mg	11 (8.8)	7 (63.6)	4 (36.4)	
50-100 mg	80 (64)	41 (51.3)	39 (48.7)	
>100mg	34 (27.2)	13 (38.2)	21 (61.8)	
	125	61	64	

5.4 The characteristics of Intraoperative Ramsay sedation score

At 10 minutes post-induction, adequate sedation was observed predominantly in Group II (51.8%), whereas all cases of inadequate sedation occurred in Group I. Similarly, at 20 minutes post-induction, most patients with adequate sedation (54.4%) were in Group II, and the majority of inadequate sedation cases (47.6%) were from Group I. These differences at 10 and 20 minutes were statistically significant ($p < 0.05$). However, at 30 minutes post-induction, there was no significant difference between the two groups in terms of either adequate or inadequate sedation.

Table 5: Maintenance dose related characteristics of the study participants undergoing procedural sedation, in TASH from December 1, 2024 to February 30, 2025 (n=128):

Variable	Total (%)	Ketofol combination		p-value
		Group1 (1:1)	group 2(2:1)	
Ramsay sedation score after induction				0.438
Adequate sedation	120(93.8)	59(41.3)	61(50.7)	
Inadequate sedation	8(6.3)	5(62.5)	3(37.5)	
	128	64	64	
Ramsay sedation score after 10 min of induction				0.037
Adequate sedation	123(96.9)	59(47.9)	64(51.8)	
Inadequate sedation	5(3.1)	5(100)	0	
	128	64	64	
Ramsay sedation score after 20min of induction				0.043
Adequate sedation	118(95.9)	56(47.6)	62(52.4)	
Inadequate sedation	5(3.9)	4(80)	1(20)	
	123	60	63	
Ramsay sedation score after 30min of induction				1.000
Adequate sedation	88(97.8)	45(51.2)	43(48.8)	
Inadequate sedation	2(2.2)	1	1	
	90	46	44	

5.5 The characteristics of Intraoperative adverse events

Among the participants who showed signs of respiratory depression or apnea during the procedure (8.6%, n = 11), the majority (n=9) were from Group I. In contrast, signs of hallucination during the procedure and recovery period were more frequently observed in Group II, with 19 cases (79.2%), compared to 5 cases in Group I. This difference was statistically significant ($p < 0.002$). Similarly, vomiting during the procedure and recovery period was significantly more common in Group II, with 10 cases compared to only 2 cases in Group I ($p = 0.015$).

Table 6: The characteristics of Intraoperative adverse event of the study participants undergoing procedural sedation, in TASH from December 1, 2024 to February 30, 2025 (n=128)

Variable	Total (%)	Ketofol combination		p-value
		Group1 (1:1)	group 2(2:1)	
Bradycardia during the procedure				0.227
Yes	7(5.5)	5(71.4)	2(28.6)	
No	121(94.5)	59(48.8)	62(51.2)	
	128	64	64	
sign of respiratory depression/apnea at any time during the procedure				0.024
Yes	11(8.6)	9(81.8)	2(18.2)	
No	117(91.4)	55(47)	62(53)	
	128	64	64	
Desaturation				0.078
Yes	34(26.8)	21(61.8)	13(38.2)	
No	94(73.2)	43(45.7)	51(54.3)	
	128	64	64	
Vomiting during procedure and recovery period				0.015
Yes	12(9.4)	2(16.7)	10(83.3)	
No	116(90.6)	62(53.4)	54(56.6)	
	128	64	64	
Signs of hallucination during the procedure and recovery period				0.002
Yes	24(18.8)	5(20.8)	19(79.2)	
No	104(81.2)	59(56.7)	45(43.3)	
	128	64	64	

Chapter 6. Discussion

According to the findings of this study, at both 10 and 20 minutes post-induction, a significantly higher proportion of patients in Group II achieved adequate sedation compared to Group I ($p < 0.05$). This finding contrasts with a study by M. Woubshet, E. Melese, Z. Ashebir et al., which reported no significant difference in sedation levels between ketofol 1:2 and 1:3 groups when assessed by the Ramsay Sedation Scale (RSS) [9]. The improved sedation profile observed in the 2:1 ketofol ratio in the present study may be attributed to the higher ketamine content, which has a longer half-life and prolonged anesthetic effects,

The mean recovery time was significantly shorter in Group I (13.59 minutes) compared to Group II (16.25 minutes), with a p-value of 0.000. This result is consistent with findings from Kip et al., where lower ketamine concentrations in ketofol mixtures (group-1:4) were associated with shorter recovery durations [11]. Similarly, Ayatollahi V. et al. reported shorter recovery times in patients receiving lower ketamine doses. The longer recovery time in Group II may be due to ketamine's longer half-life and psychotropic effects, while the shorter half-life of propofol in the 1:1 ratio facilitates faster emergence from sedation.

Oxygen desaturation events were also more common in Group I, although the difference was not statistically significant ($p = 0.078$). This trend is consistent with findings by Kip et al. and Woubshet et al. Conversely, Daabiss et al. reported hypoxia in both 1:1 and 1:4 ketofol groups. The lower incidence in our study might be explained by the routine use of 100% oxygen via facemask or nasal cannula throughout the procedures, potentially masking early signs of desaturation.

Regarding side effects, hallucinations and vomiting were significantly more frequent in Group II ($p < 0.05$). This is in line with findings from Ayatollahi V. et al. where higher ketamine concentrations in ketofol mixtures were associated with increased psychomimetic effects and emesis. However, Woubshet et al. reported no significant difference in these adverse events between groups [9]. The higher incidence of hallucinations and vomiting in Group II in our study can be attributed to the greater ketamine-to-propofol ratio, as ketamine is well-known for its psychomimetic side effects, especially at higher doses.

Conclusion: The findings of this study demonstrate that the ketofol combination used in Group II provided significantly better anesthesia outcomes compared to Group I. Specifically, Group II showed a longer duration of anesthesia and more adequate sedation as measured by the Ramsay Sedation Scale (RSS). Additionally, patients in Group II experienced fewer adverse events, including respiratory depression/apnea, desaturation, bradycardia, and the need for rescue airway interventions. However, the Group II combination was associated with a higher incidence of hallucinations and vomiting, as well as a greater requirement for maintenance dosing. Overall, the results suggest that the ketofol combination used in Group II offers a more effective and safer sedation profile, with better sedation quality and fewer critical airway-related complications, making it a preferable choice for procedural sedation in pediatric patients.

Chapter 7: Strength and limitation of the study

7.1. Strength of the study

Fairly adequate sample size

It also clearly addressed its main objectives

We could evaluate multiple outcomes

It could help further future researches

7.2. Limitation of study

The study was done single center referral hospital

Majority of patients were oncologic patients

The study does not include patients for whom endoscopy, MRI, bronchoscopy and other procedure

7.3. Recommendation

Based on the findings of this study, the ketofol 2:1 ratio is recommended for pediatric procedural sedation in resource-limited settings. This combination provided more adequate sedation with lower incidences of rescue airway interventions, bradycardia, and respiratory depression/apnea. In our context, where ketamine is more readily available and affordable than propofol, and where procedural sedation is typically administered by anesthetists rather than anesthesiologists—as is more common in higher-resource settings—this ratio offers both clinical and practical advantages. However, the 1:1 ketofol ratio may still be a reasonable alternative in certain circumstances. Specifically, it may be preferable for shorter procedures or in high-volume settings due to its association with faster recovery times and a lower risk of vomiting and hallucinations. These side effects, which are more common with the 2:1 ratio, can prolong recovery room stays and increase overall procedural time. Therefore, the choice of ketofol ratio should be tailored to the specific clinical scenario, procedural duration, patient throughput demands, and resource availability.

Chapter 9. References

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10. annex

Questionnaire

Hello, my name is……., and I am here on behalf of Dr. Kassahun Abebayehu, a student at the School of Medicine, Addis Ababa University. She is conducting a research study titled Comparison of Ketamine-Propofol Admixture Ratios (1:1 and 2:1) for Procedural Sedation in Pediatric Patients at Black Lion Hospital, Addis Ababa, Ethiopia, 2024. This study has received official approval from Addis Ababa University and Tikur Anbessa Specialized Hospital.

You have been invited to participate in this study because you or your child is currently admitted to the hospital and has undergone elective surgery. Participation in this study is entirely voluntary. You have the right to decline participation or withdraw from the study at any time without having to provide a reason, and without facing any negative consequences or changes in the care you receive. Although there is no direct benefit to you from participating, the findings of this study may help inform future treatment guidelines, assist policymakers, and guide researchers in improving procedural sedation practices.

All information you provide will remain strictly confidential. Personal identifiers will be replaced with codes, and all data will be securely stored. Only the study team will have access to non-coded data, which will be used solely for research purposes. Your cooperation and willingness to participate are greatly appreciated and are vital to the success of this study.

Section I: Socio Demographic Data and preoperative Data

Card number:		Bed no:	Code
	Question	Response	
	Age (years)		
	Sex	1. Male 2. Female	
	Weight (kg)		

	Height (cm)		
	BMI		
	ASA physical status	1. ASA I 2. ASA II 3. ASA III	
	Preoperative Diagnosis		
	Planned procedure		

Section II: Question related to anesthesia management

	Question	Response	Code
	Ketofol combination Ratio used for induction	1.group 1 (1:1 ratio) 2.group 2 (2:1 ratio)	
	Did additional bolus drug given for maintenance of anesthesia ?	1. YES 2. NO	
	If yes, specify type and dose	1.Ketamine ____mg 2.Propofol ____mg 3.other ____mg	
	Interventions for airway rescue given	1.YES 2.NO	
	If yes, what was used	1. Oral airway insertion	

		2. jaw thrust 3. Intubation	
	Duration of procedure (min)		
	Duration to recover from anesthesia after the procedure (min)		

Section III: Intraoperative Ramsay Sedation score (RSS)

Time	Ramsay Sedation score (RSS)
After induction	
10 min	
20 min	
30 min	

Ramsay Sedation Score(RSS)

Score	Definition
1	Patient is anxious and agitated, restless
2	Patient is cooperative, oriented and quite
3	Patient responds to commands only

4	Patient exhibits brisk response to light glabellar tap or loud auditory stimulus
5	Patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus
6	Patient exhibits no response

Section IV: intraoperative adverse events observed

s.no	Question	Response	Code
	Did the patient had bradycardia at any time during the procedure?	1. yes 2.no	
	If yes ,how much was the lowest pulse rate		
	Did the patient show sign of respiratory depression/apnea at any time during the procedure?	1. YES 2. NO	
	Did the patient show any desaturation at any time during the procedure?	1.yes 2.no	
	If yes, how much was the lowest the SPO2		
	Did the patient develop vomiting at any time	1. YES	

	during the procedure and recovery period	2. NO	
	Did the patient show signs of hallucination at any time during the procedure and recovery period?	1. YES 2. NO	