ADDIS ABABA UNIVERSITY-COLLAGE OF HEALTH SCIENCES
SCHOOL OF MEDICINE TIKURANBESSA SPECIALIZED HOSPITAL

INCIDENCE OF DELAYED AWAKENING AND ASSOCIATED FACTORS AMONG PATIENTS UNDERGOING SURGERY VIA GENERAL ANESTHESIA AT TIKUR ANBESA SPECIALIZED TEACHING HOSPITAL, ADDIS ABABA, ETHIOPIA BY TESFAYE SEBSBIE

A Research Thesis To Be Submitted To Addis Ababa University School Of Medicine, Department of Anesthesiology, Critical Care and Pain Medicine In Partial Fulfillment Of The Requirement For Specialty Certificate In Anesthesiology, Critical Care, and Pain Medicine

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Incidence and risk factors of Delayed emergence in surgical patients following general anesthesia at Tikur Anbesa Specialized Hospital, Addis Ababa, Ethiopia, 2024

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Declaration

I hereby declare that this thesis titled **"Incidence of delayed awakening and associated factors among patients undergoing surgery via general anesthesia at Tikur Anbesa Specialized Teaching Hospital"** has been carried by me in partial fulfillment of the requirement for specialty Certificate in Anesthesiology, Critical Care, and Pain Medicine with the support and guidance of my advisers, Dr. Fetiya A. and Dr. Faiza H. of Department of Anesthesiology, Critical Care, and Pain Medicine. The information derived from the literature has been duly acknowledged in the text and a list of reference provided. I also reveal that the work has not been submitted for any other degree or professional qualification.

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Acknowledgment

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Acroym

ASA……American Society of Anesthesiologist

AVPU……. Alert, Verbal, Pain, Unresponsive

BMI…. ……...Body Mass Index

CPB……. Cardiopulmonary Bypass

DE…….....Delayed Emergence

GCS….....Glasco Coma Scale

GA……...General Anesthesia

ISA……. Indian Society of Anesthesiologists

ICU……...Intensive Care Unit

MAC…….. Minimum Alveolar Concentration

OR……...Operation Room/ Odds Ratio

PACU…… Post Anesthesia Care Unit

RA….....Regional Anesthesia

ROC…….....Return of Consciousness

TASH…….....Tikur Anbesa Specialized Hospital

ABSTRACT

Background: Delayed awakening can lead to various challenges in perioperative care, such as prolonged hospital stays, increased healthcare costs, unexpected ICU admissions, reduced patient satisfaction, and hindered postoperative care activities. However, there is scarce research on this topic in our study area.

Objective: To evaluate the incidence as well as risk factors of delayed awakening among patients undergoing surgery under general anesthesia at Tikur Anbesa Specialized Teaching Hospital.

Methods: A hospital-based cross-sectional study was conducted, involving 317 patients who underwent surgery under general anesthesia at Tikur Anbesa Specialized Teaching Hospital from May 1, 2023, to May 10, 2024. Data were collected and entered using epi info version 7 and analyzed using SPSS version 27 after data cleaning. The association between categorical variables was assessed using correlation and logistic regression. Odds ratios were calculated to determine the associations through binary and multivariable logistic regressions.

Results: Out of the 317 patients included in the study, 31.2% experienced delayed awakening after surgery. Multivariable logistic regression analyses indicated that smoking (AOR=0.056, 95% CI:0.005-0.638), presence of medical comorbidity, premedication(AOR= 0.087,95% CI: 0.023-0.333), intraoperative crystalloid administration >3L for adult patients(AOR =9.810 ,95% CI: 2.78-34.613), presence of intraoperative hypotension(AOR= 0.148 ,95% CI: 0.056-0.393), type opioid at induction, duration of surgery ≥220minutes(AOR =5.815 , 95% CI:1.477-22.893), duration of anesthesia ≥230minutes(AOR= 0.244 ,95% CI :0.066-0.905), moderate surgical risk classification(AOR= 0.089 ,95% CI :0.018-0.426) and severe surgical risk classification (AOR =0.049, 95% CI: 0.007-0.321) were the independent risk factors found to have a significant association with delayed awakening ($P<0.05$).

Conclusion: Although it was single-center study, the number of patients experiencing delayed awakening is substantial, and it has significant implications, including prolonged hospital stays, increased healthcare costs, and adverse patient outcomes. It is clinically necessary to take early countermeasures against such significant various risk factors to reduce the occurrence of delayed awakening, and to improve the prognosis of patients. Multi-center studies are necessary to determine the true impact on clinical patient outcomes and its economic impact to the national level.

1.Introduction

1.1 Background of the study

Delayed awakening is defined as a delay of recovery of consciousness and cognitive function more than 30–60 minutes after the end of general anesthesia (1–4). There is no universally agreed single time window to define delayed awakening and different centers use different time to diagnose it. However: Indian Society of Anesthesiologist (ISA)defined delayed emergence as the inability to regain consciousness within 30 minutes of the completion of surgery or the cessation of anesthetics (5, 6).

The incidence of delayed awakening varies widely, ranging from 2.6 % to 72%, depending on the patient population and the definition used (7–10).This wide discrepancy in prevalence may be explained by differences in the diagnostic criteria, the quantity of samples used, and the risk factors that were taken into account. There are factors that contribute to delay awakening: such as patient characteristics, anesthetic agents, duration and type of surgery, metabolic disorders and electrolyte derangements (1, 6, 11)

There is no universal tool that could be used to assess recovery from anesthesia. However clinical assessment using conducted using many scales are being implemented to assess level of awareness after anesthesia (10). Some of these tools used to evaluate delayed emergence are GCS, AVPU and RASS score (2, 10, 11. AVPU score was used for adult patients for this study. However, for pediatric patients ASA recommends using other clinical parameters like eye opening, conjugate gaze, purposeful movement, facial grimacing and tidal volume greater than 5 ml/kg(12). If two to three out five predictors are present, child considered awake from anesthesia(12).

Delayed awakening after general anesthesia has a significant impact on patient outcomes and healthcare costs. Patients who experience delayed awakening may exhibit confusion, disorientation, and grogginess upon regaining consciousness, which can impede their ability to participate in postoperative care activities and hinder the recovery process. Additionally, extended time spent in the operation theater and recovery room due to delayed awakening can lead to increased healthcare costs, as patients occupy valuable resources and staff time for an extended period, unanticipated postoperative ICU admissions and increased case cancellations

rate(1,3,12).Even though we routinly encouter delayed awakening in our perioperative settings, not much research has been done in Ethiopia regarding the condition's prevalence and risk factors.

This study aims to close the knowledge gap by researching the incidence and risk factors of delayed emergence in our patient population. By conducting this study, we aim to provide valuable insights into the local prevalence and specific risk factors contributing to delayed emergence. The findings of this study will contribute to reduce healthcare costs, healthcare providers can improve patient outcomes, and enhance the overall quality of perioperative care and enabling healthcare professionals to enhance patient safety and optimize perioperative practices. It is also important step towards filling the existing research gap and providing evidence-based recommendations for the prevention and management of delayed emergence in surgical patients.

1.2 Statement of the problem

Delayed awakening after general anesthesia has a significant impact on patient outcomes and healthcare costs particularly in low income countries where resources are scarce. Statistics on the incidence of delayed awakening after general anesthesia among patients undergoing surgery vary depending on several factors, but incidence might be high in resources limited countries like us where we still use old anesthetic agents with limited monitoring available.

It poses various challenges in perioperative care, which includes prolonged hospital stays, increased healthcare costs, cause unanticipated postoperative ICU admissions, decreased patient satisfaction, and hindered postoperative care activities. It can also impede the ability of the patient to participate in postoperative care actives, hinder the recovery process, and increase the risk of complications. Additionally, extended time spent in the operation theater and recovery room due to delayed emergence can result in increased healthcare costs, as valuable resources, staff time are occupied for longer durations and increased case cancellations rate.

In our area of study, there is a lack of information regarding the prevalence and risk factors of delayed emergence following surgery under a general anesthetics'. This knowledge gap hinders healthcare professionals' ability to implement targeted preventive measures and interventions. Therefore, there is a pressing need to conduct this to determine the local incidence of delayed emergence and identify the specific risk factors contributing to this phenomenon.

1.3. Significance of the study

Overall, this study carries substantial significance such as, improving patient outcomes, reducing healthcare costs, and improve patient satisfaction. By conducting this study, we aim to fill this knowledge gap and provide valuable insights into the prevalence of delayed emergence and the specific risk factors relevant to our patient population. It also helps healthcare professionals in our setting to develop evidence-based protocols for risk assessment, prevention and timely management of delayed emergence and to minimize its occurrence.

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2. Literature review

Delayed awakening after general anesthesia is a common occurrence among surgical patients, and several factors influence its incidence. The reported incidence of delayed awakening varies widely, ranging from 2.6% to 64% in different studies. Developed countries generally have lower rates of delayed emergence, compared to developing countries. However, limited research has been conducted in sub-Saharan Africa on this topic. A study from Debre Markos University reported a lower incidence of 2.6%, but no explanation was provided for this low incidence of delayed awakening. In the study area, there is a lack of research on delayed awakening, highlighting the need for further investigation to determine its incidence and associated risk factors.

Delayed awakening has been associated with various factors. These factors include patient characteristics, anesthetic factors, surgical factors, as well as metabolic and electrolyte imbalances. Patient factors such as gender, advanced age, smoking, obesity, and presence medical comorbidities have been implicated.

A prospective study from China investigated by Zhang et al showed that elderly Patients whose **age ≥70** years has greater risk of delayed awakening than patients younger than 70 years (AOR 1.454, 95% CI: (1.146–1.904))(3). The reason may due to age-related decrease central nervous system function and the slower metabolism of anesthetic drugs(3). Another study conducted in conducted in the USA between October 1994 and May 1995 by Pavalin et al on 1088 adult outpatient surgery patients, unlike the above studies this study shows neither body weight nor age was a reliable indicator of awakening time(8).

A study done at China demonstrated the association between obesity and delayed awakening (AOR 1.303, 95% CI 1.102–1.912)(4). The fact that obese patients' extra adipose tissue might change drug distribution and metabolism, resulting in prolonged drug effects and delayed clearance, supports these findings(2,4,5). A study conducted at Debre Markos University by Bayable et al.

also showed that patients who are out of normal body weight delayed awakening from general anesthesia than patients with normal body weight (AOR 1.38 (1.34–5.21))(6).

A study by Zhang et al, found significant association between smoking and delayed awakening (OR 1.128, 95% CI 1.007–2.261)(3). This may be due to its detrimental effects on lung function, which followed by cerebrum hypoxia and destroy its function(3). Another factor that may contribute to delayed awakening is gender, men were 1.4 times more likely than women to experience a delayed awakening ($p<0.05$)(7,9).

Numerous studies have also found that the existence of various medical comorbidities, such as diabetes, cardiovascular disease, and renal dysfunctions, is associated with an increased risk of delayed awakening and may have an impact on the pharmacokinetics and pharmacodynamics of anesthetic drugs(1–3).While the precise mechanism remains unclear, an alternative reason could be that patients with liver and kidney disorders, particularly those who were not thoroughly assessed before to surgery, may have received an excessive amount of anesthetic medication, which could cause a delay in awakening(1–3).

Surgical factors, including the duraton and invasiveness of the procedure,, urgency of surgery, and, in the case of cardiac surgeries, the duration of the bypass or cross-clamp time (HR=0.96)(9) have been implicated in delayed emergence. A study from China done by Zhang et al revealed that patients who had surgery for longer than 220 minutes had associated with delayed emergence (OR 1.239, 95% CI 1.039–1.735)(4). Extended surgical procedures and those requiring significant tissue manipulation may cause a patient's recovery to be delayed, potentially because of the buildup of anesthetic drugs and systemic inflammatory reaction responses. According another study from China by Wang et al on patients undergoing aortic arch surgery are at a higher risk of delayed awakening if they had emergency surgery and CBP more than 240 minutes(9,10).One possible explanation is that when CPB time increased, more inflammatory cytokines were generated, exacerbating the ischemia-reperfusion injury. Furthermore, if patients needed emergency surgery, they were in critical preoperative condition and had an increased risk of brain injury.

Another factors that may contribute to delayed awakening is the duration of surgery and invasiveness of the procedure. Studies have shown only moderate and major surgical procedures

such as cardiac surgeries or organ transplantation, (p=0.04) and surgeries lasting longer than 2 h (AOR: 1.91, 95% CI: 1.83–6.14), can contribute to delayed awakening(5,13,14) (14,17).This may be due to the longer duration of surgery and the use of more potent anesthetic agent and use of neuromuscular blocking agents during surgery.

Anesthetic factors that have been linked to delayed awakening include length of anesthesia, types of anesthetic agent, intraoperative hypotension, estimated blood loss greater than 1.5L, and administration of crystalloids greater than 3L(6,11,12). Similar factors that cause delayed awakening have been linked to prolonged fasting, use of premedication, type of muscle relaxant and opioid used(6,13). According to a study done by, Zhang et the duration of anesthesia ≥230 minutes emerge as key factors that contribute to delayed awakening (OR 1.223, 95% CI 1.013–1.926)(4,12).

A study conducted at Debre Markos University which released after data collection of this study was started and it indicates that the following factors may also play a significant role in delayed awakening after general anesthesia: the presence of intraoperative hypotension (AOR: 3.37, 95% CI: 2.93–9.41), strong intraoperative opioid administration (AOR: 2.3, 95% CI: 2.20–5.76), extended preoperative fasting (AOR: 2.72, 95% CI: 2.11–6.35), estimated blood loss >1.5L (AOR: 1.20, 95% CI: 0.62–11.30), and crystalloid administration >3L (AOR:3.12, 95% CI: 2.19–7.32)(12). An observational prospective study conducted in the USA by Pavalin et al. from October 1994 to May 1995 on 1088 adult patients found that the induction by thiopental led to a slower regain in cognitive function than the induction with propofol (11). This investigation shows, recovery from thiopental induction with isoflorine maintenance takes 22 minutes longer than that from propofol induction with isoflorine maintenance (*pro/iso < thio/iso (P = 0.005))(14).

Other factors: given that delayed emergence is multifactorial, there may be additional risk factors that were not included in the list of risk variables that came before it(14,15). Metabolic problems such electrolyte imbalances and glucose dysregulation have been proposed as an additional risk

factor for delayed emergence. The imbalances in calcium, potassium, and magnesium levels, together with hyper- or hypoglycemia, may affect neuronal activity and delay the return of consciousness(2,14).

Moreover, unexpected delayed emergence can also result from other causes such as thrombosis, embolism, or bleeding (13,16). Additional rare case reports and case studies of delayed emergence have been connected to hypernatremia, dysglycemia, hypothyroidism, and central anticholinergic syndrome(13,14).

3. Objectives

3.1. General objective

- To assess incidence and associated risk factor of delayed awakening after general anesthesia in patients who undergo surgery from May 1, 2023, to May 10, 2024 at TASH, Addis Ababa, Ethiopia

3.2. Specific objectives

- To assess the incidence of delayed recovery after general anesthesia from May 1, 2023, to May 10, 2024.
- To evaluate the risk factors that are connected to prolonged emergence for surgeries under general anesthesia from May 1, 2023, to May 10, 2024.

4. Methodology

4.1. Study Area and period

The study was carried out at TASH, which is located in Addis Ababa, the capital and largest city of Ethiopia. Opened since 1972, then in 1998, the TASH, the largest referral hospital in the country, with 700 beds, and it has since become a university teaching hospital. The TASH now the main teaching hospital for both clinical and preclinical training of most disciplines. It is also an institution where specialized clinical services that are not available in other public or private institutions are rendered to the whole nation. Total of 18 OR tables give surgical service in the following departments: Gastroenterology, neurosurgery, pediatric surgery, urological surgery, orthopedics, obstetrics, ENT, Emergency operations and cardio-thoracic surgery are the specialties in which TASH now provides surgical services. Anesthesia services are provided by anesthesiology, critical care and pain medicine department. The study was conducted from May 1, 2023, to May 10, 2024.

4.2. Study Design

Hospital based prospective cross-sectional research has been employed.

4.3 Population

4.3.1. Source population

All patients who underwent surgery at TASH during the duration of the study were included.

4.3.2. Study population

All patients that fulfill inclusion criteria who have undergone surgery under GA at TASH from May 1, 2023, to May 10, 2024

4.4. Eligibility Criteria

4.4.1. Inclusion Criteria

All patients who undergoing surgery under general anesthesia were included

4.4.2. Exclusion Criteria

Patients who are not extubated after surgery, had a reoperation due to surgical complications within six hours, have known neurological deficits, and psychiatric illness were exclude

4.5. Sample Size

To estimate sample size, a formula based on the single proportion populations was applied. According to an investigation done in Iraq, 31.8% of people had delayed awakening (6). Using a 95% confidence interval and a 10% margin of error

$$\text{Sample size} = Z^2 \times p(1-p)\frac{1}{d^2}$$

n= Sample Size

P= Prevalence=0.318

d=Margin of error

$n=1.96^2*0.318(1-0.318)/0.05^2$

n= 333

and non-response (333*10%) rate which is approximately 33

with adding 10% none response rate, the final sample size was, n = 366

4.6. Sampling Technique

We included all patients for whom surgery was done via GA in the study area who fulfill the inclusion criteria and willing to participate in the study was included.

4.7. Data Collection Procedurs

Data was gathered using self-administered questionnaires by 18 trained data collectors (three third-year anesthesiology residents, four second-year anesthesiology residents, eight first-year anesthesiology residents, and three anesthetists) after a 24-hour follow-up. The components of the

questionnaire were explained to them and around 10% of the data collection was supervised by the principal investigator. The data collection questionnaire was adopted from research conducted in Iraq, USA and China at 2019,2010 and 2020 respectively and tailored, developed, and contextualized for this specific study.

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4.8. Data Analysis Procedure

After being manually checked for accuracy and input using the Epi-data, the data was cleaned and then exported to SPSS version 27 for further analysis. For the participant's sociodemographic and clinical variables as well as operator factors, descriptive statistics including frequency, percent, mean, median, and standard deviation were used. Binary logistic and multivariable logistic regression was conducted to evaluate the level of correlation between the covariates and the outcome variables. To determine the strength of the association, 95% confidence intervals were employed along with crude and adjusted odds ratios. In order to examine further associations, variables having a P-value of less than 0.20 in the binary analysis were included to the multivariable logistic regression analysis. Covariates with a p-value of less than 0.05 in multivariable logistic regression analysis were regarded as statistically significant.

4.9.Study Variables

4.9.1 Dependent Variable (Outcome Variable)

Delayed awakening after general anesthesia

4.9.2. Independent Variables:

Patient related factors: Include Age, Gender, BMI, ASA Physical Status, Comorbidity, History Of Smoking, and History Of Alcohol Use.

Surgery related factors: Urgency Of Surgery, Duration Of Surgery, and Surgical Risk Classification Of The Procedure

Anesthesia related factors: Use Of Premedication, Extended Preoperative Fasting, Induction And Maintenance Anesthetic Agent, Use Of Muscle Relaxant For Maitenance and Type Of Opioid Used For Induction And Maintenance, Presence Of Intraoperative Hypotension, Visual Estimated Blood Loss And Amount Of Crystalloid Administration.

4.10. Operational Definition

Delayed emergence: Inability the patient to regain consciousness within 30 minutes of the cessation of anesthetic drug.

Chronic alcohol consumption defined as more than three alcoholic drinks per day for more than 03 month

4.11 Ethical Issue

The Addis Ababa University College of Health Science's department of anesthesiology, critical care, and pain medicine provided a letter of support and ethical permission for the study. Patients or legal guardians were educated about the procedure's aim, potential risks and benefits, and study objectives before verbally providing their consent.

Trial participants were informed that there would be no immediate advantages and that they might discontinue the study at any time. The confidentiality of the proceduralists and their patients was maintained by hiding personal identifiers in favor of codes and by not disclosing any of their data to anybody besides the study team.

4.12 Result dissemination plan

The study's findings will be submitted to the Department of Anesthesiology, Critical Care, and Pain Medicine. We will work very hard to get the results of the study published in a scientific journal that is peer-reviewed.

5. Result

5.1 Sociodemographic Details Of Patients

In this study 317 patients were enrolled, with a response rate of 86.6%. Among the study participants 64.7% belonged to the 15–64 age group, with a median age of 29. Table 1 below illustrates the nearly equal distribution of sexes among the participants, and 55.2% of them had a normal body mass index.

TABLE 1. FREQUENCY AND PERCENTAGE OF SOCIODEMOGRAPHIC AND PATIENTS RELATED FACTORS OF STUDY PARTICIPANT IN TIKUR ANBESSA SPECIALIZED HOSPITAL FROM JAUARY TO APRIL 2024, ADDIS ABABA, ETHIOPIA, (N=317)

Variables	Category	Frequency	Percent
Sex	Male	157	49.5
	Female	160	50.5
Age			
	under 14 years	94	29.7
	15-64 year	205	64.7
	65 year and older	18	5.7
BMI (kg/m2)	Pediatric age group	42	13.3
	<18.5	19	6
	18.5–24.9	175	55.4
	25–29.9	67	21.2
	≥ 30	11	3.5
ASA status	ASA I	118	37.2
	ASA II	153	48.3
	ASA III and above	46	14.5
Alcoholic history	Yes	15	4.7
	No	302	95.3
Smokers	Yes	9	2.8
	No	308	96.2
Medical comorbidity of the patient	Yes	124	39.2
	No	192	60.8
Premedication	Yes	46	14.5
	No	271	85.5
NPO hour of the patient	less than 12 hours	290	91.5
	more than 12 hours	27	8.5

5.2 Patient Related Factors

In this study, ASA II 153 patients made up the majority (48.3%), with the remaining patients being ASA I 118 (37.2%) and ASA III and above 46 (14.5%). Table 1 below shows that of the respondents, 124 (or 39.1%) had a chronic condition, 15 (or 4.7%) drank alcohol, 9 (or 2.8%) were smokers, and 54.9% had a normal body mass index.

5.3 Anesthesia Related Factors and Surgical Procedures

Anesthetic aspects of study participants revealed that 91.5% had NPO hours less than twelve hours. 14.5% of the patients received premedication, which usually included fentanyl (4.4%), diazepam (1.3%), lidocaine (1.3%), ketamine + atropine (1.3%), ketamine alone (1.9%), and dexamethasone (0.6%). During intubation, (164, 51.7%) succinylcholine was employed using modified rapid sequence induction (RSI) and normal (151, 47.6%) situations that used vecuronium. To induce patients, 192 (60.6%) propofol, 124 (391%) ketofol, and 1 (0.3%) other medication were utilized. The maintenance of anesthesia was achieved with volatile anesthetics (isoflurane 94% and halothane 5.7%), and these were supplemented with opioids (fentanyl 12%, morphine 57.7%, and 30.3% of them did not require any opioid for maintenance).

Opioids for induction (fentanyl 78.9% and morphine 14.8%) were used as induction of anesthesia). vecuronium were used as a muscle relaxants maintenance in 282(89%) of patients. Most of the study participants procedure were elective 248 (78.2%) while the rest 63 (19.9%),6(1.9%) were emergency and urgency respectively. As presented in table 2 below when we look the pattern of surgical procedures its Pediatric, ENT, cardiovascular, git and hepatobiliary surgery followed by obstetrics and gynecology operations were the highest in this study, accounting for 15.5, 15.2, 13.9, 13.9 and 12.9% respectively.

Table 2.: FREQUENCY AND PERCENTAGE OF RISK FACTORS OF THE STUDY PARTICIPANTS IN TIKUR ANBESSA SPECIALIZED HOSPITAL,FROM JAUARY TO APRIL 2024,ADDIS ABABA, ETHIOPIA, (N=317)

Variables	Category	Frequency	Percent
Induction anesthetic agent	Propofol	192	60.6
	ketofol	125	39.4
Use of NMB for maintenance	Yes	279(88)	88
	No	38	12
Type of opioids used for induction			
	Fentanyl	250	78.9
	Morphine	47	14.8
type of opioids for maintenance	Fentanyl	134	42.3
	Morphine	183	57.7
EBL (for adult)	<1500ml	251	79.2
	≥ 1500ml	16	5
Intraoperative crystalloid used (for adult)	<3000ml	219	69.1
	≥ 3000	48	15.1
Intraoperative hypotension	Yes	81	25.6
	No	236	74.4
Duration of anesthesia	<230 minutes	211	66.6
	≥230 minutes	106	33.4
Duration of surgery	< 220 minutes	244	77
	≥220 minutes	73	23
surgical risk classification	Low risk	112	35.3
	Moderate risk	122	38.5
	high risk	83	26.2
Type of operations			
	Pediatrics	49	15.5
	Cardiovascular	69	13.9
	Gynecologic and Obstetrics	41	12.9
	GIT and Hepatobiliary	44	13.9
	ENT	39	12.3
	Orthopedics	29	9.1
	Neurosurgery	26	8.2

General surgery and Emergency surgery	19	6
Urology	16	5

5.4 Prevalence Of Delayed Awakening

There were 317 patients undergoing surgery via general anesthesia, 218 (68.8%) of them were with normal recovery after anesthesia and 99(31.2%) were with delayed recovery after anesthesia.

5.5 Factors Associated with Delayed Awakening

Binary logistic regression was used to evaluate the relationship between each independent variable and dependent variable. In order to determine which independent variables were statistically significant, factors with a p-value of 0.2 or less were incorporated to the multivariate regression model.

By using binary logistic regression, variables like **ASA status, the existence of comorbidities, and premedication use, alcoholic history, anesthetic agent used for induction, use of muscle relaxant for maintenance, type opioid at induction, use of opioids for maintenance, duration of anesthesia ≥230minutes, duration of surgery ≥220minutes and urgency of surgery ,intraoperative hypotension, surgical risk classification, EBL ≥ 1500 for adult and intraoperative crystalloid administration of ≥ 3000ml for adult** were entered to multivariate analysis.

By using multi-variant logistic regression, factors such as, **use of premedication, presence of intraoperative hypotension, duration of surgery ≥220minutes, duration of anesthesia ≥230minutes, intraoperative crystalloid administration of more than 3000 ml for adult patients, and surgical risk classification were found to be significantly associated.** The study found no statistically significant association between many variables, including age, sex, the patient's NPO hour, the kind of NMB used during induction, the induction and maintenance agent, alcohol intake, the type of surgery, the type of operation, the use of inhalations, and the use of analgesics.

Table 3. Bi-variant and multi-variant logistic regression among patients who develop delayed awakening in Tikur Anbessa Specialized Hospital Addis Ababa, Ethiopia, 2024 (N=317

Variables	Frequency (%)	Bi-variant		Multivariate	
		Crude OR	P value	Adjusted OR	P value
Sex					
Male	157(49.5)	0.84(0.522-1.351)	0.472	1.431(0.46-4.449)	0.536
Female	160(50.5)	1	1		
Premedication	46(14.5)	**0.284(0.149-0.539)**	**<0.001**	**0.087(0.023-0.333)**	**0.0**
Yes	270(85.2)	1	1	1	1
No					
Age					
under 14 years	94(29.7)	1	1	1	1
15-64 year	205(64.7)	0.956(0.562-1.628)	0.869	0.365(0.057-2.331)	0.287
65 year and older	18(5.7)	0.53(0.189-1.485)	0.227	0.052(0.004-0.73)	0.028
BMI (kg/m2)					
<18.5	19(6)	1	1	1	1
18.5–24.9	175(55.4)	1.418(0.528-3.808)	0.488	36.959(2.248-6607.54)	0.011
25–29.9	67(21.2)	1.333(0.46-3.863)	0.596	7.209(0.465-111.848)	0.158
≥ 30	11(3.5)	0.583(0.135-2.527)	0.471	1.296(0.039-43.275)	0.885
ASA status					
ASA I	118(37.2)	1	1	1	1
ASA II	153(48.3)	0.526(0.3-0.922)	0.025	0.816(0.291-2.287)	0.7
ASA III and above	43(13.6)	0.214(0.103-0.446)	<0.001	0.283(0.079-1.012)	0.052
Alcohol					
Yes	15(4.7)	0.283(0.098-0.819)	0.02	0.808(0.118-5.537)	0.829
No	302(95.3)	1	1	1	1
Comorbidity status					
Yes	124(39.1)	0.558(0.344-0.985)	0.018	2.145(0.750-6.133)	0.155
No	192(60.6)	1	1	1	1
Induction anesthetic agent					
propofol	192(60.6)	1	1	1	1
ketofol	125(39.4)	0.378(0.232-0.616)	<0.001	1.418(0.517-3.888)	0.497
Use of NMB for maintenance					
Yes	279(88)	0.393(0.158-0.976)	0.044	0.671(0.075-5.961)	0 .720
No	37(11.7)	1	1	1	1
Type of opioids for induction					

Fentanyl	250(78.9)	1	1	1	1
Morphine	47(14.8)	1.839(0.872-3.879)	0.11	6.152(0.983-38.5)	0 .052
Use of opioids for maintenance					
Yes	229(72.2)	0.229(0.115-0.454)	<0.001	1.912(0.363-10.053)	0 .444
No	88(27.8)	1	1		
type of opioids for maintenance	134(42.3)	1	1	1	1
Fentanyl	183(57.7)	0.338(0.2-0.571)	< 0.001	0.848(0.199-3.605)	0 .823
Morphine					
EBL (for adult)					
<1500ml	251(79.2)	1	1	1	1
≥ 1500ml	16(5)	0.152(0.012-1.842)	0.139	0.199(0.000-94.727)	0.608
Intraoperative crystalloid used (for adult)					
<3000ml	219(69.1)	1	1	1	1
≥ 3000	48(15.1)	0.29(0.177-0.476)	<0.001	**9.810(2.780-34.613)**	**0.0**
Intraoperative hypotension					
Yes	81(25.6)	0.087(0.049-0.152)	<0.001	**0.148(0.056-0.393)**	**0.0**
No	236(74.4)	1	1		
Duration of anesthesia					
<230 minutes	211(66.6)	1	1	1	1
≥230 minutes	106(33.4)	0.263(0.159-0.435)	<0.001	**0.244(0.066-0.905)**	**0.035**
Duration of surgery					
< 220 minutes	244(77)	1	1	1	1
≥220 minutes	73(23)	0.61(0.354-1.052)	0.076	**5.815(1.477-22.893)**	**0.012**
surgical risk classification					
Low risk	112(35.3)	1	1	1	1
Moderate risk	122(38.5)	0.194(0.091-0.41)	<0.001	**0.089(0.018-0.426)**	**0.002**
high risk	83(26.2)	0.071(0.033-0.156)	<0.001	**0.049(0.007-0.321)**	**0.002**

1= indicate for reference * Significant p-value(P<0.05)

6. DISCUSSION

Delayed awakening after surgery and anesthesia is a significant concern as it can prolong hospital stays, increase healthcare costs, and impact patient outcomes. In this study, we aimed to explore the incidence and factors associated with delayed recovery in patients undergoing surgery via general anesthesia. In the current study, we defined delayed awakening if inability to regain consciousness within 30 minutes of the completion of surgery or the cessation of anesthetics.

In this study, out of the 317 patients undergoing surgery via general anesthesia, 97 (31.2%) experienced delayed recovery after anesthesia, while 219 (68.8%) had a normal recovery, which is almost the same as the study done in Iraq (31.81%)(12). This suggests that delayed awakening is not an uncommon occurrence and warrants further investigation into its underlying causes. In comparison with other studies, the rate of delayed awakeninig.was higher than that of studies from Debre Markos University in Ethiopia (2.6%), Indonesia (5% and 10% of ASA I and II patients, respectively) and China (25%) (2,13,14). However, it was less than an American study that discovered 72% of participants had delayed awakeninig (20). The difference would be attributed to variations in study populations, surgical procedures, and different anesthesia protocols.

Our study population consisted of patients undergoing a variety of surgical procedures, including emergency surgery, different elective surgeries, and pediatric surgeries. We analyzed various factors, including patient characteristics, surgery-related variables, anesthetic and metabolic variables, to identify independent risk factors for delayed recovery.

According to a multivariate logistic regression analysis, using **premedication**, **intraoperative crystalloid administration of more than 3000 ml for adult patients, presence of intraoperative hypotension, duration of surgery ≥220minutes, duration of anesthesia ≥230minutes and, surgical risk classification** were significantly associated delayed awakeninig.

The current study showed that there were statistical significant association between **duration of surgery ≥220 minutes as well as duration of anesthesia ≥230 minutes and delayed awakening (AOR 5.815(1.477-22.893), p value 0.012), (AOR 0.244(0.066-0.905), p value 0.035)respectively**. The possible explanation may be prolonged duration of surgery and anesthesia can affect a number of aspects, including drug accumulation, drug interactions, and

also predispose patients to hypothermia, which can all lengthen the time it takes to wake up(1).The longer the surgery, the more tissue manipulation and blood loss that may occur which further results in hypotension and later followed by a decreased metabolism and medication excretion(13,21).

Another significant factor associated with delayed awakening in our study is the existence of intraoperative hypotension **(AOR 0.148(0.056-0.393), p value 0.0).** The reasons underlying this include decreased perfusion, which subsequently led to decreased drug metabolism and clearance and amplified anesthetic effects(1).

The other parameter that showed statistically significant association with delayed awakening in this study was crystalloid administration of more than 3000 ml intraoperatively **(AOR 9.810(2.78-34.613), p value 0.0).** Although the precise mechanism remains unclear, fluid-induced hypothermia is one potential explanation. hypothermia prolongs the return of consciousness by reducing drug metabolism and clearance, by increased oxygen affinity for hemoglobin, which predisposes to tissue hypoxia and sometimes hypothermia can also cause direct CNS depression(1,2).

The other parameter which showed statistically significant association with delayed awakening were if the operation was moderate or high risk surgical procedures**(AOR 0.089(0.018-0.426), p value 0.002) or (AOR 0.049(0.007-0.321), p value 0.002)** for respectively. The possible explanation may due Extended surgical procedures and those requiring significant tissue manipulation may cause a patient's recovery to be delayed, potentially because of the buildup of anesthetic drugs and systemic inflammatory reaction responses. Another study from Indonesia conducted by Djoni et al showed that patients with ASA I physical status recovered faster than patients with ASA II in the conscious recovery room(2). 90% of ASA I patients were conscious within 30 minutes, while 80% of ASA II patients achieved consciousness within the same timeframe. Bayable et al also demonstrated that patients with estimated blood loss greater than 1500 ml has an association with delayed awakening following general anesthesia(21).

Multivariate logistic regression analysis for the **use of Premedication** showed that patients who took premedication had an association with delayed awakening **(AOR 0.087(0.023-0.333), p value 0.0.** The reason may be that, as some studies have shown, many premeditations, particularly if

taken in large doses, reduce the need for anesthesia(1). However, a large dose may cause a delay in the recovery process from anesthesia unless the anesthetic depth is titrated by monitoring brain function (for example, using BIS) and unless the standard dose is modified accordingly(1).

7. Conclusion and Recommendation

7.1 Conclusion

This study demonstrated that the incidence of delayed awakening is high which make this concerning because it can prolong hospital stays, increase healthcare costs, and impact overall patient outcomes. In our study, smoking history, use of premedication, intraoperative crystalloid administration of more than 3000 ml for adult patients, presence of intraoperative hypotension, duration of surgery ≥220minutes, duration of anesthesia ≥230minutes and,moderate and high risk surgical risk surgeries was found to have association with delayed awakening. These findings provide insights into patient care and anesthetic management for clinicians in related fields.

9.2 Recommendation

We recommend cautious monitoring, early treatment of intraoperative hypotension, and goal-directed crystalloid delivery tailored to each patient. We recommend multidisciplinary team discussions prior to surgery for extended and high-risk procedures in order to establish an early postoperative and intraoperative care plan.

We also recommend develop local perioperative care protocols. Multi-center studies are necessary to determine the true impact on clinical patient outcomes and its economic impact to the national level.

8. Strength and Limitation

8.1 Strength

It included patients of all ages and almost all surgical specialties who underwent surgery via general anesthesia. As far as we could find, this is the first of its kind in our study area.

8.2 Limitation

In this study we are unable to include hypothermia as an independent variable because core body temperature monitoring is not available in the study setting. Therefore, future research addressing this aspect is necessary. The study was conducted at a single institution, which limits the generalizability of the findings.

9. Work plan

Appendix-I: Time Plan

SRN	Activity	March	April	May	June	July	August	September	October	November	December	January	February	march	April	may
1	Title selection															
2	Literature review															
3	Proposal writing															
4	Proposal submission															
5	Proposal defence															
6	Ethical review															
7	Data collection															
8	Data analysis															
9	Report writing															
10	Submission															
11	Final defence															
12	Dissemination of result															

10. Budget Breakdown

Appendix- II: Cost Estimation

No	Budget category	Measurement unit	Unit cost in Ethiopian Birr (ETB)	Multiplying factor	Total cost (ETB)	Justification
	Supplies					
1	pen	Item	10	10	50	For data collection
2	pencil	Item	5	5	15	For data collection
3	Clip board	Item	20	2	40	For data collection
4	CD-R	Item	10	5	50	For data collection
5	Flash drive	Item	300	1	300	For data collection
	Miscellaneous					
1.	Payment for data collectors	Cost per study subject	50	366	18,300	Peridium for a data colle
2.	Internet (CDMA)	Per package	1,000	2	2000	internet
3.	Typing and Printing of proposal, research paper and questionnaire	Cost per study subject	2	(60+120+10)	360	Duplication of paper and questionnaire
4.	Photocopy of questionnaire	Cost per paper	1	2500	2500	Duplication of paper
5.	Mobile card for P				2,000	Used for communicatior
6.	Total				25,615	
7.	Contingency (5%)				1280.75	
8.	Grand Total			Total + Contingency	26,895.75	

11. Reference

1. Choi J, Kim S. Delayed awakening time from general anesthesia for dental treatment of patients with disabilities. J Dent Anesth Pain Med. 2021;21(3):219-26.
2. frOST Eam. <Differential Diagnosis Of Delayed Awakening From General Anesthesia A Review(3).pdf>. Google Scholar. 2014;M.E.J. ANESTH 22 (6), 2014.
3. Djoni Kusumah Himsani Pohan* GA, Elly Noer Rochmah, Rizki Bunawa. <Description of ASI & ASA II paitents from GA.pdf>. ATLANTIS PRESS. 2021.
4. Misal US, Joshi SA, Shaikh MM. Delayed recovery from anesthesia: A postgraduate educational review. Anesth Essays Res. 2016;10(2):164-72.
5. <Delayed Awake ISA.pdf>.
6. Karim S. Factors Related to Delayed Recovery After Anesthesia. Iraqi Journal of Medical Sciences. 2021;19(1):39-48.
7. Zelcer J WD. Anaesthetic-related recovery room complications

Anaesth Intensive Care. 1987;vol.15:168-74.
8. Sher-Lu Pai M. <Delayed emergence and emergence delirium in adults.pdf>. Jun 23, 2022.
9. Shaikh SI, *, R aLR. Delayed awakening Achallenge for anesthesiologists. International Journal of Biomedical and Advance Research.
10. Cascella M, Bimonte S, Di Napoli R. Delayed Emergence from Anesthesia: What We Know and How We Act. Local Reg Anesth. 2020;13:195-206.
11. Sinclair RCF, Faleiro RJ. Delayed recovery of consciousness after anaesthesia. Continuing Education in Anaesthesia Critical Care & Pain. 2006;6(3):114-8.
12. Templeton TW, Goenaga-Diaz EJ, Downard MG, McLouth CJ, Smith TE, Templeton LB, et al. Assessment of Common Criteria for Awake Extubation in Infants and Young Children. Anesthesiology. 2019;131(4):801-8.

13. Thomas E, Martin F, Pollard B. Delayed recovery of consciousness after general anaesthesia. BJA Educ. 2020;20(5):173-9.
14. <Factors_Affecting_Discharge_Time_in_Adult.14.pdf>.
15. Myles PS, McLeod AD, Hunt JO, Fletcher H. Sex differences in speed of emergence and quality of recovery after anaesthesia: cohort study. Bmj. 2001;322(7288):710-1.
16. Tsai HJ, Chen CC, Chang KY. Patients and surgery-related factors that affect time to recovery of consciousness in adult patients undergoing elective cardiac surgery. J Chin Med Assoc. 2011;74(8):345-9.
17. <Differential Diagnosis Of Delayed Awakening From General Anesthesia A Review(6).pdf>.
18. Chittleborough M, Osborne G, Rudkin G, Vickers D, Leppard P, Barlow J. Double-blind comparison of patient recovery after induction with propofol or thiopentone for day-case relaxant general anaesthesia. Anaesthesia and intensive care. 1992;20(2):169-73.
19. AR B. Delayed awakening from anesthesia following electrolyte and acid-base disorders, two cases. Journal of Patient Safety & Quality Improvement. 2014;2(1):65-8.
20. Davarcı I, Dağlı C, Karcıoğlu M, Tuzcu K, Turhanoğlu S. Delayed Emergence from Anesthesia Associated with Undiagnosed Central Sleep Apnea Syndrome. Mustafa Kemal Üniversitesi Tıp Dergisi. 2014;5(18).
21. Garg R, Punj J, Pandey R, Darlong V. Delayed recovery due to exaggerated acid, base and electrolyte imbalance in prolonged laparoscopic repair of diaphragmatic hernia. Saudi Journal of Anaesthesia. 2011;5(1):79.

12. Annexes

Annex 1: Subject information sheet

Addis Ababa University

School of medicine

Subject information sheet

Hello there, I'm Dr. Tesfaye Sebsbie, a medical student at Addis Ababa University School of Medicine studying anesthesiology. My research topic involves evaluating the incidence and associated factors of delayed emergence after general anesthesia in patients undergoing surgery via general anesthesia at TASH, Addis Ababa, Ethiopia, 2023/24.

You are the participant in this study because you currently get perioperative service at TASH now. Whether or if you engage in this study will only depend on your willingness to do so. It is entirely up to you whether or not to take part in this study. If you would like to cease at any time and withdraw without explanation, you will not be treated unfairly. While taking part in this study won't directly benefit you, over time the information gathered will help improve the quality of treatment offered at TASH and other hospitals.

Your provided information will be kept private because only code numbers will be used, and the data will be locked. The non-coded data will only be accessible to the study team members, and it will not be utilised for any other reason than the study. Your willingness to participate fully in this study is crucial to its success.

You can get in touch with this address if you require any further details or clarification about the study.

Name: Dr Tesfaye Sebsbie Tel- +251-982133293 Email- tesfayesebsbie1@gmail.com

Annex 2: Informed Consent and/or Ascent form

Having read the aforementioned details, are you willing to take part in this study?

A) Yes B) No

If yes, Signature ---------- Date----------

Data collector Name ----------

Questionnaire ID Number ----------

Date of data collected ----------

Result of data collected

A) Completed

B) Not completed

C) Partially completed

D) Refused

Checked by supervisor: Name ---------- Signature ----------

For further explanation, use the principal investigator‟s address: Name: Dr. Tesfaye Sebsbie

Tel- +251-982133293 Signature ----------Email- tesfayesebsbie1@gmail.com