ADDIS ABABA UNIVERSITY COLLEGE OF HEALTH SCIENCES

DEPARTMENT OFANESTHESIA

Magnitude of Delirium and associated factors in intensive care units of selected governmental hospitals in Addis Ababa, Ethiopia.

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FULL TITLE OF THESIS	Magnitude of Delirium and associated factors at intensive care units of selected governmental hospitals in Addis Ababa, Ethiopia from September 2022 to November 2022
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STUDY AREA	TIKUR ANBESSA SPECIALIZED HOSPITAL, ST. PAUL, Minilik, yekatit 12HOSPITAL.
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Declaration

I, the undersigned, declare that this thesis is my original work in partial fulfillment of the requirements for the MSc in Anaesthesia. I understand that plagiarism will not be tolerated, and all directly quoted materials have been appropriately referenced.

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Date of submission _____

This thesis work has been submitted for examination with our approval as advisors and tutors on the MSc in Advanced Clinical Anesthesia course.

Approval of the advisors:

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Approval

This is to certify that the thesis prepared by Kirubel Behailu, entitled: Magnitude of Delirium and associated factors in intensive care units of selected governmental hospitals in Addis Ababa, Ethiopia.2022, in partial fulfillment of the requirements for the degree of Master's of Science in Advanced Clinical Anesthesia, complies with the regulations of the university and meets the accepted standards with respect to originality and quality.

Signed by the Examining Committee:

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ABSTRACT

Background: Delirium is defined as mental disorder of acute onset and fluctuating course characterized by disturbances in consciousness, orientation, memory, thought, perception, and behavior and its incidence is nearly 50% in ICU in those non intubated patients whereas in intubated patients it rises approximately to 80% according to different studies. Furthermore, ICU delirium is associated with negative outcomes such increases length of ICU stay, prolonged mechanical ventilation, a high rate of admission after discharge and over all increased patient mortality according to varieties of studies.

Objectives: The objective of this study is to assess the magnitude of delirium and associated factors in intensive care units of selected governmental hospitals in Addis Ababa, Ethiopia.

Methods: Institution based multicenter cross-sectional study was conducted on patients admitted to intensive care units of selected governmental hospitals in Addis Ababa from September1, 2022 to November 30, 2022.Froma total of 403patientsselected from Four hospital using simple random sampling technique 388 Patients were included in the final analysis. Before being imported into STATA/MP version 17, the data were originally input into Epidata version 4.6. The analysis fitted bivariable and multivariable binary logistic models to find the explanatory variables. The 95% confidence interval of the odds ratio (OR) was calculated, and factors with a p-value less than 0.05 in the multivariable model were declared significantly associated with the dependent variable.

Results: incidence of delirium in the ICU at selected Addis Ababa hospitals was 31.44% (95% CI: 27.00%, 36.25%).age(AOR= 5.29, 95%CI: 2.28, 12.84), coexisting illness (AOR= 4.23, 95%CI: 1.97, 9.78), alcohol history (AOR= 6.72, 95%CI: 2.68, 20.48), and APACHE II score (AOR= 1.11 95% CI: 1.05, 1.17) were significantly associated with delirium in ICU.

Conclusion: Delirium was high at Four Addis Ababa government hospitals' ICUs. Age, concurrent disease, alcohol history, and APACHE II score were significant ICU delirium predictors.

Keywords: intensive care unit, Delirium, CAM-ICU, ICDSC, APACHE score.

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Acronyms

AOR	Adjusted odds ratio
CAM-ICU	Confusion assessment method- Intensive care unit
CI	Confidence interval
ICU	Intensive care unit
RA	Research assistant
RASS	Richmond Agitation-Sedation Scale
SD	Standard deviation
ICDSC	Intensive care delirium screening checklist
APHACHE	Acute Physiology and Chronic Health Evaluation

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1. Introduction

1.1 Background

The Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) defines delirium as a disturbance in cognition and higher functioning with the short onset and fluctuating course,whether from an acute illness, drug intoxication, or withdrawal but not fromother neurocognitive disorders.Deliriumis a frequent clinical scenario observed in hospitalized patients where inattention, altered consciousness, or disorganized thinkingare other features (1, 2).

Delirium is a syndrome that commonly affects patients admitted to the intensive care unit (ICU), but the incidence of delirium in the intensive care setting varies from 7% to 87%. These marked variations exist as there are differences in studies done regarding population characteristics, type of ICU used (medical, surgical, both), study methodology, an assessment tool used for diagnosis of delirium, staff training, medications used,and individual ICU practices(3-5).

In developing areas of the world, especially Africa, ICU delirium is a new concept.A few ICU-attending health professionals are aware of it, and its assessment is not routinely performed in the setting.Withincreasing access to critical care, even in low-income countries, thenumberof patients admitted to ICU with a mechanical ventilator is increasing, placing more patients at risk of delirium and its adverse outcomes(6).

Detecting and monitoring ICU delirium is made possible by applying Confusion Assessment Method for the ICU (CAM-ICU) and the Intensive Care Delirium Screening Checklist (ICDSC), validated and reliable ICU delirium assessment tools. These tools allow clinicians without psychiatric training to diagnose delirium, even in nonverbal, mechanically ventilated patients(7).

With proper identification of risk factors by ICUnurses, delirium is a preventable clinical condition. Additionally,identifying high-risk patients and the early detection and prevention of ICU delirium isessentialfor rapid recovery.Its appropriate management is also based onearly identification and risk factor assessment(8, 9).

In Ethiopia,studies are done on the magnitudeof delirium and its associated factors,emphasizing the area of postoperative emergency delirium at PACU, among postoperative patients after elective surgery, and among hospitalized patients. The findings of the studies showed the

magnitude of delirium to be 37.1%, 27.6%&16.6%, respectively. Despitethese, studies onthemagnitude of ICU delirium and its associated factors have not been studied yet(10-12).

1.2 Statement of the problem

They are improving medical care in modern medicine resulting in an increment of ICU survivors considerably these days. On the contrary, recent studies demonstrate that ICU survivors can experience substantial long-term morbidity;to further improve care for survivors of critical illness, it is essential to identify common factors like delirium, which can increase the risk of long-term morbidity and mortality. Delirium is a significant problem in ICU due to the increased risk factors in these patients compared with non-ICU patients(13, 14).

Higher age(Age>70), benzodiazepine exposure,increased APACHE II score, abnormal electrolyte values,disease severity, having pneumonia, previous cognitive impairment, depression, or previous stroke, mechanical ventilation, a higher number of total medication received and use of sedative, functional status and physical restraints were common factors indicated as a precipitating factor for ICU delirium. Most of the patients had delirium within five days of ICU admission,which is associated with a longer intensive care unit (ICU) stay and higher mortality rates(15, 16).

ICU Delirium is mostly undiagnosed and undermined clinical scenarios by health professionals in developing countries like Ethiopia. It usually gets little attention in ICUs since it is often believed that it is the expected way of ICU patients without considering its unfavorable outcomes. Due to its difficulty in management, it also signifies a poor prognosis in the hospital, and beyond the diagnosis of delirium is crucial in ICU. Further,The effect of delirium on relevant clinical outcomes is not restricted to the hospital setting, as it is also an independent predictor of mortality and long-term cognitive impairment (17).

From research done on the ways for prevention and management of delirium in ICU, a recent study by Michael E. Reznik et al. has shownmulticomponent non-pharmacologic interventions to be the best strategies for delirium prevention, with real-world evidence favoring the use of the ABCDEF bundle which is specially used in mechanically ventilated patients. The research further elaborated that avoiding high-risk medications such as benzodiazepines and anticholinergicsprevents delirium, especially in older patients. Whereas potential pharmacologic

treatments for ICU delirium with promising results include dexmedetomidine and, to a lesser extent, ramelteon, more data, and further research are needed for recommendation(18).

In low-income countries like Ethiopia where, malnutrition, infectious disease, sepsis, and trauma are common clinical scenarios that might need intensive care unit admission and follow-up, but very little is known about the magnitude of delirium, especially in critically ill and the associated factors with it, so this study will determine the magnitude of delirium specifically in ICU and will also explore associated factors.

Even though different studies were done on the prevalence of delirium and associated factors at different hospital units and a general patient population, little is known about delirium in ICU, particularly in our country. Furthermore, this study employs a multi-center cross-sectional study is aims to know the magnitude and factors associated with delirium.

1.3 significance of the study

Different studies were done on trends of ICU admissions and their outcomes in Ethiopia, showing increased admission rates and high mortality for different reasons. Delirium is considered an independent risk factor for increased mortality of ICU patients according to many studies done in high income and some African countries, so the exact burden, associated factors, and possible consequences should also be known in our county.

Although delirium harms patient outcomes in ICU, the condition usually stays unrecognized and untreated So this study was used as a means to start assessment of ICU Delirium as a routine clinical practice in different hospitals of Addis Ababa using validated tools like The Confusion Assessment Method for the ICU (CAM-ICU) and the Intensive Care Delirium Screening Checklist.

This research will also help healthcare providers, governmental and non-governmental organizations make the most of efforts to design preventive and treatment strategies for ICU delirium in our country and the study area while also serving as a valuable resource for other researchers. It will also serve as a guide for future research, including developing local Guidelines on ICU delirium.

2. Literature review

2.1. Magnitude of ICU delirium

An observational study done in Italy on the Prevalence and risk factors of delirium in the intensive care unit has participated patients admitted to ICU. From 165 patients, where 38.8% had been subjected to trauma, 37.6% had undergone general surgical interventions, and 23.6% had undergone medical interventions, results revealed that 55.8% of patients were Delirious(19). In a similar study but with a prospective cohort study design done in Brazil from 149 patients, 69 (46.3%) patients developed delirium in the ICU(20).Additionally, Studies from Portugal, with 562 participants, and the Netherlands,with412 participants, showed the prevalence of ICU delirium to be 16% and 37%,respectively(21, 22).

Since delirium is a common condition in older adults, which can have devastating outcomes, different Studies were done on the magnitude of ICU delirium, specifically on older patients, showing significant prevalence in a study on the prevalence, incidence, and risk factors of delirium among older Thailand adults in ICU where Delirium was rated by trained clinical personnel using the Confusion Assessment Method for the ICU (CAM-ICU). The Results showed delirium occurred in 44 of 99 patients (44.4%) with an incidence rate of 22.2% (22/99) (15). Unlike the result found in Thailand, research on the incidence of ICU delirium among old age in Australia and Canada showed slightly low results, with 499 elderly at about 17% and 548 elderly at 11%, respectively (23, 24).

As COVID-19 emerged as a public health threat in December 2019 and was declared a pandemic by WHO in March 2020, delirium has been becoming evident in COVID-19 patients admitted to ICU. An observational study done in the USA on Delirium Incidence, Duration, and Severity in Critically Ill Patients with Coronavirus Disease showed that the incidence of delirium without coma occurred in 29.1% of patients, delirium prior to coma in 27.9%, and delirium after coma in 23.1%(25). Whereas another cohort study was done in USA on Delirium and neuropsychological outcomes in critically Ill patients with COVID-19 results showed delirium was identified in 108/148 (73%) patients, with a median (IQR) duration lasting 10 (4–17) days. In the delirium cohort, 50% (54/108) of patients were African American, and delirious patients were more likely to be female (76/108, 70%) (Absolute standardized differences >0.30)(26).

Even though literature is explicitly limited on the magnitude and associated factors of ICU delirium, few pieces of research have been carried out on the issue of delirium in different settings of hospitals and on post-surgical patients in Africa and Ethiopia in particular. In an Observational Multi-center Study done in South Africa on incidence and Risk Factors for Delirium among Mechanically Ventilated Patients, results showed that Of 160 patients, 81 (51%) had delirium, with the Median time to onset of delirium being 3.7 days. In Ethiopia, the studies on the incidence of emergency delirium at PACU in a study done at the black lion and a Cross-Sectional Study done Magnitude and Associated Factors of Delirium among Hospitalized Patients showed incidences of 37.1% and 16.6%, respectively (10, 12, 27).

2.2. Factors associated with ICU delirium

In different studies done on risk and associated factors of ICU delirium with different study designs from socio-demographic variables, patients' age where Patients with delirium were significantly older (mean age = 65.7, SD = 8.1), $t(243) = -3.66$, $P < .05$) are associated with the occurrence of delirium according to a study Abla Habeeb-Allah ., results from a study by Satomi Mori as well showed as age is significantly associated, and further more a study by Akhilesh Sharmahas also showed higher age to be statistically significant(3, 16, 19). In contrast, sex is not significantly associated with ICU delirium.

In a Systematic Review of Risk Factors for Delirium in the ICU by Irene J. Zaal et al., in which 33 studies were included, 70% were high quality. There was strong evidence that age, dementia, hypertension, pre-ICU emergency surgery or trauma, Acute Physiology and Chronic Health Evaluation II score(APHACHEII), mechanical ventilation, metabolic acidosis, delirium on the previous day, and coma are risk factors for delirium. Consistent with these findings, a study by Akhilesh Sharma etal., in addition to the above factors, abnormal laboratory values such as hyperuricemia; hypoalbuminemia; abnormal alkaline transferase levels; higher number of total medication received and use of sedatives, steroids, and insulin in ICU are considered to be significantly associated with delirium in ICU(3, 28). In addition to the above results, Panita Limpawattana et al. studies after multivariate regressions, stroke, multiple bed changes, and physical restraints were found to be the significant factors for Delirium in ICU (15).

In a systematic review and meta-analysis by Jorge I F Salluh etal.The outcome of delirium in critically ill patients: Delirium was identified in 5280 of 16595 (31.8%) critically ill patients

reported in 42 studies. When compared with control patients without delirium, patients with delirium had significantly higher mortality during admission (risk ratio 2.19, 94% confidence interval 1.78 to 2.70; P<0.001)as well as longer durations of mechanical ventilation and lengths of stay in the intensive care unit and hospital (standard mean differences 1.79 (95% confidence interval 0.31 to 3.27; P<0.001) respectively(29).

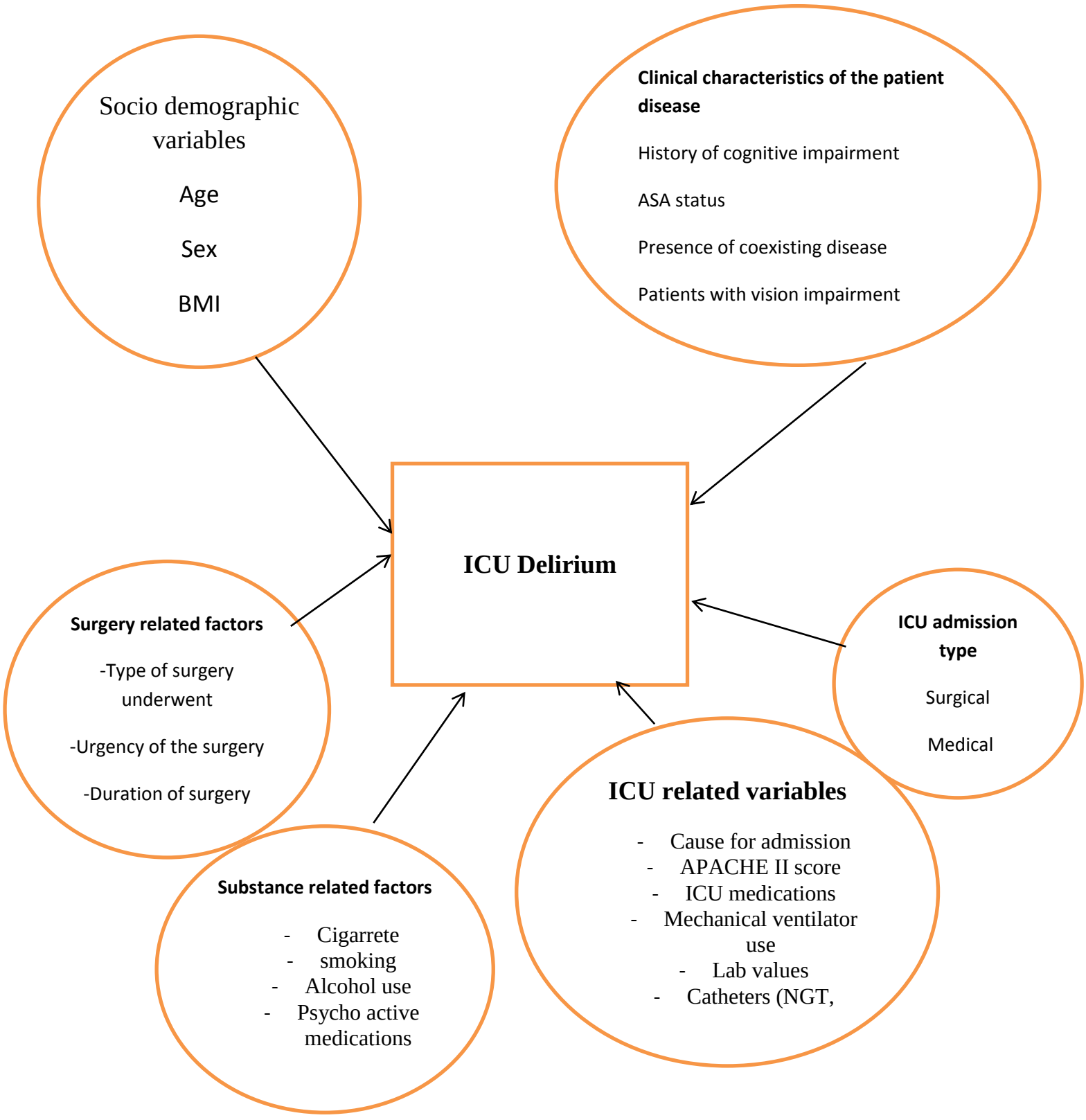

Figure 1: Conceptual framework for assessing the factors of ICU delirium, developed after literature review.

3. Objective

3.1 General objective

- To assess the magnitude and associated factors of Delirium in intensive care units of governmental hospitals in Addis Ababa from September 1 to November 30, 2022.

3.2 Specific objective

- To determine the magnitude of delirium in patients admitted to intensive care units of governmental hospitals in Addis Ababa.
- To identify factors associated with delirium among patients admitted to intensive care units of governmental hospitals in Addis Ababa.

4. Methods

4.1 Study design

A cross sectional study design was conducted from September 1toNovember 30, 2022.

4.2 Study Area

The study was conducted in four purposively selected governmental hospitals based on their high number of patient admissions to ICU in Addis Ababa.

Tikur Anbessa Specialized hospital, Saint Paul hospital, Minilik II Referral hospital and yekatit 12 hospital Medical College. Addis Ababa is the capital and largest city of Ethiopia. According to World Population Review 2021, the population size of Addis Ababa town is estimated to be 5,005,524.TikurAnbessa Specialized Hospital was established in 1972 and is the largest referral hospital in the country, with 700 beds. MinilikII Referral Hospital provides health services for the catchment population of about one million and six hundred thousand people. Saint Paul Hospital (affiliation with AaBET hospital) was built in 1969 and medical college was formed in 2007. The hospital has 350 beds sees an annual average of 300,000. It has a catchment population of more than 5 million. 16 ICU beds in Tikur Anbessa hospital, 8 in Minilik II Referral hospital, 8 in yekatit 12 hospital Medical College and 14 in Saint-Paul Hospital (affiliation with AaBET hospital) are used for critically ill patients.

4.3 Population

4.3.1 Source population

Critically ill patients admitted to the intensive care unit of the four hospitals.

4.3.2 Study population

All critically ill patients admitted to intensive care of the four hospitals from September 1, 2022 to November30,2022.

4.4. Sample size and sampling techniques

4.4.1 Sample size determination

Sample size determined by modified Cochran single population proportion formula.

$$X = \frac{Z\alpha/_2{}^2 * P * (1 - P)}{w^2}$$

Confidence interval = 95%

α= 0.05% (critical value 1.96)

w= 0.05

Prevalence of Delirium in ICU = 51 % where (p=0.51) from study done at South Africa(27).

Thefinalsample is calculated by adding 5% of contingency and the final sample size was 403.

4.4.2. Sampling procedure

Study subjects were selected in the study using a proportion allocation algorithm, which divides the number of admissions in each ICU by the total number of admissions in the Four ICUs multiplied by the sample size (**n** = 403).

TASH = n1/**N*n, SPHMMC =** n2/**N*n, MIIRH =** n3/**N*n and Y12MC=**m4/**N*n**

Where N is the total number of admission to all four hospitals, n1, n2, n3 and n4are the total admission in **TASH**, **SPHMMC**, **MIIRH** and **Y12MC** hospitals. Simple random sampling method was used to choose the needed number of participants from all newly admitted ICU patients in the study period from September 1, 2022 to November 30, 2022.The calculated total sample size was allocated to selected hospital based on the above proportional allocation formula.

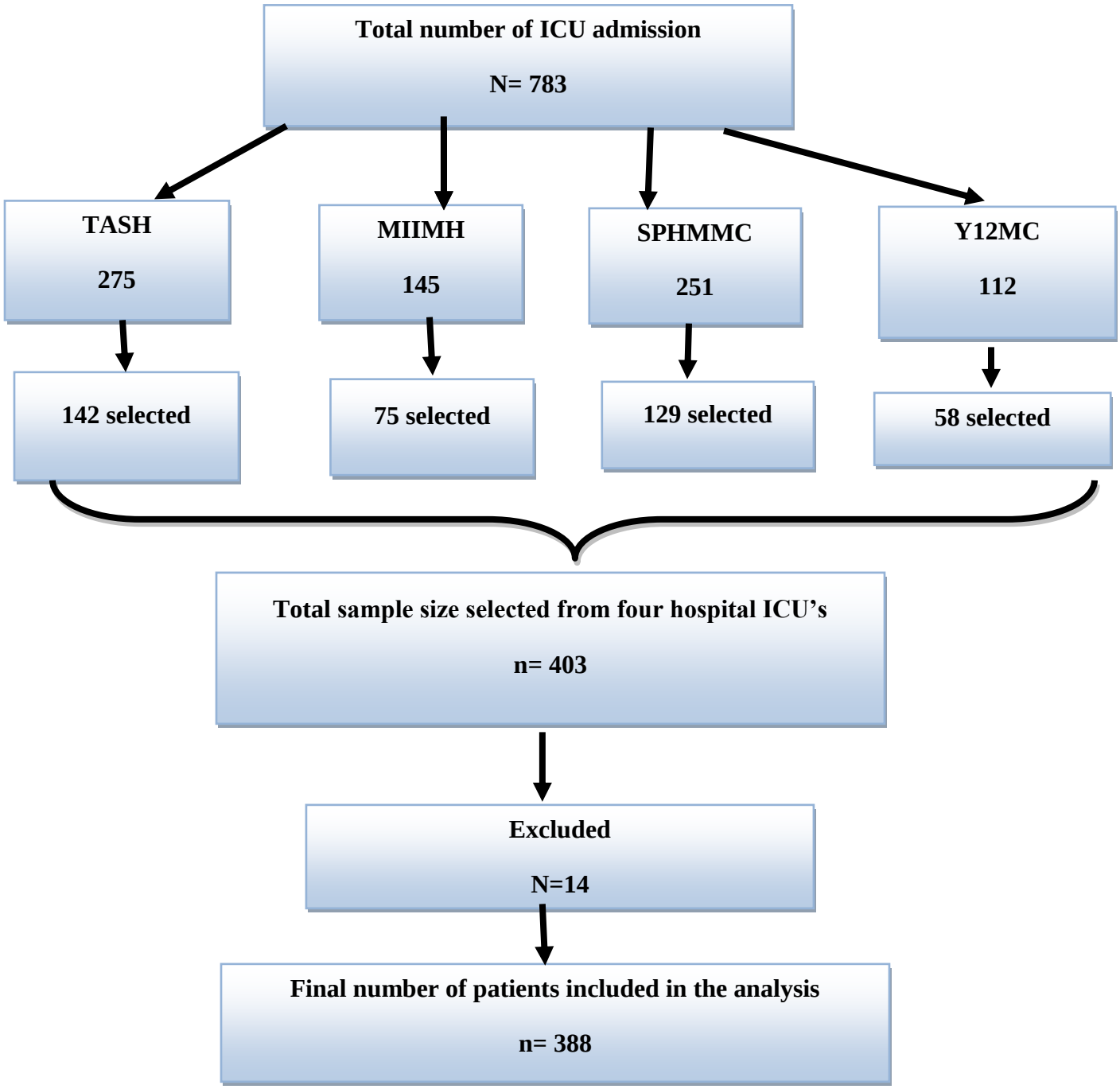

Figure 1 Flow diagram of proportional allocation and sampling

4.5 Inclusion and exclusion criteria

4.5.1 Inclusion criteria

All adult age > 18 newly admitted patients to intensive care unit between September 1st, 2022to November 30,2022were included.

4.5.2 Exclusion criteria

-Patients with RASS score <-3

- Patients who died during follow up period.

-patients who were discharged from ICU during follow up

4.6 Variable of the study

4.6.1 Dependent variable

Delirium in ICU (yes/no)

4.6.2 Independent variable

Socio-demographic variables: Age, Sex, BMI

Surgery related Variables: Type of surgery underwent, urgency of the surgery and duration of the surgery.

Presence of coexisting illness: Hypertension, DM, Asthma, COPD, Cancer, Cardiac illness, renal illness, infectious disorder, psychiatric disorder, Neurologic disorder.

Clinical characteristics of the patient disease: History of cognitive impairment, visual impairment, ASA status

Type of ICU Admission: Medical or Surgical

Substance related factors: Cigarette smoking, Alcohol use and Psycho active medications.

ICU related variables: Cause for admission, APACHE II score, and Mechanical ventilator use Catheters (NGT, bladder, rectal, cvc).

ICU Medications: Analgesics, sedatives, steroids

Lab values at ICU: Hemoglobin, Platelet, serum albumin, urea, Cr, Na^+, K^+

4.7 Data collection, analysis and quality control

4.7.1 Data collection procedures

Data collectors: Two intensive care unit nurses in each of the selected hospitals collected the data by the supervision of 1 head ICU nurse professionals having a minimum qualification of BSc degree at Tikur Anbessa Hospital ICU, Saint-Paul Hospital ICU Minilik II Hospital and yekatit 12hospital Medical College.

Data were collected using structured, pre-tested, internationally validated data-collecting format and a checklist prepared for this purpose. Socio demographic and independent variables are collected through chart review. CAM-ICU, a validated tool for delirium assessment by non-psychiatrist health professionals, was used to assess delirium in ICU. Patients were screened for delirium after 24 hours of ICU admission, and assessment was conducted two times daily every 12 hours during vital sign sand RASS assessment by ICU Nurses for 5days.Forpatients who are aggressive (RASS>+3) during delirium assessment re assessment was done after decreasing environmental stimuli, early and frequent mobilization, providing hydration to the ICU patient.

4.7.2 Data quality control

Two nurses in each of the selected hospitals who collect the data were given a group training session conducted by the principal investigator and under taken actual personalized training. They will also be provided with a detailed training manual on ICU Delirium. To ensure data quality, a pre-test was conducted on study subjects (5% of the calculated sample size) at Minilik II referral hospital those included in pre-test was excluded from analysis. The principal investigator, with another supervisor, will supervise the overall process. The filled formats were checked for completeness by the principal investigator and the supervisor daily.

4.7.3 Data processing and analysis

The collected data was cleaned, coded, and analyzed by SPSS 25 statistical package. Using STATA version 17 basic descriptive statistics like frequency was done for socio demographic variables and for the outcome variable. Multivariable logistic regression is used to assess the association of variables. Adjusted and crude odds ratios and their 95% confidence interval are used as indicators of the strength of association. A $p< 0.05$ or less are used as cut off level to declare statistical significance. Model fitness for logistic regression analysis was checked by

Hosmer-Lmeshow goodness of fit test (p-value=0.1125). Results were narrated and expressed in tables and graphs after analysis.

4.7.4 Operational definitions

Confusion Assessment Method for the ICU (CAM-ICU): is modified from the Confusion Assessment Method and assesses four features 1) Acute change or fluctuation in mental status from baseline,2) inattention, 3) altered level of consciousness and 4) disorganized thinking. The CAM-ICU is positive, and the patient is considered to have delirium, if Features 1 and 2 and either Feature 3 or 4 is present.

Incomplete records: If important data are not written on the card, such as demographic data, variables related to the disease condition and variables related to the laboratory values.

APACHE II score: A widely used method for assessing severity of illness in acutely ill patients in intensive care units, taking into account a variety of routine physiological parameters.

The Richmond Agitation and Sedation Scale (RASS):is a validated and reliable method to assess patients' level of sedation in the intensive care unit. As opposed to the Glasgow Coma Scale (GCS), the RASS is not limited to patients with intracranial processes.

4.7.5 Ethical consideration

Ethical clearance was obtained from the Institutional Review Board (IRB) of the College of health science, Addis Ababa University. After getting consent from the responsible bodies in each hospital, data was collected after an informed consent obtained from the family members of the patients prior to recruitment. Confidentiality was ensured by avoiding personal identification from the questionnaire.

4.7.6 Dissemination of results

The final result of the research will be submitted to the Department of Anesthesia, College of Health Science, and Addis Ababa University. Next, the study findings will be disseminated to the regional health bureau and respective health facilities. Lastly, an attempt will be made to publish the findings in a peer-reviewed scientific journal.

5. Results

5.1 Socio-demographic characteristics of study subjects

Seven hundred eighty-three were hospitalized to the intensive care units of the four government hospitals between September 1, 2022 and November 30, 2022.14 out of 403 randomly selected Study participants were excluded according to predefined exclusion criteria, and 388 patients were included in the final analysis. Approximately 210 (55.50%) of individuals aged 34 to 64 years. About 54.64% of the whole sample consisted of male subjects, and more than 85% of study subjects had a BMI within the normal range. (Table **1**)

Table 1 Socio-demographic characteristics of study subjects

Variable	Category	Frequency	Percentage
Age (year)	18-33	117	30.15%
	34-65	213	54.90%
	>65	58	14.95%
Gender	Male	212	54.64%
	Female	176	45.36%
BMI (kg/m2)	<18.5	36	9.42%
	18.5-24.9	330	86.39%
	>=25.0	16	4.19%

5.2 Behavioral characteristics of the study participants

Regarding behavioral factors, 85 (23.45%) had a smoking history, 118 (30.41%) had an alcohol history, and 48 (12.37%)had substance abuse. (Table 2)

Table 2 Behavioral characteristics of study subjects

Variable	Category	Frequency	Percentage
Alcohol history	Yes	118	30.41%
	No	270	69.59%
Smoking history	Yes	91	23.45%
	No	297	76.55%
Substance abuse	Yes	48	12.37%
	No	340	87.63%

5.3. Clinical and physiologic characteristics of the study subjects

Of 388 critically ill patients, 216 (55.67%) were admitted to the medical ICU. Among 172 surgical patients, 74 exhibiting ASA physical status II, 33 subjects underwent neurosurgery, and nearly two-thirds of patients (106) underwent emergency surgery. Respiratory failure was the most frequent cause of ICU admission, followed by traumatic brain injury and postoperative monitoring, with regards to the cause of ICU admission surgery From all study subjects,116 (29.64%) had comorbidity, More than a three-fourth of patients admitted to ICU have no history of use of psychoactive medication, cognitive impairment, and visual impairment. On admission, the mean hemoglobin and creatine were 12.75 (SD ± 1.72), and 1.241 (SD ± 0.38) mg/dl, respectively. The mean APACHE II score was 20.07 (SD ± 6.07).During the ICU stay, the percentage of study subjects who received analgesic and sedative steroidal agents were 40.21%, 36.01%, and 32.73%, respectively. One hundred fifty-one critically ill patients received nasogastric tube feeding, and 330 had urinary catheterization. (Table 3)

Table 3 Clinical and physiologic characteristics of study subjects

Variable	Category	Frequency	Percentage
ICU	Medical	216	55.67%
	Surgical	172	44.33%
Cause of admission	Respiratory failure	102	26.29%
	Traumatic head injury	87	22.42%
	Sepsis/septic shock	58	14.95%
	Postoperative monitoring	84	21.65%
	Other	57	14.69%
Comorbidity	Yes	189	29.64%
	No	199	70.36%
Cognitive impairment	Yes	20	5.16%
	No	368	94.84%
Psychoactive medication	Yes	73	18.82%
	No	315	81.18%
Visual impairment	Yes	11	2.84%
	No	377	97.16%
Hemoglobin	12.75 (SD ± 1.72)		
Creatinine	1.241 (SD ± 0.38)		
APACHE II score	25(SD ± 6.07)		
Analgesia	Yes	232	59.79%
	No	156	36.01%
Sedative	Yes	248	63.99%
	No	139	36.01%
Steroid	Yes	127	32.73%
	No	261	67.27%
NG tube	Yes	151	38.92%
	No	237	61.08%
Catheter	Yes	58	14.95%
	No	338	85.05%

5.4. The magnitude of delirium in ICU

Of 388 study subjects included in the final analysis, 122 developed delirium in ICU. The overall prevalence of delirium in the ICU at selected Addis Ababa hospitals was 31.44% (95% CI: 27.00%, 36.25%). (Figure 2)

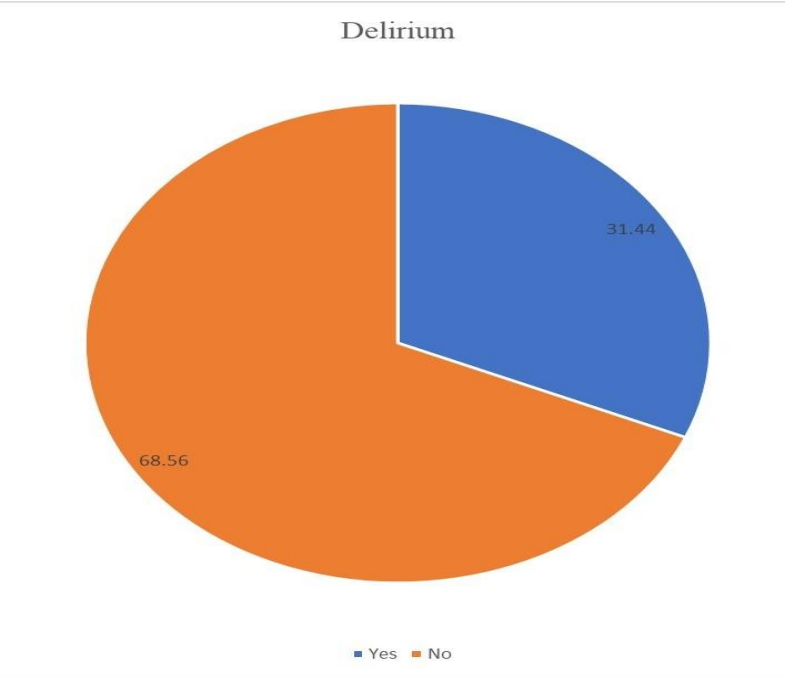

Figure 2 Magnitude of delirium in ICU

5.5 Factors associated with delirium in ICU

After assessing the assumptions of logistic regression, the binary logistic regression model was fitted to identify significant predictors of delirium among patients admitted to the ICU.

In multivariable binary logistic regression covariates, age, coexisting illness, alcohol history, and APACHE II score were significant predictors for delirium in ICU. (Table 4)

The odds of developing delirium in ICU among patients aged >65years was 5.29 (**AOR= 5.29, 95%CI: 2.28, 12.84**) times higher than those aged 18-33 and 34-64 years On the other hand presence of comorbidity had 4.23 (**AOR= 4.23, 95%CI: 1.97, 9.78**) times increased risk of delirium in ICU compared with patients with no comorbidity. Those patients who had alcohol history have a 6.72 (**AOR= 6.72, 95%CI: 2.68, 20.48**) times increased odds of developing delirium in ICU compared to their counterparts. In addition, there will be an 11% (**AOR= 1.11**

95% CI: 1.05, 1.17) increased risk of delirium in the ICU for every one-unit increment in the APACHE II score.

Table 4 Bivariable and multivariable binary logistic regression to identify factors associated with delirium in ICU

Variable	Category	Delirium in ICU		COR (95% CI)	AOR (95% CI)
		Yes	No		
Gender (5980)	Male	76	136	1.57 (1.01, 2.44)	1.04 (0.45, 2.38)
	Female	46	130	1	
Age	18 – 33	23	94	1	
	34- 64	66	147	1.83 (1.06, 3.15)	1.83 (0.69, 4.80)
	>65	33	25	5.39 (2.70, 10.79)	5.29 (2.28, 12.84)**
BMI	<18	16	26	1.89 (0.94, 3.80)	2.49 (0.61, 10.41)
	18 – 4	98	232	1	
	>24.9	6	10	1.42 (0.50, 4.01)	0.47 (0.14, 3.84)
Alcohol history	Yes	54	64	2.50 (1.59, 3.94)	6.72 (2.68, 20.42)***
	No	68	202	1	
Smoking history	Yes	31	54	1.29 (0.78, 2.15)	3.08 (0.11, 8.63)
	No	91	206	1	
Comorbidity	Yes	97	92	2.86(1.68, 4.87)	4.23 (1.97, 9.78)*
	No	71	128	1	
Creatinine		1.29 (±0.45)	1.21 (±0.34)	1.70 (0.98, 2.94)	1.49 (0.69, 3.24)
Hemoglobin		13.84 (±1.14)	13.54 (±1.49)	0.81 (0.68, 0.97)	1.01 (0.80, 1.27)
APACHE II score		23.59 (±7.11)	18.45 (±5.48)	1.13 (1.09, 1.18)	1.11 (1.05, 1.17)***
Analgesia	Yes	91	141	2.60 (1.62, 4.17)	1.59 (0.63, 3.99)
	No	31	125	1	
Sedative	Yes	64	75	2.78 (1.78, 4.33)	2.06 (0.88, 4.84)
	No	58	189	1	

*p-value <0.05 **p-value<0.001

6. Discussion

This study studied the prevalence and determinants of delirium among patients hospitalized in intensive care units of three selected Ethiopian government hospitals. Delirium in the ICU is associated with increased morbidity and mortality. While previous research has identified several potential risk factors for delirium in ICU, our study went a step further by analyzing socio-demographic, behavioral, clinical, and physiological factors. Among potential factors contributing to delirium in ICU, age, coexisting illness, alcohol history, and APACHE II score were significantly associated with delirium in ICU.

In this study, the prevalence of delirium among patients admitted to the ICU in three hospitals in Addis Ababa, Ethiopia, was 31.44% (95% CI: 27.00%, 36.25%). Our results were consistent with studies conducted in Latin America(30), Switzerland (30), and Nigeria (31). The result of this study was higher than reports from Saudi Arabia (32), India (33), Thailand (34) and Canada (35). This discrepancy might be due to differences in the level of medical care in which a high level of medical care reduces the incidence of delirium in the ICU. On the contrary, our results were lower than studies from Uganda (27) and Japan (36). The possible explanation for this contradiction might be a difference in the study population and sample size.

Our study found that the incidence of delirium in the ICU increased with age>65 years. This finding is inline with multiple studies, as age is reported to be an independent risk factor for delirium..(32-34, 37). This link could be the loss of central cholinergic neurons in older adults with a diminished ability to respond to stress and adjust to an altered metabolism (38). Additionally, age-related disruptions of several neurotransmitter systems may be the leading pathogenic cause of delirium in the ICU. These alterations increase elderly susceptibility to delirium in ICU (39).

In this study, comorbidity increased the likelihood of delirium in the ICU. This finding agrees with a study by *Bart Van Rompaey et al* (40). The association between comorbidity and delirium in ICU could be explained by patients with comorbid conditions who have a severe disease upon admission, which contribute to a deteriorated central nervous system function that increases the chance of delirium developing in the ICU(41). Moreover, patients with the comorbid condition

are highly likely to be on invasive mechanical ventilation, venous catheter, and arterial catheter, increasing the ICU's risk of delirium.

The result of our study is that patients with a history of alcohol intake have an increased risk of delirium in the ICU. This result is consistent with studies done in the United Kingdom (42) and Italy (20); the possible reason might be that patients who have a history of alcohol intake have a significant risk of autonomic hyperactivity, hallucinations, agitation, and seizures in which these conditions aggravate the risk of delirium (42). In addition, patient with a history of alcohol intake has a risk of alcohol-induced psychosis, which affect the likelihood of delirium in the ICU (43).

As evidenced by multiple pieces of literature, a higher APACHE II score predict the likelihood of delirium ICU delirium (25, 30, 44). Although the sensitivity and specificity of the APACHE scoring system are still under investigation, it remains a vital scoring system for assessing the severity and prognosis of critically ill patients. Apart from delirium prediction, this scoring system helps predict mortality among patients who developed delirium in the ICU using changes in scores from the baseline. APACHE score incorporates various physiological parameters to predict delirium. An increase in the APACHE score shows a significant hemodynamic and physiologic disturbance which is suggestive of the development of delirium in critically ill patients (45). Early prediction of delirium in the ICU is essential to identify a patient with a higher risk of delirium and execute target-specific interventions. Hence, an effective delirium prediction model is a potent instrument for ICU clinicians to assist early deployment of preventative measures(46).

The clinical significance of this investigation was to provide patients and healthcare providers with information about factors associated with the risk of delirium in the ICU so that they could act to minimize the risk and maximize their efforts in preventing the problem while the public health significance of this study was to prevent economic loss associated with delirium and its complications.

6.1 Strength and limitation

6.1.1 Strength of the study

- A multi-center study
- Application of simple random sampling technique
- Low non-response rate

6.1.2 Limitations of the study

- The study design was cross-sectional, in which causal relationships could not be identified
- Due to the unavailability of laboratory investigation, variables like albumin and electrolytes were not assessed as a potential predictor of delirium

7. Conclusion and recommendations

7.1 Conclusion

In this longitudinal study, we found that the magnitude of delirium among patients admitted to the ICU of the four governmental hospitals in Addis Ababa was high. Age, coexisting illness, alcohol history, and APACHE II score were significant determinant factors associated with delirium in ICU.

7.2 Recommendation

Based on the findings of this study, we forwarded the following recommendations

For clinicians

- We recommend clinicians use APACHE II score up on admission and during ICU stay to predict ICU delirium.
- Target-specific interventions are recommended among older age, patients with comorbidity and alcohol history in order to minimize the risk of delirium in the ICU

For Researchers

- Further studies are recommended by including variables like nutritional variables
- Cohort studies with long follow-up time are regarded in order to identify causal-relationship
- Studies with large sample sizes are recommended in order to estimate the magnitude of delirium in ICU better

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Annex I

This data extraction checklist is prepared to collect socio-demographic and other related variables for assessing delirium and associated factors in ICU in Tikur Anbessa, Minilik, and Saint Paul hospitals. All this information will be retrieved from individual patient cards and the CAM-ICU assessment tool was used to assess delirium in ICU without mentioning the name of clients. This information was collected by health care providers (ICU nurse).

Table 1. Assessing Consciousness: Linking Level of Consciousness & Delirium Monitoring

Step 1 Level of Consciousness: Richmond agitation and sedation score (RASS*)

Scale	Level	Description
+ 4	COMBATIVE	Combative, violent, immediate danger to staff
+ 3	VERY AGITATED	Pulls to remove tubes or catheters; aggressive
+ 2	AGITATED	Frequent non-purposeful movement, fights ventilator
+ 1	RESTLESS	Anxious, apprehensive, movements not aggressive
0	ALERT & CALM	Spontaneously pays attention to caregiver
-1	DROWSY	Not fully alert, but has sustained awakening to voice
-2	LIGHT SEDATION	Briefly awakens to voice (eyes open & contact
-3	MODERATE SEDATION	Movement or eye opening to voice (no eye contact)
	If RASS is ≥ -3 proceed to CAM-ICU (Is patient CAM-ICU positive or negative?)	
-4	DEEP SEDATION	No response to voice, but movement or eye opening to physical stimulation
-5	UNAROUSABLE	No response to voice or physical stimulation
	If RASS is -4 or -5 ,STOP (patient unconscious), RECHECK later	

Step 2: Content of Consciousness: CAM-ICU

.

……

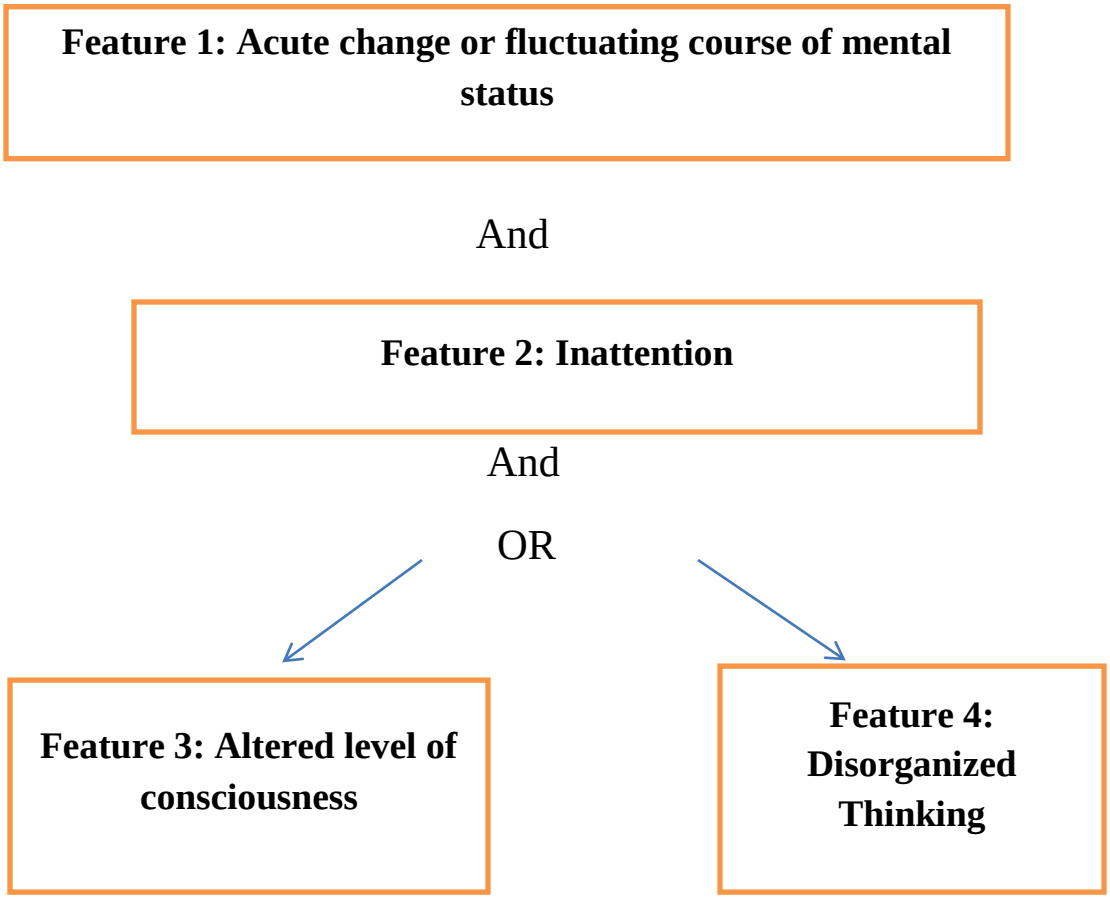

Table 4: CAM-ICU Worksheet

Feature 1: Acute Onset or Fluctuating Course	Score	Check here if Present
Is the patient different than his/her baseline mental status? OR Has the patient had any fluctuation in mental status in the past 24 hours as evidenced by fluctuation on a sedation/level of consciousness scale(RASS)	Either question Yes →	☐
Feature 2: Inattention		
Letters Attention Test Directions: Say to the patient, "I am going to read you a series of 10 letters. Whenever you hear the letter 'A,' indicate by squeezing my hand." Read letters from the following letter list in a normal tone 3 seconds apart. S A V E A H AA R T or C A S A B L A N C A or A B A D D A Y **Errors are counted when patient fails to squeeze on the letter "A" and when the patient squeezes on any letter other than "A."**	Number of Errors >2 →	☐
Feature 3: Altered Level of Consciousness		
Present if the Actual RASS score is anything other than alert and calm (zero)	RASS anything other than zero →	☐
Feature 4:Disorganized Thinking		
Yes/No Questions (See training manual for alternate set of questions) 1. Will a stone float on water? 2. Are there fish in the sea? 3. Does one pound weigh more than two pounds? 4. Can you use a hammer to pound a nail? **Errors are counted when the patient incorrectly answers a question**. **Command**; Say to patient: "Hold up this many fingers" (Hold 2 fingers in front of patient) "Now do the same thing with the other hand" (Do not repeat number of fingers) *If the patient is unable to move both arms, for 2nd part of command ask patient to "Add one more finger"**An error is counted if patient is unable to complete the entire command**	Combined number of errors >1 →	☐

Overall CAM-ICU **Feature 1 plus 2 and either 3 or 4 present = CAM-ICU positive**	Criteria Met →	 CAM-ICU Positive (Delirium Present)
	Criteria Not Met →	 CAM-ICU Negative (No Delirium)

Table 5: A checklist to assess socio-demographic and other variables of the study.

101	Age	----------years			
102	Sex	1. Male 2. Female			
103	Weight	----------kg			
104	Height	……cm			
105	BMI	…… kg/cm2			
201	Types of ICU Admission	Medical Surgical			
202	For surgicaladmission urgency of surgery	1. Elective 2. Emergency			
203	For surgical admission Specify surgery specialty	1. Abdominal 2. Neurologic 3. Orthopedic		4. Vascular 5. Endocrine 6. Cardiothoracic 7. Urologic 8. ENT surgery	
204	Presence of coexisting disease	1. Yes 2. No			
205	If yes to 203, coexisting disease present	1. Hypertension 2. DM 3. Asthma 4. COPD 5. Cancer		6. Cardiac illness, 7. Renal illness, 8. infectious disorder, 9. psychiatric disorder, 10. Neurologic disorder 11. Other	
206	ASA Classification of the patient	1. ASA I 2. ASAII 3. ASAIII 4. ASA IV 5. ASA V			
207	Duration of surgery	1.[1-2) hr.	2. [2-3) hrs.	3. [3-4) hrs.	4.[4hrs and more)
301	Cigarette smoking	1. Yes		2. No	

302	Alcohol use	1. Yes 2. No		
303	Use of psychoactive medication	1. Yes 2. No		
401	Does the patient have history of cognitive impairment?	1. Yes 2. No		
403	Does patient have visual impairment?	1. Yes 2. No		
501	Laboratory result at ICU	1.Hgb	4. Na+	7. urea
		2. Platelet count	5. K+	
		3. Cr	6. Serum albumin	
502	Cause for ICU Admission	1…….		
503	APACHE II Score of the patient	1……..		
504	ICU Medications	A. Analgesics used 1. YES 2. NO , If yes name of the drug B. Sedatives used 1. Yes 2. No If yes name of the drug…… C. Steroids used 1. Yes 2. No If yes name of the drug……		

505	Catheters used in ICU	1) NG tube 1.Yes 2. No 2) Bladder 1. Yes 2. No 3) Rectal 1. Yes 2. No 4) Central venous Catheter 1. Yes 2. NO

Annex II

Bi-variable and multivariable logistic regression result to identify factors associated with delirium in ICU

Variable	Category	Delirium in ICU		COR (95% CI)	p-value	AOR (95% CI)	p-value
		Yes	No				
Gender	Male	76	136	1.57 (1.01, 2.44)	0.041	1.04 (0.45, 2.38)	0.825
	Female	46	130	1			
Age	18 – 33	23	94	1			
	34- 64	66	147	1.83 (1.06, 3.15)	0.023	1.83 (0.69, 4.80)	0.272
	>65	33	25	5.39 (2.70, 10.79)	<0.001	5.29 (2.28, 12.84)	<0.001
BMI	<18	16	26	1.89 (0.94, 3.80)	0.071	2.49 (0.61, 10.41)	0.288
	18 - 4	98	232	1			
	>24.9	6	10	1.42 (0.50, 4.01)	0.508	0.47 (0.14, 3.84)	0.608
Alcohol history	Yes	54	64	2.50 (1.59, 3.94)	<0.001	6.72 (2.68, 20.42)	<0.001
	No	68	202	1			
Smoking history	Yes	31	54	1.29 (0.78, 2.15)	0.020	3.08 (0.11, 8.63)	0.511
	No	91	206	1			
Substance abuse	Yes	28	20	1.90 (0.51, 3.25)	0.331		
	No	94	246	1			
ICU	Medical	60	165	1			
	Surgical	62	101	2.27 (0.06, 5.36)	0.506		
Cause of admission	Respiratory failure	34	68	0.97 (0.49, 1.65)	0.764		
	Traumatic head injury	28	59	0.85 (0.45, 1.60)	0.626		
	Sepsis/septic shock	16	42	0.68 (0.33, 1.42)	0.310		
	Postoperative monitoring	30	54	1			
	Other	14	43	0.58 (0.27, 1.24)	0.363		
Comorbidity	Yes	97	92	2.86 (1.68, 4.87)	<0.001	4.23 (1.97, 9.78)	<0.001
	No	71	128	1			
Cognitive impairment	Yes	6	14	0.93 (0.34, 2.48)	0.887		
	No	116	252	1			
Psychoactive	Yes	28	45	1.84 (0.12, 3.34)	0.486		

medication							
	No	94	221				
Visual impairment	Yes	8	3	7.97 (1.63, 38.97)	0.010	1.42 (0.41, 3.69)	0.709
	No	115	262	1			
Creatinine		1.29 (±0.45)	1.21 (±0.34)	1.70 (0.98, 2.94)	0.059	1.49 (0.69, 3.24)	
Hemoglobin		13.84 (±1.14)	13.54 (±1.49)	0.81 (0.68, 0.97)	0.029	1.01 (0.80, 1.27)	
APACHE II score		23.59 (±7.11)	18.45 (±5.48)	1.13 (1.09, 1.18)	<0.001	1.11 (1.05, 1.17)***	
Analgesia	Yes	91	141	2.60 (1.62, 4.17)	<0.001	1.59 (0.63, 3.99)	0.457
	No	31	125	1			
Sedative	Yes	64	75	2.78 (1.78, 4.33)	<0.001	2.06 (0.88, 4.84)	0.091
	No	58	189	1			
Steroid	Yes	88	173	1.39 (0.87, 2.22)	0.681		
	No	34	93	1			
NG tube	Yes	81	156	1.39 (0.89, 2.18)	0.311		
	No	41	110	1			
Urinary catheter	Yes	110	220	1.91 (0.97, 3.76)	0.056	1.23 (0.41, 3.69)	0.709
	No	12	46	1			