

## ORIGINAL ARTICLE

### Incidence and predictors of delirium among the intensive care unit patients at Jimma Medical Center, Southwest Ethiopia

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#### Abstract:

**Objective:** Delirium is characterized by impaired attention and awareness, accompanied by cognitive deficits. It develops rapidly and poses a considerable burden on healthcare systems. Patients in the intensive care unit (ICU) are particularly vulnerable to developing delirium. This study aims to determine the incidence and predictors of delirium among ICU patients at Jimma Medical Center in southwest Ethiopia in 2023.

**Methods:** A prospective observational cohort study was conducted on 403 patients aged  $\geq 18$  years admitted to emergency, surgical, and medical ICUs at Jimma Medical Center in southwest Ethiopia. Patients were assessed twice daily for delirium using the Richmond agitation sedation scale (RASS) and confusion assessment method (CAM). The association between independent variables and delirium incidence was analyzed using Cox proportional hazards (PH) regression. A univariate Cox PH model screened variables at a 0.25 significance level, followed by a multivariable Cox PH model for significant variables. Variables with a  $P$ -value  $\leq 0.05$  were considered significantly associated with delirium incidence among ICU patients.

**Results:** The findings of this study revealed that the overall occurrence of delirium among critically ill ICU patients was 118 (29.3%) (95% CI: 25%,34%), and the rest, 70.7% of the participants, were censored (95% CI: 66,75). The incidence rate of delirium among intensive care unit patients was 21.2 (95% CI: 17.8,25.4) per 1000 person-days of observation. Chronic obstructive pulmonary disease (AHR: 1.94; 95% CI: 1.23,3.56), stroke (AHR: 1.8; 95%CI: 1.98,3.73), Oxygen Saturation less than 90% (AHR:1.61; 95% CI: 1.11,2.34) and Obesity (AHR: 0.35; 95%CI: 0.13,0.84) were independent predictors of delirium among ICU patients.

**conclusion:** This study found that, with an incidence rate of 21.2 occurrences per 1000 person-days of observation, delirium greatly affects the outcome of intensive care unit patients in the Jimma Medical Center. The study identifies several factors that independently predict the occurrence of delirium in ICU patients, including obesity, stroke, low oxygen saturation levels, and COPD. Interestingly, our findings suggest that admission for heart failure may have a protective effect against delirium. Therefore, health professionals ought to give special attention to patients with identified predictors.

**Keywords:** Delirium; Incidence; Intensive Care Unit, Jimma Medical Center

**1. Introduction:** Delirium is a prevalent and serious neurological complication encountered in patients admitted to the intensive care unit (ICU). Characterized by acute confusion, impaired consciousness, cognitive decline, and fluctuations in mental status, delirium poses significant challenges in patient management and is associated with increased morbidity

and mortality rates (1,2). The condition can arise suddenly and is often linked to systemic diseases, making its recognition and management critical in the ICU setting (3,4).

The prevalence of delirium varies significantly across different populations. Studies indicate that between 20% and 83% of ICU patients may develop this condition, with particularly high rates observed among elderly patients requiring mechanical ventilation (5,6). The burden of delirium extends beyond immediate clinical outcomes; it can lead to long-term cognitive impairments, further complicating recovery and rehabilitation (7). Given its profound implications for patient care, understanding the risk factors associated with delirium is essential for effective prevention and intervention strategies (8).

Delirium arises from a complex interplay of patient-centric predisposing factors—such as advanced age, pre-existing cognitive impairments, and comorbid conditions—and hospital-centric precipitating factors, including sedative use and mechanical ventilation (9-11). In particular, studies conducted in sub-Saharan Africa (SSA) reveal a distinct pattern of delirium prevalence that diverges from trends observed in developed nations. In SSA, delirium affects a broader demographic range, including younger adults often suffering from infectious diseases like HIV, which has been identified as a leading cause of delirium in specific populations (12-15).

Several predictors have been identified that increase the likelihood of delirium among ICU patients. Research indicates that older age, pre-existing cognitive impairment, severity of illness, and the use of sedatives and opioids are significant predictors (16). Additionally, factors such as a history of alcohol abuse, sepsis, and higher acute physiology and chronic health evaluation (APACHE) scores have also been associated with an increased risk of delirium (17). Early identification of these predictors is vital for implementing preventive measures and managing delirium effectively.

To facilitate the detection of delirium in the ICU setting, several assessment tools have been developed. The confusion assessment method for the ICU (CAM-ICU) and the intensive care delirium screening checklist (ICDSC) are among the most widely utilized and validated instruments for assessing delirium in critically ill patients (18). Emerging research into biomarkers for delirium also holds promise for enhancing diagnostic accuracy and monitoring disease progression, potentially transforming approaches to managing this complex condition in the future (19). Delirium represents a significant challenge within the ICU environment, necessitating ongoing research into its prevalence, risk factors, and effective management strategies tailored to diverse patient populations. Understanding these dynamics is critical for improving patient outcomes and reducing the burden of this condition on healthcare systems.

Despite the recognized prevalence and serious implications of delirium in ICU patients, particularly in sub-Saharan Africa, there remains a significant gap in understanding the specific incidence and predictors of delirium among patients at Jimma Medical Center in Southwest Ethiopia. Existing literature highlights a broader demographic affected by delirium, yet localized studies focusing on this particular healthcare setting are limited. This creates an urgent need for research that systematically investigates the incidence rates and identifies the unique risk factors contributing to delirium in this population. Such insights are crucial for developing targeted prevention and management strategies tailored to the socio-cultural and clinical context of the region, ultimately enhancing patient outcomes and informing healthcare practices in similar settings.

## **2. Methods**

### **2.1. Study area and period**

The study was conducted at Jimma Medical Center Hospital on 403 patients admitted to emergency, surgical, and medical ICUs, located in the Oromia region of southwest Ethiopia, approximately 365 km away from the capital city of Addis Ababa. It offers various medical services, such as surgery, obstetrics and gynecology, emergency and trauma treatment, and serves as a referral hospital for the catchment area. Jimma Medical Center also provides critical care services to patients in need of advanced care in the medical, surgical, and emergency ICUs. The study period was from

January 1, 2023, to December 30, 2023, by prospectively following ICU patients who were admitted from January 1, 2023, to December 30, 2023.

## **2.2. Study design**

An institutional-based prospective follow-up study was conducted among patients who were admitted to the intensive care units of Jimma Medical Center Hospital.

## **2.3. Source of population**

All adult patients who were admitted to the ICUs of Jimma Medical Center Hospital.

## **2.4. Study Population**

The study included all patients aged 18 years and older admitted to the ICUs at Jimma Medical Center Hospital from January 1, 2023, to the end of December 2023.

## **2.5. Eligibility criteria**

All adult patients whose age is greater than or equal to 18 years were admitted to ICUs for more than 24 hours from January 1, 2023, to December 30, 2023. Patients with confirmed delirium at ICU admission, those in a deep coma without sedative exposure, patients with cognitive impairment, mental illness, nervous system diseases, brain injury, Glasgow coma scale  $\leq 8$ , serious auditory or visual disorders, and those transferred from other ICUs were excluded.

## **2.6. Sample size determination and sampling procedure**

To determine the sample size for our study at the intensive care center, we used a single population proportion formula. Given the lack of prior research on the topic, we conservatively assumed a proportion of 50% to ensure a balanced estimate. With a 95% confidence level and a 5% margin of error, the calculated sample size was determined to be 403 participants. To select study participants, we employed a consecutive patient sampling technique. This method involved enrolling patients in the study as they were admitted to the ICU until the target sample size of 403 was reached. This approach ensured that all eligible patients had an equal opportunity to participate in the study and helped minimize selection bias.

## **2.7. Operational definition and measurements**

- **The CAM-ICU assessment** was positive if patients demonstrated an acute change or fluctuation in the course of their mental status (as determined by abnormalities), plus inattention, and either disorganized thinking or an altered level of consciousness (34).
- **In terms of ICDSC**, the checklist is scored out of eight categories that include the level of consciousness, inattention, disorientation, delusions, psychomotor agitation, inappropriate speech or mood, sleep disturbance, and symptom fluctuation (35). Each category is coded as present (i.e., a score of 1) if the patient meets the criteria listed, for a maximum score of 8. Patients who scored  $\geq 4$  on the ICDSC at any time during the ICU stay were categorized as ever having delirium and those with all their ICDSC scores  $< 4$  on all ratings were categorized as never having delirium.
- **The event was censored**: patients who were moved out of the ICU and those who passed away without having experienced delirium during the follow-up period were categorized as censored.

## **2.8. Data collection and procedure**

The semi-structured questionnaire used to collect the data from the patients was prepared in the English language and then translated to the local language (Oromo) by language experts to keep its consistency. The questionnaire was adapted from intensive care unit patient monitoring, and triage sheets, and by reviewing different related articles (4,8,9,14,28,35,37,38,49). The tool comprised the confusion assessment method for the ICU (CAM-ICU), an intensive care unit delirium screening checklist, socio-demographic details, the date of the patient's admission to the ICU, the diagnosis, the baseline vital signs, the baseline laboratory results, comorbidities, the medication administered, the vital signs at the end of the follow-up, the laboratory results at the end of the follow-up, complications, and the date of the last follow-up (the date of the developing delirium, the patient's recovery or death from the ICU, or stayed in the ICU after 24 hours of ICU admission). Three data collectors and one supervisor were employed, and data collection was

accomplished during the study period from January 1, 2023, to the end of December 2023. Regular follow-up and monitoring were important during data collection.

### **2.9. Data quality control**

The checklist was pretested on 20 (5% of the participants) randomly selected patients to maintain data quality before starting the actual data collection period, and those patients were excluded from the study during the study. Two days of training were given to data collectors and a supervisor working outside of the study area regarding the data collection process and tool before data collection began. The data collection procedure was closely monitored by the supervisor and principal investigators daily for the completeness and consistency of the collected data.

### **2.10. Data processing and analysis**

At the end of data collection, the collected data were checked for completeness, and then the data were entered into Epi-Data Manager version 4.6.0.6 and exported to STATA version 14 for cleaning, editing, coding, and analysis. Explanatory data analysis was done to determine missing values, normality tests, and the presence of outliers before data analysis. Then the data were described using relative frequency, percent, mean with standard deviation, and median with interquartile range based on their applicability. A life table was used to estimate the cumulative probability of delirium at different time intervals. Kaplan-Meier's survival curve was used to estimate the median survival time during the follow-up period, and log-rank tests were also used to compare survival curves for the presence of differences in the incidence of delirium among the groups.

The bi-variable analysis was computed to identify possible associations between delirium and each dependent variable using the Cox proportional hazard model. Variables that were significant at the P-value less than 25% level in the bi-variable analysis were collectively included in the multi-variable analysis to identify independent predictors of delirium. Using variable inflation factors (VIF) between independent variables, multi-co-linearity was checked, and all outputs fell within the acceptable range (mean VIF=1.12). The proportional hazard assumptions were also checked using the global test with a value of  $P=0.2476$ , which was insignificant. The Cox-Snell residuals were also used to assess the Cox regression model's fitness for the data. Finally, we could conclude that the final model fits and succeeds. In multivariable analysis, any statistical value was considered significant at  $P<0.05$ . The association between the incidence of delirium and independent variables was declared using an adjusted hazard ratio (AHR) with a 95% confidence interval. Finally, data was presented using tables, frequency, graphs, and texts.

### **2.11. Ethical considerations**

The Jimma University Medical Center Ethics Committee reviewed and approved the study protocol (JU-IRB, REC, 1356.564). After approval, official letters of cooperation were written for the hospital administrators. Documentation of informed written consent was provided for each participant. Before asking patients or their representatives to take part in the study, they were given information about the study and any potential risks involved. They were told that participating was entirely up to them and would not impact their treatment. To protect their privacy, all data was made anonymous before being analyzed. The data was stored securely on password-protected computers and kept in a locked office.

## **3. Results**

From the beginning of January 2023 to the end of December 2023, a total of 679 patients were admitted to the ICUs of Jimma Medical Center. About 276 patients were excluded using exclusion criteria 163 of them were aged less than 18 years, 43 of them were confirmed with delirium during admission, 35 patients were a deep comma, 15 had a severe traumatic brain injury, 10 patients had a mental illness, 6 patients were cognitive impairment, and 4 patients were transferred from other health facility ICU. Hence, 403 patients were candidates for the study, and all of them were included using a consecutive sampling method until the end of the study period.

### **3.1. Socio-demographic characteristics**

A total of 403 consecutive patients' admissions to ICUs were included for final analysis. In this analysis, 236 (58.6%) of the participants were male, of which 70 (29.7%) experienced delirium. The average age among the participants was 55 years (SD=18.1), and regarding the age category, 188 (46.7%) of participants were under 60 years of age or older, of

which 54 (28.7%) developed delirium. More than half of the participants (53.3%) were from urban areas. Additionally, 77.7% of the participants showed a respiratory rate greater than or equal to 24 breaths per minute, of which 27.8% developed delirium. Furthermore, more than half (51.4%) of the participants had oxygen saturation levels greater than ninety, with 43.1% of them experiencing delirium. Among the 168 (41.7%) patients admitted to the ICU with a severe Glasgow coma scale, 52 (31%) developed delirium. The majority of 365 (90.6%) of the participants were admitted to ICUs with severe triage scores, of which 29.3% developed delirium (Table 1).

**Table 1** Distribution of Socio-demographic characteristics and vital signs at baseline among patients admitted to the ICU

Variables	Categories	Outcome		
		Delirium, n (%)	Censored, n (%)	Total, n (%)
Age	18-39 years	30 (25.4%)	56 (19.7%)	86 (21.3%)
	40-59 years	34 (28.8%)	95 (33.3%)	129 (32)
	≥60 years	54 (45.8%)	134 (47.0%)	188 (46.7%)
Sex	Male	70 (59.3%)	166 (58.3%)	236 (58.6%)
	Female	48 (40.7%)	119 (41.7%)	167 (41.4%)
Residency	Rural	44 (37.3%)	144 (50.5%)	188 (46.7%)
	Urban	74 (62.7%)	141 (49.5%)	215 (53.3%)
Respiratory rate, breaths per minute	<24	31 (26.3%)	59 (20.7%)	90 (22.3%)
	≥24	87 (73.7%)	226 (79.2%)	313 (77.7%)
Pulse rate at baseline, beats per minute	<60	18 (15.3%)	23 (8.07%)	41 (10.2%)
	60-100	63 (53.4%)	172 (60.4%)	235 (58.3%)
	>100	37 (31.4%)	90 (31.6%)	127 (31.5%)
Temperature at baseline, (°C)	<36.5	30 (25.4%)	65 (22.8%)	95 (23.6%)
	36.5-37.5	24 (20.3%)	85 (29.8%)	109 (27.1%)
	>37.5	64 (54.2)	135 (47.4 %)	199 (49.4%)
Mean arterial pressure, mmHg	≥65	77 (65.8%)	174 (61.1%)	251 (62.3%)
	<65	41 (34.8%)	111 (38.9%)	152 (37.7%)
Oxygen saturation, %	<90	67 (56.8%)	129 (52.6%)	196 (48.6%)
	≥90	51 (43.1%)	156 (54.7%)	207 (51.3%)
Glasgow coma scale at admission	14-15 (Mild)	13 (11.0%)	37 (12.9%)	50 (12.4%)
	9-13 (Moderate)	53 (44.9%)	132 (46.3%)	185 (45.9%)
	≤8 (Severe)	52 (44.1%)	116 (40.7%)	168 (41.7%)
Triage score at admission	Mild	6 (5.08%)	7 (2.46%)	13 (3.23%)
	Moderate	5 (4.24%)	20 (7.02%)	25 (6.20%)
	Severe	107 (90.7%)	258 (90.5%)	365 (90.6%)

°C: degree Celsius; mmHg: Mill meter of mercury

### 3.2. Diseases-related variables of ICU patients

The study results indicated that 56 (13.9%) of the subjects were diagnosed with severe pneumonia, and 18 (32.1%) of them developed delirium. A majority of the participants (237, 58.8%) were diagnosed with shock upon admission to the ICU, and 29.1% of them developed delirium while in the ICU. Furthermore, 96 (23.8%) of the subjects admitted to the ICU had cardiovascular disease. The reasons for ICU admission were as follows: thoracic-abdominal injury (16%), traumatic brain injury (16.6%), diabetic ketoacidosis (10.2%), and post-operative conditions (9.2%). The findings also revealed that 177 (43.9%) of the subjects had at least one comorbid condition, about 120 (29.8%) of them developing delirium. The most frequently recorded comorbidities were obesity (120, 29.8%), hypertension (97, 24.1%), diabetes mellitus (90, 22.3%), and chronic kidney disease (56, 13.9%) (Table 2).

**Table 2** Reason for ICU admission and comorbidities among patients admitted to the ICU

Variables	Categories	Outcome status		
		Event	Censored	Total, n (%)

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**Reason for ICU admission**

Severe Pneumonia	No	100 (84.8%)	247 (86.7%)	347 (86.1%)
	Yes	18 (15.3%)	38 (13.3%)	56 (13.9%)
Shock	No	49 (41.5%)	117 (41.1%)	166 (41.1%)
	Yes	69 (58.5%)	168 (58.9%)	237 (58.8%)
Traumatic brain injury	No	98 (83.1%)	238 (83.5%)	336 (83.4%)
	Yes	20 (16.9%)	47 (16.5%)	67 (16.6%)
Thoraco abdominal injury	No	104 (88.1%)	234 (82.1%)	338 (83.9%)
	Yes	14 (11.9%)	51 (17.9%)	65 (16.1%)
Cardiovascular disease (CHF, CAD, MI)	No	88 (74.6%)	219 (76.8%)	307 (76.2%)
	Yes	30 (25.4%)	96 (23.8%)	96 (23.8%)
DKA	No	109 (92.4%)	253 (88.8%)	362 (89.8%)
	Yes	9 (7.63%)	32 (11.2%)	41 (10.2%)
Post-operative	No	103 (87.3%)	263 (92.3%)	366 (90.8%)
	Yes	15 (12.7%)	22 (7.7%)	37 (9.2%)
Meningitis	No	55 (93.2%)	273 (95.8%)	383 (95.0%)
	Yes	8 (6.8%)	12 (4.2%)	20 (5.0%)
Bronchial asthma	No	113 (95.7%)	253 (88.8%)	366 (90.8%)
	Yes	5 (4.2%)	32 (11.2%)	37 (9.2%)

**Comorbidity**

At least one comorbidity	No	61 (51.7%)	165 (57.9%)	226 (56.1%)
	Yes	57 (48.3%)	120 (42.1%)	177 (43.9%)
Diabetics mellitus	No	94 (79.7%)	219 (76.8%)	313 (77.7%)
	Yes	24 (20.3%)	66 (23.2%)	90 (22.3%)
Hypertension	No	85 (72.0%)	221 (77.5%)	306 (75.9%)
	Yes	33 (28.0%)	64 (22.5%)	97 (24.1%)
Malignancy	No	55 (93.2%)	270 (94.7%)	380 (94.3%)
	Yes	8 (6.8%)	15 (5.3%)	23 (5.7%)
Stroke	No	104 (88.1%)	262 (91.9%)	366 (90.8%)
	Yes	14 (11.9%)	23 (8.07%)	37 (9.2%)
Chronic kidney disease	No	102 (86.4%)	245 (85.9%)	347 (86.1%)
	Yes	16 (13.6%)	40 (14.1%)	56 (13.9%)
HIV/AIDS	No	111 (94.1%)	259 (90.9%)	370 (91.8%)
	Yes	7 (5.9%)	26 (9.12%)	33 (8.2%)
COPD	No	107 (90.7%)	271 (95.1%)	378 (93.8%)
	Yes	11 (9.32%)	14 (4.9%)	25 (6.2%)
Bronchial asthma	No	113 (95.7%)	253 (88.8%)	366 (90.8%)
	Yes	5 (4.2%)	32 (11.2%)	37 (9.2%)
Obesity	No	94 (79.7%)	189 (66.3%)	283 (70.2%)
	Yes	24 (20.3%)	96 (33.7%)	120 (29.8%)

DKA: Diabetic ketoacidosis; COPD: Chronic obstructive pulmonary disease; HIV: Human immune Virus; AIDS: Acquired immune deficiency syndrome; CHF: Chronic heart failure; MI: Myocardial infarction; CAD: Coronary artery disease

**3.3. Baseline laboratory findings among ICU patients**

The baseline laboratory findings in this study revealed several prevalent abnormalities among the participants. The most common abnormalities were leukocytosis, hyponatremia, hyperkalemia, thrombocytopenia, and elevated serum

creatinine levels. Specifically, 79.2% of individuals had leukocytosis, followed by hyperkalemia (35.7%), hyponatremia (37.2%), thrombocytopenia (27.3%), and increased blood creatinine levels (13.4%). Among participants with leukocytosis, a significant proportion (79.7%) developed delirium by the end of the follow-up period. Additionally, the majority of participants (73%) had a platelet count greater than or equal to 150,000/mcL at baseline, with 76.3% of these individuals developing delirium compared to 24.3% of those with platelet counts below 150,000/mcL. Furthermore, a subset of patients (16.4%) presented with elevated blood urea nitrogen (BUN  $\geq$ 45 mg/dl) upon admission. These findings underscore the importance of monitoring and addressing these laboratory abnormalities in patients, as they may be associated with the development of delirium and other adverse outcomes (Table 3).

**Table 3** Baseline laboratory results related variables among patients admitted to the ICU

Variables	Category	Outcome status		Total
		Event	Censored	
WBC Baseline	$\leq$ 11,000	24 (20.3%)	84 (20.8%)	84 (20.8%)
	$>$ 11,000	94 (79.7%)	225 (79%)	319 (79.2%)
Hgb baseline	$<$ 12 mg mg/dl	28 (23.7%)	64 (22.5%)	92 (22.8%)
	$\geq$ 12mg/dl	90 (76.3%)	221 (77.5%)	311 (77.2%)
Platelet baseline	$<$ 150,000	28 (23.7%)	111 (27.5%)	115 (27.3%)
	$\geq$ 150,000	90 (76.3%)	292 (72.5%)	307 (72.7%)
Cr level baseline	$\leq$ 1.2mg/dl	104 (88.4%)	245 (85.9%)	349 (86.6%)
	$>$ 1.2md/dl	14 (11.9%)	40 (14.0%)	54 (13.4%)
BUN at the baseline	$<$ 45mg/dl	97 (82.2%)	241 (84.6%)	338 (83.9%)
	$\geq$ 45mg/dl	21 (17.8%)	44 (15.4%)	65 (16.4%)
Serum sodium at baseline	$<$ 135 meq/l	43 (36.4%)	107 (37.5%)	150 (37.2%)
	135-148 meq/l	75 (63.6%)	178 (62.5%)	253 (62.8%)
	$<$ 3.5mEq/l	16 (13.6%)	18 (6.3%)	34 (8.4%)
Serum potassium at baseline	3.5-5mEq/l	71 (60.2%)	154 (54.0%)	225 (55.8%)
	$>$ 5mEq/l	31 (26.3%)	113 (39.7%)	144 (35.7%)

BUN: Blood urea nitrogen; Cr: Creatinine; Hgb: Hemoglobin; mg/dl: Mill gram per Deci liter; WBC: white blood cells

### 3.4. Management and complication-related variables

According to the study result, 222 (55.1%) study subjects were intubated, of whom 29.3% (65/222) developed delirium. In contrast, the remaining 44.9 % of the patients were not intubated, of which only 41.4% (53/118) of the participants developed delirium. The proportion of delirium was higher (33.9%) among patients who took blood transfusions than among those who did not receive blood transfusions. The majority of study participants (359, or 89.1%) took thromboprophylaxis during their ICU stay, of which 106, or 29.5%, developed delirium. Furthermore, findings revealed that 70.5% (284/403) of study participants had at least one ICU complication. Acute kidney injury (AKI) (70.2%=283), hospital-acquired infections (HAIs) (38.7), cardiac arrests (73.2%), electrolyte imbalance (23.8), and thromboembolism (22.3) were the most prevalent recorded ICU complications among study participants. The study findings also showed that the occurrence of delirium among patients who have ICU complications was 71.8 %. Conversely, 68.9 of the study subjects who did not have any ICU complications developed delirium during their ICU stay (Table 4).

**Table 4** Interventions and complications related variables among patients admitted to the ICU

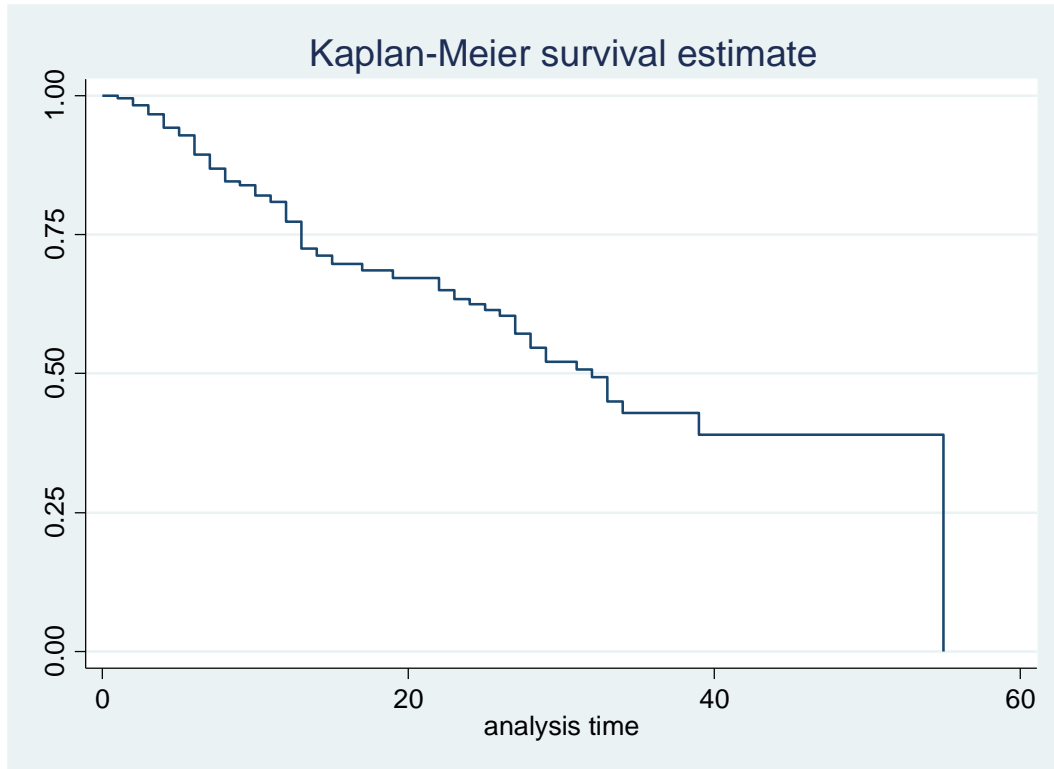
Variables	Categories	Outcome		
		Event	Censored	Total
<b>Management related variables</b>				
Method of ventilation	Non-invasive	53 (44.9%)	128 (44.9%)	181 (44.9%)
	Invasive	65 (55.1%)	157 (55.1%)	222 (55.1%)
Blood transfusion	No	97 (82.2%)	244 (85.6%)	341 (84.6%)
	Yes	21 (17.8%)	41 (14.4%)	62 (15.4%)

Systematic steroid	No	89 (75.4%)	196 (68.8%)	285 (70.7%)
	Yes	29 (24.6%)	89 (31.2%)	118 (28.3%)
Thromboprophylaxis	No	12 (10.2%)	32 (11.2%)	44 (10.9%)
	Yes	106 (89.8%)	253 (88.8%)	359 (89.1%)
Vasopressors	No	80 (67.8%)	174 (61.1%)	254 (63.1%)
	Yes	38 (32.2%)	111 (38.9%)	149 (36.9%)
Sedation	No	63 (53.4%)	152 (53.3%)	215 (53.4%)
	Yes	55 (46.6%)	133 (46.7%)	188 (46.7%)
Diuretics	No	86 (72.8%)	207 (72.6%)	293 (72.7%)
	Yes	32 (27.1%)	78 (27.4%)	55 (27.3%)
<b>Complications</b>				
At least one complication	No	82 (28.77%)	37 (31.2%)	119 (29.5%)
	Yes	203 (71.2%)	81 (68.6%)	284 (70.5%)
Acute kidney injury	No	88 (30.9%)	32 (27.1%)	120 (29.8%)
	Yes	197 (69.1%)	86 (72.9%)	283 (70.2%)
Electrolyte imbalance	No	91 (77.1%)	216 (75.6%)	307 (76.2%)
	Yes	27 (22.9%)	69 (24.2%)	96 (23.8%)
Hospital-acquired infection	No	77 (65.3%)	170 (59.7%)	247 (61.3%)
	Yes	41 (34.8%)	115 (40.4%)	163 (38.7%)
Thromboembolism	No	95 (80.5%)	218 (76.5%)	313 (77.67%)
	Yes	23 (19.5%)	67 (23.5%)	90 (22.3%)
Acute lung injuries	No	32 (27.1%)	120 (29.8%)	321 (76.1%)
	Yes	86 (72.9%)	238 (70.2%)	101 (23.9%)
Congestive heart failure	No	88 (74.6%)	219 (76.8%)	307 (76.2%)
	Yes	30 (25.4%)	66 (23.2%)	96 (23.8%)
DKA	No	109 (92.4%)	253 (88.8%)	362 (89.8%)
	Yes	9 (7.6%)	32 (11.2%)	41 (10.2%)
Acute liver injury	No	32 (27.1%)	88 (30.9%)	120 (29.8%)
	Yes	86 (33.9%)	197 (69.1%)	283 (70.2%)
Cardiac arrest	No	40 (33.9%)	68 (23.9%)	108 (26.8%)
	Yes	78 (66.1%)	217 (76.2%)	295 (73.2%)

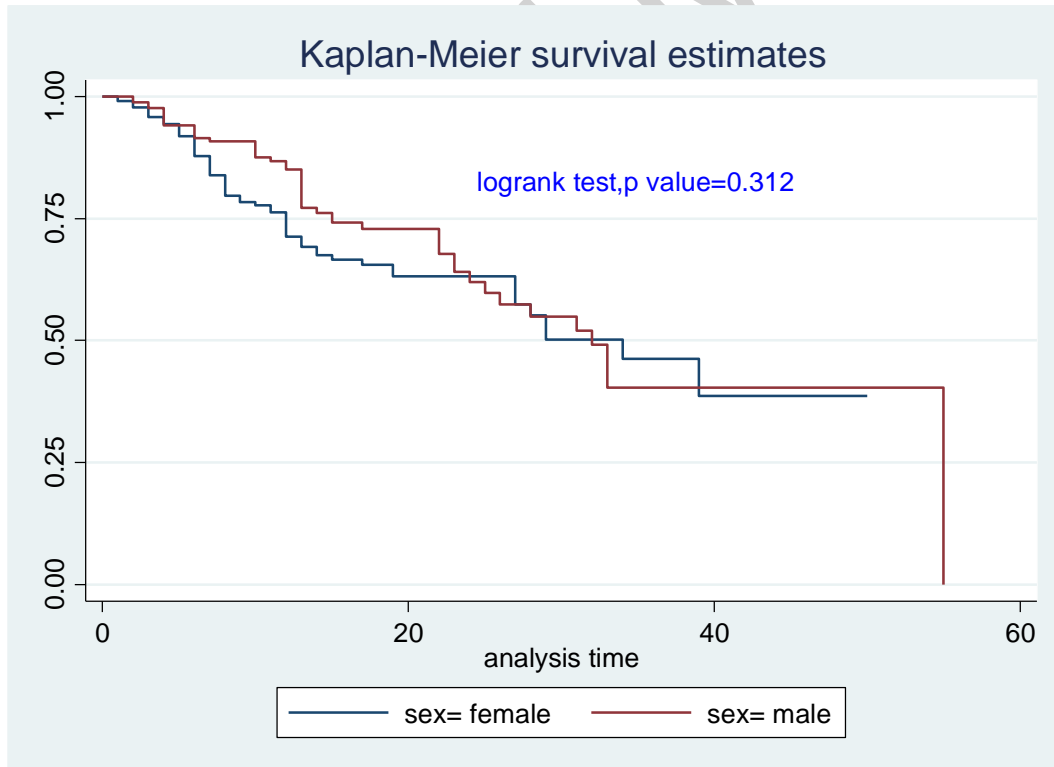
### 3.5. Kaplan-Maier Survival Estimating of Delirium

Kaplan-Meier survival curve decreases stepwise, and it crosses the survival function at a survival probability of 0.5 (50%). The overall Kaplan Meier estimates identified that the probability of developing delirium in patients admitted to the ICU is low on the first day of admission, which relatively increases as follow-up time increases. The overall median time of developing delirium of admitted ICU patients in this study was 37 (95% CI: 32,41) days. During the first day of hospital stay, a 98.82 % survival probability was observed (95% CI: 0.9718,0.9951) (Figures 1, 2).





**Figure 1** Overall Kaplan-Meier curve for ICU patients in the Jimma Medical Center, Southwest Ethiopia, 2023 (N=403)



**Figure 2** shows the overall Kaplan-Meier survival curve estimate based on the gender of critically ill ICU patients in the Jimma Medical Center, southwest Ethiopia, 2023 (N=403). The blue middle line survival of being female and the middle red line shows the survival time of being male. The horizontal axis (X): shows the time of analysis in (days). The vertical axis (Y): indicates cumulative survival and Middle line (downward) Survival function

### 3.6. Survival function and Incidence density rate of delirium

In this study, the patients were followed for a minimum of 1 day to a maximum of 55 days, with the overall median follow-up period being 32 days (95% CI: 27,36). The total person-time observation was 5613 person-days. The findings of this study revealed that the overall occurrence of delirium among critically ill ICU patients was 118 (29.3%; 95% CI: 25%,34%), and the rest, 70.7% of the participants, were censored (95% CI: 66,75). The incidence rate of delirium among ICU patients was 21.2 (95% CI: 17.8,25.4) per 1000 person-days of observation. The cumulative probability of survival at the end of 5 and 55 days was 0.8486 and 0.000, respectively. This life table provides information on the number of individuals who develop delirium within specific 5-day intervals. The table starts with an initial total of 403 individuals and records the number of individuals who develop delirium within each interval. The survival rate, represented as a proportion, indicates the likelihood of not developing delirium at each interval. As individuals progress through the intervals, the number of individuals developing delirium increases while the survival rate decreases. The table ends with an interval where all individuals have developed delirium, resulting in a survival rate of 0. This indicates that all individuals in the initial population have experienced delirium during this interval. Overall, the life table provides a comprehensive overview of the development of delirium within the 5-day intervals (Table 5).

**Table 5** The life tables of patients admitted to the ICUs

Interval	Event	Delirium	Lost	Survival	95% CI	
0	5	403	61	0	0.8486	0.8098 0.8801
5	10	342	116	0	0.5608	0.5109 0.6077
10	15	226	79	0	0.3648	0.3179 0.4117
15	20	147	52	0	0.2357	0.1955 0.2782
20	25	95	32	0	0.1563	0.1228 0.1935
25	30	63	24	0	0.0968	0.0704 0.1280
30	35	39	22	0	0.0422	0.0256 0.0650
35	40	17	8	0	0.0223	0.0110 0.0405
40	45	9	5	0	0.0099	0.0034 0.0239
45	50	4	2	0	0.0050	0.0010 0.0168
50	55	2	1	0	0.0025	0.0002 0.0132
55	60	1	1	0	0.0000	

### 3.7. Predictors of delirium in ICU patients

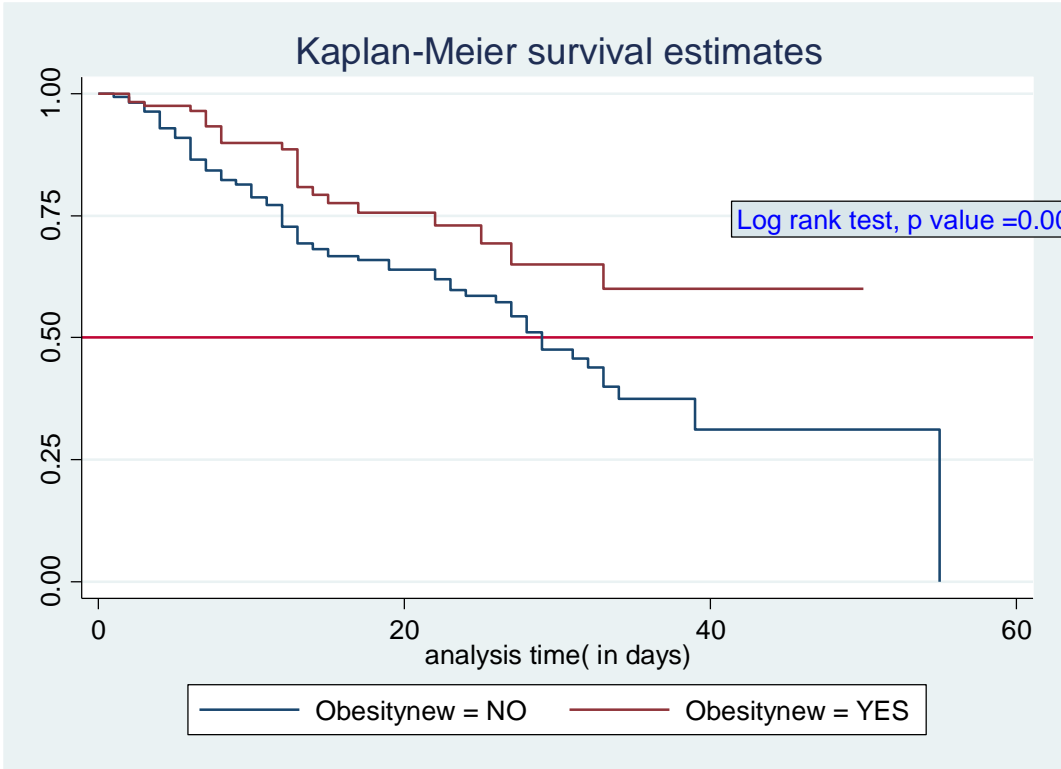
After determining the nature of the data, the Kaplan-Meier (KM) curve and the life of tables were used for data descriptions. Then, a long-rank statistic test was used to identify the presence of significant differences between independent variables. Afterward, a bivariate analysis was conducted using Cox proportional hazard regression to identify variables that had an association with the dependent variable, and variables to be included in the final model for multivariate analysis were identified. Accordingly, in the bivariable analysis, eleven variables were included: the presence of diabetes mellitus, being obese, developing DKA, method of ventilation, stroke, thromboprophylaxis, oxygen saturation, COPD, thoracic abdominal injury, heart failure, and electrolyte imbalance, collectively transferred to multivariate analysis. However, acute kidney injury was excluded since it violated the proportional hazard assumptions with a value of less than 0.05 during the Schoenfeld residual test.

In multivariable analysis, patients with chronic kidney disease, hypoxia, delirium, intubation, and patients admitted to the ICU with cardiovascular disease were found to be independent predictors of delirium in the ICU at a 95% confidence interval. This study revealed that obesity (AHR: 0.35, [95% CI: 0.13,0.84]; P=0.007), stroke (AHR: 1.81, [95% CI: 1.98,3.73]; P=0.048\*), oxygen saturation levels (AHR: 1.61, [95% CI: 1.11,2.34]; P=0.001\*), COPD (AHR: 1.94, [95% CI: 1.23,3.56]; P=0.004\*), and heart failure (AHR: 0.56, [95% CI: 0.38,0.82]; P=0.003) were found to be a significant predictor of developing of delirium in ICU patients (Table 5 and figure 3).

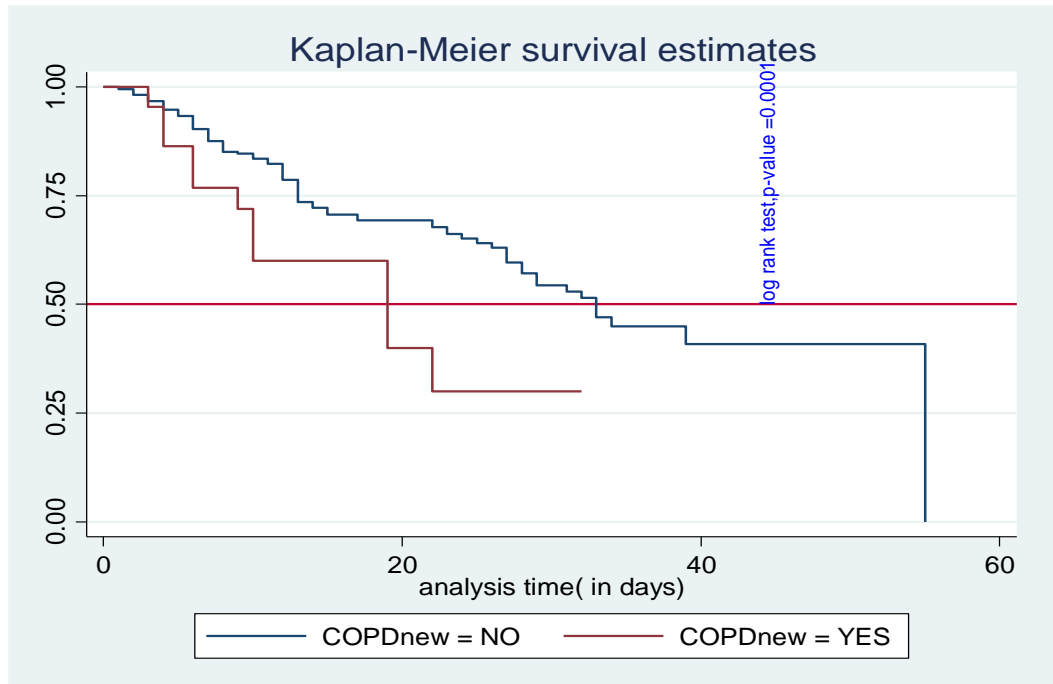
**Table 6** This table presents the results of a bivariate and multivariate analysis of Cox proportional hazard regression for delirium among ICU

Covariate	Categories	Outcome		CHR 95% CI	AHR 95% CI	P-value
		Event	Censored			
Diabetics mellitus	No	94 (79.7%)	219 (76.8%)	Reference	Reference	0.235
	Yes	24 (20.3%)	66 (23.2%)	0.851 (0.45,1.12)	0.74 (0.46,1.40)	
Obesity	No	94 (79.7%)	189 (66.3%)	Reference		0.007*
	Yes	24 (20.3%)	96 (33.7%)	0.502 (.34,.85)	0.35 (0.13,0.84)	
DKA	No	109 (92.4%)	253 (88.8%)	Reference	Reference	0.325
	Yes	9 (7.6%)	32 (11.2%)	1.8 (1.03,3.56)	0.76 (0.34,1.89)	
Method ventilation	Non-invasive	53 (44.9%)	128 (44.9%)	Reference	Reference	0.633
	invasive	65 (55.1%)	157 (55.1%)	1.426 (1.09,2.89)	0.81 (0.35,1.98)	
Stroke	No	104 (88.1%)	262 (91.9%)	Reference	Reference	0.048*
	Yes	14 (11.9%)	23 (8.07%)	1.53 (1.2,2.86)	1.81 (1.98,3.73)	
Thromboprophylaxis	No	12 (10.2%)	32 (11.2%)	Reference	Reference	0.951
	Yes	106 (89.8%)	253 (88.8%)	0.55 (0.31,0.96)	1.03 (0.54,2.1)	
Oxygen saturation, %	<90%	67 (56.8%)	129 (52.6%)	1.56 (1.08,2.25)	1.61 (1.11,2.34)	0.001*
	≥90%	51 (43.1%)	156 (54.7%)	Reference	Reference	
COPD	No	107 (90.7%)	271 (95.1%)	Reference	Reference	0.004*
	Yes	11 (9.32%)	14 (4.9%)	2.13 (1.54,4.23)	1.94 (1.23,3.56)	
Thoracic abdominal injury	No	104 (88.1%)	234 (82.1%)	reference	reference	0.909
	Yes	14 (11.9%)	51 (17.9%)	2.01 (1.14,3.55)	.96 (0.67,1.06)	
Heart failure	No	40 (33.9%)	68 (23.9%)	Reference	Reference	0.003
	Yes	78 (66.1%)	217 (76.1%)	0.61 (.012,0.89)	0.56 (0.38,0.82)	
Electrolyte imbalance	No	91 (77.1%)	216 (75.6%)	reference	Reference	0.954
	Yes	27 (22.9%)	69 (24.2%)	1.43 (1.02,2.22)	0.99 (0.64,1.5)	

AHR: adjusted hazard ratio; CHR: Crude hazard ratio; CI: Confidence interval; DKA: Diabetic ketoacidosis; GCS: Glasgow coma scale; COPD: Chronic obstructive pulmonary disease; \*: Statistically significant at P<0,05 with 95% confidence interval



figure=A



figure= B

**Figure 3** A shows the Kaplan-Meier survival estimate by obesity of study participants from the intensive care unit at Jimma Medical Center in southwest Ethiopia in 2023. (n=403); B: Kaplan–Meier survival estimate by chronic obstructive pulmonary disease of study participants from intensive care unit at Jimma Medical Center, southwest Ethiopia, 2023. (n=403). The horizontal axis (X): shows the time of analysis in (days). The vertical axis (Y): indicates cumulative survival. Middle-blue line: survival without obesity. Middle-red line: survival with obesity. Middle-blue line (downward): survival of those having COPD as comorbidities. Middle-red line: (downward) survival of those not having COPD as a comorbidity

#### 4. Discussion

This prospective observational study aimed to assess the incidence of delirium and its predictors among critically ill ICU patients at JMC in southwest Ethiopia. This study is the first to report on delirium incidence in this patient population in Ethiopia. The current study revealed that obesity, stroke, oxygen saturation levels, COPD, and heart failure were found to be significant predictors of ICU delirium.

At the end of the follow-up, about 118 (29.3%) (95% CI: 25%,34%) of the patients developed delirium. In this study's findings, the incidence density rate of delirium among intensive care unit patients was 21.2 (95% CI: 17.8,25.4) per 1000 person-days of observation. This finding was lower than the study conducted at China Medical University Hospital, which reported that 36.1% of ICU patients developed delirium (39). The disparity might be due to the difference in sample size and study design that was conducted on 456 patients and case-control, whereas the current study was conducted on 403 ICU patients and used a prospective cohort study design. The current findings are also in line with the study conducted in Iran and Jordan on delirium incidence in the ICU reported at 27 and 31.5% (37,40) respectively. The discrepancy in findings may be attributed to the recent implementation of delirium assessment tools in our facility, potentially resulting in missed diagnoses of delirium. However, scientific evidence on the incidence of delirium in the ICUs limited, particularly in developing countries like Ethiopia.

In contrast, the current study findings were higher than previously reported in Germany at the Freiburg Heart Center, which reported a delirium rate of 10.9% among all patients (41). The difference in results could be attributed to the variation in the study population. The previous study specifically focused on patients with myocardial infarction, while

our study included all patients in the ICU regardless of their underlying condition. This led to a higher or inconsistent incidence of delirium in our study compared to the more specific patient population studied in the previous report.

Patients with obesity as a comorbidity were found to have a lower hazard of developing delirium than their counterparts (AHR: 0.35, [95% CI: 0.13,0.84]; P=0.0007). This study is similar to the one done in South Korea, where reportedly being underweight is an independent risk factor for delirium in the ICU (42).

The study results also showed that having oxygen saturation of less than ninety was a significant predictor of increasing development delirium among patients in the ICU than those who had oxygen saturation of greater than ninety (AHR:1.61, [95%CI: 1.11,2.34]; P=0.001\*). It is consistent with the study done in Canada that reported low oxygen saturation is an independent risk factor for the subsequent development of delirium and Also, this finding is in line with a study done on cerebral oximetry monitoring to maintain normal cerebral oxygen saturation during high-risk cardiac surgery which stated a significant decrease in brain cell oxygen saturation can increase the risk of developing postoperative cognitive decline or delirium (P<0.0001) (41-43).

Additionally, this research has shown that among ICU patients, having chronic obstructive pulmonary disease (COPD) as a comorbidity throughout the follow-up period was a significant predictor of developing delirium (AHR: 1.94, [95% CI: 1.23,3.56]; P=0.001). This finding was consistent with a previous study conducted in China, which reported that there is a strong association between COPD and developing delirium in ICUs (4). Additionally, this study is almost similar to the exploration done on It was created by eHealthMe based on reports of 264 people who have chronic obstructive pulmonary disease from the food and drug administration (FDA), which stated that individuals with COPD have a notably higher likelihood of developing delirium compared to those without COPD. This increased risk is primarily attributed to factors like hypoxia, inflammation, and the medications commonly used to manage COPD symptoms, all of which can contribute to the onset of delirium (44).

Finally, the hazard of developing delirium among patients who had heart failure at admission to the ICU decreased by 54% compared to their counterparts (AHR: 0.54, [95% CI: 0.23,0.91]; P=0.001). This study's findings were not in line with previous studies done in China and Italy (45). The decreased hazard of developing delirium among patients with heart failure at admission to the ICU in the current study compared to previous studies in China and Italy could be due to differences in patient characteristics, healthcare practices, cultural factors, study design, and advancements in care. These factors, such as unique patient profiles, variability in treatment protocols, cultural influences, methodological variations, and temporal advancements, may contribute to the observed discrepancies. Further research and collaborative efforts are needed to better understand the underlying reasons for these differences in delirium risk among patients with heart failure across different healthcare settings and populations. This finding was supported by a previous study done on delirium in the cardiac ICU that reportedly no significant association was found between delirium and cardiovascular disease (46,47). It needs further study to magnify the association between delirium and primary cardiac failure conditions.

##### **5. Limitations:**

To the best of our knowledge, this is the first study in Ethiopia to investigate the incidence and predictors of delirium in patients who were admitted to ICUs. The purpose of this study was to address the knowledge gaps about the burden of delirium and possible risk factors that were preventable in the ICU. The prospective observation cohort study design allows for the collection of data over time, providing a more comprehensive understanding of the incidence and risk factors of delirium in ICU patients. By focusing on a specific geographical location and setting, the study results may have implications for improving delirium management and prevention strategies in similar healthcare settings.

The study's findings may not be generalizable to other populations or healthcare settings due to the specific patient population and location being studied. The study's results may be influenced by factors unique to the study area, such as staffing levels, resources, and clinical practices, which may limit the broader applicability of the findings.

## **6. Conclusion**

The study focuses on delirium as a significant problem that affects ICU patients in the study area. It reveals that delirium occurs in 21.2% of patients after admission to the ICU. The study identifies several factors that independently predict the occurrence of delirium in ICU patients, including obesity, stroke, low oxygen saturation levels, and COPD. Interestingly, our findings suggest that admission for heart failure may have a protective effect against delirium. This indicates that, despite the complexity of heart failure as a condition, it may somehow mitigate the risk of developing delirium in critically ill patients. It underscores the importance of early intervention in addressing these modifiable risk factors to improve patient outcomes. The study also suggests that future research should include larger sample sizes and consider additional variables that were not covered in the current study to further investigate delirium in ICU settings.

## **7. Declarations**

### **7.1. Acknowledgment**

We extend our heartfelt gratitude to all the participants, data collectors, supervisors, hospital staff, and administrators who contributed their time and effort to make this study possible. We would also like to express our sincere appreciation to Jimma Medical Center for providing us with the opportunity to conduct this research. Your support and cooperation have been invaluable in advancing our understanding of delirium in ICU patients. Thank you for your dedication and commitment to improving patient care and outcomes.

### **7.2. Authors' contribution**

Initially, AHS comes with the study topic. AHS, TMA, AWF, BLT, AKS, and FTG, were involved in the study design and tool preparation. AHS wrote the research proposal. EG, A& and AHS, AWF edited and revised the proposal. Then, AHS, TMA, AWF, BLT, AKS FTG, and EG participated in the data collection and entry. AHS, TMA, AWF, BLT, and FTG conducted the statistical analysis, and AHS drafted the manuscript. AHS, TMA, AWF, BLT, and FTG edited the manuscript and formatted it for publication. Afterward, all the authors read, critically revised, approved the manuscript, and agreed to be accountable for all aspects of this research.

### **7.3. Conflict of interest**

None.

### **7.4. Funding**

None.

### **7.5. data availability statement**

Extra data that support the findings of this study are accessible from the corresponding author upon reasonable request and can be shared upon legal request via [asaminewhbtamu@gmail.com](mailto:asaminewhbtamu@gmail.com).

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