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ORIGINAL ARTICLE

Incidence and risk factors of delirium in the intensive care unit of SIUT Karachi.

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ABSTRACT… Objective: To estimate the incidence and risk factors of delirium in intensive care unit (ICU) of Sindh Institute of Urology and Transplantation (SIUT), Karachi. **Study Design:** Cross-sectional study. **Setting:** The ICU of SIUT, Karachi, Pakistan. **Period:** February 2023 to August, 2023. **Methods:** Patients over 18 years of age who were admitted to the ICU for more than 24 hours were analyzed. Patient with Richmond agitation sedation score (RASS >-2) were assessed for delirium using the confusion assessment method (CAM)-ICU method. Delirium subtypes were also evaluated. Domographic and clinical risk factors were evaluated for possible relationship with the existence of delirium. **Results:** Total 96 patient were enrolled in the study, 64 (66.7%) were male and 32 (33.3%) female. The mean age was 49.1±17.3 years. Mean RASS and CAM-ICU scores were 0.53±1.31 and 1.0±1.42 respectively. Delirium was present in 32 (33.3%) patients. It was noted that 45.4% patients had hypoactive delirium, 31.8% hyperactive delirium, and 22.7% mixed type. Patients aged 50 years or above had higher odds of delirium (OR: 0.41 [0.17-0.98], p=0.045), On multivariable regression model, BMI <25 Kg/m^2, coexistence of ischemic heart disease and chronic kidney disease, patients with septic shock, post-operative patients, need of sedation were significantly associated with higher odds of delirium. **Conclusion:** Delirium is a frequent condition in ICU patients, with a higher occurrence of hypoactive delirium. The leading risk factors associated with delirium were older age, ischemic heart disease, chronic kidney disease and use of sedative drugs.

Key words: Body Mass Index, Delirium, Ischemic Heart Disease, Sedation, Septic Shock.

INTRODUCTION

Patients in critical care units often experience and are distressed by delirium. Acute mental status change or fluctuation from baseline, inattention, disordered thought, and changed degree of awareness describe the condition known as delirium in the intensive care unit (ICU).[1] In clinical settings, hyperactive delirium, characterized by extreme restlessness, is by far the most often reported category, but is often incorrectly labeled as either a psychotic condition or agitated dementia.[2] Due to under recognition by doctors, hypoactive delirium is common yet has a poor prognosis.[3]

In the ICU, delirium can occur anywhere between 45% and 87% of the time. It was reported that 60% delirium incidence among mechanical ventilated (MV) patients.[4] Study from Pakistan reported an incidence rate of 21.8%.[5] Delirium is a prominent morbidity and death cause in ICU settings. It results in longer ICU stays, longer mechanical ventilation, a decrease in 6-month survival, and cognitive damage that lasts for years following discharge.[6] In a recent observational study, researchers discovered that keeping an eye on patients' delirium in the ICU was linked to better results down the line.[7]

However, in ICU patient's prevention and treatment of delirium may be complicated by baseline risk factors, including history of hypertension, pre-existing dementia, alcoholism, and high disease severity at admission.[8] Although the precise pathophysiology of delirium is still being investigated, we know that an imbalance of neurotransmitters, ischemic brain damage, and brain inflammation are key causes of delirium.[9,10] Acute illnesses and environmental factors such as sedation, lack of daylight, fever, tubes, pain,

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catheters, and prolonged ICU stays are modifiable factors..[11] Elderly patients, those admitted to ICU with cognitive impairments, patients with terminal illnesses, and patients undergoing major surgery are vulnerable for delirium development.[12-14] The "Confusion Assessment Method for the Intensive Care Unit (CAM-ICU)" and the "Intensive Care Delirium Screening Checklist (ICDSC)" assessment tools are most frequently used for delirium in ICU with CAM-ICU sensitivity varying from 47-100% and specificity of 81-100%, while sensitivity of ICDSC ranged from 64 - 99% and specificity of 61- 88%.[15]

A major risk factor for unfavorable outcomes in terms of morbidity and mortality is delirium. To our knowledge we don't know delirium incidence in general ICU population in Pakistan. This study is expected to find out the incidence of delirium in general ICU population admitted in multi-disciplinary ICU and associated risk factors and thus help in working on prevention strategies to lessen the impact and burden of delirium. Hence, the study was designed to assess the incidence and risk factors for delirium at SIUT Karachi's ICU.

METHODS

This cross-sectional study was carried out at Sindh Institute of Urology and Transplantations (SIUT), Karachi, in the general ICU. The institutional committee gave the approval (SIUT-ERC-2023/A-428). Sample size of 96 patients was calculated through Open-Epi online calculator with confidence level of 95% with margin of error 5% taking frequency of delirium to be 21.8%.[5] Non-probability consecutive sampling method was used.

Patients of both genders of age ≥18 years, admitted in ICU > 24hours were included in the study. The patient with CNS infection, TBI, epilepsy, history of cognitive impairment, dementia, hearing impairment and patient taking any type of antipsychotic medications were excluded. Patients who received reversal agent Naloxone/Flumazenil, with deep sedation Richmond Agitation Sedation Scale (RASS) ≤ –2), and severe injuries of brain (Glasgow Coma Scale (GCS) ≤ 8), and if the patient was unable to be evaluated for delirium. Written informed consent was taken from all the patients or their surrogate decision makers for becoming the part of the study.

The patients on invasive mechanical ventilation was sedated, sedation was stopped and assessed daily for delirium while sedation level was assessed by using "Richmond Agitation and Sedation Scale (RASS)". Patients was daily evaluated until their RASS score > -2, so they could be assessed for delirium using the CAM-ICU. The CAM-ICU assesses four features of delirium: (1) acute onset or fluctuating course, (2) inattention, (3) disorganized thinking, and (4) altered level of consciousness. The participant must display features 1 and 2, and either 3 or 4 to be considered CAM-ICU positive. If the RASS score was observed 0 to – 2 with consistent symptoms of delirium was labeled as hypoactive delirium and hyperactive type if the RASS score > 0 with consistent symptoms. If the patient once labeled delirious, not followed for subsequent delirium episodes. Severity was assessed by using "Acute Physiology and Chronic Health Evaluation II (APACHE II)" score. Daily use of sedatives, analgesics, and other risk factors were recorded on proforma.

All the data were entered into SPSS 22.0 and analyzed using the same software. The continuous variable reported as mean ± SD or median ± IQR given normality. Frequencies and percentages were reported for categorical variables. Risk factors were independently assessed using univariate logistic regression. Multivariate logistic regression was applied to adjust confounders for evaluation of risk factors. Odds ratio with respective confidence intervals reported for recorded risk factors. P values ≤0.05 was considered as statistically significant.

RESULTS

In a total of 96 patients, the mean age was 49.5±17.3 years. Nearly, two-third of patients were males (66.7%). The mean APACHE II score was 15.3±5.8. Delirium was present among 33.3% patients. Frequency of patients with hypoactive delirium was 45.4%, following hyperactive delirium 31.8%, and mixed type of delirium as

22.7%. Table-I displays socio-demographic and clinical features of patients.

Age Groups	Frequency (%)
≤50 years	50 (52.1%)
≥50 years	46 (47.9%)
Body mass index	
<25 kg/m^2	70 (72.9%)
≥25kg/m^2	26 (27.1%)
Addiction habits	
Alcohol addiction	6 (6.3%)
Smokers	15 (15.6%)
Comorbidity	
Diabetes	31 (32.3%)
Hypertension	52 (54.2%)
Ischemic heart disease	11 (11.5%)
Chronic kidney disease	11 (11.5%)
Reason of ICU admission	
Acute respiratory failure	11 (11.5%)
Septic shock	65 (67.7%)
Pneumonia	18 (18.8%)
Metabolic acidosis	27 (28.1%)
Heart failure	4 (4.2%)
Post-operative	49 (51%)
Types of drugs	
Analgesic	64 (66.7%)
Sedatives	50 (52.1%)
Mechanical ventilator	54 (56.3%)
RASS Score#	0.53±1.31
CAM-ICU Score#	1.0±1.42
Delirium	32 (33.3%)

Table-I. Summary of socio-demographic and clinical features of patients

#Numerical variables are presented as mean ± standard deviation

Table-II shows comparison of patients' features among those with and without delirium and their univariate association with delirium. On univariate analysis, odds of delirium were significantly lower among patients of age <50 years than those with age 50 years and above. Increasing Apache II score were significantly associated with increasing risk of delirium. Patients with septic shock and those underwent MV were significantly at higher risk of developing delirium.

Table-III represents multivariable association of patients' features with delirium. On multivariable model, age of <50 years was significantly associated with lower risk of delirium. BMI <25 Kg/m^2 and presence of septic shock were significantly associated with higher odds of delirium.

DISCUSSION

Patients in the ICU frequently suffer from delirium, a dangerous psycho-organic condition. The frequency of delirium in patients in ICUs is not well-documented, and reported incidence rates are highly variable.[16] Research on the delirium incidence in low- and middle-income countries is few; the majority of studies have concentrated on high-income European countries. This lack of data makes it challenging to determine the risk of delirium in these regions. Addressing this knowledge gap is crucial for understanding delirium patterns and outcomes. This study was conducted to evaluate the incidence as well as risk factors associated with delirium among general ICU patients of Sindh institute of urology and transplantations (SIUT), Karachi.

The patients in our study were 49.1±17.3 years old on average, whereas mean age was 55±18 years in a study conducted by Abazid et al. in 2021.[17] In our study, 66.7% patients were male which was similar to finding of Lobo et al. (2021), who reported that male were 62.3% in total sample.[18]

Our study found that the incidence of delirium was 33.3% after admission. On other hand, findings of Shaughnessy et al.[19], suggested that that delirium was common in ICU patients, occurring 21% of the time.[19] Rahimi et al.[20], found a slightly higher frequency of delirium which was 27% in such patients in Iranian population. The incidence of delirium was 31.8% and hypoactive type was the most frequent 41.5% in a study done by Dalli et al.[21] Frequency of patients with hypoactive delirium was high in this study (45.4%) following hyperactive delirium which was present in (31.8%) patients and mixed type of delirium was observed in 22.7% patients. Similar to the study by Kumar et al., 44.5% of patients were classified as hypoactive type delirium, with 33.3% as hyperactive and 22.2% as mixed.[22] In our study the most common comorbidity among ICU patients in the delirium group, hypertension (54.2%) and diabetes (32.3%). Comorbidities of our study were in accordance with early study which stated that 58.4% patients had diabetes mellitus, 17.8% had hypertension.[23]

Variables	Delirium		Odds ratio (95% CI)	P-Value
	Yes n=22	No n=74		
Age groups				
≤50 years	12(24)	38(76)	0.41 (0.17-0.98)	0.045
≥50 years	20(43.5)	26(56.5)	Reference category	
Male	23(35.9)	41(64.1)	0.69 (0.27-1.75)	0.445
Female	9(28.1)	23(71.9)	Reference category	
Body mass index				
<25 kg/m^2	27(38.6)	43(61.4)	2.64 (0.88-7.82)	0.081
≥25kg/m^2	5(19.2)	21(80.8)	Reference category	
APACHE II score	19(13.3-20.8)	14(11-18)	1.11 (1.02-1.20)	0.011
Addiction habits				
Alcohol	1(16.7)	5(83.3)	0.38 (0.04-3.40)	0.387
Smoking	7(46.7)	56(69.1)	1.96 (0.64-5.99)	0.238
Comorbidity				
Diabetes	13(21)	49(79)	0.74 (0.29-1.88)	0.538
Hypertension	16(30.8)	36(69.2)	0.77 (0.33-1.82)	0.563
Ischemic heart disease (IHD)	5(45.5)	6(54.5)	1.79 (0.50-6.38)	0.369
Chronic kidney disease (CKD)	5(45.5)	6(54.5)	1.79 (0.50-6.38)	0.369
Reason of ICU admission				
Acute respiratory failure	3(27.3)	8(72.7)	0.72 (0.17-2.93)	0.652
Septic shock	29(44.6)	36(55.4)	7.51 (2.07-27.23)	0.002
Pneumonia	7(38.9)	11(61.1)	1.35 (0.46-3.89)	0.580
Metabolic acidosis	9(33.3)	18(66.7)	1 (0.38-2.57)	1.000
Heart failure	1(25)	3(75)	0.65 (0.06-6.56)	0.720
Post-operative patients	19(38.8)	30(61.2)	1.65 (0.70-3.91)	0.250
Drugs				
Analgesic drugs	24(37.5)	40(62.5)	1.80 (0.69-4.63)	0.224
Sedatives	23(46)	27(54)	3.50 (1.40-8.75)	0.007
Mechanical ventilator	24(44.4)	30(55.6)	3.40 (1.33-8.69)	0.011

Table-II. Univariate analysis of risk factors for delirium

Variables	Adjusted Odds Ratio	95% CI	P-Value
Age groups			
≤50 years	0.23	0.07-0.76	0.017
≥50 years	Reference category		
Body mass index			
<25 kg/m^2	6.54	1.49-28.57	0.013
≥25kg/m^2	Reference category		
APACHE II score	1.07	0.96-1.19	0.176
Addiction Habit			
Smoking	2.01	0.42-9.56	0.378
Reason of ICU admission			
Septic shock	9.88	1.53-63.75	0.016
Post-operative patients	3.31	0.94-11.64	0.061
Drugs			
Analgesic drugs	0.58	0.15-2.17	0.424
Sedatives	3.62	0.91-14.33	0.066
Mechanical ventilator	0.50	0.10-2.40	0.383

Table-III. Multivariable logistic regression - factors associated with delirium

Patients with a history of diabetes and hypertension were not associated delirium, according to our findings. Researchers have shown a correlation between hypertension and delirium. Vyveganathan et al.[24], and Nagari et al.[25], found that having a hypertension history doubled the likelihood of developing delirium. Patients with hypertension are more likely to develop vascular disease, which increases their risk of cerebral hypoperfusion and possibly cerebral cellular hypoxia. Sedation was revealed to be an independent risk factor for the daily onset of delirium, as reported by Nagari et al.[25] The reason of conflicting finding could be due to limited sample size. However, this study found that patients with septic shock and post-operative patients had higher risk of delirium development. This finding is consistent with existing literature which reports sepsis associated delirium and delirium in post-operative patients is common.[26,27]

Delirium is a side effect of many medication classes. Prescription, over-the-counter, complementary/alternative, and illegal goods are all included in this. In this study we found that in univariate analysis use of sedatives was significantly associated with higher delirium risk which is in line with earlier findings.[27,28] The use of anaesthetic medications was revealed to be a significant risk factor for delirium in this patient population by Tilouche et al.[28]

Surprisingly, this study did not find association of mechanical ventilation and delirium on final regression model. However, patients in ICUs on mechanical ventilation have a heightened vulnerability to delirium due to a multitude of circumstances, including drugs, comorbidities, and multisystem acute diseases.[29]

This study possesses notable strengths. We utilized an innovative statistical model, enabling the identification of the group at the highest risk for delirium development. The findings from this research have generated various strategies aimed at addressing this specific high-risk group, which may potentially lead to significant changes in our daily practices. Recognizing and mitigating risk factors is a crucial aspect of delirium management. Our study holds significant clinical relevance, as it identifies key risk factors for delirium in the ICU setting. Future research endeavors should expand this scope to encompass patient's post-ICU admission in different hospital settings and ICUs to provide a more comprehensive understanding of delirium in diverse clinical contexts.

The study's limitations stem from the fact that it was conducted at only one location. We were unable to assess the effect of delirium on long-term morbidity and death in our cohort since our follow-up period was just 5 days. Delirium was also evaluated using a binary scale, which ignores the severity and length of the condition. In our study, we exclusively focused on patients who exhibited delirium symptoms during their ICU/CCU admission. It's important to note that this selection criterion could potentially account for the relatively lower incidence of delirium observed in our study.

CONCLUSION

Delirium is a prevalent condition among ICU patients, with a higher occurrence of hypoactive delirium. The leading risk factor associated with delirium were younger age, ischemic heart disease, chronic kidney disease and use of sedative drugs.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

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2	Fakhir Raza Haidri	Designed the study protocol, Critically revised the initial manuscript draft.	
3	Bushra Zafar	Data collection, Initial manuscript writing.	
4	Ravi Kumar	Performed data analysis and involved in result writing.	
5	Abdul Rehman Azam	Performed data analysis and involved in result writing.	
6	Sumera Imran	Performed data analysis and involved in result writing.	