Original Article

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Clinical Profile and Outcome of Delirium in Patients in The Semi-Closed Intensive Care Unit

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ABSTRACT

Background: Delirium is an underdiagnosed condition in the intensive care unit. This study was conducted to know clinical profile and outcome of delirium in patients in the mixed semi-closed intensive care unit of medical college.

Methods: This prospective observational study was done in 284 patients of age≥18 years admitted for more than 24 hours in level three intensive care unit of tertiary care hospital for one year. The Confusion Assessment Method-ICU and Richmond Agitation Sedation Scale were used to diagnose and motor subtype delirium, respectively, Hyperactive delirium was defined as a persistent rating of +1 to +4 during all assessments. Hypoactive delirium was defined as a persistent rating of 0 to −3 during all assessments and mixed subtype was defined as present when the patients have rating of both hyperactive and hypoactive values. There was a checklist to assess risk factors. All data was transferred to the excel sheet and transferred to a statistical package for the social sciences-16. Chi-square test and Fisher's exact probability test were used to detect the difference between groups in the univariate analysis, as appropriate.

Results: Of the 284 ICU admissions 109(38.4%) patients developed delirium. Mixed delirium was the most common motor subtype 39(35.7%) in this study. The mean duration of delirium was 3.69±4.06 days. APACHE II score, SOFA score, presence of co-morbidities, history of alcohol intake, presence of hypoxemia, presence of metabolic acidosis, and use of mechanical ventilation were identified as risk factors for delirium. Delirious patients had longer length of ICU stay (5.8 ±5.4 vs 4.2±4.3 days) and higher reintubation rate.

Conclusions: APACHE II score, SOFA score, presence of co-morbidities, history of alcohol intake, presence of hypoxemia, presence of metabolic acidosis, and use of mechanical ventilation were identified as risk factors for delirium in the intensive care unit patients that should be identified early to prevent complication such as longer length of ICU stay and higher reintubation rate.

Keywords: Delirium; intensive care units; mortality.

INTRODUCTION

Delirium is defined as a disturbance of consciousness with inattention accompanied by change in cognition or perceptual disturbance that develops over short period of time (hours to days) and fluctuates over time.[1] Studies have shown that an incidence of delirium in the intensive care unit (ICU) varies between 3.6% to 67% [1-3] depending upon the severity of the illness, group of patients studied, and the diagnostic method used. The risk factors of delirium can be modifiable and non-modifiable [4] and it affects the patient outcome in the intensive care unit.

Risk factors, and outcomes of delirium can vary depending upon the protocol for sedation, pain management, and models of the ICU in the same country or between different countries. There are limited studies about delirium from developing countries including Nepal.

This study was conducted to know profile, risk factors, and outcome of delirium in mixed semi-closed intensive care unit.

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METHODS

It was a prospective observational study in a level three intensive care unit of National medical college, Birgunj between August 1,2023 to July 31, 2024. The ethical approval from the Institutional Review Committee was obtained before enrolment in this study. The ethical approval number was F-NMC/630/079-080. Written informed consent was obtained from the patients or surrogate decision-makers.

Patients ≥18 years admitted to the mixed intensive care unit of a tertiary care hospital for more than 24 hours were included in this study. Patients younger than 18 years, surrogate decision-maker, or patient did not give written informed consent, whose length of stay in the ICU was less than 24 hours, required cardiopulmonary resuscitation with no return of spontaneous circulation, previously diagnosed disorders like senile dementia, Alzheimer's disease, psychosis, depression, patients having intracranial injury, ischemic or hemorrhagic strokes, do not resuscitate orders given by surrogate members, patient who was blind and deaf were not included in this study.

Sedation management and delirium assessment is a routine procedure in our ICU by treating physicians and ICU staff. The nurse performed and recorded the result of sedation and delirium assessment by using Richmond Agitation-Sedation Scale (RASS) and confusion assessment method (CAM-ICU) for every patient admitted in the intensive care unit twice a day and whenever a patient experiences a change in mental status. Each day during rounds, the target RASS score for the patient for the following 24 hours was set by the critical care team. The critical care team decided on sedation drug, regimen, the route of administration, and whether the administration was by bolus or infusion. All sedation was stopped between 6 to 8 am daily to assess the Glasgow coma scale.

Risk factors associated with delirium was documented and were subdivided into predisposing factors present before ICU admission and precipitating factors that occurred during critical illness that can be changed by preventing or therapeutic intervention.

The following information was collected from each patient meeting inclusion criteria on the day of study. Age, sex, ethnicity, occupation, Acute physiology and chronic health evaluation II (APACHE II), Sequential organ failure assessment (SOFA), injury severity score, diagnosis, temperature, hemoglobin, hematocrit, serum sodium, potassium, magnesium, calcium, blood sugar, creatinine, urea, albumin, bilirubin, a ratio of aspartate aminotransferase/alanine aminotransferase (AST/ALT). Other information included co-morbidity, history of blood transfusion, exposure to a sedative, analgesic, and other drugs, the reason for admission in the ICU, and the category of surgical admission (elective versus emergency).

Eligible patients were screened daily for delirium by applying the CAM-ICU score until the day of discharge from the ICU. Level of arousal was measured by using the RASS score which rates a patient's level of agitation or sedation on a 10 point scale ranging from -5 (unarousable, not responsive to voice or physical stimulation) to +4 (combative). Those having a RASS score of -3 to +4 were taken to step two on whom the CAM-ICU scale was applied. 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. To be CAM-ICU positive, the patient must display features 1 and 2, and either 3 or 4.

The patients who were CAM-ICU positive were labeled as patients having delirium. Then, the details of individual patient including the type of delirium, duration, drugs that were used to treat delirium, and duration of the drugs used was recorded. Hyperactive delirium is defined as a persistent rating of +1 to +4 during all assessments. Hypoactive delirium is defined as a persistent rating of 0 to −3 during all assessments and mixed subtype is defined as present when the patients have rating of both hyperactive and hypoactive values.

The outcome of delirium was assessed in terms of mortality, length of stay in the ICU, duration of mechanical ventilation, extubation and reintubation.

At the time of discharge from ICU, duration of mechanical ventilation, length of stay in the ICU, reintubation, unplanned extubation, and mortality in the ICU were recorded.

Bias was reduced by collecting data from all groups of patients.

Data collection was done in a preformed sheet. The preformed sheet included all physiologic variables and demographic variables. All data was transferred to the excel sheet and transferred to SPSS-16. The descriptive data are presented as the number and percentage for categorical data and mean ± standard deviation for continuous data according to their distribution. Chi-square test and Fisher's exact probability test were used

to detect the difference between groups in the univariate analysis, as appropriate.

The risk factors were analyzed using binary logistic regression. Any variables which had P<0.2 after the univariable risk regression and all other potential variables associated with the delirium were included for the multivariable risk regression. The level of significance was P<0.05.

RESULTS

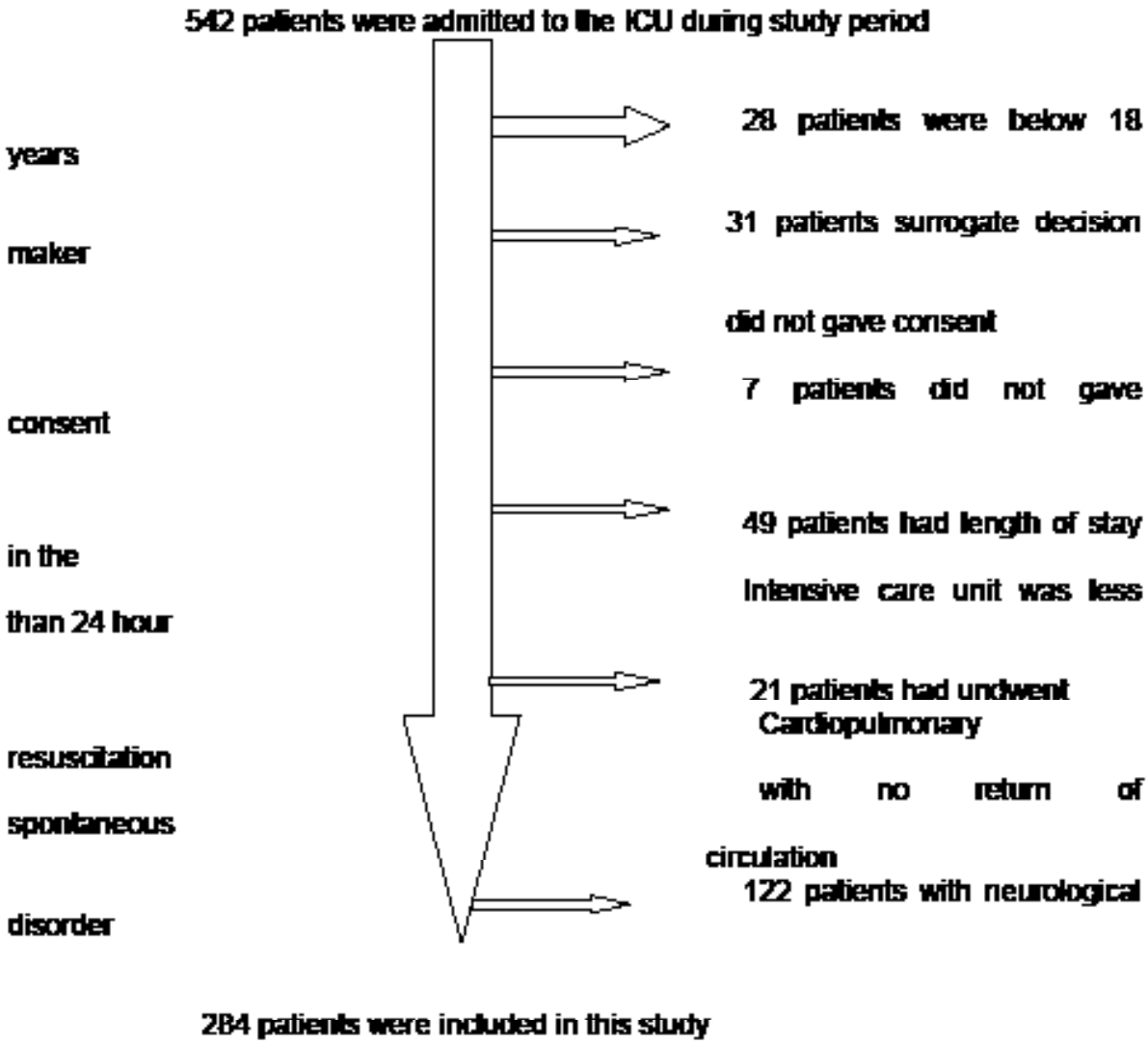

Figure 1. Flow diagram of patients included in this study.

Figure 1 shows that 284 patients were included in this study.

Table 1. Baseline characteristics of patients with and without delirium.

Characteristics	Delirious patients (n=109)	Non-delirious patients (n=175)	P value
Age (Years), Mean±SD	53.7±18.1	49.3±22.4	0.072
Sex (Male/ Female),n	67/42	102/73	0.564
APACHE II, Mean±SD	11.7±7	8.3±5.9	<0.001
SOFA, Mean±SD	4.3±3.2	2.6±2.5	<0.001
Injury Severity Score, Mean±SD	14.8±8.3	14.1±10.7	0.789
Comorbidity,n	101	135	0.001
COPD, n(%)	15(13.8)	16(9.1)	0.225
Chronic renal failure, n(%)	6(5.5)	3(1.7)	0.076
Hypertension, n(%)	25(22.9)	34(19.4)	0.479
Diabetes mellitus, n(%)	13(11.9)	31(17.7)	0.192
Alcohol. n(%)	63(57.8)	60(34.3)	<0.001
Trauma, n(%)	17(15.6)	60(34.3)	0.001
Emergency surgery, n(%)	14(12.8)	27(15.4)	0.018
Abdominal surgery, n(%)	3(2.8)	14(8)	0.071
Chest surgery, n(%)	3(2.8)	10(5.7)	0.245
Ortho surgery, n(%)	7(6.4)	10(5.7)	0.807
Reason for ICU admission			
Acute respiratory failure, n(%)	23(21.1)	17(9.7)	0.007
Septic shock, n(%)	10(9.2)	14(8)	0.729
Other, n(%)	65(59.6)	113(64.6)	0.403
Specialty			
Medicine, n(%)	78(71.6)	81(46.3)	<0.001
Surgery, n(%)	16(14.7)	54(30.9)	0.002
Orthopedics, n(%)	10(9.2)	35(20)	0.015

APACHE II: Acute physiology and chronic health evaluation, COPD: Chronic obstructive pulmonary disease, ICU: Intensive care unit, SD: Standard deviation SOFA: Sequential organ failure assessment.

Table 1 shows the baseline characteristics of patients. The incidence of delirium was 109(38.4%). Delirium was mixed in 39(35.7%), hypoactive 38(34.8%), and hyperactive 35(32.1%) patients. The mean duration of delirium was 3.69±4.06 days. Delirious patients had higher APACHE II, SOFA score, higher incidence of co-morbidities,had a history of alcohol, emergency surgery, Trauma, and delirium was more in medical and surgical patients while it was less in orthopedics patients.

Table 2. Univariate analysis of metabolic risk factors in delirious and non-delirious patient.

Characteristics	Delirious patients (n=109) n(%)	Non-delirious patients (n=175) n(%)	P value
Anemia	59 (54.1)	75(42.9)	0.064
Raised Urea	31(28.4)	26(14.9)	0.005
Raised Creatinine	32(29.4)	41(23.4)	0.266
Raised AST/ ALT	59(54.1)	80(45.7)	0.168
Hyperbilirubinemia	42(38.5)	55(31.4)	0.221
Hypoalbuminemia	30(27.5)	51(29.1)	0.769

Table 2. Univariate analysis of metabolic risk factors in delirious and non-delirious patient.

Characteristics	Delirious patients (n=109) n(%)	Non-delirious patients (n=175) n(%)	P value
Mechanical ventilation	36(33)	31(17.7)	0.041
Metabolic disorder			
Hypoglycemia	11(10.1)	7(4)	0.041
Hyponatremia	26(23.9)	33(18.9)	0.313
Hyperkalemia	5(4.6)	5(2.9)	0.442
Hypocalcemia	39(35.8)	74(42.3)	0.276
Hypomagnesemia	28(25.7)	37(21.1)	0.375
Hypoxemia	65(59.6)	63(36)	<0.001
Hypercarbia	20(18.3)	24(13.7)	0.294
Metabolic acidosis	76(69.7)	100(57.1)	0.034
Respiratory acidosis	14(12.8)	13(7.4)	0.131
Blood Transfusion	24(22)	31(17.7)	0.372
Analgesic	63(58.6)	56(32)	0.006
Vasopressor	10(9.2)	14(8)	0.121

AST/ALT: Aspartate aminotransferase/Alanine aminotransferase, Anemia: Hemoglobin <12g/dl for females and <13g/dl for males, Raised Urea: Urea>45mg/dl, Raised Creatinine: Creatinine>1.2 mg/dl, Raised AST/ALT: >37/45U/L, Hyperbilirubinemia: Bilirubin >1.2 mg/dl, Hypoalbuminemia: Albumin<3.5 gm/dl, Hypoglycemia: Blood sugar<60 mg/dl. Hyponatremia: Serum sodium<135 MEq/L, Hyperkalemia: Serum potassium>5.5 MEq/L, Hypocalcemia: Serum calcium <8.8 mg/dl, Hypomagnesemia: Serum magnesium<1.7 mg/dl.

Table 2 shows the univariate analysis of metabolic risk factors in delirious and non-delirious patients. Metabolic disorders like raised urea, hypoglycemia, hypoxemia, metabolic acidosis were higher in delirium patients. The use of mechanical ventilation and analgesic drug was higher in delirious patients.

Table 3. Multivariate analysis of risk factors related to mortality.

Characteristics	OR	OR(95% CI)	P
Alcohol	3.096	5.368-1.786	<0.001
Hypoxemia	1.878	3.277-1.076	0.026
Metabolic acidosis	1.716	0.961-3.065	0.048
Mechanical ventilation	1.793	3.370-0.954	0.046

CI: Confidence interval, OR: Odds ratio

Table 4. Clinical outcomes, complications and mortality

Characteristics	Delirious patients (n=109)	Non-delirious patients (n=175)	P Value
Duration of MV, Mean±SD, days	3.2 ± 2	2.5±1.6	0.126
ICU LOS, days, Mean±SD	5.8 ±5.4	4.2±4.3	0.006
Mortality n(%)	19(17.4)	24(13.7)	0.395
Complications			
Unplanned extubation, n(%)	5(4.6)	2(1.1)	0.154
Reintubation, n(%)	4(3.7)	0	0.021

ICU: Intensive care unit, LOS: length of stay, MV: Mechanical ventilation, SD: Standard deviation

Table 4 shows the clinical outcomes, complications, and mortality of the study population. Delirious patients had a significantly longer length of stay in the ICU and reintubation. Mortality was similar between the two groups.

Table 5. Dose and duration of drugs used to treat delirium in the intensive care unit.

		N	Minimum	Maximum	Mean	Std. Deviation
Lorazepam	Dose, mg	65	3	400	31.92	51.598
	Duration, days	65	1	40	4.34	5.360
Midazolam	Dose, mg	9	2	40	15.33	12.288
	Duration, days	9	1	12	4.67	3.775
Quetiapine	Dose, mg	35	100	2000	290.00	340.156
	Duration, days	35	1	15	3.49	2.748
Haloperidol	Dose, mg	5	20	20	20.00	.000
	Duration, days	5	2	6	3.20	1.789

Lorazepam and Quetiapine were the most common drugs used to treat delirium in the intensive care unit in this study.

DISCUSSION

The incidence of delirium in our study was 38.4%. In a systemic review of 48 studies, Krewulak et al[5] reported that the pooled incidence of delirium was 31% in all ICU (medical, surgical, and specialty). There is only one study from Nepal conducted in the ward that has shown the incidence of delirium 16%.[2] Indian studies in the ICU setting have reported prevalence rates ranging from 16% to 53.6%.[6-9] Study by Tilouche et al [9] and other studies [1,3] have shown the incidence in the range of 19% to 67%. This difference may be due to differences in definitions, type of ICU population, the severity of illness, diagnostic tool used, model of ICU, the protocol for sedation and pain management, and hospital setting. Delirium was not assessed in the night, neurological, and do not resuscitate patient.

Mixed subtype constituted 39(35.7%) of the cases of delirium in our study which is similar to other studies.[1,10,11] while other studies [3,5-9] have shown that hypoactive is most common subtype. This difference may be due to differences in definitions, type of ICU population, the severity of illness, diagnostic tool used, model of ICU, the protocol for sedation and pain management, and hospital setting.

Variables like Hypoglycemia, COPD, high urea, trauma, medicine, surgery, orthopedics, acute respiratory failure, and use of analgesics were statistically significant in univariate analysis but in multivariate analysis, it was not statistically significant. It is because it was a non-randomized and cross-sectional study.

Seven risk factors for delirium were identified in our study which includes High APACHE II, SOFA score, presence of co-morbidities, history of alcohol intake, hypoxemia, metabolic acidosis, and mechanical ventilation.

Raised APACHE II score was an important risk for delirium in our study which is similar to other studies. [1,5,6,12] This can be explained by the vulnerability of sick patients to develop delirium.

A high SOFA score was an important risk factor for delirium in our study which is similar to study by Salluh et al [13], and Pipanmekaporn et al. [1] This is explained by the physiological derangement in a patient with high SOFA score.

The presence of co-morbidities in patients increases the risk of delirium in our study though the individual co-morbidity was not statistically significant. This may be due to the small number of patients with individual comorbidity in our study.

Alcohol was an important risk factor for delirium in our study which is similar to the study by Stewart et al [14] and Sarkar et al. [15] It is because alcohol causes the change in the brain neurotransmitters along with physiological and metabolic changes that predisposes patients to delirium.

Hypoxemia was risk factor for delirium which is similar to the study by a Jayaswal et al [9]and Li et al. [12]

Mechanical ventilation was risk factor for delirium in our study which is similar to other studies. [3,5,6,8]

The presence of metabolic acidosis was risk factor for delirium in our study which is similar to the study by a Sharma et al. [6]

This study showed that the length of stay in the ICU was higher in delirious patients that is similar to other studies. [1,6-8,12]

The mortality was similar in delirious and non-delirious patients in our study which is similar to the study by Tilouche et al[9] This is different in the literature with higher mortality in delirious patients.[1,6-8] This may be due to different study populations in other studies.

The duration of mechanical ventilation was not statistically significant in delirious and non-delirious patients while other studies have shown that the duration of mechanical ventilation is prolonged in the delirious patient.[6-8] This may be due to the protocolized management of patients by the full-time intensivist.

Reintubation was more in the delirious patient in our study which is similar to the study by a Brummel et al .[16]

Unplanned extubation was similar in both group in our study while other studies [16,17] have shown that unplanned extubation is more common in delirious patients.

Lorazepam was a most common drug used to treat delirium in the intensive care unit in our study because 57.8% of patient in our study were alcoholic and benzodiazepines is a drug of choice to treat delirium in alcoholic patient. and non-benzodiazepines in non-alcoholic patients which were used in our study.

Our study has limitations like it was a single-center, non-randomized study. Delirium was not assessed in the night. Long term outcome to detect persistent cognitive impairment was not assessed in our study.

CONCLUSIONS

High APACHE II, SOFA score, presence of co-morbidities, history of alcohol intake, hypoxemia, metabolic acidosis, and mechanical ventilation were identified as risk factors for delirium in the intensive care unit patients that should be identified early to prevent complications such as longer length of ICU stay and higher rate of reintubation.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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