

Short-Term Outcome of Patients in Delirium at Medical Intensive Care Unit

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ABSTRACT

Background: Delirium is highly prevalent in the Intensive Care Unit (ICU), and managing it in critically ill patients with severe comorbidities is challenging due to transient nature of symptoms. However its significance is underestimated, often overlooked and misdiagnosed by healthcare providers. In Nepal, limited studies has been done on delirium in medical ICUs hence this study aims to assess short-term outcome of admitted patients in delirium.

Methods: Descriptive cross-sectional observational study was conducted among 92 patients referred from medical ICU with history of disorientation and altered sensorium, assessed during consultation liaison and meeting the criteria for delirium. Data were collected using semi-structured proforma. Richmond Agitation Sedation Scale and Delirium Rating Scale-Revised 98 were used to know the pattern and severity of delirium at day 0 and seven respectively and phone follow-up was done at three months. Data were tabulated and analyzed using SPSS version 25.0.

Results: Hyperactive delirium (57.6%) was most common in medical ICU. Out of total patients, 63.2% improved, 23% became worse and 13.8% remain static with treatment. Mean length of hospital stay was 11.1 days. Hypoactive delirium was associated with longer hospital stay and increased mortality. Significant association was found between length of ICU stay and outcome in terms of mortality and response to treatment.

Conclusions: Study underscores the prevalence of hyperactive delirium as the predominant pattern in MICU settings. However, it is crucial to highlight the significance of hypoactive delirium due to its poor treatment response and prolonged ICU stays compared to other forms.

Keywords: Delirium; length of ICU stay; mortality pattern; outcome.

INTRODUCTION

Delirium in Intensive Care Units (ICU) is a challenging condition due to its high comorbidity, use of high doses of analgesics and sedatives, and presence of life support systems like ventilators.¹ The prevalence of delirium is 20-50% in lower severity patients and 60-80% in patients with Mechanical Ventilation.² Short-term outcomes include increased hospital mortality and longer stay, while long-term outcomes include higher mortality rates, functional disability, residential care admission, cognitive impairment, and dementia.³⁻⁶ Delirium is

preventable in 30-40% cases but often goes undetected and misdiagnosed due to its transient nature, overlap with other psychiatric syndromes, and heterogenic presentations.⁷⁻⁹ Knowledge of subtype-specific delirium risk factors could help develop risk prediction models for effective interventions in high-risk patients. However, limited studies have evaluated short-term outcomes of delirium in ICUs, making it often unrecognized. This study aims to assess the short-term outcome of delirium in ICUs, supporting the development of screening and intervention strategies for early diagnosis and treatment.

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METHODS

A descriptive cross-sectional observational study was conducted among patients admitted in medical ICU of Tribhuvan University Teaching Hospital (TUTH), Nepal. Ethical approval for the study was obtained from Institutional Review Committee, Institute of Medicine, TUTH (Ref: 231(6-11) E2 076/077). Study was conducted from December 2019 to November 2020. All the study participants were explained about the research and asked if they would like to participate, and when asserted, they were asked to sign consent. The participants were assured that the information provided by them would be maintained confidential. Participants were selected using purposive sampling technique. All patients admitted at MICU of TUTH and meeting the inclusion criteria were enrolled in the study until the adequate sample size was achieved.

Tools used in the study were International Classification of Diseases, Tenth Revision Diagnostic criteria for Research (ICD-10 DCR), Delirium Rating Scale- revised 98 (DRS-R98) and Richmond Agitation Sedation Scale (RASS). ICD-10 DCR was developed by the World Health Organization, outlines the specific diagnostic criteria derived from the ICD-10 Chapter V(F) which is detailed in the Clinical Descriptions and Diagnostic Guidelines (CDDG).¹⁰ For assessing delirium, DRS-R98 was employed, featuring 16 items divided into diagnostic (3 items) and severity (13 items) categories, with higher scores indicating more severe delirium; a cutoff score over 15 suggested a delirium diagnosis.¹¹ It requires 1-2 hours for information gathering and 20-30 minutes for scoring, based on 24-hour patient observations, and has demonstrated high sensitivity and specificity. Additionally, RASS was used to identify delirium subtypes within a very short assessment time, helping categorize delirium as hyperactive, hypoactive, or mixed based on the patient's agitation and sedation levels.¹²

Population included for study were patients aged more than 16 years and all those admitted in medical ICU who had been consulted to Psychiatric Department and meeting ICD-10 DCR criteria for delirium. Patients diagnosed with dementia, delirium due to alcohol or benzodiazepine withdrawal (last intake at least two weeks back), comorbid psychotic or mood disorder and severe aphasia interfering with assessment were excluded in the study.

Procedure

A total of 103 patients in medical ICU who were consulted to psychiatry department for delirium were

assessed from December 2019 to November 2020. After applying inclusion and exclusion criteria, 92 patients were included in the study [Figure 1] and 11 patients were excluded as four patients were diagnosed as psychiatric illness, five patients were using alcohol within two weeks and two patients were found to have dementia. Among 92 patients, nine were lost to follow up as five died after day 0 and four patients did not receive call on follow-up after discharge from hospital. Consequently, 83 participants were included in the analysis of the length of hospital stay and other relevant outcomes. Furthermore, the five patients who died post day 0 were excluded from the follow-up assessments of DRS-R98 and RASS at day seven. Thus, the total sample size for the analysis of these measures and mortality at day seven was 87.

Written and informed consent was obtained from the nearest relative of the patient. After receiving consent, the semi structured proforma was filled. ICD -10 DCR was used for making diagnosis of delirium in these patients. After applying both the inclusion and exclusion criteria participants were selected then assessment of enrolled patient was done by using DRS-R98 and RASS at day 0 and day seven and then phone follow up was done at three months. The response to treatment was categorized as improving, static and worse based on DRS-R98 score which was calculated as continuous scores. Etiological factors were broadly divided into three categories as diagnosis based on system (system-based diagnosis), diagnosis based on risk factors (risk factors) and diagnosis based on number of drugs used which were further categorized as more than three drugs used and less than three drugs used. Diagnosis based on system such as respiratory, cardiac, central nervous system, renal system, cardiothoracic and vascular surgery, gastrointestinal etc., risk factors such as electrolyte abnormalities, deranged renal function test (RFT) and liver function test (LFT), acid base imbalance, infection and anemia and number of drugs used.

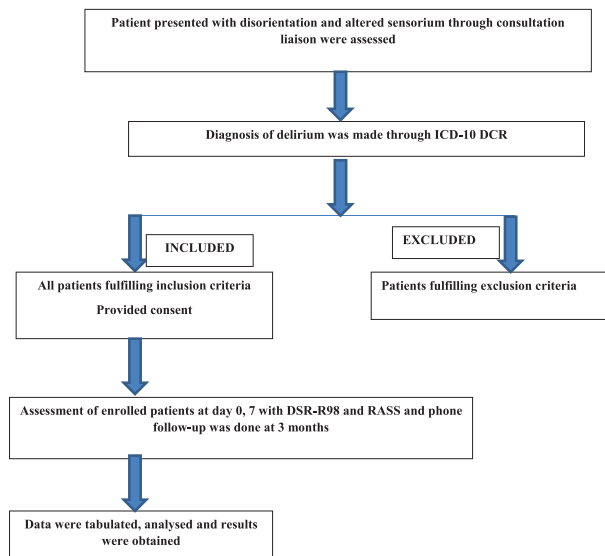


Figure 1. Flow chart of the study.

Data were edited, coded, categorized and then analyzed using SPSS version 25. All the data were normally distributed except length of ICU stay and pattern of delirium. Descriptive analysis was carried out in the form of frequency, percentages, means, and standard deviations. Independent t-test was used to determine association between the means of length of ICU stay and mortality. ANOVA was used to measure association between the means of length of ICU stay and response to treatment as usual. Kruskal Wallis test was used to see statistically significant differences between length of ICU stay and pattern of delirium. Chi square (x2) and Fischer's exact test were used to evaluate difference between etiology and pattern of delirium, response to treatment as usual and pattern of delirium, mortality, and pattern of delirium as appropriate. P value of less than 0.05 was considered statistically significant in all tests.

RESULTS

Table 1. Characteristics of patients admitted in medical ICU.

Characteristics	n=92
Age in years; (mean±SD)	55.9 ± 20
Length of ICU stay; (mean±SD)	11.1 ± 2.4
Gender	
Male	56 (60.9%)
Female	36 (39.1%)

Table 1. Characteristics of patients admitted in medical ICU.

Marital status	
Married	68 (73.9%)
Unmarried	24 (26.1%)

Religion	
Hindu	78 (84.8%)
Others	14 (15.2%)

Ethnicity	
Others (Mongolian, Chhettri, Newar)	64 (69.6%)
Brahmin	28 (30.4%)

Occupation	
Employed (skilled, semiskilled, unskilled worker)	53(57.6%)
Unemployed	39 (42.4%)

Comorbidity	
No	48 (52.2%)
Yes	44 (47.8%)

Diagnosis	
Others (Renal, Respiratory, Cardiac, Gastrointestinal, CTVS)	66 (71.7%)
CNS	26 (28.3%)

Number of drugs used	
>3	67 (72.8%)
<3	25 (27.2 %)

Risk factors	
Dearranged RFT, LFT, electrolyte and acid base imbalance	56(60.9%)
Others (anemia, pancytopenia, and infection)	36(39.1%)

Table 1 reveals that mean age was 55.9 years where majority of participants with delirium were in age group range of 70-79 years. Mean of length of ICU stay at 3 months follow up was 11.1 days. Majority were male participants 56(60.9%), married 68(73.9%) who belong to Hindu 78(84.8%) religion and Mongolian, Chhettri, Newar and others ethnicity 64 (69.6%) Majority of participants were employed (skilled, semiskilled and unskilled worker) 53(57.6%). The majority of participants were illiterate 30(32.6%) followed by primary level education 27(29.3%), higher secondary level 17 (18.5%), university level 12 (13%) and secondary level 6 (6.5%). Participants without any comorbidities were 48(52.2%) and 44(47.8%) had comorbidities. Majority of the participants had disease affecting renal, respiratory, cardiac, gastrointestinal, CTVS 66(71.7%). Similarly, 67(72.8%) participants had used more than three drugs

and majority of participants with the risk factors of delirium were dearranged RFT, LFT, electrolyte imbalance and acid base imbalance 56(60.9%).

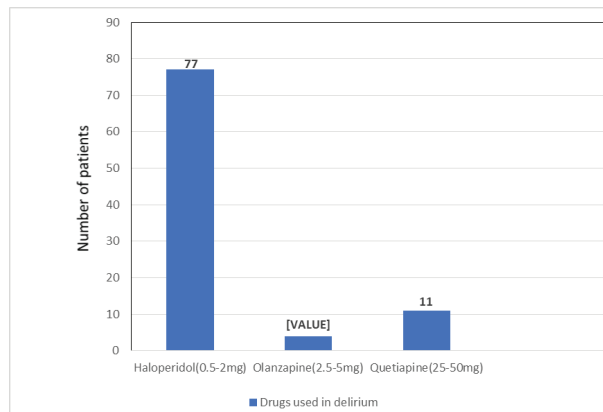


Figure 2. reveals more than 3/4th of the patients were prescribed haloperidol. Rest of the patients were prescribed quetiapine and only four patients were given olanzapine.

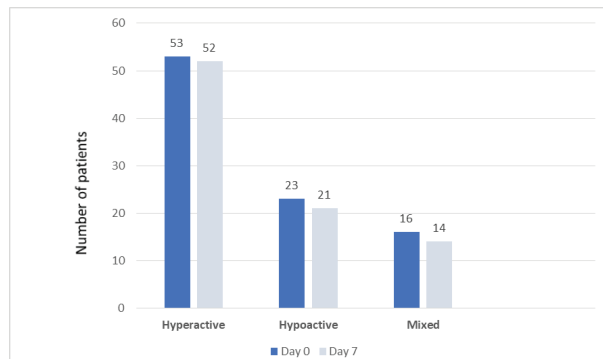


Figure 3. Bar diagram showing distribution of patients on the basis of RASS at day 0 and day 7.

The pattern of delirium at day 0 and day 7 [Figure 3], majority of the participants were hyperactive delirium 53(57.6%) and 52(59.8%) respectively.

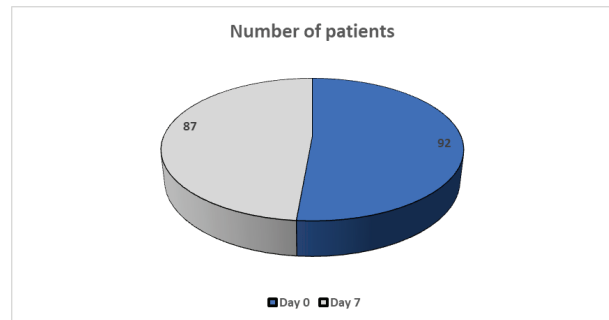


Figure 4. Distribution on the basis of DRS R98 at day 0 and day 7.

The total number of patients on day 0 and at day 7 [figure 4] were 92 and 87 respectively. The mean score for DRS on day 0 was 20.6 with S.D 2.0 while on day seven the mean score was 14.4 and S.D 7.3.

Table 2. Association between length of ICU stay and outcome (mortality and response to treatment).

Outcome		N	Length of ICU stay		P
			Mean	S. D	
Mortality	Yes	36	13.25	1.422	<0.001
	No	47	9.4	1.346	
Response to treatment	Improving	52	10	2.1	<0.001
	Static	11	12.5	2.1	
	Worst	20	13.1	1.3	

Table 2 reveals that mortality was higher with longer ICU stay and association was statistically significant as p-value was less than 0.05. Similarly, study showed that the mean length of ICU stay was shorter who responded well with treatment as compared to others and the association between them was statistically significant as p-value was less than 0.05.

Table 3. Association between RASS at day 0 and 7 with length of hospital stay.

Length of stay (in days)	RASS at day 0 and day 7																		p
	Hyperactive						Hypoactive						Mixed						
	Median		Q1		Q3		Median		Q1		Q3		Median		Q1		Q3		
	D 0	D 7	D 0	D 7	D 0	D 7	D 0	D 7	D 0	D 7	D 0	D 7	D 0	D 7	D 0	D 7	D 0	D 7	
	10	10	9	9	12	12	13.5	13	12	12	15	15	9	9	8.7	9	10.5	10	

Table 3 showed that at day 0, length of ICU stay was highest with hypoactive delirium and lowest with mixed delirium and the association was statistically significant as p-value was <0.05. Similarly, at day seven, length of ICU stay was highest with hypoactive delirium and lowest with mixed delirium and the association was statistically significant as p-value was <0.05.

Table 4. Association between Response to treatment and RASS at day 7.

Response to treatment	RASS at day 7			P
	Hyperactive (n=52)	Hypoactive (n=21)	Mixed (n=14)	
Improving	38(73.1%)	6(28.6)	11(78.6%)	<0.001
Static	8(15.4%)	2(9.5%)	2(14.3%)	
Worse	6(11.5%)	13(61.9%)	1(7.1%)	

Table 4 reveals that mixed delirium showed greater improvement to treatment and hypoactive delirium showed worse response to treatment. The association between response to treatment and RASS at day seven was statistically significant as p-value was less than 0.05.

Table 5. Association between Pattern of delirium and mortality at 3 months follow up.

Mortality at 3 month F/U	Pattern of delirium			P
	Hyperactive (n=52)	Hypoactive (n=21)	Mixed (n=14)	
Yes	15 (30%)	18 (85.7%)	3 (25%)	<0.001
No	35 (70.0%)	3 (14.3%)	9 (75%)	

Table 5 reveals that mortality was highest with hypoactive delirium and lowest with mixed delirium. The association of pattern of delirium and mortality at three months follow- up was statistically significant with p-value less than 0.05.

DISCUSSION

In the present study, hyperactive delirium (57.6%) was the most common pattern followed by hypoactive delirium (25%) and mixed delirium (17.4%). Study done by Ayush Kumar et al., has shown similar result as our study which reported hyperactive delirium (30%) more common than mixed (22.2%) and hypoactive delirium (2.04%). In contrast, study done by Karla et al., showed the range of prevalence for hyperactive delirium was 0.3% to 6.5%, hypoactive delirium was 7.3% to 29.2% and mixed delirium was 1.3% to 33.6% that varied across the 20 studies.¹³ Another study from India showed hypoactive delirium (45.33%) more common followed by hyperactive delirium (37.33%) and mixed delirium (17.33%) in ICU setting. This difference might be due to nature of hypoactive delirium which did not seem to be as problematic as hyperactive delirium and failed to draw the attention of the ICU staff. Therefore, many patients with hypoactive delirium were not referred for psychiatric consultations and were missed while making diagnosis.¹⁴

Our study showed that the majority of patients improved with treatment 55% followed by worse response to treatment 20% and static response to treatment 12%. The association between response to treatment and pattern of delirium was found to be statistically significant. Similar findings were shown in studies done on antipsychotic medication for the treatment of delirium and found improvement in delirium severity after using antipsychotics.¹⁵ However, a systematic review done on efficacy of antipsychotic in delirium found that antipsychotics did not reduce delirium severity or resolve symptoms.¹⁶ The reason for these contrast finding might be due to use of different types and doses of medication for treating delirium in different studies.

The present study showed the mean of length of ICU stay at three months follow up was 11.1 days. A systematic review reported that the length of hospital stays among studies ranged from a mean of 10 to 24 days.¹³ Mortality of patient with delirium at three months follow up was 46.6%. The association between mortality and length of ICU stay was found to be statistically significant. Indian studies by Sharma et al., and Lahariya et al., have found a significant difference in both duration of ICU stay and ICU mortality rates in delirious patients 14,17 as critical patients are usually admitted in ICU and need a longer ICU stay.^{14,17} As critical patients are usually admitted in ICU and need a longer ICU stay. Another study done by Ayush Kumar et al., reported that patients showed greater mortality rates (15.9%) within a month of discharge from the hospital.^{18,19} Thus, the impact of delirium, even when reversed or managed in the ICU seemed to impact post discharge outcomes of patients. The reason for this findings have shown that physicians usually have poor knowledge about delirium that was often missed and remained untreated and was not given as much importance as other organ dysfunction.

Our study showed that the mortality rate was higher in hypoactive delirium (85.7%) followed by hyperactive delirium (30%) and mixed delirium (25%). Studies done by Krewulak et al., and Indian studies have shown that hypoactive delirium was associated with higher mortality which resembles with our study.^{13,14,18} The cause of higher mortality in hypoactive delirium might be due to difficulty in early recognition of hypoactive delirium which leads to delayed treatment strategies. Besides hypoactive delirium was frequently dismissed as depression and dementia leading to different choice of medication ending up with worsening of medical condition.

In the present study the length of ICU stay was greater with hypoactive delirium (13 days) followed by hyperactive delirium (ten days) and with mixed delirium (nine days). The association was statistically significant as p value was <0.05. In contrast study conducted by Shirkey et al., found a significantly longer ICU stay for patients with hyperactive/mixed delirium (11 days) compared to patients with hypoactive delirium (five days).²⁰ Another study reported that patients with mixed delirium had a significantly longer median length of ICU stay (nine days) compared to patients with hypoactive delirium (five days) and patients with hyperactive delirium (three days).²¹ These inconsistent findings in length of ICU stay in pattern of delirium might be due lack of an appropriate standardized tool for assessment of delirium and under recognition of hypoactive delirium due to which patient were missed and remained untreated. Along with that hypoactive delirium was mistaken with depression and frequent prescription of antidepressant drugs to patient which prolonged ICU stay.

Our study showed the etiology of delirium broadly divided into three categories as diagnosis based on system, risk factors and number of drugs used. It included risk factors as others (anemia, fever, pancytopenia), deranged renal function test, electrolyte imbalance, acid base imbalance, deranged liver function test, diagnosis involving various system like CNS, renal, respiratory, gastrointestinal, CTVS and use of more than three drugs. Such risk factors were not statistically significant with pattern of delirium. Earlier studies have reported fever, infections, anemia, azotemia, elevated hepatic enzymes, hyperbilirubinemia, hypertension, hypocalcemia, hyponatremia, hypotension, morphine use, etc., with development of delirium in ICU patients.^{22,23} Another study done by Ayush Kumar et al, showed that increased bilirubin, increased creatinine, fever, mechanical ventilation, hypoxia and benzodiazepine use were significantly associated with ICU delirium.¹⁸ These differences possibly reflects the differences in various types of ICU set ups studied (medical versus surgical) and patient selection practices. This may also be due to inconsistent reporting of risk factors and outcomes between studies and variation in statistical models used to analyze the data.

Age and delirium

Our study showed majority of study population who had delirium falls in age group between 70-79 years (20.7%) and mean age of study population was 55.92 which was similar to the study conducted by Meagher et al. and

Maldonado and colleagues.²⁴ Similar result done in Nepal reported patients aged above 65 were more predisposed to develop delirium.²⁵ This may be due to the facts that elderly patients were more vulnerable so, any precipitating factors or noxious might precipitate delirium.

Gender and delirium

In the current study, 60.9% were males while 39.1% were female and similar study of male preponderance in delirium were found by Sharma et al. and Bhattarai et al.^{14,25}

Our study showed that majority of the participants were married (73.9%) as compared to unmarried. In another study too married participants developed delirium more than unmarried.²⁶

Our study showed that majority of participants were unemployed 39(42.2%) and minority were semi-skilled worker two (2.2%). Study by Franco et al, showed 50 % were homemaker, 20.59 were unemployed and 26 % were retired and disabled.²⁷ Older age group (more than 65 years) were most commonly predisposed to delirium so majority of them were unemployed or retired.

In present study, 32.6% were illiterate, 29.3% achieved primary level education, 18.5% achieved higher secondary, 18.5% achieved university and secondary level education. Two studies have identified educational attainment as an important risk factor for delirium. Galanakis et al. and Pompei et al. identified low education as a risk factor and found that patients with delirium were less likely than those without delirium to have completed some education beyond the 12th grade (22% vs 30%).^{28,29} This effect was statistically significant. By contrast, at least three previous studies have failed to demonstrate a significant effect of education on the risk of delirium.³⁰ Low education level identified as risk factor for delirium which was in concordance with cognitive reserve hypothesis, which assumed that education would protect against delirium.

CONCLUSIONS

The study underscores the prevalence of hyperactive delirium as the predominant pattern in MICU settings. However, it is crucial to highlight the significance of hypoactive delirium due to its poor treatment response and prolonged ICU stays compared to other forms. Comprehensive understanding of delirium's prevalence, risk factors, patterns, and outcomes is imperative for healthcare providers.

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