Prevalence, risk factors and outcome of delirium in intensive care unit

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Abstract

Introduction: Delirium causes serious in-hospital morbidity.

Aims: Prevalence, risk factors and outcome of delirium were studied in a medical ICU.

Materials and Methods: This prospective study in the medical ICU identified delirium by CAM (Confusion Assessment Method). Comorbidities were assessed by Charlson Comorbidity Index. Socio-demographics, clinical parameters and outcome required a structured questionnaire. Data was analyzed using chi- square test, Pearson correlation and independent sample t test.

Results: Of 467 patients assessed, 101satisfied CAM diagnosis of delirium (prevalence-21.6%). Females predominated (51.5%); average age was 59.6 years. Acute exacerbation of chronic obstructive pulmonary disease (COPD) was the most common illness, diabetes mellitus (58.4%) followed by hypertension (17.8%) the most common co-morbidities. Leukocytosis, raised serum creatinine and abnormal EEG were observed. 77.2% had nasogastric feeding, 22.8% needed ventilator support.76.2% of patients were on some medication. Delirium was hyperactive in 78.2%, idiopathic in 38.6%. Hypoactive delirium, the least common, was associated with acute pulmonary oedema and sepsis (51.3%). (p=0.009). Delirium resolved completely in 80.2%. Mortality rate was 13.9%. 78.6% patients died within 72 hours (p=0.008); death was increased in those with respiratory findings (p=0.01) and ventilator (p<0.001).

Conclusion: A high prevalence of delirium was found in the Medical ICU. This was mostly hyperactive and idiopathic. Hypoactive delirium, the least common, was found associated with acute pulmonary oedema, sepsis. Acute exacerbation of COPD was the most common cause. Those with respiratory findings and on ventilator had higher mortality.

Keywords: Delirium, Intensive care, Hypoactive delirium, Ventilator, Mortality.

Introduction

Delirium is defined as an acute disorder of attention and cognition that poses a common and serious health problem for hospitalized patients.[1] It is characterized by a reduced ability to focus, sustain or shift attention, disorganized thinking or altered level in consciousness. Estimates of the incidence of delirium have ranged from 25% to 60% with case fatality rates from 25% to 33%.[1] Development of delirium within the hospital is associated with increased morbidity, closer nursing surveillance, higher hospital costs, longer stay in hospital and increased need for post-discharge care.[2] Levkoff and co-workers estimated that if the length of stay for each acutely confused elderly hospitalized patient was reduced, the health care cost could be brought down.[3] The clinical importance of delirium has been overlooked for want of adequate studies on the subject, lack of uniform diagnostic criteria and due to nonspecific presentations of delirium. It was estimated that up to 32% of cases went unrecognized by physicians.[4] Delirium was often mistaken for depression or psychosis or misinterpreted as dementia or senescence.[4]

In ICU patients, delirium is associated with multiple complications and adverse outcomes including removal of catheters,[5] self extubation, failed extubation,[6] prolonged hospital stay,[7] increased health care cost[8] and increased mortality.[9-11] Delirium may be a predictor of long term cognitive impairment in survivors of critical illness. A study by Jackson and colleagues[12] reported that delirium was associated with cognitive decline over 1-3 years after hospital discharge.

Despite its clinical importance, few studies have looked at the prevalence of delirium in medical intensive care. Lack of standardized assessment tools led to large variations in estimates of prevalence. Several protocols have been in use for identifying dementia, but few were validated for use in delirium till Sharon K. Inouye et al[1] from the University of Chicago School of Medicine devised a Confusion Assessment Method (CAM) to enable non-psychiatrically trained clinicians to identify delirium quickly and accurately in clinical and research settings. Many studies have looked individually at-risk factors, etiology, outcome and mortality of delirium in the general hospital, ward and ICU but none comprehensively examined these variables in an intensive care setting.

The current study was designed to estimate the prevalence, risk factors, co-morbidities, precipitants, course, outcome and mortality of delirium in the medical ICU in a comprehensive manner.

Materials and Methods

This study was performed on in-patients of the medical intensive care unit of a tertiary care hospital. It was approved by the Ethics Committee of the institute. All patients were recruited after obtaining proper

informed consent. Consecutive ICU patients above 18 years of age whose relatives had given written informed consent, with recent onset of fluctuating consciousness and who satisfied the CAM- ICU score was included in the study.[13] Patients with dementia, traumatic brain injury, mental retardation and other organic causes of cognitive impairment were excluded. Socio-demographic and clinical data was recorded using a semi-structured questionnaire designed for the study. The Charlson Comorbidity Index,[14] which represents the sum of a weighted index that takes into account the number and seriousness of pre-existing co-morbid conditions, was used to assess the role of co-morbidities. All ICU patients were screened and diagnosed using the CAM-ICU scale. Medical causes were excluded by routine tests, CBC, ESR, blood sugar, blood urea, serum creatinine, electrolytes, liver function tests, routine urinalysis, ECG, chest radiograph and EEG. Where indicated, specific investigations like peripheral blood smear, CSF examination, thyroid function and antibodies, ANA and imaging (USG, CT, MRI) were done.

All patients were followed up till delirium subsided or until shifted out of ICU. The data represented as categorical and continuous variables were further analyzed via chi-square test, pearson correlation, independent sample t test; analysis was done using SPSS version 16.

Results

467 patients were included in the study after informed consent. Of these 101 patients (21.6%) satisfied the CAM-ICU diagnosis of delirium. The socio-demographic data of our patients showed that more females (51.5%) developed delirium than males (48.5%). The average age of our population was 59.6 years (SD=18.3). The duration of ICU stay ranged between 24-192 hours, mean duration of ICU stay being 79.6 hours. The most common co-morbidity was diabetes mellitus (58.4%) followed by hypertension (17.8%). No co-morbidities were detected in15.8%. While most of the patients had no addictions (68.3%), smoking was the most prevalent addiction observed (29.7%). The majority of patients (76.2%) were on medication; of these, most were on oral anti-diabetics or insulin (56.4%).

In those with delirium, respiratory findings were found in 45.5%, followed by gastrointestinal in 14.9%; 34.7% patients had no abnormal findings on clinical examination. The majority of patients with delirium (61.4%) had no abnormality in investigation results, but16.8% had leukocytosis and 11.9% had elevated serum creatinine; 10.8% had EEG abnormalities, the most common being occasional generalized slowing followed by triphasic waves. The most common primary diagnosis among patients with delirium was acute exacerbation of chronic obstructive pulmonary disease (19.8%) followed by chronic kidney disease (CKD) with associated acute pulmonary oedema (11.9%). In 38.6% patients, no diagnosis was reached during their period of ICU stay. (Fig. 1) 77.2% of our delirious patients were on nasogastric tube feeding, 22.8% needed ventilator support. Among the precipitating factors in the ICU, nasogastric tube (in 77.2%) was the commonest precipitant associated.

The most common type of delirium observed was the hyperactive type (78. 2%). Hypo-active delirium was found in 21.8% cases- these were most commonly associated with acute pulmonary oedema (100%) and sepsis (51.3%). ($\chi 2$= 20.03, d.f. =8, p=0.009). No cases of mixed delirium were identified.

The mortality rate among the patients with delirium in ICU was 13.9%. Delirium resolved in 80.2% of the patients during their period of ICU stay, while 5.9% continued to be delirious even after 192 hours of ICU stay. The average duration of ICU stay was 79.6 hours (SD=35.7). (Table 1)

The mortality among patients with delirium in ICU was maximal within the first 72 hours of ICU stay, 78.6% of patients dying within this time period. ($\chi 2$= 15.67, d.f. =5, p=0.008). In terms of duration of stay in the ICU in hours, those who expired had a stay duration of 58.3 hours (SD=32.2), while those who survived stayed for 83.03 hours (S.D. =58.2). (t= 2.46, p=0.01) on the average. Of the 14 patients who expired, 12 (85.71%) had respiratory findings. ($\chi 2$= 10.12, d.f. =3, p=0.01). Ventilator stay was associated with significant mortality: around 85.71% of those who died were on ventilator support. ($\chi 2$= 45.39, p<0.001) (Table 1)

There was a higher rate of mortality among males (20.4%) than females (7.69%) but this fell slightly short of statistical significance ($\chi 2$=3.41, p=0.059). Age was higher in those who expired (60.2 years) with respect to survivors (59.6 years) but was not statistically significant (p=0.89). There was no significant association between mortality and variables like co-morbidity, medication use, type of delirium, and medical diagnosis. (Table 1)

Table 1: Association of variables with delirium mortality

Variable	Distribution	Test Value	Significance
Sex	Cured= F:M= 55.2%: 44.8% Expired= F:M= 28.6% :71.4%	X^2=3.41 d.f.= 1	P=0.059
Medical Co-morbidity	Cured= Yes: No=83.9%: 16.1% Expired= Yes: No = 85.7%: 14.3%	X^2=1.56 d.f.=2	P= 0.98
Addiction	Cured= Yes: No=29.9%: 70.1%	X^2=1.52	P=0.57

	Expired= Yes: No = 43.9%: 57.1%	d.f.=3	
Drugs	Cured= Yes: No=77.1%: 22.9% Expired= Yes: No = 71.5%: 28.5%	X^2=0.49 d.f.=1	P=0.91
Respiratory Findings	Cured= Yes: No= 39.1%: 60.9% Expired= Yes: No = 85.7%: 28.5%	X^2=10.92 d.f.=3	P=0.012
Ventilator Stay	Cured= Yes: No= 88.5%: 11.5% Expired= Yes: No = 92.8%: 7.2%	X^2=45.4 d.f.=1	P<0.001
Abnormal Investigations	Cured= Yes: No= 39.1%: 60.9% Expired= Yes: No = 64.2%: 35.8%	X^2=3.26 d.f.=6	P=0.77
Primary Diagnosis	Cured= Yes: No= 59.8%: 40.2% Expired= Yes: No = 64.2%: 35.8%	X^2=9.46 d.f.=8	P=0.31
Type of Delirium	Cured= Hyperactive: Hypoactive= 79.4%: 20.6% Expired= Hyperactive: Hypoactive = 71.5%: 28.5%	X^2=0.44 d.f.=1	P=0.36
Age	Cured= 59.6 years Expired= 60.21 years	T= -0.14 d. f.= 99	P=0.91
Charlson Co-morbidity Score	Cured= 3.21 Expired= 3.92	T= -1.45 d. f.= 99	P=0.15
ICU Stay (in hours)	Cured= 83.03 Expired= 58.2	T= 2.46 d. f.= 99	P=0.015

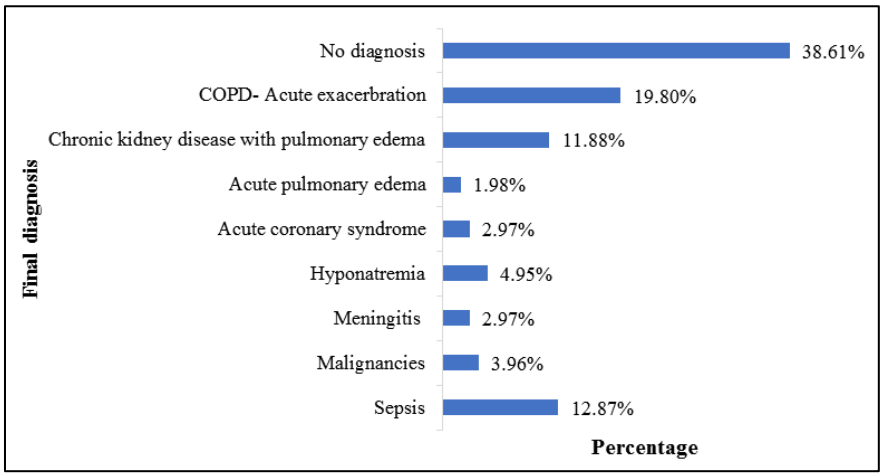

Fig. 1: Diagnostic distribution in delirium

Discussion

The prevalence of delirium in this study was 21.6%, comparable to the prospective studies done by Francis et al[15] by Bart Von Rompaey et al [16] who found the prevalence of delirium to be 30%. A prospective study by Aldemir et al[17] found the prevalence of delirium to be 11% in the ICU. Across studies, it was found that the prevalence of delirium in ICU cohorts varied from 20 to 80%.[1,15-17] This discrepancy may reflect differences in patient characteristics, interpretation of delirium, the screening instrument and its application, local sedation practices, and the confounding influence of medication-associated coma.[5]

The mean age of our study sample was 59.69±18.38 years, with a range of 17 years to 94 years. The prevalence rate of our study was in accordance with that of Von Rompaey et al [16] which showed the mean age was 64 years with an age range of 19 to 90 years similar to that reported in an earlier study (64.5± 14.1 years).[5]

There were more females (51.5%) in our study group. Our results were not in concordance with that by Von Rompaey et al which showed the prevalence to be more in males (59%). The male sex was said to be a risk factor for delirium in the general population,[16] However studies in ICU population including ours have echoed discordant prevalence rates. Larger trials are necessary to elucidate the true gender prevalence in this population.

Among the co-morbidities, 58.4% of our patients had diabetes mellitus, 17.8% had hypertension and 15.8% had no co-morbidities, in accordance with earlier studies.[5,17]

The most common primary diagnosis among our patients with delirium was acute exacerbation of chronic obstructive pulmonary disease (19.8%) followed by CKD with acute pulmonary oedema

(11.9%). No diagnosis was reached during the period of ICU stay in 38.6% of our patients. This is in accordance with earlier studies which noted that infections were associated with delirium and that idiopathic delirium was seen in 30-50% patients.[5, 17]

The most common type of delirium observed was the hyperactive type (78.2%) as reported in earlier studies.[1,5,17] The remaining (21.8%) had hypoactive delirium. Acute pulmonary oedema and sepsis had a significant association with hypoactive delirium this finding has not been not reported previously and merits further study.

Among the precipitating factors in the ICU, nasogastric tube was the commonest association. This is in accordance with a standard study done in ICU patients.[18] Mustafa et al also showed an association with nasogastric tube with an odds ratio 7.8.[19]

The mortality rate among our patients with delirium in ICU was 13.9%, in concordance with the rate of 19% reported by a study on 558 patients with delirium.[20] We found that mortality was related to abnormal respiratory findings. However, this finding has never been reported previously and further studies have to be done to ascertain this association.

We found the duration of ICU stay ranged between 24-192 hours with a mean duration of 79.6 hours, similar to findings in earlier studies which showed there was an association of delirium with increased ICU stay.[1,5,17,18] A significant association was also seen between mortality and ICU stay duration. The mortality was more within the first 72 hours of ICU stay with 78.6% of the patients dying within this time frame. This finding was reflected in a study that delirium in the ICU was independently associated with fewer median days alive.[21] Ventilator stay was also associated with significant mortality; around 85.71% of patients who died were on ventilator support. Mechanical ventilation in delirium has been found to be a risk factor for mortality in a prospective attributable mortality study.[21] There was a higher but non-significant rate of mortality among males than females in our study. There was no significant association between mortality and variables like co-morbidity, medication use, type of delirium, and medical diagnosis. Age though higher in those who expired with respect to survivors in our study was not statistically significant. These factors have to be studied further as studies have yielded discordant results in terms of age, and sex.[11,13,16]

The type of delirium and co-morbidities had no significant association. This echoes the observation that though co-morbidities predispose a patient to delirium, they do not influence the type of delirium.[13] No significant association was found between diagnosis at admission and outcome of delirium. Similar findings were reported by an earlier study which looked into outcome of delirium including mortality.[22] The type of delirium also had no significant association with the outcome of disease, as 86.1% cases were cured. This was as reported in another study on delirium.[22]

This study had an adequate sample size, had used standardized tools; patients had been followed up till their discharge from the ICU.

The limitation of our study was that all patients could not be followed up till their delirium subsided; also, we did not rate the delirium.

Conclusion

This study clearly elucidates the prevalence, risk factors, types and outcome of delirium. Delirium was more in females and associated with precipitants like nasogastric tube. The study showed a significant association of acute pulmonary oedema and sepsis with hypoactive delirium. We found that mortality in delirium was associated with respiratory involvement, duration of ICU stay and mechanical ventilation. Therefore, proper identification of pre-disposing factors, thorough clinical examination, necessary investigations and supportive care can reduce the morbidity and mortality due to delirium.

References

1. Inouye SK, van Dyek CH, Alessi CA, Balkin S, Seigal AP, Horwitz RI. Clarifying Confusion: The Confusion Assessment Method. *Ann Intern Med* 1990;113:941-8.
2. BhatRS, Rockwood K. The prognosis of delirium. Psychogeriatrics 2002;2:165-79.
3. LevkoffSE, Besdine RW, Wetle T. Acute confusional states (delirium) in the hospitalized elderly. *Annu Rev Gerontol Geriatr* 1986;6:1-26.
4. Francis J, Strong S, Martin D, Kapoor W. Delirium in elderly general medical patients: common but often unrecognised (Abstract). *Clin Res* 1988;36:711.
5. Ouimet S, Kavanagh BP, Gottfried SB, Skrobik Y. Incidence, risk factors and consequences of ICU delirium. *Intensive Care Med* 2007;33:66-73.
6. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. *Crit Care Med* 1985;13:818-29.
7. Lacasse H, Perreault MM, Williamson DR. Systematic review of antipsychotics for the treatment of hospital-associated delirium in medically or surgically ill patients. *Ann Pharmacother* 2006;40:1966-73.
8. Miranda DR, de Rijk A, Schaufeli W. Simplified Therapeutic Intervention Scoring System: The TISS-28 items--Results from a multicenter study. *Crit Care Med* 1996;24:64-73.
9. Van Eijk MMJ, Kesecioglu J, Slooter AJ. Intensive care delirium monitoring and standardised treatment: a complete survey of Dutch intensive care units. *Intensive Crit Care Nurs* 2008;24:218-21.
10. World Health Organization: Prevalence of current tobacco use among adults. 2005 [http://www.who.int/whosis/data/ Search.jsp]. WHO Statistical Information System (WHOSIS).
11. Cole MG. Delirium in elderly patients. *Am J Geriatr Psychiatry* 2004;12:7-21.
12. Inouye SK, Charpentier PA. Precipitating factors for delirium inhospitalized elderly persons. Predictive model and interrelationship with baseline vulnerability. *JAMA* 1996;275: 852-7.

13. Inouye SK. Delirium in older persons. *NEngl JMed* 2006;354:1157-65.
14. Santos DV, Eleazar J. Delirium in Elderly-A silent cry for help. *Phil J. Internal Medicine* 2000;38:192-6.
15. Francis J, Martin D, Kapoor WN. A prospective study of delirium in hospitalized elderly. *JAMA* 1990;263:1097-101.
16. Bart Van Rompaey, Monique M Elseviers, Marieke J Schuurmans, Bart Van Rompaey, Monique M Elseviers, Marieke J Schuurmans. Risk factors of delirium in intensive care unit patients: a prospective cohort study. *Crit Care* 2009;13:R77.
17. Aldemir M, Ozen S, Kara IH, Sir A, Baç B. Predisposing factors for delirium in the surgical intensive care unit. *Crit care* 2001;5:265-70.
18. Timothy DG, Pandharipande PP, Ely EW. Delirium in intensive care unit. *Crit Care* 2008;12:S3.
19. Liptzin B, Levkoff SE. An empirical study of delirium subtypes. *Br J Psychiatry* 1992; 161:843-5.
20. Klein Klouwenberg PMC, Zaal IJ, Cristian S, Ong David S Y, van der Kooi Arendina W, Bonten Marc J M et al. The attributable mortality of delirium in critically ill patients: prospective cohort study. *BMJ* 2014;349:g6652.
21. Ely E, Shintani A, Truman B, Theodore S, Gordon SM, Harrel FE, et al. Delirium as a Predictor of Mortality in Mechanically Ventilated Patients in the Intensive Care Unit. *JAMA* 2004;291:1753-62.
22. Al-Qadheeb NS, Balk EM, Fraser GL, Skrobik Y, Rike RR, Kress JP, et al. Randomized ICU trials do not demonstrate an association between interventions that reduce delirium duration and short-term mortality: a systematic review and meta-analysis. *Crit Care Med* 2014;42:1442-54.