

Correlates & Risk factors for ICU delirium

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Abstract:

Background: Delirium is a disturbance in attention awareness which develops in short period of time & fluctuate in severity. Its associated with functional disability, cognitive impairment, dementia & death in ICU inpatients.

Objective: To Study the incidence & risk factors of delirium in intensive care unit (ICU) patients .

Method: In an observational, non-interventional study, 486 ICU patients were assessed in a tertiary care center for delirium. 163 patients had a Richmond Agitation Sedation Scale value (RASS) ≤ -3 were excluded from the study. Remaining, 323 subjects were evaluated for delirium using CAM-ICU (Confusion Assessment Method for ICU). Apart from socio-demographic profile, admission details, clinical profiles, use of invasive mechanical ventilation, invasive devices & medication were examined. SPSS version 14.0 was used for statistical analysis.

Results: Among 323 subjects evaluated by CAM-ICU, 31 (9.6%) patients had delirium. Medical causes being most common reason for ICU admission & sepsis being the commonest medical ailment. Use of Invasive mechanical ventilation, central vein catheter, arterial catheter, urinary catheter & midazolam use; significantly increased risk of delirium. Prolonged ICU (5 vs 3) and hospital (10 vs 6) length of stay (LOS) was associated with delirium.

Conclusion: One in every ten patients admitted to an intensive care unit develop delirium, which is postulated to be associated with poor prognosis, cognitive impairment & mortality risk. Burden of delirium can be reduced by controlling for several modifiable risk factors.

Keywords: Correlates, Delirium, ICU, Risk factors

I. Introduction

The word delirium is derived from Latin, meaning "off the track". The DSM 5 revised diagnostic criteria for Delirium, defined it as a (a) Disturbance in attention awareness (b) which develops in short period of time & fluctuate in severity (c) additional disturbance in cognition (d) not explained by a pre-existing neurocognitive or severely reduced arousal such as coma (e) as a direct physiological consequence of another medical condition substance intoxication or withdrawal or exposure to a toxin, or is due to multiple etiologies.

Delirium has been linked to adverse short term outcomes, including up to threefold increases hospital mortality^[1,2,3] which place considerable burdens on caregivers^[4,5] and healthcare services.^[6,7] Delirium can also have long term consequences, with studies indicating an association between delirium and a higher likelihood of death,^[8] functional disability,^[9] admission to residential care, cognitive impairment,^[10] and dementia after discharge.^[11] The risk of delirium is particularly high in selected subsets of hospital patients such as elderly people and those with pre-existing cognitive impairments,^[12] people with terminal illnesses,^[13] patients undergoing major surgery,^[14] and those who are admitted to an intensive care unit.^[15]

Delirium often goes unrecognized by clinicians as being considered as an expected, inconsequential complication of critical illness. The common risk factors for under-recognition being hypoactive delirium; advanced age, vision impairment and dementia^[16]. Despite prognostic significance, Indian literature on ICU delirium is limited, this is an effort to study incidence, risk factors for delirium in a tertiary care center in Northern India.

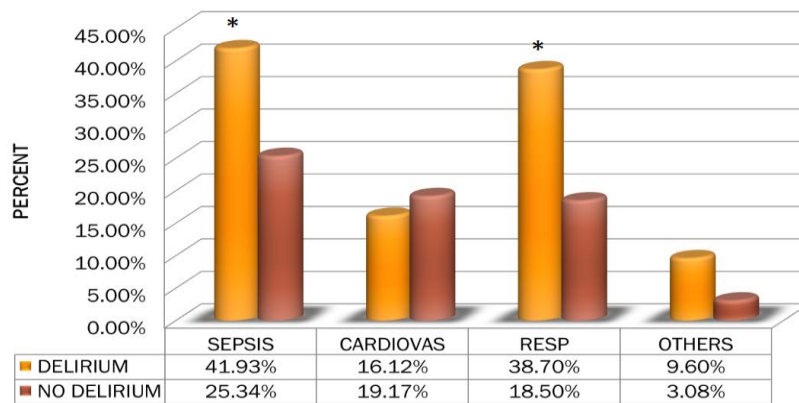
II. Method

In an observational study, at Mahatma Gandhi Medical College & Hospital, Jaipur, 486 patients (≥ 18 years), admitted in ICU (at least one day) were evaluated with Richmond Agitation Sedation Scale to assess the patients eligibility for Confusion Assessment Method for ICU (CAM ICU), which is recommended tool for routine monitoring of delirium in adult ICU patients by American College of Critical Care Medicine (ACCM) & Society of Critical Care Medicine (SCCM). Schedules for Clinical Assessment in Neuropsychiatry (SCAN) was applied for neuropsychiatric diagnosis. Admission details, use of invasive mechanical ventilation, invasive devices & sedation use was evaluated. SPSS version 14.0 was used for descriptive & analytical, statistical analysis.

III. Results

Among a total of 486 patients in ICU assessed, 163 (34%) were found to be sedated with a RASS score ≤ -3 . These patients could not be evaluated using CAM-ICU & were excluded from the study. Remaining 323 subjects were evaluated for delirium using CAM-ICU. 31 (9.6%) patients had a positive CAM ICU score for delirium. 69% patients were admitted for medical causes and remaining 31% for surgical. Sepsis was the commonest medical reason for admission in ICU, followed by cardiovascular and respiratory causes. Sepsis & respiratory disorders were significant correlated with delirium ($p < 0.05$) (Figure 1).

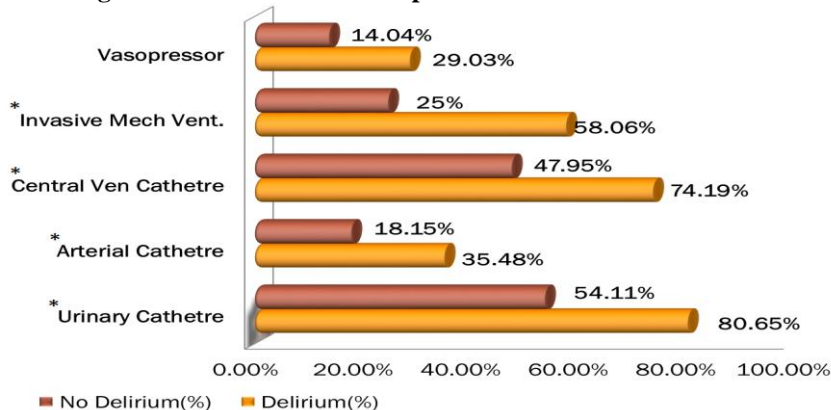
Figure 1: Reason for ICU Admission: Comparison of Delirium & No Delirium study groups



* $p < 0.05$

The use of Invasive mechanical ventilation, central vein catheter, arterial catheter & urinary catheter; significantly increased risk of delirium ($p < 0.05$) (Figure 2).

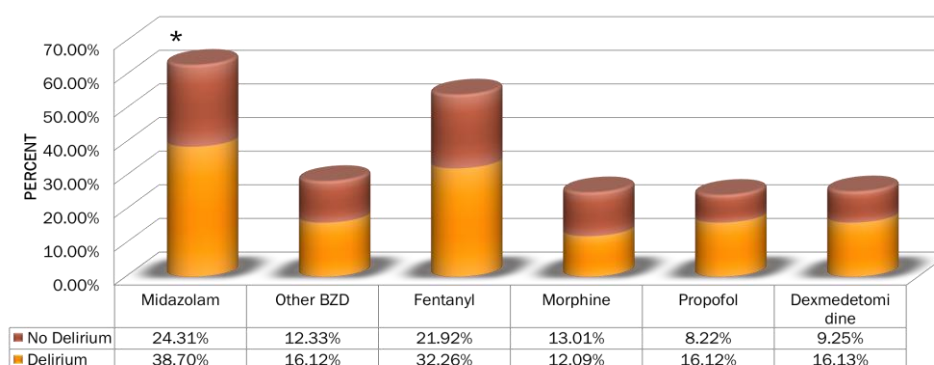
Figure 2: Association of therapeutic interventions with delirium



* $p < 0.05$

Use of sedatives is a common practice, especially in hyperactive form of delirium. Midazolam use was correlated with higher incidences of delirium in ICU in our study (Figure 3).

Figure 3: Association of Sedative used with Delirium



* p<0.05

Table 1: Comparing Length of Stay (LOS) in patients with Delirium & with No delirium

	DELIRIUM (DAYS)	NO DELIRIUM (DAYS)	P VALUE
ICU LOS, Median days	5(3-11)	3(2-5)	<0.001
HOSPITAL LOS	10(6-20)	6(3-11)	<0.001

ICU, intensive care unit; LOS, length of stay

ICU Length of Stay (LOS) & Hospital LOS were significantly higher in patients with delirium ($p<0.001$), implying significant raised financial burden on patients (Table 1).

IV. Discussion

In our study 9.6% of subjects suffered from delirium. Several Studies have reported similar incidence ranging between 11–31%^[17-20]. Approximately 70% of delirium cases are missed clinically in practice, when compared to use of a standardized screening tool such as the Confusion Assessment Method for the ICU (CAM-ICU). The CAM-ICU is a validated delirium screening tool, which can be applied in few minutes and with minimal training.

In our study, midazolam use was significantly associated with delirium. Hypoactive delirium has been attributed to cause outcomes such as reintubation, increased susceptibility to nosocomial pneumonia with aspiration, pulmonary embolism, decubitus ulcers related to immobility. Whereas, hyperactive delirium is responsible for risk of self-extubation, pulling of central lines and other invasive catheters, causing self-harm. These hyperactive variety of patients are often given higher doses of sedatives that may prolong the duration of mechanical ventilation and leave them in a state of prolonged cognitive dysfunction^[21]. Prolonged ICU (5 vs 3) and hospital (10 vs 6) length of stay (LOS), was found in patients with delirium in our study. Several other studies show similar results^[1,22].

Delirium is considered as a response of the central nervous system to any systemic inflammation in body^[23]. Several factors associated with systemic inflammation like cytokine cascade, imbalance between the excitatory dopaminergic neurotransmitters and the inhibitory GABA and cholinergic system are postulated to be responsible for delirium. GABA agonists like benzodiazepines are known to cause impaired cognitive function and delirium^[24,25,26]. The altered pharmacokinetics of several sedatives and analgesics in ICU patients, especially in the older patients, makes the responses difficult to predict.^[27] Dexmedetomidine, an alpha agonist, produced significantly less delirium than GABA agonists like propofol or midazolam^[28]. Inhibition of acetylcholine (anticholinergic drugs), which normally inhibits pro-inflammatory cytokine release; may also trigger a CNS inflammatory response.

Our study suggests that, mechanical ventilation increases the risk of delirium. Several studies have found similar results. Studies also suggest that increasing age and severity of illness too increase the risk for delirium manifold.^[29,30]

The Society of Critical Care Medicine (SCCM) recommends monitoring of level of sedation and for delirium in all critically ill patients^[31]. Care must be taken for early titration of sedatives, early mobilization and maintenance of sleep-wake cycles. Delirium should be monitored for and once diagnosed management should focus on identifying precipitating factors, providing supportive care and preventing further complications.^[32] Once life-threatening complications such as metabolic derangements, hypoxemia, organ hypoperfusion and

severe pain and infection have been excluded, patient's medications and environment should be analysed in an attempt to remove any factor that might exacerbate delirium.^[23]

V. Conclusion

ICU patients should be actively screened for delirium. Identification of its risk factor, potential preventive measures, and timely management is critical. Early removal of invasive devices & titration of sedation should be emphasised.

References

- [1]. Ely EW, Shintani A, Truman B, et al. Delirium as a predictor of mortality in mechanically ventilated patients in the intensive care unit. *JAMA*2004;291:1753-62.
- [2]. Lin S, Liu C, Wang C, et al. The impact of delirium on the survival of mechanically ventilated patients. *Crit Care Med*2004;32:2254-59.
- [3]. Pompei P, Foreman M, Rudberg MA, et al. Delirium in hospitalized older persons: outcomes and predictors. *J Am Geriatr Soc*1994;42:809-15.
- [4]. Buss MK, Vanderwerker LC, Inouye SK, et al. Associations between caregiver-perceived delirium in patients with cancer and generalized anxiety in their caregivers. *J Palliat Med*2007;10:1083-92.
- [5]. Shankar KN, Hirschman KB, Hanlon AL, et al. Burden in caregivers of cognitively impaired elderly adults at time of hospitalization: a cross-sectional analysis. *J Am Geriatr Soc*2014;62:276-84.
- [6]. Milbrandt EB, Deppen S, Harrison PL, et al. Costs associated with delirium in mechanically ventilated patients. *Crit Care Med*2004;32:955-62.
- [7]. Leslie DL, Marcantonio ER, Zhang Y, et al. One-year health care costs associated with delirium in the elderly population. *Arch Intern Med*2008;168:27-32.
- [8]. Pisani MA, Kong SY, Kasl SV, et al. Days of delirium are associated with 1-year mortality in an older intensive care unit population. *Am J Respir Crit Care Med*2009;180:1092-7.
- [9]. O'Keefe S, Lavan J. The prognostic significance of delirium in older hospital patients. *J Am Geriatr Soc*1997;45:174-8.
- [10]. Pandharipande PP, Girard TD, Jackson JC, et al. Long-term cognitive impairment after critical illness. *N Engl J Med*2013;369:1306-16.
- [11]. Witlox J, Eurelings LS, de Jonghe JF, et al. Delirium in elderly patients and the risk of postdischarge mortality, institutionalization, and dementia: a meta-analysis. *JAMA*2010;304:443-51.
- [12]. Levkoff SE, Evans DA, Liptzin B, et al. Delirium. The occurrence and persistence of symptoms among elderly hospitalized patients. *Arch Intern Med*1992;152:334-40.
- [13]. Lawlor PG, Gagnon B, Mancini IL, et al. Occurrence, causes, and outcome of delirium in patients with advanced cancer: a prospective study. *Arch Intern Med*2000;160:786-94.
- [14]. Balas MC, Happ MB, Yang W, et al. Outcomes associated with delirium in older patients in surgical ICUs. *Chest*2009;135:18-25.
- [15]. Ely EW, Inouye SK, Bernard GR, et al. Delirium in mechanically ventilated patients: validity and reliability of the confusion assessment method for the intensive care unit (CAM-ICU). *JAMA*2001;286:2703-10.
- [16]. Inouye, S.K., Foreman, M.D., Mion, L.C. et al. Nurses' recognition of delirium and its symptoms: comparison of nurse and researcher ratings. *Arch Intern Med.* 2001; 161:2467-2473.
- [17]. Aldemir M, Ozen S, Kara IH, Sir A, Bac B (2001) Predisposing factors for delirium in the surgical intensive care unit. *Crit Care* 5:265-270
- [18]. Kishi Y, Iwasaki Y, Takezawa K, Kurosawa H, Endo S (1995) Delirium in critical care unit patients admitted through an emergency room. *Gen Hosp Psychiatry* 17:371-379
- [19]. Lin SM, Liu CY, Wang CH, Lin HC, Huang CD, Huang PY, Fang YF, Shieh MH, Kuo HP (2004) The impact of delirium on the survival of mechanically ventilated patients. *Crit Care Med* 32:2254-2259
- [20]. McNicoll L, Pisani MA, Zhang Y, Ely EW, Siegel MD, Inouye SK (2003) Delirium in the intensive care unit: occurrence and clinical course in older patients. *J Am Geriatr Soc* 51:591-598
- [21]. Ely EW. In: Vincent JL, editor. *Yearbook of Intensive Care and Emergency Medicine*. Springer-Verlag: Berlin; 2005. p. 721-34.
- [22]. Salluh JJ, Soares M, Teles JM, Ceraso D, Raimondi N, Nava VS, Blasquez P, Ugarte S, Ibanez-Guzman C, Centeno JV, Laca M. Delirium epidemiology in critical care (DECCA): an international study. *Crit Care.* 2010 Nov 23;14(6):R210.
- [23]. Meyer NJ, Hall JB. Brain dysfunction in critically ill patients – the intensive care unit and beyond. *Critical Care* 2006;10:223.
- [24]. Dubois MJ, Bergeron N, Dumont M, Dial S, Skrobik Y. Delirium in an intensive care unit: A study of risk factors. *Intensive Care Med* 2001;27:1297-304.
- [25]. Pandharipande P, Shintani A, Peterson J, Pun BT, Wilkinson GR, Dittus RS, et al. Lorazepam is an independent risk factor for transitioning to delirium in intensive care unit patients. *Anesthesiology* 2006;104:21-6.
- [26]. Marcantonio ER, Juarez G, Goldman L, Mangione CM, Ludwig LE, Lind L, et al. The relationship of postoperative delirium with psychoactive medications. *JAMA* 1994;272:1518-22.
- [27]. EW. In: Vincent JL, editor. *Yearbook of Intensive Care and Emergency Medicine*. Springer-Verlag: Berlin; 2005. p. 721-34. Wise MG, Terrell CD. In: Hall JB, Schmidt GA, Wood LD, editors. *Principles of Critical Care* p. 1757-69. 1st ed. McGraw-Hill Inc: New York; 1992
- [28]. Nelson LE, Lu J, Guo T, Saper CB, Franks NP, Maze M. The alpha2-adrenoceptor agonist dexmedetomidine converges on an endogenous sleep-promoting pathway to exert its sedative effects. *Anesthesiology* 2003;98:428-36.
- [29]. Peterson JF, Pun BT, Dittus RS, Thomason JW, Jackson JC, Shintani AK, et al. Delirium and its motoric subtypes: A study of 614 critically ill patients. *J Am Geriatr Soc* 2006;54:479-84.
- [30]. McNicoll L, Pisani MA, Zhang Y, Ely EW, Siegel MD, Inouye SK. Delirium in the intensive care unit: Occurrence and clinical course in older patients. *J Am Geriatr Soc* 2003;51:591-8
- [31]. Jacobi J, Fraser GL, Coursin DB, Riker RR, Fontaine D, Wittbrodt et, et al. Clinical practice guidelines for the sustained use of sedatives and analgesics in the critically ill adult. *Crit Care Med* 2002;30:119-41.
- [32]. Inouye SK. Delirium in older persons. *N Engl J Med* 2006, 354:1157-65