Delirium Incidence and Risk Factors in Adult Critically Ill Patients in Saudi Arabia

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Abstract

Background: Delirium in intensive care units (ICUs) is associated with long ICU stay, long hospital stay and increased costs of treatment. Unfortunately, delirium in ICU is significantly underestimated and overlooked by healthcare providers. Aims: The aim of this study is to determine the incidence and associated risk factors of delirium among critically ill patients in Saudi Arabia. Methods: This is a prospective study. Patients were assessed for delirium using the confusion assessment method for the ICU. Delirium was the independent variable in this study. Results: Fifty-nine patients (17.3%) showed positive delirium at least once compared to 283 patients (82.7%) who did not show positive delirium. Certain factors for delirium found to be significantly correlated with delirium \((P < 0.005)\); including receiving sedation, mode of sedation, receiving mechanical ventilation, resistance to mechanical ventilator, and baseline Glasgow Coma Scale. Conclusion: Delirium occurred in >17% of our ICU patients. More efforts should be directed to consider ICU delirium and to minimize its triggering factors.

Keywords: Delirium, incidence, intensive care unit, risk factors

Introduction

The American Psychiatric Association’s Diagnostic and Statistical Manual, 5th edition (DSM-5) defines delirium as a disturbance of consciousness characterized by acute onset and fluctuating course of inattention accompanied by either a change in cognition or a perceptual disturbance, so that a patient’s ability to receive, process, store, and recall information is impaired. A lot of intensive care unit (ICU) patients (30%–80%) are showing delirium at some point during their stay in ICU. Delirium in ICU was found to be associated with longer ICU stay, longer hospital stay, and increased costs of treatment. Unfortunately, delirium is significantly underestimated and overlooked by healthcare providers. There are many validated tools that have been used to assess delirium in ICU. One of the most common recommend tools is the confusion assessment method for the ICU (CAM-ICU). This tool can help healthcare providers to better estimate and diagnose delirium and recommended to be included in the routine daily assessment of ICU patient. Several factors have been proven to be associated with the risk of delirium. Use of sedation and analgesics is linked to increased delirium. Searching several research databases and to the best of our knowledge, there are only little data regarding delirium among critically ill patients in ICUs of Saudi Arabia and the middle east countries.

Aim of the study

The aim of this study is to determine the incidence and associated risk factors of delirium among critically ill patients in Saudi Arabia.

Methods

This prospective study was carried out between March 2017 and March 2018. A total number of 494 ICU patients who had met the inclusive criteria were assessed independently for delirium by well-trained bedside nurses using valid delirium tool; the CAM-ICU is used as a validated screening tool for delirium.
Inclusion criteria
All ICU patients after 24 h of admission to ICU, older than 14 years old were assessed for delirium using CAM-ICU tool. Exclusion criteria are patients with structural or metabolic neurological deficit (as identified by admission medical diagnosis), patients with unknown baseline mental status and patients who were found to be “Unable to Assess (UTA)” as defined by CAM-ICU, patients who had been readmitted to the ICU after participating in the trial were also excluded after readmission. Informed consent had been obtained from each patient guardian/relative. Study participants were observed for any incidence of delirium over 24 h on a daily basis for 1 week, any single observed delirium incidence was counted as positive delirium. Any repeated delirium incidence for the same patient during the same admission stay was not counted in study incidence.

For all study participants, delirium was the independent variable in this study; positive delirium or negative delirium as evidenced by CAM ICU tool, other factors included in data collection and considered as dependent variables included: patients demographics and variables (i.e., age, gender, admission diagnosis, any sedatives, sedation mode, sedation vacation opportunity, any assisted mechanical ventilation, resistance (asynchrony) to assisted mechanical ventilator, and discharge outcome. This is observational study, so no treatment or specific therapy was given to any patients who were found to have positive delirium. The decision to start any treatment was left for treating physician/s.

The study has been approved by the Institutional Review Board (IRB) (Reference number: H1R1-20-Apr17-01, IRB registration Number with KACST, KSA: H-01-R-053) and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. All authors declare that there is no conflict of interest regarding the publication of this article.

Setting
The research was conducted in the ICU of King Saud Medical City which has 120-bed capacity and provides care for different categories of critically ill patients who need comprehensive stabilization. Averagely, 196 patients are admitted every month. Around 100 patients are receiving care in ICU every day, 50–60 patients on an average are connected to assisted mechanical ventilation (MV) and needs some amount of sedation based on the clinical decision.

Sampling technique
Cohort sampling technique was used for selecting the patients for the study. All newly admitted patients who had been admitted from the 1st day of the month (May–September 2018) and had met the inclusive criteria were recruited for the study.

Statistical analysis
The data were analyzed using SPSS version 22 (IBM Corp., Armonk, NY, USA), and the results are presented as descriptive statistics—frequency, percent, age, mean, standard deviation, and inferential statistics—Chi-square test, risk ratio (RR) with 95% confidence interval (CI), Student’s–t-test for independent samples for $\alpha = 0.05$ and 5% level of significance.

Results and Discussion
We had observed 494 patients for this study and 342 patients (69.23%) were qualified for delirium assessment and found to have positive or negative delirium, compared to 152 patients (30.76%) who were not qualified (labeled as “UTA”) for delirium assessment as they had been deeply sedated, discharged, or died before completion of assessment. Figure 1 presents the Flow Chart of the study.

The incidence of delirium in ICU was 17.3%. Of 342 patients who had been qualified for delirium assessment, 59 patients (17.3%) showed positive delirium at least once compared to 283 patients (82.7%) who did not show any single delirium incidence during the study period. Table 1 presents the association between observed delirium and other associated factors and Table 2 presents associated factors RRs.

Sedation and delirium
Data analysis has shown a strong statistically significant association between delirium and sedation; the patient has sedation started in ICU during the study period or not, Chi-square $= 17.405$ ($P = <0.001$). RR analysis has shown that patients who received sedation ($n = 75$, 21.9%) had 2.61 times the risk of developing delirium compared to patients who did not receive any sedation during stay in ICU ($n = 267$, 78.1%). RR 2.618; 95% CI 1.67–4.09, $P = <0.001$). This result is consistent with other studies findings in the reviewed literature. Ouimet et al. observed that the use of sedation was significantly associated with delirium; (odds ratio [OR] = 3.2, 95% CI = 1.5–6.8). Pandharipande et al. had defined that midazolam (OR 2.75, CI 1.43–5.26, $P = 0.002$) exposure as the strongest independent risk factor for transitioning to delirium among surgical ICU (SICU) and trauma ICU (TICU) patients.

Another study conducted by Pandharipande et al. concluded...
that patients treated with lorazepam on a given ICU day are more likely to be delirious on the following day than if lorazepam were not administered; (OR = 1.2, 95% CI = 1.2–1.4). Pisani et al. concluded that receipt of a benzodiazepine or opioid (RR = 1.64, 95% CI = 1.27–2.10) was associated with increased delirium duration in medical intensive care. Vasilevskis et al. had concluded in their study, that among a large number of risk factors discovered, administration of potent sedative medications, most notably benzodiazepines, is most consistently and strongly associated with an increased burden of delirium.\[19\]

### Table 1: Chi-square test of association for the factors and observation of delirium

| Characteristics                      | n (%)       | Delirium observed n | Delirium not observed n | \( \chi^2 \), (P) |
|--------------------------------------|-------------|---------------------|-------------------------|------------------|
| **Gender**                           |             |                     |                         |                  |
| Male                                 | 264 (77.2)  | 46                  | 218                     | 0.024            |
| Female                               | 78 (22.8)   | 13                  | 65                      | (P=0.876)        |
| **Sedation**                         |             |                     |                         |                  |
| Receiving Sedation                   | 75 (21.9)   | 25                  | 50                      | 17.40            |
| Not Receiving Sedation               | 267 (78.1)  | 34                  | 233                     | (P<0.001)        |
| **Mode of Sedation Administration (only for sedated patients)** |             |                     |                         |                  |
| Infusion                             | 60 (80.0)   | 19                  | 41                      | 20.09            |
| Intermittent                         | 5 (6.67)    | 3                   | 2                       | (P<0.001)        |
| Mixed                                | 10 (13.33)  | 3                   | 7                       |                  |
| Ventilated                           |             |                     |                         |                  |
| Yes                                  | 119 (34.8)  | 33                  | 86                      | 14.04            |
| No                                   | 223 (65.2)  | 26                  | 197                     | (P<0.001)        |
| **Mechanical Ventilator (MV) Resistance** |             |                     |                         |                  |
| Yes                                  | 11 (3.2)    | 6                   | 5                       | 20.14            |
| No                                   | 108 (31.6)  | 27                  | 81                      | (P<0.001)        |
| Not connected to MV                  | 223 (65.2)  | 26                  | 197                     |                  |
| **Discharge Outcome**                |             |                     |                         |                  |
| Alive                                | 317 (92.7)  | 52                  | 265                     | 2.18             |
| Dead                                 | 25 (7.3)    | 7                   | 28                      | (P=0.140)        |

*Statistically significant at 5% level

### Table 2: Risk Ratio of Significant associated factors with delirium observation

| Parameter                        | Number of patients | Risk ratio | 95% CI |
|----------------------------------|--------------------|------------|--------|
| Sedation - Received              | 75                 | 2.618*     | 1.67-4.09 |
| Did not receive                  | 267                | 1          | ---    |
| Mode of sedation - Infusion      | 60                 | 0.53       | 0.23-1.18 |
| Intermittent                     | 5                  | 1          | ---    |
| Patient on - Sedation Vacation    | 43                 | 2.10*      | 1.17-3.79 |
| NOT on Sedation Vacation          | 80                 | 1          | ---    |
| Patient - received assisted MV    | 119                | 2.37*      | 1.49-3.78 |
| Did not receive assisted MV       | 223                | 1          | ---    |
| Patient on assisted MV            | 11                 | 2.18*      | 1.16-4.10 |
| Showed resistance to MV           | 108                | 1          | ---    |

*Statistically significant

who received sedation as continuous or as intermittent. Junior and Park had investigated the association of sedation mode (continuous or intermittent) with delirium and found no differences between both groups (\( P = 0.472 \)). In our study for patients who received sedation, there was a strong statistically significant association between delirium incidence and mode of sedation (intermittent versus continuous) Chi-square = 20.090 (\( P = <0.001 \)).

RR analysis has shown that patients who received sedation as “infusion mode”\( (n = 60, 80\%) \) had a 47% reduction in risk of developing delirium compared to patients who received sedation as “intermittent mode” \( (n = 5, 6.7\%) \) dosages during length of stay in ICU; \( RR = 0.53,95\% CI 10.23–1.18, P = <0.001 \). Svenningsen et al. had investigated the impact of fluctuating sedation levels on the incidence of delirium in ICU and found that continuous infusion of sedatives (midazolam) was associated with a decrease in delirium incidence (OR: 0.38; \( P = 0.002 \)).

### Daily sedation interruption and delirium

Holding sedation on a daily basis to assess neurological status (daily sedation interruption [DSI]) is a common practice for sedated patients that can reduce sedation. Our data analysis showed no statistically significant association between delirium and DSI \( (P = 0.412 \). Many other studies had shown similar finding; no significant association between DSI and delirium.

### Assisted mechanical ventilation and delirium

Out of the 342 qualified patients for delirium assessment, 119 patients (34.80%) received assisted MV during the study period compared to 223 (65.20%) patients who did not receive any assisted MV during the study period. Many studies had
found a strong association between the incidence of delirium and ventilation time.\[^{29,30}\] Studies had shown that the prevalence of delirium is reaching 80% among ventilated patients in medical, surgical, and ICU.\[^{31}\] Data analysis in this study showed a strong statistically significant association between delirium and assisted MV (i.e., the patient received assisted MV during the study period); Chi-square = 14.04 (\(P < 0.001\)). RR analysis has shown that patients who received assisted MV (\(n = 119, 34.8\%\)) had 2.37 times the risk of developing delirium compared to patients who did not receive assisted MV (\(n = 223, 65.2\%\)) during stay in ICU. RR = 2.37, 95% CI 1.49–3.78, \(P < 0.001\).

Patients who are MV may experience unpleasant effects as a result of asynchrony in breathing, some ventilator settings, distress from ventilator devices and tubes, difficult communication with others while ventilated. Patient-ventilator dyssynchrony (PVD) is defined as ineffective patient triggering, double-triggering, short-cycle, and long-cycle breaths.\[^{34}\] It suggests a faulty interaction between the patient and ventilator that is commonly managed by sedation and advanced ventilator modes and adjustments.\[^{35}\] PVD can be identified by direct observation of “patient fight with ventilator” as described by nurses or by detecting changes in the pressure/flow waveform as described by respiratory therapists.\[^{35}\] In this study, we had found that of 119 patients connected to ventilator, only 11 patients (9.24%) had shown resistance (asynchrony) to MV. Analysis has shown a strong statistically significant association and resistance to MV; Chi-square = 20.14 (\(P < 0.001\)). RR analysis has shown that patients who showed resistance/asynchrony to MV (\(n = 11, 3.2\%\)) had 2.18 times the risk of developing delirium compared to patients who did not show any resistance/asynchrony to MV (\(n = 108, 31.6\%\)) during stay in ICU. RR = 2.18, 95% CI = 1.16–4.10, \(P < 0.001\).

### Baseline level of consciousness and delirium

Glasgow Coma Scale (GCS) has been used to measure the level of consciousness for patients, especially those with brain injury.\[^{36,37}\] Data analysis has shown a strong statistically significant association between delirium incidence and baseline GCS. Chi-square = 72.69 (\(P < 0.001\)). Figure 2 presents the frequency distribution of patients eligible for delirium assessment (\(n = 342\)) and their baseline GCS score. In one study investigated delirium among 115 trauma patients admitted to the SICU, GCS Score <15 on admission was found to be one of the positive predictors of delirium.\[^{38}\] Another study investigated traumatic brain injury patients in the neurosurgical ward, concluded that those with low GCS score on admission in the emergency department were more likely to have delirium in the first 4 days after admission.\[^{39}\]

### Other factors and delirium

Data analysis showed no statistically significant association between delirium incidence and ICU admitting diagnosis, age, gender, and discharge outcome; \(P = 0.95, 0.58, 0.88,\) and 0.14, respectively. Chi-square = 2.183 \((P = 0.140)\). Ely et al. had investigated 275 MV patients and found similar findings; no significant difference in age and admission diagnosis between group of patients with delirium and group of patients without delirium.\[^{40}\] Aldemir et al. investigated the predisposing factors for delirium for 818 patients in a SICU; in their findings, there was no significant correlation between delirium and age, gender, and admission diagnosis.\[^{40}\] On the other hand, Zaal et al. included 33 studies in their systematic review of risk factors for delirium in the ICU. Among findings, age and admission diagnosis/status were strong risk factors for delirium in >70% of studies included but not gender.\[^{41}\] Mattar et al. had reviewed 22 published articles about delirium predisposing factors in ICUs (medical, surgical, or cardiac) from 1990 to 2012; they concluded that old age is a common risk factor for delirium in critically ill adult patients.\[^{42}\]

### Conclusion

Despite methodological limitations, delirium occurred in >17% of our ICU patients populations. Certain factors for delirium have been found to be significantly correlated with delirium \((P < 0.005)\). These factors include receiving sedation, mode of sedation, receiving MV, resistance to MV, and baseline GCS score. Other factors found to be not significantly contributed to developing of delirium among studied populations, including age, gender, admission diagnosis, and discharge outcome. Given the fact that delirium is extremely overlooked syndrome in ICUs of the Middle East and Saudi Arabia; additional studies are necessary to investigate delirium and its associated factors.

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### Conflicts of interest

There are no conflicts of interest.

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