





*Review Article*

**Epidemiology, risk factors, diagnosis, and potentially effective strategies to improve delirium in patients admitted to intensive care units: A narrative review**

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**Abstract**

Delirium is prevalent in intensive care units (ICUs), causing significant financial burden and devastating consequences. The primary objective of this article is to furnish comprehensive insights into delirium, encompassing its epidemiology, risk factors, diagnosis, and strategies for preventing its occurrence among patients in the ICUs. A comprehensive literature search was conducted using electronic databases PubMed, Web of Science, and Scopus to identify relevant studies published until September 16, 2023. The search items included the terms “Delirium” and “Intensive Care Unit”. It is better to implement the pain, agitation, and delirium bundle to diagnose delirium in children admitted to the pediatric ICU. Therefore, methods are suggested to improve the sensitivity and specificity of diagnostic tools, such as training nurses, developing guidelines, and using electroencephalogram and automated infrared pupillometry. It should be noted that delirium significantly impacts mortality and morbidity and imposes heavy costs on the healthcare system. Therefore, finding methods to improve the quality and speed of delirium detection is important.

**Keywords:** Epidemiology, Risk Factor, Diagnosis, Delirium, Intensive Care Unit, Review.

**1 | Introduction**

Delirium, as defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), is an acute, fluctuating, reversible disorder characterized by a disturbance in attention or awareness and cognition or an altered level of consciousness [1-4]. It is commonly observed in behavioral and neuropsychiatric disorders during critical illness, affecting sleep patterns, psychomotor activity, and emotions [5, 6]. Delirium is prevalent in intensive care units (ICUs), causing significant financial burden and devastating consequences [7, 8]. It has been found to impact perception, memory, and sleep quality, leading to changes in anxiety levels,

fearfulness, and euphoria [3, 6]. This condition develops rapidly and fluctuates throughout the day due to cerebral dysfunction [9, 10]. Delirium is associated with extended hospital stays, prolonged mechanical ventilation, greater reintubation, short and long-term cognitive impairment, and posttraumatic stress disorder [2, 10].

It has a considerable impact on morbidity and mortality rate, higher hospital and ICU costs, which appear to increase linearly with the severity of delirium, and a 3-fold increase in the 6-month mortality rate [1, 5, 7, 11, 12]. Delirium, a common and serious condition, can be classified into three subtypes: hyperactive, hypoactive, and mixed. Hyperactive delirium is characterized by

increased psychomotor activity, leading to agitation and restlessness. On the other hand, hypoactive delirium is marked by decreased psychomotor activity, resulting in lethargy, stupor, drowsiness, withdrawal, and inactivity. The mixed form of delirium fluctuates between hypo and hyperactivity [7, 13]. Individuals with any of these subtypes exhibit limited movement, impaired communication skills, and an inability to respond to interactions [13, 14]. Various factors contribute to the development of delirium, including baseline developmental delays, the need for mechanical ventilation, severity of illness, age younger than five years old, aggressive medical procedures, metabolic disorders, and visual and auditory impairments [2, 3]. Understanding these subtypes and associated factors is crucial for effectively diagnosing and managing delirium [13, 15]. The Confusion Assessment Method for the ICU (CAM-ICU) and the intensive care delirium screening checklist (ICDSC) have emerged as the preeminent measures for evaluating delirium in ICU settings due to their well-documented high sensitivity and specificity [8, 11, 13, 16, 17].

However, despite these practical assessment tools, nurses need help detecting delirium in their patients. These barriers encompass a lack of sufficient knowledge about delirium and its screening tools, inadequate pain control, heightened anxiety levels, the complexity of standardized assessment tools, excessive workload pressure, avoidance of oversedation, maintenance of day-night routines, and providing a comforting environment [2, 3, 10]. The primary objective of this article is to furnish comprehensive insights into delirium, encompassing its epidemiology, risk factors, diagnosis, and strategies for preventing its occurrence among patients in the ICU.

## 2 | Methods

A comprehensive literature search was conducted using electronic databases PubMed, Web of Science, and Scopus to identify relevant studies published until September 16, 2023. The search was conducted using the terms (“Delirium” OR “Subacute Delirium” OR “Subacute Deliriums” OR “Mixed Origin Delirium” OR “Mixed Origin Deliriums”) AND (“Intensive Care Units” OR “Intensive Care Unit” OR “ICU”). All terms were extracted from the medical subject heading in PubMed. Articles in English were filtered. Overall, 997 articles were initially identified. Through skimming the titles and removal of duplicates, 894 articles were eliminated. The title and abstract of the remaining 103 articles were screened to identify eligible studies in line with the improvement of delirium detection in the ICU, excluding 47 articles. Out of the 56 remaining articles, the full text

of 25 articles was unavailable. The full text of 31 articles was thoroughly screened, the final 18 studies were selected for our research, and their data was extracted.

## 3 | Results

### 3.1 | Delirium

For the past 2,500 years, delirium has been characterized as having or not having specific behavioral characteristics [18]. The American Psychiatric Association, however, defined it in 1983 using clinical symptoms and mental characteristics. This organization defines delirium as an acute and fluctuating disturbance in attention or awareness accompanied by a change in baseline cognition [1]. In the Diagnostic and Statistical Manual for Mental Disorders (Fifth Edition), delirium is a consciousness condition that affects hospitalized patients, particularly those in the ICU, and is marked by its abrupt onset and fluctuating cognitive alterations. It is important to distinguish this illness from dementia, especially in older adults. Dementia is a general cognitive condition that progresses more slowly than delirium and produces memory and speech problems [19].

### 3.2 | Epidemiology delirium in patients admitted to ICU

Numerous studies demonstrate a wide range of delirium occurrences, which may vary depending on the features of the population under investigation and the available diagnostic techniques. This rate was reported as 27% by Rahimi-Bashar *et al.*, (2021) [15] in a study on 400 hospitalized ICU patients. Additionally, Al-Hoodar *et al.*, (2022) [1] reported this percentage as 26.1% in research with 153 patients, of which 64.1% were men and 35.9% were women. The prevalence of delirium varies between 9% [2] and 87% [3] across several studies. This rate is 45-50% in patients after surgery, 80% in ICU patients under mechanical ventilation, and 20% in patients under acute care.

### 3.3 | Risk factors delirium in patients admitted to ICU

Risk factors that cause delirium in patients can be divided into three general categories. The first group of factors includes old age, underlying primary cerebral diseases such as cognitive impairment and memory impairment, and underlying chronic diseases [20]. A prospective observational study in 2021 showed that sepsis, metabolic acidosis, nasogastric tube use, Acute Physiology and Chronic Health Evaluation II (APACHE II) score, sedation use, and creatinine level are associated with the incidence of delirium [2]. In another study conducted in 2021, it was shown that the age factor is unrelated to delirium. This study showed that

the factors that increase the chance of delusions include male gender, being single, smoking, using mechanical ventilation, and the occurrence of hard trauma. It was also shown that these patients' mean scores of APACHE IV, Sequential Organ Failure Assessment Score (SOFA), and Richmond Agitation-Sedation Scale (RASS) were significantly higher [4]. The second category includes medicinal agents such as taking sedatives and the use of almost all drugs, especially opioids, anticholinergic agents (e.g., promethazine, diphenhydramine, amitriptyline, doxepin, chlorpromazine), and benzodiazepines (e.g., clonazepam, diazepam, lorazepam, estazolam) [5]. Studies have shown that those who used sedatives during their stay in the ICU were 2.61 times more likely to experience delirium [2]. Opioids that have a longer duration of action, such as morphine and meperidine, have a more significant effect on the occurrence of delirium, especially in patients with kidney and liver diseases [11]. Studies have shown that delirium can be considered as one of the side effects of steroid drugs [3]. A study by Rahimi-Bashar *et al.*, (2021) showed that the consumption of sedatives and painkillers like morphine, methadone, fentanyl, midazolam, dexamethasone, diazepam, and hydrocortisone was higher in patients with delirium. This study also showed that a higher percentage of these patients were treated with antibiotics than those who did not suffer from delirium [4]. The third category includes environmental factors contributing to delirium, including sleep disruption, pain, which can increase with its lack of proper management after trauma or surgery, noise, and sensory overload [5]. Mechanical ventilation, the amount of time spent in the hospital or ICU, and the usage of restraints on patients are other factors that can contribute to delirium in patients [2].

### 3.4 | Diagnosis of delirium in patients admitted to ICU

The CAM-ICU and the ICDSC are the most commonly used tools to assess delirium in the ICU because the examination of the patients using these tools requires less time and education, and are also suitable for individuals who are unable to speak [3]. The CAM-ICU identifies delirium by evaluating four diagnostic characteristics, including abrupt shifts in mental state, inattention, disorganized thinking, and changes in levels of consciousness. On the other hand, ICDSC evaluates eight diagnostic criteria, including changes in consciousness, inattention, altered psychomotor activity, psychosis, disorientation, inappropriate speech or mood, sleep problems, and symptom fluctuations [19]; this test is based on the DSM-IV definition of delirium [5]. In children and the pediatric ICU (PICU), the diagnosis of delirium is more challenging [4]; Cloedt LD *et al.* have concluded that the implementation of the Pain, Agitation, and Delirium (PAD) bundle in PICU

increases the potential to improve the detection of delirium in this population. Allegedly, implementing the PAD bundle was found to be most beneficial for patients who did not undergo invasive ventilation since, before its implementation, delirium was predominantly diagnosed in patients who received invasive ventilation [4]. Al-Hoodar *et al.*, (2022) [1] have utilized APACHE II and SOFA other than ICDSC to identify the predictors of delirium; APACHE II was composed to measure disease severity and SOFA measures the failure degree of each system.

### 3.5 | Potentially effective strategies to improve delirium in patients admitted to ICU

Despite efforts to implement regular delirium screenings using the ICDSC or the CAM-ICU, many assessments are still incorrect, even when these reliable tools are used [7]. In CAM-ICU, Inadequate documentation, unclear responses (IUTA responses), and incorrect scoring, especially in patients suffering from hypoactive delirium (which is harder to diagnose), have led to many unrecognized ICU delirium cases, despite its importance and apart from the staff-related factors, Awan *et al.*, (2021) [2] investigated the patient-related barriers that may precipitate to this phenomenon, their research demonstrated that mechanical ventilation and sedative infusions play a significant role in inaccurate CAM-ICU evaluations. Also, patients of older age (more than 80) and races other than white had higher IUTA responses. The CAM-ICU accuracy in delirium assessment is lower in individuals suffering from mild delirium, dementia, and mild cognitive impairment and has lower sensitivity in hypoactive cases of delirium [18]. Therefore, Mulkey *et al.*, (2019) suggest that the utility of electroencephalogram (EEG) can improve early detection of delirium since neurochemical changes and, therefore, their impact on the neuro-electrical activity occur before delirium's behavioral symptoms; in other words, physiologic monitoring might be able to yield the detection of delirium before the onset of symptoms [18]. Nurses, who play a critical role in detecting delirium despite having a good understanding of delirium, tend not to prioritize delirium assessment, mostly because of their lack of knowledge of its significance [3]. Krupa *et al.*, (2022) [6] conducted training plans containing different parts such as an introduction to delirium, watching a video on a patient's experience of delirium, raising awareness on the consequences of their decisions, talking to delirious patients and their families, etc. Furthermore, surveying nurses can better understand any deficit nurses may experience concerning preventing, detecting, or managing delirium [21]. Quality improvement, which is defined as "A process through which an organization or department can improve an aspect of patient care" by the health foundation (2015),

consists of different models to improve the detection of delirium [22]. Different research examines different models for quality improvement of delirium detection. Stewart & Bench (2018) [22] studied the plan, do, study, act (PDSA) model and agreed upon two interventions: “developing a guideline for practice” and “education and awareness”. They educated the staff on delirium, its common symptoms, and the CAM-ICU tool using short presentations. Since no significant improvement was shown and the results were skewed, they concluded that perhaps evaluating the potential barriers before the implementation would have made the results more useful. Dilibero *et al.*, (2018) [7] also mention that coaching at the bedside, case-based education, auditing in real-time, and incorporating quality improvement models are proven effective. They utilized the Standards for Quality Improvement Reporting Excellence (SQUIRE 2.0) guidelines as their model for quality improvement. Their intervention was designed based on the identified barriers in their research and played out in two phases; the first phase was mostly general education provided, such as hands-on education and case-based scenarios, but no feedback; the second phase included assessments of nurses’ evaluation and feedback on their evaluation accuracy. Eken *et al.*, (2022) [13] implemented a two-cycle PDSA intervention in pediatric and pediatric cardiovascular ICU. The interventions included training, educational hand-outs, and an electronic medical record (EMR) embedded flowsheet for documentation. They proved effective and sustainable; their work also emphasizes the importance of EMR documentation tools for sustaining accurate delirium assessments. Rohlik *et al.*, (2018) [10] began by conducting a nursing survey in pediatric ICU, identifying barriers such as difficulty remembering to fill out the assessment, intubated patients, completing documentation after working hours, and busy patients. They also went on to form a quality improvement team, including registered nurses of PICU and others. They used two methods: education and increasing awareness of detection rates and using the failure mode and effects analysis, a quality improvement tool utilized in various industries, to pinpoint the process steps with the highest probability of failure. They concluded that education combined with identifying and eliminating barriers increases the success rate of delirium screening. Devlin *et al.*, (2008) [23] studied the positive impact of the intervention using a didactic lecture and clinical-based scenario scripts. They measured the effectiveness by assessing the nurses’ ability to identify delirium and their ability to operate delirium scales properly. Also, Sinvani *et al.*, (2021) [14] identified lack of knowledge on delirium as the most important barrier and therefore conducted a multicomponent education and training program including testimonials of patients, group discussions,

didactics, role-plays, and tele-delirium training to improve knowledge on the subject. Moreover, Al-Hooadar *et al.*, (2022) [1] believe that recognition of delirium predictors can be helpful for early detection of delirium; the results of their research show a remarkable correlation between sepsis and delirium, and consistent with other research that metabolic acidosis, a disruption in electrolyte equilibrium and therefore lack of the brain’s acetylcholine activity, severity of illness, and individuals with nasogastric tubes are all associated with delirium precipitation. As a result, looking out for these signs can be useful for early detection. another predisposing factor that may contribute to the early detection of delirium in the ICU is the slower dilation velocity of pupils in patients with delirium based on research done by Okamoto *et al.*, (2022) [9] which claims that disruption in neurons of the sympathetic system and cholinergic neurons can cause delirium by disturbing overall neurotransmitter balance, and the fact that the cholinergic system is responsible for pupillary constriction in response to light stimulation, we can use automated infrared pupillometry (AIP) to measure the dilation velocity and associate it with potential delirium.

#### 4 | Limitations

It is possible that some pertinent studies were overlooked even though a thorough search strategy was implemented.

#### 5 | Implications for clinical nursing practice

Delirium is a common disorder in hospitalized patients, particularly those admitted to the ICU. Nurses in the ICU play a crucial role in preventing, diagnosing, and caring for patients with delirium. However, it has been found that nurses do not use standard tools while assessing patients for sedation levels and delirium. Delirium is often underdiagnosed, and earlier detection could lead to more effective nursing interventions and reduce long-term consequences. It is suggested that nurses use bedside clinical assessment tools such as the CAM-ICU and provide high-quality primary nursing care to prevent and treat delirium.

#### 6 | Recommendations for future research

It is suggested that forthcoming studies concentrate on enhancing the precision of forecasting delirium commencement by utilizing AIP parameters upon admission to the ICU, the attentiveness of nurses in detecting alterations in cognitive function, and prompt identification and treatment of delirium which could result in decreased ICU stays, improved patient outcomes, and minimized reliance on pharmaceutical interventions.

## 7 | Conclusions

Considering the importance of delirium, especially in patients hospitalized in ICU and its high incidence rate, much research has been conducted to investigate its causes, risk factors, diagnosis methods, epidemiology, and strategies to improve the diagnosis of this mental disorder. According to the definition of the American psychiatric association, delirium is an acute and fluctuating disturbance in attention or awareness that is accompanied by a change in baseline cognition. From the point of view of epidemiology, a wide range of the incidence of this disorder has been reported in patients. However, the noteworthy point is that most of these studies report a high and non-negligible percentage. Also, several factors have been reported as delirium risk factors, including demographic characteristics, underlying diseases, drugs, and environmental conditions. Currently, tools CAM-ICU and ICDSC are the most used to diagnose delirium in the ICU. Studies have shown that even using these tools often causes non-diagnosis or misdiagnosis of delirium; it is better to implement the PAD bundle to diagnose delirium in children admitted to the PICU. Therefore, methods are suggested to improve the sensitivity and specificity of diagnostic tools, such as training nurses, developing guidelines, and using EEG and AIP. It should be noted that delirium significantly impacts mortality and morbidity and imposes heavy costs on the healthcare system. Therefore, finding methods to improve the quality and speed of delirium detection is important.

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### Authors' contributions

Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work: AMN, ME, HZ, ZFA, AD, YM; Drafting the work or revising it critically for important intellectual content: AMN, ME, HZ, ZFA, AD, YM; Final approval of the version to be published: AMN, ME, HZ, ZFA, AD, YM; Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved: AMN, ME, HZ, ZFA, AD, YM.

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We do not have potential conflicts of interest with respect to the research, authorship, and publication of this article.

### Availability of data and materials

The datasets used during the current study are available from the corresponding author on request.

### Using artificial intelligent chatbots

None.

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