

## Delirium in Elderly

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### Abstract

**Introduction:** Delirium is defined as a clinical syndrome which is characterized by acute and fluctuating cognitive dysfunction, or acute state of confusion, which is usually transient, and happens as a result of another underlying medical condition. The prevalence of delirium is about 14 - 24% in hospital setting and 1 - 2% in community. The incidence is higher among the elderly, especially those in post-operative stage, in palliative care, or those requiring intensive care. Patients over age 65 in the intensive care unit (ICU) can have an incidence of delirium as high as 85%. Delirium is also greatly associated with patients on ventilators. Delirium is associated with a cost of 4 - 16 billion dollars per year in the United States alone. It is also associated with increased duration of mechanical ventilation, rates of self extubation and prolonged hospital stay. Prolonged delirium in the ICU is directly associated with increased mortality, as well as long term cognitive dysfunction. Therefore, understanding the cause behind the condition, and its management is imperative.

**Objectives:** In this review, we will discuss the management of delirium of patients in the intensive care department.

**Methodology:** We did a systematic search for management of delirium of patients in the intensive care department using PubMed search engine (<http://www.ncbi.nlm.nih.gov/>) and Google Scholar search engine (<https://scholar.google.com>). All relevant studies were retrieved and discussed. We only included full articles.

**Conclusion:** Delirium is a serious condition and a complication of hospitalization patients, especially in the elderly. It must be considered to be a medical emergency until proven otherwise. Delirium has the potential to significantly affect the overall outcome and prognosis of severely ill patients in the ICU. It also substantially increases the health-care utilization and costs. Interdisciplinary team approach with new guidelines for managing delirium leads to use minimum sedation, reduced duration of mechanical ventilation, increase ventilator-free days, and better sleep hygiene. Restraints should only be used in refractory cases. More studies are needed to understand causes and risk factors for delirium to reduce incidence and enhance prevention in the ICU patients.

**Keywords:** Delirium; Acute Confusion; Intensive Care Unit; Palliative Care; Treatment of Delirium

### Introduction

Delirium is defined as a clinical syndrome which is characterized by acute and fluctuating cognitive dysfunction, or acute state of confusion, which is usually transient, and happens as a result of another underlying medical condition [1]. The prevalence of delirium is about 14 - 24% in hospital setting and 1 - 2% in community. The incidence is higher among the elderly, especially those in post-operative stage, in palliative care, or those requiring intensive care. Patients over age 65 in the intensive care unit (ICU) can have an incidence of delirium as high as 85%. Delirium is also greatly associated with patients on ventilators. Delirium is associated with a cost of 4 - 16 billion dollars per year in the United States alone. It is also associated with increased duration of mechanical ventilation, rates of self extubation, and prolonged hospital stay. Prolonged delirium in the ICU is directly associated with increased mortality, as well as long term cognitive dysfunction. Therefore, understanding the cause behind the condition, and its management is imperative [2].

Causes of delirium are diverse, and can result from multifactorial reasons, such as predisposing factors, medical condition and medications or infections. Studies have shown delirium to be associated with decreased cerebral blood flow and metabolism, cerebral inflammation, and cholinergic deficiency. The presentation of delirium can include disturbed consciousness, inattention, and sudden psychotic features. Memory loss and language and emotional disturbances may be hard to detect in ICU patients. For ICU patients, delirium can be diagnosed with Sedation Agitation Scales (SAS) to categorize severity [3].

Factors such as new drug administration, change in medication regimen, underlying infection, alcohol withdrawal, and changes in environment must be given special consideration. As up to 40% of delirium is preventable, prevention is the key to management. One example is avoiding use of benzodiazepine in elderly. Once delirium is confirmed, the underlying cause should be addressed. For critically ill patients requiring mechanical ventilation, often sedation and analgesia is offered. Additionally, nonpharmacologic strategies, such as behavioral intervention, offering clear instructions, keeping a calm and uninterrupted environment, minimizing psychoactive drugs, and music therapy is the first choice. In refractory cases, however, use of antipsychotics, especially haloperidol, is the standard approach [4].

### Methodology

We did a systematic search for management of delirium of patients in the intensive care department using PubMed search engine (<http://www.ncbi.nlm.nih.gov/>) and Google Scholar search engine (<https://scholar.google.com>). All relevant studies were retrieved and discussed. We only included full articles.

The terms used for search were delirium, acute confusion, intensive care unit, palliative care, treatment of delirium.

### Causes of delirium

Upon exposure to precipitating factors delirium can be triggered. Precipitating factors can include medications, stress, pain, dehydration or infection. The precipitating factors have been found to affect in a cumulative manner with the severity of delirium being proportional to the severity/number of stressors. These factors are mostly modifiable so one must be vigilant to identify them for treatment and prevention. Complex interrelationships exist between predisposing and precipitating factors of delirium. Patients who have low vulnerability to delirium require a strong precipitating factor for delirium to set in, such as sepsis or another precipitating factor just as strong. In patients who with high vulnerability even a mild precipitating factor can cause delirium or lead to prolongation of its duration.

In addition, changes in the pathophysiology which are associated with delirium can add to the pre-existing cerebral disease and worsen the neurodegenerative processes [5]. Development of delirium and its long-term sequelae pathophysiologic pathways including inflammation, cerebral hypoperfusion, oxidative stress, mitochondrial dysfunction, hypothalamic-pituitary-adrenal axis hyperresponsiveness, and others seem to be involved in the genesis of delirium and may contribute to its long-term sequelae. While the precise mechanisms remain still incompletely understood, there is evidence that a disturbed interaction between various neurotransmitters including acetylcholine, dopamine, noradrenaline, glutamate and gamma-amino hydroxybutyric acid (GABA) underlies the symptoms of delirium [6].

Possible risk and precipitating factors, must be kept in consideration, evaluated, and if possible, treated in any patient with delirium. Major and mild neurocognitive disorders (dementia and mild cognitive impairment) old age, visual and/or hearing impairment; poorer functional ability; male gender, long-term use of medications (prescribed or non-prescribed), co-morbid illnesses such as hypertension, chronic obstructive pulmonary disease, coronary artery disease, anemia, malignancy and past psychiatric illness, history of falls, alcohol abuse and immobility are all common risk factors [7].

Factors that precipitate to delirium are any iatrogenic event during hospitalization; physical restraints or bladder catheter; intensive care treatment; malnutrition, more than three newly prescribed medications; excessive number of procedures during early hospitalization (X-rays, blood tests, etc.); mechanical ventilation; infection; extended waiting period prior to surgery; type and duration of operation; intra-operative hemorrhage; postoperative pain and malpractice in pain management; and use of drugs with a high anticholinergic activity, opiates, benzodiazepines and corticosteroids.

A study in India showed that the predisposing risk factors that are found for delirium in intensive care individuals were older age, greater Glasgow Coma Scale, hyperuricemia, hypoalbuminemia, active acidosis, irregular alkaline transferase levels, mechanical ventilation usage, greater number of total drugs received and use of sedative, steroids and insulin, increased APACHE II score. Few significant risk factors that precipitate for mortality in patients with delirium are age, multi organ failure, hypoactive delirium and higher Delirium Rating Scale-Revised-98 (DRS-R-98) (delirium severity) scores. In hospitalized elderly in medicine wards, Khurana, *et al.* [8] showed that sepsis and metabolic abnormalities were the most common etiologies. Multiple causes were observed in most patients this shows how important is the multifactorial nature of delirium and need for thorough evaluation to unravel these. Most of the causes were curable and had a great outcome (83% recovered). Multiple important risk factors were identified by Guenther, *et al.* [9] that lead to the development of postoperative delirium including patients undergoing elective cardiac surgery higher age, higher Charlson's comorbidity index, impaired cognition (lower MMSE) and length of cardiopulmonary bypass. Intraoperative monitoring of the depth of anesthesia was associated with less incidence of delirium, the possible reason behind it is the reduction of extreme low BIS (Bispectral index) values which was shown in a study conducted by Radtke, *et al* [10]. Hence, the anesthesiologist can influence at least one precipitating factor in the complex genesis of delirium in high-risk surgical patients.

### Clinical presentation

According to DSM-IV-TR criteria, delirium is featured by the rapid onset of symptoms (usually hours or days) and tends to fluctuate, associated with confusion, focus impairment, sustain or shift attention, and a change in cognition (that includes memory impairment, disorientation, language disruption) or establishment of a perceptual disturbance that is not better accounted for by dementia. In addition, there is evidence based on history, physical exam, or laboratory results that the disturbance is originated from direct physiological consequences of a general medical condition, or substance abuse/withdrawal, or due to multiple causes [11].

Although this definition implies great complexity, it has the advantage of covering a broad clinical spectrum. It is difficult to pinpoint or attribute the activity to a discrete cerebral structure, despite the identified areas of neurological function are wide. In addition, controversial is defining that the syndrome is caused by the ability of different etiological factors to impact on a final common pathway producing stereotyped clinical consequences [11].

The core features of delirium are the Sudden and acute onset and fluctuating course. Therefore, establishing the patient's level of baseline cognitive functioning and the course of cognitive change becomes a priority. Fluctuation in symptoms is unpredictable. Which can be intermittent and are usually worse at night [12].

Consciousness is a brain function that lets the awareness of self and of the surrounding environment and is characterized by two important aspects: Consciousness level and the content. Consciousness level is defined as arousal and vigilance: wakefulness, being asleep, or comatose. The experience of the individual as awareness of themselves and the environment when awake or normally alert is the

content of consciousness, or part of it. The only way to examine the content of consciousness and cognition is by preservation of at least a certain degree of wakefulness and alertness. Impairment of consciousness appears to be the primary change in acute organic disorders and should also be considered as a continuum from full alertness and awareness to coma. therefore, it covers an important role in the assessment of brain function severity, as well as disturbances of brain function [13].

Conscious disturbance is one of the initial manifestations in delirium, which often fluctuates, primarily in the evening when environmental stimulation is at its lowest. Consciousness level can alternate between extremes in the same individual, or instead can manifest with more subtle signs, such as mild drowsiness, or impaired attention level. In fact, in more advanced cases, individuals may appear with obviously drowsy, lethargic, or even semi-comatose. Hyper-vigilance which is considered as the opposite extreme can also occur, especially in cases of sedative drug withdrawal or alcohol (less common in elderly people) [14].

Attention can be defined as a process that enables the individual to pick relevant stimuli from the environment, to focus and to keep behavioral responses to such stimuli, and to shift mental activity toward new stimuli, reorienting the individual behavior, depending on the relevance of the stimulus. Consciousness and attention function differently however, attention depends on consciousness. Therefore, attention with variable degrees can occur with full consciousness yet, full attention and concentration are impossible with decreased levels of consciousness. In fact, pathologic decrease can happen in attention in organic states, usually with lowering consciousness [15].

One of the main important features of delirium is inattention which occurs with affected patients. most patients can get easily distracted by irrelevant stimuli, or have a hard time keeping track of what the doctor mentions during clinical interview. Furthermore, in most cases questions must be repeated due to attention impairment of the individual. Usually cognition deficiency can be multiple or global, this includes disorientation and memory impairment. In fact, the function of memory and orientation can be affected by impairment of new information registration due to this inattentiveness [12].

Short-term memory is usually affected in the first case. but retention of saved information can also be disrupted. For example, instructions that were given to individuals are difficult to remember or they found to have an inability to remember events [16].

Other common feature is disorientation, usually starts in reference to time and then to place. However, it can be considered normal in seriously chronically ill patients, without references of days or months. Both functions of thinking and speaking can be impaired in delirium, they can overlap and cannot be readily separated from one another however, they are clearly different [14].

Deficiency in Language and its impoverishment individuals with delirium are probably more related to the disorder of arousal and attention levels, than a precise cause, or they may reveal a change in thought process. Frank confabulation can show dominance in cases of severe global impairment, giving only little opportunity to assess language, memory and thought content. In mild or early stages, language and speech, including reading, are often less affected than writing. In the course of delirium only Few specific observations on language disturbances were found available. In one study, it was found that misnaming has been common, as frequent as observed in demented patients, but they were different in being more often of the types of word intrusion and unrelated misnaming. Perseveration explains word intrusion. It is defined as the repetition of a previously uttered word (therefore perseverating) rather than the expected word that he/she is not able to find or pronounce. Unlike paraphasia, unrelated misnaming is when a word is used which wildly differs in meaning from the intended word and therefore has no link with the word appropriate for the context [17].

Impaired thinking is one other clinical feature which present as incoherent speech and rambling or irrelevant conversation, unclear or illogical flow of ideas. Individuals can have a hard time making appropriate decisions or execute simple tasks. In these patients, delusions can happen in around 30% of cases, and their judgment and insight may be poor, especially of persecutory or paranoid nature [18].

Patients with delirium can also have perceptual disturbances which may include misinterpretations and illusions, which manifests as a false impression of a real stimulus. For instance, agitation and fear can strike a patient, believing that a shadow in a dark room is actually an attacker. Hallucinations, where no objects are actually present is included as perceptual disturbance. Most frequent hallucinations are

of visual type. They often occur at night, and in a few cases, they can present during the day as soon as the patient shuts his eyes. Contents of hallucinations can be as simple as colors, lines, or shapes. At times it may include, for example, fearful animals or random images [13].

Other clinical features that are not included in the diagnostic criteria can commonly present with delirium. This can include sleep-wake cycle disturbance, which presents as excessive daytime sleepiness with insomnia during night time, fragmentation, and decrease of sleep or complete sleep-cycle reversal [16].

Studies suggest circadian rhythm disorder and sleep fragmentation in particular are important contributing factors to sundowning syndrome, also the studies observed the potential role of these disorders on sleep-wake cycle disturbance. In delirium this phenomenon has been observed and is featured by worsening of disruptive behavior in the late afternoon or evening. Fatigue and reduced sensory input toward the evening are possible causes [13].

Disturbed psychomotor activity which is featured by increased or decreased motor activity is another clinical feature of delirium. Restlessness or frequent sudden changes of position are observed in the first case. However, individuals can also present with sluggishness or lethargy, approaching stupor. Other presentations such as emotional disturbances, anxiety, fear, irritability, anger, depression, and euphoria can be seen in these patients. Recent life events, medical or surgical diseases, personality types, or premorbid psychiatric disorders, can influence these symptoms [12].

Some caveats must be taken into consideration while discussing classification and criteria currently used in delirium according to some authors. For example, although the tendency to make the criteria explicit, according to the specificity of the clinical manifestations of delirium, it should be remembered that some clinical situations, hospitalization, or physical symptoms, such as pain or breathing difficulty, can give rise to pseudo-delirious signs [19].

Furthermore, a deficient correlation has been proven between the different sets of diagnostic criteria (DSM-IV, ICD-10). Especially, a study reported different delirium prevalence rates in old age individuals presented to hospital or nursing homes, as stated by the criteria used (24.9% by DSM-IV and 10.1% by ICD-10). These outcomes clearly show that too inclusive or too restrictive criteria may cause noticeable differences in estimated prevalence rates of delirium [20].

Keeping this controversy in mind, few authors go beyond this criticism of delirium in the DSM-IV criteria. The notion of delirium was questioned by these authors reflecting it as "altered level of consciousness." As an alternative, these authors have suggested that delirium is defined as the decline of cognitive functions (attention, working memory, and executive functions), in direct proportion to the severity of any confusional state, and given that these processes are considered the base for every other cognitive process, their decline sets the entire cognitive apparatus in danger. These functions lay a base for the cognitive pyramid and are functionally deeply interdigitating, and hard to neatly separate. The current DSM criteria does not appear to contain this perspective [21].

Clinicians often miss Another limitation which is related to the severity of delirium, it is inadequately represented in this classification, as the complete clinical spectrum ranges from very severe deliriums where patients are minimally conscious, to low-grade encephalopathic states in a broad continuum, frequently missed by clinicians. Therefore, these authors report that delirium might originate from a broader category of diseases of consciousness. Suggestions from them apply that the following as a rough heuristic, with disorders of consciousness ranging from the most severe to the least severe: Coma; Persistent Vegetative State; Stupor; Akinetic Mutism; State of minimal consciousness; Delirium or states of confusion. This kind of taxonomy can provide a continuum, with "gray zones," or regions of transition demarcating one disorder from the other. This type of method would continue to allow a continuum of severity in relation to delirium itself, which is now disregarded in DSM-IV [21].

Despite this, clinical evaluation according to the phenomenon of symptom and the nosographic criteria shows as a reference standard for the diagnosis of delirium. Furthermore, many others reported that the correct examination of patients with delirium symptoms for epidemiological reasons, research, and clinical purposes is important and has been reported by many authors [22].

### Management

In elderly patients with delirium Both pharmacological and non-pharmacological interventions have shown great impact on health status. Non-pharmacological interventions did contribute to improved function in the medium term and reduced complications. While not greatly affecting the severity and duration of delirium, or mortality; a lot of medications were experimented to treat agitation of hyperactive delirium, with shown improvement in delirium severity, duration and rate of remission, positively affecting length of hospital stay and burden of caregiver. Managements in which combine cognitive impairment treatment, sleep hygiene, early mobility, visual and hearing support, and hydration care (HELP protocol) with light therapy have contributed to great improvement in functional status and lack of physical restraints for the care of delirium in geriatric wards [23].

Combining Strategies orientation interventions (clock, calendar, daily schedule chart, visual and hearing support, language interpreters); interventions that help in familiarizing with objects and family members; physiotherapy; hip protectors and nutritional supplements with the prescription of cholinesterase inhibitors when needed and restriction of the use of neuroleptics provided more pronounced and acute reduction in the severity of delirium and improvement cognitive function after discharge [24].

Combination of entertainment Intervention (radio, television); sleep hygiene (dark room and decreased sound); orientation interventions; interventions with familiarity in the presence of objects and people they recognize; attention to visual and auditory acuity, communication intervention with visual contact, empathy, calm speech; initial mobility stimulation, and psychiatric and geriatric specialist consultation was related with more rapid cognitive improvement [25].

The small number of participants in the reviewed studies could be due to a possible underdiagnosis of delirium and an inclusion of frail populations. Dementia prevalence difference between the groups can as well have influenced the outcome, since it is a risk factor and affects delirium prognosis. The intervention with non-pharmacological methods for delirium in general were applied together, encompassing several domains, and demonstrated less effectiveness in managing symptoms. As observed, it was found hard to differentiate the effectiveness of each patient therapeutic approach. studies where pharmacological intervention were applied have included cholinesterase inhibitors, typical (haloperidol and droperidol) and atypical antipsychotics (olanzapine and others). Pharmacological treatment greatly improved delirium severity and duration although there have only been a few published studies, involving a small number of cases. One of the cholinesterase inhibitors Rivastigmine, applied as a treatment for dementia, decreased the duration of delirium, improved cognitive function and reduced caregiver stress in elderly patients with ischemic stroke [26].

Elderly patients admitted to medical wards who suffer from delirium found that both olanzapine and haloperidol decreased the severity, and recovery was slightly faster with olanzapine. Droperidol usage have reduced the length of stay in the hospital and increased postoperative delirium remission rate in elderly patients who suffer colorectal cancer [27].

Immediate treatment should be initiated once elderly patients have developed acute cognitive decline; delirium must be diagnosed. Management must include swift detection and treatment of underlying critical conditions. Pharmacological treatment of agitation preferentially with atypical antipsychotics, improving cognitive function with cholinesterase inhibitors, and associating multiple interventions to hydrate, sleep-wake cycle restoration, initiating early mobility, support visual and hearing deficits, beginning temporal orientation and familiarity sensation, and improve communication. Therapeutic action in multiple domains can help lessen the severity of mental illness, duration to delirium recovery, and guarantee improved long-term cognitive function [27].

### Conclusion

Delirium is a serious condition and a complication of hospitalization patients, especially in the elderly. It must be considered to be a medical emergency until proven otherwise. Delirium has the potential to significantly affect the overall outcome and prognosis of severely ill patients in the ICU. It also substantially increases the health-care utilization and costs. Interdisciplinary team approach with new guidelines for managing delirium leads use minimum sedation, reduced duration of mechanical ventilation, increase ventilator-free days, and

better sleep hygiene. Restraints should only be used in refractory cases. More studies are needed to understand causes and risk factors for delirium to reduce incidence and enhance prevention in the ICU patients.

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