

Research Article

Delirium in Internal Medicine Intensive Care: An Overlooked Complication

 Ozden Yildirim Akan,¹  Pinar Ortan,²  Ismail Demir¹

¹Department of Internal Medicine, University of Health Sciences, Izmir Bozyaka Training and Research Hospital, Ringgold Standard Institution, Izmir, Turkey

²Department of Neurology, University of Health Sciences, Izmir Bozyaka Training and Research Hospital, Ringgold Standard Institution, Izmir, Turkey

Abstract

Objectives: The aetiology and risk factors of the patients that were diagnosed with delirium were investigated in this study. We aimed at revealing the risk factors for the development of delirium in intensive care unit.

Methods: Patients that were participated in our study were assessed with the Confusion Assessment Method and examined by a neurologist for the existence of delirium. Patients with and without delirium were statistically compared with Student's T-test and Chi-square test. Logistic regression analysis was performed to determine independent risk factors.

Results: All of 283 patients with 143 (51%) female and 140 (49%) male were included in this study. Delirium was detected in 144 (51%) patients. Delirium was higher in patients with the history of neurological diseases and the usage of medications for the central nervous system ($p=0.012$). The most common reasons of the delirium were infections (97%) and electrolyte imbalances (80%). The length of stay was longer in the delirium group ($p<0.0001$).

Conclusion: This study showed that the rates of delirium was high in ICU. We want to emphasize the importance of delirium in diagnose that can easily be overlooked by physicians.

Keywords: Delirium, intensive care units, length of stay

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The delirium is an organic brain syndrome that is characterized by several nonspecific findings including the sudden onset, general impairment of cognitive functions, changes in consciousness, attention disorders, increased or decreased psychomotor activity, and disorder of the sleep-wake cycle.^[1] Delirium is a serious disturbance in mental abilities and usually occurs acutely as well as it fluctuates during the day. As a term, delirium is originated from a Latin word "delirare" which means "to go out of the furrow" or "crazy or deranged".^[2] It is also known as a geriatric syndrome affecting the elderly patients that not only charged

in ICU, but also in community and despite the fact it is the most common mental state disorders, up to the 60% of older adults it is overlooked by physicians.^[3,4] But the hypoactive subtype of the delirium is the most common one that remains unrecognised by many healthcare practitioners.^[5] In many studies, the presence of delirium is known to increase the length of stay in hospital and increase the morbidity and mortality.^[6] The economic impact of delirium in the population is enormous and reducing delirium might lead to considerable cost savings in the ICU.^[7] The aetiologies of delirium are often multi-factorial and the predisposing

Address for correspondence: Ozden Yildirim Akan, MD. Izmir Bozyaka Egitim ve Arastirma Hastanesi, Saglik Bilimleri Universitesi İc Hastaliklari Klinigi, Ringgold Standart Enstitüsü, Izmir, Turkey

Phone: +90 505 484 21 69 **E-mail:** ozdenyldrm@gmail.com

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Table 1. DSM v diagnostic criteria

A	Disorder of consciousness (eg reduced awareness of the environment) characterized by focus and attention of attention;
B	Short-term development of disorders (usually within hours or days) and fluctuation and severity of the disorder within the same day,
C	Disorders in cognitive domains such as memory, orientation, language, visual spatial functions, perception,
D	Criteria A and C cannot be better explained by any other underlying disease. A state of advanced alertness such as coma,
E	The cause of the disorder can be attributed to one of the following by history, physical examination or laboratory tests; As a physiological consequence of the general situation, Depending on the drug or toxic substances, Due to withdrawal syndrome, More than one of the above reasons.

(non-modifiable) and precipitating (modifiable) risk factors are dementia, serious pathologies and surgery, infections, sedative medications etc, respectively.^[8-10] Delirium is diagnosed according to DSM V as shown in Table 1.

In the diagnosis of delirium, ICU confusion assessment scale (CAM-ICU) was developed to be used by non-psychiatrists such as nurses and intensive care physicians in a ICU.^[11] In 2005, Akıncı et al.^[12] have done the reliability and validity study of the CAM-ICU Turkish version. This test may provide early detection of delirium which is overlooked or neglected in the intensive care units, and give possibility to take precautions and treatments. CAM-ICU evaluates the acute onset of cognitive impairment, the fluctuations of mental state, the lack of attention, the disruption of thinking, and the change of consciousness. It is also easy and reliable to use in patients that cannot communicate verbally and/or who are connected to the ventilator. In this test, less than eight correct answers are considered as the delirium. The patients are diagnosed with the delirium when two items are positive and one of the third or fourth items is positive (Table 2).

The aim of this study was to determine the likelihood of the delirium in patients in the internal medicine intensive care unit without any primary neurological diseases and to determine the risk factors in the development of delirium.

Methods

All of the 283 patients who were charged in the intensive care unit of our hospital were included in the study from 2017 to 2019 years. In ICU, we routinely used the ICAM-ICU, Acute Physiology and Chronic Health Evaluation (APACHE II) scores, Sequential Organ Failure Assessment Scores (SOFA). We evaluated the files of the patients retrospectively. Patients who were on mechanical ventilators and those under 18 years of age were excluded. The patients that were charged in with the primary neurological disease, trauma, etc. were not included in the study. All patients included in the study were administered an ICAM-ICU by a physician in the ICU. The aetiologies and risk factors of all patients with and without delirium were investigated and the labo-

ratory examinations (blood and urine), HIV serology, ESR, CRP, WBC, HCT, hemoglobin, neutrophil, lymphocyte and platelet counts, PDW, RDW, MPV, HBA1C, urea, creatinine AST, ALT, BNP-TRIAG, albumin, total bilirubin levels were recorded in files. The lung graphy, ECG, cranial CT/MRI and EEG were performed in patients with delirium. The SOFA scores and APACHE II scores of all patients were calculated.

The age, educational status, alcohol-smoking habit, diagnosis of primary diseases, comorbid diseases, history of demantia, neurological diseases, the history of surgery and medications were reviewed. The length of stay and outcomes (death or discharge from hospital) were recorded. The aetiology of delirium was evaluated for the fluid-electrolyte imbalance, uremic encephalopathy, hepatic encephalopathy, hypoxic encephalopathy, hypo/hyperglycemia, infection-sepsis, narcotic and/or anticholinergic drug use, drug intoxication, and alcohol withdrawal syndrome. Patients with and without delirium were statistically compared with Student's T-test, Chisquare test. Logistic regression analysis was performed to determine independent risk factors.

Results

All of 283 patients with 143 (51%) female and 140 (49%) male were included in this study. The mean age was 71 ± 14.2 years. Delirium was detected in 144 (51%) of these patients. The age and sex of patients with and without delirium were compared and there was not a statistically significant value in results ($p=0.17$, $p=0.51$, respectively). The incidence of delirium was higher in patients with a history of neurological disease (stroke, dementia, Parkinson's disease, etc.) ($p=0.03$). Delirium rate was similar in patients taking more than four drugs ($p=0.11$). Delirium was more frequent in patients using central nervous system medications ($p=0.012$).

When all the risk factors were evaluated, the use of central nervous system medicationa was determined As an independent risk factor. In terms of the aetiology of delirium, fluid electrolyte disorder was detected in 115 patients, hypotension in 69 patients, infection in 140 patients, ure-

Table 2. CAM-ICU for delirium assessment

CAM-ICU Criteria		Delirium present
FEATURE 1 <i>Alteration/Fluctuation in Mental Status</i>	if yes for either question	+
1. Is the patient's mental status different than his/her baseline?		
2. Has the patient had any fluctuation in mental status in the past 24 hours as evidenced by fluctuation on a sedation scale (eg, RASS, Glasgow Coma Scale), or previous delirium assessment?		
FEATURE 2 <i>Inattention 1: Alteration/Fluctuation in Mental Status Letters Attention Test</i>	If number of errors >2	+
Tell the patient "I am going to read to you a series of 10 letters. Whenever you hear the letter 'A,' squeeze my hand." S A V E A H A A R T Count errors (each time patient fails to squeeze on the letter "A" and squeezes on a letter other than "A").		
FEATURE 3 <i>Altered Level of Consciousness</i>		
• Present if the RASS score is anything other than Alert and Calm (zero) OR	If RASS ≠ 0 OR SAS ≠ 4	+
• If SAS is anything other than Calm (4)		
FEATURE 4 <i>Disorganized Thinking Yes/No Questions</i>	Count errors if patient is unable to complete the entire command.	+
• Ask the patient to respond:		
1. Will a stone float on water?		
2. Are there fish in the sea?		
3. Does 1 kilogram weigh more than 2 kilogram?		
4. Can you use a hammer to pound a nail? Count errors (each time patient answers incorrectly).		
• <i>Commands:</i> Ask the patient to follow your instructions:		
a) "Hold up this many fingers." (Hold 2 fingers in front of the patient).		
b) "Now do the same thing with the other hand." (Do not demonstrate the number of fingers this time.) If unable to move both arms, for part "b" of command ask patient to "Hold up one more finger."		

If combined number of errors >1 if features 1 and 2 are both present and either features 3 or 4 are present: CAM-ICU is positive, delirium is present.

Table 3. Demographic finding of the patients

	Delirium found	Delirium not found	p
The length of stay	9.24±7.56 days	4.82±4.32 days	<0.0001
Age	72.90±13.51years	69.03±14.95years	0.16
SOFA	9.94±2.70	10.65±2.89	0.035
APACHE II	22,97±4,77	22.29±4.60	0.07

SOFA: Sequential organ failure assessment; APACHE: Acute physiology and chronic health evaluation.

mia in 13 patients, hypoxia in 9 patients, and elevated blood glucose levels in 43 patients. Infections and fluid electrolyte disturbances were the most common causes of the delirium in participants. The length of stay in patients with delirium was 9.24±7.56, and in patients without delirium was 4.82±4.32 days. The length of stay was significantly longer in the delirium group ($p<0.0001$). The SOFA score of the patients with delirium was 9.94±2.70 and the patients without delirium was 10.65±2.89 and the results between groups were statistically significant

($p=0.035$). The APACHE II scores were not significant between groups ($p=0.07$) (Table 3).

Discussion

In present study, the detected rate of delirium in patients charged in ICU was 51%. According to the available studies in literature, various rates of delirium in patients that were charged in ICU were noticed. In a meta-analysis, 9357 patients in 19 articles that were studied from 2005 to 2016, the incidence of delirium ranged from 4% to 55% (the mean was 29±14).^[13] But in an Indian study the prevalence of delirium was higher at 64% in mechanically ventilated patients.^[14] In a study geriatric patients were diagnosed with delirium in ICAM-ICU, the rates of the delirium at admission and during the stay in ICU were 3% and 8%, respectively but the patients were sampled from intensive care unit.^[15] Most of these studies were performed in general intensive care units where mixed patients such as trauma and cerebrovascular disease were accepted. Our study is important because all the patients that were included in

the study were diagnosed only with internal diseases and this formed a homogeneous group at the end. In ICU, it is important to use the scales to avoid delirium. Our ability to detect delirium at such a high rate is due to our delirium research. Two types of delirium have been identified as follows: Hyperactive delirium and hypoactive delirium. The hyperactive delirium is often noticed after agitation in a major problem because of the catheter, tube withdrawal. The hypoactive delirium is frequently missed and as result the risk of aspiration and reintubation increases. Therefore, the use of these scales should be routinely used in ICU to avoid the morbidity and mortality in patients with delirium. Using ICAM scale will allow early and easy diagnosis of patients with hypoactive delirium.

In present study, the length of stay was significantly longer in patients with delirium ($p < 0.0001$). This is consistent with the literature and no significant difference was found in terms of mortality. However, our study and findings were recorded after short-term period and so long-term results of patients were not evaluated. In present study, when the risk factors for the development of delirium were examined, the presence of a primary neurological disease and cognitive dysfunction before hospitalization was significant in the delirium group. Similar results have been reported in the literature. Fluid and electrolyte disturbance is an important cause of delirium.^[16] In present study, the most common cause was fluid electrolyte imbalance and infection. Age, male sex, nutritional disorders, multiple drug use, neuroleptic or narcotic medications have been reported as the initiators of delirium.

Fraser et al. reviewed 14 studies about the effect of benzodiazepine in intensive care patients and it was proposed that benzodiazepines increase hospital stay, time of ventilation, delirium prevalence, short term mortality.^[6,17] Jawaswal et al.^[18] found delirium incidence as 31.4% among patients in tertiary intensive care unit. They underlined high hypoactive delirium rates that can easily overlooked. The tobacco use, chronic liver disease, and past episodes of delirium were predisposing factors and mechanical ventilation, hypoxia, fever and benzodiazepine usage significantly precipitated

ICU delirium. In the Indian study, the authors reported the risk factors as higher Glasgow coma scale scores, hyperuricemia, increased APACHE II scores, mechanic ventilation, polypharmacy, use of sedative drugs. In our study, the use of central nervous system drugs was an independent risk factor. There was no difference in terms of age and gender. Based on the results of our study, in order to prevent the development of delirium in all patients hospitalized in intensive care unit, patients with central nervous system drugs such as narcoleptic should be closely examined, fluid electrolyte balance, infection and nutrition should be paid attention, early mobilization should be provided and cognitive functions should be supported.^[19-23]

In present study, APACHE II and SOFA scores were analyzed in all patients. APACHE II scoring is a disease severity assessment scale used in intensive care units, which was similar in patients with and without delirium, because delirium was not related to disease severity. In the literature the results are conflicting. The reason may be that the nonhomogeneous disease groups are include in different studies. Prognostic scoring systems and organ failure scoring systems showing morbidity are recommended in sequential intensive care units. For this purpose, SOFA defined in 1994 is used. It was developed by the European Society of Intensive Care to assess organ failure in sepsis, and was subsequently used in patients without sepsis. The SOFA score were similar in our group. This may be the result of high frequency of infections and sepsis (97%) in the delirium group (Table 4).

Conclusion

The scales routinely used in intensive care units (APACHE II, SOFA score) are not sufficient to evaluate the delirium. In particular, we recommend that the delirium assessment scales to into daily practice in order to overlook hypoactive delirium.

Disclosures

Ethics Committee Approval: The ethics committee of University of Health Sciences, Izmir Bozyaka Training and Research Hospital provided the ethics committee approval for this study (11.03.2020/n=01)

Peer-review: Externally peer-reviewed.

Conflict of Interest: The author has no conflicts of interest to report.

Authorship Contributions: Concept – O.Y.A., P.O.; Design – O.Y.A.; Supervision – O.Y.A.; Materials – I.D.; Data collection &/or processing – I.D.; Analysis and/or interpretation – P.O.; Literature search – O.Y.A.; Writing – O.Y.A.; Critical review – P.O.

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Table 4. The aetiology of the delirium

Aetiology	Number of patients	%
Fluid and electrolyte disorders	115	80
Hypotension	69	48
Infection	140	97
Uremia	13	0.09
Hypoxia	9	0.06
Hyperglycemia	43	30

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