



## Incidence and factors related to delirium in an Intensive Care Unit

Incidência e fatores relacionados ao delirium em Unidade de Terapia Intensiva

Incidencia y factores relacionados con el delirium en Unidad de Cuidados Intensivos

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### ABSTRACT

**Objective:** To identify the incidence of delirium, compare the demographic and clinical characteristics of patients with and without delirium, and verify factors related to delirium in critical care patients. **Method:** Prospective cohort with a sample made up of patients hospitalized in the Intensive Care Unit (ICU) of a university hospital. Demographic, clinical variables and evaluation with the Confusion Assessment Method for Intensive Care Unit to identify delirium were processed to the univariate analysis and logistic regression to identify factors related to the occurrence of delirium. **Results:** Of the total 149 patients in the sample, 69 (46.3%) presented delirium during ICU stay, whose mean age, severity of illness and length of ICU stay were statistically higher. The factors related to delirium were: age, midazolam, morphine and propofol. **Conclusion:** Results showed high incidence of ICU delirium associated with older age, use of sedatives and analgesics, emphasizing the need for relevant nursing care to prevent and identify early, patients presenting these characteristics.

### DESCRIPTORS

Delirium; Intensive Care Units; Nursing Care.

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## INTRODUCTION

Delirium is an acute neurological disorder that is frequently observed in Intensive Care Unit (ICU) patients. It is characterized by transitory changes of consciousness and cognition, generally for a short period of time<sup>(1)</sup>. The prevalence of delirium is almost 70% and incidence can reach up to 89%. In addition, patients that developed this disorder performed worst in the clinical outcomes, contributing to extended length of hospital stay, an increase in the possibility of adverse events such as respiratory and neurological complications and higher mortality rate<sup>(1-3)</sup>.

Considering the negative aspects of delirium on patients' prognosis, the evaluation and recognition of this clinical condition by health professionals is important in the context of intensive care. These aspects were observed by 1,384 ICU professionals from 41 North American hospitals who completed a questionnaire about beliefs and practices related to delirium. Among respondents, 86% have recognized that delirium was underdiagnosed, 90% agreed that delirium damaged weaning from mechanical pulmonary ventilation (MPV) and 95% agreed that the occurrence of delirium increased length of hospital stay. Regarding the identification of delirium, 59% agreed to make evaluation to detect it<sup>(4)</sup>. These data reinforce the idea that preventive care and identification should be improved.

Health professionals in the ICU, notably the nursing team, care for confused or agitated patients due to adverse events that can endanger their safety and cause detrimental consequences. Generally, the nursing team is the first to identify behavioral changes in ICU patients<sup>(2)</sup>. This reinforces the importance and need for early identification of delirium by nurses using valid tools, and also for knowledge about potential factors related to the occurrence of delirium in critical care patients.

Therefore, the use of assessment tools to facilitate the recognition of delirium should be encouraged. Among those available to identify delirium in ICU, a review study identified the following instruments: Cognitive Test for Delirium, Intensive Care Delirium Screening Checklist, Neecham Scale, Delirium Detection Score e Confusion Assessment Method for Intensive Care Unit (CAM-ICU)<sup>(5)</sup>.

The CAM-ICU has been broadly used to identify delirium in ICU patients, including those with orotracheal intubation under MPV. It was adapted to the Brazilian Portuguese language and has high sensitivity (72.5%) and specificity (96.2%). Moreover, CAM-ICU is easy to apply and can be used by professionals of the multi-disciplinary team<sup>(6)</sup>. Results from the use of CAM-ICU showed that 91.5% of nurses said that their knowledge about delirium was expanded when they started systematically using the CAM-ICU, while 85.1% said that the tool was user-friendly<sup>(7)</sup>.

Nurses' knowledge about factors that could cause the occurrence of delirium is crucial in planning nursing care and in effectively establishing the communication network with patients and their family members. This knowledge is

also crucial in fostering communication with other members of the multi-disciplinary team to achieve positive improvement in the patients' clinical conditions<sup>(2)</sup>.

Considering the relevance of ICU delirium, it is worth noticing the importance of effective participation by nurses in the prevention and identification of delirium in critical care patients. The study guiding questions were: *Which is the delirium incidence in ICU? Which are the potential factors that contribute to the occurrence of delirium in ICU?* To answer these questions, these were the objectives of this study: identify the incidence of delirium; compare the demographic and clinical characteristics of patients with and without delirium; and verify factors related to delirium in critical care patients.

## METHOD

This prospective, observational cohort design study was carried out in the ICU (Pneumology, Medical and Emergency) of a university hospital in São Paulo, Brazil. These units totaled 17 beds for adult patients from emergency room, operating room and hospitalization units. The study was approved by the Unifesp Research Ethics Committee (report # 1509/11).

The following inclusion criteria were observed to select the convenience sample: minimum age of 18; length of stay in ICU for at least 24 hours. Patients with previously diagnosed cognitive disorders like senile dementia and Alzheimer's illness were not included in the sample.

The data collection form was prepared after an integrative review of the literature composed of items related to patients' characteristics such as: age, sex, comorbidities evaluated through the Age-Adjusted Charlson Comorbidity Index (ACCI), ICU admission type, medical diagnosis, severity of illness according to the Simplified Acute Physiology Score III (SAPS-III), use of sedatives and analgesics, use of MPV, use of physical restraint with strips, length of ICU stay, outcome (discharge and death) and presence or absence of delirium according to the CAM-ICU.

The criteria that define delirium through the CAM-ICU are as follows: 1. acute change or fluctuating course of mental state; 2. inattention; 3. altered level of consciousness; and 4. disorganized thinking. The presence of delirium is defined by the following composition: 1 + 2 + 3 or 1 + 2 + 4<sup>(6)</sup>.

The first CAM-ICU criterion evaluates the presence of acute changes or fluctuating course of mental state in the past 24 hours, through oscillation of the consciousness level according to the Richmond Agitation-Sedation Scale (RASS) or Glasgow's Coma Scale. Evaluation must be performed in sedated patients and patients with no sedation, as well as in those submitted to MPV. Criterion 2 evaluates the patient's attention level through the identification of letters or figures defined by the CAM-ICU. Criterion 3 evaluates the level of consciousness by the time of CAM-ICU application, while in criterion 4 the evaluation of disorganized thinking presence is analyzed by means of simple questions structured by the CAM-ICU<sup>(8)</sup>.

Data were collected by four nurses experienced in intensive care who underwent a 15-hour practical training. By that time, doubts about the detection of delirium using the CAM-ICU were clarified by applying it to ICU patients, and achieving agreement among these applications. This process resulted in 20 applications.

When the training was concluded, nurses went through the ICUs and presented the study objectives to patients meeting the inclusion criteria to obtain their sign in the written informed consent form. When the patient's clinical conditions impaired their cooperation, nurses made contact with a family member or tutor.

The CAM-ICU was applied every 12 hours in the first five days of ICU stay. After that period, if the patient remained in the ICU without presenting the disorder, evaluation was made every other day until the patient's discharge or death. If the patient developed delirium after the 5<sup>th</sup> day, the CAM-ICU was applied every day again for five consecutive days or until interruption.

From January 02 to June 19, 2012, there were 262 hospitalizations, of which 10 patients refused to participate in the study and 103 did not meet the inclusion criteria, totaling 149 patients.

Categorical variables were described in absolute numbers and percentage, whereas the quantitative variables were expressed through mean and standard deviation, or by median and interquartile range. The two-tailed Fisher's test was applied to compare the groups of patients with and without delirium for categorical variables, and the t test or Mann-Whitney test to the ordinal quantitative variables according to data distribution. To identify factors related to delirium, variables with  $p < 0.05$  in univariate analysis were selected, as well as the backward selection method ( $\alpha$  0.05) to process multiple logistic regression. If a variable strongly prevailed over the others, a new model was processed and the variable was excluded from the new analysis. The Hosmer-Lemeshow's test was applied to analyze the regression model goodness-of-fit<sup>(9)</sup>. Analyses were performed using the R 3.0.1 (R Core Team, 2012) software and the significance level adopted was  $p < 0.05$  and confidence interval (CI) of 95%.

## RESULTS

According to the selection criteria, the sample was made up of 149 patients. Of these, 69 (46.3%) presented delirium during ICU stay.

The sample characterization data show significant differences between the groups of patients with and without delirium. Among those presenting delirium the mean age was higher ( $p = 0.001$ ) with higher SAPS-III scores ( $p < 0.001$ ), higher ACCI mean ( $p = 0.001$ ), the prevailing type of ICU admission was medical ( $p < 0.001$ ) and length of ICU stay was longer ( $p < 0.001$ ). Despite the larger number of deaths in the group of patients with delirium, the difference between the groups was not statistically significant (Table 1).

**Table 1** – Patients with and without delirium according to demographic and clinical variables – São Paulo, São Paulo, Brazil, 2012.

Variables	With delirium (n=69)	Without delirium (n=80)	p
Age, median (IQ*)	65 (22.0)	54 (24.25)	0.001 <sup>†</sup>
Sex: Women, n (%)	27 (39.1)	31 (38.8)	1 <sup>‡</sup>
Men, n (%)	42 (60.9)	49 (61.2)	
SAPS-III <sup>§</sup> , mean (SD <sup>  </sup> )	58.2 ( $\pm$ 16.1)	44.5 ( $\pm$ 16.8)	<0.00 <sup>†</sup>
ACCI <sup>**</sup> , median (IQ*)	3 (3.0)	2 (2.25)	0.001 <sup>†</sup>
ICU admission type:			
Surgical, n (%)	7 (10.0)	33 (41.0)	<0.00 <sup>†</sup>
Medical, n (%)	62 (90.0)	47 (59.0)	
ICU <sup>††</sup> stay, median (IQ*)	11 (16.0)	4 (4.0)	<0.00 <sup>†</sup>
Death, n (%)	16 (23.2)	9 (11.2)	0.077 <sup>‡</sup>

\*Interquartile interval; <sup>†</sup>Mann-Witney; <sup>‡</sup>Fischer; <sup>§</sup>Simplified Acute Physiology Score III; <sup>||</sup>Standard deviation; <sup>††</sup>t test;

<sup>\*\*</sup>Age-adjusted Charlson's Comorbidity Index; <sup>††</sup> Intensive Care Unit.

Comparing frequencies between the group of patients with delirium and those without, there are significant differences ( $p < 0.001$ ) regarding the use of MPV, physical restraint, midazolam, fentanyl, propofol, tramal and morphine ( $p = 0.027$ ) (Table 2).

**Table 2** – Patients with and without delirium according to mechanical pulmonary ventilation, physical and therapeutic restraint – São Paulo, São Paulo, Brazil, 2012.

Variables	With delirium (n=69) n (%)	Without delirium (n = 80) n (%)	p*
MPV <sup>†</sup>	54 (78.3)	15 (18.8)	<0.001
Physical restraint	57 (82.6)	8 (10.0)	<0.001
Midazolam	41 (59.4)	9 (11.3)	<0.001
Fentanyl	48 (69.6)	16 (20.0)	<0.001
Propofol	23 (33.3)	6 (7.5)	<0.001
Tramal	48 (69.6)	32 (40.0)	<0.001
Morphine	20 (29.0)	11 (13.8)	0.027

\*Fischer; <sup>†</sup>mechanical pulmonary ventilation.

To identify factors related to delirium, the variables with  $p < 0.05$  in the univariate analysis were firstly related, as follows: age, SAPS-III, ACCI, ICU admission type, ICU stay, MPV, physical restraint, midazolam, fentanyl, propofol and morphine.

The model shows that age ( $p = 0.019$ ) and physical restraint ( $p < 0.001$ ) variables are related to delirium. At every increased year of life the chance for the patient to have delirium increases by 4%, whereas the presence of physical restraint increases by 44.3 times the patient's chance of having delirium. The Hosmer-Lemeshow's test did not reject the model adequacy ( $p = 0.646$ ) (Table 3).

**Table 3** – Logistic regression model according to the delirium dependent variable – São Paulo, São Paulo, Brazil, 2012.

Variable	Estimate	Standard error	OR*	CI <sup>†</sup> 95%	p
Interceptor	-3.85	0.98	0.02	0.00 - 0.15	<0.001
Age	0.04	0.02	1.04	1.01 - 1.07	0.019
Physical restraint	3.79	0.51	44.30	16.15 - 121.48	<0.001

\*Odds ratio; <sup>†</sup>Confidence interval.

The logistic regression model in Table 3 shows that in the inclusion of variables the effect of some factors prevailed over the others, then a new processing was made using the backward method. The logistic regression was processed keeping the midazolam, fentanyl and propofol medicines jointly with the age and physical restraint variables (Table 4).

In the model presented the midazolam, fentanyl and propofol medicines did not reach statistical significance ( $p=0.522$ ,  $0.578$  and  $0.747$ , respectively) (Table 4). Moreover, the Odds Ratio of the variables age (OR 1.04) and physical restraint (OR 40.41 versus 44.3, respectively) remained equal or close to those in Table 3. However, the Hosmer-Lemeshow's test did not reject the model adequacy ( $p=0.557$ ).

**Table 4** – Logistic regression model according to the delirium dependent variable – São Paulo, São Paulo, Brazil, 2012.

Variable	Estimate	Standard error	OR*	CI <sup>†</sup> 95%	p
Interceptor	-3.87	1.01	0.02	0.00 - 0.15	<0.001
Age	0.04	0.02	1.04	1.01 - 1.07	0.019
Physical restraint	3.70	0.73	40.41	9.74 - 167.62	<0.001
Midazolam	0.55	0.85	1.73	0.32 - 9.20	0.522
Fentaniil	-0.48	0.87	0.62	0.11 - 3.38	0.578
Propofol	0.24	0.74	1.27	0.30 - 5.44	0.747

\*Odds ratio; <sup>†</sup>Confidence interval.

Since these variables, notably physical restraint, prevailed over medications in the global logistic regression, a third model was processed, including the medications that reported a significant association with the presence of delirium in the univariate analysis: tramal, midazolam, fentanyl, propofol and morphine. To prevent biases because the model is not controlled by age and sex, these variables were maintained in the analysis.

As observed, the factors related to delirium were age ( $p=0.004$ ) and the following medications: midazolam ( $p<0.001$ ), morphine ( $p=0.036$ ) and propofol ( $p=0.007$ ). In patients taking midazolam the chance of occurrence of delirium was seven times higher; for those taking propofol it was nearly five times higher; and for those taking morphine it was almost three times higher. The

Hosmer-Lemeshow's test did not reject the final model adequacy ( $p = 0.918$ ) (Table 5).

**Table 5** – Logistic regression model according to the delirium dependent variable – São Paulo, São Paulo, Brazil, 2012.

Variable	Estimate	Standard error	OR*	CI <sup>†</sup> 95%	p
Interceptor	-3.52	0.88	0.03	0.01 - 0.17	<0.001
Age	0.04	0.01	1.04	1.01 - 1.07	0.004
Midazolam	1.96	0.46	7.09	2.86 - 17.57	<0.001
Morphine	1.08	0.52	2.95	1.07 - 8.12	0.036
Propofol	1.58	0.59	4.85	1.54 - 15.30	0.007

\*Odds Ratio; <sup>†</sup>Confidence Interval.

## DISCUSSION

Delirium is a complex disorder related to many factors such as: severity of illness; environment; patient care; and iatrogenic factors. Because of these factors, the disorder should be treated using multi-disciplinary care that currently consists of weaning from sedation and early mobilization therapeutic activities, optimization of hearing and vision, and promotion of patients' sleep, among others. Despite the knowledge acquired so far, the everyday use of these kinds of interventions remains sparse<sup>(10)</sup>. Nurses must actively participate in patient care and broaden their knowledge related to delirium to improve their care practices.

The analyses about delirium incidence in the ICU show that it can vary according to patients' characteristics and factors such as therapeutic measures. In the sample of this study made up of medical and surgical patients, the incidence of delirium was 46.3%, similar to the results described in the literature. Studies carried out among populations with the same characteristics found that the incidence of delirium ranged from 9% to 64%<sup>(3,11-12)</sup>. In cardiac surgery ICU it was 13.3% to 34.78%<sup>(1,13)</sup>.

Although the incidence of delirium in these units is considerable, it can be reduced through care delivered by nurses and their staff. Results concerning the efficiency of strategies oriented to preventing delirium among patients in post cardiac surgery showed that in the intervention group the occurrence of delirium was lower in comparison with the group that did not receive it (respectively: 12.24% and 34.78%,  $p=0.009$ )<sup>(13)</sup>. Another study was carried out in a medical and surgical ICU where patients were called by the first names, informed about the place of hospitalization and the development of their clinical condition. These interventions were considered to be protective against the occurrence of delirium<sup>(14)</sup>. It is worth noticing that these are simple interventions that help in preventing delirium, and that nurses should appraise and use these interventions in the nursing care and encourage the staff to do the same.

Among data related to the patients' characteristics, it was observed that older age was associated with delirium, a fact also observed in other studies<sup>(1, 12, 13)</sup>. It is

worth mentioning that the presence of old people in ICU has increased. Severity of illness is another aspect typically associated with delirium. However, this study found that although patients with delirium presented worst clinical conditions according to the SAPS III, this was not a risk factor associated with the disorder. A systematic review carried out to identify risk factors with a strong connection to developing delirium in ICU patients found that, in addition to age and higher severity of illness evaluated through the Acute Physiology and Chronic Health Evaluation II, other clinical conditions were considered to be risky. These were dementia, high blood pressure, emergency surgeries or traumas previous to ICU admission, MPV, metabolic acidosis and coma<sup>(15)</sup>.

Among the variables analyzed in this study, physical restraint was frequently found in the group of patients with delirium and was associated with the disorder. However, due to the shortage of information about the time when restraint was applied, it could not be confirmed as a risk factor. The analysis of this variable was a limitation of the study. Likewise, another study that analyzed this relation only found that the presence of delirium increased the use of sedatives and physical restraint, emphasizing that further investigations will be required to better understand the influence of the use of physical restraint on delirium<sup>(16)</sup>.

Physical restraint may be required in many situations to prevent the occurrence of adverse events. However, nurses and the multidisciplinary team should establish good communication to promote a more judicious use of physical restraint. A study found that ineffective communication not only between professionals, but also between them and patients or family members, negatively influences decisions and practices related to the use of restraint<sup>(17)</sup>.

When it comes to the use of sedatives and analgesics, the results of this study showed that the use of midazolam, morphine and propofol were risk factors in developing delirium.

The results of some studies showed that the use of benzodiazepines like midazolam for critically ill patients favors the emergence of delirium<sup>(3, 18-19)</sup>. However, this hypothesis was not confirmed by the systematic review that analyzed the use of this drug in patients submitted to MPV. Patients that used benzodiazepines stayed longer in the ICU and were more dependent on the MPV. The review suggested the use of dexmedetomidine or propofol instead of benzodiazepines to sedate patients, which reduces the length of ICU stay and MPV duration<sup>(20)</sup>. Other studies found that the use of dexmedetomidine can offer advantages in terms of reducing patient ICU stay and lower risk of delirium<sup>(21-22)</sup>.

Many studies currently recommend the use of protocols or interdisciplinary goals in the use of sedatives and early relief of pain in order to improve the control of delirium in ICU patients<sup>(23-25)</sup>. In this context, the nurse's participation is important because it contributes to reduction of sedative use to the minimum levels sufficient to provide comfort and safety to patients. This practice may lead to a reduced need

for using mechanical restraint devices, allowing for an early start to physical mobilization contributing to better clinical conditions of patients. Moreover, it reduces costs related to therapy and the prevention of delirium<sup>(21-26)</sup>.

Among the protocols involving nurses' participation, the following stand out: Awakening and Breathing Coordination; Delirium Monitoring and Management; and Early Mobility (ABCDE Bundle). These protocols describe a wide range of means to monitor and manage sedation level, MPV, delirium and early mobilization of patients. In the ABCDE Bundle nurses actively participate in the patient's evaluation to define the safe interruption of sedatives and their tolerance<sup>(27)</sup>. Results of this protocol implementation pointed out reduction of delirium from 62.3% to 48.7%, and reduction of MPV time length<sup>(28)</sup>.

Evidence is favorable regarding the use of the set of measures proposed by the ABCDE Bundle. The results of the isolated use of the daily awakening protocol did not confirm reduced occurrence of delirium<sup>(29)</sup>. New studies are needed to discuss the controversies related to risk factors and the preventive and therapeutic measures related to delirium.

Considering that the incidence of delirium in ICU patients is high, and that there are several factors related to the disorder, it is worth highlighting the importance of systematized care and use of specific instruments to detect it. Such care can not only achieve positive results in preventing delirium, but would also raise the team's awareness in performing these measures in a conscious way aimed at controlling the disorder in the ICU.

The study's limitations were related to the sample size; different clinical characteristics of patients included in the analysis; and, lack of detailed information about the exact time when restraint was applied to patients. These factors may have influenced the results found.

## CONCLUSION

Results showed that the incidence of delirium in ICU patients was 46.3%, and factors related to occurrence were older age and use of sedative and analgesics like midazolam, propofol and morphine.

The study reinforces the relevance of nurse's care to prevent delirium through non-pharmacological measures mainly among old patients with higher chances of developing this cognitive disorder in the ICU environment. Nurses can implement strategies to systematically monitor the presence of pain or discomfort and, in this way, better fit the use of analgesics and sedatives.

Regarding early identification of delirium, tools like the CAM-ICU should be used to favor communication using uniform language in the multi-disciplinary team. Many aspects related to delirium are still to be clarified. Specific to nursing, further studies are required to evaluate the use of physical restraints and its occurrence, as well as the use of non-pharmacological interventions to prevent their use.

**RESUMO**

**Objetivo:** Identificar a incidência de delirium, comparar as características demográficas e clínicas dos pacientes com e sem delirium e verificar os fatores relacionados ao delirium em pacientes internados em Unidade de Terapia Intensiva (UTI). **Método:** Coorte prospectiva, cuja amostra foi constituída de pacientes internados em UTI de um hospital universitário. Variáveis demográficas, clínicas e da avaliação com o *Confusion Assessment Method for Intensive Care Unit* para identificação de delirium foram processadas para análise univariada, e regressão logística para identificar fatores relacionados à ocorrência do delirium. **Resultados:** Do total de 149 pacientes da amostra, 69 (46,3%) apresentaram delirium durante a internação na UTI, observando-se que a média da idade, o índice de gravidade e o tempo de permanência nas UTI foram estatisticamente maiores. Os fatores relacionados ao delirium foram: idade, midazolam, morfina e propofol. **Conclusão:** Os resultados mostraram elevada incidência de delirium na UTI e sua ocorrência associada às idades mais avançadas e o uso de sedativos e analgésicos, ressaltando-se a importância da atuação do enfermeiro na prevenção e identificação precoce do quadro nos pacientes com essas características.

**DESCRITORES**

Delírio; Unidades de Terapia Intensiva; Cuidados de Enfermagem.

**RESUMEN**

**Objetivo:** Identificar la incidencia de delirium, comparar las características demográficas y clínicas de los pacientes con y sin delirium y verificar los factores relacionados con el delirium en pacientes ingresados en Unidad de Cuidados Intensivos (UCI). **Método:** Cohorte prospectiva, cuya muestra estuvo constituida de pacientes ingresados en la UCI de un hospital universitario. Variables demográficas, clínicas y de evaluación con el *Confusion Assessment Method for Intensive Care Unit* para identificación de delirium fueron procesadas para análisis univariado y regresión logística a fin de identificar factores relacionados con la ocurrencia del delirium. **Resultados:** Del total de 149 pacientes de la muestra, 69 (46,3%) presentaron delirium durante la estancia en la UCI, observándose que el promedio de edad, el índice de gravedad y el tiempo de estancia en las UCI fueron estadísticamente mayores. Los factores relacionados con el delirium fueron: edad, midazolam, morfina y propofol. **Conclusión:** Los resultados mostraron elevada incidencia de delirium en la UCI y su ocurrencia estuvo asociada con las edades más avanzadas y el uso de sedativo y analgésicos, resaltándose la importancia de la actuación del enfermero en la prevención e identificación precoz del cuadro en los pacientes con dichas características.

**DESCRIPTORES**

Delirio; Unidades de Cuidados Intensivos; Atención de Enfermería.

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