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Delirium in elderly patients: association with educational attainment

Martins S, Paiva JA, Simões MR, Fernandes L. Delirium in elderly patients: association with educational attainment.

Objective: Among cognitive reserve markers, educational attainment is the most widely studied, with several studies establishing a strong association with risk of dementia. However, it has not yet been fully examined in delirium. This study aims to analyse the relationship between educational attainment and delirium.
Methods: The study included elderly hospitalised patients admitted (≥48 h) into an intermediate care unit (IMCU) of Intensive Care Medicine Service. Exclusion criteria were as follows: Glasgow Coma Scale (total ≤ 11), blindness/deafness, inability to communicate or to speak Portuguese. The European Portuguese Version of the Confusion Assessment Method (CAM) was used for delirium assessment.
Results: The final sample (n = 157) had a mean age of 78.8 (SD = 7.6) the majority being female (52.2%), married (51.5%) and with low educational level (49%). According to CAM, 21% of the patients had delirium. The delirium group presented the fewest years of education (median 1 vs. 4), with statistical significance (p = 0.003). Delirium was more frequent among male patients [odds ratio (OR) 0.32; 95% confidence interval (CI) 0.12–0.86; p = 0.023], as well as those patients with lower education (OR 0.76; 95% CI 0.62–0.95; p = 0.016), and with respiratory disease (OR 3.35; 95% CI 1.20–9.33; p = 0.020), after controlling for age and medication.
Conclusion: Similar to previous studies, these findings point to a negative correlation between education and delirium. This study appears as an attempt to contribute to the knowledge about the role of cognitive reserve in risk of delirium, particularly because is the first one that has been carried out in an IMCU, with lower educated elderly patients. Further studies are needed to clarify this relationship considering other markers (e.g. cognitive activities), which can contribute to the definition of preventive strategies.

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Keywords: aged; cognitive reserve; delirium; educational status

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Significant outcomes

- Lower educational levels may be associated with higher risk of delirium development in hospitalised elderly patients.
- Delirium was more frequent among male patients, those patients with lower education and with respiratory disease, after controlling for age and medication.
- These findings might point out in the negative correlation between education and delirium in elderly hospitalised patients, which is in line with some previous studies.

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Limitations

- This is an one-site study, with the selection of a sample recruited from an intermediate care unit in the referred hospital (São João Hospital Centre). So, the generalisability of these findings will need to be confirmed in future studies.
- The sample presented low education. Thus, the restricted range of educational levels may have resulted in attenuated correlations of education with delirium.

Introduction

Delirium, an acute disorder of attention and cognition, is a common and serious complication among elderly hospitalised people, affecting as many as 50% of these patients (1). It has been associated with negative outcomes, such as risk of death, institutionalisation and dementia (2–4). This syndrome is usually multifactorial, resulting on a complex interrelationship between the patient´s baseline vulnerability (predisposing factors) and exposure to noxious insults (precipitating factors) during hospitalisation (4,5).

Taking this into consideration, the concept of reserve capacity can represent an important new conceptualisation to capture this vulnerability to delirium (6,7). This concept was proposed, as a theoretical framework, to explain individual differences in the relationship between neuropathology and cognitive performance (8), in a range of clinical disorders, such as dementia (e.g. 9–13) or brain injury (e.g. 14–16), and in cognitive ageing (17).

Reserve capacity has been examined with respect to the brain and cognitive reserve (18). The first one is related to the structure and integrity of the brain and considers that there are individual differences (accounted for by structural features, such as head size) in the amount of damage that the brain can tolerate before reaching a critical threshold for clinical expression. Cognitive reserve refers to the efficiency with which an individual can use alternate neural networks or cognitive strategies to cope with the brain's pathology. There are two distinct mechanisms underlying this concept: neural reserve (the brain's capacity to cope with pathology by using pre-existing cognitive processes) and neural compensation (recruitment of compensatory networks) (9,18).

Differences in cognitive reserve have been explained as a result of mental stimulation that individuals are exposed to over a lifetime, including educational attainment, complex occupational performance, pre-morbid intelligence or participation in cognitive and stimulating leisure activities (11,19,20). In this context, some instruments have been developed to assess the participation in these activities, such as the Lifetime of Experiences Questionnaire (21). Regarding the pre-morbid intelligence, this indicator has usually been assessed by literacy or vocabulary measures (e.g. National Adult Reading Test) (22,23).

Among the markers of cognitive reserve, educational attainment is the most widely studied, and it is not uncommon to find research where education alone stands in for this concept (19,20).

The robust association between lower educational levels and higher prevalence of dementia suggests that education may be the most important protective factor for dementia (e.g. 13, 24–26). In the context of delirium, studies that analyse the relationship between education and delirium are scarce (6). Among these works, some have reported that individuals with low levels of educational attainment are at greater risk of delirium than individuals with more education (6,27–29). Particularly, Pompei et al. (27) found that low educational levels and living alone were significant risk factors for delirium, whereas more education (beyond 12th grade) was a protective factor. Low educational level was also identified as a risk factor for acute confusional state in elderly patients following hip surgery (28). After these studies, Jones et al. (6) verified in two large prospective cohorts involving hospitalised elderly patients that a 5-year difference in educational attainment was associated with 1.6-fold decrease in the odds of delirium.

Nonetheless, some other studies have not found any association between education and the risk of delirium (30–34). More recently (34), a study examined the relation of brain and cognitive reserve markers (including education) to the risk of postoperative delirium in elderly patients without dementia, in whom the markers, except for vocabulary knowledge, failed to predict delirium.

In spite of these previous studies, it is important to consider that most of them have been carried out in populations with high levels of educational attainment [e.g. in Jones et al. (6), 61% had 7–12 years of education], and in surgical wards (27,28,30,33,34).

In this context, carrying out the present work in a different setting, that is, in intermediate care units (IMCU), could complement the previous studies, aiming to analyse the relationship between educational attainment and delirium in severely ill elderly hospitalised patients. In this way, it is hypothesised that patients with lower education would be more likely

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to develop delirium during hospitalisation than patients with higher levels of education.

Materials and methods

Sample

This study was carried out with a sample of elderly patients recruited from an IMCU of the Intensive Care Medicine Service in the university hospital – São João Hospital Centre (CHSJ), in Porto, Portugal. Inclusion criteria were as follows: aged 65 years and over and admission for at least 48 h. Patients with a total score ≤11 on the Glasgow Coma Scale (35), blindness/deafness, inability to communicate or to speak Portuguese were excluded.

Procedures

The European Portuguese Version of the Confusion Assessment Method (CAM) (36,37) was used for delirium assessment. This instrument assesses the presence, severity and fluctuation of nine delirium features: acute onset and fluctuating course*, inattention*, disorganised thinking*, altered level of consciousness*, disorientation, memory impairment, perceptual disturbances, psychomotor agitation or retardation and altered sleep–wake cycle. It also includes a diagnostic algorithm, based on the four cardinal features of delirium (previously marked with an asterisk). A diagnosis of delirium requires the presence of features 1, 2, and either 3 or 4.

In the original study (36), CAM demonstrated high levels of sensitivity (94%–100%) and specificity (90%–95%), when validated against the ratings of geriatric psychiatrists, and high inter-rater reliability ($k = 0.81–1.0$). In the Portuguese validation study (37), the CAM had a moderate sensitivity (79%) and an excellent specificity (99%), using the *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition (DSM-IV-TR), as reference standard (38), and also good convergent validity, as well as a high inter-rater reliability ($k = 0.65–1.00$).

In the present study, the CAM was rated by a trained interviewer based on observations made during a clinical structured interview and a formal cognitive assessment, using the Mini Mental State Examination (39), a cognitive global measure, and the Digit Span Test (40), an attention and work memory measure. The patient's family or caregivers and nurses, were also interviewed about the patient's prior cognitive performance and any recent cognitive change.

Complete socio-demographic and clinical characteristics of patients and hospital-related data were also obtained through chart review.

The hospital ethics committee approved the present study. Informed consent was obtained from the patient or their closest family, if the patient was unable to decide for him/herself.

Data analysis

The statistical analyses were performed using the Statistical Package for the Social Sciences Version 21.0 for Windows software (SPSS). Patient characteristics are presented as raw frequencies and percentages for categorical variables and as median, minimum and maximum for continuous variables, as normality could not be assumed.

For analysis of differences between the two groups, with and without delirium (according CAM rating), the Mann–Whitney test for continuous variables, χ^2 test for paired categorical variables and Fisher's exact test for dichotomous variables were used at a significance level of 0.05.

A logistic regression analysis was conducted to test whether differences in the risk of delirium during hospitalisation were related to educational attainment, controlling for variables known to be risk factors for delirium (1,41,42). The OR and its 95% CI were calculated. A p-value < 0.05 was considered statistically significant. Education attainment was treated as a continuous variable, considering the total years of formal education that patients had.

Results

In the final sample ($n = 157$), with a mean age of 78.85 (SD = 7.61), the majority was female (52.2%), married (51.5%) and with low education level (0–3 years, 49%). Most of the patients lived with partner (37.6%) at home (93.6%) and had a caregiver (60.9%), in most of cases the son or daughter (45.7%). These socio-demographic characteristics did not differ significantly between the groups with and without delirium, classified by CAM, except for education ($p = 0.003$), with the delirium group presenting the lowest value (Table 1). The median years of education among those who developed delirium was 1 (minimum 0 maximum 9), compared with 4 (minimum 0 maximum 17) years among those who did not (Fig. 1).

In relation to the clinical characteristics, the most common reason for admission was cardiorespiratory problems (56.1%). Concerning the admission type, the most frequent was emergency department (68.6%). The mean of length of stay in IMCU was 7.99 (SD = 5.88) days. The average of the number of comorbidities was 7.86 (SD = 3.40) and most of the patients (78.6%) presented poly-medication major (≥5 medication/day). In this sample, the majority (69.7%) did not consume alcohol (or did not report alcohol intake). According to the CAM, 21% of the

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Table 1. Demographic characteristics of sample

Characteristics	Overall (n = 157)	Delirium (n = 33)	No delirium (n = 124)	p-Value
Age [median (min.–max.)]	79 (65–96)	80 (67–95)	78 (65–96)	0.143*
Gender [n (%)]				
Female	82 (52.2)	15 (45.5)	67 (54.0)	0.381†
Male	75 (47.8)	18 (54.5)	57 (46.0)	
Education [years, median (min.–max.)]	4 (0–17)	1 (0–9)	4 (0–17)	**0.003***
Marital status [n (%)]				
Single	8 (5.1)	1 (3.0)	7 (5.6)	
Married	81 (51.5)	23 (69.7)	58 (46.9)	0.087‡
Divorced/separated	7 (4.5)	–	7 (5.6)	
Widowed	61 (38.9)	9 (27.3)	52 (41.9)	
Living situation [n (%)]				
Alone	33 (21.0)	3 (9.1)	30 (24.2)	
With partner	59 (37.6)	14 (42.4)	45 (36.3)	
With son or daughter	36 (22.9)	9 (27.3)	27 (21.8)	
With partner and son/daughter	15 (9.6)	3 (9.1)	12 (9.7)	0.447‡
With other relatives	6 (3.8)	1 (3.0)	5 (4.0)	
Others	8 (5.1)	3 (9.1)	5 (4.0)	
Place of living/care [n (%)]				
Home	147 (93.6)	30 (90.9)	117 (94.4)	0.439§
Nursing home	10 (6.4)	3 (9.1)	7 (5.6)	
Has a caregiver? [n (%)]				
Yes	92 (60.9)	17 (60.7)	75 (61.0)	0.980†
No	59 (39.1)	11 (39.3)	48 (39.0)	
Caregiver relationship [n (%)]				
Son or daughter	42 (45.7)	9 (52.9)	33 (44.0)	
Spouse	15 (16.3)	4 (23.5)	11 (14.7)	0.356†
Other	35 (38.0)	4 (23.4)	31 (41.3)	

Bold values significant at $p < 0.05$.
Max., maximum; min., minimum.
* Mann–Whitney test.
† χ^2 independent test.
‡ χ^2 exact test.
§ Fisher's exact test.

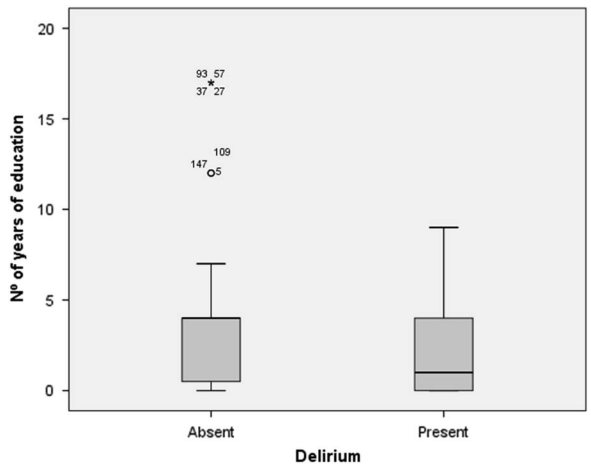


Fig. 1. Number of years of education and delirium. The dots and stars represent outliers and extreme values in the data.

patients had delirium. Comparing the two groups (with and without delirium), significant differences were only verified for admission type ($p = 0.012$) and length of stay in the IMCU ($p = 0.005$), with the delirium group presenting the highest duration of hospitalisation (Table 2).

The Table 3 contains the results of the logistic regression model testing the linear effect of years of education as a predictor of delirium risk during hospitalisation. Through this analysis, it was possible to verify that delirium was more frequent among male patients (OR 0.32; 95% CI 0.12–0.86; $p = 0.023$), as well as those patients with lower education (OR 0.76; 95% CI 0.62–0.95; $p = 0.016$), and with respiratory disease (OR 3.35; 95% CI 1.20–9.33; $p = 0.020$), after controlling for age and total number of medication.

Discussion

The main results of the present study, found that delirium was more frequent among male patients,

Table 2. Clinical characteristics of sample

Characteristics	Overall (n = 157)	Delirium (n = 33)	No delirium (n = 124)	p-Value
Admission type [n (%)]				
Emergency department	107 (68.6)	16 (50.0)	91 (73.4)	
Operating room	16 (10.3)	2 (6.3)	14 (11.3)	
Inter-hospital transfer	23 (14.7)	9 (28.0)	14 (11.3)	**0.012**‡
Intensive care units	7 (4.5)	3 (9.4)	4 (3.2)	
Wards	3 (1.9)	2 (6.3)	1 (0.8)	
Reason for admission [n (%)]				
Cardiorespiratory	88 (56.1)	16 (48.5)	72 (58.1)	
Gastrointestinal	19 (12.1)	3 (9.1)	16 (12.9)	
Urology/nephrology	26 (16.5)	6 (18.1)	20 (16.2)	
Cancer	4 (2.5)	-	4 (3.2)	0.289‡
Neurology	8 (5.1)	4 (12.1)	4 (3.2)	
Fall	7 (4.5)	2 (6.1)	5 (4.0)	
Other	5 (3.2)	2 (6.1)	3 (2.4)	
IMCU length of stay [(days), median (min.–max.)]	6 (3–36)	8 (4–21)	6 (3–36)	**0.005***
Total of comorbidities [median (min.–max.)]	8 (2–16)	7 (2–14)	8 (2–16)	0.068*
Medication [(daily), median (min.–max.)]	7 (0–16)	7 (0–16)	7 (0–16)	0.785*
Poly-medication [n (%)]				
Minor ≤4	33 (21.4)	7 (23.3)	26 (21.0)	0.777†
Major ≥5	121 (78.6)	23 (76.7)	98 (79.0)	
Alcohol consumption [n (%)]				
Yes	36 (30.3)	7 (41.2)	29 (28.4)	0.392§
No	83 (69.7)	10 (58.8)	73 (71.6)	

Bold values significant at $p < 0.05$.
IMCU, Intermediate Care Unit; max., maximum; min., minimum.
* Mann–Whitney test.
† χ^2 independent test.
‡ χ^2 exact test.
§ Fisher's exact test.

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Table 3. Regression model of risk of delirium on educational attainment and control variables

Characteristics	Odds ratios (95% CI)	*p*-Value
Education	0.76 (0.62–0.95)	**0.016***
Age (years)	1.04 (0.98–1.10)	0.169
Gender (women vs. men)	0.32 (0.12–0.86)	**0.023***
Medication	1.02 (0.90–1.17)	0.687
Respiratory disease (yes vs. no)	3.35 (1.20–9.33)	**0.020***

95% CI = 95% confidence interval.
*$p < 0.05$.

those with lower education and with previous respiratory disease.

Male gender is presented as a risk factor for delirium in previous review studies in mixed hospital settings (43,44). In Noimark's review (44), from eight studies analysed, six had reported an association between delirium and male gender, in accordance with the present results.

In agreement with prior studies (e.g. 45–47) the presence of chronic respiratory diseases was recognised as a predisposing risk factor for delirium in hospitalised patients, suggesting that they had some background brain vulnerability to delirium.

In relation to education, the findings of the present study might point to a negative correlation between education and delirium in elderly hospitalised patients, which is in line with some previous studies (6,27–29). Among these, two early prospective studies (27,28) have identified low educational level as a predictor for delirium, but only with a moderate to large effect size. In particular, Pompei et al. (27) found that elderly patients with delirium were less likely than those without delirium to have completed some education beyond the 12th grade (22% vs. 30%, $p < 0.05$), and living alone was also identified as a risk factor. Likewise, Galanakis et al. (28) verified that elementary education only (OR 3.59; 95% CI 1.14–11.25; $p = 0.016$), was a risk factor for delirium in elderly patients undergoing hip surgery.

In another study (6), with two large prospective cohorts of elderly hospitalised patients, a significant statistical difference in the mean years of education was found, with the delirium group presenting the lowest mean (9 vs. 11 years). In the present study, a significant difference regarding years of education was also found (1 vs. 4 years), in spite of the lower levels of educational attainment.

The association between education and delirium found in this work could be explained by the cognitive reserve concept. Accordingly, a higher educational attainment may enhance cognitive reserve by generating new or compensatory cognitive strategies (9,48) and it may increase brain reserve by promoting synaptic growth (49). Considering this, lower education may lead to low cognitive reserve and increased vulnerability to stressor events that could precipitate delirium (50,51). However, since education typically occurs in early lifetime, it is important to consider other forms of complex activities when assessing cognitive reserve (21,52), such as occupational achievement, pre-morbid intelligence and cognitive activities (7,9). On the other hand, higher education can often lead to employment that involves high levels of intellectual and cognitive challenges, and can also lead to larger income, increased well-being, and to other factors that can shape lifestyle and promote involvement in physical, cognitive and social activities over a lifetime (7,53). In this way, it is important to consider that all these factors can contribute to cognitive reserve. In this context, a more recent study (29), which evaluated the same cohorts as the Jones study (6), with hospitalised elderly patients, focussing on the role of activities in the delaying of clinical manifestations of delirium, found that not only education but also leisure activity participation (namely regular physical exercise) were protective against delirium. In addition, activity participation mediated the relationship between education and this syndrome.

It is also important to bear in mind some heterogeneity in the methodological issues between these previous studies and the present work, particularly regarding the setting and sample characteristics. The majority of these studies were carried out in surgical wards, focussing on the relationship between education and postoperative delirium. Despite the increased number of IMCUs in hospitals, there are few studies in the literature regarding delirium in this context, compared with the information on critically ill patient settings. In fact, the present study is the first one on the association between education and delirium in elderly patients recruited from IMCUs.

Moreover, most of these studies included highly educated samples, which is distinct from the current work, with lower educated patients. This may contribute to clarification of the role of only a few years of education in cognitive reserve, considering the scarce number of studies available on the present data.

The importance of assessment with standardised and referenced tools is also noteworthy. Thus, the inclusion of a standardised delirium assessment instrument is an undoubted strength of this study, particularly the recent European Portuguese Version of the CAM (37).

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Nevertheless, this is a one-site study, with the selection of a sample recruited from an IMCU in the CHSJ hospital. So, the generalisability of these findings will need to be confirmed in future studies. Another limitation is related to the sample that presented low education. Thus, the restricted range of educational levels may have resulted in attenuated correlations of education with delirium.

In conclusion, lower educational levels may be associated with higher risk of delirium development in hospitalised elderly patients. These findings simply point out that the previously established hypothesis might be true in this population. Bearing this in mind, future studies are needed to clarify this association, as well as the role of other cognitive reserve markers, such as previous professional occupations, pre-morbid intelligence, cognitive, leisure and physical activities. This pinpoints the increasing interest in specific interventions that could promote cognitive reserve that can contribute to delirium prevention in elderly hospitalised patients.

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Conflicts of Interest

None.

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