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Predictors of Delirium Severity in Intensive Care Unit Patients: Emphasizing the Clinical Importance of Hypoactive Delirium

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SUMMARY

Background: Delirium is a common neuropsychiatric condition in ICU patients, particularly among older adults, and is strongly associated with poor clinical outcomes. However, predictors of delirium severity, especially hypoactive delirium, remain underexplored in the literature. This study aimed to identify predictors of delirium severity, including age, comorbidities, steroid use, and metabolic acidosis, while underscoring the clinical significance of hypoactive delirium.

Methods: This cross-sectional study included 160 ICU patients admitted from September 2016 to June 2017. Potential predictors such as age, steroid use, comorbidities, metabolic acidosis, and ventilator duration were evaluated. Delirium severity was assessed using the Delirium Index (DI).

Results: Multiple regression analysis showed that age ≥ 65 years, number of comorbidities, metabolic acidosis, steroid use, and ventilator duration were significant predictors of delirium severity ($p < 0.05$) and explained 24.4% of the variance. Hypoactive delirium was the most prevalent subtype (90.9%), but its subtle clinical presentation often led to underdiagnosis.

Conclusions: Advanced age, comorbidities, corticosteroid use, metabolic acidosis, and prolonged ventilator support were significant predictors of delirium severity in ICU patients. Although hypoactive delirium was not statistically linked to severity, its high prevalence (90.9%) underscores its relevance. These findings support cognitive assessments in ICUs for early detection and timely intervention. In resource-limited environments, improving delirium recognition and management through focused nursing education and non-pharmacological strategies — such as environmental reorientation, sleep optimization, and individualized care — may enhance patient outcomes. Further multicenter studies are needed to validate these findings across diverse settings and develop tailored protocols for low-resource health-care systems.

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1. Introduction

Delirium is a common and severe condition in ICU patients, especially among older adults, with incidence rates as high as 70–80%.¹ Elderly ICU patients face heightened risks due to delirium's association with adverse outcomes, such as prolonged hospitalization, cognitive decline, post-discharge institutionalization, increased mortality, and substantial healthcare costs stemming from extended ICU stays and additional treatments.² ICU patients with delirium have a two-to-four fold higher mortality risk than those without delirium do.³ Delirium often develops within the first 1–2 days of ICU admission, with the hypoactive subtype frequently underdiagnosed, leading to poorer recovery and higher mortality rates.^{4,5}

The pathophysiology of delirium is multifactorial. The risk factors include advanced age, infections, mechanical ventilation, sedative use, polypharmacy, and metabolic disturbances such as metabolic acidosis,⁶ characterized by arterial pH < 7.35 and plasma bicar-

bonate ($\text{HCO}_3^- < 22$ mmol/L). Metabolic acidosis is common in critically ill patients and may manifest as fatigue, nausea, vomiting, and altered consciousness — symptoms highly relevant to ICU care.⁷ Despite extensive research on delirium onset, the severity and impact of overlapping factors, particularly in hypoactive delirium, remain underexplored. Identifying how factors such as metabolic acidosis influence severity can improve clinical management and preventive strategies.⁶

This study aimed to identify the key predictors of delirium severity in ICU patients, with a particular focus on metabolic acidosis and hypoactive delirium. Conducted in a regional teaching hospital, it highlights the challenges of resource limitations and specialized care demands, providing actionable insights to improve ICU management and patient outcomes.

2. Methods

2.1. Study design and setting

This cross-sectional study was conducted in two intensive care units (ICUs) at a regional teaching hospital in Tainan between Sep-

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tember 2016 and June 2017. The primary objective was to identify factors associated with the severity of delirium by examining patient characteristics, health status, disease severity, and medical treatments.

2.2. Study population

Eligible participants were ICU patients aged 20 years or older admitted to the ICU within 12 hours from the emergency department or general ward, with a Glasgow Coma Scale (GCS) score of 15 or an EVM (eye, verbal, and motor response) score of 10–11 for intubated patients who had been on mechanical ventilation for at least 12 hours. Exclusion criteria included patients with brain injury, pre-existing cognitive impairments, or medication with high doses of morphine (> 50 mg/day), as these factors may influence delirium assessments and confound the results.

2.3. Outcome measure: delirium severity

Delirium severity was measured using the Delirium Index (DI), which scores seven domains — attention, organized thinking, consciousness, orientation, memory, perceptual disturbances, and mobility — from 0 (normal) to 3 (severe), for a total score of 0–21. The DI, chosen for its simplicity, ICU validation, and quick assessment (5–10 minutes), showed strong reliability with a Content Validity Index (CVI) of 0.864.

2.4. Sample size calculation

The sample size, calculated using G*Power for a target power of 0.8 and alpha of 0.05, required at least 138 participants. To account for dropouts, 160 participants were recruited.

2.5. Data collection

Data were collected daily from 11 a.m. to 3 p.m. by the primary investigator for consistency, including demographics, health status, disease severity, and treatment data from electronic records and patient assessments. Quality control involved inter-rater reliability checks and training for DI scoring. The DI, translated into Mandarin using standardized methods, achieved a CVI of 0.86 and a Cronbach's alpha of 0.74, indicating strong validity and reliability.

2.6. Measures

2.6.1. General characteristics

Patient demographics, including gender, age, number of comorbidities, medication use in the past three months, and history of steroid use, were recorded.

2.6.2. Health status

Health status data included physiological parameters, such as arterial blood gas analysis, and assessment of pain levels and delirium subtypes. Arterial blood gas analysis was conducted using the NOVA Stat Profile Critical Care Xpress. Pain was assessed on the 11-point Numeric Rating Scale (NRS-11). Delirium subtypes were categorized as hypoactive, hyperactive, or mixed based on the Richmond Agitation-Sedation Scale (RASS).

2.6.3. Disease severity

Disease severity was evaluated using the Acute Physiology and Chronic Health Evaluation II (APACHE II) score, number of complica-

tions, types of infections, and ICU stay duration. APACHE II provides an estimate of mortality risk based on disease severity within the first 24 hours of ICU admission.

2.6.4. Medical treatment

Medical treatment variables included the duration of mechanical ventilation, the number and types of medications administered, use of physical restraints, and the number of tubes (e.g., intravenous lines, endotracheal tubes) present. Data were collected from medical records and verified through direct observation.

2.7. Statistical analysis

Statistical analysis was conducted in SPSS 20.0. Descriptive statistics summarized demographic and clinical variables. Independent-sample t-tests, one-way ANOVA, chi-square tests, Pearson correlations, and multiple regression were used to identify predictors of delirium severity. Blood biochemistry was analyzed using one-way ANOVA with Tukey's post hoc tests for group comparisons.

2.8. Ethical considerations

This study was approved by the Institutional Review Board of Chi Mei Medical Center (Approval No. 10507_J01), with informed consent obtained and confidentiality strictly maintained.

3. Results

3.1. Participant characteristics and delirium risk factors (Table 1)

Table 1 shows that there were no significant differences between the delirium and no-delirium groups in terms of age, gender, pre-existing conditions, medication use, or steroid history. Metabolic acidosis was significantly more frequent in the delirium group ($p < 0.001$) than in the no-delirium group, while other acid-base imbalances, pain levels, and delirium subtypes showed no meaningful differences.

Patients with delirium experienced more complications ($p = 0.005$) and longer ICU stays ($p = 0.015$) than did those without delirium, despite having similar APACHE II scores and infection rates. Delirium severity scores were numerically higher in the delirium group ($p = 0.102$) than in the no-delirium group, although this difference did not reach statistical significance. Detailed results are provided in Table 1.

3.2. Univariate analysis of ICU patient characteristics and delirium severity (Table 2)

3.2.1. General characteristics

Although female participants had a higher average delirium score than males, the difference was not statistically significant ($p = 0.139$), indicating no clear gender-based variation in this sample. In contrast, participants aged 65 years and older had significantly higher scores compared to those under 65 ($p < 0.001$), suggesting a positive association between advanced age and delirium severity. A statistically significant difference was also observed with respect to steroid use; individuals with a history of steroid use had higher delirium scores than those without ($p = 0.046$).

3.2.2. Health status

3.2.2.1. Blood gas analysis

A significant association was found between blood gas status

Table 1
Participant demographics and delirium-associated risk factors (N = 160).

Variable	No delirium (n = 138) n (%) or M \pm SD	Delirium (n = 22) n (%) or M \pm SD	p-value
General characteristics			
Age			0.216
< 65 years old	50 (36.2)	5 (22.7)	
\geq 65 years old	88 (63.8)	17 (77.3)	
Gender			0.616
Female	58 (42)	8 (36.4)	
Male	80 (58)	14 (63.6)	
Number of past diseases	1.54 \pm 1.29	1.68 \pm 1.13	0.618
Number of medications used in the past 3 months	0.43 \pm 0.65	0.68 \pm 1.00	0.271
History of steroid used	0.07 \pm 0.25	0.14 \pm 0.35	0.369
Health status			
Physiological parameters			
Blood gas analysis			< 0.001
Not collected	34 (24.6)	2 (9.1)	
Normal	51 (37)	3 (13.6)	
Respiratory acidosis	5 (3.6)	0 (0.0)	
Respiratory alkalosis	16 (11.6)	1 (4.5)	
Metabolic acidosis	10 (7.3)	15 (68.2)	
Metabolic alkalosis	22 (15.9)	1 (4.5)	
Pain (Mean)	2.14 \pm 1.85	1.55 \pm 1.55	0.146
Delirium subtypes			0.192
Hypoactive	134 (97.1)	20 (90.9)	
Hyperactive	4 (2.9)	2 (9.1)	
Mixed-type	0 (0.0)	0 (0.0)	
Disease severity			
Number of complications	(0.05 \pm 0.21)	(0.22 \pm 0.43)	0.005
The number of types of infection (Mean)	0.01 \pm 0.09	0.05 \pm 0.21	0.415
ICU stay	3.63 \pm 1.46	4.45 \pm 1.54	0.015
APACHE II score	14.85 \pm 4.81	15.86 \pm 4.30	0.352
Medical treatment			
Number of days of ventilator used	0.53 \pm 1.34	0.77 \pm 1.72	0.448
Number of the types of drugs used	1.67 \pm 1.12	2.00 \pm 1.98	0.200
The body restraint device used	0.04 \pm 0.19	0.05 \pm 0.21	0.834
Number of tubes on the body	3.36 \pm 1.56	3.86 \pm 1.75	0.170
Delirium severity	0.33 \pm 0.58	0.88 \pm 1.46	0.102

Note: 1. p-values were calculated using the chi-square test for categorical variables and the independent samples t-test for continuous variables.

2. Percentages may not total 100% due to rounding.

3. APACHE II, Acute Physiology and Chronic Health Evaluation II.

Table 2
Univariate analysis of ICU patient characteristics and delirium severity (N = 160).

Variable	n	Mean	SD	t/F	p-value	Post hoc
General characteristics						
Gender						
Female	66	0.52	0.92	1.489	0.139	
Male	94	0.32	0.66			
Age						
< 65 years old	55	0.13	0.39	-4.106	< 0.001	
\geq 65 years old	105	0.54	0.89			
Medical history of steroid use						
No	148	0.34	0.70	-2.238	0.046	
Yes	12	1.17	1.27			
Health status						
Physiological parameters						
Blood gas analysis (N = 124)						
1. Normal blood gas	54	0.33	0.58	3.259	0.008	
2. Respiratory acidosis	5	0.20	0.45			
3. Respiratory alkalosis	17	0.35	0.49			
4. Metabolic acidosis	25	0.92	1.41			4 > 1
5. Metabolic alkalosis	23	0.43	0.66			
Delirium subtypes						
Hypoactive delirium	154	0.41	0.79	0.558	0.456	
Hyperactive delirium	6	0.17	0.41			
Mixed-type delirium	0	0.00	0.00			

Note: F = one-way ANOVA; t = Independent t-test.

and delirium severity scores ($p = 0.008$, one-way ANOVA). Post hoc comparisons revealed that patients with metabolic acidosis had significantly higher delirium scores compared to those with normal blood gas profiles. However, no significant differences were observed between the normal group and those with respiratory acidosis, respiratory alkalosis, or metabolic alkalosis. Among the various blood gas abnormalities assessed, only metabolic acidosis was significantly associated with increased delirium severity.

3.2.2.2. Delirium subtypes

Among the delirium subtypes, hypoactive delirium was the most prevalent, while hyperactive delirium occurred less frequently. No cases of mixed-type delirium were observed. There were no statistically significant differences in delirium severity scores among the subtypes ($p = 0.456$).

3.3. Correlation analysis of risk factors for delirium severity (Table 3)

3.3.1. General characteristics

Delirium severity was positively associated with both the number of comorbid conditions and the number of drugs used in the past three months, suggesting that a higher medical burden and polypharmacy are linked to more severe symptoms.

3.3.2. Health status

There was no significant correlation between pain level and delirium severity.

3.3.3. Disease severity

None of the variables examined — including the number of complications, types of infection, ICU length of stay, and APACHE II score — were significantly associated with delirium severity in this sample.

3.3.4. Medical treatment

Among medical treatment variables, only the number of days on mechanical ventilation showed a significant positive correlation with delirium severity. Other treatment-related factors, including

physical restraint use, number of tubes, and number of drug types administered, were not significantly associated.

3.4. Key predictive risk factors for delirium severity (Table 4)

Hierarchical regression analysis identified several key predictors of delirium severity:

Model 1, which included age ≥ 65 ($\beta = 0.191$, $p = 0.013$), number of pre-existing diseases ($\beta = 0.184$, $p = 0.018$), and steroid use ($\beta = 0.224$, $p = 0.010$), explained 16% of the variance.

Model 2, which added health status variables, increased the explained variance to 22%, with metabolic acidosis emerging as a significant predictor ($\beta = 0.247$, $p = 0.001$).

Model 3, further included medical treatment variables, raising the explained variance to 24.4%, with ventilator duration identified as a significant factor ($\beta = 0.164$, $p = 0.028$).

In the final Model, age ($\beta = 0.184$, $p = 0.015$), number of pre-existing diseases ($\beta = 0.175$, $p = 0.021$), steroid use ($\beta = 0.175$, $p = 0.042$), metabolic acidosis ($\beta = 0.238$, $p = 0.002$), and ventilator dura-

Table 3
Correlation analysis of factors affecting delirium severity (N = 160).

Variable	<i>r</i>	<i>p</i> -value
General characteristics		
Number of diseases developed in the past	0.23	0.003
Number of drugs used in the past 3 months	0.24	0.002
Health status		
Pain	0.08	0.292
Disease severity		
Number of complications	-0.11	0.183
The number of types of infection	-0.06	0.466
ICU stay days	0.12	0.144
APACHE II score	0.12	0.118
Medical treatment		
Number of days of ventilator use	0.214	0.007
Body restraint device used	0.025	0.750
Number of tubes on the body	0.124	0.118
Number of the types of drugs used	0.037	0.647

Note: 1. *r* = Correlation coefficient.

2. APACHE II, Acute Physiology and Chronic Health Evaluation II.

Table 4
Hierarchical regression analysis of predictors of delirium severity (N = 160).

Variable	Model 1		Model 2		Model 3	
	β	<i>p</i>	β	<i>p</i>	β	<i>p</i>
General characteristics						
Age						
≥ 65 years old (ref: < 65)	0.191	0.013*	0.167	0.027*	0.184	0.015*
Number of diseases developed in the past	0.184	0.018*	0.178	0.020*	0.175	0.021*
Number of drugs used in the past 3 months	0.024*	0.792	0.028*	0.753	0.011	0.905
Medical history of steroid use (ref: no use)	0.224	0.010**	0.197	0.023*	0.175	0.042*
Health status						
Blood gas analysis (ref: normal)						
Respiratory acidosis			-0.035	0.634	-0.025	0.731
Respiratory alkalosis			0.038	0.615	0.034	0.648
Metabolic acidosis			0.247	0.001**	0.238	0.002**
Metabolic alkalosis			0.062	0.409	0.036	0.627
Medical treatment						
Number of days of ventilator use					0.164	0.028*
Model statistics						
R	0.400		0.468		0.494	
R ²	0.160		0.219		0.244	
R ² change	0.160		0.059		0.025*	
Adjusted R ²	0.138		0.178		0.199	
F	7.382	< 0.001***	5.295	< 0.001***	5.377	< 0.001***

Note: β : standardized coefficients.

tion ($\beta = 0.164$, $p = 0.028$) remained significant predictors, collectively explaining 24.4% of the variance in delirium severity.

4. Discussion

This study employed hierarchical regression analysis to examine multiple factors associated with the severity of delirium in ICU patients. Age ≥ 65 years, the number of diseases developed in the past, steroid use, metabolic acidosis, and duration of ventilator use emerged as significant independent predictors of delirium severity. These findings have important implications for ICU clinical management and offer valuable insights for early identification and targeted intervention strategies, particularly in resource-limited settings.

4.1. Delirium subtypes and clinical outcomes

Hypoactive delirium was the predominant subtype observed in this study, accounting for 90.9% of all delirium cases. This finding is consistent with previous research indicating that hypoactive delirium, characterized by symptoms such as lethargy, apathy, and reduced responsiveness, is frequently under-recognized in clinical settings. Due to its subtle presentation, this subtype is often misdiagnosed or missed entirely, potentially delaying appropriate intervention. Prior studies have linked hypoactive delirium to higher mortality rates and poorer long-term outcomes, emphasizing the need for heightened clinical vigilance.⁵

The present study, conducted in a regional teaching hospital, also reflects the challenges of delirium management in resource-limited environments. Compared to tertiary medical centers, which have more robust staffing and infrastructure, smaller hospitals may face barriers such as insufficient training in delirium recognition and limited implementation of standardized cognitive assessments. These findings underscore the importance of context-appropriate interventions, including simplified screening tools and targeted education programs, to enhance early detection and management of delirium — particularly the hypoactive subtype — in diverse care settings.

4.2. Risk factors influencing delirium severity

4.2.1. Impact of age

Older patients experienced more severe delirium, consistent with previous studies highlighting age as a key risk factor. Impaired cortisol regulation in older adults may contribute to this vulnerability, reinforcing the importance of regular assessments to enable timely intervention.⁸

4.2.2. Number of diseases developed in the past

The number of pre-existing diseases showed a consistent and statistically significant positive correlation with delirium severity across multiple analyses. This repeated association suggests that a greater comorbidity burden is not only linked to the occurrence of delirium but may also contribute to its severity. Recent evidence highlights that patients with multiple chronic conditions are more susceptible to heightened systemic inflammation, diminished physiological reserve, and increased cognitive vulnerability in critical care settings.⁹ These findings underscore the clinical importance of early identification and close monitoring of patients with high comorbidity burdens, who may be at elevated risk for more severe delirium trajectories and poorer recovery outcomes.

4.2.3. Effects of steroid use

Steroid use was significantly associated with delirium severity.

Steroids can disrupt sleep and induce psychostimulant effects such as mood swings, exacerbating delirium symptoms. Future research should explore the mechanisms by which steroid use affects sleep quality and delirium severity in ICU patients.¹⁰

4.2.4. Association of metabolic acidosis

Metabolic acidosis emerged as a significant predictor of delirium severity, in line with previous findings. This association was identified in a subgroup of 124 patients with available blood gas analysis data. ICU patients with metabolic acidosis require close monitoring and timely interventions to address delirium symptoms and prevent further complications.¹¹ Integrating metabolic acidosis monitoring into routine assessments can enhance early detection and intervention.

4.2.5. Polypharmacy and ventilator use

Both polypharmacy and prolonged ventilator use^{12,13} were correlated with increased delirium severity. Thorough medication review upon ICU admission and regular reorientation strategies for ventilated patients may mitigate these risks.

4.3. Nursing implications and recommendations

To address the challenges of delirium management, especially in resource-limited settings, several strategies are recommended, as follows.

4.3.1. Routine screening and assessment

Nursing staff should prioritize cognitive assessments for high-risk patients, such as older adults, patients with metabolic acidosis, or those on ventilators. The use of tools such as the CAM-ICU, DI, or RASS daily can facilitate the early detection of subtle symptoms, particularly those associated with hypoactive delirium.¹⁴

4.3.2. Non-pharmacological interventions

Strategies such as environmental orientation, optimizing sleep hygiene, and promoting social interaction can reduce delirium risk and improve patient outcomes. For example, maintaining a familiar and supportive environment helps reduce anxiety and cognitive disorientation.¹⁴

4.3.3. Personalized care plans

Individualized care plans are essential for managing high-risk patients. For those with metabolic acidosis, intensive monitoring to maintain acid–base balance can optimize outcomes, even in resource-constrained settings.¹⁴

4.3.4. Enhanced nursing training

Regular training sessions focused on delirium recognition and management, including case-based learning, can empower nursing staff to better address hypoactive delirium symptoms and apply evidence-based interventions effectively.¹⁵

4.4. Clinical implications and preventive measures

The identification of risk factors such as age, steroid use, metabolic acidosis, and ventilator use supports targeted preventive measures. The NICE guidelines¹⁴ emphasize early delirium detection in high-risk patients through reorientation, hydration, and sleep hygiene. For resource-limited hospitals, low-cost solutions like brief nursing training programs and simplified tools such as the DI or RASS can improve early detection and management. These scalable strate-

gies are practical for diverse settings. This study highlights specific risk factors and preventive approaches suited to resource-constrained environments, offering actionable insights to enhance delirium care and improve patient outcomes.

4.5. Limitations and future directions

This study identified age, number of diseases developed in the past, metabolic acidosis, steroid use, and ventilator duration as key predictors of delirium severity in ICU patients. Conducted in a resource-limited regional hospital, it has highlighted challenges such as the need for enhancement of staff training and implementation of streamlined screening protocols, particularly for hypoactive delirium.

Limitations included its single-center design and cross-sectional nature, which restrict causal inference. Additionally, factors like sleep quality were not assessed. Blood gas analysis was available for 124 out of the 160 participants, with two delirium patients excluded from this analysis due to missing data. Although this slightly reduced the subgroup size, the significant association between metabolic acidosis and delirium remained robust.

Future research should focus on multicenter longitudinal studies to validate these findings and explore the impact of environmental and staffing factors on delirium severity. Further studies are also needed to investigate the long-term effects of hypoactive delirium on patient recovery and strategies to reduce associated mortality.

5. Conclusions

This study identified age, number of diseases developed in the past, steroid use, metabolic acidosis, and ventilator duration as significant predictors of delirium severity in ICU patients. Although hypoactive delirium was not statistically associated with severity, it accounted for 90.9% of all delirium cases, underscoring its critical clinical importance. This highlights the need for routine cognitive assessments, as hypoactive delirium is often overlooked in clinical practice, making timely intervention more challenging. Conducted in a resource-limited regional hospital, this study emphasizes the challenges of delirium management, including limited training and constrained resources. Enhanced nursing education and the implementation of non-pharmacological interventions, such as environmental orientation, optimizing sleep hygiene, and personalized care plans, are crucial for mitigating delirium risk and improving outcomes.

Future multicenter studies are needed to validate these findings in diverse clinical settings and to explore tailored protocols for resource-limited environments aimed at reducing the long-term impact of delirium on critical care outcomes.

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Competing interests

None declared.

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