

Delirium incidence, risk factors and outcomes in a New Zealand tertiary intensive care unit: a retrospective, observational, single-centre study

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ABSTRACT

AIM: Our aim was to determine the incidence of delirium in a tertiary intensive care unit (ICU) in Auckland, New Zealand compared to other Australasian ICUs. To determine the incidence of delirium among different ethnicities and identify risk factors and outcomes of patients experiencing delirium.

METHODS: The design was a retrospective observational study. The setting was a single-centre, 24 bed, tertiary ICU in Auckland, New Zealand. The participants were two hundred and twenty-two patients admitted to the ICU over 10 months in 2019. The main outcome measures were incidence of delirium, identified using the Confusion Assessment Method – ICU (CAM-ICU) screening, antipsychotic prescription, 12-month mortality, and ICU discharge disposition.

RESULTS: Fifty of the 222 (23%) patients had delirium. There was no association between the incidence of delirium and ethnicity ($p=0.39$). The risk of delirium increased with ICU duration of stay (odds ratio [OR]: 1.003, 95% CI, 1.001–1.005, $p=0.004$), days on vasopressors ($p<0.001$) and days on mechanical ventilation ($p<0.001$). Thirty-three of the 50 (66%) patients received at least one antipsychotic medication. Twelve-month mortality was not associated with delirium (OR: 0.97, 95% CI 0.73–1.22, $p=0.81$). Delirium was not associated with ICU discharge disposition ($p=0.20$).

CONCLUSIONS: The incidence of delirium in this single-centre, tertiary Auckland ICU was comparable to other Australasian ICUs. There was no difference in the incidence of delirium between different ethnicities. Positive associations to delirium included length of stay in ICU, number of days on vasopressors and duration of mechanical ventilation. Delirium was not associated with an increased risk of 12-month mortality and was not associated with ICU discharge disposition.

Delirium is the acute onset of potentially reversible cerebral dysfunction characterised by disturbances in awareness and attention, accompanied by changes in cognition.¹ The prevalence of delirium in patients in the intensive care unit (ICU) is high, ranging from 20–40% overall^{2,3} and up to 80% in patients who are mechanically ventilated.⁴ The presence of delirium is associated with higher mortality,⁴ longer ICU admission,⁴ longer hospital length of stay^{3,4} and long-term cognitive impairment⁵ compared to the absence of delirium. Delirium is also a distressing experience for patients and their families.

Delirium is under-diagnosed in the ICU.⁶ The Society of Critical Care Medicine (SCCM) recommends using validated tools such as the Confusion Assessment Method – ICU (CAM-ICU) and Intensive Care Delirium Screening Checklist (ICDSC) to screen for delirium.⁷ In addition to a variety of non-pharmacological interventions, antipsychotics are commonly used to treat delirium in patients in

the ICU.^{8,9} A point prevalence study conducted by the Australian and New Zealand Intensive Care Society (ANZICS) in 2019 found that across 44 ICUs in Australia and New Zealand, 54% of patients had a delirium assessment and of those 20% had delirium.⁹ Eighteen percent of patients had been prescribed an antipsychotic drug and 41% of those having an antipsychotic drug did not have a delirium assessment.

Multinational models have been used to predict the likelihood of delirium in the ICU. The E-PRE DELIRIC¹⁰ model uses nine risk factors (age, history of cognitive impairment, history of alcohol misuse, blood urea nitrogen [BUN], admission category, urgent admission, mean arterial blood pressure, use of corticosteroids, and respiratory failure) collected at the time of ICU admission, and the PRE-DELIRIC¹¹ model uses 10 risk factors (age, Acute Physiology and Chronic Health Evaluation II [APACHE-II] score, coma, urgent admission [unplanned ICU admission], admission category

[surgical, medical, trauma, neurological/neurosurgical], infection, coma, use of sedatives, morphine use, BUN, and the presence of metabolic acidosis) collected within 24 hours of ICU admission. Additional risk factors that have been found to have a strong association with delirium include coma 24 hours before delirium assessment, pre-ICU emergency surgery, high American Society of Anesthesiologists (ASA) score, and blood transfusions.⁷

Inequity in health service delivery and outcomes between Māori and non-Māori are well documented in the New Zealand health system.¹² Previous studies have shown that Māori patients in the ICU are younger and more likely to be admitted with sepsis and trauma, and they are more likely to require dialysis.¹³ A recent study has also suggested Māori have higher mortality at day 180 post-ICU admission than non-Māori.¹⁴ However, it is unclear how these inequities relate to the development and treatment of delirium in the ICU.

Middlemore Hospital serves approximately half a million people, and its catchment area includes a higher proportion of Māori and Pacific peoples than that of other metropolitan ICUs in New Zealand.¹⁵ There are specific demographic factors in this patient population that may influence the rate of ICU admission and subsequent development of delirium, including high levels of social disadvantage, prevalence of comorbidities and high rates of alcohol misuse.¹⁵

We hypothesised that because of the unique demographics of Middlemore Hospital, the incidence of delirium would be different compared to other metropolitan ICUs in Australia and New Zealand. Further, we hypothesised that the incidence of delirium would differ in Māori and Pacific peoples compared to non-Māori and non-Pacific peoples.

Methods

We did a single-centre, retrospective, observational study of delirium in adult patients admitted to the Middlemore Critical Care Complex over 10 months in 2019. The Middlemore Critical Care Complex is a 24-bed adult and paediatric tertiary intensive ICU located in South Auckland, New Zealand.

Ethics approval

The study was approved by the Auckland Health Research Ethics Committee (AH23443).

Research question

Our primary research question was to determine the incidence of delirium in patients admitted to Middlemore Hospital ICU and compare the incidence to published data from other metropolitan ICUs. Our secondary research question was to determine the incidence of delirium among different ethnic groups admitted to the ICU at Middlemore Hospital. A further secondary research question was to determine risk factors for delirium and outcomes among patients experiencing delirium.

Inclusion and exclusion criteria

We included all patients 18 years or older admitted to ICU for more than 24 hours from January 2019 to September 2019. We included repeat presentations if the patient had not developed delirium during the first presentation or if the episode of delirium had resolved at the time of the repeat presentation. We excluded patients readmitted with persisting delirium from their first presentation.

Data source and data collection

National Health Index (NHI) numbers of patients admitted to ICU were obtained from the ICU admission logbook. NHI numbers were used to collect patient data from the electronic medical record. Outcome and illness severity scores were obtained from the ANZICS Adult Patient Database (ANZICS-APD), a binational clinical quality registry dataset, collected by the ANZICS Centre for Outcomes and Resources Evaluation. Data were collected during the period between January 2021 and September 2021.

Daily CAM-ICU assessment was either positive or negative for delirium. An unable to assess (UTA) was documented if the patient was comatose, with a Richmond Agitation-Sedation Scale (RASS) score of -5 to -4. Other appropriate reasons for UTA include a physical limitation to perform CAM-ICU, such as the inability to squeeze hands, hearing impairment or a language barrier.¹⁶ Days in which no assessment was performed were recorded as absent.

We collected data on age, sex, ethnicity, admission diagnostic category, the presence of infection in the first 24 hours of ICU admission, illness severity (APACHE III score), comorbidities, duration of mechanical ventilation, duration of vasopressor support, ICU length of stay, use of drugs for treating delirium, post-ICU disposition and date of death (if applicable). Comorbidities comprised a history of

alcohol misuse, a history of cognitive impairment, a history of mental health diagnosis and preadmission antipsychotic prescription. Data were collected on the use of the following drugs for treating delirium, as these were the most common antipsychotics used in our unit: quetiapine, haloperidol and risperidone.

Definitions of terms

Delirium was defined as the presence of at least one positive CAM-ICU score. Ethnicity was defined using the Ministry of Health – Manatū Hauora definition, “*The ethnic group or groups that people identify with or feel they belong to*”,¹⁷ as identified by the patient or a family member at the time their NHI was first assigned. Admission diagnosis was categorised as medical, surgical, neurological or trauma. The presence of infection in the first 24 hours was defined as the administration of antibiotics or documented suspicion of infection in the clinical record.

Data analysis and presentation

Categorical variables are presented as proportions (%) and continuous variables as median (interquartile range [IQR]) or mean (standard deviation [SD]). The association between delirium and categorical variables was assessed using a Chi-squared test (multiple categories) or a Fisher’s exact test (binary categories). The association

between delirium and continuous variables was assessed using univariate logistic regression. The association between delirium and survival was assessed using univariate Cox regression. The association between delirium and ethnicity was also assessed using multivariable logistic regression; model covariates comprised age, sex, diagnostic category and APACHE III score. Data analyses are presented as odds ratios (ORs) and 95% confidence intervals (95% CIs) (logistic regression) or p-values (Fisher’s exact and Chi-squared tests). In all cases $p \leq 0.05$ or a 95% CI that excluded one was considered statistically significant.

Data were tabulated in Microsoft Excel (Microsoft Corporation, Redmond, Washington, United States of America [USA]) and analysed in SAS (v9.4; SAS Institute, Cary, North Carolina, USA) and R (v4.2.2, R Foundation for Statistical Computing, Vienna, Austria).

Results

Patients

A total of 514 patients were admitted to the ICU over the 10-month study period. Two hundred and ninety-two (57%) patients were excluded (Figure 1). No potential participants were excluded due to ICU readmission with persisting delirium. Table 1 summarises the demographic characteristics

Figure 1: Flow diagram of patients included in the study.

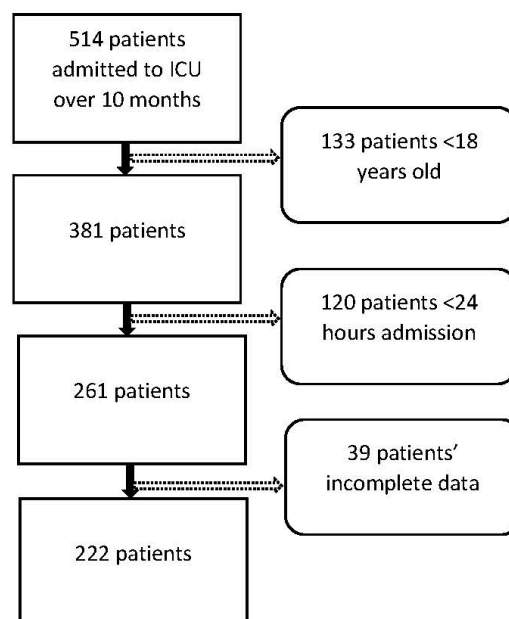


Table 1: Patient description.

		Mean (SD)	Median (IQR)	Range
Age		50±17.8	52 (37–65)	18–83
Illness severity	Length of stay in ICU (hours)	127±160.3	70 (43–140)	22–1224
	Acute Physiology and Chronic Health Evaluation (APACHE) III	70±33.8	67 (44–91)	5–174
	Days on vasopressors	2.8±3.4	2 (0–4)	0–24
	Days on mechanical ventilation	3.8±5.9	2 (1–4)	0–38
		N/222 (%)		
Gender	Male	146 (66)		
	Female	76 (34)		
Ethnicity	European	78 (35)		
	Māori	46 (21)		
	Asian	28 (13)		
	Pacific	65 (29)		
	Other	5 (2)		
Diagnosis category	Medical	118 (53)		
	Surgical	46 (21)		
	Trauma	43 (19)		
	Neurological	15 (7)		
Emergency admission	Yes	207 (93)		
Infection in the first 24 hours	Yes	119 (54)		
Medical history	Mental health	26 (12)		
	Cognitive impairment	0 (0)		
	Alcohol misuse	14 (6)		

Table 2: Age by ethnicity.

Ethnicity	Mean (SD)	Median (IQR)	Range
European	57±17.9	57 (45–71)	19–83
Māori	44±17.4	43 (28–60)	18–80
Asian	49±16.2	49 (37–59)	20–74
Pacific	48±16.2	48(38–62)	18–78
Other	50±16.9	50 (44–62)	21–70

of patients included in the analysis.

The age of patients by ethnicity group is shown in Table 2.

Primary outcome

Fifty of 222 (23%) patients had delirium. From a total of 1,490 ICU days, 109/1,490 (7%) were CAM-ICU positive, 758/1,490 (51%) were CAM-ICU negative, 535/1,490 (36%) were UTA and 88/1,490 (6%) were not performed and not UTA. Among patients who were CAM-ICU positive, the median (IQR) duration of delirium was 1 day (1–3 days).

Secondary outcomes

There was no association between the incidence of delirium and ethnicity ($p=0.39$) (Table 3).

The risk of delirium was not associated with age ($p=0.20$), sex ($p=0.97$), diagnostic category ($p=0.67$), emergency of admission ($p=0.79$) or infection in the first 24 hours ($p=0.30$) (Appendix Table 1). A history of alcohol misuse ($p=0.90$) and a history of mental illness ($p=0.41$) were not associated with delirium (Appendix Table 1).

Higher APACHE III score was not associated with delirium (OR: 1.01, 95% CI, 1.00–1.02, $p=0.28$), but ICU length of stay (OR: 1.003, 95% CI, 1.001–1.005, $p=0.004$), days on vasopressors ($p<0.001$) and days on mechanical ventilation ($p<0.001$) were associated with increased delirium (Appendix Table 1). In the multivariable model, there was no association between delirium and ethnicity after controlling for age, sex, diagnostic category and illness severity (APACHE III).

The most commonly used antipsychotic was quetiapine, followed by haloperidol and risperidone (Table 4). Thirty-three of 50 (66%) patients with delirium received at least one antipsychotic medication. In patients with no delirium, 40 of 172 (23%) were prescribed an antipsychotic. Of the 20 patients who were already on an antipsychotic before hospital admission, 10 had their medications continued in the ICU.

One-year mortality was not associated with delirium (OR: 0.97, 95% CI, 0.73–1.22, $p=0.81$) but was significantly associated with days where the patient was UTA (OR: 1.14, 95% CI, 1.05–1.26, $p=0.004$) (Appendix Table 2). Delirium was not associated with ICU discharge disposition ($p=0.20$) (Appendix Table 3).

Discussion

In this single-centre, retrospective observational study from a metropolitan, tertiary ICU in South Auckland, the incidence of delirium was 23%. There was no association between ethnicity and the incidence of delirium. However, delirium was associated with ICU length of stay, number of days treated with vasopressors and number of days on mechanical ventilation. Most patients (66%) with delirium were given at least one antipsychotic. Delirium was not associated with increased 12-month mortality or post-ICU disposition. The incidence of delirium observed in this study is similar to that reported in other Australasian ICUs, which ranges from 18–45%.^{9,18,19}

Table 3: Incidence of delirium by ethnicity.

Ethnicity	N/N (%)
European	22/78 (28)
Māori	11/46 (24)
Asian	6/28 (21)
Pacific	11/65 (17)
Other	0/5 (0)

Table 4: Antipsychotic prescription.

Medication	N/50 (%)
Haloperidol	12 (24)
Quetiapine	31 (62)
Risperidone	1 (2)

Studies in patients in ICU in New Zealand have shown differences between Māori and Pacific peoples compared to European patients. Māori and Pacific peoples are younger, more comorbid and have a higher illness severity score compared to their European counterparts.^{13,14,20} Mortality among Māori (but not Pacific peoples) is also higher.¹⁴ Additionally, Māori patients are more likely to be admitted with sepsis and trauma and more likely to require dialysis than non-Māori.¹³ Multivariable regression in our study did not demonstrate an association between ethnicity and delirium when controlling for age, sex or illness severity. There was no disparity between the proportion of Māori and Pacific people in the community and those admitted to the ICU in the two studies performed on behalf of the ANZICS CORE Management Committee.^{14,20} In our study, the proportion of Māori and Pacific people admitted to the ICU was higher than in the community. The Middlemore Hospital catchment comprises 16% Māori and 22% Pacific peoples. By comparison, Māori and Pacific patients accounted for 21% and 29% of our study population, respectively.¹⁵

To our knowledge, this is the first study to examine the incidence of ICU delirium between Māori and non-Māori. We are aware of only one study investigating ethnicity as a risk factor for ICU delirium. That study, from the USA, found African Americans aged between 18 and 49 years had lower rates of delirium compared to Caucasians of similar age.²¹ This difference was not found in older age groups.

The study has obvious limitations. The relatively small sample size and retrospective, observational nature of the study mean there is a risk of missing real associations (i.e., of a type II error statistical error). In particular, we cannot be sure there is no relationship between delirium and ethnicity. As a single-centre study, we must also be cautious about generalising our findings in the ICU in different jurisdictions. We did not correct for multiple statistical testing. Consequently, there is an increased risk of observing false positive findings (i.e., type I statistical error),²² even though the associations found are plausible and consistent with other findings in the literature.⁴

Although the CAM-ICU assessment is accurate and reliable across multiple ICU settings,^{23,24} it has not been examined in our unit. Furthermore, inappropriate assignment of UTA in evaluations may be significant, with rates ranging from 19–30% in the literature.²⁵ A USA study by Awan

et al. suggested that inappropriate UTA scores were also more likely in non-white patients.²⁶ As such, it is possible that inappropriate UTA scores contributed to the lack of association between delirium and ethnicity. Furthermore, inappropriate UTA may explain why our study did not find an association between delirium and the APACHE III score and delirium and mortality. It is likely that patients with high APACHE III scores were comatose or sedated to facilitate intensive care therapies, such as mechanical ventilation, and therefore categorised as UTA (either appropriately or inappropriately) and not CAM-ICU positive. This is further supported by the finding that those with more UTA days had a higher mortality.

Despite recognised differences in the South Auckland population,¹⁵ there does not appear to be a notable difference in delirium incidence compared with other metropolitan ICUs. While the lack of association between ethnicity and delirium may appear reassuring, the finding should be viewed with caution for the reasons outlined above.

Future investigations to explore possible inequities in this area could include qualitative studies of the experience of delirium among different ethnicities in the ICU. It would also be important to understand the relationship between CAM-ICU assessments, treatment decisions, and patient and family satisfaction. Because family engagement and empowerment have been shown to reduce delirium²⁷ and improve survival in the ICU, it may be even more important when considering the greater emphasis on family kinship and community in Māori and Pacific populations.^{28,29} Leveraging these cultural values may be essential to preventing delirium and delivering more patient-centred care and satisfaction to these groups.

Conclusion

The incidence of delirium in our study, despite recognised differences in our local population, is comparable to other Australasian ICUs. We found no difference in the incidence of delirium between different ethnic groups, although the sample size was too small to draw definitive conclusions. We found positive associations with delirium and length of ICU stay, number of days on vasopressors and mechanical ventilation. Delirium was not associated with a difference in mortality or post-ICU disposition.

COMPETING INTERESTS

Nil.

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Appendix

Appendix Table 1: Delirium in subcategories.

	Delirium present N=50			Delirium not present N=172		
	Mean (SD)	Median (IQR)	Range	Mean (SD)	Median (IQR)	Range
Intensive care unit length of stay (hours)	193 (169.8)	137 (61–287)	28–766	108 (152.0)	64 (40–102)	22–1,224
Acute Physiology and Chronic Health Evaluation (APACHE) III	75 (34.8)	70 (48–98)	5–174	69 (33.4)	67 (42–89)	11–161
Days on mechanical ventilation	6.2 (6.8)	5 (1–8)	0–31	3 (5.5)	2 (1–3)	0–38
Days on vasopressors	4.7 (4.9)	3 (1–6)	0–24	2 (2.6)	2 (0–3)	0–14
		N/50 (%)		N/172 (%)		
Gender	Male	33 (66)		113 (66)		
	Female	17 (34)		33 (19)		
Diagnosis category	Medical	27 (54)		91 (53)		
	Surgical	8 (16)		38 (22)		
	Trauma	12 (24)		31 (18)		
	Neurological	3 (6)		12 (7)		
Emergency admission	Yes	47 (94)		160 (93)		
	No	3 (6)		12 (7)		
Infection in the first 24 hours	Yes	30 (60)		89 (52)		
	No	20 (40)		83 (48)		
Mental health	Yes	8 (16)		18 (10)		
	No	42 (84)		154 (90)		
Cognitive impairment	Yes	0 (0)		0 (0)		
	No	50 (100)		172 (100)		
Alcohol misuse	Yes	3 (6)		11 (6)		
	No	47 (94)		161 (94)		

Appendix Table 2: Twelve-month mortality.

	All patients N/58 (%)
Delirium present	14 (24)
Delirium absent	44 (76)

Appendix Table 3: Intensive care unit (ICU) outcomes in patients with and without delirium.

	Delirium present N/50 (%)	Delirium not present N/172 (%)
Ward	46 (92)	140 (81)
Died	3 (6)	24 (14)
Other hospital/ICU	1 (2)	8 (5)