Risk factors for incident delirium in an acute general medical setting: a retrospective case – control study

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Risk Factors for Incident Delirium in an Acute General Medical Setting: A Retrospective Case – Control Study.

Authors:

Emily J Tomlinson, RN PhD[1], Nicole M Phillips, Associate Professor PhD [1,2], Mohammadreza Mohebbi, Senior Research Fellow Biostatistics PhD[3] Alison M Hutchinson, Professor of Nursing PhD[1, 2, 4]

1. Deakin University, Geelong, Australia, School of Nursing and Midwifery
2. Centre for Quality and Patient Safety Research, Faculty of Health, Deakin University
3. Deakin University, Geelong, Australia, Faculty of Health, Biostatistics Unit
4. Centre for Nursing Research - Deakin University and Monash Health Partnership, Monash Health, Clayton, Australia

Correspondence to:

Dr Emily Jane Tomlinson

Deakin University
221 Burwood Hwy
Burwood VIC 3125
Australia
Ph: 61 3 9246 8715.
Email: emily.cull@deakin.edu.au

Data Sharing

Extra data are available in the form of raw de-identified information extracted from patient medical records. Data is also available regarding a small group of patients that were not identified as cases or controls and were examined separately. These data are available in an

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SPSS data sheet. Our statistical analysis is also available on request. Extra data are available by emailing emily.cull@deakin.edu.au

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ABSTRACT

Aims and Objectives: To determine predisposing and precipitating risk factors for incident delirium in medical patients during an acute hospital admission.

Background: Incident delirium is the most common complication of hospital admission for older patients. Up to 30% of hospitalised medical patients experience incident delirium. Determining risk factors for delirium is important for identifying patients that are most susceptible to incident delirium.

Design: Retrospective case-control study with two controls per case.

Methods: An audit tool was used to review medical records of patients admitted to acute medical units for data regarding potential risk factors for delirium. Data was collected between August 2013 and March 2014 at three hospital sites of a healthcare organisation in Melbourne, Australia. Cases were 161 patients admitted to an acute medical ward and diagnosed with incident delirium between 1st January 2012 and 31st December 2013. Controls were 321 patients sampled from the acute medical population admitted within the same time range, stratified for admission location and who did not develop incident delirium during hospitalisation.

Results: Identified using logistic regression modelling, predisposing risk factors for incident delirium were: dementia, cognitive impairment, functional impairment, previous delirium, and fracture on admission. Precipitating risk factors for incident delirium were: use of an indwelling catheter, adding more than three medications during admission and having an abnormal sodium level during admission.

Conclusions: Multiple risk factors for incident delirium exist; patients with a history of delirium, dementia and cognitive impairment are at greatest risk of developing delirium during hospitalisation.

Relevance to clinical practice: Nurses and other health care professionals should be aware of patients that have one or more risk factors for incident delirium. Knowledge of risk factors for delirium has the potential to increase the recognition and understanding of patients who are vulnerable to delirium. Early recognition and prevention of delirium can contribute to improved patients safety and reduction in harm.

Keywords: delirium, risk factor, medical patients, acute care, case-control

ARTICLE SUMMARY

What does this paper contribute to the wider global clinical community?

- This study has provided a preliminary understanding of the risk factors for delirium in the medical setting in an Australian setting and further research can be conducted to compare findings between Australian hospitals.
- Information and education can be provided to nursing staff in the clinical setting regarding risk factors that contribute to a patient's vulnerability to delirium. Increased knowledge and understanding may lead to increased awareness of delirium and identification of patients at risk.
- Patients who have a prior diagnosis of dementia, or cognitive impairment are at greatest risk. Nurses should observe and screen for signs of cognitive deterioration in order to detect a possible delirium. Nurses should also be vigilant about speaking with patients and their families about any cognitive impairment and also past history of a delirium in order to adequately estimate the risk of delirium.

Keywords: Incident delirium, Case-control study, Risk factor, Cognitive Impairment, Recognition, Medical Patients.

INTRODUCTION

Delirium is a clinical syndrome that has potentially serious personal, social, and financial consequences for patients (Cole 2005). It can lead to increased morbidity and mortality with worse cognitive recovery for patients following an episode of delirium (Young & Inouye 2007). Delirium is defined by the American Psychiatric Association (APA) as "a disturbance of attention or awareness that is accompanied by a change in baseline cognition that cannot be better explained by a pre-existing or evolving neurocognitive disorder (NCD)"(American Psychiatric Association 2013). The onset of delirium can be short, presenting within a few hours or days of admission to hospital (Inouye 2006). Delirium may be categorised as prevalent delirium, which is present on admission to hospital, or incident delirium, which develops during hospitalisation (Gofton 2011). Because incident delirium has potential to be prevented, healthcare professionals should be particularly concerned with identifying patients at risk and implementing preventative strategies to reduce the risk of harmful consequences of incident delirium in hospitalised patients (Leslie & Inouye 2011).

BACKGROUND

Delirium is a complex syndrome that may be due to the interaction of physiological illness and pre-existing risk factors (Elie et al. 1998, Elmore 2002, Inouye et al. 2014). Researchers have attempted to explain the physiological processes that cause delirium (Choi et al. 2012, Flacker & Lipsitz 1999, MacLullich et al. 2008) and proposed various hypotheses and multiple interacting theories including: reduced blood flow to the brain due to ageing (Flacker & Lipsitz 1999), dysfunction in metabolism within the brain or an overall insufficiency of the cerebral cortex (Dasgupta & Hillier 2010, Engel &

Romano 1959), cholinergic deficiency (Flacker & Lipsitz 1999), and an overreaction of the body's natural stress response, with a corresponding increase in systematic inflammation (MacLullich et al. 2008). Despite these theories, the specific neurological processes that occur in the brain remain unclear (Rigney 2010). This may be because a number of clinical conditions such as sepsis or severe illness can cause a delirium. However, the clinical conditions may not necessarily occur in the same combinations for each case of delirium (Kamholz 2010). That is, for two patients with similar clinical characteristics, one may develop delirium, while the other may not. Although delirium may be caused by just one factor, in older people the cause of delirium is usually multifactorial and involving many different factors (Inouye et al. 2014). This is particularly concerning for nurses as it is difficult to detect which patient may be more susceptible to developing delirium and knowledge of these factors is important.

Development of delirium is not confined to a particular hospital setting; in fact, it is one of the most widespread clinical disorders across all health care settings (O'Hanlon et al. 2014). Incidence rates for delirium have been reported to range between 3 – 29% in acute medical settings and as high as 80% in intensive care settings (Siddiqi et al. 2006). While signs and symptoms of delirium are consistent across settings, the mechanisms behind its development may be very different (Rigney 2010), indicating a potentially unique set of factors that may increase the risk for delirium. Patients in a different clinical areas will be exposed to a different set of risk factors and research that examines these differing set of risk factors in patient populations (such as surgical, intensive care unit (ICU) or medical) will help to isolate factors related to delirium in particular diagnostic or clinical groups. For example, anaesthetic drugs can increase the risk of delirium in patients who undergo surgery. However, patients in medical settings, who have not been exposed to this risk will have a different set of factors which could increase their vulnerability. A number of studies have investigated delirium in the intensive care unit (ICU) setting (Divatia 2006, McNicoll et al. 2003) and

the surgical setting (Adunsky et al. 2003, Marcantonio et al. 1994, Pandharipande et al. 2008), but relatively few studies specific to the general medical setting have been undertaken. This information is important, as risk factors found only in the medical settings can be monitored for patients who are admitted for to hospital for medical reasons. Nurses working in these areas can be more attentive to specific risk factors for delirium.

Risk factors known to increase a patient's vulnerability to delirium include: dementia, cognitive impairment, severe medical illness, functional impairment, hearing or vision impairment and use of restraints (Bjoro 2008, Dahl et al. 2010, Elie et al. 1998, Inouye 1999, Inouye 1998, Inouye & Charpentier 1996). A recent systematic review investigated incident delirium in acute medical in-patients (Cull et al. 2013) and the results indicated that factors such as dementia, cognitive impairment and functional impairment were strongly association with incident delirium in medical in-patients. Advanced age of greater than 80 years was not indicated as a risk factor for delirium in this population, suggesting other factors like dementia were more predictive of incident delirium (Cull et al. 2013). Limitations of the studies in this systematic review included the potential for bias in the reporting of only significant results and the omission of certain patient data when reporting the results of modelling for possible risk factors. A further limitation of some studies was the failure to compare characteristics of study participants who developed delirium against the characteristics of those who did not, which prevented the use of those data in meta-analysis. Furthermore, none of the included studies were undertaken in the Australian setting.

The development of delirium can lead to significant and serious consequences for the patient. These can include increase mortality and morbidity, increased risk of long term cognitive impairment, higher rates of falls, and longer lengths or stay in hospital (Inouye et al. 2014). Health-care professionals, especially nurses, should be aware of risk factors for delirium in order to implement

proactive strategies to prevent its onset (Voyer et al. 2007). Rates of delirium have been shown to be reduced if screening procedures are put in place (Martinez et al. 2015). This information is clinically important for nurses who are frequent bedside caregivers and have the potential to improve the safety of care provided and also reduce harm to patients. This case-control study therefore aimed to identify both predisposing and precipitating risk factors for incident delirium in patients admitted to acute medical wards in the Australian hospital setting.

METHODS

Study design

We undertook a retrospective case-control study, auditing the medical records of patients admitted to a medical setting over a 2-year period (1st January 2012 to 31st December 2013) at an acute public healthcare organisation in Melbourne, Australia.

The healthcare organisation comprised of seven hospitals. Three of the hospitals had acute medical wards, so these three sites were included in this study.

Participants

Cases

A report containing the medical record numbers for potential cases were obtained from the hospital discharge data. Cases were determined by a diagnosis of delirium coded in the medical record discharge summary. The report also contained the date of discharge and the type of admission (e.g. medical), enabling the relevant records to be retrieved via an online patient record system used within the organisation. Following a patient's discharge from hospital the paper medical record is

scanned electronically and filed in the electronic record system. Records scanned into the record system include all in-patient progress notes, emergency progress notes, admission forms, assessment tools, medication charts and discharge summaries. Records of the patients coded for delirium were assessed to confirm whether or not the patient had a delirium. This was confirmed using a chart review method for delirium and included documenting evidence from the medical record regarding words used to describe patients with delirium (e.g. confused, agitated, aggressive, vague), date of onset of symptoms, who documented the signs of delirium and date delirium diagnosed. Records were also assessed to confirm inclusion in the review based on the inclusion criteria. Inclusion criteria for cases were: patients aged 18 years and over, admitted to a medical unit with no evidence of delirium, and developed incident delirium during hospitalisation (diagnosed in the medical history). Exclusion criteria were: patients with a diagnosis of delirium on admission to hospital, patients with delirium tremens or drug and alcohol intoxication, patients admitted to an intensive care unit (ICU) or critical care unit (CCU), a psychiatric or sub-acute facility, surgical patients, and patients who had surgery during admission.

Controls

Control patients were selected randomly from medical patients who had no diagnosis of delirium during admission. The decision support services department at the health-care organisation used a random number generator to identify patients in the control group. Cases were all over the age of 42, and therefore a random sample of patients aged 42 years and older without a code for delirium was retrieved for the controls. Inclusion criteria for controls were: admitted to a medical unit with no evidence of delirium, and did not develop incident delirium during hospitalisation. Exclusion criteria were the same as for cases. Cases and Controls were stratified according to admission location and equal ratio of one case and two controls were selected for the three hospitals sampled.

Sample size

Sample size was calculated based on Type I error of 0.05, power of 0.8 and 2 controls per case ratio. Based on these assumptions 151 cases and 302 controls enabled us to detect a minimum odds ratio (OR) of 2.0.

Data collection

A structured audit tool developed by the researchers was used to extract data from medical records. The audit tool was customised into a digital form, created using the 'Tap Forms' (©2013 Tap Zapp Software Inc) application on an iPad. Data were obtained using the entire patient medical record for the admission episode under examination.

Data collected from each of the medical records included age, gender, diagnosis on admission, living status prior to admission, length of stay in hospital, and place of discharge. Possible predisposing risk factors were also assessed. These included: dementia, cognitive impairment, functional decline (scored by the Katz Index of Activity of Daily living using information in the medical history), visual impairment, hearing impairment, depression, previous delirium and other comorbid conditions. Documentation of the diagnosis must have been included in the medical record and was considered present if included. If the patient was described as having cognitive impairment, they were considered to have cognitive impairment (although degree of cognitive impairment may not have been measured). Any Mini Mental State Exam (MMSE) scores recorded on admission were also extracted.

Information regarding possible precipitating risk factors was also extracted. Factors were considered to be present if documentation in the medical record supported the presence of these factors, including use of indwelling catheter, use of restraints, abnormal sodium levels (from routine blood

tests) and addition of new medications (by using medication chart during hospitalisation compared to medication reconciliation from filled in by pharmacist on patient admission to hospital).

Data collection was conducted over an eight-month period, from August 2013 to March 2014. Following data collection, data files were exported from the iPad application 'Tap Forms' (©2013 Tap Zapp Software Inc) to an excel spread sheet. The data were first checked for errors, specifically looking for values that fell outside the range of possible values for a variable. Errors or missing information were subsequently corrected if detected. Evidence of missing data prompted a re-review of the medical record to obtain the missing information. As a result, there is minimal missing data for this study. For three patients certain documentation was missing from their file in which case, for the respective variable, a code to indicate the data were not available was entered into the field. In order to reduce potential bias regarding outcomes and the presence of delirium, only patients that had been diagnosed with delirium in the medical record were included as cases. During the review of control patients, if delirium was suspected but not diagnosed, this record was excluded.

Statistical analysis

Data analysis was performed using IBM SPSS (Statistical Package for the Social Sciences) Version 22.0. The relationships between potential predisposing and precipitating factors of incident delirium were examined. To assess the difference between cases and controls, Chi-square was used to explore the relationship and the differences among categorical variables. When exploring the differences in mean scores between cases and controls, the independent samples t-test was used. Logistic regression modelling was also used to analyse the relationship between multiple independent variables and the presence of delirium. Selection of predictors for the logistic regression modelling was determined by using the results of the bivariate analysis performed with potential risk factor variables. Backward variable selection method with entry p-value = 0.1 and exit

p-value = 0.05 has been implemented. Logistic regression was therefore performed on all important (p-value < 0.1) variables detected in the bivariate analysis (Abbott 2014).

Ethical approval

The ethical guidelines and principles as set out in the National Statement on Ethical Conduct in Human Research (National Health and Medical Research Council 2007 (updated 2015)) and the Australian Code for the Responsible Conduct of Research (the Code) (Australian Research Council 2007) were adhered to in this study. A waiver of consent was sought for reviewing medical records and formal ethics approval was obtained from both the Human Research Ethics Committee at Deakin University and the respective healthcare organisation.

RESULTS

Two hundred and ninety three medical patients were coded for an episode of incident delirium during admission to hospital between 1st January 2012 and 31st December 2013. Consistent with exclusion criteria, 137 patient records were excluded, most because there were documented signs of delirium on admission to hospital. The remaining 156 patient records were included as cases. During the record review for the control group, a further five cases were identified as having a documented medical diagnosis of delirium during their hospital stay and their records were included as cases. The total number of cases was 161 and total number of controls was 321 (selected to preserve the 2 by 1 ratio).

The difference in mean ages of the case (M = 84.11, SD = 7.3) and control groups (M = 77.69, SD 11.8, *t* (457.35) = 7.30, p < 0.00) was significant. The mean age difference between the groups was 6.4 years (95% CI: 4.69 to 8.14). Refer to Table 1 for the baseline characteristics of patients in the case and control groups.

Predisposing Risk factors

Results for the Chi-square tests to examine the relationship between possible predisposing risk factor variables and presence of incident delirium are presented in Table 2.

Risk factors found to have a significant association with incident delirium at the p = 0.1 level in bivariate analysis were simultaneously analysed using logistic regression to determine factors associated with delirium. The logistic regression model indicated that eight independent variables were strongly associated with incident delirium in this medical patient population (Table 3). Patients who previously experienced delirium had just over 16 times greater odds of developing delirium compared to controls. Similarly, patients that had a diagnosis of dementia or who had cognitive impairment had two times greater odds of developing delirium. Having a fracture on admission or functional impairment also significantly increased a patient's likelihood of developing delirium.

Precipitating Risk factors

Results of the Chi-square tests to determine precipitating risk factors associated with delirium are presented in Table 4.

Logistic regression models indicated that three independent variables for precipitating factors were strongly associated with delirium (Table 5). Adding more than three new medications during an admission to hospital increased the patients' odds of developing delirium by just over three times. Using an indwelling catheter during admission also increased the odds of developing incident delirium by two times, and having an abnormal sodium level during admission also increased the odds of developing delirium compared to controls.

DISCUSSION

Risk factors identified in this study highlight a variety of factors that can contribute to incident delirium. The findings of this study support existing research findings that dementia is one of the leading risk factors for delirium across a range of hospital settings (Inouye 2006). Patients that developed delirium were also likely to be older than patients with no delirium and this also supports previous research (Elie et al. 1998). However, logistic regression models including age greater than 80 years did not find this to be a significant risk factor for delirium. This suggests that advanced age *alone* does not contribute individually to an increased risk of delirium.

Cognitive impairment was identified as a risk factor for incident delirium in this medical patient population. The relationship between cognitive impairment and delirium has frequently been examined in the literature and evidence shows an increased risk for delirium if cognitive impairment is present (Harwood et al. 1997, Jackson et al. 2004, MacLullich et al. 2009). As a result, assessment of cognition on admission is important in order to determine a patient's possible risk for delirium. Voyer et al. (2007) identified that when determining risk for delirium, severity of prior cognitive impairment was less important than the patient's cognitive status on admission. That is, recent deterioration in level of cognition appeared to be more important in determining delirium risk. Although the Mini Mental State Exam (MMSE) was not used to assess level of cognition of patients in the case-control study, a patient whose family was documented to state that the patient had some cognitive impairment (which was not previously diagnosed) had greater odds of developing incident delirium than a patient who had not been described as having cognitive impairment. Therefore, health professionals should be listening to and considering the input of family members in regards to reporting the patient's cognition status. Health professionals should also consider information from family members regarding a patient's cognition as a cue to conduct a formal cognitive assessment on the patient.

Patients who had a history of a previous episode of delirium had a higher risk for incident delirium in this study. This finding is supported by previous research (Inouye et al. 2014). However, because this case-control study was conducted retrospectively, inclusion of these data required documentation of the previous episode of delirium. It is possible that patients who developed delirium were more likely to have a previous delirium documented because health professionals were more inclined to investigate for evidence of previous delirium when the patient was currently experiencing delirium. The presence of delirium could therefore have resulted in more patients with delirium having an episode of previous delirium documented and therefore influenced the results. Results of this study indicate that patients who experience delirium during hospitalisation should be informed of the diagnosis and the risk of subsequent episodes of delirium during future admissions.

Functional impairment was also found to be an independent predictor for incident delirium. This finding is consistent with the findings of other research. Specifically, previous research has shown that functional dependence, immobility, low levels of activity and a history of falls are risk factors for delirium (Inouye et al. 1999, Margiotta et al. 2006). These findings highlight the importance of providing a safe environment in the clinical setting where patients can be encouraged to undertake activities independently. Patients with pre-existing functional impairment, therefore, need to be well supported in the hospital setting in order to reduce the risk of developing delirium or becoming more functionally dependent during hospital admission.

Findings of the study also revealed that having a fracture on admission increased the risk of incident delirium. This finding concurs with other research on this topic (Radinovic et al. 2015). The most common fractures experienced by patients in the current study were hip fractures. In this study, the type of fracture was not independently investigated for its relationship with incident delirium. It is important to note that patients in this study were treated conservatively for their hip fractures (such

as bed rest); patients who underwent surgery to treat hip fractures were excluded, as surgery was an exclusion criteria for the study. Factors such as pain and narcotic use were also not included in the logistic regression model. Future prospective studies will need to include these factors in relation to fractures and risk for delirium in medical patients. Schor et al. (1992) also found that fracture on admission was an independent risk factor for delirium. However, the authors do not identify the type of fracture present on admission and low numbers of patients experienced a fracture. Schor et al. (1992) also included patients from both the medical and surgical populations and it was not clear how patients with fractures were managed or if they had undergone surgical intervention. Much research has been undertaken to assess the risk factors for delirium among hip fracture patients following surgery, yet little research has investigated the risk of fracture among patients receiving conservative management. The findings of this study suggest that patients admitted with a fracture and managed conservatively should be carefully monitored for incident delirium.

Factors previously identified as precipitating risk factors for delirium in patients during an acute admission are: use of physical restraints, malnutrition, more than three medications added, use of a bladder catheter, and any iatrogenic event (Inouye & Charpentier 1996). This information informed the selection of precipitating factors examined in our case-control study. However, due to the nature of retrospective analysis it was difficult to assess some risk factors. For example, malnutrition was defined in the study by Inouye and Charpentier (1996) as an albumin less than 30 g/L. Albumin levels were rarely measured by the medical team for patients included in this study and therefore could not be assessed. Pain was also not assessed as a precipitating factor for delirium due to the inconsistencies of documenting pain scores experienced by patients. Data was unable to be retrieved retrospectively regarding pain. Use of narcotics was also not examined as a precipitating risk factor and should be considered in future prospective research.

Other potential precipitating risk factors examined in our study included use of an indwelling catheter, benzodiazepines, physical restraints, adding more than three medications, abnormal sodium, and one environmental factor: moving wards. Consistent with the findings of Inouye and Charpentier (1996) multivariate logistic regression showed that having an indwelling catheter and adding more than three medications during admission, were independently associated with delirium. We also found that evidence of an abnormal sodium level during admission was independently associated with incident delirium supporting the findings of a systematic review by Elie et al.(1998). Use of benzodiazepines was associated with an increased risk for delirium in bivariate analysis, but was not independently associated with delirium risk in the logistic regression.

Bivariate analysis indicated use of physical restraints was also associated with delirium. However, as there was no documented use of restraint for control group patients, this variable could not be included in the logistic regression model. There is evidence to suggest a relationship between restraint use and delirium (Inouye & Charpentier 1996), but in our study it is unclear if the relationship is causative or reactive. In our study, patients who developed delirium were often restrained in order to control behaviours exhibited after delirium developed. Therefore, the results do not definitively show that restraints are a risk factor for incident delirium, or if they are used in response to patients displaying behaviours common to delirium, such as aggression and agitation. However, restraints do pose a serious threat to patients with delirium and should be avoided.

The limitations of this research should be acknowledged. One of the limitations was the retrospective analysis of medical records. Identifying incident delirium from retrospective reviews of medical records is likely to underestimate the true extent of the syndrome. In order to minimise this uncertainty, the review was limited to the medical records of patients diagnosed with delirium, based on discharge summary documentation and was confirmed using chart review methods for

delirium. The other consideration is that there was no documented evidence of the diagnosis of delirium based the DSM criteria using a diagnostic tool. It is possible that patients who had delirium may have been missed using this method. Retrospective reviewing of medical records also inhibited the inclusion of potential precipitating risk factors for delirium including pain, as this was not able to be assessed retrospectively and documentation of patient pain scores was inconsistent.

Another limitation of this retrospective case-control study is the potential for differential reporting of information between cases and controls. For example, for patients exhibiting signs of delirium, doctors may have been more likely to investigate for evidence of a past history of delirium. Conversely, patients who did not develop delirium during admission may not have had a previous episode of delirium documented, even if they had previously had delirium. External validity and generalisability of the findings may be limited to the Australian setting.

As limited previous research has been conducted in the Australian setting regarding risk factors for delirium, this study has provided some fundamental building blocks for further prospective research into risk factors for delirium in an Australian setting. Data found in this research will help to inform future research into risk factors for delirium in medical settings in an Australian context. This research will also help to inform nursing staff working in the clinical setting about which patients may be more vulnerable to developing incident delirium.

CONCLUSION

To the best of the authors' knowledge, this is the first study that examined risk factors specific to medical patients in the Australian setting. Factors that are of particular concern include dementia, cognitive impairment, previous delirium, and functional impairment. This study builds on international research that also shows both dementia and cognitive impairment have a strong

relationship with incident delirium in the acute general medical setting. Further research is needed in this setting to test the likelihood that the presence of these factors will predict delirium and how they can be used to assess a patient's level of risk for incident delirium.

RELEVANCE TO CLINICAL PRACTICE

- Delirium is a serious neurocognitive disorder which has the potential to have significant harm for patients. The knowledge and understanding that certain predisposing and precipitating factors can contribute to an increased risk for delirium is important and should be understood by all healthcare professionals working at the bedside. This research has provided further clinical evidence for both predisposing and precipitating factors that can increase a patients risk for delirium.
- Clinical nurses should have an understanding of the risk factors for delirium in order to implement preventative strategies for patients at high risk and be aware of the potential for patients to develop delirium.
- Early recognition and implementation of risk reduction interventions can significantly impact on the incidence of delirium in acute medical settings.

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ETHICS APPROVAL

Deakin University Human Research Ethics Committee, Project ID 2013 – 201 and the Eastern Health Human Research Ethics Committee, Project ID LR05/1314.

COMPETING INTERESTS

None declared

LICENCE TO PUBLICATION

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TRANSPARENCY DECLARATION

The lead author affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

CONTRIBUTORSHIP STATEMENT

Contributors: ET initiated project, developed study protocol, designed data collection tools, conducted data collection, cleaned and analysed the data with the assistance of MM, and drafted and revised the paper. She is guarantor. NP and AH contributed to the study design, monitored data collection and contributed to the drafting and revision of the paper. MM developed and wrote the

statistical analysis plan, conducted sample size calculations, assisted with data analysis and contributed to drafting and revising the paper.

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Table 1. Baseline characteristics of cases and controls

	Case Delirium N = 161 N (%)	**Control N= 321 N (%)**
Mean age (SD)	84.11 (7.4)	77.69 (11.8)
Gender		
Female	94 (58.4)	172 (53.6)
Male	67 (41.6)	149 (46.4)
Living status on admission		
Home alone	49 (30.4)	86 (26.8)
Home with services	9 (5.6)	14 (4.4)
Living with family	72 (44.7)	178 (55.5)
Low level care	18 (11.2)	27 (8.4)
High level care	13 (8.1)	16 (5.0)
Level of functioning		
Independent with all ADL (Katz score 5 - 6)	88 (54.7)	255 (79.4)
Independent with most ADL, requires assistance with some (Katz score 3-4)	42 (26.1)	38 (11.8)
Assistance required for most ADL (Katz score 2)	17 (10.6)	23 (7.2)
Full assistance required (Katz score 0)	14 (8.7)	5 (1.6)
Reported Cognition on admission		
Cognition reported as normal	76 (47.2)	246 (76.6)
Reported cognitive issues (no diagnosis)	13 (8.1)	6 (1.9)
Mild cognitive impairment	6 (3.7)	0
Some memory loss	40 (24.8)	49 (15.3)
Dementia	26 (16.1)	20 (6.2)

Note: ADL – Activities of Daily Living

Table 2. Chi-square comparisons of predisposing risk factors for incident delirium

Predisposing Factor present	Case (N = 161) n (%)	Control (N = 321) n (%)	Odds Ratio (95 % CI)	*p*
Age > 80 years	124 (77.0)	178 (55.5)	2.69 (1.75 – 4.13)	<0.01
Anaemia	6 (3.7)	13 (4.0)	1.09 (0.41 – 2.92)	1.0
Cancer	21 (13.0)	44 (13.7)	0.94 (0.54 – 1.65)	0.95
COAD	27 (16.8)	77 (24.0)	1.57 (0.96 – 2.55)	0.09
Cognitive impairment	61 (37.9)	54 (16.8)	3.01 (1.96 – 4.65)	<0.01
Depression	35 (21.7)	53 (16.5)	1.41 (0.87 – 2.26)	0.20
Dementia	26 (16.1)	20 (6.2)	2.90 (1.56 – 5.37)	<0.01
Diabetes	40 (24.8)	72 (22.4)	0.86 (0.56 – 1.36)	0.63
Functional impairment	71 (44.1)	66 (20.6)	3.05 (2.02 – 4.60)	<0.01
Fall on admission	51 (31.7)	53 (16.5)	2.34 (1.50 – 3.65)	<0.01
Fracture on admission	29 (18.0)	31 (9.7)	2.06 (1.19 – 3.55)	0.01
Male gender	67 (41.6)	149 (46.4)	0.82 (0.56 – 1.21)	0.37
Hearing impairment	30 (18.6)	48 (15.0)	1.30 (0.79 – 2.15)	0.37
Hypertension	92 (57.1)	185 (57.6)	1.02 (0.70 – 1.49)	0.99
Hypercholesterolemia	54 (33.5)	76 (23.7)	1.61 (1.08 – 2.44)	0.03
Ischemic heart disease	28 (17.4)	51 (15.9)	0.90 (0.54 – 1.49)	0.77
Joint replacement	22 (13.7)	27 (8.4)	1.72 (0.95 – 3.13)	0.10

Osteoporosis	59 (36.6)	87 (27.1)	0.64 (0.43 – 0.96)	0.04
Parkinson's disease	12 (7.5)	9 (2.8)	2.79 (1.15 - 6.76)	0.03
Previous delirium	16 (9.9)	2 (0.6)	17.54 (3.99 – 77.55)	<0.01
Recent admission to hospital (within 6 months)	59 (36.6)	137 (42.7)	0.77 (0.53 – 1.15)	0.24
Renal failure	19 (11.8)	34 (10.6)	1.13 (0.62 – 2.05)	0.81
Stroke or TIA	38 (23.6)	38 (11.8)	2.30 (1.40 – 3.78)	<0.01
Visual impairment	31 (19.3)	39 (12.1)	1.72 (1.03 – 2.89)	0.05

Note: TIA – Transient Ischemic Attack

Table 3. Logistic regression model of predisposing risk factors for incident delirium

	Odds	**95% C.I.**		**p**
Predisposing risk factor present	**Ratio**	**Lower**	**Upper**	
Age (continuous)	1.04*	1.02	1.07	<0.01
Cognitive impairment	2.63	1.61	4.32	<0.01
Dementia	2.70	1.31	5.54	<0.01
Fracture on admission	2.46	1.33	4.53	<0.01
Functional impairment	2.01	1.22	3.29	<0.01
Hypercholesterolemia	1.71	1.05	2.77	0.03
Previous delirium	16.48	3.57	75.07	<0.01
Stroke or TIA	1.69	.96	2.97	0.07

Note: TIA – Transient Ischemic Attack

*Odds Ratio for each one year increase in age

Table 4. Chi-square results for precipitating factors for development of incident delirium

Precipitating risk factor present	Case *N* = 161 *n* (%)	Controls *N* = 321 *n* (%)	Odds Ratio (95 % CI)	*p*
Abnormal sodium	72 (44.7)	101 (31.5)	1.76 (1.19 - 2.60)	<0.01
Administered benzodiazepines	74 (46.0)	114 (35.5)	1.55 (1.05 - 2.27)	0.03
Add more than three new medications	85 (52.8)	71 (22.1)	3.94 (2.62 - 5.91)	<0.01
Moved wards	39 (24.2)	58 (18.1)	1.44 (0.92 - 2.29)	0.14
Use of IDC	57 (35.4)	60 (18.7)	2.38 (1.55 - 3.66)	<0.01
Use of restraints	18 (11.2)	0	3.25 (2.83 - 3.72)	<0.01

Note: IDC – Indwelling catheter

Table 5. Logistic regression model of precipitating risk factors for incident delirium.

		95% C.I.		
Precipitating risk factor present	**Odds Ratio**	**Lower**	**Upper**	**p**
Use of IDC	2.00	1.27	3.15	<0.01
Add more than 3 medications	3.58	2.36	5.41	<0.01
Abnormal sodium	1.54	1.02	2.33	0.04

Note: IDC – Indwelling Catheter