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published in
Journal of Clinical Nursing
2019

DOI (link to publisher)
10.1111/jocn.14833

document version
Publisher's PDF, also known as Version of record

Received: 27 May 2018 | Revised: 6 February 2019 | Accepted: 9 February 2019

DOI: 10.1111/jocn.14833

ORIGINAL ARTICLE

WILEY Journal of Clinical Nursing

Undiagnosed delirium is frequent and difficult to predict: Results from a prevalence survey of a tertiary hospital

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Abstract

Aims and objectives: To study the prevalence and determinants of undiagnosed delirium in a tertiary hospital.

Background: Delirium is a common inpatient condition. It is frequently undiagnosed in a variety of settings, but determinants of undiagnosed delirium are largely unknown, and the frequency of undiagnosed delirium across all inpatient units is uncertain. The utility of hospital-wide screening then is also uncertain.

Methods: Hospital-wide prevalence study conducted over 4 months, using a chart-based method. Gender, age, admitting unit, history of dementia and comorbidity were used in univariate and multivariate analyses to search for differences in patients with no delirium, with undiagnosed delirium and with diagnosed delirium. Sensitivity, specificity and number needed to screen were calculated from proportions in each group. Study was conducted in concordance with STROBE guidelines.

Results: Delirium was prevalent in 12.5% of all patients and undiagnosed in 24.1% of patients. Only age ≥65 years and a history of dementia predicted delirium, and undiagnosed delirium in both univariate and multivariate analyses. Age ≥65 years accounts for 92.3% sensitivity and 50.8% specificity for undiagnosed delirium in this group. History of dementia had a 23.0% sensitivity and 97.0% specificity. Twenty-eight patients would need to be screened to detect a case of undiagnosed delirium.

Discussion: There was a high rate of delirium and undiagnosed delirium in this cohort. Known risk factors for delirium also independently predict undiagnosed delirium; other factors were not found.

Conclusion: Undiagnosed delirium is common and difficult to predict from patient baseline characteristics other than age.

Relevance to clinical practice: Assessment of all inpatients for delirium is recommended.

KEYWORDS

delirium, delirium diagnosis, delirium epidemiology, delirium prevention and control, undiagnosed delirium

This study was approved by the local Human Research Ethics Committee.

1 | INTRODUCTION

Delirium is a common condition affecting 17.3%–22.9% of hospitalised older people (Bellelli et al., 2016; Travers, Byrne, Pachana, Klein, & Gray, 2013a) and is associated with poor outcomes, including an independent association with mortality (Kiely et al., 2009), long-term cognitive decline (Fong, Tulebaev, & Inouye, 2009), increased risk of functional decline and institutionalisation (Krogseth, Wyller, Engedal, & Juliebo, 2014). Delirium follows an acute, fluctuating course with disturbance of attention, awareness and perception (Khurana, 2017). Undiagnosed delirium is common. Prevalence has been reported to be 42% in an internal medicine setting (Gonzalez Pezoa, Carrillo Venezian, & Castillo Rojas, 2015), 56% in a general hospital population (Ryan et al., 2013), 6.0% at hospital admission from the emergency department (Han et al., 2009) and incident delirium developing in 7.6% (Travers et al., 2013a; Travers, Byrne, Pachana, Klein, & Gray, 2013b) in older medical inpatients during admission.

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

- Delirium is common and frequently undiagnosed.
- Older age and dementia diagnosis increase risk of delirium and undiagnosed delirium.
- Assessment of all hospitalised patients for delirium is recommended to improve diagnosis of delirium.

2 | BACKGROUND

Very little is known about factors which predict undiagnosed delirium. Two studies examined predictors of undiagnosed delirium in patients referred for consultation-liaison psychiatry assessment from other nonpsychiatric inpatient units (Kishi et al., 2007; Swigart, Kishi, Thurber, Kathol, & Meller, 2008). Both reported a past history of psychiatric disease, the first also pain (Kishi et al., 2007), the second general medical or surgical admitting unit and absence of disorientation (Swigart et al., 2008), as predictive of undiagnosed delirium. However, these patients were selected for referral to psychiatry and do not represent a general inpatient population. A point prevalence study of all assessable inpatients in a single hospital showed severity of inattention, memory impairment and admission under an internal medicine specialty were independently associated with diagnosed delirium (Ryan et al., 2013). However, factors at admission to hospital associated with undiagnosed delirium in unselected hospitalised inpatients have not been evaluated.

2.1 | Aims and objectives

The authors aimed to study the prevalence of undiagnosed delirium and the determinants of undiagnosed delirium of patients referred to a tertiary hospital.

3 | METHODS

The study involved prospective review of inpatients' medical records to diagnose delirium in the Royal Melbourne Hospital, a tertiary hospital in the state of Victoria, Australia, with 490 inpatient beds and 140 sub-acute inpatient beds. All patients admitted to ward beds at 11:00 on the day of assessment of that ward were included in the chart review. At the time of the study, delirium screening was not standard practice. The point prevalence data collection occurred over a 4-month period from February–May 2016, on a ward-by-ward basis. Additional follow-up of patient's status continued until July 2016 using the hospital admissions database, determining whether the patient had been discharged from hospital, deceased or was still in hospital.

Delirium was diagnosed according to the chart-based method described by Inouye et al. (2005). This method determines a DSM-IV diagnosis of delirium from a review of the patient's chart and has been validated compared to interview by a specialist in the area (Inouye et al., 2005). Undiagnosed delirium was defined as delirium positive according to the chart-based method, without a diagnosis of delirium, acute confusional state or equivalent term implying the diagnosis of delirium as documented by the treating clinician. Delirium was considered diagnosed if one of these terms were present, or appropriate actions according to local guidelines for delirium were taken though no diagnostic term was entered.

Inpatient Palliative medicine/care unit, psychiatry units, Hospital in the Home and ventilated Intensive Care Unit patients were excluded as the method has not been validated in these patient groups and charts for Hospital in the Home patients were not available for review. The Charlson Comorbidity Index (CCI) (Charlson, Pompei, Ales, & MacKenzie, 1987) was calculated from diagnoses obtained from separation coding data. CCI was dichotomised into greater than or equal to 4 points or not to separate cohorts at different risk of mortality (Testa et al., 2009). Age was dichotomised into ≥65 years consistent with current recommendations for care for delirium ("Delirium Clinical Care Standard," 2016). Other data collected were the patient's gender, ability to speak English, admission under an internal medicine unit, diagnosis of dementia, and whether deceased in hospital. Nonfluent English was operationally defined as patients who were not able to effectively communicate with nursing staff to the point that orientation was not able to be established each shift. The Royal Melbourne Hospital has a catchment area with a high proportion of residents born outside of Australia (Australian Bureau of Statistics, 2014) who do not have English as their first language. Dementia diagnosis was taken from coding data.

All analyses were conducted using Stata 14.2 (Statacorp, USA). Analysis used binomial logistic regression analysis. Multivariate

binomial logistic regression analysis was conducted using variables with a *p*-value less than 0.1 on univariate testing. Two multi-variable binomial logistic regression analyses were performed: the first compared nondelirium to undiagnosed delirium patients and the second nondelirium versus all (both diagnosed and undiagnosed) delirium patients. All variables significant on univariate analysis in the respective models were used in multi-variable binomial logistic regression analysis to determine factors independently associated with the outcome of interest.

This study conformed to the STROBE guidelines for improving reporting of observational research, see Supporting information Appendix S1.

The ability of patient characteristics—such as age, dementia status—to identify undiagnosed delirium from nondelirium was of interest, as it may indicate the ability to rule-out undiagnosed delirium in the absence of these characteristics. The sensitivity of these characteristics was therefore defined as participants with the characteristic and undiagnosed delirium (true positives) as a proportion of all with undiagnosed delirium. The specificity was also of interest, as it may indicate the ability to rule-in undiagnosed delirium in the presence of that characteristic. This was defined as participants without the characteristic and without undiagnosed delirium (true negatives) as a proportion of all without undiagnosed delirium. Number needed to screen was calculated as the reciprocal of the absolute rate of undiagnosed delirium in the group of interest. Diagnosed delirium was not included in these analyses, as the outcome of interest was the ability to differentiate those who did not have a diagnosis from usual clinical care, indicating the possible contribution of screening guided by these characteristics to routine clinical care, rather than replacing usual clinical care.

4 | RESULTS

In total, 496 patients were included in the point prevalence study. In the Intensive Care Unit, 10 of 22 patients were ventilated and not able to be assessed. Eighteen Hospital in the Home patients and 36 psychiatry patients were excluded. In total, 432 patients were available for analysis.

The baseline characteristics of the inpatient cohort are presented in Table 1. Mean age was 63.9 years (standard deviation 20.4 years), and 34.7% were female. 12.5% of all inpatients and 22.7% of patients ≥65 years had delirium, and 24.1% (13/54) of these had undiagnosed delirium.

Table 2 shows the comparison of patients without delirium to those with undiagnosed delirium. Twelve out of 13 patients with undiagnosed delirium were ≥65 years of age, and 3/13 had a history of dementia; these characteristics were the only ones associated with undiagnosed delirium on univariate analysis. These findings remained significant on multi-variable binomial logistic regression analysis.

Table 3 presents the characteristics of the nondelirium patients compared to delirium patients (diagnosed and undiagnosed). In the univariate analysis, age ≥65 years, nonfluent English, admission under an internal medicine unit, a coded history of dementia and CCI > 4 points were associated with an increased risk of delirium. In the multi-variable binomial logistic regression analysis of these factors, only older age and dementia remained independently predictive of delirium.

TABLE 1 Baseline characteristics

Characteristic	*n* = 432
Gender, female	150 (34.7)
Age (years) Mean, (*SD*)	63.88 (20.4)
Diagnosed delirium	41 (9.49)
Undiagnosed delirium	13 (3.5)
Nonfluent English	64 (14.8)
Internal medicine unit	77 (17.8)
CCI > 4	69 (16.0)
Dementia	26 (6.0)
Deceased in hospital	18 (4.2)

Note. All values are given as *n* (%) unless otherwise indicated.

Considering the utility of risk factors to capture cases of undiagnosed delirium, in this study age ≥65 years would have a sensitivity of 92.3% for the detection of undiagnosed delirium, and specificity of 50.8% in those without diagnosed delirium. Dementia would give a sensitivity of 23.0%, and specificity of 97.0% for undiagnosed delirium. Universal screening of inpatients in this study would have required a Number Needed to Screen of 28 to detect one undiagnosed of delirium. Screening only older inpatients would have a Number Needed to Screen of 15 to detect one undiagnosed case of delirium.

5 | DISCUSSION

This study demonstrated 12.5% of patients had delirium, of which 24.1% was undiagnosed.

The percentage of undiagnosed delirium in our study is concordant with the literature ranging from 21.0%–79% depending on the diagnostic method used, the point during admission diagnosis was made, the study nation and the type of hospital (Forman et al., 1995; Iseli, Brand, Telford, & LoGiudice, 2007; Press et al., 2009). Higher rates were reported in an earlier study published in 1995 (Forman et al., 1995) and emergency department (Press et al., 2009), and are comparable with a study of older medical inpatients in 2006 at this hospital (21%) (Iseli et al., 2007). A prevalence survey in Ireland found just 43.6% of patients with delirium had confusion noted by medical staff though overall prevalence of undiagnosed delirium was similar (Ryan et al., 2013). Frequency of any delirium in point prevalence surveys of older hospital inpatients was also comparable to other recent studies ranging from 17.3%–19.1% (Gonzalez Pezoa et al., 2015; Ryan et al., 2013; Travers et al., 2013b; Wand et al., 2013).

The authors sought determinants of undiagnosed delirium, using factors that could be determined from chart review such as age,

TABLE 2 Characteristics of nondelirium versus undiagnosed delirium patients

Characteristic	Nondelirium, *n* = 340 (%)	Undiagnosed delirium, *n* = 13 (%)	Univariate		Multivariate	
			Odds ratio (95% CI)	*p*-value	Odds ratio (95% CI)	*p*-value
Age >=65 years	167 (49.1)	12 (92.3)	12.4 (1.60–96.7)	**<0.001**	8.92 (1.11–71.6)	**0.039**
Female gender	128 (37.6)	7 (53.8)	1.93 (0.635–5.88)	0.246		
Nonfluent English	50 (14.7)	3 (23.1)	1.74 (0.463–6.54)	0.412		
Internal medicine unit	199 (58.5)	5 (38.4)	0.443 (0.142–1.38)	0.161		
Dementia	10 (2.9)	3 (23.0)	10.8 (2.54–46.2)	**<0.001**	6.41 (1.16–28.1)	**0.014**
CCI > 4	52 (15.2)	4 (30.8)	2.46 (0.730–8.29)	0.146		

Note. CI: Confidence interval CCI: Charlson Comorbidity Index.
Bold values are statistically significant ($P<0.05$).

TABLE 3 Characteristics of nondelirium versus delirium (including diagnosed and undiagnosed)

Characteristic	Nondelirium, *n* = 378 (%)	Delirium, *n* = 54 (%)	Univariate		Multivariate	
			Odds ratio (95% CI)	*p*-value	Odds ratio (95% CI)	*p*-value
Age >=65 years	184 (48.7)	50 (92.6)	13.2 (4.67–37.2)	**<0.001**	9.71 (3.33–28.3)	**<0.001**
Female gender	145 (38.4)	23 (42.6)	1.19 (0.669–2.12)	0.552		
Nonfluent English	56 (14.8)	14 (25.9)	2.01 (1.03–3.94)	**0.0499**	0.650 (0.280–1.51)	0.314
Internal medicine unit	199 (52.6)	37 (68.5)	1.96 (1.07–3.60)	**0.0264**	1.19 (0.583–2.48)	0.633
Dementia	10 (2.70)	16 (30.1)	15.7 (6.65–37.1)	**<0.001**	10.1 (3.81–26.8)	**<0.001**
CCI > 4	40 (10.6)	10 (18.5)	1.92 (0.897–4.11)	**0.093**	1.59 (0.650–3.88)	0.310

Note. CI: Confidence interval, CCI: Charlson Comorbidity Index.

gender, English proficiency, admitting unit, history of dementia and comorbidity. Of the factors studied, only older age (≥65 years) and a history of dementia predicted undiagnosed delirium in the univariate and multivariate analysis. Similarly in comparing patients without delirium to patients with delirium, the same factors were again independently predictive of delirium in the multivariate analysis. This suggests that delirium and undiagnosed delirium have similar risk factors, suggesting they follow similar patterns, and that causes of failure to diagnose may not be amongst these patient factors. In contrast, Ryan et al. (2013) in a prevalence survey, and two studies in patients referred to psychiatric liaison services (Kishi et al., 2007; Swigart et al., 2008), found that admission under a surgical unit was associated with undiagnosed delirium. In this study, admitting unit was not associated with undiagnosed delirium. This may be related to the higher rate of undiagnosed delirium in the study by Ryan et al. (2013), allowing detection of a signal that was not significant in this study, and possible referral bias in the other studies. One study reported that severity of inattention was associated with delirium diagnosis, and another reported that the absence of disorientation was associated with undiagnosed delirium (Swigart et al., 2008), supporting the possibility that absence of core features of delirium hampers diagnosis. In a sample of hospital inpatients referred for psychiatric evaluation, pain and a past history of psychiatric disease were associated with undiagnosed delirium (Kishi et al., 2007), suggesting these factors may also contribute to undiagnosed delirium. In this study, it was not possible to examine these characteristics as this was not an interview but a chart review. As such, it is not possible to determine whether delirium was undiagnosed due to factors related to the symptoms or signs of delirium, or characteristics of the patient with delirium. Further studies in this area could include prospective study design with interviews of participants, searching for characteristics that might be predictive of undiagnosed delirium.

Strengths of this study include the inclusion of patients in every multi-day stay bed suitable, resulting in a comprehensive assessment of prevalence of delirium not limited to age or certain types of wards, units or patients. Limitations of the study are the chart-based method may have resulted in bias, as documentation of delirious signs and symptoms may be lacking. Reassuringly however the prevalence in the older cohort was similar to studies using interview methods (Khurana, 2017). As a point prevalence study, the in-hospital incidence could not be differentiated from prevalent delirium, and factors predicting incident undiagnosed delirium rather than prevalent undiagnosed delirium warrant further evaluation.

Though a large study, the total number of undiagnosed delirium cases was small. A larger, multi-site prevalence study may help to address these limitations, providing more information about this important group (Bellelli et al., 2016).

Clinical guidelines ("Delirium: Prevention, Diagnosis, & Management", 2010) and standards ("Delirium Clinical Care Standard," 2016) recommend a systematic search for risk factors for

delirium at admission, followed by interventions and vigilance for patients at risk. These strategies have been based on studies of risk factors for delirium, but not undiagnosed delirium. For this strategy to be effective, those same risk factors must predict undiagnosed delirium. Lack of risk factors for delirium may lead to lower vigilance for the diagnosis, so that patients without risk factors may be more likely to be undiagnosed. The findings of this study, though based on a small group of patient with undiagnosed delirium, are reassuring that these strategies are likely to be effective, as the risk factors for diagnosed delirium were the same as those for undiagnosed delirium.

6 | CONCLUSIONS

There was a significant proportion of undiagnosed delirium in this cohort. Older age and dementia predicted delirium and undiagnosed delirium. This study supports recommendations for screening of inpatients for delirium, and for risk factors for delirium.

7 | RELEVANCE TO CLINICAL PRACTICE

Undiagnosed delirium is common, and factors other than age that strongly predict undiagnosed delirium have not been identified in this study or previous literature. A high level of vigilance for delirium and systematic methods for detection are therefore recommended.

ACKNOWLEDGEMENTS

The authors wish to thank the Royal Melbourne Hospital for financial support and assistance in the conduct of this study.

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How to cite this article: Lange PW, Lamanna M, Watson R, Maier AB. Undiagnosed delirium is frequent and difficult to predict: Results from a prevalence survey of a tertiary hospital. *J Clin Nurs*. 2019;28:2537–2542. https://doi.org/10.1111/jocn.14833

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