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EDITORIAL

Delirium in COVID-19: common, distressing and linked with poor outcomes. . . can we do better?

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Key Points

- Delirium was one of the challenges health professionals caring for patients with COVID-19 faced, yet little attention has been devoted to its prevalence, and outcomes.
- A recent systematic review showed that nearly one in three COVID-19 patients had delirium on or during hospital admission with a pooled mortality approximately three times higher than in those without delirium.
- Policy, research and education must better serve patients at risk of this common and devastating syndrome in COVID-19 and beyond.

Introduction

Managing delirium is one of the challenges health professionals caring for patients with coronavirus disease 2019 (COVID-19) have faced in the past year. Delirium, a neuropsychiatric syndrome characterised by acute change in attention, awareness and cognition [1], is often due to the coexistence of predisposing and precipitating factors including sensory impairment, frailty, acute disease, surgery and polypharmacy [2, 3]. Delirium is independently associated with increased hospital-acquired complications, longer stay, admission to long-term care and cognitive decline [4, 5]. Generally difficult to prevent and manage, delirium in COVID-19 poses additional challenges, including logistical and ethical issues around pathways of care, infection control, staff time and visiting. Health policies have impacted delirium prevention and non-pharmacological management, with isolation requirements increasing vulnerability and affecting treatment [6]. Why, then, has there been a relative lack of attention on delirium in COVID-19? Early policy was slow to recognise delirium as a common presenting feature of COVID-19; however, Public Health England included delirium from October 2020 [7]. Historic underdetection of delirium and persisting use of alternative terms for delirium in practice and research likely contributed [8]. There is now substantial emerging evidence around delirium in COVID-19. Shao et al. [16] provide a systematic review and meta-analysis of available evidence regarding prevalence, incidence and mortality of delirium in COVID-19.

Discussion

The authors analysed 48 observational studies with 11,553 patients to December 2020, assessing delirium prevalence, incidence and subsequent mortality. The authors should be commended for examining this important and underscrutinised issue, with rapid synthesis of many studies. Their results have important real-world implications.

Delirium in COVID-19 is common. This review found prevalence—delirium on admission—was 28.2% (95% CI: 23.5–33.1%) in people aged 65 and over and 15.7% (95% CI: 9.2–23.6%) in those under 65. Strikingly, in patients with dementia, prevalence was 45.3%. Incidence—new delirium during hospitalisation—was 25.2% (95% CI: 16.0–35.6%) and 71.4% (95% CI: 58.5–82.7%) for over and under 65 s, respectively. Put simply, nearly one in three COVID-19 patients had delirium on or during hospital

admission. When one considers total cases of COVID-19 (as of 30 May 2021: 466,758 cumulative patients admitted in the UK [9]), this number is staggering.

Delirium in COVID-19 is not only common, but also serious. The authors reported a pooled mortality of 44.5% ($P < 0.01$) (evaluated in 17 studies), approximately three times higher than in those without delirium (OR 3.2, 95% CI: 2.1–4.8). Mortality was higher in patients over 65 (48.4% (95% CI: 40.6–56.1%)) than under 65 (21.2% (95% CI: 15.4–27.6%)). It is not clear if delirium is only a powerful predictor of poor outcomes or if it directly causes increased mortality. Observed excess mortality may reflect a frail patient group. Age and frailty have been independently associated with increased mortality in COVID-19, as well as increased care needs in survivors [10, 11]. The Geriatric Medicine Research Collaborative study (published after this review's inclusion cut-off) found, when adjusting for frailty, the relationship between delirium and mortality was removed [10]. In clinical practice, however, frailty and delirium are often concomitant; frailty precedes and is a risk factor for delirium [12]. It may be of limited clinical relevance to separate these when assessing mortality outcomes and guiding practice.

There was marked heterogeneity in study populations. This may account for some variability observed. The authors ran subgroup analyses, some being difficult to interpret due to the low number of studies included. Furthermore, delirium-identification methods varied in sensitivity and specificity. Some studies did not present detailed information about how delirium was assessed; only 29.2% of studies used validated instruments, raising the issue of diagnostic accuracy. The authors attempted correction for this in subgroup analyses using validated tools. Most included studies were hospital-based, limiting generalisability for community settings, including care homes, which remain poorly explored in delirium research.

Clinical implications

The main findings of this review are delirium is common in COVID-19, and delirium is a strong indicator of worse prognosis, particularly in people aged over 65. This suggests healthcare systems need robust processes to detect delirium and provide specific care.

Multifactorial interventions to prevent delirium may reduce incident delirium by around one-third [13], but most delirium is prevalent. Identification and treatment of active delirium is therefore a priority. Trial evidence on multidomain treatment is lacking. Current recommendations are based mainly on expert consensus [1, 14] and focus on treating acute precipitants, reducing complications, and treating distress. COVID-19 is deliriogenic—from physiological risk factors (hypoxia, inflammation) to psychological factors (stress, isolation), and drug and respiratory device use [1, 6]. Many of these factors are hard to modify, particularly in time and space-pressured pandemic settings. When considering difficult decisions regarding delirium management in COVID-19, such as steroid use to help distressing respiratory features but with potential to worsen delirium, or antipsychotics to reduce agitated behaviour (e.g. pulling off oxygen masks), further research may demonstrate where the balance of benefit lies.

Delirium can cause distress, not only in patients, but in family and professionals who witness it. Post-delirium trauma can persist. Clear explanation and reassurance during and after delirium can help reduce distress and psychological morbidity [15]. Given the results of this review, communication to families and professionals should include prognosis: delirium should alert everyone to increased risk of a poor outcome. In addition to giving rationale for active management of delirium, understanding high mortality rates may give practitioners confidence to inform families and consider appropriate palliative care strategies.

Delirium must be at the heart of COVID-19 policy, research and education. Delirium has important implications for patient experience and outcome, length of stay and ongoing care needs [5]. Resources should be directed towards research into effective delirium prevention, identification and management, not just for COVID-19, but for all patients.

Conclusion

This review confirms our clinical experience that delirium in COVID-19 is common and associated with poor prognosis. Practitioners must prevent and treat delirium where possible. We must also communicate with patients and families to reduce distress. Policy, research and education must serve patients at risk of this common and devastating syndrome in COVID-19 and beyond.

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References

1. Wilson JE, Mart MF, Cunningham C *et al.* Delirium. Nat Rev Dis Primers 2020; 6: 90. 10.1038/s41572-020-00223-4.
2. Aloisi G, Marengoni A, Morandi A *et al.* Drug Prescription and Delirium in Older Inpatients: Results From the Nationwide Multicenter Italian Delirium Day 2015-2016. J Clin Psychiatry 2019; 80: 18m12430. 10.4088/JCP.18m12430.
3. Jin Z, Hu J, Ma D. Postoperative delirium: perioperative assessment, risk reduction, and management. Br J Anaesth 2020; 125: 492–504.
4. Richardson SJ, Lawson R, Davis D *et al.* Hospitalisation without delirium is not associated with cognitive decline in a population-based sample of older people-results from a nested, longitudinal cohort study. Age Ageing 2021; afab068. 10.1093/ageing/afab068.
5. O'Keeffe S, Lavan J. The prognostic significance of delirium in older hospital patients. J Am Geriatr Soc 1997; 45: 174–8.

6. Manca R, De Marco M, Venneri A. The Impact of COVID-19 Infection and Enforced Prolonged Social Isolation on Neuropsychiatric Symptoms in Older Adults With and Without Dementia: A Review. Front Psych 2020; 11: 585540. 10.3389/fpsyt.2020.585540.
7. COVID-19: investigation and initial clinical management of possible cases, Public Health England, 2020. Available: https://www.gov.uk/government/publications/wuhan-novel-coronavirus-initial-investigation-of-possible-cases/investigation-and-initial-clinical-management-of-possible-cases-of-wuhan-novel-coronavirus-wn-cov-infection#other-clinical-situations-when-sars-cov- (3 June 2021, date last accessed).
8. Slooter A, Otte WM, Devlin JW *et al.* Updated nomenclature of delirium and acute encephalopathy: statement of ten Societies. Intensive Care Med 2020; 46: 1020–2.
9. Coronavirus (COVID-19) in the UK. Available: https://coronavirus.data.gov.uk/details/healthcare (3 June 2021, date last accessed).
10. Geriatric Medicine Research Collaborative, Covid Collaborative, Welch C. Age and frailty are independently associated with increased COVID-19 mortality and increased care needs in survivors: results of an international multi-centre study. Age Ageing 2021; 50: 617–30.
11. Marengoni A, Zucchelli A, Vetrano DL *et al.* Beyond Chronological Age: Frailty and Multimorbidity Predict In-Hospital Mortality in Patients With Coronavirus Disease 2019. J Gerontol Series A, Biol Sci Med Sci 2021; 76: e38–45.
12. Zhang XM, Jiao J, Xie XH, Wu XJ. The Association Between Frailty and Delirium Among Hospitalized Patients: An Updated Meta-Analysis. J Am Med Dir Assoc 2021; 22: 527–34.
13. Ludolph P, Stoffers-Winterling J, Kunzler AM *et al.* Non-Pharmacologic Multicomponent Interventions Preventing Delirium in Hospitalized People. J Am Geriatr Soc 2020; 68: 1864–71.
14. Scottish Intercollegiate Guidelines Network. Risk reduction and management of delirium. Edinburgh: SIGN, 2019.
15. Partridge JS, Martin FC, Harari D *et al.* The delirium experience: what is the effect on patients, relatives and staff and what can be done to modify this? Int J Geriatr Psychiatry 2013; 28: 804–12.
16. Shao S-C, Lai C-C, Chen Y-H, Chen Y-C, Hung M-J, Liao S-C. Prevalence, incidence and mortality of delirium in patients with COVID-19: a systematic review and meta-analysis. Age Ageing 2021; afab103. 10.1093/ageing/afab103..

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