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Delirium in COVID-19: Common, distressing and linked with poor outcomes

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[Editorial to accompany: "Prevalence, incidence and mortality of delirium in patients with COVID-19"]

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

Journal:	<i>Age and Ageing</i>
Manuscript ID	Draft
Manuscript Category:	Editorial
Keywords:	delirium, covid-19, mortality
Subject Section:	Covid-19
Keypoints:	Delirium was one of the challenges health professionals caring for patients with COVID-19 faced, yet little attention has been d, A recent systematic review showed that nearly one in three COVID-19 patients had delirium on or during hospital admission with a, Policy, research, and education must better serve patients at risk of this common and devastating syndrome in COVID-19 and beyon

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

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 COVID-19 have faced in the past year. Delirium, a neuropsychiatric syndrome characterized 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 under-detection 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. [XX-ANONYMOUS-XX] 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 under-scrutinised 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 65s, 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 May 30, 2021: 466,758 cumulative patients admitted in the UK [9]), this number is staggering.

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3 Delirium in COVID-19 is not only common, but also serious. The authors reported a pooled mortality of 44.5%
4 (p<0.01) (evaluated in 17 studies), approximately three times higher than in those without delirium (OR 3.2,
5 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%
6 (95% CI: 15.4-27.6%)). It is not clear if delirium is only a powerful predictor of poor outcomes or if it directly
7 causes increased mortality. Observed excess mortality may reflect a frail patient group. Age and frailty have
8 been independently associated with increased mortality in COVID-19, as well as increased care needs in
9 survivors [10] [11]. The Geriatric Medicine Research Collaborative study (published after this review's inclusion
10 cut-off) found, when adjusting for frailty, the relationship between delirium and mortality was removed [10].
11 In clinical practice, however, frailty and delirium are often concomitant; frailty precedes and is a risk factor for
12 delirium [12]. It may be of limited clinical relevance to separate these when assessing mortality outcomes and
13 guiding practice.
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17 There was marked heterogeneity in study populations. This may account for some variability observed. The
18 authors ran subgroup analyses, some being difficult to interpret due to the low number of studies included.
19 Furthermore, delirium-identification methods varied in sensitivity and specificity. Some studies did not present
20 detailed information about how delirium was assessed; only 29.2% of studies used validated instruments,
21 raising the issue of diagnostic accuracy. The authors attempted correction for this in subgroup analyses using
22 validated tools. Most included studies were hospital-based, limiting generalisability for community settings,
23 including care homes, which remain poorly explored in delirium research.
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26 CLINICAL IMPLICATIONS

27 The main findings of this review are delirium is common in COVID-19, and delirium is a strong indicator of
28 worse prognosis, particularly in people aged over 65. This suggests healthcare systems need robust processes
29 to detect delirium and provide specific care.
30

31 Multifactorial interventions to prevent delirium may reduce incident delirium by around one third [13], but
32 most delirium is prevalent. Identification and treatment of active delirium is therefore a priority. Trial evidence
33 on multidomain treatment is lacking. Current recommendations are based mainly on expert consensus [1] [14]
34 and focus on treating acute precipitants, reducing complications, and treating distress. COVID-19 is deliriogenic
35 – from physiological risk factors (hypoxia, inflammation) to psychological factors (stress, isolation), and drug
36 and respiratory device use [1] [6]. Many of these factors are hard to modify, particularly in time and space-
37 pressured pandemic settings. When considering difficult decisions regarding delirium management in COVID-
38 19, such as steroid use to help distressing respiratory features but with potential to worsen delirium, or
39 antipsychotics to reduce agitated behaviour (e.g., pulling off oxygen masks), further research may
40 demonstrate where the balance of benefit lies.
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44 Delirium can cause distress, not only in patients, but in family and professionals who witness it. Post-delirium
45 trauma can persist. Clear explanation and reassurance during and after delirium can help reduce distress and
46 psychological morbidity [15]. Given the results of this review, communication to families and professionals
47 should include prognosis: delirium should alert everyone to increased risk of a poor outcome. In addition to
48 giving rationale for active management of delirium, understanding high mortality rates may give practitioners
49 confidence to inform families and consider appropriate palliative care strategies.
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52 Delirium must be at the heart of COVID-19 policy, research, and education. Delirium has important
53 implications for patient experience and outcome, length of stay, and ongoing care needs [5]. Resources should
54 be directed towards research into effective delirium prevention, identification, and management, not just for
55 COVID-19, but for all patients.
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58 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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