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Delirium is a good predictor for poor outcomes from coronavirus disease 2019 (COVID-19) pneumonia: A systematic review, meta-analysis, and meta-regression

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ABSTRACT

Aim: Delirium is a common presenting symptom among older patients. Patients who presented with delirium may have a higher morbidity and mortality rate due to older age, other comorbidities, and atypical COVID-19 presentation. Currently, the evidence supporting delirium as one of the predictors of poor outcome of COVID-19 is still insufficient. This study aims to explore the potential association between delirium and poor outcomes from COVID-19.

Methods: We systematically searched the PubMed and Google Scholar databases using specific keywords related to our aims until January 30th, 2021. All articles published on COVID-19 and delirium were retrieved. The quality of the study was assessed using the Newcastle Ottawa Scale (NOS) tool for observational studies and Joanna Briggs Institute (JBI) Critical Appraisal Tools for case-series studies. Statistical analysis was done using Review Manager 5.4 software.

Results: Our meta-analysis of 20 studies showed that delirium symptoms on admission was associated with poor outcomes from COVID-19 [OR 2.36 (95% CI 1.80–3.09), $p < 0.00001$, $I^2 = 76\%$, random-effect models] and its subgroup which consist of severe COVID-19 [OR 3.89 (95% CI 1.72–8.75), $p = 0.001$, $I^2 = 91\%$, random-effect models], and mortality from COVID-19 [OR 1.90 (95% CI 1.55–2.33), $p < 0.00001$, $I^2 = 36\%$, random-effect models]. Meta-regression showed that the association was influenced by age ($p = 0.005$).

Conclusions: Our study suggests delirium as an important marker to identify patients at higher risk for developing poor COVID-19 outcomes. The physicians should add delirium as one of the common presenting symptoms of COVID-19 in older populations.

1. Introduction

Since March 2020, Coronavirus disease (COVID-19) has been declared a pandemic by the World Health Organization (WHO). Initially, the novel virus was called the 2019 novel Coronavirus (2019-nCoV), which officially changed into severe acute respiratory syndrome coronavirus 2 by the WHO. The number of confirmed and death cases of COVID-19 is increasing in several countries and has over-capacitated the hospital capacity. As of January 30, 2021, COVID-19 has caused 2,2182,867 deaths globally (World Health Organization, 2020). Previous meta-analysis studies have demonstrated several comorbidities (Putri et al., 2021; Hariyanto and Kurniawan, 2021; Hariyanto et al., 2021a, 2021b, 2021c) and laboratory markers (Hariyanto et al., 2020a; Ivan Hariyanto and Kurniawan, 2020) which are associated with severe COVID-19 and mortality.

The manifestations of COVID-19 are non-specific and may appear as an asymptomatic disease to fatal pneumonia resulting in death (Kwenandar et al., 2020; Sheleme et al., 2020; Hariyanto et al., 2021d). Studies have reported atypical presentations of COVID-19 which may impede early recognition and management of COVID-19 (D'Adamo et al., 2020). A study from Wuhan, China reported neurological symptoms in 36.4% patients and were more frequent in severe COVID-19

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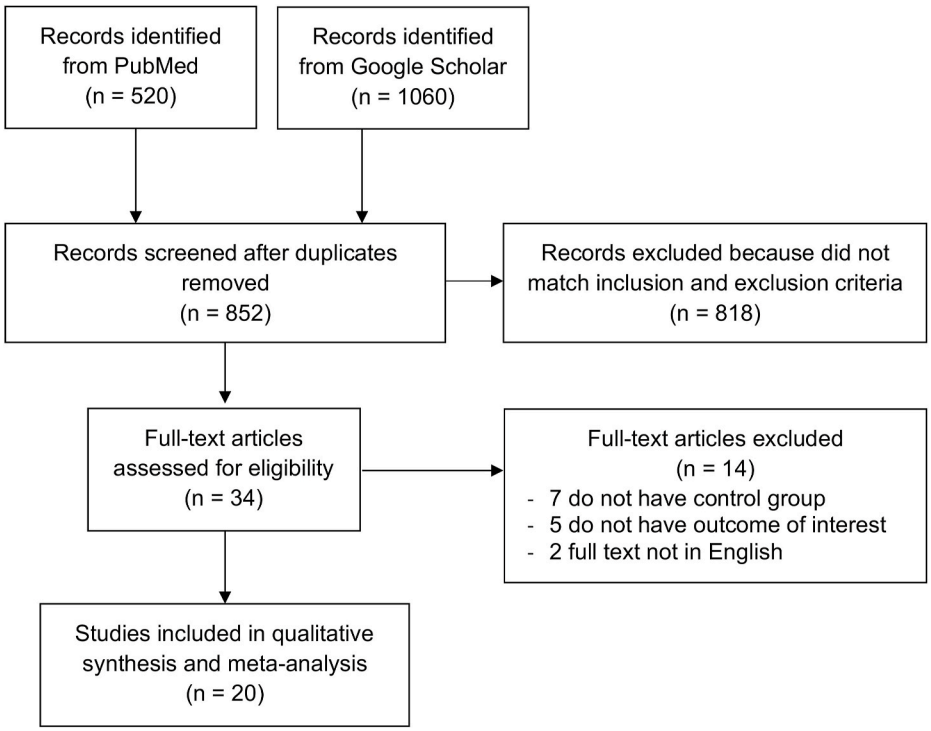

Fig. 1. PRISMA diagram of the detailed process of selection of studies for inclusion in the systematic review and meta-analysis.

patients showing atypical symptoms (Mao et al., 2020). Delirium, defined as an acute neuropsychiatric syndrome of altered level of consciousness or cognitive disturbances, presents in 11–12% of COVID-19 patients (Ticinesi et al., 2020; Garcez et al., 2020). Some patients may suffer from delirium during the clinical course of COVID-19, but it is also known to be a common presenting symptom in older patients with severe disease, thus complicates the diagnosis and management of COVID-19 (Kennedy et al., 2020; Suffoletto et al., 2013a). Patients who presented with delirium may have a higher morbidity and mortality rate due to older age, other comorbidities (e.g. dementia, epilepsy), atypical COVID-19 presentation, and worse gas exchange at the moment of admission (Ticinesi et al., 2020). Age-related changes in the immune system may reduce the ability to fight against newly encountered antigens in elderly (Aiello et al., 2019). Moreover, they usually suffer from dementia and other medical conditions with chronic inflammatory states that contribute to the increased risk of developing severe COVID-19 (Czick et al., 2020; Bianchetti et al., 2020; Hariyanto et al., 2020b, 2020c). Increased levels of blood urea nitrogen (BUN), C-reactive protein (CRP) and pro-inflammatory cytokines in delirium patients are also associated with worse COVID-19 outcome (Cheng et al., 2020; Leisman et al., 2020). There is currently insufficient evidence supporting delirium as one of the predictors of poor outcome of COVID-19. The ability to predict severe COVID-19 may help clinicians to accelerate decisions and referrals. This study aims to explore the potential association between delirium and poor outcomes from COVID-19 infection.

2. Materials and methods

2.1. Eligibility criteria

This is a systematic review and meta-analysis study. The IRB approval was not applicable for this type of article because this study did not involve human and animal subjects directly. We did not adopt a registered pre-specified protocol. Included articles in this study are selected as potentially fulfilling the entry criteria: comply the PICO framework (P: COVID-19 patients; I: patients presenting with delirium on hospital admission; C: patients who were admitted into the hospital without delirium symptoms; O: poor outcomes from COVID-19 which consist of severe COVID-19 and mortality), type of study was a randomized control trial, cohort, clinical trial, case-cohort, and cross-over design, and if the full-text article was available. The exclusion criteria are articles other than original research (e.g., review articles, letters, or commentaries); case reports; articles reported other than in English language; articles focusing on the populations of young age (below 18 years old) and women during their pregnancy.

2.2. Search strategy and study selection

The papers were searched systemically and obtained from PubMed and Google Scholar. Search terms used include “delirium” OR “confusion” OR “acute confusional state” OR “acute mental change” AND “SARS-CoV-2” OR “coronavirus disease 2019″ OR “COVID-19″ in a time range from 2019 until the present time (January 30th, 2021) with English-language restriction. Studies evaluating the delirium symptoms in patients with COVID-19, with a valid each outcome of interest definition, were included in this study. Potential eligible articles searching was done by analyzing the papers cited by authors of all identified studies. The search strategy was presented in the PRISMA diagram (Moher et al., 2009).

2.3. Data extraction and quality assessment

Two authors performed the data extraction process. An extraction form was developed to list the essential information on the authors, year of study, study design, number of participants, age, gender, number of patients with delirium symptoms, number of patients without delirium, and proportion of patients with each outcome of COVID-19.

The outcome of interest was poor outcomes from COVID-19 that consist of severe COVID-19 and mortality. Severe COVID-19 manifestation was the one having either of the mentioned features at the time of, or after, admission: (1) respiratory distress ($\geq$30 breaths per min); (2) oxygen saturation at rest $\leq$93%; (3) ratio of the partial pressure of arterial oxygen (PaO2) to a fractional concentration of oxygen inspired air (FiO2) $\leq$300 mmHg; or (4) critical complication (respiratory failure,

Table 1
Characteristics of included studies.

Study	Sample size	Design	Outcome	Age (years)	Male (%)	Patients with dementia (%)	Patients with history of stroke (%)	Patients with delirium n (%)	Delirium diagnosis
Atkins JL et al. (Atkins et al., 2020) 2020	507	Retrospective cohort	Mortality	74.3	61.3	2.8	4.5	5 (1%)	Using the DSM-V criteria
De Smet R et al. (De Smet et al., 2020) 2020	81	Retrospective cohort	Mortality	85.3 (88 vs 84.5)	41 (42 vs 40)	44 (52.6 vs 43)	N/A	34 (42%)	Not described
Emmerton D et al. (Emmerton and Abdelhafiz, 2020) 2020	71	Case-series	Severity, Mortality	73.5 (83 vs 68)	57.7 (58.3 vs 57.6)	14 (33 vs 10)	33.8 (50 vs 31)	12 (17%)	Using the 4AT tool
Garcez FB et al. (Garcez et al., 2020) 2020	707	Retrospective cohort	Severity, Mortality	66 (70 vs 64)	57 (61 vs 55)	4 (9 vs 2)	7 (12 vs 5)	234 (33%)	Using the Chart-Based Delirium Identification Instrument (CHART-DEL)
Hammes J et al. (Hammes et al., 2020) 2020	144	Retrospective cohort	Mortality	N/A	N/A	N/A	N/A	106 (73.6%)	Using the Confusion Assessment Method for the ICU (CAM-ICU)
Helms J et al. (Helms et al., 2020) 2020	140	Prospective cohort	Mortality	61.3 (62 vs 65)	71.4 (75.4 vs 50)	2.9 (2.7 vs 4.5)	6.4 (8 vs 0)	118 (81.9%)	Using the Confusion Assessment Method for the ICU (CAM-ICU)
Karlsson LK et al. (Karlsson et al., 2020) 2020	102	Retrospective cohort	Mortality	84.6	47	N/A	N/A	30 (29.4%)	Not described
Kennedy M et al. (Kennedy et al., 2020) 2020	817	Prospective cohort	Mortality	77.7 (83.2 vs 74.3)	47 (45.5 vs 47.8)	30 (42 vs 25.8)	13 (20.3 vs 10.3)	226 (28%)	Using the Confusion Assessment Method (CAM)
Khan SH et al. (Khan et al., 2020) 2020	268	Retrospective cohort	Severity, Mortality	58.4 (58.9 vs 55.7)	59.7 (54.7 vs 65.8)	3.5 (3.8 vs 2.6)	N/A	215 (80.2%)	Using the Confusion Assessment Method for the ICU (CAM-ICU)
Knopp P et al. (Knopp et al., 2020) 2020	217	Retrospective cohort	Mortality	80	62	33	N/A	64 (29%)	Not described
Marengoni A et al. (Marengoni et al., 2020) 2020	91	Retrospective cohort	Severity, Mortality	79.5 (81.7 vs 78.6)	60.4 (64 vs 59.1)	N/A	N/A	25 (27.4%)	Screened by using 4AT tool and confirmed by the DSM-V criteria
Mattace-Raso F et al. (Mattace-Raso et al., 2020) 2020	123	Retrospective cohort	Severity	70.7 (71.3 vs 70.4)	71.5 (78.7 vs 67)	N/A	N/A	47 (38.2%)	Using the DSM-V criteria
Poloni TE et al. (Poloni et al., 2020) 2020	57	Retrospective cohort	Mortality	82.8 (85.4 vs 81.2)	33.3 (42.9 vs 27.8)	100 (100 vs 100)	N/A	21 (36.8%)	Using the DSM-V criteria
Rawle MJ et al. (Rawle et al., 2020) 2020	134	Retrospective cohort	Mortality	86	54.5	26.1	N/A	55 (41%)	Using the 4AT tool
Rebora P et al. (Rebora et al., 2020) 2020	516	Prospective cohort	Mortality	78.3 (84 vs 77)	62 (47 vs 64)	16 (48 vs 11)	N/A	73 (14.1%)	Screened by using 4AT tool and confirmed by the DSM-V criteria
Romero-Sanchez CM et al. (Romero-Sánchez et al., 2020) 2020	841	Retrospective cohort	Severity	66.4 (71.5 vs 63.1)	56.2 (56.5 vs 56.1)	8.4 (12.5 vs 5.9)	6.3 (8.3 vs 5.1)	69 (8.2%)	Not described
Steinmeyer Z et al. (Steinmeyer et al., 2020) 2020	94	Retrospective cohort	Mortality	85.5 (88.6 vs 84.8)	44.7 (35.3 vs 46.8)	45.7 (52.9 vs 44.2)	N/A	8 (8.5%)	Using the Confusion Assessment Method (CAM)
Ticinesi A et al. (Ticinesi et al., 2020) 2020	852	Retrospective cohort	Mortality	73 (82 vs 75)	52.9 (55 vs 53)	18.3 (40 vs 16)	6.3 (12 vs 6)	758 (88.9%)	Using the Confusion Assessment Method (CAM)
Vrillon A et al. (Vrillon et al., 2020) 2020	76	Prospective cohort	Mortality	89.3 (89.5 vs 90)	44.7 (68.2 vs 35.2)	63.2 (45.5 vs 70.4)	28.9 (22.7 vs 31.5)	54 (71.1%)	Not described
Zerah L et al. (Zerah et al., 2020) 2020	821	Retrospective cohort	Mortality	86 (87 vs 86)	42 (50 vs 39)	54 (52 vs 55)	22 (24 vs 21)	205 (25%)	Using the Confusion Assessment Method (CAM)

vs = Group A vs Group B.

septic shock, and or multiple organ dysfunction/failure) or Intensive Care Unit (ICU) admission. Mortality outcome from COVID-19 was defined as the number of patients who were dead because of COVID-19.

Two investigators independently evaluated the quality of the included cohort and case-control studies using the Newcastle–Ottawa Scale (NOS) (Margulis et al., 2014). The selection, comparability, and exposure of each study were broadly assessed and studies were assigned a score from zero to nine. Studies with scores ≥7 were considered of good quality. Meanwhile, the quality of the included case-series studies was assessed by using the Joanna Briggs Institute (JBI) Critical Appraisal Tools For Case-Series (Moola et al., 2017).

2.4. Statistical analysis

Review Manager 5.4 (Cochrane Collaboration) software was used to perform the meta-analysis. Generic Inverse Variance formula with random-effects models was used to calculate each outcome's risk. The effect size was reported as odds ratio (OR) and its 95% confidence interval (CI). The heterogeneity was assessed by using the I^2 statistic with a value of <25%, 26–50%, and >50% were considered as low, moderate,

Table 2
Newcastle-Ottawa quality assessment of observational studies.

First author, year	Study design	Selection	Comparability	Outcome	Total score	Result
Atkins JL et al. (Atkins et al., 2020) 2020	Cohort	***	**	***	8	Good
De Smet R et al. (De Smet et al., 2020) 2020	Cohort	***	**	***	8	Good
Garcez FB et al. (Garcez et al., 2020) 2020	Cohort	***	**	****	9	Good
Hammes J et al. (Hammes et al., 2020) 2020	Cohort	***	**	**	7	Good
Helms J et al. (Helms et al., 2020) 2020	Cohort	***	**	***	8	Good
Karlsson LK et al. (Karlsson et al., 2020) 2020	Cohort	***	**	***	8	Good
Kennedy M et al. (Kennedy et al., 2020) 2020	Cohort	***	**	***	8	Good
Khan SH et al. (Khan et al., 2020) 2020	Cohort	***	**	****	9	Good
Knopp P et al. (Knopp et al., 2020) 2020	Cohort	***	**	***	8	Good
Marengoni A et al. (Marengoni et al., 2020) 2020	Cohort	***	**	***	8	Good
Mattace-Raso F et al. (Mattace-Raso et al., 2020) 2020	Cohort	**	**	***	7	Good
Poloni TE et al. (Poloni et al., 2020) 2020	Cohort	****	**	***	9	Good
Rawle MJ et al. (Rawle et al., 2020) 2020	Cohort	***	**	***	8	Good
Rebora P et al. (Rebora et al., 2020) 2020	Cohort	***	**	***	8	Good
Romero-Sanchez CM et al. (Romero-Sánchez et al., 2020) 2020	Cohort	***	**	***	8	Good
Steinmeyer Z et al. (Steinmeyer et al., 2020) 2020	Cohort	***	**	***	8	Good
Ticinesi A et al. (Ticinesi et al., 2020) 2020	Cohort	***	**	***	8	Good
Vrillon A et al. (Vrillon et al., 2020) 2020	Cohort	***	**	***	8	Good
Zerah L et al. (Zerah et al., 2020) 2020	Cohort	***	**	****	9	Good

Table 3
Joanna Briggs Institute Critical Appraisal tool for case series.

	Emmerton D et al. (Emmerton and Abdelhafiz, 2020) 2020
1. Were the criteria for inclusion in the sample clearly defined?	No
2. Were the study subjects and the setting described in detail?	Yes
3. Was the exposure measured in a valid and reliable way?	Yes
4. Were objective, standard criteria used for measurement of the condition?	Yes
5. Were confounding factors identified?	Yes
6. Were strategies to deal with confounding factors stated?	No
7. Were the outcomes measured in a valid and reliable way?	Yes
8. Was appropriate statistical analysis used?	Yes
Quality	Include study

and high degrees of heterogeneity, respectively. P-value was two-tailed, and the statistical significance was set at ≤ 0.05. Subgroup analysis was performed for each component of poor outcomes from COVID-19. Random effects meta-regression was performed using a restricted-maximum likelihood for pre-specified variables including age, gender, dementia, and history of stroke. The qualitative risk of publication bias was assessed with Begg's funnel plot analysis.

3. Results

3.1. Study selection and characteristics

In electronic databases, 1580 studies were found. A total of 852 records remained following the elimination of duplicates. By screening the titles/abstracts and matching the inclusion and exclusion criteria, 818 studies were removed. Among the 34 full-text articles evaluated for their eligibility, 7 articles were excluded due to no control/comparison group in the studies, 5 articles because they do not have the outcome of interest, 2 articles because the articles were not in English. At last, the meta-analysis included 20 studies (Ticinesi et al., 2020; Garcez et al., 2020; Kennedy et al., 2020; Atkins et al., 2020; De Smet et al., 2020; Emmerton and Abdelhafiz, 2020; Hammes et al., 2020; Helms et al., 2020; Karlsson et al., 2020; Khan et al., 2020; Knopp et al., 2020; Marengoni et al., 2020; Mattace-Raso et al., 2020; Poloni et al., 2020; Rawle et al., 2020; Rebora et al., 2020; Romero-Sánchez et al., 2020; Steinmeyer et al., 2020; Vrillon et al., 2020; Zerah et al., 2020) with a total of 6659 COVID-19 patients. (Fig. 1). Amongst them, 15 were retrospective cohort studies, 4 studies were prospective cohort design, and the remaining 1 study was a case-series study. Table 1 presents the essential characteristic of the included studies.

3.2. Quality of study assessment

Studies with various study designs including cohort and case-control were included in this review and assessed accordingly with the appropriate scale or tool. The Newcastle Ottawa Scale (NOS) was used to assess the cohort and case-control studies (Table 2), while the Joanna Briggs Institute Critical Appraisal checklist was used for case series studies (Table 3). All included studies were rated 'good' based on the criteria used in the Newcastle Ottawa Scale (NOS) and the Joanna Briggs Institute Critical Appraisal checklist. In conclusion, all studies were deemed fit to be included in the meta-analysis.

3.3. Delirium symptoms and outcomes

Our pooled analysis showed that delirium symptoms on admission was associated with poor outcomes from COVID-19, with high heterogeneity [OR 2.36 (95% CI 1.80–3.09), $p < 0.00001$, $I^2 = 76\%$, random-effect modelling] (Fig. 2). Subgroup analysis showed that delirium symptoms on admission was associated with severe COVID-19 [OR 3.89 (95% CI 1.72–8.75), $p = 0.001$, $I^2 = 91\%$, random-effect modelling], and mortality from COVID-19 [OR 1.90 (95% CI 1.55–2.33), $p < 0.00001$, $I^2 = 36\%$, random-effect modelling].

3.4. Meta-regression

Meta-regression showed that the association between delirium symptoms on admission and poor outcome from COVID-19 was affected by age ($p = 0.005$) (Fig. 3A), meaning that the magnitude of poor COVID-19 outcomes in patients with delirium was increased according to age. However, the relationship between delirium symptoms on admission and poor COVID-19 outcome was not affected by gender ($p = 0.215$) (Fig. 3B), dementia ($p = 0.656$) (Fig. 3C), and history of stroke ($p = 0.224$).

3.5. Publication bias

The funnel-plot analysis showed a qualitatively symmetrical inverted funnel-plot for the association between delirium symptoms and poor outcomes from COVID-19 (Fig. 4), showing no indication of publication bias.

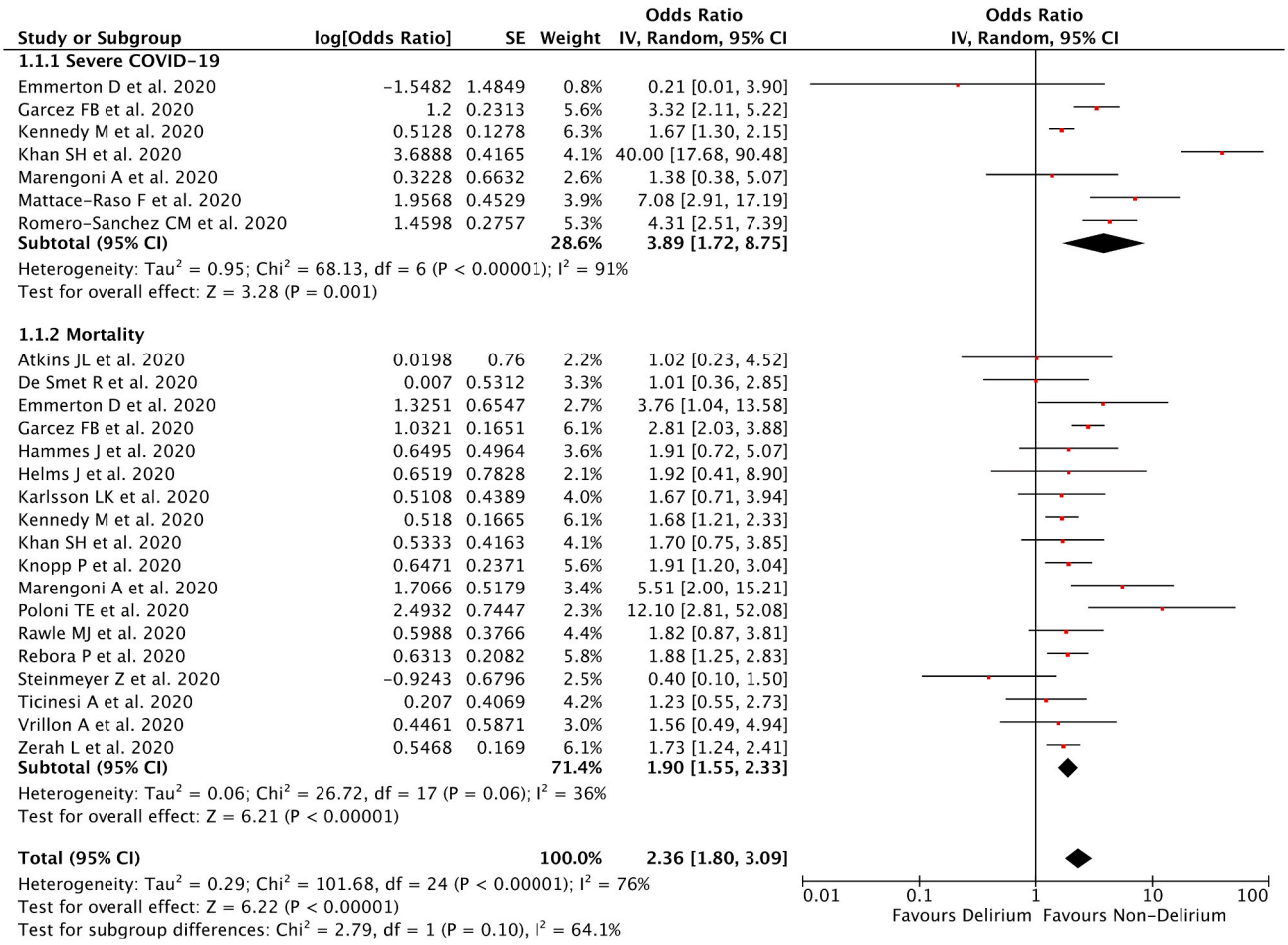

Fig. 2. Forest plot that demonstrates the association of delirium symptoms with poor outcomes and its subgroup which comprises of severe COVID-19 and mortality.

4. Discussion

This is the first systematic review and meta-analysis which analyzes the potential ability of delirium symptoms on admission to predict poor outcomes from COVID-19. Based on our pooled analysis of available data, delirium is associated with greater morbidity and mortality among COVID-19 patients and this association was influenced by age. Therefore, delirium at presentation can serve as an important marker to identify COVID-19 patients at high risk of poor outcomes.

Several reasons can be proposed to explain these findings. First, delirium (either hypo- or hyperactive) is a common presenting symptom of COVID-19 infection in older adults (Nanda et al., 2020). The prevalence of delirium among older people admitted into the hospitals ranges from 11 to 25%, higher than the general population which is only 1–2% (Vasilevskis et al., 2012; Wass et al., 2008). Although the prevalence was quite high in older people, delirium often went unidentified during hospital admission or stay in two-third of the cases (Suffoletto et al., 2013b; Bellelli et al., 2015). In COVID-19 elderly patients, delirium may be the only presenting symptom in the absence of other typical COVID-19 symptoms. The prevalence of typical COVID-19 symptoms, such as fever (>38°) and cough were only 39–47% and 32–54%, respectively in elderly patients admitted into the hospital when compared with younger/middle-aged patients (77–80% and 58–75%, respectively) (Mori et al., 2021; Gómez-Belda et al., 2021). The presence of atypical symptoms such as delirium and the lack of typical COVID-19 symptoms may impede the early identification of COVID-19, and will increase the risk of developing poor outcomes, including prolonged ICU stay and death. Second, the old age itself in patients who present with delirium is an independent risk factor for poor COVID-19 outcomes. A previous meta-analysis study has shown an exponential relationship between age and infection fatality rate (IFR) for COVID-19 (Levin et al., 2020). Older people have disrupted the capability to fight against newly encountered antigens. These age-related changes in the immune system, called immunosenescence, lead to a progressive reduction in the ability to trigger antibody and cellular responses against infection. This phenomenon affects both acquired and innate immunity (Aiello et al., 2019). Older people usually also have other comorbidities inducing chronic inflammatory states such as hypertension, obesity, diabetes mellitus that contribute to the development of severe COVID-19 by activating RAS which then activates Angiotensin II type 1 receptor (AT1R) and produces proinflammatory cytokines, vasoconstriction, fibrosis, thrombosis, and Reactive Oxygen Species (ROS). Moreover, patients with old age have a reduced expression of ACE2 and therefore reduced capacity to produce vasodilator, anti-inflammation, anti-fibrosis, anti-thrombosis, and ROS Neutralizer (Czick et al., 2020). All of these conditions will contribute to the development of poor outcomes from COVID-19 in patients who present with delirium symptoms which usually have older age. Third, patients with central nervous system diseases, such as Alzheimer's Dementia (AD), are more prone to develop delirious states, and the diagnosis of delirium superimposed on dementia (DSD) is being studied recently (Maclullich et al., 2008; Morandi and Bellelli, 2020). In a study among dementia patients infected with COVID-19, delirium was the most common presenting symptom at admission (Bianchetti et al., 2020). On the other side, meta-analysis studies have reported that dementia was associated with poor outcomes of COVID-19 (Hariyanto et al., 2020b, 2020c). Fourth, delirium was associated with an increased level of blood urea nitrogen (BUN) (Chu et al., 2011). An increase in BUN levels is an indication of impaired

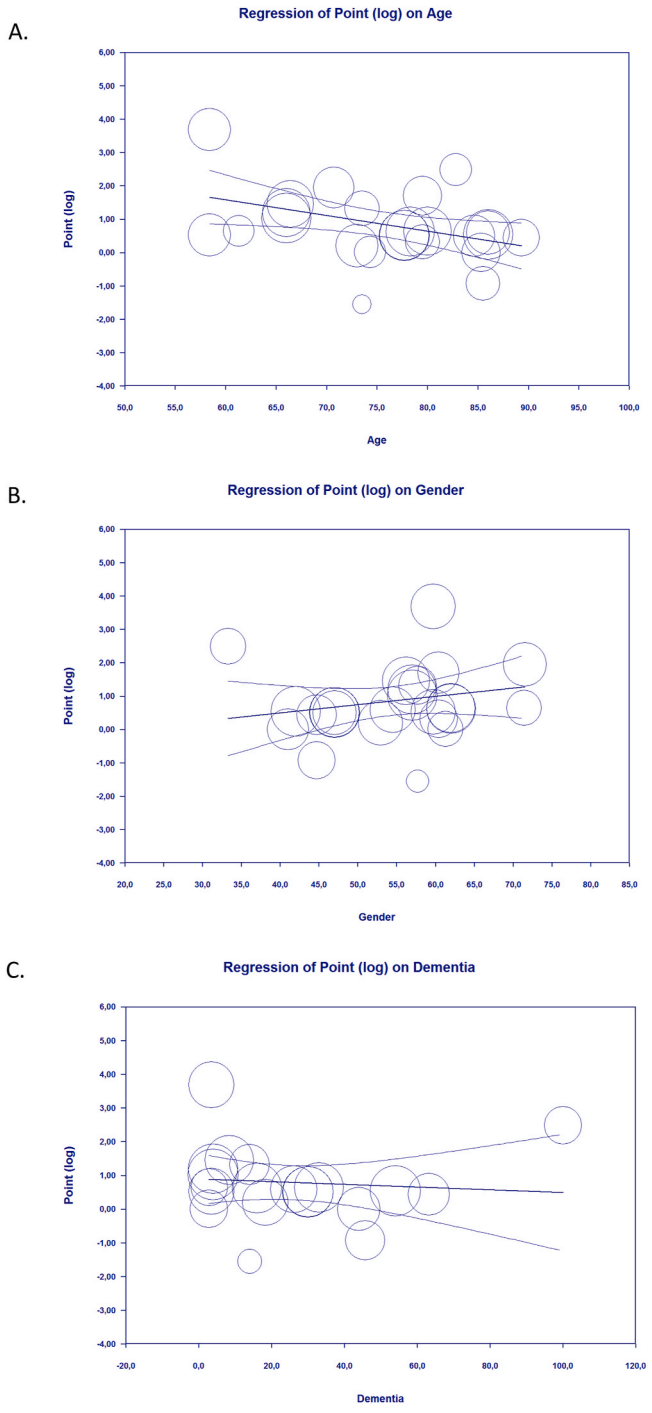

Fig. 3. Bubble-plot for Meta-regression. Meta-regression analysis showed that the association between delirium on admission and poor outcome was affected by age [A], but not by gender [B] and dementia [C].

perfusion and dehydration of peripheral organs, including the central nervous system in COVID-19 patients (Li et al., 2020). COVID-19 patients are indeed at higher risks of dehydration and related acute kidney failure due to negative fluid balance caused by fever, tachypnea, and oxygen supply. Elevated BUN was an independent risk factor for an unfavorable prognosis of COVID-19 (Cheng et al., 2020). Not only that, delirium was also associated with higher C-reactive protein (CRP) and pro-inflammatory cytokines levels such as IL-2, IL-6, and TNF-α, and these laboratory values were often used as biomarkers for delirium (Chu et al., 2011; Toft et al., 2019). Elevated levels of CRP and pro-inflammatory cytokines serve as an indication of

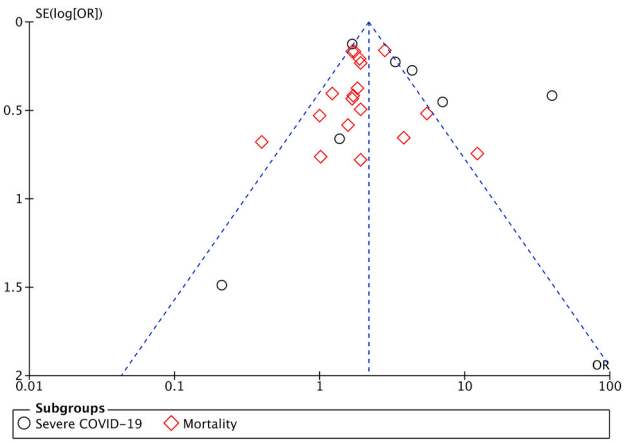

Fig. 4. Funnel plot analysis for the association of delirium symptoms with poor outcomes and its subgroup which comprises of severe COVID-19 and mortality.

hyperinflammatory response and cytokine storm which are associated with severe COVID-19 (Hariyanto et al., 2020a; Leisman et al., 2020). Therefore, the presence of delirium can be used as a marker of impaired peripheral perfusion and hyperinflammatory conditions in COVID-19 patients, which are associated with higher morbidity and mortality rates.

The limitation of this study is that the information regarding the other factors which can influence the relationship between delirium and COVID-19 outcomes such as patients' nutritional status, daily medication, and duration of delirium symptoms are lacking in the included studies, therefore cannot be analyzed. Moreover, some of the included studies did not mention the criteria they used for delirium diagnosis, while the mentioned criteria for delirium diagnosis were varied among the included studies which may increase the heterogeneity in the analysis. However, with this study, we hope that delirium can further be considered as a marker for identifying patients that are at high risk of developing severe COVID-19 and mortality.

Our study suggests delirium as an important marker to identify patients at higher risk for developing severe COVID-19 and related death. Understanding the variations in COVID-19 presentation is essential to prompt early recognition and management of the disease. The physicians should add delirium as one of the common presenting symptoms of COVID-19 in older populations, to better identify COVID-19 cases that are at high risk of poor outcomes and related mortality.

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Author statement

Timotius Ivan Hariyanto: Conceptualization; Data curation; Methodology; Investigation; Validation; Visualization; Writing – original draft; Writing – review & editing. Cynthia Putri: Conceptualization; Data curation; Methodology; Investigation; Validation; Visualization; Writing – original draft; Writing – review & editing. Joshua Edward: Conceptualization; Data curation; Methodology; Investigation; Validation; Visualization; Writing – original draft; Writing – review & editing. Jessie Arisa: Conceptualization; Data curation; Methodology; Investigation; Validation; Visualization; Writing – original draft; Writing – review & editing. Rocksy Fransisca V Situmeang: Conceptualization; Validation; Resources; Writing – original draft; Writing – review & editing; Supervision. Andree Kurniawan: Conceptualization; Validation; Resources; Writing – original draft; Writing – review & editing; Supervision.

Data availability statement

The data that support the findings of this study are openly available in PubMed at https://pubmed.ncbi.nlm.nih.gov/, reference number 14–16, and 21–37.

Declaration of competing interest

The authors declare no conflict of interest.

Acknowledgment

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jpsychires.2021.08.031.

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