



Parkinson's disease and COVID-19: a systematic review and meta-analysis

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Abstract

Background Patients with Parkinson's disease (PD) are at higher risk of COVID-19 infection as most of them are at older age. The goal of this study is to update the pooled prevalence of COVID-19 infection in patients with PD.

Methods Two researchers systematically searched PubMed, Scopus, EMBASE, Web of Science, Google Scholar, and also gray literature including references of the included studies which were published before September 2021. We extracted data regarding the total number of participants, first author, publication year, the country of origin, mean age, number with COVID-19, symptoms, hospitalization, and death.

Results We found 1693 articles by literature search; after deleting duplicates, 798 remained. Thirty articles remained for meta-analysis. The pooled prevalence of COVID-19 infection in PD cases was 5% (95%CI: 4–6%) ($I^2=98.1%$, $P<0.001$). The pooled prevalence of fever in cases with PD was 4% (95%CI: 2–6%) ($I^2=96%$, $P<0.001$). The pooled prevalence of cough in cases with PD was 3% (95%CI: 2–4%) ($I^2=95.9%$, $P<0.001$). The pooled prevalence of hospitalization in cases with COVID-19 infection was 49% (95%CI: 29–52%) ($I^2=93.5%$, $P<0.001$). The pooled prevalence of mortality in COVID-19 cases was 12% (95%CI: 10–14%) ($I^2=97.6%$, $P<0.001$).

Conclusion The results of this systematic review and meta-analysis show that the pooled prevalence of COVID-19 infection in PD cases is 5% besides hospitalization and mortality rates which are 49% and 12%.

Keywords COVID-19 · Parkinson's disease · Prevalence

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Introduction

The new coronavirus was first introduced in December 2019, and now, it is in pandemic stage [1]. The most frequent manifestations are fever, cough, and malaise while underlying diseases, advanced age, and medications play an important role in prognosis [2]. Following Alzheimer's disease, Parkinson's disease (PD) is the second common neurodegenerative disease which could have a negative effect on COVID-19 prognosis in affected cases [3]. The prevalence of PD is between 113 and 873 cases per 100,000 people and is higher in Europe and lowest in Asia [4]. As the patients with PD are elderlies and they have underlying diseases, they are at higher risk of developing COVID-19 and quarantine will affect the presence of the symptoms [5].

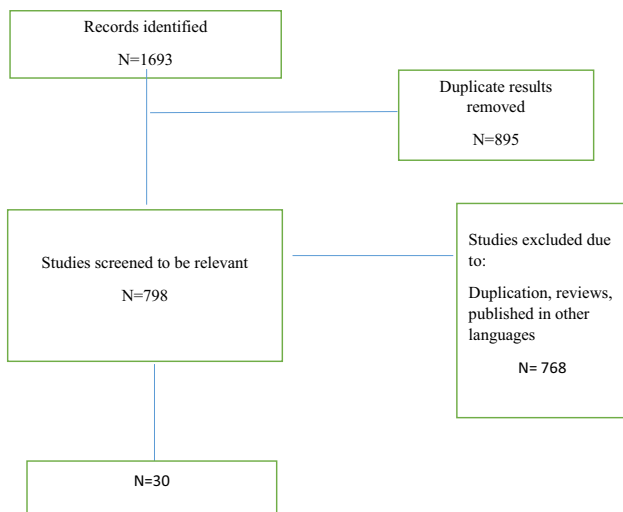


Fig. 1 Flow diagram summarizing the selection of eligible studies

Up to now, systematic reviews and meta-analysis have been done and reported various pooled prevalence of COVID-19 infection in patients with PD. The goal of this study is to update the pooled prevalence of COVID-19 infection in patients with PD.

Methods

Two researchers systematically searched PubMed, Scopus, EMBASE, Web of Science, Google Scholar, and also gray literature including references of the included studies which were published before September 2021.

The search strategy was as follows:

“Idiopathic Parkinson Disease” OR “Lewy Body Parkinson Disease” OR (“Parkinson Disease” AND Idiopathic) OR (“Parkinson Disease” AND “Lewy Body”) OR (“Parkinson Disease” AND Idiopathic) OR “Parkinson Disease” OR “Idiopathic Parkinson Disease” OR “Lewy Body Parkinson Disease” OR “Primary Parkinsonism” OR (Parkinsonism AND Primary) OR “Paralysis Agitans” OR Parkinson) AND (“COVID 19” OR “COVID-19 Virus Disease” OR “COVID 19 Virus Disease*” OR “COVID-19 Virus Disease*” OR (Disease AND “COVID-19 Virus”) OR (“Virus Disease” AND COVID-19) OR “COVID-19 Virus Infection*” OR “COVID 19 Virus Infection” OR (Infection AND “COVID-19 Virus”) OR (“Virus Infection” AND COVID-19) OR “2019-nCoV Infection” OR “2019 nCoV Infection*” OR (Infection AND 2019-nCoV) OR “Coronavirus Disease-19” OR “Coronavirus Disease 19” OR “2019 Novel Coronavirus Disease” OR “2019 Novel Coronavirus Infection” OR “2019-nCoV Disease” OR “2019 nCoV Disease” OR “2019-nCoV Diseases” OR (Disease AND 2019-nCoV) OR “COVID19” OR

Table 1 Basic characteristics of included studies

Author	Year	Country	Type Study	Total PD	Number Covid ¹	Number confirm PCR ²	Ag Case ³	Age SD_Case	Female Case	Male Case	Disease Duration case	Disease Duration SD Case	Fever	Cough	Dyspnea	Hospitalized	Death	NOS Quality assessment
Heng Zhai [7]	2021	China	Retrospective cohort	10	10	10	72.1	11.46	7	3	8.6	5.9	8	10	3	10	3	5/9
Lynda Nwabuobi [8]	2021	USA	Retrospective cohort	25	25	25	Median: 82	IQR: 73–88	6	19	NR	NR	12	11	NR	17	8	5/9
Raphael Scherbaum [9]	2021	Germany	Cross-sectional	64,434	693	693	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	245	8/10
Mehri Salari [10]	2021	Iran	Cross-sectional	647	73	73	60.57	12.46	NR	NR	NR	NR	30	26	16	10	NR	6/10
Ana C. Tahiria [11]	2021	Brazil	Cross-sectional	182	35	35	NR	NR	NR	NR	NR	NR	NR	NR	NR	25	14	5/10
Maria Bucufusca [12]	2021	Italy	Cohort	12	12	12	73.33	10.73	6	6	13.5	6.34	4	2	1	9	0	5/9
Raminder Parihar [13]	2021	USA	Cross-sectional	70	53	53	Mean: 78.7	IQR: 12	22	31	NR	NR	NR	NR	NR	NR	19	5/10
Valentina Leta [14]	2021	UK	Cross-sectional	27	27	27	59	12.7	11	16	9.2	7.8	NR	NR	NR	6	NR	5/10
Mehri Salari [15]	2021	Iran	Cross-sectional	87	87	NR	75.8	7.3	NR	NR	NR	NR	NR	NR	NR	31	31	5/10

Table 1 (continued)

Author	Year	Country	Type, Study	Total, PD	Number, Covid ¹	Number confirm Number PCR ²	Ag Case ³	Age, SD_Case	Female Case	Male Case	Disease, Duration case	Disease, Duration, SD Case	Fever	Cough	Dyspnea	Hospitalized	Death	NOS Quality assessment
Ousseny Zerbo [16]	2021	USA	Cross-sectional	9100	325	325	NR	NR	NR	NR	NR	NR	NR	NR	NR	172	39	7/10
Hossein Estiri [17]	2021	USA	Cross-sectional	165	165	165	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	32	6/10
Megan P. Feeney [18]	2021	USA	Cross-sectional	1342	17	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	6/10
Christian Ineichen [19]	2021	Switzerland	Retrospective cohort	264	4	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	5/9
Ladan Akbarian-Tefaghi [20]	2020	UK	Cross-sectional (abstract)	28	12	12	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NA
Joy Antonelle de Mar [21]	2020	United States	Retrospective cohort	21	21	21	75.19	5.41	8	13	9.95	6.45	10	9	14	16	6	5/9
Jeanine J.S [22]	2020	Netherlands	Prospective cohort	280	99	99	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	6/9
Alfonso Fasano [23]	2020	Italy	Case-control	1486	105	NR	70.5	10.1	50	55	9.9	6.4	74	62	NR	18	6	7/9
Carlo Alberto Artusi [24]	2020	Italy	Cross-sectional	1407	8	8	74	7.52	3	5	12.14	7.62	6	2	3	8	6	6/10
Sanz-Amo [25]	2020	Spain	Case-control	211	39	NR	75.9	9	16	23	8.9	6.2	NR	NR	NR	21	8	6/9
Roberto Cilia [26]	2020	Italy	Case-control	12	12	NR	65.5	8.9	7	5	6.3	3.6	10	9	4	1	0	5/9
Santos Garcia	2020	Spain	Cross-sectional	568	15	NR	65.6	9.4	8	7	6.8	4.9	NR	NR	NR	5	0	6/10
Mehri Salari	2020	Iran	Cross-sectional	137	2	2	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	5/10
Angelo Antonini	2020	Italy, UK	Case series	10	10	NR	78.3	0.0847	4	6	12.7	8.09	6	8	2	10	4	NA
Eleonora Del Prete	2020	Italy	Case-controlled	740	7	7	75.71	8.9	3	4	9.29	3.59	NR	NR	NR	4	1	7/9
Luca Vignatelli	2020	Italy	Cohort	696	4	NR	76.5	NR	1	3	NR	NR	NR	NR	NR	4	1	6/9
Alfonso Fasano	2020	Italy, Iran	Cohort	2238	117	NR	71.4	10.8	43	74	9.4	5.8	NR	NR	NR	37	23	7/9
Ethan G. Brown	2020	United States	Cross-sectional	5429	51	22	65	NR	27	24	NR	NR	32	36	NR	5	0	6/10
Qiang Zhang	2020	United States	Cross-sectional	694	694	NR	Median: 79	NR	276	418	NR	NR	NR	NR	NR	NR	148	6/10

¹Number of PD patients who has effected by COVID-19

²Number of PD patients who has confirmed as COVID-19 case, by Polymerase chain reaction (PCR)

³Case means all PD patients who has effected by COVID-19

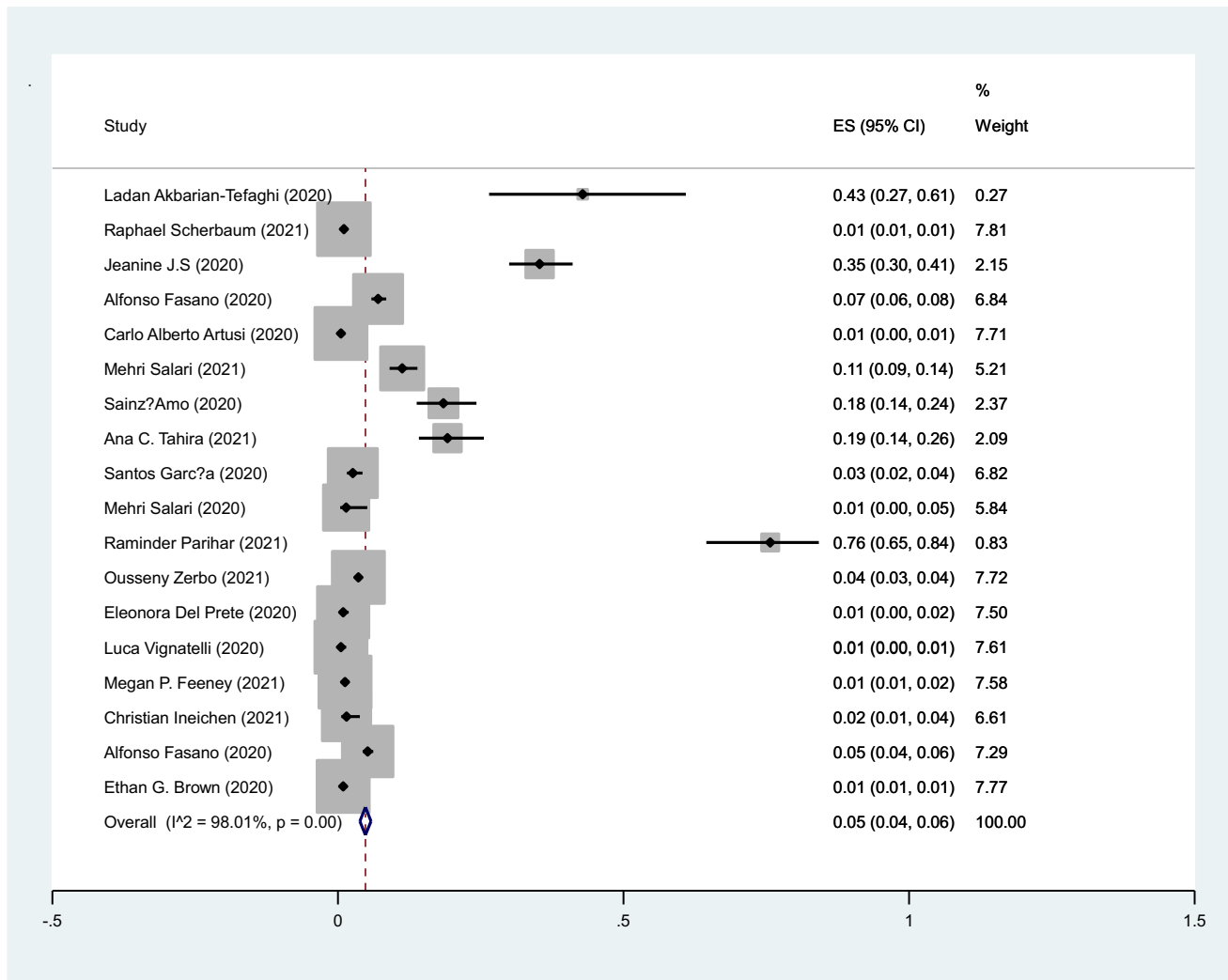


Fig. 2 The pooled prevalence of COVID-19 infection in PD cases

“Coronavirus Disease 2019” OR (“Disease 2019” AND Coronavirus) OR “SARS Coronavirus 2 Infection” OR “SARS-CoV-2 Infection” OR (Infection AND SARS-CoV-2) OR “SARS CoV 2 Infection*” OR “COVID-19 Pandemic*” OR “COVID 19 Pandemic” OR (Pandemic AND COVID-19).

Inclusion criteria were as follows:

We included cross-sectional studies which had reported the number of patients with Parkinson’s disease who had COVID-19 infection.

Exclusion criteria were as follows:

Letters to the editor, case–control, case reports, and cross-sectional studies which had no clear data.

We extracted data regarding the total number of participants, first author, publication year, the country of origin,

mean age, number with COVID-19, symptoms, hospitalization, and death.

Risk of bias assessment

Using Newcastle–Ottawa Quality Assessment scale (adapted for cross-sectional studies), we evaluated the risk of bias [6].

Statistical analysis

All statistical analyses were performed using STATA (Version 14.0; Stata Corp LP, College Station, TX, USA). We used random effects.

To determine heterogeneity, Inconsistency (I^2) was calculated.

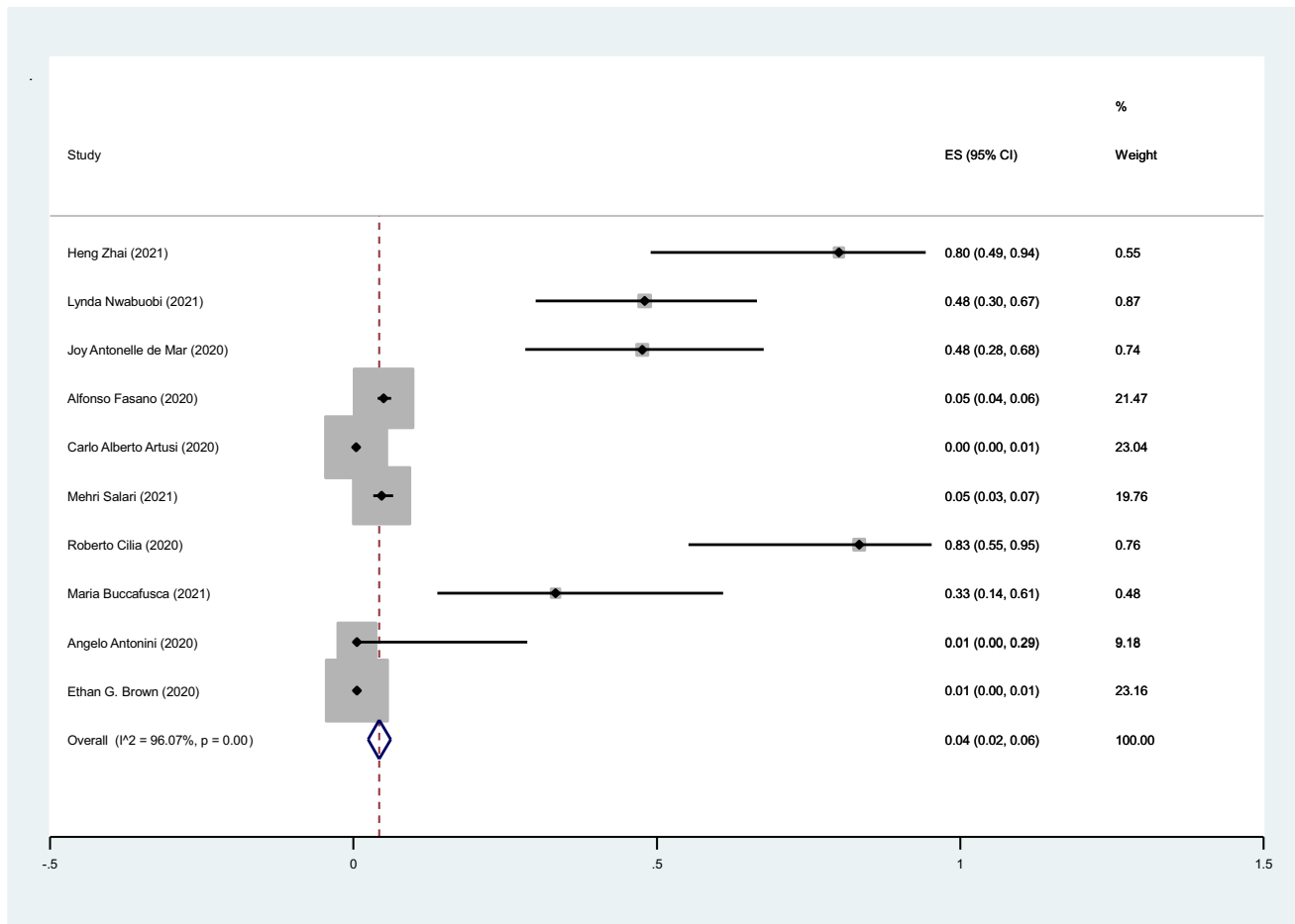


Fig. 3 The pooled prevalence of fever in cases with PD

Results

We found 1693 articles by literature search, after deleting duplicates 798 remained. Thirty articles remained for meta-analysis (Fig. 1).

Thirty articles were included. The number of included patients differed between 10 and 64,434, and mean disease duration varied between 6 and 13 years. Most studies were conducted in the United States of America (USA). Minimum and maximum quality assessment scores were 4–9.

The basic characteristics of the included studies are shown in Table 1.

The pooled prevalence of COVID-19 infection in PD cases was 5% (95%CI: 4–6%) ($I^2=98.1\%$, $P<0.001$) (Figure 2).

The pooled prevalence of fever in cases with PD was 4% (95%CI: 2–6%) ($I^2 = 96\%$, $P < 0.001$) (Fig. 3).

The pooled prevalence of cough in cases with PD was 3% (95%CI: 2–4%) ($I^2 = 95.9\%$, $P < 0.001$) (Fig. 4).

The pooled prevalence of hospitalization in cases with COVID-19 infection was 49% (95%CI: 29–52%) ($I^2: 93.5\%$, $P < 0.001$) (Fig. 5).

The pooled prevalence of mortality in COVID-19 cases was 12% (95%CI: 10–14%) ($I^2 = 97.6\%$, $P < 0.001$) (Fig. 6).

Discussion

The results of this systematic review and meta-analysis showed that the pooled prevalence of COVID-19 infection in patients with Parkinson's disease is 5% which is higher than the pooled prevalence reported in previous systematic reviews. In two previous systematic reviews,

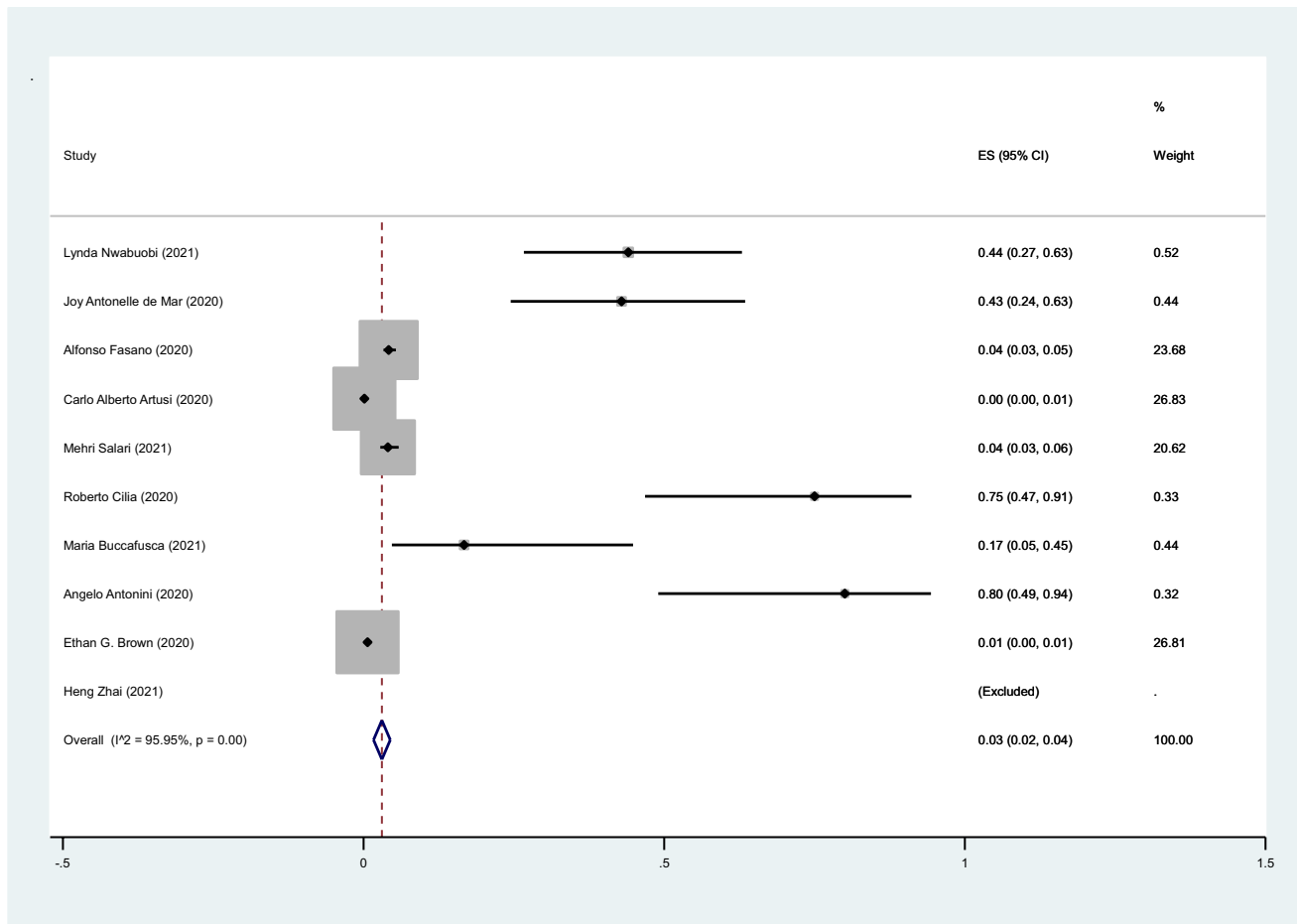


Fig. 4 The pooled prevalence of cough in cases with PD

the pooled prevalence of COVID-19 in PD reported was 2% [5, 27]. The difference could be due to the higher number of included studies. The prevalence of COVID-19 infection in PD cases ranged between 1 and 43% in different studies. We also found that the pooled hospitalization rate was 49% while the pooled mortality rate was 12%.

A recent systematic review and meta-analysis showed that the pooled prevalence of COVID-19 infection in patients with MS was 4% and pooled hospitalization rate was 10% [28]. The pooled hospitalization rate in this study for PD cases was 49% which is more higher than it was estimated for patients with MS. It could be due to higher age, advanced disease, and more comorbidities among patients with PD.

Zhang et al. found that patients with Alzheimer's disease (AD) had significantly higher odds of dying from COVID-19 compared with the no AD group [29].

El-Qushayri et al. published a systematic review and meta-analysis and reported the pooled hospitalization rate as 39.8% and the mortality rate as 25.1% [27].

Alberto Artusi et al. evaluated 1407 PD cases and reported COVID-19 infection in 8. They also found that six out of eight cases died due to COVID-19 infection while the fatality rate was 11.5%. The most common symptoms were fever and weakness [30].

Del Prete et al. enrolled 740 PD cases and reported COVID-19 infection in 7 (0.9%) and mortality rate as 0.13%. They reported hypertension and diabetes as predisposing factors of infection [31].

There are controversies regarding predisposing factors of COVID-19 infection in PD cases including higher susceptibility according to age and disease duration [23, 26, 32].

Patients with PD suffer from a wide range of comorbidities and they have twofold higher risk of hospitalization due

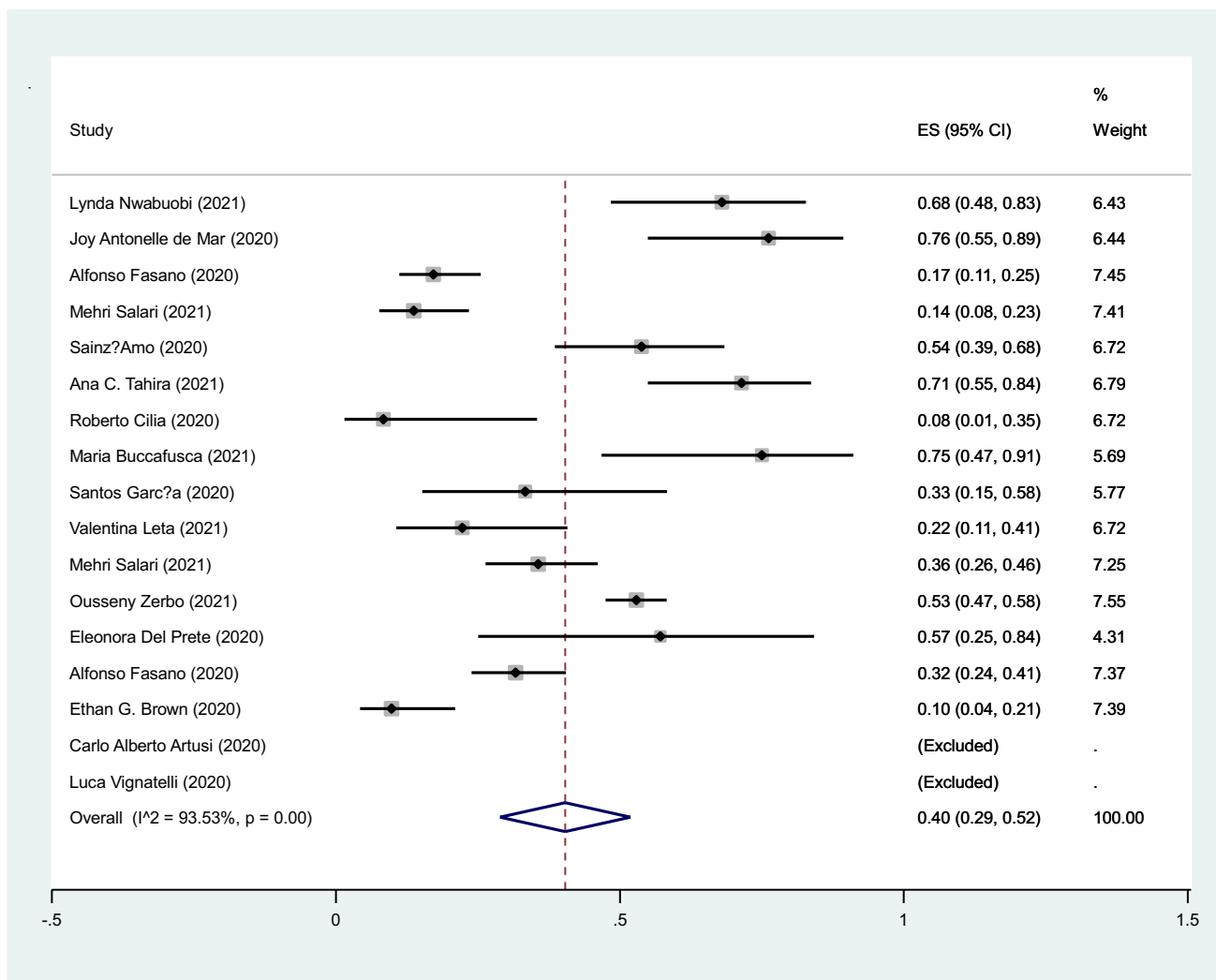


Fig. 5 The pooled prevalence of hospitalization in cases with COVID-19

to comorbidities [33]. On the other hand, PD may predispose cases to the risk of severe COVID-19 and higher rate of mortality based on disease complications such as delirium, drug adverse effects, syncope, aspiration pneumonia, falls, and fractures [34].

It should be considered that lock downs and social isolation during pandemic stage will result in reduction of outside activity which affects health being in PD cases. Being at home and having no activity affect motor function of patients with PD and also their psychological status. Literature shows that during COVID-19 pandemic stage, patients with PD suffer MORE from anxiety, and sleep disturbances [35–37].

On the other hand, case fatality rate is higher in PD cases after adjusting for different factors such as age, sex, and race

and the mortality rate is reported as 30% which is more than general population [38].

SARS-CoV-2 enters the host through cellular receptor angiotensin-converting enzyme 2 (ACE2) which highly is expressed in human airway epithelia and also dopaminergic neurons [39]. On the other hand, brain angiotensin system has role in neurodegeneration in PD cases [36]. Literature also shows that antibodies against different forms of coronaviruses were detected in cerebrospinal fluid of PD patients [40]. All of these findings could show that PD patients are at higher risk of catching SARS-Co V-2 infection.

This study had some strength. First, the number of included studies is high. Second, we calculated the pooled prevalence of COVID-19 infection, hospitalization rate, and mortality in PD cases.

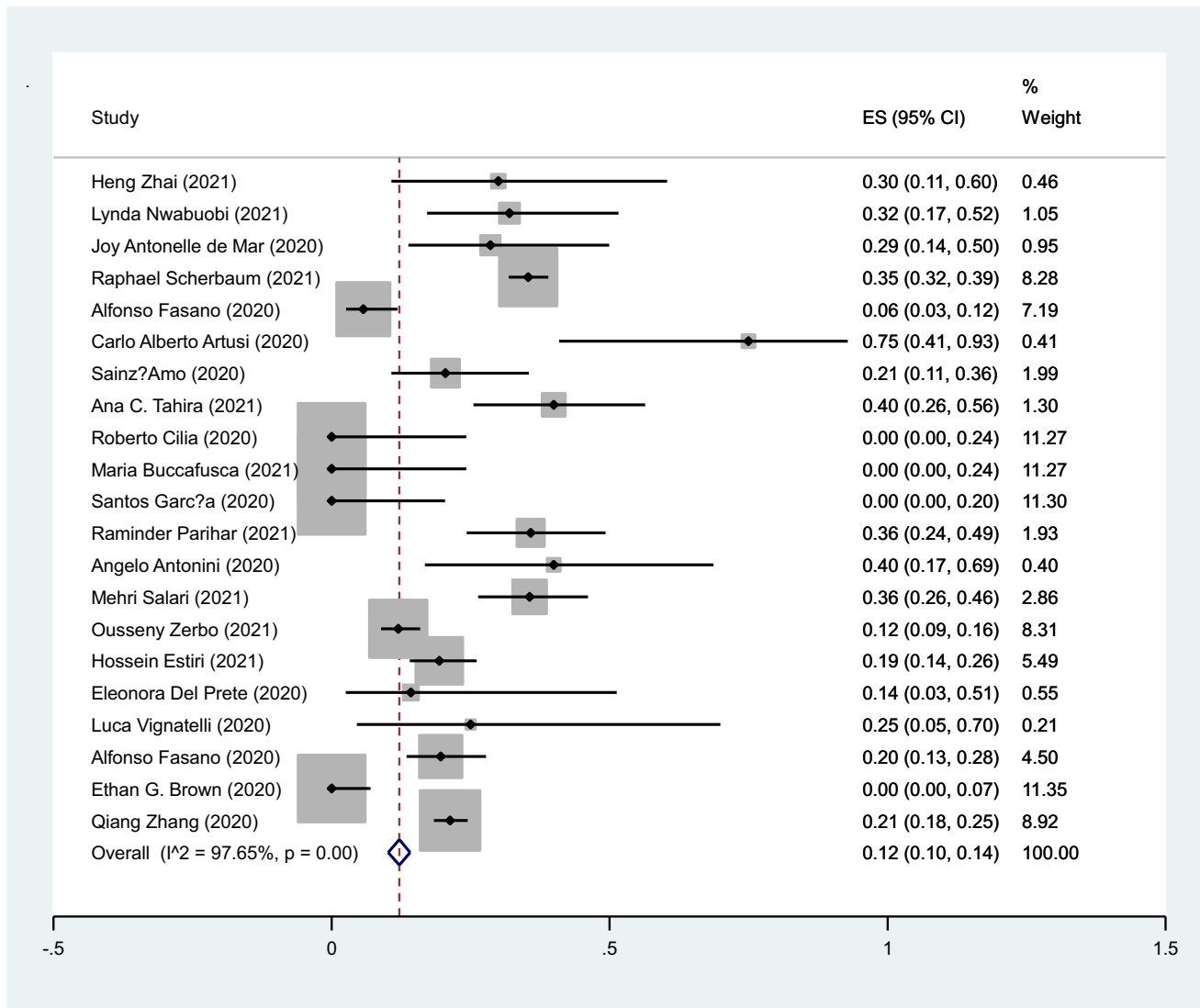


Fig. 6 The pooled prevalence of death in COVID-19 cases

Conclusion

The results of this systematic review and meta-analysis show that the pooled prevalence of COVID-19 infection in PD cases is 5% besides hospitalization and mortality rates are 49% and 12%.

Declarations

Ethical approval None.

Informed consent Not applicable.

Conflict of interest The authors declare no competing interests.

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