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Original Article

Conundrum of re-positive COVID-19 cases: A systematic review of case reports and case series

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ABSTRACT

Background: The systematic review was conducted to summarize and synthesize evidence from all available case series and case reports published on re-positive COVID-19 cases.
Methods: The systematic review was registered with Prospero (CRD42020210446). PRISMA guidelines were followed for conducting the systematic review. Inclusion criteria for studies included case reports and case series which have documented cases of positive reverse transcriptase polymerase chain reaction (RT-PCR) after a period of clinical improvement or a negative RT-PCR report. Reviews, opinions, and animal studies were excluded. Methodological quality was assessed using the modified Murad scale.
Results: A total of 30 case reports/case series were included in the study, wherein a total of 219 cases were included. In re-positive cases, the age range varied from 10 months to 91 years. The pooled proportion of positive cases after follow-up using random-effects was 12% (95% confidence interval [CI]: 09%–15%). Among the re-positives, a total of 57 cases (26%) had comorbidities. A total of 51 (23.3%) and 17 (7.8%) re-positive cases had been treated with antivirals and corticosteroids, respectively. Only a few studies have confirmed the presence of antibodies after the first episode. Studies that included contact tracing of re-positives did not find any positive cases among close contacts of re-positive cases.
Conclusion: The systemic review found that reinfection is a possibility within 123 days of a negative RT-PCR test in a small number of cases of COVID-19. This has wider ramifications in framing clinical, preventive, and public health policy guidelines.

Introduction

Clusters of atypical pneumonia cases were reported from Wuhan city, China, in December 2019 in the Hubei province.[1] The agent was identified as severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) and the disease was named as COVID-19.[2] World Health Organization declared it as Public Health Emergency of International Concern on 30 January 20 and subsequently as a pandemic on 11 March 20.[3]

Although scientific knowledge of the novel SARS-CoV-2 in the context of characteristics, transmission dynamics,

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pathophysiology, and clinical spectrum of disease manifestations has considerably increased over the past one year, knowledge gaps continue to persist in the natural history of the disease. The immune response to the infection (humoral versus cellular Immunity, the persistence of acquired immunity, and natural immunity to the disease) are still plagued with uncertainty.

Case reports and case series have documented COVID-19 cases with reverse transcriptase polymerase chain reaction (RT-PCR)—positive test reports at two different time frames following a symptom free period and/or RT-PCR—negative test. These cases may include re-positives, reactivated, and reinfection cases. It is unknown whether these cases share common characteristics or features that may help identify re-positive cases before discharge. The systematic review of the case reports and case series of the re-positives may help in better understanding of the natural history of the disease. Hence, a systematic review to summarize and synthesize evidence from all the published case series and case reports was conducted.

Materials and methods

The present systematic review was registered with Prospero with registration number CRD42020210446. We followed PRISMA guidelines for conducting the systematic review. A detailed literature search was carried out until 12 November 2020 for studies with reported cases of COVID-19 after a symptom-free interval. The databases that were searched included Medline through Pubmed and Cochrane databases. The key terms used were COVID-19, severe acute respiratory syndrome corona virus, relapse, re-activation, re-positive, and re-infection. The detailed search for Pubmed is given in Supplementary Table 1. Hand searches of the references of articles were also carried out. Observational studies, including case reports and case series, which had reported COVID-19 cases positive for RT-PCR on different occasions following a symptom-free interval and/or negative RT-PCR test were considered for the systematic review. Studies published in English language only were considered for the systematic review. Inclusion criteria for studies included case reports and case series that have documented positive RT-PCR cases after a period of clinical improvement or after a negative RT-PCR report. Review, opinions, and animal studies were excluded. Case reports which described clinical presentation or manifestations of COVID-19 cases were also excluded from the studies if they did not specify the positive molecular test after a symptom-free period or negative RT-PCR test.

Case definition

For this systematic review, the words relapse, re-activation, and re-positives were used interchangeably to include anyone who had become RT-PCR positive again after a symptom-free interval or negative RT-PCR test. Reinfection was restricted to only those studies where genomic characterization of the virus at two different time frames following a negative RT-PCR test proved fresh infection. The term "Recurrence" was used for encompassing both reinfection and re-positive/relapse/reactivation.

A data extraction form was developed, and data were extracted by two authors independently. The data items consisted of age and sex of the patients, clinical comorbidities, date of initial positive RT-PCR test, date of negative RT-PCR test based on which the patient was declared as cured, and date of positive RT-PCR test in recovered individuals who reported with new onset of symptoms suggestive of COVID-19 reinfection after a disease-free interval. Data on serology (if performed) and the clinical outcome of patients were also collated. If there was a mismatch in data extraction by the two authors, the same was resolved through discussion with a senior epidemiologist.

Methodological quality was assessed using the existing Murad scale.[4] The scale consists of eight items that converge into four domains: selection, ascertainment, causality, and reporting. Two items pertaining to adverse drug events (dose—response effect and challenge and rechallenge phenomenon) were not considered relevant. The data were extracted for remaining six items by two independent authors, and in case of mismatch, consensus was made in consultation with a senior epidemiologist. Narrative synthesis of the results was carried out. Random-effects model was used for the pooling of results. The description of variable was carried out as mean and standard deviation for continuous variables and proportion for categorical variables. 95% confidence interval (95% CI) was calculated. The statistical analysis was carried out using StataCorp. 2019. Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC.

Results

The selection for the study is shown as PRISMA Chart in Fig. 1. A total of 30 case reports/case series with 219 cases were included in the study. The patients' details and characteristics in the case series and case reports are shown in Table 1.[5–33] A study carried out in China among children with a median age of age of 5.7 years which studied recurrence in 14 children[22] and another Chinese study among 10 elderly subjects which did not mention the age and gender of the participants[20] were also included in the study. The pooled mean age of 195 cases was 44.3 ± 19.2 years. A total of 111 (50.68%) of 195 were women. The age range of the recurrence cases varied from 10 months to 91 years of age.

Molecular test for COVID-19 among discharged patients had been performed on sputum (lower respiratory tract), nasopharyngeal and anal swab. The details are shown in Table 1.

The majority of the cases (197, 89.9%) had mild to moderate clinical presentation. The clinical severity at initial presentation was not specified for 10 cases. Only 12 cases (5.5%; 95% CI: 2.8%–9.4%) had severe disease manifestation at initial presentation. A total of 64 (29.2%) reported cases were symptomatic during the second episode with the majority of them having less severe disease manifestation compared with the first episode. One hundred fifty (68.5%) cases were asymptomatic, and the status of five was unknown.

A total of 57 cases (26%) among the re-positives cases had comorbidities. A total of 51 and 17 re-positive cases had received

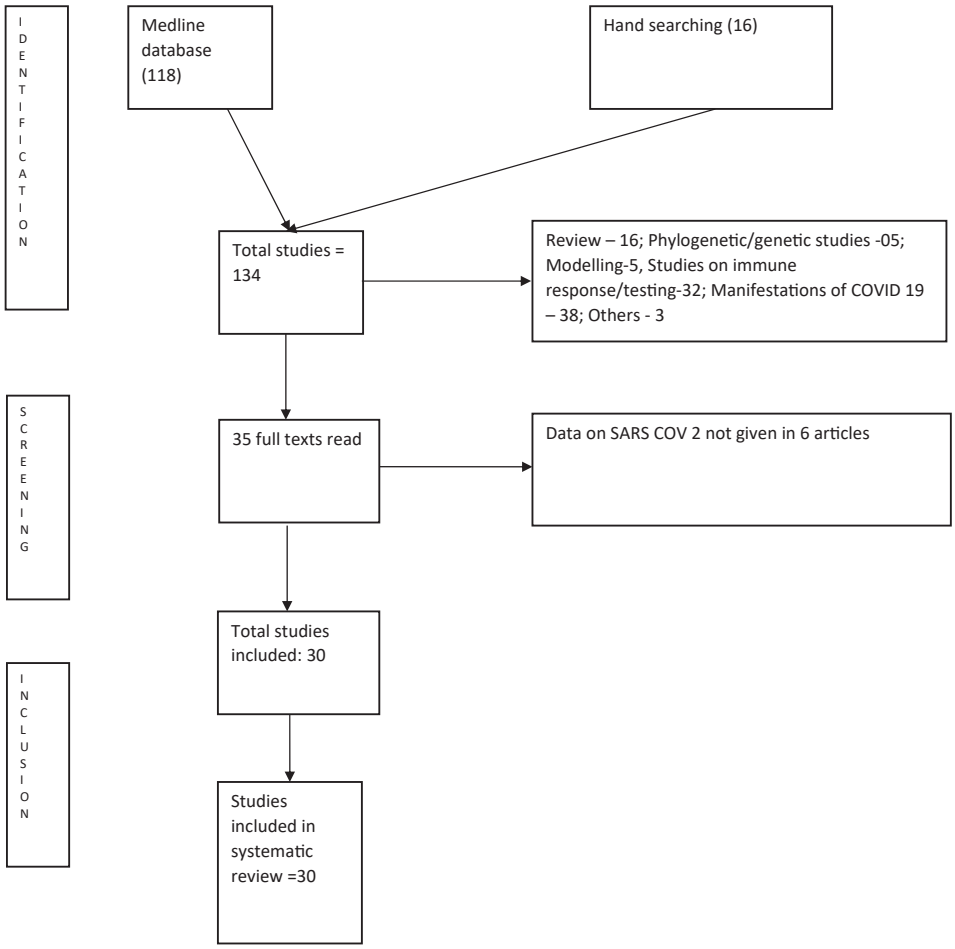

Fig. 1 – Prisma chart for the inclusion of studies in the systematic review.

antivirals and corticosteroids, respectively. Time interval between discharge/preceding a RT-PCR–negative report and a positive molecular test report ranged from 03 days to 123 days.

Eight studies have mentioned the proportion of cases that became re-positives after a negative RT-PCR test during follow-up period. The summary of proportions and their pooled ratio is given in Fig. 2. The pooled proportion using random-effects was 12% (95% CI: 09%–15%). All studies had a follow-up period in the range of 4–17 days except one which had a follow-up period of 14–46 days.[26]

Only a few studies confirmed the presence of antibodies after the first episode of clinical illness (Table 1). Even after the development of antibodies, studies had reported re-positivity (Table 1). A few studies had conducted contact tracing of re-positives. The studies did not find any positive cases among high risk contact with re-positives (Table 1). Mortality was reported in seven re-positive cases. The age range of these cases ranges from 73 to 91 years. All of them had multiple comorbidities.

Only a few studies had looked into the genetic analysis of the SARS-COV-2 to confirm reinfection.[30–35] These studies had found reinfection to occur even after a period of 123 days after the last RT-PCR negative test.

The quality of studies was assessed by using the modified Murad et al scale as shown in Fig. 3. In most of the studies, selection methods of COVID-19 cases were not clear; in addition, there were no precautions taken for ruling out false positives or rule out an alternate pathogen, which could produce similar signs and symptoms.

Korea Centers for Disease Control and Prevention reported 141 cases positive by RT-PCR after they recovered from COVID-19.[34] However, the probable reason given was relapse or inconsistent tests. The details were not available on the site.

Discussion

The systematic review was carried out for all case reports and case series to identify common characteristics and evidence available for re-positive cases. Although during review of available literature, we found evidence of re-positives after symptom free and negative RT-PCR test, yet it is difficult to ascertain whether it was due to continuous shedding of the virus, relapse, or reinfection by the virus. Only six studies that have carried out the genetic analysis of the COVID-19 virus in

Table 1 – Characteristics of studies.

S no	Study	Age and sex	Country	Sympt-omatic	Comor-bidity	Clinical severity	First COVID 19 (PCR)	Test Done	Serological test done after first episode	RT PCR negative after first episode	Symptomatic again after period of weeks	Date of Second COVID 19	Test done	Outcome
1	Batisse et al.[6]													
	1	19, F	France	Yes	7 Cormo-	Mild	D2	RT-PCR[a]	Available	NM	Yes	D29,	RT- PCR[a]	3 Dead
	2	32, F		Yes	bidity:	Mild	D18		for 9	NM	Yes	D36,55		and 8
	3	33, F		Yes	4 No co-	Mild	D3		patients	NM	Yes	D28		Alive
	4	43, M		Yes	morbitiy	Mild	D1		5 were	NM	Yes	D38		
	5	85, M		Yes		Mild	D16		positive, one	NM	Yes	D46		
	6	54, M		Yes		Mild	D38,44		slightly	NM	Yes	D45		
	7	91, F		Yes		Mild	D3		positive	NM	Yes	D26		
	8	55, M		Yes		Mild	D6		and three	NM	Yes	D31		
	9	72, M		Yes		Mild	D7		negatives	NM	Yes	D23, 32, 36		
	10	73, M		Yes		Mild	D6			NM	Yes	D35		
	11	84, F		Yes		Mild	D11			NM	Yes	D50		
2	Lafai et al.[7]													
	1	84, F	France	Yes	Yes	Severe	26 March	PCR	Yes**	No	Yes	26 days	RT PCR[a]	Death
	2	90, F		Yes	Yes	Severe	05 April	PCR	No	No	Yes	15 days		Death
	3	84, F		Yes	Yes	Severe	15 April	PCR[a] (neg)	Yes**	Yes	Yes	11 days		Death
3	Enrico et al.[8]	69, F	Italy	Yes	Yes	Mild	24 March	RT-PCR	Yes IgG Positive	Yes (two)	Yes	32 days	RT PCR	Alive
4	Ye et al.[9]													
	1	30, M	China	Yes	No	Mild	NM	NM	NM	Yes	NM	4–17 days	RT PCR[a]	Alive
	2	42, M		Yes	No	Mild	NM	NM	NM	Yes	NM	after		Alive
	3	32, F		Yes	No	Mild	NM	NM	NM	Yes	NM	negative		Alive
	4	27, F		No	No	Mild	NM	NM	NM	Yes	NM	test		Alive
	5	31, F		Yes	No	Mild	NM	NM	NM	Yes	NM			Alive
5	Ravioli et al.[10]													
	1	81, F	Switzerland	Yes	Yes	Moderate	09 March	RT-PCR[a]	NM	Yes	Yes	21	RT-PCR[a]	Died
	2	77, F		Yes	Yes		23 March		NM	Yes	Yes	14		Alive
6	Loconsole et al.[11]	48, M	Italy	Yes	No	Severe	17 March	RT-PCR	Yes	Yes	Yes	30	RT PCR	Alive
7	Jiang et al.[12]													
	1	35 F	China	Yes	No	Mild	30 January	RT-PCR[a]	No	Yes	Yes	9 days	RT-PCR[a]	Re-hosp
	2	56 F		Yes	Yes	Mild	30 January		No	Yes	No	14 days		Alive
	3	F		Yes	No	Mild	03 February		No	Yes	Yes	8 days		Alive
	4	F		Yes	No	Mild	03 February		No	Yes	No	7 days		Alive
	5	F		Yes	Yes	Mild	05 February		No	Yes	No	9 days		Alive
	6	F		Yes	No	Mild	06 February		No	Yes	No	5 days		Alive

8	Chang et al.[13]													
	1	14M	China	No	No	Mild-6	01 February	RT-PCR[a]	No	Yes	No	7	4RS	Alive
	2	13M		No	No	Moderate - 1	01 February		No	Yes	No	11	2 RT-PCR[a]	Alive
	3	0.8F		Yes	No		05 February		No	Yes	No	9	1RT-PCR[a] and 1 Rs	Alive
	4	35M		Yes	No		02 February		No	Yes	No	9		Alive
	5	35M		No	No		31 January		No	Yes	No	8		Alive
	6	33M		No	No		27 January		No	Yes	No	5		Alive
	7	26M		Yes	No		26 January		No	yes	No	11		Alive
9	Yoo et al.[14]	8M	Korea	Yes	No	Mild	03 March	RT-PCR	No	Yes	Yes	14	RT-PCR	Alive
10	Liu et al.[15]	35 M	China	yes	No	Mild	30 January	RT-PCR	Yes	Yes	Yes	15	RT-PCR	Alive
11	Yuan et al.[16]													
	1	38M	China	19- Yes	6 people had	Mild to	NM for all	RT-PCR[a]	14 were	Yes	No for all	13- retested	14	Alive (all)
	2	53M		1 - No	comorbidities	moderate			tested			at 07 days	nasophary	
	3	40F							and all of				ngeal	
	4	61F							them have			7 retested	and 7 anal	
	5	64F							antibodies			14 days	swabs	
	6	53F												
	7	33F												
	8	1F												
	9	34F												
	10	43M												
	11	34F												
	12	38M												
	13	50F												
	14	50F												
	15	5F												
	16	55F												
	17	72F												
	18	54M												
	19	8M												
	20	12M												
12	Lan et al.[17]													
	1	30-36, 2 M	China	3-Yes	NM	Mild to	NM	RT-PCR[a]	NM	Yes	No	5–13 days	RT-PCR[a]	Alive
	2			1- No	NM	moderate	NM		NM	Yes	No	after		Alive
	3				NM		NM		Nm	Yes	No	discharge		Alive
	4				NM		NM		NM	Yes	No			Alive

(*continued on next page*)

Table 1 – (*continued*)

S no	Study	Age and sex	Country	Sympt-omatic	Comor-bidity	Clinical severity	First COVID 19 (PCR)	Test Done	Serological test done after first episode	RT PCR negative after first episode	Symptomatic again after period of weeks	Date of Second COVID 19	Test done	Outcome
13	Cao et al.[18]													
	1	54F	China	Yes	No	Severe	NM	RT-PCR[a]	NM	Yes	No	12	RT-PCR[a]	Alive
	2	72F		Yes	No	Moderate	NM		NM	Yes	No	14		Alive
	3	60F		Yes	No	Moderate	NM		NM	Yes	No	09		Alive
	4	65F		Yes	Yes	Moderate	NM		NM	Yes	No	12		Alive
	5	58M		Yes	No	Moderate	NM		NM	Yes	No	16		Alive
	6	64M		Yes	No	Severe	NM		NM	Yes	No	29		Alive
	7	36F		Yes	No	Moderate	NM		NM	Yes	No	06		Alive
	8	26M		No	No	Moderate	NM		NM	Yes	No	06		Alive
14	Deng et al.[19]	Age - 54.8 years, F- 36	China	NM	24 (39.3%)	Severe-3 (4.9%)	NM	RT-PCR[a]	Not done	Yes	38-No	0 (7–13)	36-RT-PCR 17- AS; 8-sputum	Alive (All)
15	Peng et al.[20]													
	1	67M	China	Yes	NM	Mild	24 January	PCR	NM	Yes	No	4	RT-PCR	Alive
	2	- M		Yes	NM	Mild	24 January	PCR	NM	Yes	No	6	RT-PCR	Alive
	3	- F		Yes	NM	Mild	27 January	PCR	NM	Yes	No	3	RT-PCR	Alive
	4	- M		Yes	NM	Mild	28 January	PCR	NM	Yes	No	7	RT-PCR	Alive
	5	38F		Yes	NM	Mild	24 January	PCR	NM	Yes	No	6	AS	Alive
	6	29M		Yes	NM	Mild	29 January	PCR	NM	Yes	No	6	AS	Alive
	7	21F		Yes	NM	Mild	31 January	PCR	NM	Yes	No	5	RT-PCR	Alive
16	Wu et al.[21]													
	1	>70	China	NM	Yes	NM	01 February	NM	NM	NM	Yes	3	RT-PCR	Alive
	2	>70		NM	Yes	NM	02 February'	NM	NM	NM	Yes	5	RT-PCR/AS	Alive
	3	NM		NM	NM	NM	02February	NM	NM	NM	No	6	AS	Alive
	4	NM		NM	NM	NM	23 January	NM	NM	NM	No	25	RT-PCR	Alive
	5	NM		NM	NM	NM	27 January	NM	NM	NM	No	16	RT-PCR	Alive
	6	NM		NM	NM	NM	30 January	NM	NM	NM	No	9	RT-PCR	Alive
	7	NM		NM	NM	NM	29 January	NM	NM	NM	No	22	AS	Alive
	8	NM		NM	NM	NM	28 January	NM	NM	NM	No	23	AS	Alive
	9	NM		NM	NM	NM	07 February	NM	NM	NM	No	11	AS	Alive
	10	NM		NM	NM	NM	07 February	NM	NM	NM	No	07	AS	Alive
17	Zhou et al.[22]	40M	China	Yes	Yes	Severe	23 January	RT-PCR	Yes	Yes	Yes	5 days after discharge	RT-PCR	Alive

18	Zhao et al[23] (7/14)	5.7 (Median) (2.9–7.3) Range F-4	China	5 Yes 2 No	No Co-morbidity	Mild (All)	NM (All)	RT-PCR[a]	NM (All)	Yes(all)	6-No 1- Yes	14 days from discharge (7–17)	RT-PCR[a]	Alive (All)
19	Li et al.[24]	50M	China	Yes	Yes	Mild	D13	RT-PCR	Yes on D 40. IgM and IgG positive	Yes	No	14	RT-PCR	Alive
20	Chen et al.[25]													
	1	29M	China	Yes	NM	Mild	01 February	RT-PCR[a]	NM	Yes	No	3	RT-PCR[a]	Alive
	2	49F		Yes	NM	Mild	02 February		NM	Yes	No	3		Alive
	3	12F		No	NM	Mild	05 February		NM	Yes	No	3		Alive
	4	38M		Yes	NM	mild	30 January		NM	Yes	No	3		Alive
21	Hu et al[26] (11)	median age 27, range 4–58 years F-4	China	Yes (All)	3-Co-morbidities	Mild-1 Moderate- 9 Severe-1	NM(All)	RT-PCR[a]	NM(All)	Yes (All)	No (All)	14 (9–17)	RT-PCR[a]	Alive (All)
22	Jianghong An et al.[27]	Median age 20 (5–64) 7-F (Mild) 38 (2–60) 15-F	China	Yes	1/11 1/27	Mild –11 Moderate 27	Patient were discharged, January 23 to February 25 (14 days)	RT PCR, Anal swab	Yes no difference between the two groups	Yes (All)	No (All)	Weekly after discharge	RT PCR[a]	Alive (All)
23	Chen et al.[28]	46 F	China	Yes	No	Mild	24 January	RT-PCR	No	Yes	No	03 days after last negative test	RT-PCR	Alive
24	Duggan et al.[29]	82 M	USA	Yes	Yes	Severe	Early April	RT-PCR	No	Yes	No	10 days post discharge	RT-PCR	Alive
25	Ye-min et al.[30]	49 M	China	Yes	NM	Mild	22 January	RT-PCR	NM	Yes	No	3 days after discharge	Sputum positive PCR -ve	Alive
26	To et al.[31]	33M	Hong kong	Yes	No Co-morbidity	Mild	29 March	RT- PCR	NM	Yes	No	123 days after discharge	RT-PCR	Alive
27	Tillet et al.[32]	25M	USA	Yes	No	Mild	18 April	RT- PCR	Yes	Yes	Yes	10 days after last negative test	RT-PCR	Alive

(*continued on next page*)

Table 1 – (continued)

S no	Study	Age and sex	Country	Sympt-omatic	Comor-bidity	Clinical severity	First COVID 19 (PCR)	Test Done	Serological test done after first episode	RT PCR negative after first episode	Symptomatic again after period of weeks	Date of Second COVID 19	Test done	Outcome
28	Elslande et al.[33]	51F	Belgium	Yes	Asthma	Moderate	March 20	RT-PCR	Yes (second time)	No	Yes	10 weeks after home quarantine	RT-PCR	Alive
29	Prado-Vivar B et al.[34]	46M	Eucadorian	Yes	NM	Mild	May 12	RT-PCR	Yes	Yes	Yes	6 weeks after being negative	RT-PCR	Alive
30	Gupta et al.[35]	25M	India	Yes	No	No	05 May	RT-PCR[a]	NM NM	Yes	No	100 days after tested negative	RT-PCR	Alive
		28F		No			17 May			Yes	No	101 days	RT-PCR	Alive

AS, anal swab; F, female; M, male; NM, not mentioned; RT-PCR, reverse transcriptase polymerase chain reaction (naso-pharyngeal swab).
[a] Same for all.

re-positives found genomic diversity, thus establishing reinfection.

Recurrence has been observed across all ages, from 10 months to 91 years of age. Mortality after reinfection is seen in the older age group with multiple comorbidities which is consistent with primary infection. Innate and acquired immunity of the individual may also influence recurrences.[35] Hence, immune-senescence of the old age and immunosuppressant drugs may affect recurrence. However, the majority (92.2%) of the COVID-19 re-positive cases had not been given corticosteroids for management during the primary episode of illness. Many re-positive cases were also given antivirals. However, in absence of control group, it is difficult to draw any inference for association of corticosteroids or antivirals. Second, the denominator in case reports or case series is difficult to ascertain, hence rate can also be not calculated. The effect of other immunomodulators and antiviral drugs on recurrence may be studied in a well-designed study with control group.

Pooled proportion of studies that have specified the proportion of COVID-19 re-positives was carried out. Approximately 12% of discharged COVID-19 cases after the first episode of infection were detected positive during subsequent molecular testing. The reasons may be related to Intermittent shedding of virus, the persistence of the virus, testing technique including sampling, or host characteristics. There was no evidence of secondary cases arising from these re-positives. Study carried out on nine patients of COVID-19 cases noted prolonged viral shedding in sputum.[36] However, there is a little residual risk of infectivity with viral load less than 100,000 viral RNA copies per ml of sputum.[36] This viral shedding in sputum needs to be further explored for infectivity of virus during recurrences as infectiousness of recurrence cases would have major implication on public health policy.

A notable area of scientific interest is the role of seroconversion among re-positives. Although animal studies suggest that antibody formation is protective against reinfection, yet in present systematic review we found that re-positives can occur even after seroconversion.[37] The relation between seroconversion and re-positives further need to be explored.

Different anatomical sampling sites may also have some effect on viral detection. In many cases, even if the sample from the nasopharyngeal is negative, the samples from sputum (lower respiratory tract) and anal swab have been positive. There is evidence that the virus may be shed longer from the extrapharyngeal sites. There are reports that virus shedding from asymptomatic patients may continue from extrapulmonary sites in various bodily fluids (saliva, tears, faeces, throat, or nasal discharge) for a longer duration of time.[38,39] Its role in reinfection is still not known.

Antibody-dependent enhancement is a known phenomenon in viral disease and responsible for increased severity of subsequent infections.[40] However, in this systematic review, we found that clinical manifestations in majority of re-positive cases were milder than the initial infection. This may be because most of the cases were not true reinfections but persistence of the same infection or due to intermittent virus shedding. Even in the six studies with documented genomic analysis, clinical manifestations in the reinfection

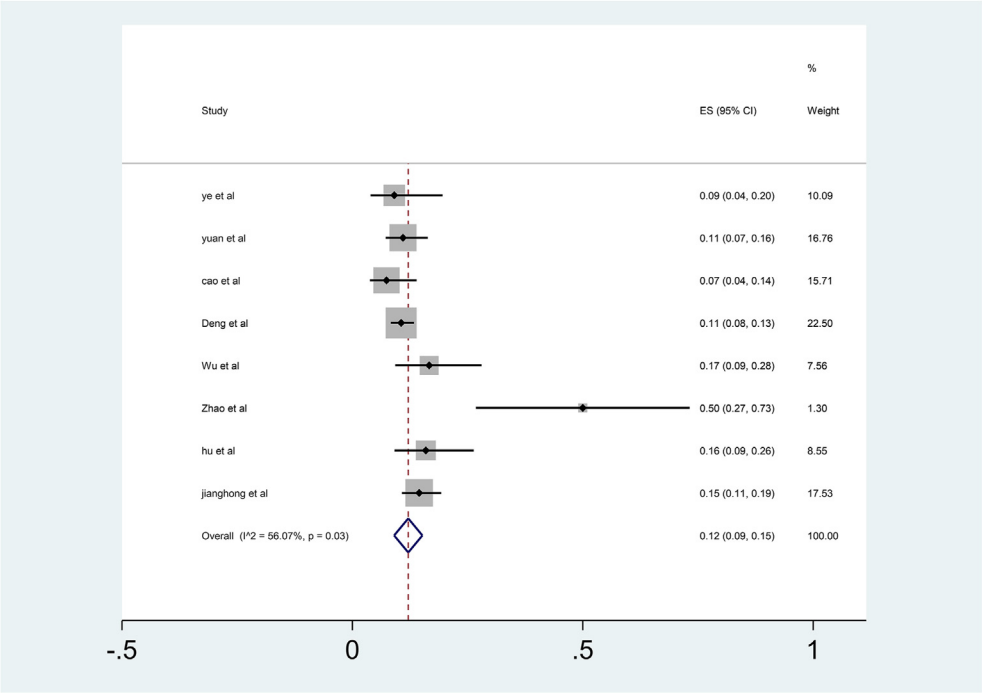

Fig. 2 – Pooled proportions of re-positives from studies.

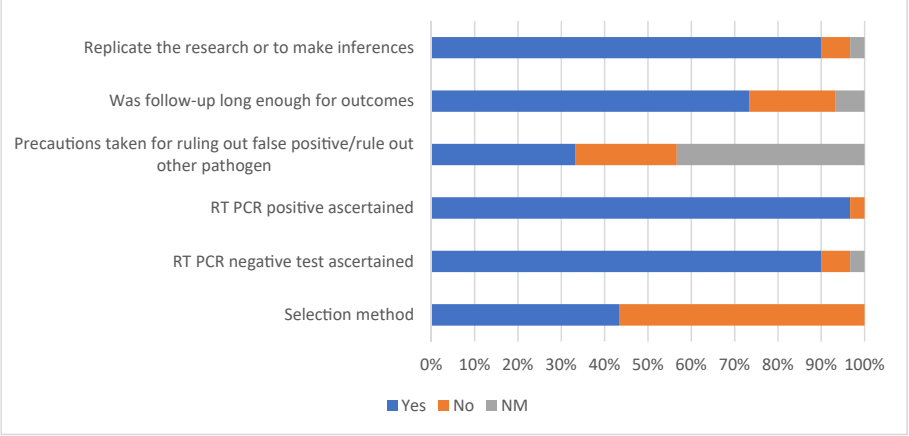

Fig. 3 – Quality of study as assessed using the modified Murad scale. *NM- Not Mentioned.

cases were mild to moderate. A model for reinfection has concluded that the rate of reinfection in the recovered population would decline to zero over time as the virus is cleared clinically from the system of the recovered cases.[41]

Risk of bias

Although there are no set guidelines for estimating the risk of bias in case reports and case series, the authors feel that initial RT-PCR positive, subsequent RT-PCR negative, serological testing, and RT-PCR positive after symptom-free period are essential for drawing conclusion about relapse or reinfection. Few case reports did not mention a negative RT-PCR test after the first COVID-19 infection.[5,9]

One of the limitations of our study is that the literature search has been restricted to only English language and to Medline and Cochrane database. Hence, we may have missed articles published in Chinese and other non-English languages.

Since these patients of recurrence may represent a special subset of COVID-19 cases, the findings may not be generalizable to all COVID-19 cases. More research is needed to delineate the factors responsible for recurrence in recovered cases.

As the pandemic progresses, more conclusive evidence in this context would be gathered. Nevertheless, there is a strong case for proper documentation of all the cases to further refute or confirm the findings.

Disclosure of competing interest

The authors have none to declare.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.mjafi.2021.05.025.

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