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REVIEW

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Comparison of confirmed COVID-19 with SARS and MERS cases - Clinical characteristics, laboratory findings, radiographic signs and outcomes: A systematic review and meta-analysis

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Summary

Introduction: Within this large-scale study, we compared clinical symptoms, laboratory findings, radiographic signs, and outcomes of COVID-19, SARS, and MERS to find unique features.

Method: We searched all relevant literature published up to February 28, 2020. Depending on the heterogeneity test, we used either random or fixed-effect models to analyze the appropriateness of the pooled results. Study has been registered in the PROSPERO database (ID 176106).

Result: Overall 114 articles included in this study; 52 251 COVID-19 confirmed patients (20 studies), 10 037 SARS (51 studies), and 8139 MERS patients (43 studies) were included. The most common symptom was fever; COVID-19 (85.6%, $P < .001$), SARS (96%, $P < .001$), and MERS (74%, $P < .001$), respectively. Analysis showed that 84% of Covid-19 patients, 86% of SARS patients, and 74.7% of MERS patients had an abnormal chest X-ray. The mortality rate in COVID-19 (5.6%, $P < .001$) was lower than SARS (13%, $P < .001$) and MERS (35%, $P < .001$) between all confirmed patients.

Conclusions: At the time of submission, the mortality rate in COVID-19 confirmed cases is lower than in SARS- and MERS-infected patients. Clinical outcomes and findings would be biased by reporting only confirmed cases, and this should be considered when interpreting the data.

KEYWORDS

coronavirus, COVID-19, meta-analysis, Middle East respiratory syndrome coronavirus, SARS virus, severe acute respiratory syndrome

Abbreviations: ACE2, angiotensin-converting enzyme 2; ARDS, acute respiratory distress syndrome; CDC, Centre for Disease Controls; CI, confidence interval; COVID-19, coronavirus disease 2019; CRP, C-reaction protein; CT scan, computed tomography scan; ESR, erythrocyte sedimentation rate; GGO, ground-glass opacity; ICU, intensive care unit; IL, interleukin; IQR, interquartile range; MCP-I, monocyte chemoattractant protein I; MERS, Middle East respiratory syndrome; N, number; NA, not known; PRISMA, preferred reporting items for systematic reviews and meta-analyses statement; RT-PCR, real-time polymerase chain reaction; SARS, severe acute respiratory syndrome; SARS-Cov-2, severe acute respiratory syndrome coronavirus-2; TNF-α, tumor necrosis factor-α; WBCs, white blood cells; WHO, World Health Organization.

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1 | INTRODUCTION

During the last two decades, coronaviruses have been recognized as one of the most critical human pathogenic viruses that affect global health and cause concern in the world health system.[1] Coronavirus is classified into four genera: alpha, beta, delta, and gamma. Major human pathogenic viruses belong to the beta genus, including Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS), and the 2019 novel coronavirus (COVID-19).[2]

Although coronaviruses are recognized as causes of the common cold, SARS was the first coronavirus to cause a life-threatening respiratory infection in humans. It was endemic in Guangzhou China in 2002-2003 and quickly spread to other countries in Asia, the Americas, Europe, and South Africa. A total of 8098 SARS infected cases and 774 deaths (about 10% mortality) were reported.[3]

About a decade later, MERS caused respiratory infection in the Middle East. Most of these patients had a history of travel to the Arabian Peninsula, or they were in contact with infected people, of which some were camel shepherds. After the Middle East, the second outbreak of MERS occurred in 2014-2017 in South Korea, indicating the circulation of the virus and a more significant concern for the world health community. At that time, MERS was responsible for infecting 2458 people and 848 deaths (about 35% mortality).[4]

In December 2019, a cluster of Covid-19 patients with symptoms of pneumonia complicated with acute respiratory distress syndrome (ARDS) was observed in Wuhan, China.[5,6] In comparison to SARS and MERS, Covid-19 has a higher rate of spread and became a pandemic in about 4 months. The high power of this large-scale dissemination led to the quarantine of several cities in different countries.[7] Based on the World Health Organization (WHO) 57th report on 17 March 2020; worldwide there have been 179 112 confirmed cases, with 7426 deaths (about 4% mortality).[8] There is no vaccine or targeted treatment currently available for COVID-19 infection. Treatment is mostly supportive, although multiple experimental antiviral medications are being evaluated.[9,10] Thus, prevention and rapid diagnosis of infected patients are crucial. The trigger for rapid screening and treatment of COVID-19 patients is based on clinical symptoms, laboratory, and radiographic findings that are similar to SARS and MERS infections.

In this study, we attempted to distinguish the clinical symptoms, laboratory findings, radiographic signs, and outcomes of confirmed COVID-19, SARS, and MERS patients. All findings are compared to determine unique features among each of them. These data could be helpful in the early diagnosis and prevention of infection as well as providing more reliable epidemiological data on a large-scale for health care policies and future studies.

2 | METHODS

2.1 | Search strategy

This study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Statement (PRISMA) guidelines, and it has been registered in the PROSPERO database (ID 176106).[11] We searched all studies published up to 28 February 2020, from the following databases: Embase, Scopus, PubMed, Web of Science, and the Cochrane library. Search medical subject headings (MeSH) terms used were: "COVID-19," "Coronavirus," "Severe Acute Respiratory Syndrome," "SARS Virus," "severe acute respiratory syndrome coronavirus 2", "Coronavirus Infections," "Middle East Respiratory Syndrome Coronavirus," and all their synonyms like "Wuhan Coronavirus," "SARS-CoV-2," and "COVID-19," "2019-nCoV" and MERS. Moreover, we searched for unpublished and grey literature with Google scholar, Centre for Disease Controls (CDC) and WHO databases. We also examined references of included articles to find additional relevant studies. There was no language restriction, and all included studies were written in English or Chinese languages; the latter was translated by https://translate.google.com/. Additional search strategy details are provided in Table S1.

2.2 | Study selection

Duplicate studies were removed using EndNote X7 (Thomson Reuters, New York, NY, USA). Records were initially screened by title and abstract by independently four authors (AP, SG, AK, and RF). The full-text of potentially eligible records was retrieved and examined, and any discrepancies were resolved by consensus.

2.3 | Eligibility and inclusion criteria

Studies had to fulfill the following predetermined criteria to be eligible for inclusion in our meta-analysis. All case-control, cross-sectional, cohort studies, case reports, and case series peer-reviewed studies were included if they reported the number of confirmed cases of patients with demographic data, [AND] [OR] clinical data, [AND] [OR] laboratory data, [AND] [OR] risk factor data.

2.4 | Exclusion criteria

Studies were excluded if they did not report the number of confirmed cases. Letters to the editor, individual case reports, review articles, and news reports were also excluded. Duplicate information from the same patient was combined and counted as a single case when the data was reported twice.

2.5 | Data extraction

All COVID-19 included publications were published in 2020, and all patients were from China. The following items were extracted from each article: first author, center and study location in China, countries, sample collection time, patient follow-up time, the reference standard for infection confirmation, number of confirmed cases, study type, and all demographic, clinical, laboratory data, and risk factor data. Three of our authors (SG, AK, and RF) independently extracted data, and all extracted data were checked randomly by another author (AP); differences were resolved by consensus.

2.6 | Quality assessment

Quality assessments of studies were performed by two reviewers independently according to the Critical Appraisal Checklist recommended by the Joanna Briggs Institute,[12] and disagreements were resolved by consensus. The checklist is composed of nine questions that reviewers addressed for each study. The "Yes" answer to each question received one point. Thus, the final scores for each study could range from zero to nine (Table S2).

2.7 | Analysis

Data cleaning and preparation were done in Microsoft Excel 2010 (Microsoft©, Redmond, WA, USA), and further analyses were carried out via Comprehensive Meta-Analysis Software Version 2.0 (Biostat, Englewood, NJ). Determination of heterogeneity among the studies was undertaken using the chi-squared test (Cochran's Q) to assess the appropriateness of pooling data. Depending on the heterogeneity test, we used either random or fixed-effect models for pooled results. In the case of high heterogeneity (I2 > 50%), a random effect model (M-H heterogeneity) was applied, while in low heterogeneity cases (I2 < 50%), a fixed-effect model was used.[13] Percentages and means ± SDs were calculated to describe the distributions of categorical and continuous variables, respectively. *P* values reflect study heterogeneity with <.05 being significant. We also used the funnel plot, Begg's, and Egger's tests based on the symmetry assumption to detect publication bias (Figure S1).

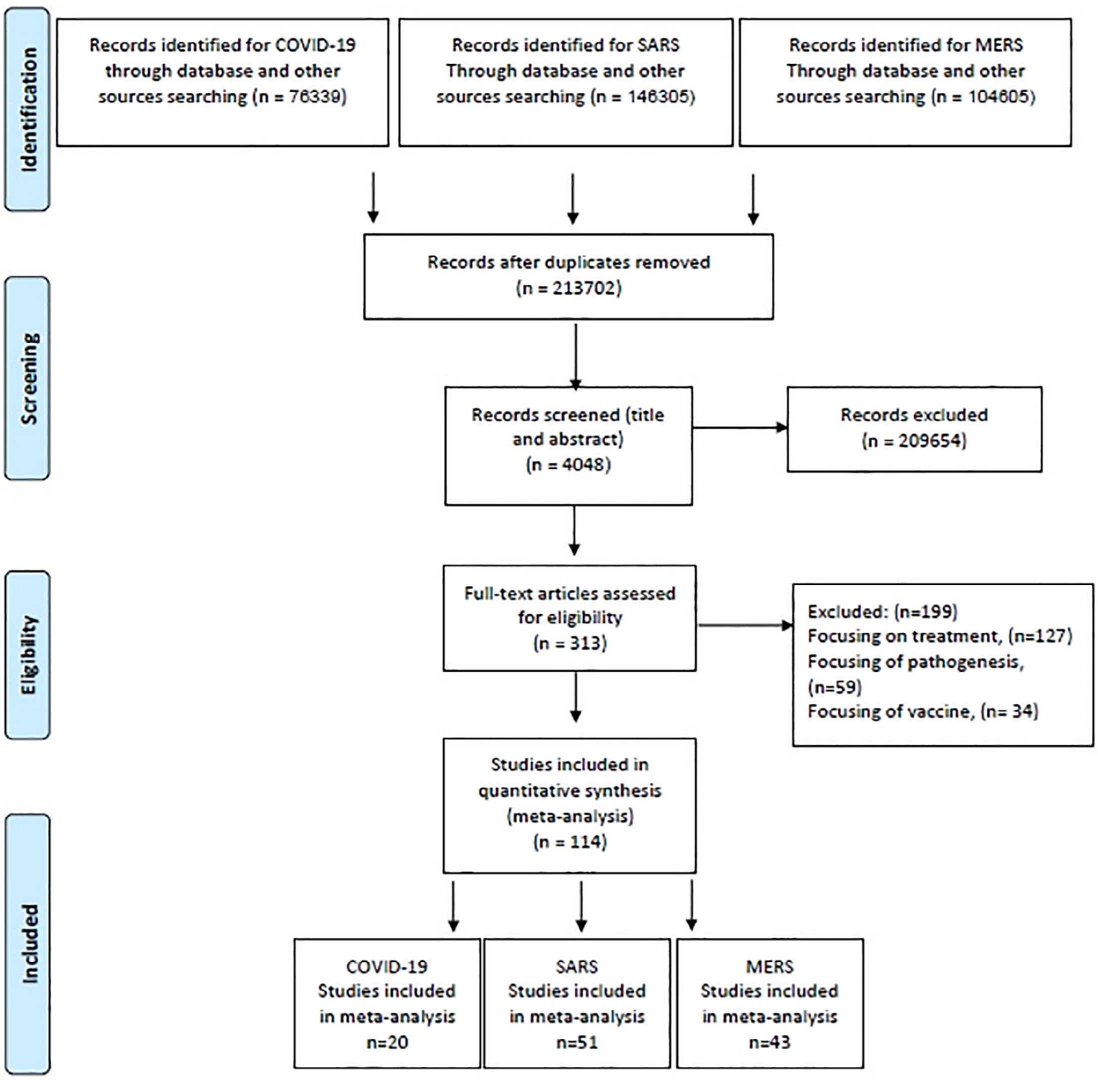

FIGURE 1 Flow diagram of literature search and study selection (PRISMA flow chart)

TABLE 1 Characterization of included studies

First author	Sampling center/Country	Sample collection time	Published year	Patient follow-up (d)	N Confirmed patients	Mean age in years (IQR)	N sex (male)	Reference standard	Study type
	COVID-19 studies (Total of 20 studies, 52 251 patients)								
Nanshan Chen [14]	Wuhan Jinyintan Hospital	1 Jan to 20 Jan 2020	2020	5-24	99	55·5 (21-82)	67	RT-PCR	Retrospective
Kaiyuan Sun [15]	Multicenter	20 Jan-Jan 29, 2020	2020	42	288	49 (2-89)	62.3	CDC guideline	Retrospective
Jie Li [16]	Dazhou Central Hospital	22 January-10 February 2020	2020	1-21	17	45.1 (32-65)	9	RT-PCR	Retrospective
Dawei Wang [17]	Zhongnan Hospital of Wuhan	1 January-28 January 2020	2020	6-34	138	56 (42-68)	75	RT-PCR	Retrospective
Chaolin Huang [18]	Jin Yintan Hospital (Wuhan)	31 Dec 2019-UN	2020	NA	41	49 (41-58)	30	RT-PCR	Retrospective
Weijie Guan[19]	Multicenter	NA	2020	NA	1099	47 (35-58)	640	RT-PCR	Retrospective
Yang Yang[20]	NA	NA	2020	51 d	4021	49	2211	NA	Retrospective
Lei Chen (Chinese)[21]	Tongji hospital in Wuhan	14-29 January 2020	2020	15 d	29	56 (26-79)	21	RT-PCR	Retrospective
Adam Bernheim[22]	Multicenter	18 January-2 February 2020	2020	12 d	121	45 (18-80)	61	RT-PCR & CT scan	retrospective
Feng Pan[23]	Union Hospital	12 Jan-6 Feb 2020	2020	NA	21	40 (25-63)	15	RT-PCR	Retrospective
Jin Zhang[24]	No.7 hospital of Wuhan	16th Jan to 3rd Feb 2020	2020	NA	140	57 (25-87)	71	RT-PCR	Retrospective
Yichun Cheng[25]	Tongji hospital in Wuhan	28 January-11 February 2020	2020	10 (7-13)	710	63 (51-71)	374	RT-PCR	Retrospective
Ming-Yen[26]	Hong Kong-Shenzhen Hospital	NA	2020	NA	21	56 (37-65)	13	RT-PCR	Retrospective
Sijia Tian[27]	Beijing Emergency Medical Service	20 Jan to 10 Feb 2020	2020	Feb. 10 20	262	47.5 (1-94)	127	RT-PCR	Retrospective
Qun Li[28]	NA	NA	2020	NA	425	15-89 (26-82)	240	WHO guideline	Retrospective
De Chang[29]	Three hospitals in Beijing	16 January-29 January 2020	2020	4 Feb. 2020	13	34 (34-48)	10	NA	Retrospective
Xiao-Wei Xu[30]	Zhejiang province	10 January-26 January 2020	2020	10 d	62	41 (32-52)	36	WHO guideline	Retrospective
Fengxiang Song[31]	Center for Disease Control, Shanghai	20 January-27 January 2020	2020	NA	51	49 (16-76)	25	CT scan & nucleic acid test	Retrospective
Michael Chung[32]	Multicenter	18-27 January 2020	2020	NA	21	51 (29-77)	13	CT scan, NA	Retrospective
Zunyou Wu (CDC)[33]	Multicenter	through 11 February 2020	2020	15 d	44 672	30-79	22 981	nucleic acid test result	Retrospective
	SARS studies (Total of 51 studies, 10 037 patients)								
First author	**Sampling center/Country**	**Sample collection time**	**Published year**	**Patient follow**	**N confirmed patients**	**Mean age in years (IQR)**	**N sex (male)**	**Reference standard**	**Study type**

TABLE 1 (Continued)

First author	COVID-19 studies (Total of 20 studies, 52 251 patients) Sampling center/Country	Sample collection time	Published year	Patient follow-up (d)	N Confirmed patients	Mean age in years (IQR)	N sex (male)	Reference standard	Study type
Ali S. Omrani[34]	Saudi Arabia	2013	2013	NA	3	UN	UN	RT-PCR	Case series
Owen Tak-Yin Tsang[35]	Hong Kong	26 January 2003-31 March 2003	2003	NA	156	UN	90	RT-PCR	Retrospective
Li-Yang Hsu[36]	Singapore	2003	2003	NA	20	(19-73)	5	RT-PCR	Retrospective
Christl A Donnelly[37]	Hong Kong	2003	2003	NA	1425	UN	UN	RT-PCR	Prospective
Christopher[38]	Canada	2003	2003	NA	144	(34-57)	NA	RT-PCR	Retrospective
Monali Varia[39]	Canada	2003	2003	NA	128	42 (21 m-86 y)	51	RT-PCR	Retrospective
Robert A Fowler[40]	Canada	2003	2003	NA	38	(39-69.6)	23	RT-PCR	Retrospective
J S M Peiris[41]	China	2003	2003	NA	50	(23-74)	NA	RT-PCR	prospective
J S M Peiris[42]	Hong Kong	2003	2003	NA	75	UN	36	RT-PCR	Prospective
J W M Chan[43]	Hong Kong	2003	2003	NA	115	UN	NA	RT-PCR	Retrospective
Jann-Tay Wang[44]	Taiwan	2003	2003	NA	76	46.5 (24-87)	34	RT-PCR	Retrospective
K L E Hon[45]	China	2003	2003	NA	10	NA	2	RT-PCR	Retrospective
K. T. Wong[46]	Hong Kong	2003	2003	NA	138	39 (20-83)	66	RT-PCR	Retrospective
Kamaljit Singh[47]	Singapore	2003	2003	NA	14	58 (21-84)	5	CT scan and RT-PCR	Retrospective
Kenneth W. Tsang[48]	China	2003	2003	NA	10	52.5 ± 11	5	RT-PCR	Retrospective
Marianna Ofner-Agostini[49]	Canada	2003	2006	NA	17	39.2 (27-58)	4	RT-PCR	Retrospective
N S Zhong[50]	China	2002	2003	NA	50	38.4	28	RT-PCR	Retrospective
Nelson Lee[51]	China	2003	2004	NA	17	34 (22-57)	6	RT-PCR	Retrospective
Nelson Lee[52]	China	2003	2003	NA	138	NA	NA	RT-PCR	Cohort
P.L. Ho[53]	China	2003	2005	NA	44	39.27 ± 11.26	22	RT-PCR	Retrospective
Ping Tim Tsui[54]	China	2003	2003	NA	323	41 ± 14 (18-83)	NA	RT-PCR	Retrospective
Raymond S M Wong[55]	China	2003	2003	NA	157	NA	64	RT-PCR	Retrospective
Thomas W[56]	Singapore	2003	2003	NA	199	NA	65	RT-PCR	Cohort
Timothy H Rainer[57]	China	2003	2003	NA	97	37.0 ± 15.4	37	RT-PCR	Prospective
W.N. Wong[58]	Hong Kong	2003	2003	NA	205	35.9 ± 16.2	90	RT-PCR	Cohort
Z. Zhao[59]	China	2002	2003	NA	190	NA	NA	RT-PCR	Prospective
Susan M. Poutanen[60]	Canada	2003	2005	NA	10	NA	NA	RT-PCR	Retrospective
I.F.N. Hung[61]	China	2004	2004	NA	154	41.5 (20-80)	92	RT-PCR	Retrospective
Hoang Thu Vu[62]	Vietnam	2003	2004	NA	62	NA	NA	RT-PCR	Retrospective

(Continues)

TABLE 1 (Continued)

First author	Sampling center/Country	Sample collection time	Published year	Patient follow-up (d)	N Confirmed patients	Mean age in years (IQR)	N sex (male)	Reference standard	Study type
	COVID-19 studies (Total of 20 studies, 52 251 patients)								
F. Chena[63]	Hong Kong	2002	2004	NA	10	NA	5	RT-PCR	Retrospective
C.W. Leung[64]	China	2004	2004	NA	64	11.7	29	RT-PCR	Retrospective
Monica Avendano[65]	Canada	2003	2003	NA	14	42 ± 9 (27-63)	3	RT-PCR	Retrospective
Padmini Srikantiah[66]	Us	2003	2005	NA	8	NA	NA	RT-PCR	Retrospective
Kwok H. Chan[67]	Hong Kong	2004	2004	NA	322	NA	NA	RT-PCR	Cohort
Wannian Liang[68]	China	2003	2003	NA	2443	33 (1.0-90)	NA	RT-PCR	Prospective
Xinchun Chen[69]	China	2004	2004	NA	36	30.39 ± 12.15	20	RT-PCR	Retrospective
Chi-wai Leung[70]	Hong Kong	2004	2004	NA	44	12 (17-50)	20	RT-PCR	Prospective
LCL Heung[71]	Hong Kong	2006	2006	NA	93	NA	18	IF	Cross-sectional
Ming-Han Tsai[72]	Taiwan.	2003	2008	NA	124	NA	NA	ELISA	Retrospective
Hy A. Dwosh[73]	Us	2003	2003	NA	16	(24-80)	4	RT-PCR	Retrospective
Ari Bitnun[73]	Canada	2003	2003	NA	15	NA	6	RT-PCR	Prospective
Alice S. Ho[74]	Hong Kong	2003	2003	NA	40	(24-50)	9	RT-PCR	Retrospective
Leonard Grinblat[75]	Canada	2003	2003	NA	40	42.7 ± 13.5 (17-73)	18	RT-PCR	Retrospective
Cheng-Kuo Fan[76]	Taiwan	2005	2005	NA	43	41.0 ± 17.1	22	RT-PCR	Descriptive
Kin Wing Choi[77]	Hong Kong	2003	2003	NA	227	39 (18-96)	75	RT-PCR	Retrospective
GM Leung[78]	Hong Kong	2003	2003	NA	1755	NA	777	RT-PCR	Retrospective
Chung-Ming Chu[79]	China	2005	2005	NA	79	39.4 ± 11.5 (20-72)	38	RT-PCR	Retrospective
Kwok Hong Chu[80]	Hong Kong	2004	2004	NA	536	NA	NA	RT-PCR	Retrospective
T.-N. Jang[81]	Taiwan	2003	2004	NA	29	42.9 (22-82)	9	RT-PCR	Retrospective
Tze-wai Wong[82]	China	2004	2004	NA	16	22.3	8	RT-PCR	Retrospective
Wei-Kung Wang[83]	Taiwan	2003	2004	NA	17	21-54	9	RT-PCR	Retrospective
	MERS studies (Total 43 studies, 8, 139 patients)								
First author	**Sampling center/Country**	**Sample collection time**	**Published year**	**Patient follow**	**N Confirmed patients**	**Mean age in years (IQR)**	**N Sex (male)**	**Reference standard**	**Study type**
Asad S. Aburizaiza[84]	Saudi Arabia	2012	2012	NA	8	(16-62)	NA	IFA	Cross-sectional
Marcel A Müller[85]	Saudi Arabia	2012-2013	2015	NA	15	37·13 ± 8·64 (15-62)	NA	ELISA, IFA	Cross-sectional
Abdulkarim Alhetheel[86]	Saudi Arabia	2016	2017	NA	30	NA	NA	RT-PCR	Cross-sectional
Abdulaziz A. Bin Saeed[87]	Saudi Arabia	2015	2016	NA	384	(1-66)	226	NA	Cross-sectional

TABLE 1 (Continued)

First author	COVID-19 studies (Total of 20 studies, 52 251 patients)								
	Sampling center/Country	Sample collection time	Published year	Patient follow-up (d)	N Confirmed patients	Mean age in years (IQR)	N sex (male)	Reference standard	Study type
Boyeong Ryu[88]	South Korea	2015	2015	NA	34	(34-56.7)	20	RT-PCR	Cross-sectional
Jamal Ahmadzadeh[89]	Iran	2019	2019	NA	107	50 ± 17	80	NA	Cross-sectional
Kazhal Mobaraki[90]	Iran	2019	2019	NA	229	NA	171	RT-PCR	Epidemiological analysis
Abdullah Assiri[91]	Saudi Arabia	2013	2013	NA	47	55	36	RT-PCR	Retrospective
Korea Centers for Disease[92]	South Korea	2015	2015	NA	186	55 (42-66)	111	RT-PCR	Retrospective
Abdullah Assiri[93]	Saudi Arabia	2013	2013	NA	23	56 (24-94)	17	RT-PCR	Retrospective
Abdullah Assiri[94]	Saudi Arabia	2014	2016	NA	38	51 (17-84)	28	RT-PCR	Retrospective
Abdullah M. Assiri[95]	Saudi Arabia	2015	2016	NA	143	58 (2.0-99)	91	RT-PCR	Retrospective
Ashraf Abdel Halim[96]	Egypt	2015	2016	NA	32	43.99 ± 13.03	20	RT-PCR	Retrospective
Deborah L. Hastings[97]	Saudi Arabia	2014	2016	NA	78	53	59	RT-PCR	Retrospective cohort
F S Alhamlan[98]	Saudi Arabia	2012-2015	2016	NA	1275	50 (0-109)	807/1246	RT-PCR	Retrospective
H.E. El Bushra[99]	Saudi Arabia	2015	2016	NA	52	NA	31	RT-PCR	Retrospective
Hanan H. Balkhy[99]	Saudi Arabia	2016	2016	NA	130	56.3	66	RT-PCR	Retrospective
Ikwo K. Oboho[100]	Saudi Arabia	2014	2015	NA	255	45 (30-59)	174	RT-PCR	Retrospective
Kyung Min Kim[101]	South Korea	2015	2015	NA	36	51	20/36	RT-PCR	Retrospective
Ziad A. Memish[102]	Saudi Arabia	2013	2013	NA	7	(29-59)	0	RT-PCR	Retrospective
Won Suk Choi[103]	South Korea	2015	2015	NA	186	5 (16-86)	111	RT-PCR	Retrospective observational
Mohammad Mousa Al-Abdallat[104]	Jordon	2012	2014	NA	9	40 (25-60)	6	RT-PCR	Retrospective
Mustafa Saad[105]	Saudi Arabia	2012-2014	2014	NA	70	62 (1-90)	46	RT-PCR	Retrospective
Yaseen M. Arabi[106]	Saudi Arabia	2012-2013	2014	NA	12	59 (36-83)	8	RT-PCR	Case series
Maimuna S. Majumder[107]	South Korea	2015	2015	NA	159	55 ± 15.9 (16-87)	94	RT-PCR	Retrospective
Victor Virlogeux[108]	South Korea	2015	2016	NA	107	54.6	96	NA	Retrospective
Jaffar A. Al-Tawfiq[109]	Saudi Arabia			NA	17	60.7	11	RT-PCR	Case-control
Thamer H. Alenazi[110]	Saudi Arabia	2015	2017	NA	130	56.5	66	RT-PCR	Prospective
Abdullah J. Alsahafi[111]	Saudi Arabia	2012-2015		NA	939	NA	624	NA	
Karuna M. Das[112]	Saudi Arabia	2015	2015	NA	55	54 ± 16 (12 to 85)	16	RT-PCR	Retrospective
Anwar E. Ahmed[113]	Saudi Arabia	2014-2016	2017	NA	660	53.9 ± 17.9 (2-109)	452	NA	Retrospective
Anwar E. Ahmed[114]	WHO website	2015-2017	2017	NA	537	55 ± 17.9 (2-109)	370	NA	Retrospective

(Continues)

TABLE 1 (Continued)

	COVID-19 studies (Total of 20 studies, 52 251 patients)								
First author	Sampling center/Country	Sample collection time	Published year	Patient follow-up (d)	N Confirmed patients	Mean age in years (IQR)	N sex (male)	Reference standard	Study type
Basem M. Alraddadi[115]	Saudi Arabia	2014	2014	NA	535	49	518	NA	Retrospective
Benjamin J Cowling[116]	South Korea	2015	2015	NA	166	56	101	NA	Retrospective
Chang Kyung Kang[117]	South Korea	2015	2017	NA	186	54	111	RT-PCR	Retrospective
Christian Drosten[118]	Saudi Arabia	2014	2014	NA	12	(3-74)	7	PRNT and RT-PCR	Cross-sectional
Daniel R. Feikin[119]	Saudi Arabia	2014	2015	NA	102	NA	76	NA	retrospective
Hamzah A. Mohd[120]	Saudi Arabia	2014-2015	2016	NA	80	40	48	RT-PCR	Cohort
Jung Wan Park[121]	South Korea	2015	2017	NA	26	71 (38-86)	13	RT-PCR	Retrospective
Nahid Sherbini[122]	Saudi Arabia	2014	2016	NA	29	45 ± 12	20	RT-PCR	Retrospective
Oyelola A. Adegboye[123]	Saudi Arabia	2012-2015	2017	NA	959	NA	642	NA	
Ghaleb A. Almekhlafi[124]	Saudi Arabia			NA	31	59 ± 20	22	RT-PCR	Retrospective cohort
Sun Hee Park[125]	South Korea			NA	23	NA	13	RT-PCR	Retrospective

Abbreviations: CDC, Centers for Disease Control and Prevention; CT scan, CT scan of chest; IQR, interquartile range; N, number; NA, not known; RT-PCR, real-time polymerase chain reaction; WHO, World Health Organization.

3 | RESULTS

3.1 | Characteristics of included studies

The process of study selection is displayed in Figure 1. A total of 36 115 reports were screened for the analysis of patients with COVID-19, 36 014 were excluded after the title, and abstract screening and the full text of 81 reports were reviewed in full text. We excluded studies that did not report sufficient data. Out of 114 included studies, 20 studies met the inclusion criteria for COVID-19, 51 for SARS, 43 for MERS. The characteristics of the selected articles are summarized in Table 1. Of the 20 COVID-19 studies that were included in the analysis, 19 studies were in English, and one was in Chinese.[21] All COVID-19 studies were retrospective, published in 2020, and all patients were from China.

3.2 | Quality assessment

Quality assessment of included studies was performed based on the Critical Appraisal Checklist, and the final quality scores of the included studies are represented in Table S2. In brief, studies by Chen et al,[14] Wang et al,[17] Huang et al,[18] Guan et al,[19] Zhang et al,[24] Cheng et al,[25] Li et al,[28] Xu et al,[30] and Song et al[31] had the highest quality of the COVID-19 studies available in the purpose of this study.

3.3 | Demographics, baseline characteristics, and clinical characterization

Overall, 52 251 confirmed patients with COVID-19 infection, 10 037 with SARS, and 8139 with MERS were included in the meta-analysis, of which 53.7% (95% CI 50-56.8, $P < .001$) of COVID-19, 43% (95% CI 40-46.5, $P < .001$) of SARS, 66% (95% CI 63-69, $P < .001$), of MERS included patients were male. Funnel plots for included studies did not detect significant publication bias (Figure S1). Table 2 shows that most COVID-19 85.6% (95% CI 73-93, $P < .001$), SARS 96% (95% CI 93-97.6, $P < .001$), and MERS 74% (95% CI 63.5-83.5, $P < .001$) had a fever (Figure S2). Cough was the second most common symptom presenting in COVID-19 63% (95% CI 55.5-70, $P < .001$), SARS 54.2% (95% CI 49-59, $P < .001$), and MERS 61% (95% CI 51-70, $P < .001$) of patients (Figure S3).

Shortness of breath was less common in Covid-19 patients 17% (95% CI 9-31.5, $P < .001$), in comparison to SARS 32% (95% CI 20-46, $P < .001$), and MERS 51% (95% CI 41-63, $P < .001$). Likewise, chills were less common in Covid-19 patients 17% (95% CI 6.5-38, $P < .001$), in comparison to SARS 57.5% (95% CI 50-64, $P < .001$), and MERS 41% (95% CI 16-72, $P < .001$).

A much smaller proportion of COVID-19 patients had sore throat 12.3% (95% CI 7.8-17, $P < .06$), headache 12.2% (95% CI 8.3-18, $P < .001$), diarrhea 7.3% (95% CI 4.6-11.4, $P < .001$), rhinorrhea 6% (95% CI 3-12, $P < .43$), nausea and vomiting 6%

TABLE 2 Demographics, baseline characteristics, and clinical outcomes of patients with confirmed COVID-19

	COVID-19 (Total of 20 Studies, 52, 251 Patients)			SARS (Total of 51 Studies, 10, 037 Patients)			MERS (Total 43 Studies, 8, 139 Patients)		
	Clinical presentation[a] (CI 95%)	Included studies number	Included patients number	Clinical presentation[a] (CI 95%)	Included studies number	Included patients number	Clinical presentation[a] (CI 95%)	Included studies number	Included patients number
Age, y	49.5 (mean) (46-52.5)	20	52 251	37.5 (34.5-40.5)	24	4309	52 (51-54.5)	30	5174
Sex (Male)	53.7 (50-56.8)	20	52 248	43 (%) (40-46.5)	35	6254	66 (63-69)	40	8086
Fever	85.6 (73-93)	15	2832	96 (93-97.6)	34	6194	74 (63.5-83.5)	22	1583
Cough	63 (55.5-70)	15	2135	54.2 (49-59)	32	5904	61 (51-70)	21	1453
Fatigue	40.3 (29-52.5)	11	1959	-	-	-	28 (21-35)	6	516
Sputum production/ Expectoration	28 (19-39)	7	1378	21 (16-27)	11	2320	31.5 (22-43)	9	757
Myalgia	26 (14-43)	6	1350	49.5 (44.5-55)	22	2872	33.3 (26.5-41)	10	785
Dyspnea	20 (12.6-32)	7	1730	32 (20.5-45.5)	18	2412	40 (23-57)	11	777
Shortness of breath	17 (9-31.5)	3	1260	32 (20-46)	11	2335	51 (41-63)	9	695
Chill	17 (6.5-38)	2	1120	57.5 (50-64)	21	2767	41 (16-72)	6	667
Sore throat	12.3 (7.8-17)	6	1429	17 (14-21)	20	2452	16.5 (10-26)	12	992
Headache	12.2 (8.3-18)	10	1815	38 (30-46)	20	2617	15 (11-20)	12	1170
Diarrhea	7.3 (4.6-11.4)	11	1710	24 (17.5-31.5)	20	2452	17.3 (14.5-20.5)	13	1017
Rhinorrhea	6 (3-12)	3	129	13 (8.5-20)	6	840	6 (1-20)	6	479
Nausea and vomiting	6 (2.7-13)	4	1387	18.5 (13-25	14	2410	20 (16-25)	12	863
Runny nose	4 (1-14)	1	51	18 (9-30)	6	870	21 (4-61)	5	246
Comorbid conditions									
	COVID-19			**SARS**			**MERS**		

(Continues)

TABLE 2 (Continued)

	COVID-19 (Total of 20 Studies, 52, 251 Patients)			SARS (Total of 51 Studies, 10, 037 Patients)			MERS (Total 43 Studies, 8, 139 Patients)		
	Clinical presentation[a] (CI 95%)	Included studies number	Included patients number	Clinical presentation[a] (CI 95%)	Included studies number	Included patients number	Clinical presentation[a] (CI 95%)	Included studies number	Included patients number
	Clinical presentation[a] (CI 95%)	Included studies number	Included patients number	Clinical presentation[a] (CI 95%)	Included studies number	Included patients number	Clinical Presentation[a] (CI 95%)	Included studies number	
Recent travel or contact with endemic people resident of Wuhan		69.5 (54.5-81)	7	45 443	26.5 (20-34)	1	156	-	- -
Chronic diseases	41.2 (20-66)	3	1227	-	-	-	-	-	-
Exposure to seafood market	24.3 (9.6-49)	5	732	-	-	-	-	-	-
Sick contacts with respiratory illness	15 (4.5-39.6)	4	829	-	-	-	-	-	-
Hypertension	15 (8.5-24.6)	10	46 270	14 (5.5-31)	4	504	36 (28-45)	10	677
ARDS	10.6 (4-26.7)	5	1439	51 (6-94)	2	204	29 (14-51)	2	55
Diabetes	8 (4-15)	8	46 232	9.9 (5-16.5)	10	2304	46 (34.5-58)	17	1086
Current smoker	7.7 (3.7-15)	5	1348	7.5 (5-11)	4	347	21.5 (14-32)	9	144
Chronic liver disease	5.7 (3.8-8.4)	8	499	13.5 (5-30)	6	604	9 (4-21)	5	53
Digestive system disease	3.5 (2.5-4.9)	2	1198	10.5 (6.5-6)	5	504	16.5 (10-25)	11	152
Health care worker	3 (2-4.6)	3	46 196	28.5 (18-43)	12	2328	21 (17-25.5)	20	1232
Past smoker	3 (1.1-7.5)	2	1239	-	-		-	-	-
Cardiovascular and cerebrovascular diseases	2.3 (2.2-2.5)	8	46 302	9.5 (5-22)	8	1045	20.5 (15-27)	15	407
Chronic respiratory disease	2.2 (0.6-8)	4	45 911	30 (15-50)	10	2224	9 (6.5-12	1	939
Cancer	1.7 (0.4-7.4)	6	46 078	1.3 (0.2-10)	3	504	12 (7-20)	10	182
Renal failure	2.3 (1-4)	7	2289	4 (2.5-7)	8	1103	20.5 (14-24.5)	15	366

TABLE 2 (Continued)

	COVID-19 (Total of 20 Studies, 52, 251 Patients)			SARS (Total of 51 Studies, 10, 037 Patients)			MERS (Total 43 Studies, 8, 139 Patients)		
	Clinical presentation[a] (CI 95%)	Included studies number	Included patients number	Clinical presentation[a] (CI 95%)	Included studies number	Included patients number	Clinical presentation[a] (CI 95%)	Included studies number	Included patients number
Bacteria co-infection	-	-	-	20 (12-31)	3	281	17.7 (6-42)	4	21
Camel exposure	-	-	-	-	-	-	20 (12-32)	9	657
Chest X-ray and CT scan									
	COVID-19			**SARS**			**MERS**		
	Clinical presentation[a] (CI 95%)	**Included studies number**	**Included patients number**	**Clinical presentation[a] (CI 95%)**	**Included studies number**	**Included Patients Number**	**Clinical presentation[a] (CI 95%)**	**Included studies number**	**Included patients number**
Abnormal chest X ray	84 (78-8.5)	12	1706	86 (77-92)	20	1209	74.7 (56.5-87)	10	258
Bilateral involvement	76.8 (62.5-87)	12	46 270	-	-	-	-	-	-
Consolidation	75.5 (50.5-91)	6	1378	41.5 (11-80)	2	78	18 (10-30)	1	10
Ground-glass opacity	71 (40-90)	12	46 270	41 (14-76	3	340	65 (52-77)	1	36
Unilateral involvement of chest radiography	16.5 (8.5-29.5)	6	1378	-	-	-	-	-	-
Outcome									
	COVID-19			**SARS**			**MERS**		
	Clinical presentation[a] (CI 95%)	**Included studies number**	**Included patients number**	**Clinical presentation[a] (CI 95%)**	**Included studies number**	**Included patients number**	**Clinical presentation[a] (CI 95%)**	**Included studies number**	**Included patients number**
Hospitalized	85.4 (%) (68-94)	3	1378	33 (11-66)	3	87	8 (1-40)	5	1400
Discharged	14 (%) (5.55-31.5)	3	1378	-	-	-	40 (28-53)	7	1660
Critical condition/ICU	20.6 (%) (6.7-48)	6	45 951	-	-	-	-	-	-
Mortality	5.6 (%) (2.5-12.5)	8	47 200	13 (9-17)	20	5501	35 (31-39)	32	6987

Abbreviations: ARDS, acute respiratory distress syndrome; CI, confidence interval; CT scan, CT scan; ICU, intensive care unit.
[a]Age is an exception, presented in mean age in years.

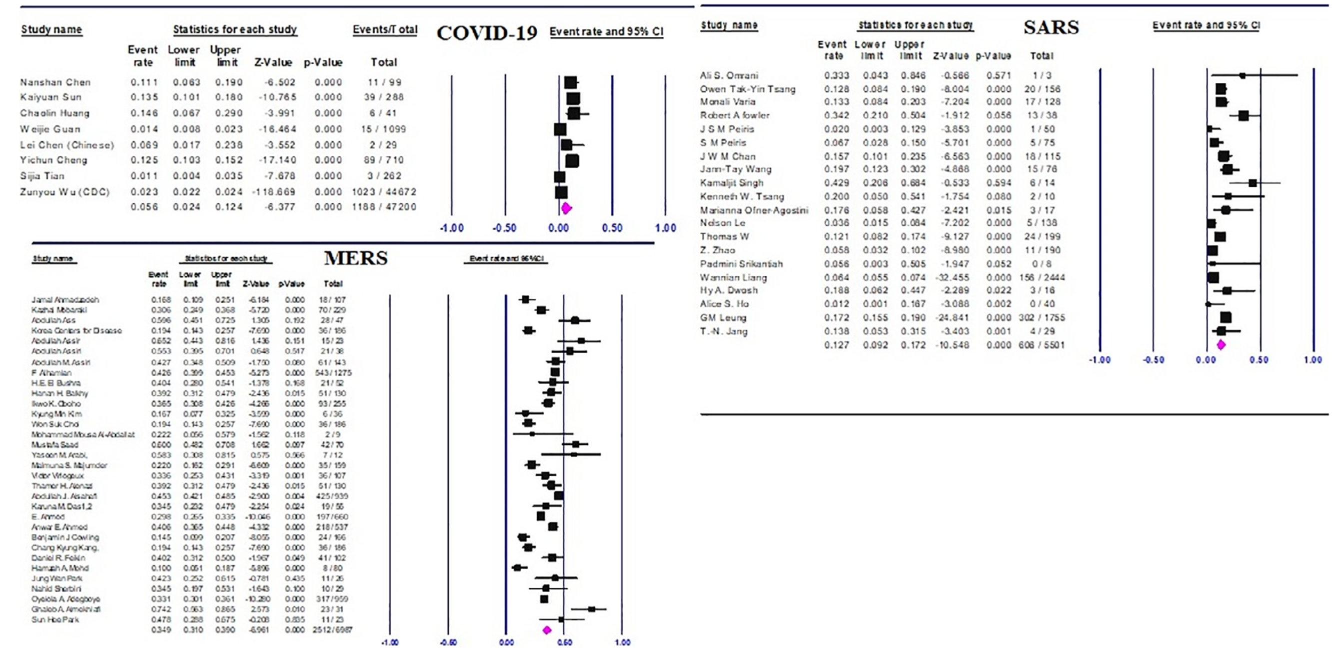

FIGURE 2 Forest plot of the meta-analysis on **mortality** outcome in patients with confirmed COVID-19 (upper left), SARS (upper right), and MERS (lower left)

(95% CI 2.7-13, $P < .001$), or runny nose 6% (95% CI 1-14, $P < .001$). More detail information about demographics and clinical characterization of COVID-19 (Table S3), SARS (Table S4), and MERS patients (Table S5) demonstrated in the supplementary material.

3.4 | Risk factors and clinical characteristics of patients infected with COVID-19

The greatest risk for COVID-19 patients 69.5% (95% CI 54.5-81, $P < .001$) up to 28 February 2020, is a history of recent travel to Wuhan, contact with people from Wuhan, or were Wuhan residents, and 24.3% (95% CI 9.6-49, $P < .001$) had exposure at the seafood market(s). The most common comorbid chronic condition for COVID-19 and SARS is hypertension, and for MERS diabetes, 46% (95% CI 34.5-58, $P < .001$). Overall, 41.2% (95% CI 20-66, $P < .001$) of COVID-19 patients had a history of chronic diseases. Acute respiratory syndrome (ARDS) occurred more frequently in SARS 51% (95% CI 6-94, $P < .001$) compared to MERS 29% (95% CI 14-51, $P < .001$) and COVID-19 10.6% (95% CI 4-26.7, $P < .001$). More detailed information about comorbid conditions of COVID-19 (Table S6), SARS (Table S7), and MERS (Table S8) patients is demonstrated in the supplementary material.

3.5 | Chest X-ray and CT scan findings in patients infected with COVID-19

Analysis showed that 84% (95% CI 78-8.5, $P < .001$) of COVID-19 patients, 86% (95% 77-92, $P < .001$) of SARS patients, and 74.7% (95% 56.5-87, $P < .001$) of MERS patients had abnormal radiological findings on chest X-ray and CT scans. The radiological abnormalities in COVID-19 patients were bilateral involvement of chest X-ray 76.8% (95% CI 62.5-87, $P < .001$), consolidation 75.5% (95% CI 50.5-91, $P < .001$), and ground-glass opacity 71% (95% CI 40-90, $P < .001$) (Table 2). More detailed information about chest X-ray and CT scan findings of COVID-19 (Table S9), SARS (Table S10), and MERS patients (Table S11) is demonstrated in the supplementary material.

3.6 | Outcome

Most COVID-19 confirmed patients required hospitalization 85.4% (95% CI 68-94, $P < .001$) and 20.6% (95% CI 6.7-48, $P < .001$) were deemed to be in critical condition. The mortality rate of COVID-19 confirmed cases was 5.6% (95% CI 2.5-12.5, $P < .001$), SARS 13% (95% 9-17, $P < .001$), and MERS 35% (95% CI 31-39, $P < .001$) (Figure 2).

3.7 | Laboratory findings of patients infected with COVID-19

The laboratory findings showed that among a subset of patients 4.5% (2361/52 251) where data were available, thrombocytosis in COVID-19 patients was 61% (95% CI 45-72, $P < .001$) which is more than double that of SARS at 41.5% (95% CI 35-56.4, $P < .001$) and MERS 30% (95% CI 22-58, $P < .001$) (Table 3). The most SARS patients 71% (95% CI 62-78, $P < .001$) had decreased lymphocytes, and the most of MERS patients had decrease platelets 62% (95% 52-74, $P < .001$) in their laboratory findings (Table 3).

TABLE 3 Laboratory features for confirmed patients with COVID-19

	Normal range	Mean (CI 95%)	Total patient number	Number of studies	Mean (CI 95%)	Total patient number	Number of studies	Mean (CI 95%)	Total patient number	Number of studies
		COVID-19			SARS			MERS		
Leucocytes (WBCs)	3.5-9.5	5.55 ($\times 10^9$ per L) (5.1-5.9)	2361	11	5.1 ($\times 10^9$ per L) (3.3-7)	367	8	7.4 ($\times 10^9$ per L) (6-8.7)	280	5
Increased		13.3 (%)			28 (%)			30 (%)		
Decreased		26 (%)			32 (%)			41 (%)		
Neutrophils	1.8-6.3	3.6 ($\times 10^9$ per L) (3.1-4.1)	412	8	4.6 (4.6-7.1)	614	5	5.3 (5-5.5)	150	2
Increased		-			5 (%)			-		
Decreased		-			17.5 (%)			-		
Lymphocytes	1.1-3.2	0.98 ($\times 10^9$ per L) (0.9-1.06)	2361	11	0.74 ($\times 10^9$ per L) (0.66-0.816)	825	10	-	210	4
Decreased		62.5 (%)			71 (%)			50 (%)		
Platelets	125-350	186.5 ($\times 10^9$ per L) (167-205)	2200	9	179 ($\times 10^9$ per L) (159-199)	1912	5	-	178	3
Decreased		13 (%)			0.2 (%)			62 (%)		
Increased		61 (%)			41.5 (%)			30 (%)		
CRP[a]	0-0.5	29.6 (mg/L) (16.7-42.5)	290	5	22.8 (mg/L) (22-35)	256	2	-	156	3
Increased		81 (%)			93 (%)			45 (%)		
Hemoglobin	130-175	119 (g/L) (106-132)	2062	8	-	-	-	-	-	-
ESR[b]	0-15	42 (mm/h) (46-57)	120	2	-	-	-	-	-	-
Albumi Decreased	40-55	36.8 (g/L) (24.5-46) 80%	120	2	-	-	-	-	-	-
Interleukin-6 Increased	0.0-7	7.9 (mg/mL) (6.8-8.6) 52%	99	2	-	-	-	-	-	-
LDH[c]	120-250	280 (268-294)	1783	9	-	-	-	-	-	-
Increased		70.3 (%)								

Abbreviations: CRP, C reaction protein; ESR, erythrocyte sedimentation rate; WBCs, white blood cells.
[a]Increased or decreased refers to values above or below the normal range.
[b]erythrocyte sedimentation rate.
[c]Lactate dehydrogenase.

4 | DISCUSSION

Prior to 2002, coronaviruses were associated with mild respiratory illness, but with the emergence of SARS in 2002, MERS in 2012, and now in late 2019, COVID-19, it is established that coronaviruses infections can be associated with severe respiratory disease. The virus is transmitted via respiratory droplets or infected inanimate objects, and with its rapid spread worldwide in just a few months, the WHO has officially declared the COVID 19 outbreak a pandemic.[22,126]

Our results show that fever and cough were the most common clinical symptoms in COVID-19, SARS, and MERS. Among 52 251 patients with COVID-19 infection, while fatigue, sputum production, and myalgia (muscle soreness) were the next most frequent clinical symptoms; diarrhea, rhinorrhea, nausea, and vomiting were less common. Within the 10 037 confirmed SARS patients, the next most frequent clinical manifestations were chills, myalgia, headache, and dyspnea. Moreover, 8139 MERS patients commonly exhibited shortness of breath, chills, and dyspnea.

Shortness of breath was less common in COVID-19 patients (17%), in comparison to SARS (32%) and MERS (51%). Likewise, chills were less common in COVID-19 patients (17%), in comparison to SARS (57.5%) and MERS (41%). Therefore, these clinical symptoms should help distinguish the various coronavirus infections from each other.

Our analysis indicated recent travel to Wuhan, contact with people from Wuhan or residency in Wuhan, exposure to persons with respiratory symptoms, and seafood market exposures were common risks among those contracting COVID-19. Furthermore, chronic respiratory disease and recent travel to SARS endemic areas were most common among those contracting SARS. In addition, 28% of SARS patients and 21% of MERS confirmed patients were health care workers, which is higher than COVID-19 cases (3%). This data indicate that in coronavirus outbreaks, isolating infected individuals is one of the most important ways of controlling transmission.

We find that most of the patients with COVID-19, SARS, and MERS had abnormal chest radiological findings. With ground-glass opacity and consolidation in COVID-19 patients being more frequent than in SARS and MERS patients. Other studies reported that significant similarity exists when comparing radiological findings of COVID-19 patients with those suffering from complicated viral pneumonia such as SARS and MERS.[22,32] Therefore, there appear to be no distinguishing radiological findings when comparing human coronaviruses.

The mortality rate was 5.6%, 13%, and 35% among COVID-19-, SARS-, and MERS-infected patients, respectively. While the mortality rate among COVID-19 patients is lower than SARS and MERS, COVID-19 is proving to have a higher contagious potency, resulting in a higher number of deaths. It should be recognized that these numbers are biased due to the data set, including publications related to screening practices (eg, only those with symptoms being screened) increased the percentage value. The actual mortality rate from COVID-19 is almost certainly much lower than that found in this study. As more data emerges from screening asymptomatic or mildly symptomatic individuals in China and around the world, the exact mortality rate will be better understood.

Among COVID-19, SARS, and MERS patients, leukocytosis was found in 13.3%, 28%, and 30%, respectively, and leukopenia in 26%, 32%, and 41%, respectively.

Most of the patients with coronavirus had abnormal chest radiological findings. On the other hand, runny nose and rhinorrhea are less common symptoms in coronavirus-infected patients,[127] which indicates the virus preferentially affects the lower respiratory tract. A study by Zhao et al showed that ACE2 is a COVID-19 virus receptor and that it is typically expressed on pulmonary alveolar epithelial cells.[128] Another study reported that following COVID-19 infection deregulated cytokine/chemokine response and higher virus titer causes an inflammatory cytokine storm with lung immunopathological injury.[129] Inflammation related to the cytokine storm in the lungs may then spread throughout the body via the circulation system. COVID-19 patients have been reported to have increased plasma concentration of inflammation-related cytokines, including interleukin (IL)-2,6,7,10, tumor necrosis factor-α (TNF-α), and monocyte chemoattractant protein I (MCP-I) especially in moribund patients.[130] Our data collected here show that ARDS occurred in 10.6% of reported patients with COVID-19 infection. A previous study showed that ACE2 (main receptor of COVID-19) expression is higher in people with pulmonary ARDS and acute respiratory injury.[131]

Several limitations of this study exist. Publication bias and study heterogeneity are unavoidable in this type of study. Therefore, it should be considered when interpreting the outcomes of the reports and our final data set. Furthermore, this study likely overestimates disease severity due to a lack of screening for asymptomatic or mildly symptomatic individuals and subsequent publication bias related to these factors. Likely, many infected persons have not been detected, thus falsely elevating the rates of hospitalization, critical condition, and mortality. The lower quality analysis and reporting in some of the included publications is another limitation of the study. To prevent language bias, we included reports in languages other than English. Additionally, we searched for a variety of sites and databases to prevent internet platform bias. Using Egger's regression test, we did not find significant publication bias. Journal bias is an issue facing those who carry out a meta-analysis, yet it does not usually affect the general conclusions.[132] However, we cannot reject the occurrence of other biases in this study, such as choice bias, since several journals are not indexed in Embase, Scopus, PubMed, Web of Science, and the Cochrane library and unpublished data from some regions of the world.

5 | CONCLUSIONS

Fever and cough are the most common symptoms of COVID-19-, SARS-, and MERS-infected patients. The mortality rate in COVID-19 confirmed cases was lower than SARS- and MERS-infected patients. Clinical outcomes and findings may be biased by reporting only confirmed cases, and it should be considered when interpreting the data.

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CONFLICT OF INTEREST

The authors have declared that no conflict of interests.

AUTHOR CONTRIBUTIONS

Conceived and designed the study: A.P., S.G.

Comprehensive research: S.G., A.K., A.P., R.F.

Analyzed the data: A.P.

Wrote and revised the paper: A.P., S.G., A.K., R.F., B.B., D.T., R.T., N.B., J.P.I.

Participated in data analysis and manuscript editing: A.P., S.G., A.K., R.F., B.B., D.T., R.T., N.B., J.P.I.

ETHICAL STATEMENT

The manuscript is a systematic review, so the ethical approval was not required for the study.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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