Family Medicine and Community Health

Clinicopathological characteristics of 8697 patients with COVID-19 in China: a meta-analysis

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ABSTRACT

Objective Our study aims to present a summary of the clinicopathological characteristics of patients affected by the coronavirus disease 2019 (COVID-19) that can be used as a reference for further research and clinical decisions.

Design Studies were included in the meta-analysis if they had cohort, case–control or case series designs and provided sufficient details on clinical symptoms, laboratory outcomes and asymptomatic patients.

Setting PubMed, Embase, Chinese Biomedical Literature Database, Wanfang, China Science and Technology Journal Database and China National Knowledge Infrastructure databases were electronically searched to identify related studies published between 1 January 2020 and 16 March 2020. Three reviewers independently examined the literature, extracted relevant data and assessed the risk of publication bias before including the studies in the meta-analysis.

Participants The confirmed cases of COVID-19.

Results A total of 55 unique retrospective studies involving 8697 patients with COVID-19 were identified. Meta-analysis showed that a higher proportion of infected patients were male (53.3%), and the two major symptoms observed were fever (78.4%) and cough (58.3%). Other common symptoms included fatigue (34%), myalgia (21.9%), expectoration (23.7%), anorexia (22.9%), chest tightness (22.9%) and dyspnoea (20.6%). Minor symptoms included nausea and vomiting (6.6%), diarrhoea (8.2%), headache (11.3%), pharyngalgia (11.6%), shivering (15.2%) and rhinorrhea (7.3%). About 5.4% of the patients were asymptomatic. Most patients showed normal leucocyte counts (64.7%) and elevated C reactive protein levels (65.9%). Lymphopaenia was observed in about 47.6% of the infected patients, along with abnormal levels of myocardial enzymes (49.4%) and liver function (26.4%). Other findings included leucopenia (23.5%), elevated D-dimer (20.4%), elevated erythrocyte sedimentation rate (20.4%), leucocytosis (9.9%), elevated procalcitonin (16.7%) and abnormal renal function (10.9%).

Conclusions The most commonly experienced symptoms of patients with COVID-19 were fever and cough. Myalgia, anorexia, chest tightness and dyspnoea were found in some patients. A relatively small percentage of patients were asymptomatic and could act as carriers of the disease. Most patients showed normal leucocyte counts, elevated levels of C reactive protein and lymphopaenia, confirming the viral origin of the disease.

INTRODUCTION

In the spring of 2020, the coronavirus disease 2019 (COVID-19) pandemic has spread to more than 200 countries around the world.[1 2] As of 27 March 2020, the total number of confirmed cases has exceeded 500 000.[3] This pandemic has become a serious threat to global health and continues to challenge healthcare systems worldwide. It was determined to be caused by a novel coronavirus, the severe acute respiratory syndrome coronavirus 2.[4] Therefore, it is critical to understand and identify the key clinical and laboratory characteristics of patients with COVID-19 in order to help in early detection and isolation of infected individuals, as well as minimise the spread of the disease.[5]

Although a number of studies have attempted to explore this subject, most of them were single-centre studies that were conducted in a specific hospital or region. Due to differences in study design and small samples, the clinical symptoms, laboratory findings and other key outcomes of these studies are complicated and unclear.[6–8] For example, two recent systematic reviews[9 10] of studies of patients with COVID-19 indicated a high incidence of fever (>88%) and cough (>68%), but only one[10] reported symptoms of myalgia or fatigue (35.8%). Both reviews meta-analysed small samples pooled from 10 studies.

Therefore, the present meta-analysis was performed to provide the most extensive, up-to-date description so far of clinicopathological characteristics of patients with COVID-19 and to provide a reference for clinical decisions and future research.

MATERIALS AND METHODS

Search strategy and study eligibility

This meta-analysis was carried out based on the guidelines of the Preferred Reporting

Box 1 Search strings used for the PubMed database

1 Corona virus [Title/Abstract]
2 Coronavirus [Title/Abstract]
3 2019-nCoV [Title/Abstract]
4 COVID-19 [Title/Abstract]
5 SARS-CoV-2 [Title/Abstract]
6 # 1 OR # 2 OR # 3 OR # 4 OR # 5

Items for Meta-Analyses of Observational Studies in Epidemiology Statement.[11] We systematically examined the studies on clinicopathological characteristics of patients with COVID-19 indexed in the PubMed, Embase, Chinese Biomedical Literature, Wanfang, China Science and Technology Journal Database and China National Knowledge Infrastructure databases between 1 January 2020 and 16 March 2020. All references cited in these studies were also analysed manually to ensure that eligible papers were not overlooked. If multiple studies analysed the same patient population, we included only the one with more detailed information or the one published more recently. No language restrictions were incorporated during the literature search, and only literature published online was included. The following keywords were used, both separately and in combination, as part of the search strategy in each database: 'Corona virus', 'Coronavirus', '2019-nCoV', 'COVID-19' or 'SARS-CoV-2' (box 1).

Studies were included in the meta-analysis if they had cohort, case–control or case series designs and provided sufficient details on clinical symptoms, laboratory outcomes and asymptomatic patients. Only studies of more than 40 patients were included.

Data extraction and quality assessment

The literature selected was independently assessed by three reviewers based on the eligibility criteria, and relevant data were extracted. Disagreements were resolved by consensus. The titles and abstracts were first screened to identify the eligible articles, followed by a full-text review to obtain detailed information. When required, the authors were contacted directly to obtain further information and clarifications regarding their study. The following data were extracted from each included study: surname of first author; date of publication; study design; number, age and sex of patients; clinical and laboratory outcomes; and data relevant for assessing publication bias. The quality of observational case series was independently evaluated by the three reviewers based on the British National Institute for Clinical Excellence[12] guidelines. This evaluation was conducted based on a set of eight criteria, and studies with a score greater than 4 were considered to be of high quality (total score=8).

Statistical analyses

All statistical analyses were performed using STATA V.12. Original incidence rates *r* were transformed by the double arcsine method to ensure a normal distribution, and the resulting transformed rate *tr* was used in single-arm meta-analysis. The heterogeneity between studies was analysed using a χ^2 test ($p<0.10$) and quantified using the I^2 statistic. When no statistical heterogeneity was observed, a fixed-effects model was used. Otherwise, potential sources of clinical heterogeneity were identified using subgroup and sensitivity analyses; these sources were eliminated, and the meta-analysis was repeated using a random-effects model. Pooled incidence rates *R* were back-calculated from transformed rates *tr* using the $R=[\sin(tr / 2)]$.[2] A two-tailed $p<0.05$ was considered statistically significant. Publication bias was evaluated using a funnel plot along with Egger's regression test and Begg's test.

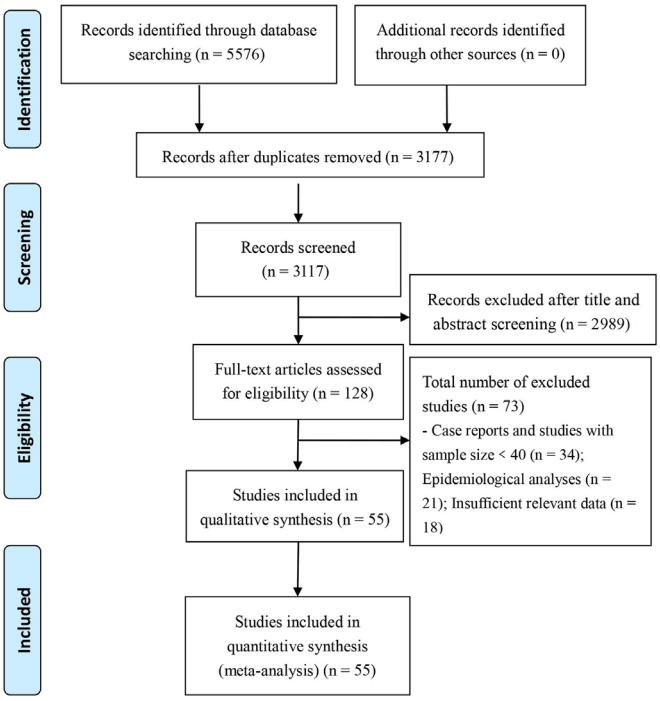

Figure 1 Flow chart depicting literature screening process.

RESULTS

Literature screening and assessment

A total of 5576 records were identified from the various databases examined. After a detailed assessment based on the inclusion criteria, 55 unique studies[6–8 13–64] involving 8697 patients with COVID-19 were included in the meta-analysis (figure 1).

Characteristics of included studies

All studies included in the meta-analysis were conducted in China and published between 6 February 2020 and 16 March 2020. These retrospective studies examined Chinese patients distributed across 31 provinces. A large proportion of these studies (n=40) were based on data collected from a single centre, with no clear explanation regarding eligibility criteria. Follow-up data were reported for most patients. All studies received quality scores of 5–8, indicating high quality (table 1).

Table 1 Characteristics of included studies

Study	Publication date	Sample size (n)	Study design	Study population	Age* (years)	Follow-up	Outcomes reported	Quality score
Zhaoet al[6]	March 3	101	Retrospective.	Patients with COVID-19 in Radiology Quality Control Center, Hunan.	21–50	NA	①	7
Xiong *et al*[7]	March 3	42	Retrospective.	Patients with COVID-19 in Tongji Hospital, Huazhong University of Science and Technology.	26–75	11 January–15 February	①②	7
Zhou *et al*[8]	March 11	191	Retrospective, multicentre.	Patients with COVID-19 in Wuhan Jinyintan Hospital and Wuhan Pulmonary Hospital.	56.0	December 2019–31 January 2020	①②	7
Li *et al*[13]	February23	54	Retrospective, single centre.	Patients with COVID-19 in Wuhan Fourth Hospital.	51.5	January–February	①②	7
Xiao *et al*[14]	February 27	143	Retrospective, single centre.	Patients with COVID-19 in Chongqing Three Gorges Central Hospital.	45.1±1.0	23 January–8 February	①②	6
Sun *et al*[15]	February 24	88	Retrospective, single centre.	Patients with COVID-19 in Tianjin Haihe Hospital.	48.5±15.7	21 January–8 February 8	①	7
Xu *et al*[16]	February 25	45	Retrospective, single centre.	Patients with COVID-19 in Hubei Provincial Hospital of Integrated Chinese and Western Medicine.	54.58±17	22 January–5 February	①	7
Lu *et al*[17]	February 10	50	Retrospective, single centre.	NA.	50.4±16.8	NA	①②	6
Wang *et al*[18]	February 25	52	Retrospective, single centre.	Patients with COVID-19 in The First Affiliated Hospital of Zhejiang University.	44±14	9 January–3 February	①	6
Liao *et al*[19]	February 26	42	Retrospective, single-centre cohort.	Patients with COVID-19 in Zhongnan Hospital of Wuhan University.	51.6	16 January–18 February	②	6
Yu *et al*[20]	February 26	40	Retrospective, single centre.	Patients with COVID-19 in Wenzhou Sixth People's Hospital.	45.9	17 January–28 January	①	6
Liu *et al*[21]	February 18	41	Retrospective, single centre.	Patients with COVID-19 in Xiaochang First People's Hospital.	48.45	NA	②	6
Cheng and Li[22]	February 19	54	Retrospective, single centre.	Patients with COVID-19 in The Affiliated Puren Hospital of Wuhan University of Science and Technology.	60.1±17	1 January–31 January	①②	7
Yang *et al*[23]	March 3	57	Retrospective, single centre.	Patients with COVID-19 in Nanjing Public Health Medical Centre.	37	NA	①②	7
Xiang *et al*[24]	March 2	49	Retrospective, single centre.	Patients with COVID-19 in The First Affiliated of Nanjing University.	42.9	21 January–27 January	①	6
Ma *et al*[25]	March 10	75	Retrospective, multicentre.	Patients with COVID-19 from four hospitals in Fuyang City.	43.9±15.1	20 January–18 February	②	7
Xue *et al*[26]	March 10	66	Retrospective, single centre.	Patients with COVID-19 in Shanghai Public Health Clinical Center.	46.0±15.6	NA	①	6
Gong *et al*[27]	March 9	225	Retrospective, single centre	Patients with COVID-19 in Chongqing Three Gorges Central Hospital.	0–82	20 January–16 February	①	7
Ran *et al*[28]	March 6	209	Retrospective, multicentre.	Patients with COVID-19 from four hospitals in Fuyang City.	46.5±15.7	25 January–10 February	①	7
Yuan *et al*[29]	March 6	223	Retrospective, single centre.	Patients with COVID-19 in Chongqing Public Medical Center.	46.5±16.1	24 January–23 February	①②	6
Shi *et al*[30]	March 5	67	Retrospective, single centre.	Patients with COVID-19 in Shanghai Public Health Clinical Center.	36±53.7	January–February	①	7

Continued

Table 1 Continued

Study	Publication date	Sample size (n)	Study design	Study population	Age* (years)	Follow-up	Outcomes reported	Quality score
Xiong *et al*[31]	March 3	89	Retrospective, single centre.	Patients with COVID-19 in Renmin Hospital of Wuhan University.	53±16.9	17 January–20 February	①	6
Chen *et al*[32]	March 13	139	Retrospective, single centre.	Patients with COVID-19 in Chongqing Three Gorges Central Hospital.	15–79	January–February	①	6
Fang *et al*[33]	Machr 12	308	Retrospective, single centre.	Patients with COVID-19 in Hubei Huangshi Chinese Medicine Hospital.	30–86	25 January–20 February	①	7
Zhou *et al*[34]	March 13	537	Retrospective, multicentre.	All cases of COVID-19 in Shandong Province.	26–86	December 2019–15 February 2020	①②	7
Li *et al*[35]	March 12	524	Retrospective, multicentre.	COVID-19 patients from hospitals in Henan Province.	45	2 January–20 February	①	8
Song *et al*[36]	March 12	60	Retrospective, multicentre.	Patients with COVID-19 in Gansu Provincial Designated Hospital.	39.5±17.7	21 January–22 February	①	7
Cheng *et al*[37]	Mar 12	463	Retrospective, single centre.	Patients with COVID-19 in Wuhan Jinyintan Hospital	15–90	December 2019–6 February 2020	①②	6
Chen *et al*[38]	March 10	76	Retrospective, single centre.	Patients with COVID-19 in Puren Hospital of Wuhan University of Science and Technology.	59.5	January–February	①②	6
Cheng *et al*[39]	March 2	1079	Retrospective, multicentre.	All cases of COVID-19 in Henan Province.	46	December 2019–29 February 2020	①	7
Han *et al*[40]	March 16	150	Retrospective.	Patients with COVID-19 from two hospitals in Wuhan.	53±14	12 January–16 February	①②	6
Xu *et al*[41]	March 16	62	Retrospective, single centre.	Critically ill patients with COVID-19 in Zhongnan Hospital of Wuhan University.	62.9	8 January–14 February	①	6
Dong *et al*[42]	March 13	135	Retrospective, multicentre.	All reported confirmed cases of COVID-19 in Tianjin.	48.6±16.8	December 2019–24 February 2020	①	7
Sun *et al*[43]	March 15	391	Retrospective.	COVID-19 cases reported in Zhejiang province.	NA	NA	①	7
Li *et al*[44]	February 29	83	Retrospective.	Patients with COVID-19 in The Second Affiliated Hospital of Chongqing Medical University	45.5±12.3	January–February	①②	7
Wu *et al*[45]	February 21	80	Retrospective, single centre.	Patients with COVID-19 from three tertiary hospitals in Jiangsu.	46.1	22 January–14 February	①②	7
Xu *et al*[46]	February 28	90	Retrospective, single centre.	Patients with COVID-19 in Guangzhou Eighth People's Hospital.	50	2 3January–4 February	①②	6
Xu *et al*[47]	February 25	50	Retrospective, single centre.	Patients with COVID-19 in The Fifth Medical Centre of Chinese PLA General Hospital.	NA	1 January–2 February	①②	6
Yang *et al*[48]	February 26	149	Retrospective, multicentre.	Patients with COVID-19 from three tertiary hospitals in Wenzhou.	45.1±13.4	17 January–10 February	①②	7
Xu *et al*[49]	February 19	62	Retrospective, multicentre.	Patients with COVID-19 from seven hospitals in Zhejiang Province.	41	10 January–26 January	①②	6
Zhang *et al*[50]	February 23	140	Retrospective, single centre.	Patients with COVID-19 in No.7 Hospital in Wuhan.	57.0	16 January–3 February	①②	6

Continued

Table 1 Continued

Study	Publication date	Sample size (n)	Study design	Study population	Age* (years)	Follow-up	Outcomes reported	Quality score
Wang *et al*[51]	February 8	138	Retrospective, single-centre case series.	Patients with COVID-19 in Zhongnan Hospital of Wuhan University.	56 (42–68)	1 January–28 January	①②	6
Liu *et al*[52]	February 18	137	Retrospective, multicentre.	Patients with COVID-19 from nine tertiary hospitals in Hubei Province.	55±16	30 December 2019–24 January 2020	①②	6
Huang *et al*[53]	February 15	41	Retrospective, single centre.	Patients with COVID-19 in Hubei Province.	49 (41–58)	December 2019–2 January 2020	①②	6
Chen *et al*[54]	February 15	99	Retrospective, single centre.	Patients with COVID-19 in Wuhan Jinyintan Hospital.	55.5±13.1	1 January–20 January	①②	6
Guan *et al*[55]	February 6	1099	Retrospective, multicentre.	Patients with COVID-19 from 552 hospitals in 31 provinces.	47.0	NA	①②	8
Bernhem *et al*[56]	February 20	121	Retrospective case series.	Patients with COVID-19 from four hospitals in four Chinese provinces.	45.3	18 January–2 February	①	8
Wu *et al*[57]	February 21	80	Retrospective, multicentre.	Patients with COVID-19 from three hospitals in Chongqing.	44±11	January–February	①②	7
Shi *et al*[58]	February 21	81	Retrospective, multicentre cohort.	Patients with COVID-19 in Wuhan Jinyintan Hospital and Union Hospital of Tongji Medical College.	49.5–11.0	18 January–2 February	①②	7
Yang *et al*[59]	February 24	52	Retrospective, single centre.	Critically ill patients with COVID-19 in Wuhan Jinyintan Hospital.	59.7–13.3	2 December 2019–23 January 2020	①	6
Zhou *et al*[60]	March 5	62	Retrospective.	Patients with COVID-19 in Huazhong University of Science and Technology.	52.8–12.2	16 January–30 January	①②	6
Wang *et al*[61]	February 28	50	Retrospective, multicentre.	Patients with COVID-19 from four hospitals in Jilin Province.	44.5±16.1	28 January–21 February	①	8
Fang *et al*[62]	February 25	79	Retrospective, single centre.	Patients with COVID-19 in Anhui Provincial Hospital.	45.1±16.6	22 January–18 February	①②	5
Yu *et al*[63]	February 17	40	Retrospective, single centre.	Patients with COVID-19 in the Chinese People's Liberation Army General Hospital.	39.9±18.2	21 January–February	①②	6
Zhang *et al*[64]	February 19	42	Retrospective, single centre.	Patients with COVID-19 in Nanjing Hospital, affiliated to Nanjing University of Traditional Chinese Medicine.	43±16.8	19 January–February	①②	5

① Clinical symptoms; ② laboratory findings.
*Reported variously as range or mean±SD or median, and IQR values.
NA, not reported.

Table 2 Clinical symptoms observed in patients with COVID-19

Symptom	No. of studies	No. of patients	Heterogeneity		Meta-analysis		
			P value	I^2 (%)	Model	R (95% CI)	P value
Fever	51	8473	<0.001	95.9	Random	0.784 (0.736 to 0.828)	<0.001
Cough	52	8539	<0.001	97.2	Random	0.583 (0.515 to 0.649)	<0.001
Fatigue	45	7848	<0.001	96.9	Random	0.340 (0.277 to 0.405)	<0.001
Myalgia	37	5625	<0.001	93.0	Random	0.219 (0.177 to 0.264)	<0.001
Headache	34	6414	<0.001	88.5	Random	0.113 (0.089 to 0.140)	<0.001
Diarrhoea	43	7904	<0.001	87.5	Random	0.082 (0.064 to 0.102)	<0.001
Expectoration	33	6408	<0.001	95.8	Random	0.237 (0.185 to 0.294)	<0.001
Dyspnoea	25	3670	<0.001	87.5	Random	0.206 (0.133 to 0.290)	<0.001
Chest tightness	30	5773	<0.001	97.2	Random	0.229 (0.163 to 0.304)	<0.001
Nausea and vomiting	24	4941	<0.001	82.2	Random	0.066 (0.048 to 0.086)	<0.001
Pharyngalgia	31	5947	<0.001	88.7	Random	0.116 (0.090 to 0.145)	<0.001
Rhinorrhoea	13	3111	<0.001	91.2	Random	0.073 (0.042 to 0.113)	<0.001
Anorexia	19	3274	<0.001	96.9	Random	0.229 (0.143 to 0.326)	<0.001
Shivering	16	4394	<0.001	96.8	Random	0.152 (0.090 to 0.228)	<0.001
Asymptomatic	10	878	0.002	66.3	Random	0.054 (0.031 to 0.084)	<0.001

Meta-analysis results

Gender distribution

Relevant data regarding the clinicopathological characteristics of 8697 patients with COVID-19 was collected.[6–8 13–64] Significant heterogeneity was observed across all included studies (I^2=93.7%), therefore, a random-effects model was used in the meta-analysis. We found that 53.3% (95%CI 50.3 to 56.4) of the patients were male.

Clinical symptoms

Two major symptoms, including fever (78.4%) and cough (58.3%), were highly prevalent among patients. Fatigue (34%), myalgia (21.9%), expectoration (23.7%), anorexia (22.9%), chest tightness (22.9%) and dyspnoea (20.6%) also occurred frequently. Less frequent symptoms were nausea and vomiting (6.6%), diarrhoea (8.2%), headache (11.3%), pharyngalgia (11.6%), shivering (15.2%) and rhinorrhea (7.3%). Only 5.4% of patients with COVID-19 were found to be asymptomatic (table 2).

Pathological characteristics

A large proportion of patients had normal leucocyte counts (64.7%) and high levels of C reactive protein (65.9%) (figures 2 and 3). Lymphopaenia was observed

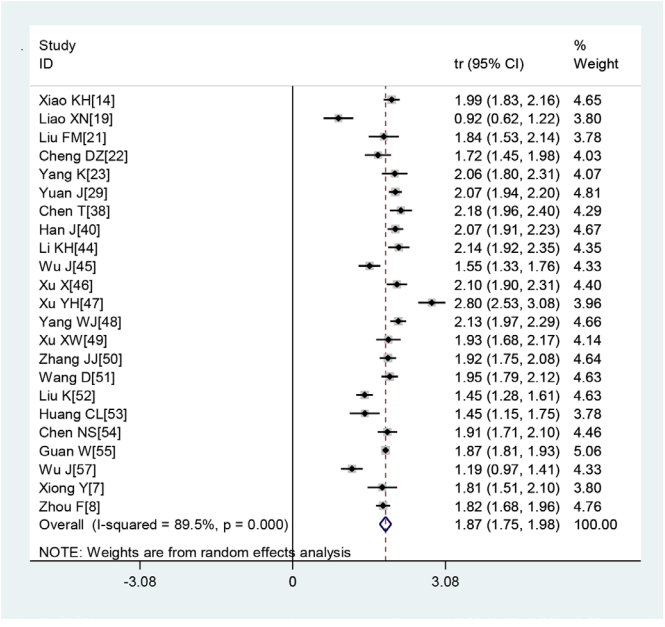

Figure 2 Transformed incidence rate of normal leucocyte count in patients with COVID-19.

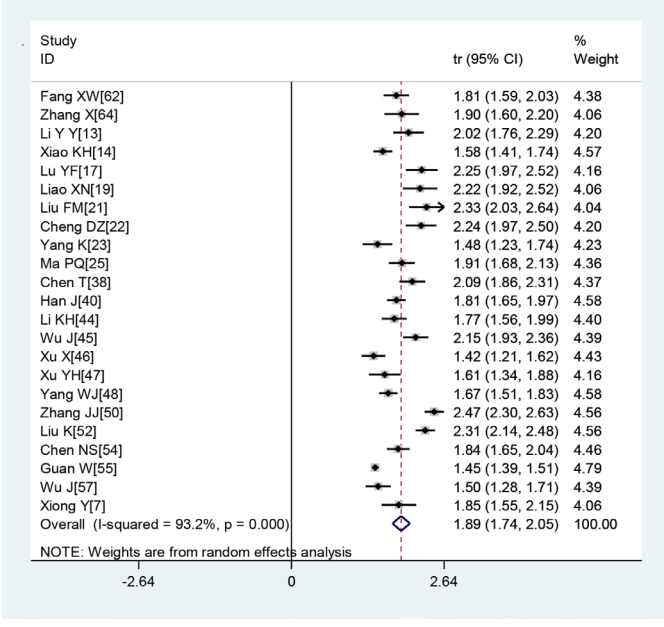

Figure 3 Transformed incidence rate of high C reactive protein levels in patients with COVID-19.

Table 3 Pathological characteristics of patients with COVID-19

Characteristic	No. of studies	No. of patients	Heterogeneity		Meta-analysis		
			P value	I^2 (%)	Model	R (95% CI)	P value
Leucocytosis	21	3936	<0.001	90.6	Random	0.099 (0.069 to 0.134)	<0.001
Normal leucocyte count	23	3267	<0.001	89.5	Random	0.647 (0.591 to 0.700)	<0.001
Leucopenia	27	4233	<0.001	89.6	Random	0.235 (0.194 to 0.279)	<0.001
Lymphopaenia	32	4660	<0.001	94.4	Random	0.476 (0.413 to 0.540)	<0.001
High C reactive protein	23	2912	<0.001	93.2	Random	0.659 (0.586 to 0.728)	<0.001
High procalcitonin	13	2190	<0.001	96.6	Random	0.167 (0.083 to 0.274)	<0.001
High D-dimer	9	2354	<0.001	90.4	Random	0.204 (0.147 to 0.267)	<0.001
High erythrocyte sedimentation rate	7	455	<0.001	90.4	Random	0.204 (0.147 to 0.267)	<0.001
Abnormal liver function	11	2524	<0.001	90.1	Random	0.264 (0.204 to 0.329)	<0.001
Abnormal renal function	8	2183	<0.001	96.1	Random	0.109 (0.045 to 0.196)	<0.001
High myocardial enzymes	11	2541	<0.001	96.1	Random	0.494 (0.264 to 0.725)	<0.001

in many patients (47.6%), along with elevated levels of myocardial enzymes (49.4%) and abnormal liver function (26.4%). Also observed were leucopenia (23.5%), leucocytosis (9.9%), abnormal renal function (10.9%), elevated levels of D-dimer (20.4%), elevated erythrocyte sedimentation rate (20.4%) and elevated procalcitonin (16.7%) (table 3).

Subgroup analysis

Patients were stratified into two groups based on the date of initial diagnosis: group 1 included all patients and group 2 included those diagnosed between December 2019 and 31 January 2020 (table 4). We found that all patients diagnosed before 31 January had higher incidence rates of fever and cough. No significant difference was observed in the heterogeneity between the subgroups and the overall heterogeneity, indicating that the date of initial diagnosis was not the main source of heterogeneity.

Sensitivity analysis

A sensitivity analysis was carried out by excluding one study at a time and reanalysing the entire dataset. We found that the pooled incidence rates did not change substantially, indicating the reliability and stability of our meta-analysis (eg, figure 4).

Evaluation of publication bias

The p values derived using the Egger's and the Begg's test for all the clinicopathological characteristics showed no obvious publication bias (table 5). A funnel plot based on the incidence rate of fever showed p values of 0.091

Table 4 Analysis of clinical symptoms observed in patients with COVID-19, stratified by date of initial diagnosis*

Clinical symptom	No. of studies	No. of patients	Heterogeneity		Meta-analysis		
			P value	I^2 (%)	Model	R (95% CI)	P value
Fever							
Group 1	51	8473	<0.001	95.9	Random	0.784 (0.736 to 0.828)	<0.001
Group 2	14	2162	<0.001	97.9	Random	0.813 (0.667 to 0.924)	<0.001
Fatigue							
Group 1	45	7848	<0.001	96.9	Random	0.340 (0.277 to 0.405)	<0.001
Group 2	11	1971	<0.001	93.9	Random	0.366 (0.268 to 0.470)	<0.001
Cough							<0.001
Group 1	52	8539	<0.001	97.2	Random	0.583 (0.515 to 0.649)	<0.001
Group 2	14	2162	<0.001	86.6	Random	0.640 (0.574 to 0.703)	<0.001
Myalgia							<0.001
Group 1	37	5625	<0.001	93.0	Random	0.219 (0.177 to 0.264)	<0.001
Group 2	10	1938	<0.001	91.7	Random	0.271 (0.193 to 0.358)	<0.001

*Group 1: all patients; group 2: diagnosed before 31 January 2020.

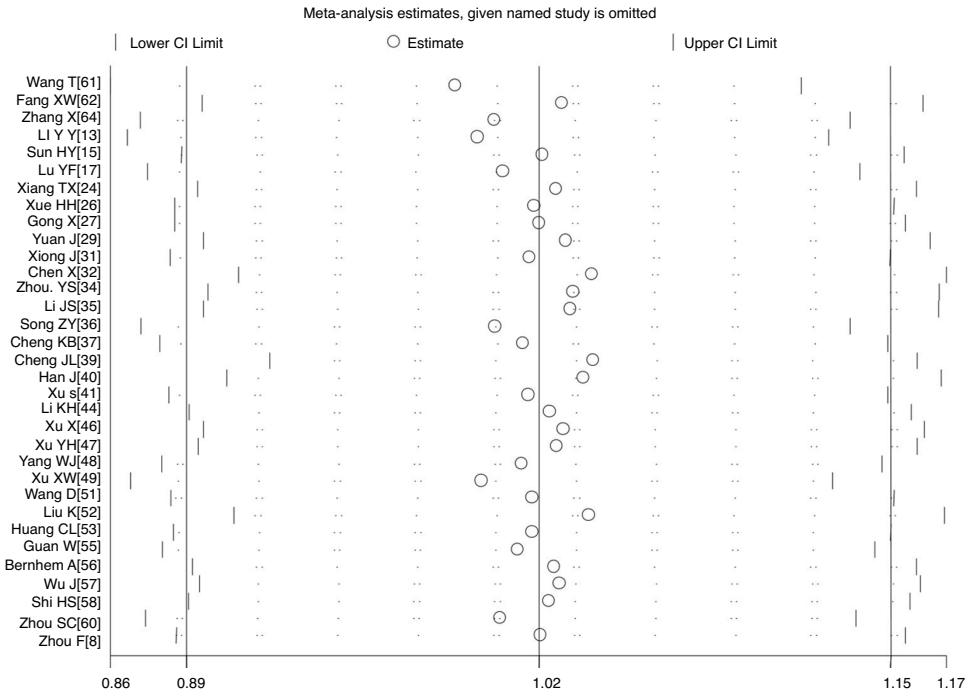

Figure 4 Sensitivity analysis of the incidence rate of expectoration in patients with COVID-19.

in Egger's test and 0.703 in Begg's test (figure 5). These results confirm that there is no publication bias.

DISCUSSION

In this meta-analysis, we examined 55 independent studies[6–8 13–64] reporting clinicopathological data on 8697 patients with COVID-19 distributed across 31 provinces in China. The studies included in this analysis comprise the latest research available on COVID-19 through 16 March 2020. Our results indicate that there is a slightly higher proportion of male patients (53.3%) and that the main symptoms of this disease are fever (78.4%), cough (58.3%) and fatigue (34%). Compared with previous results,[9 10] our findings reveal lower incidence rates of the two major symptoms of this disease, which we found to depend to some extent on whether diagnosis was made before or after 31 January 2020, reflecting with the progress of the epidemic, the number of atypical manifestations has growed gradually. For example, some patients developed gastrointestinal symptoms, such as diarrhoea, nausea and vomiting. These results highlight the importance of also taking into account non-respiratory symptoms of the disease.

Most patients with COVID-19 showed normal leucocyte counts and lymphopqenia. Few patients had leucocytosis and elevated procalcitonin levels, confirming that this

Table 5 Evaluation of publication bias using the Egger's and the Begg's test

Characteristic	P (Egger's)	P (Begg's)	Characteristic	P (Egger's)	P (Begg's)
Fever	0.091	0.703	Shivering	0.642	0.137
Cough	0.259	0.776	Asymptomatic	0.840	0.589
Fatigue	0.094	0.018	Leucocytosis	0.087	0.238
Myalgia	<0.001	<0.001	Normal leucocyte count	0.760	0.195
Headache	0.034	0.015	Leucopenia	0.790	0.587
Diarrhoea	0.001	0.004	Lymphopenia	0.062	0.910
Expectoration	0.208	0.018	High C reactive protein	0.001	0.138
Dyspnoea	0.386	0.088	High procalcitonin	0.022	0.222
Chest tightness	0.234	0.164	High D-dimer	0.363	0.466
Nausea and vomiting	0.102	0.092	High erythrocyte sedimentation rate	0.028	0.048
Pharyngalgia	0.089	0.086	Abnormal liver function	0.050	0.640
Rhinorrhea	0.748	0.059	Abnormal renal function	0.015	0.686
Anorexia	0.002	0.006	High myocardial enzymes	0.791	0.350

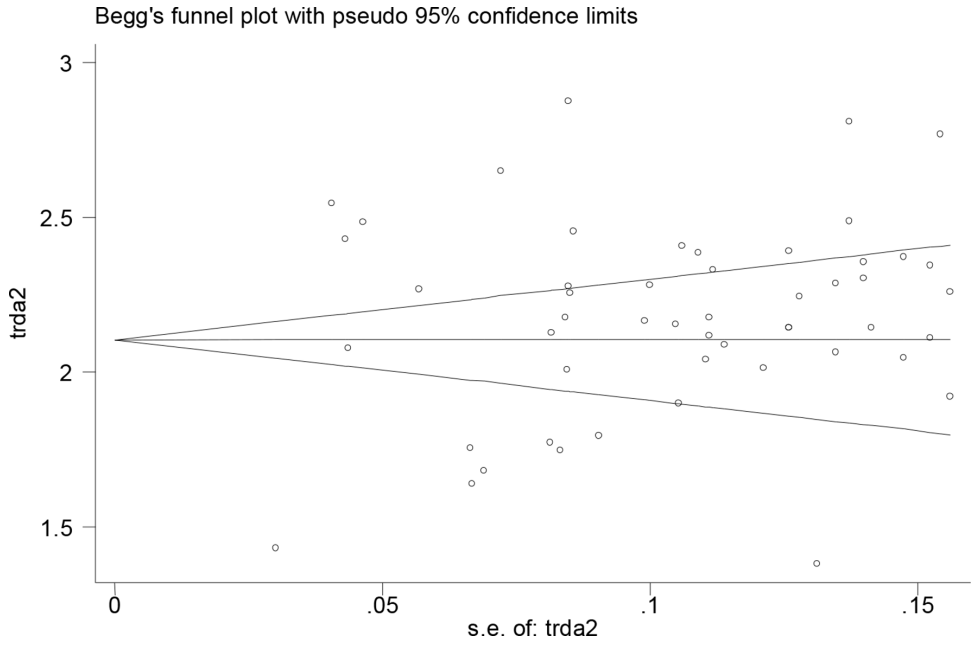

Figure 5 Evaluation of publication bias using a funnel plot based on the incidence rate of fever.

disease is transmitted by a virus. Therefore, it is essential for clinicians to use such pathological findings to rule out the presence of bacterial infections. In this study, 49.4% of the patients presented with myocardial enzyme spectrum abnormalities, which manifested as an increase in lactate dehydrogenase levels. Studies have shown that elevated levels of lactate dehydrogenase can be a risk factor for rapid progression from mild to critical COVID-19.[65] Therefore, monitoring the function of important organs during treatment is critical, and treatment should be adjusted as needed to preserve and maintain organ function.

Infected people who are asymptomatic can act as a source of infection,[66] especially since the estimated median incubation period is 5–6 days (range 0–14 days). An analysis by the Chinese Center for Disease Control and Prevention conducted through 17 February 2020 suggested that the proportion of asymptomatic patients was only around 1%,[67] but our results suggest that the proportion is closer to 5%. This increase may reflect the growing experience of hospitals with this novel disease and increasing screening of suspected COVID-19 cases for viral infection, allowing the correct diagnosis of greater proportions of patients showing no or less typical manifestations. Therefore, to control the spread of this disease, general practitioners should carefully monitor individuals with histories of contact in areas where outbreaks have occurred or who had contact with suspected or confirmed cases of COVID-19 within 14 days before onset of symptoms.[68] Epidemiological history of patients should be investigated in detail, and asymptomatic infected people in the community should be identified as quickly as possible to control spread of the disease.

A recent study suggests that, considering different scenarios, highly effective contact tracing and case isolation are sufficient to control a new outbreak of COVID-19 within 3 months.[69] Therefore, isolation, quarantine, social distancing, and community containment measures should be rapidly implemented in high-risk countries or regions.[70] In China, community engagement has been the first line of defence in the battle against the COVID-19 pandemic. General practitioners act as both gatekeepers and health promoters by educating the public and guiding the community in the fight against this disease.[71] Monitoring people at designated checkpoints, intercepting transmission routes in a timely manner and preventing local outbreaks are critical to prevent repeat epidemics.[72]

Although this study rigorously analysed clinical and laboratory data collected from a large sample of patients with COVID-19, we were unable to eliminate the significant heterogeneity observed between studies. For example, the course and the severity of the disease varied across studies. Given that most of the studies included in our meta-analysis were single-centre, retrospective studies, it was difficult for us to control for the effects of several confounding factors, including bias in patient admission and selection, as well as differences in disease severity and course. Further research is required to verify and extend our results for China. Continued surveillance across multiple countries, along with transparent and accurate reporting of patient characteristics and testing policies, will help us gain a better understanding of this global pandemic.[73]

CONCLUSION

In summary, Current evidence showed that the most commonly experienced symptoms of patients with COVID-19 were fever and cough. Myalgia, anorexia,

chest tightness and dyspnoea were found in some patients. A relatively small percentage of patients were asymptomatic and could act as carriers of the disease. Most patients showed normal leucocyte counts, elevated levels of C reactive protein and lymphopenia, confirming the viral origin of the disease. Due to limited quality and quantity of the included studies, more high-quality prospective studies are required to verify above conclusions.

Correction notice This article has been corrected since it was published Online First. The article type has been modified from 'Original research' to 'Review'.

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Correction: *Clinicopathological characteristics of 8697 patients with COVID-19 in China: a meta-analysis*

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