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

Jiyun Zhu, Zhimei Zhong, Pan Ji, Hongyuan Li, Bocheng Li, Jielong Pang, Jianfeng Zhang, Chunling Zhao

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. As of 27 March 2020, the total number of confirmed cases has exceeded 500,000. 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. 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.

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. For example, two recent systematic reviews of studies of patients with COVID-19 indicated a high incidence of fever (>88%) and cough (>68%), but only one 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
Items for Meta-Analyses of Observational Studies in Epidemiology Statement. 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 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 were transformed by the double arcsine method to ensure a normal distribution, and the resulting transformed rate was used in single-arm meta-analysis. The heterogeneity between studies was analysed using a χ² test (p<0.10) and quantified using the I² 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 were back-calculated from transformed rates using the R=[sin(πtr/2)]. A two-tailed p<0.05 was considered statistically significant. Publication bias was evaluated using an Egger’s regression test and Begg’s test.

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 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).
| Study       | Publication date | Sample size (n) | Study design                  | Study population                                                                 | Age* (years) | Follow-up                      | Outcomes reported | Quality score |
|-------------|------------------|-----------------|-------------------------------|----------------------------------------------------------------------------------|--------------|--------------------------------|-------------------|--------------|
| Zhao et al  | March 3          | 101             | Retrospective.                | Patients with COVID-19 in Radiology Quality Control Center, Hunan.                | 21–50        | NA                             |                   | 1            |
| Xiong et al | March 3          | 42              | Retrospective.                | Patients with COVID-19 in Tongji Hospital, Huazhong University of Science and Technology. | 26–75        | 11 January–15 February         | (1)              | 7            |
| Zhou et al  | March 11         | 191             | Retrospective, multicentre.   | Patients with COVID-19 in Wuhan Jinyintan Hospital and Wuhan Pulmonary Hospital. | 56.0         | December 2019–31 January 2020 | (2)              | 7            |
| Li et al    | February 23      | 54              | Retrospective, single centre. | Patients with COVID-19 in Wuhan Fourth Hospital.                                 | 51.5         | January–February               | (2)              | 7            |
| Xiao et al  | February 27      | 143             | Retrospective, single centre. | Patients with COVID-19 in Chongqing Three Gorges Central Hospital.               | 45.1±1.0     | 23 January–February            | (2)              | 6            |
| Sun et al   | February 24      | 88              | Retrospective, single centre. | Patients with COVID-19 in Tianjin Haihe Hospital.                                | 48.5±15.7    | 21 January–8 February          | (1)              | 7            |
| Xu et al    | 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–6 February          | (1)              | 7            |
| Lu et al    | February 10      | 50              | Retrospective, single centre. | NA                                                                             | 50.4±16.8    | NA                             | (2)              | 6            |
| Wang et al  | February 25      | 52              | Retrospective, single centre. | Patients with COVID-19 in The First Affiliated Hospital of Zhejiang University. | 44±14        | 9 January–3 February           | (2)              | 6            |
| Xiao et al  | February 26      | 42              | Retrospective, single-centre cohort. | Patients with COVID-19 in Zongnan Hospital of Wuhan University.              | 51.6         | 16 January–18 February         | (2)              | 6            |
| Yu et al    | 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   | February 18      | 41              | Retrospective, single centre. | Patients with COVID-19 in Xiaochang First People’s Hospital.                   | 48.45        | NA                             | (2)              | 6            |
| Cheng and Li| 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           | (2)              | 6            |
| Yang et al  | March 3          | 57              | Retrospective, single centre. | Patients with COVID-19 in Nanjing Public Health Medical Centre.                 | 37           | NA                             | (2)              | 7            |
| Xiang et al | March 2          | 49              | Retrospective, single centre. | Patients with COVID-19 in The First Affiliated of Nanjing University.           | 42.9         | 21 January–27 January          | (2)              | 7            |
| Ma et al    | 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   | 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  | March 9          | 225             | Retrospective, single centre. | Patients with COVID-19 in Chongqing Three Gorges Central Hospital.             | 0–82         | 20 January–16 February         | (2)              | 7            |
| Ran et al   | March 6          | 209             | Retrospective, multicentre.   | Patients with COVID-19 from four hospitals in Fuyang City.                     | 46.5±15.7    | 25 January–10 February         | (2)              | 7            |
| Yuan et al  | March 6          | 223             | Retrospective, single centre. | Patients with COVID-19 in Chongqing Public Medical Center.                     | 46.5±16.1    | 24 January–23 February         | (2)              | 6            |
| Shi et al   | March 5          | 67              | Retrospective, single centre. | Patients with COVID-19 in Shanghai Public Health Clinical Center.              | 36±53.7      | January–February               | (2)              | 7            |
| Study       | Publication date | Sample size (n) | Study design                          | Study population                                                                 | Age* (years ) | Follow-up                              | Outcomes reported                  | Quality score |
|------------|-----------------|----------------|---------------------------------------|----------------------------------------------------------------------------------|---------------|----------------------------------------|-------------------------------------|---------------|
| Xiong et al33 | March 3         | 89             | Retrospective, single centre.          | Patients with COVID-19 in Renmin Hospital of Wuhan University.                    | 53±16.9       | 17 January–20 February                 |                                     | 6             |
| Chen et al32 | March 13        | 139            | Retrospective, single centre.          | Patients with COVID-19 in Chongqing Three Gorges Central Hospital.                | 15–79         | January–February                       |                                     | 6             |
| Fang et al34 | March 12        | 308            | Retrospective, single centre.          | Patients with COVID-19 in Hubei Huangshi Chinese Medicine Hospital.               | 30–86         | 25 January–20 February                 |                                     | 7             |
| Zhou et al31 | March 13        | 537            | Retrospective, multicentre.            | All cases of COVID-19 in Shandong Province.                                      | 26–86         | December 2019–15 February 2020        |                                     | 7             |
| Li et al35   | March 12        | 524            | Retrospective, multicentre.            | COVID-19 patients from hospitals in Henan Province.                               | 45            | 2 January–20 February                  |                                     | 8             |
| Song et al36 | March 12        | 60             | Retrospective, multicentre.            | Patients with COVID-19 in Gansu Provincial Designated Hospital.                   | 39.5±17.7     | 21 January–22 February                 |                                     | 6             |
| Cheng et al37 | Mar 12          | 463            | Retrospective, single centre.          | Patients with COVID-19 in Wuhan Jinyintan Hospital                                 | 15–90         | December 2019–6 February 2020         |                                     | 7             |
| Zhou et al31 | March 10        | 76             | Retrospective, single centre.          | Patients with COVID-19 in Puren Hospital of Wuhan University of Science and Technology. | 59.5          | January–February                       |                                     | 6             |
| Cheng et al39 | March 2         | 1079           | Retrospective, multicentre.            | All cases of COVID-19 in Henan Province.                                         | 46            | December 2019–29 February 2020        |                                     | 7             |
| Han et al40  | March 16        | 150            | Retrospective.                         | Patients with COVID-19 from two hospitals in Wuhan.                              | 53±14         | 12 January–16 February                 |                                     | 6             |
| Xu et al41   | March 16        | 62             | Retrospective, single centre.          | Critically ill patients with COVID-19 in Zhongnan Hospital of Wuhan University.  | 62.9          | 8 January–14 February                  |                                     | 6             |
| Dong et al42 | March 13        | 135            | Retrospective, multicentre.            | All reported confirmed cases of COVID-19 in Tianjin.                               | 48.6±16.8     | December 2019–24 February 2020        |                                     | 7             |
| Sun et al43  | March 15        | 391            | Retrospective.                         | COVID-19 cases reported in Zhejiang province.                                     | NA            | NA                                     |                                     | 7             |
| Li et al44   | February 29     | 83             | Retrospective.                         | Patients with COVID-19 in The Second Affiliated Hospital of Chongqing Medical University. | 45.5±12.3     | January–February                       |                                     | 7             |
| Wu et al45   | February 21     | 80             | Retrospective, single centre.          | Patients with COVID-19 from three tertiary hospitals in Jiangsu.                 | 46.1          | 22 January–14 February                 |                                     | 7             |
| Xu et al46   | February 28     | 90             | Retrospective, single centre.          | Patients with COVID-19 in Guangzhou Eighth People’s Hospital.                    | 50            | 2 January–4 February                   |                                     | 6             |
| Xu et al47   | 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                   |                                     | 6             |
| Yang et al48 | February 26     | 149            | Retrospective, multicentre.            | Patients with COVID-19 from three tertiary hospitals in Wenzhou.                 | 45.1±13.4     | 17 January–10 February                 |                                     | 7             |
| Xu et al49   | February 19     | 62             | Retrospective, multicentre.            | Patients with COVID-19 from seven hospitals in Zhejiang Province.                | 41            | 10 January–26 January                  |                                     | 6             |
| Zhang et al50 | February 23     | 140            | Retrospective, single centre.          | Patients with COVID-19 in No.7 Hospital in Wuhan.                                 | 57.0          | 16 January–3 February                  |                                     | 6             |

Table 1 Continued
| Study            | Publication date | Sample size (n) | Study design                      | Study population                                                                 | Age* (years) | Follow-up                                      | Outcomes reported | Quality score |
|------------------|------------------|-----------------|-----------------------------------|--------------------------------------------------------------------------------|-------------|-----------------------------------------------|-------------------|--------------|
| Wang et al<sup>51</sup> | 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<sup>52</sup>  | 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<sup>53</sup> | 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<sup>54</sup> | 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<sup>55</sup> | February 6       | 1099            | Retrospective, multicentre.        | Patients with COVID-19 from 552 hospitals in 31 provinces.                     | 47.0        | NA                                           | ①②               | 8            |
| Bernhem et al<sup>56</sup> | 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<sup>57</sup>    | February 21      | 80              | Retrospective, multicentre.        | Patients with COVID-19 from three hospitals in Chongqing.                      | 44±11       | January–February                              | ①②               | 7            |
| Shi et al<sup>58</sup>    | 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<sup>59</sup>   | 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<sup>60</sup>   | 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<sup>61</sup>   | 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<sup>62</sup>   | 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<sup>63</sup>     | 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<sup>64</sup>  | 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 | \( P \) value | \( I^2 \) (%) | Model | Meta-analysis 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 rhinorrhoea (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...
Table 3  Pathological characteristics of patients with COVID-19

| Characteristic                        | No. of studies | No. of patients | Heterogeneity | Meta-analysis |
|---------------------------------------|----------------|-----------------|---------------|---------------|
|                                       |                |                 | P value | I² (%) | 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 |

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 | I² (%) | 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            |                |                 |          |        |       |           |         |
| 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          |                |                 |          |        |       |           |         |
| 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.
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, 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, 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 lymphopenia. Few patients had leucocytosis and elevated procalcitonin levels, confirming that this
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. 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, 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%, 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. 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. Therefore, isolation, quarantine, social distancing, and community containment measures should be rapidly implemented in high-risk countries or regions. 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. Monitoring people at designated checkpoints, intercepting transmission routes in a timely manner and preventing local outbreaks are critical to prevent repeat epidemics.

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.

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.

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REFERENCES

1. WHO. Who Director-General's opening remarks at the media briefing on COVID-19 -11. Available: https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19-11-march-2020 [Accessed 29 Mar 2020].

2. WHO. Coronavirus disease (COVID-19) outbreak situation. Available: https://www.who.int/emergencies/diseases/novel-coronavirus-2019 [Accessed 29 Mar 2020].

3. WHO. Coronavirus disease 2019 (COVID-19) Situation Report-67. Available: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200327-sitrep-67-covid-19.pdf?sfvrsn=b6596be8_4 [Accessed 29 Mar 2020].

4. WHO. Naming the coronavirus disease (COVID-19) and the virus that causes it. Available: https://www.who.int/mediacentre/factsheets/fsn36/en/ [Accessed 29 Mar 2020].

5. Zhang MQ, Wang XH, Chen YL, et al. [Clinical features of 2019 novel coronavirus pneumonia in the early stage from a fever clinic in Beijing]. Zhonghua Jie He He Hu Xi Za Zhi 2020;43:E013.

6. Zhao W, Zhong Z, Xie X, et al. Relationship between chest CT findings and clinical conditions of coronavirus disease (COVID-19) pneumonia: a multicenter study. AJR Am J Roentgenol 2020;214:1–6.

7. Xiong Y, Sun D, Liu Y, et al. Clinical and high-resolution CT features of the COVID-19 infection: comparison of the initial and follow-up changes. Invest Radiol 2020. doi:10.1097/RLI.0000000000000674. [Epub ahead of print: 03 Mar 2020].

8. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020;395:1054–62.

9. Sun P, Qie S, Liu Z, et al. Clinical characteristics of 50466 hospitalized patients with2019-nCoV infection. J Med Virol 2020.

10. QL L, Huang T, Wang YQ, et al. COVID-19 patients' clinical characteristics, discharge rate, and fatality rate of meta-analysis. J Med Virol 2020.

11. Stroup DF, Berlin JA, Morton SC, et al. Meta-Analysis of observational studies in epidemiology: a proposal for reporting. meta-analysis of observational studies in epidemiology (MOOSE) group. JAMA 2000;283:2088–12.

12. NICE. Appendix 4: quality of case series. Available: https://www.nice.org.uk/guidance/cg3/documents/appointment4-4-quality-of-case-series-form2 [Accessed 29 Mar 2020].

13. Li YY, Wang WN, Lei Y, et al. [Comparison of the clinical characteristics between RNA positive and negative patients clinically diagnosed with 2019-novel coronavirus pneumonia]. Zhonghua Jie He He Hu Xi Za Zhi 2020;43:E023.

14. Xiao KF, Shui LL, Pang XH, et al. The clinical features of the 143 patients with COVID-19 in north-east of Chongqing. Journal of Third Military Medical University 2020.

15. Sun HY, YF B, Zhu ZG, et al. A preliminary study on TCM syndrome characteristics of 88 patients with COVID-19 in Tianjin. J Tradit Chin Med 2020.

16. Xu B, Fan CY, Zou YL, et al. Analysis of traditional Chinese medicine syndromes of 46 cases of COVID-19. Chinese journal of experimental traditional medical formulation 2020.

17. YF L, Yang ZG, Wang M. Analysis on Chinese medical clinical characteristics of 50 patients with 2019-nCoV-infected pneumonia. Academic Journal of Shanghai University of traditional Chinese medicine, 2020.

18. Wang J, Liu JP, Wang YY, et al. [Dynamic Changes of Chest CT Imaging in Patients With Corona Virus disease-19 (COVID-19)]. Zhejiang Da Xue Xue Bao Yi Xue Ban 2020;49.

19. Liao XN, Zhou J, Cao J, et al. Chest CT features comparison between COVID-19 and bacterial pneumonia. Medical Journal of Wuhan university 2020;26.

20. XT Y, Ye H, Yang SF, et al. Chest CT features of COVID-19. The Journal of Practical Medicine. 2020.

21. Liu FM, Ding HL, Gong XM, et al. Chest CT performance and clinical characteristics of coronavirus disease 2019 (COVID-19). Radiologic Practice 2020.

22. Cheng DZ, Li Y. Clinical effective methods and case analysis in 54 NCP patients treated with lanhuanggenw granules. World Chinese Medicine 2020.

23. Yang K, Ren MH, Xiao YL, et al. Epidemiological and clinical characteristics of 57 cases of new coronavirus pneumonia in non-epidemic areas. J Third Mil Med Univ 2020.

24. Xiang TX, Liu JM, Xu F, et al. Analysis of clinical features of 49 patients with novel coronavirus pneumonia in Jiangxi Province. Chinese J Respir Crit Care Med 2020.

25. PO M, Yuan YS, Zhang L, et al. Manifestations of the initial chest CT and its association with laboratory tests in 75 COVID-19 patients. Int J Med Radiol 2020.

26. Xue HH, Zhang HY, Pang ZH, et al. Analysis on TCM clinical characteristics of 46 cases of COVID-19 in the recover period. Shan J Tradit Chin Med 2020.

27. Gong X, Mou FZ, Wei DR, et al. The clinical characteristics and medication analysis of coronavirus disease 2019. World Chinese Medicine 2020.

28. Ran J, YP L, QT L, et al. Study of TCM syndrome in 209 novel coronavirus pneumonia cases of Chongqing in 2020. Journal of Emergency in Traditional Chinese Medicine 2020.

29. Yuan J, Sun YL, Zuo YJ, et al. Clinical characteristics of 233 novel coronavirus pneumonia cases in Chongqing. Journal of Southwest University (Natural Science Edition) 2020.

30. Shi J, Yang ZG, Chen Y, et al. Clinical observation on 49 cases of non-critical coronavirus disease 2019 in Shanghai treated by integrated traditional Chinese and Western medicine, Shanghai Journal of Traditional Chinese Medicine 2020.

31. Xiong J, Jiang WL, Zhou Q, et al. Clinical characteristics, treatment, and prognosis in 88 cases of COVID-2019. Medical Journal of Wuhan University(Health Sciences) 2020.

32. Chen X, Tong J, Xiang JH, et al. Retrospective study on the epidemiological characteristics of 139 patients with novel coronavirus pneumonia on the effects of severity. Chongqing Medicine 2020.

33. Fang L, Zhu QS, Cheng W, et al. Retrospective analysis on 308 cases of COVID-19 and clinical application program of Kang Yi Qiang Shen Gong exercise prescription, Shanghai Journal of Traditional Chinese Medicine 2020.

34. Zhou SY, Wang CT, Zhang W, et al. Clinical characteristics and treatment effect of 537 cases of novel coronavirus pneumonia in Shandong Province. Journal of Shandong University(Health Sciences) 2020.

35. JS L, SY L, Xie Y, et al. Clinical characteristics and TCM syndrome distribution in 524 cases of novel coronavirus pneumonia in Henan. Journal of Traditional Chinese Medicine 2020.

36. Song ZY, Yong WX, Li J, et al. Analysis on TCM syndrome rules of 60 Casesof novel coronavirus pneumonia in Gansu area. Chinese Journal of Information on TCM 2020.
Cheng KB, Wei M, Shen H, et al. Clinical characteristics of 463 patients with common and severe type coronavirus disease 2019. *Shanghai Medical Journal* 2020.

Chen T, Jiang ZY, Xu W, et al. Clinical features and CT imaging analysis of 78 patients with coronavirus disease 2019. *Journal of Jinan University* 2020.

Cheng JL, Huang C, Zhang GJ, et al. [Epidemiological characteristics of novel coronavirus pneumonia in Henan]. *Zhonghua Jie He He Hu Xi Za Zhi* 2020;43:47-56.

Han J, Dong XF, Hu F, et al. Clinical characteristics of 120 patients infected with SARS-CoV-2. *Guangdong Medical Journal* 2020.

Xu S, HT H, YG H, et al. Clinical features of 62 cases of coronavirus disease 2019 complicated with acute renal injury. *Medical Journal of Wuhan University* 2020:1–5.

Dong XC, Li JM, Bai JY, et al. [Epidemiological characteristics of confirmed COVID-19 cases in Tianjin]. *Zhonghua Liu Xing Bing Xue Za Zhi* 2020;41:638–42.

Sun WW, Ling F, Pan JR, et al. [Epidemiological characteristics of 2019 novel coronavirus family clustering in Zhejiang Province]. *Zhonghua Jie He He Hu Xi Za Zhi* 2020;54:E027.

Li K, W, et al. The clinical and chest CT features associated with severe and critical COVID-19 pneumonia. *Radiology* 2020;395:497–506.

Huang C, W, et al. Clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020;395:507–13.

Guan WJ, ZY N, Hu Y, et al. Clinical characteristics and imaging analysis of 78 patients with coronavirus disease 2019 and its relationship with clinical features, 2020. Available: https://www.ncbi.nlm.nih.gov/pubmed/?term=32091414

Chi H, Han X, Jiang N, et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. *Lancet Infect Dis* 2020;20:425–34.

Yang X, Xu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-center, retrospective observational study. *Lancet Respir Med* 2020. doi:10.1016/S2213-2600(20)30079-5. [Epub ahead of print: 24 Feb 2020].

Zhou S, Wang Y, Zhu T, et al. Ct features of coronavirus disease 2019 (COVID-19) pneumonia in 62 patients in Wuhan, China. *AJR Am J Roentgenol* 2020;215:1046–52.

Wang T, Shi L, Chen YY, et al. Clinical efficacy analysis of 50 cases of corona virus disease 2019 in traditional Chinese medicine. *Jilin Journal of Chinese Medicine* 2020.

Fang XW, Mei G, Yang TJ, et al. Clinical characteristics and treatment analysis of 79 cases of COVID-19. *Chinese Pharmacological Bulletin* 2020.

SM Y, Cui YF, Wang ZX, et al. Analysis of the relationship between clinical features and tongue manifestations of 40 cases with novel coronavirus pneumonia. *Beijing Journal Of Traditional Chinese Medicine* 2020.

Zhang X, Li L, Dai GC, et al. A preliminary study on the clinical characteristicsandchinese medical syndrome of 42 cases of COVID-19 in Nanjing. *Journal of Nanjing University of Traditional Chinese Medicine* 2020.

Phan LT, Nguyen TV, Luong QC, et al. Importation and human-to-human transmission of a novel coronavirus in Vietnam. *N Engl J Med* 2020;382:872–4.

National Health Commission Office. The Guideline for the diagnosis and treatment of novel coronavirus pneumonia (trial version sixth) Available: http://www.nhc.gov.cn/xcs/zxxgqgf202002/8334a8326ddd9d329df35f17d7da8ae6c2/files/b2b18cf61bc54639af2279f2bbf817.pdf [Accessed 29 Mar 2020].

Strategy and Policy Working Group for NCIP Epidemic Response. [Urgent research agenda for the novel coronavirus epidemic: transmission and non-pharmaceutical mitigation strategies]. *Zhonghua Liu Xing Bing Xue Za Zhi* 2020;41:1–6.

Razai MS, Doerholt K, Ladhani S, et al. Coronavirus disease 2019 (covid-19): a guide for UK GPs. *BMJ* 2020;368:m800.

Helewel J, Abbott S, Gimma A, et al. Feasibility of controlling COVID-19 outbreaks by isolation of cases and contacts. *Lancet Glob Health* 2020;8:e488–96.

Hopman J, Allegranzi B, Mehtar S, et al. Coronavirus disease 2019 (COVID-19) in low- and middle-income countries. *JAMA* 2020. doi:10.1001/jama.2020.4189. [Epub ahead of print: 16 Mar 2020].

Li DKT, Zhu S. Contributions and challenges of general practitioners in China fighting against the novel coronavirus crisis. *Fam Med Community Health* 2020;5:e000361.

ZB H, Song C. Discovery and management of novel coronavirus pneumonia infected with latent infection. *Chinese Journal of Preventive Medicine* 2020;54.

Onder G, Rezza G, Brusaferr S. Case-Fatality rate and characteristics of patients dying in relation to COVID-19 in Italy. *JAMA* 2020. doi:10.1001/jama.2020.4683. [Epub ahead of print: 23 Mar 2020].
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