Received: 4 August 2020 | Revised: 13 November 2020 | Accepted: 22 January 2021

DOI: 10.1111/jocn.15688

Journal of Clinical Nursing WILEY

REVIEW

Diagnostic features of sars-covid-2-positive patients: a rapid review and meta-analysis

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Funding information
The authors declare that they receive no specific funding for this work.

Abstract

Aims: To identify the main diagnostic features of SARS-CoV-2-positive patients at the time of hospitalisation and their prevalence.

Background: Since the COVID-19 outbreak in China in December of 2019, several studies attempted to identify the epidemiological, viral and clinical characteristics of SARS-CoV-2. Given the rapid widespread transmission of the COVID-19 disease worldwide, a more comprehensive and up-to-date understanding of its features is needed to better inform nurses, clinicians and public health policy makers.

Methods: A rapid review and meta-analysis were carried out to identify the main diagnostic features of SARS-CoV-2-positive patients at the time of hospitalisation. All case series, cross-sectional, case–control and cohort studies published from 01/01/2020 till 30/06/2020 in English and Chinese that stated all or at least two of the outcomes of interest (clinical features, laboratory and radiological findings) were included. We performed a random-effects model meta-analysis to calculate pooled prevalence and 95% confidence intervals. Conduction of the review adheres to the PRISMA checklist.

Results: 21 studies involving 8837 patients were included in the quantitative synthesis. Fever, cough and fatigue were the most common clinical features, while the most relevant laboratory abnormalities at the time of hospitalisation were lymphopenia, elevated C-reactive protein and lactate dehydrogenase. CT images showed a bilateral lung involvement, with ground glass infiltrates and patchy shadows on most patients.

Conclusion: This review provides an up-to-date synthesis of main diagnostic features of SARS-CoV-2-positive patients at the time of hospitalisation.

Relevance to Clinical Practice: Our findings could provide guidance for nurses and clinicians to early identification of positive patients at the time of the hospitalisation through a complete definition of main clinical features, laboratory and CT findings.

KEYWORDS
COVID-19, diagnostic features, meta-analysis, review, severe acute respiratory syndrome coronavirus 2

1 | INTRODUCTION

In late December 2019, several cases of viral pneumonia of unknown aetiology were first reported in Wuhan, capital of Hubei, China, with epidemiological links to the Huanan Seafood Wholesale Market. The Chinese Centre for Disease Control and Prevention isolated the causative agent of the outbreak as a novel Coronavirus (nCoV), namely severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (Lu et al., 2020). Soon after, the number of cases increased exponentially, spreading across China and worldwide. On 11 March 2020, the World Health Organization (WHO) officially declared the COVID-19 outbreak a pandemic (Mahase, 2020). At the time of writing, more than 51 million cases of SARS-CoV-2 have been confirmed and more than 1.270.000 people have died (WHO, 2020a).

Since then, several studies attempted to identify the epidemiological, viral and clinical characteristics of SARS-CoV-2 patients. The majority of those studies were case reports, case series and cross-sectional studies, which described evolution and outcomes of the disease, as well as risk factors, clinical, laboratory and image findings (Long et al., 2020; Chu et al., 2020; Cheng et al., 2020; Ai et al., 2020). Two systematic reviews published between March and April 2020 (Rodriguez-Morales et al., 2020; Fu et al., 2020) gave a preliminary characterisation of the disease, describing the most commonly reported clinical features, the laboratory abnormalities and CT images of SARS-CoV-2 patients, mostly from China.

However, the current literature on COVID-19 is rapidly evolving, with new peer-reviewed and preprint articles published every day across the world, and its main features remain unclear (Rodriguez-Morales et al., 2020; Struyf et al., 2020). Given the rapid widespread transmission of the COVID-19 disease worldwide, a more comprehensive and up-to-date understanding of its features is needed to better inform clinicians, nurses and public health policy makers.

2 | AIMS

A rapid review was conducted to identify the main diagnostic features of SARS-CoV-2-positive patients at the time of hospitalisation, aiming to help stakeholders and clinicians optimise the diagnostic process.

To achieve our aim, we:

- synthetised and described the diagnostic features of SARS-CoV-2-positive patients at the time of hospitalisation;
- assessed the prevalence of the main diagnostic features in SARS-CoV-2-confirmed cases.

3 | METHODS

Conduction of the review adheres to PRISMA checklist for systematic reviews and meta-analyses (Moher et al., 2009). See File S1.

What does this paper contribute to the wider global clinical community?

- This review provides an up-to-date summary of the main clinical characteristics of SARS-COV-2-positive patients at the time of hospitalisation.
- Among clinical symptoms, fever, cough and fatigue showed the highest pooled prevalence.
- The most common alterations of blood routine reported at the time of hospitalisation were lymphopenia, increased infection-related biomarkers and elevated liver functions values.

3.1 | Study selection

All the articles that provide a clear description of the patient with a confirmed diagnosis of SARS-CoV-2 at the time of hospitalisation were included. The confirmation of the diagnosis of SARS-CoV-2 was ascertained in agreement with the diagnostic criteria of the Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (2020b). Therefore, all the studies which clearly stated the baseline characteristics of patient with positive RNA assay were included.

The search was limited to articles in English or Chinese, published from 01/01/2020 till 30/06/2020. Case reports, diagnostic accuracy studies without a clear statement of the baseline-positive SARS-CoV-2 characteristics and studies focused on pregnant women or paediatric patients were excluded. To speed up data extraction and synthesis, only studies with a sample size of at least 90 patients were included.

The outcomes of interest were the reported clinical and diagnostic features and the laboratory findings. We chose to include all the case series, cross-sectional, case–control and cohort studies that stated all or at least two of the outcomes of interest (e.g. clinical and diagnostic features or clinical and laboratory findings). For the clinical features, all the reported signs and symptoms were collected. In the same way, all the image characteristics and the lesions region of the diagnostic imaging as well as the stated blood routine, coagulation function, infection-related biomarkers and blood biochemistry were collected.

3.2 | Search strategies

The Europe PMC, LitCovid Database, Medline, The Cochrane Library, Science Direct, Embase and The Cumulative Index to Nursing and Allied Health Literature (CINAHL) were screened independently by two experienced reviewers with the support of Zotero Reference Manager (V.5.0). In case of disagreement between the reviewers on eligibility, a senior author was consulted. Two different search strings were used (File S2), both combining different synonyms and mesh terms for SARS-CoV-2 and diagnosis or testing.

Since this is a rapid review, no specific searches of grey literature were done. After a discussion between the authors, we decided to include only peer-reviewed published articles. All the articles published in Chinese were summarised by a team member with a certified knowledge of the Chinese language and then discussed with another team member.

3.3 | Data extraction

One experienced review author-extracted data from the included studies into a standardised table. A second review author checked the data extraction for completeness and correctness. Whether an article reported duplicate information from the same patient, the information of both reports was combined in order to obtain complete data, but only counted as a single case. Observational studies that stated the overall proportion of symptoms, laboratory characteristics and CT images or/and the mean values of clinical features or laboratory findings for SARS-CoV-2-positive patients at baseline were included for quantitative synthesis (meta-analysis). The data item included the following: author, country, year, study design, aim, characteristic of the study participants, diagnostic reference criteria, age, gender, comorbidities, clinical features (e.g. fever, cough), laboratory findings (e.g. lymphocytes count) and imaging (e.g. CT signs).

3.4 | Quality assessment

The risk of bias was assessed by one author with the Joanna Briggs institute (JBI) 'Checklist for case series'

and 'Critical appraisal checklist for cohort'. A risk of bias judgement (Low; Moderate; High) was attributed to each included study following Melo et al. (2018) scoring system. Then, the 25% of the rating judgment was checked independently by another author, as suggested by the World Health Organization guidelines for rapid review (2017). Moreover, publication bias was assessed using a funnel plot and computing the Egger's test (Egger et al., 1997).

3.5 | Statistical approach

All the different units of measure of the outcomes of interest were converted in the referred international unit (e.g. from mg/dl to mmol/L). All the data presented as median and interquartile range were converted to mean and standard deviation (SD) following the Cochrane handbook of systematic review of interventions (7.7.3.5). Percentages or mean and standard deviation (SDs) were calculated to describe the distributions of categorical and continuous variables. Pooled prevalence and its 95% confidence interval (CI) were used to summarise the weighed effect size for each study grouping variable in a random effect model. We chose a random effect model because we assumed high clinical, methodological and statistical heterogeneity. The proportion of cases (e.g. fever or lymphocytopenia) on the total number of cases for each outcome of interest was meta-analysed using the R function *metaprop*. Whether computed with function *metamean* in R, raw weighted mean and their 95% confidence intervals were reported (e.g. mean age in years).

Measure of heterogeneity, as the I^2 index and the tau squared test were estimated and reported for both pooled prevalence and pooled mean. We expected high heterogeneity from the results (Ioannidis et al., 2007); therefore, we chose to keep the pooled overall estimates but to estimate also a prediction interval for all the outcomes of interest as it presents the expected range of true effects in similar studies (IntHout et al., 2016).

4 | RESULTS

The literature search yielded 10727 references. After removal of duplicates, 7829 references were screened for title and abstract and 21 observational studies were identified, all included in the quantitative analysis (Figure 1). The main descriptive characteristics of the included studies are shown in Table 1.

The total sample of participants included 8837 adults with a laboratory-confirmed diagnosis of SARS-CoV-2 by real-time RT-PCR, accordingly to the World Health Organization or the National Health Commission diagnostic guidelines (Table 1). The reasons for excluding the other records are listed in the PRISMA flow chart case (Figure 1). All the included studies published before May 2020 were issued in Asia, while the latter were issued in USA and Europe too (Table 1). The most common type of studies included was retrospective case series or cross-sectional design (Table 1). Data were primarily collected with the support of electronic records or by retrospective manual review of the clinical record at the time of hospitalisation; therefore, only one study provided baseline data for patients admitted at the emergency department (Figure 1). All the included studies reported SARS-CoV-2 patients' clinical features and laboratory findings, while diagnostic imaging was less commonly and clearly stated especially in the recently issued articles (Table 1).

The methodological quality of included studies was assessed according to the study designs with the Joanna Briggs Institute (JBI) checklists. As shown in Table 1, nearly half of included studies were rated as 'Low' risk of bias. Only four studies were rated as 'Moderate' and even fewer as 'High' (Table 1). The lack of consecutive inclusion or a clear description of participants, as well as many imprecisely reported outcomes, elevated the risk of bias in nearly half of the included studies. None of the cross-sectional designs provide any measure or adjustment for potential confounding variables. Publication bias was assessed with a funnel plot for the standard error, with no evidence of bias (File S3). Additionally, the Egger's test (p =.61) performed by the *gender* variable suggested no notable evidence of publication bias.

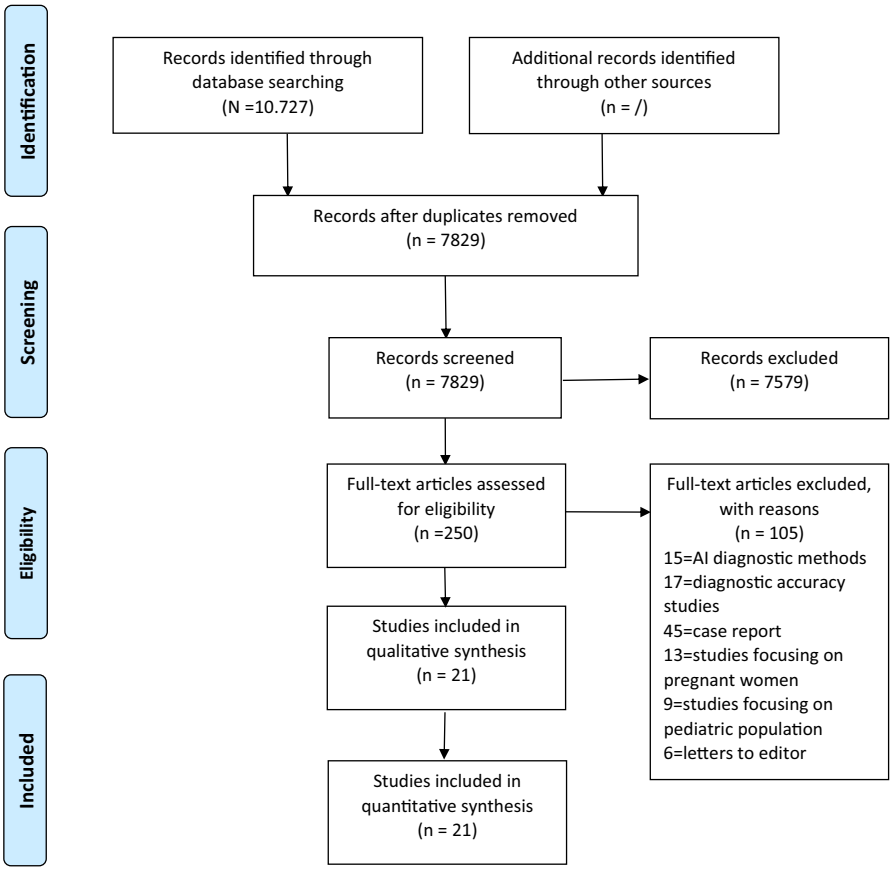

FIGURE 1 Search strategy [Colour figure can be viewed at wileyonlinelibrary.com]

4.1 | Demographical characteristics and comorbidities

The pooled mean age of the patients across the 21 studies was 51.43 years old (95%CI 48.35;54.52), with a prediction interval ranging from 41.54 to 61.32 mean years as in shown in Table 2. However, the pooled mean age of the sample was fairly lowered by the pooled mean age of the studies issued in Asia, in which the mean age was 50 years old versus 65 years old of the studies issued in Western regions (e.g. America or Europe). Male was only slightly more prevalent than female in the total sample (Table 2). Common comorbidities were hypertension (22.49%, 95%CI 15.49;31.49) and diabetes (13%, 95%CI 8.82;18.88), both with prediction intervals ranging from less than 5% to more than 50% (Table 2). The rate of obesity was reported only by two studies (Table 2) and, despite only including estimates, it appears to be the most prevalent comorbidity of hospitalised SARS-CoV-2-positive patients (40.19%, 95%CI 29.23;52.22). Surprisingly, both chronic obstructive pulmonary disease (3.66%, 95%CI 2.41;5.52) and malignancies (3.19%, 95%CI 2.07;4.87) were not very prevalent comorbidities in SARS-CoV-2-positive patients (Table 2).

4.2 | Clinical manifestations of COVID-19

Symptoms were commonly reported in the included articles, while signs were often missing or described approximately as shown in Table 3. Fever and cough were the only clinical features reported by the totality of the included studies as commonly associated to SARS-CoV-2 patients (Table 2). However, cough, which was stated in all of the included studies, showed an overall pooled prevalence of only 64% (95%CI 60.33;67.60) and a large prediction interval ranging from less than 50% to more than 80% (Table 2). Fever, as a self-reported symptom, showed a pooled prevalence of 77.5% with a pretty narrow confidence interval (95%CI 71.45;82.58) but a fairly larger prediction interval (Table 2). Only 6 studies reported the rate of SARS-CoV-2-positive patients with a temperature >38° Celsius, and the overall pooled prevalence of the sign was 38.96% (95%CI 25.65;54.14), while 5 studies clearly stated the mean temperature of the sample with thresholds ranging from 36.7° to 38.5° and with a non-statistically significant pooled mean of 36.96° Celsius (Table 2). Other signs mean values (e.g. respiratory or heart rate) were reported only by four included studies (Table 3), and despite pooled, they did not result statistically significant in the quantitative synthesis.

Diarrhoea was the most commonly reported gastrointestinal symptom (Table 3) and showed a pooled prevalence of 9.42% (95%CI 7.34;12.01). Instead, anorexia was recorded only by 7 included studies, but showed a pooled prevalence of 19.40% (95%CI 12.70;28.48) and a higher prediction interval than diarrhoea (Table 2). Respiratory symptoms, like dyspnoea, pharyngalgia and rhinorrhoea, were not commonly reported in the included studies (Table 2), and when pooled, did not show a high pooled prevalence (Table 2). However, some studies were not clear in the reporting of symptoms, often

TABLE 1 overview of all the included studies.

Authors	Country	Published	Study	N	Mean age	Data collected at	Clinical Features	Laboratory findings	Diagnostic imaging	Risk of Bias
Chen et al. (2020)	China	15/2/2020	CS	99	55	AH	✓	✓	✓	Low
Guan et al. (2020)	China	28/2/2020	CR	1099	47	AH	✓	✓	✓	Low
Cao et al. (2020)	China	13/3/2020	CS	102	54	AH	✓	✓	✓	Low
Qiu et al. (2020)	China	5/5/2020	CS	104	43	AH	✓	✓	✓	Moderate
Li et al. (2020)	China	10/4/2020	CS	225	50	AH	✓	✓	✓	High
Dai et al. (2020)	China	6/4/2020	CR	234	44	AH	✓	✓	✓	Low
Hong et al. (2020)	Korea	24/4/2020	CR	98	55	AH; ICU	✓	✓	✓	Moderate
Chen et al. (2020)	China	11/4/2020	CS	203	54	AH	✓	✓	✓	Moderate
Huang et al. (2020)	China	8/5/2020	CS	202	44	AH	✓	✓	✓	Low
Zhang et al. (2020)	China	10/5/2020	CS	194	48	AH	✓	✓	✓	Low
Lian et al. (2020)	China	12/5/2020	CS	465	45	AH	✓	✓	✓	Low
Israelsen et al. (2020)	Denmark	15/5/2020	CS	175	71	AH ICU	✓	✓	✓	Low
Li et al. (2020)	China	15/5/2020	CR	93	51	AH	✓	✓	✓	Moderate
Song et al. (2020)	China	16/5/2020	CS	111	55	AH	✓	✓	✓	Low
Argenziano et al. (2020)	USA	29/5/2020	CS	764	59	AH; ICU; ED	✓	✓		Low
Buckner et al. (2020)	USA	22/5/2020	CS	105	69	AH	✓	✓		Low
Imam et al. (2020)	USA	4/6/2020	Co	1305	61	AH	✓	✓	✓	Low
Zhao et al. (2020)	China	4/6/2020	CR	1000	61	AH	✓	✓	✓	High
Li et al. (2020)	China	11/6/2020	CS	1449	57	AH	✓	✓	✓	Low
Xu et al. (2020)	China	15/5/2020	CR	703	46	AH	✓	✓	✓	Low
Wang et al. (2020)	China	30/4/2020	CS	107	51	AH	✓	✓	✓	High

Abbreviations: AH, Admission at hospital; Co, Cohort studies; CR, Cross-sectional studies; CS, Case series studies; ED, Emergency department; ICU, Intensive unit care admission.

using terms such 'sore throats', 'shortness of breath' or 'runny nose' as synonymous for pharyngalgia, dyspnoea and rhinorrhoea. Neuromotor symptoms, such as myalgia and headache, were frequently reported in the included studies (Table 3), but both showed low prevalence with prediction interval narrow than 50% (Table 2). Other possible relevant symptoms of SARS-CoV-2, such as loss of smell or taste and conjunctivitis, were stated only by one included article.

TABLE 2 Meta-analysis outcomes (random-effects model)

Variable		K	Mean or Prevalence (%)	95%CI	Prediction Interval	n	I^2	t^2	p
Demographics	Mean age	21	51.43	48.35;54.52	41.54;61.32	8837	46%	19.85	.01
	Male	20	52.91	50.44;55.37	43.10;62.50	8821	77%	0.03	.001
	Female	20	46.91	44.50;49.34	37.5;56.48	8821	76%	0.03	.01
Comorbidities	CD	17	9.32	5.89;14.44	1.13;47.87	6944	97%	0.99	.01
	Diabetes	16	13	8.82;18.88	2.17;50.38	6845	97%	0.74	.01
	COPD	14	3.66	2.41;5.52	0.75;15.92	6632	88%	0.49	.01
	Hypertension	16	22.49	15.49;31.49	3.71;68.60	5765	98%	0.83	.01
	Malignancies	14	3.19	2.07;4.87	0.61;14.89	6585	88%	0.53	.01
	Obesity	2	40.19	29.23;52.22	Ni	1093	81%	0.32	.02
Clinical Features									
Signs	Temperature >38°	6	38.96	25.65;54.14	6.19;86.05	3483	98%	0.56	.01
	Mean temperature	5	36.96	36.53;37.39	35.75;38.18	2898	47%	0.09	.1
	Mean RR	5	20.01	19.06;20.95	18.47;21.54	2353	0%	0	.99
	Mean HR	4	83.91	75.40;92.42	65.23;102.59	1353	5%	0	.97
Symptoms	Fatigue	16	34.10	29.11;39.46	16.24;58.00	7465	95%	0.19	.01
	Cough	19	64.05	60.33;67.60	47.16;78.04	7525	89%	0.10	.01
	Fever	20	77.50	71.45;82.58	43.45;93.92	7636	97%	0.48	.01
	Diarrhoea	19	9.42	7.34;12.01	2.84;27.51	8823	93%	0.34	.01
	Myalgia	19	20.25	16.44;23.76	8.04;41.20	8719	93%	0.22	.01
	Dyspnoea	20	22.19	15.38;30.92	3.19;71.17	8944	99%	1.00	.01
	Headache	16	8.69	6.94;10.82	3.47;20.10	8294	88%	0.18	.01
	Rhinorrhoea	10	5.44	3.02;9.63	0.59;35.68	5939	97%	0.86	.01
	Sore throat	9	12.66	7.58;20.40	1.74;54.28	6417	97%	0.70	.01
	Anorexia	6	19.40	12.70;28.48	3.86;59.03	2813	94%	0.34	.01
CT Finding	Bilateral Involvement	15	65.22	49.45;77.62	10.37;96.70	7291	99%	1.53	.01
	Pleural effusion	3	3.06	0.78;11.26	0.00;99.99	2159	96%	1.44	.01
	GGO	9	38.25	24.80;53.78	5.45;86.93	5041	99%	1.30	.01
	Consolidation	3	7.20	2.62;16.51	0;99.99	3100	98%	1.14	.01
	Patchy shadows	5	58.34	36.80;76.52	4.45;97.60	2543	98%	1.33	.01
Laboratory findings	WBC ↑	9	10.23	5.70;17.67	1.07;54.35	3783	96%	1.28	.01
	WBC ↓	10	21.50	16.08;28.13	6.79;50.73	3985	95%	0.29	.01
	Lymphocytes ↓	10	50.08	33.81;65.62	7.19;92.63	2918	98%	1.05	.01
	CRP ↑	11	58.34	49.45;66.72	25.83;84.91	5022	97%	0.34	.01
	LDH ↑	9	47.38	39.59;55.29	21.85;74.35	4422	96%	0.21	.01
	ALT ↑	11	18.30	8.95;33.78	0.85;85.38	4804	99%	2.30	.01
	AST ↑	11	26.03	14.82;40.56	2.25;83.75	5593	99%	1.30	.01
	Al ↓	7	59.20	32.68;81.25	2.60;98.74	2945	99%	2.10	.01
	Cr ↑	8	22.36	5.79;56.27	0.09;98.78	3601	99%	5.16	.01
	Tbil ↑	6	16.10	4.30;45.03	0.08;97.72	3110	99%	3.24	.01
	D-Dimer ↑	7	27.04	19.53;35.22	7.99;60.29	2840	95%	0.26	.01

Abbreviations: Al, Albumin; ALT, Alanine transaminase; AST, Aspartate transaminase; CD, Cardiac disease; COPD, Chronic obstructive pulmonary disease; Cr, Serum creatinine; CRP, C-reactive protein; GGO, Ground glass opacities; LDH, Lactate dehydrogenase; Ni, not imputable; Tbil, Total bilirubin; WBC, White blood count.

TABLE 3 Qualitative summary of the findings

	Variables	*K*	Inter-study frequency (%)		Variables	*K*	Inter-study frequency (%)
Signs	Temperature	8	38	Blood Routine	WBC	13	61
	Respiratory Rate	4	19		Lymphocyte count	18	85
	Hearth rate	4	19		Lymphocyte ratio	7	33
	Systolic blood pressure	4	19		Neutrophil count	9	42
					Neutrophil ratio	6	28
Symptoms	Fever	20	95		Monocyte count	2	9
	Chills	9	42		Basophil count	1	4
	Cough	21	100		Eosinophil count	1	4
	Diarrhoea	19	90		Platelet count	11	52
	Fatigue	16	76		Haemoglobin level	11	52
	Chest distress	14	66		Haematocrit	3	14
	Pharyngalgia	12	57				
	Dyspnoea	13	61	Coagulation function	APTT	8	38
	Rhinorrhoea	8	38		D-dimer	8	38
	Anorexia	7	33		PT	3	14
	Expectoration	11	52				
	Nausea	13	61	Infection-related biomarkers	CRP	15	71
	Vomit	10	48		ESR	10	48
	Headache	14	66		IIL−6	3	14
	Myalgia	19	90		PCT	12	57
Image characteristics	GGO	12	57	Blood biochemistry	Al	9	42
	Patchy shadows	7	33		ALT	17	80
	Consolidation	4	19		AST	16	76
	Pleural effusion	3	14		Tbil	13	61
	Interstitial thickening	2	9		BUN	10	48
	Crazy-paving pattern	2	9		Cr	8	38
					LDH	10	48
Lesion region	Bilateral pulmonary	19	90		Hs-cTnT	4	19
	Subpleura	4	19		CK	9	42
	Peripheral zone	3	14		Ferratin	3	14
					Troponin I	3	14

Abbreviations: Al, Albumin; ALT, Alanine transaminase; APTT, Activated partial thromboplastin time; AST, Aspartate transaminase; BUN, blood urea nitrogen; CK, Creatine kinase; Cr, Serum creatinine; CRP, C-reactive protein; GGO, Ground glass opacities; Hs-cTnT, High-sensitive cardiac troponin T; IL-6, Interleukin; LDH, Lactate dehydrogenase; PCT, Procalcitonin; PT, Prothrombin time; Tbil, Total bilirubin; WBC, White blood count.

4.3 | Laboratory findings

Among the 21 studies which reported the laboratory findings of SARS-CoV-2 patients (Table 3), 18 studies stated a widespread decrease of the lymphocyte count. Other commonly reported alterations of the blood routine in the included articles involved a general decrease of the leucocyte count, while the haemoglobin level did not seem to vary much (Table 3). Indeed, a decrease in lymphocytes counts was present in the 50% of the total sample (95%CI 33.81;65.62), while leucocyte count showed a pooled prevalence of only 21.5% (Table 2).

Between the infection-related biomarkers, an increased level of C-reactive protein level (CRP) was stated in all the articles except six (Table 3). The pooled prevalence of the increased level of CRP was 58.3% (95%CI 49.45;66.72); however, it showed a pretty wide prediction interval (Table 2). All the other increased infection-related biomarkers (e.g. erythrocyte sedimentation rate, interleukin and procalcitonin) were less commonly reported and referred

predominantly as normal (Table 3). Eight studies also reported normal values of coagulation function (Table 3), except for D-dimer, which resulted increased in seven studies with a pooled prevalence of 27% (Table 2).

Liver function values were reported by 17 of the included studies, mostly showing normal or increased levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST) and total bilirubin (Table 2). Both ALT and AST were increased in 11 included studies with an overall pooled prevalence of 18.3% (95%CI 8.95;33.78) and 26% (95%CI 14.82;40.56), respectively, and wide prediction intervals (Table 2). Increase of total bilirubin was slightly less prevalent than ALT and AST, and it has an even wider prediction interval (Table 2). Renal function (e.g. blood urea nitrogen, serum creatinine and glomerular filtration rate) was scarcely reported and referred predominantly as normal (Table 3). Other increased blood biochemistry values reported in the included studies (Table 3) were lactate dehydrogenase (48%), serum high-hypersensitivity troponin T (19%), creatinine kinase CK (42%) and ferratin (14%). Increased values of lactate dehydrogenase (LDH) showed a pooled prevalence of 47.38% (95%CI 21.85;55.29), while increased value of serum creatinine of only 22.36% (Table 2).

4.4 | Radiologic findings

The processing of computed tomography (CT) images is often reported in the included studies as the fastest method to confirm a diagnosis of SARS-CoV-2 at the time of hospitalisation. Characteristic images of the SARS-CoV-2 patients in the CT scans were ground glass opacities (GGO) and consolidations (Table 3). However, consolidation rates were reported only by 3 studies with an overall pooled prevalence of 7.2% (Table 2). Instead, GGO were estimated in 38.2% (95%CI 24.89;53.78) of the total sample (Table 2). Moreover, only a few included studies provided a clear classification of how many patients have GGO, consolidation or both. Five articles stated the rate of observed patchy shadow without linking them to any possible causes such as pleural effusion or pneumonia (Table 3), and despite pooled they were the most prevalent CT images reported in SARS-CoV-2 patients at hospitalisation (Table 2).

The pulmonary opacifications or patchy shadows were stated in the included studies as located in the peripheral zones of both lungs (Table 3), with the lower lobe of the left lung as the more involved one. However, while bilateral involvement is a prevalent clinical gauge of SAR-CoV-2-positive patients in the included studies, pleural effusion rates were reported only by 3 included articles and showed a pooled prevalence of only 3% (95%CI 0.78;11.26) with a wide prediction interval (Table 2).

5 | DISCUSSION

A rapid diagnosis is essential to ensure SARS-CoV-2 patients receive proper care and to reduce the risks of contagion, and this rapid review updates the diagnostic features of SARS-CoV-2 patients at the time of hospitalisation. Indeed, the actual golden standard tests for SARS-CoV-2 diagnosis are real-time RT-PCR by swab, which has low sensitivity (Carver & Jones, 2020), and often it must be repeated one or more days apart. SARS-CoV-2-positive patients at the time of hospitalisation predominantly presented fever, cough, fatigue, dyspnoea, myalgia and anorexia. At least 38% (95%CI 25.65;54.14) of SARS-CoV-2-positive patients at hospitalisation show a temperature higher than 38° Celsius and 65.22% (95%CI 49.45;77.62) of them show bilateral pulmonary involvement at the CT scan. Both lymphocytes count and albumin are decreased in at least 50% of the cases, while CRP, LDH and liver function values are significantly increased. This rapid review provides an updated summary of the most commonly reported symptoms, signs, diagnostic features and laboratory findings of SARS-CoV-2 patients, to speed up the triage process and help clinician in their daily decision-making process.

More than half of the patients included in the overall sample are male, with a mean age of 51 years and comorbidities such as diabetes and hypertension being prevalent respectively in 9.32% and 22.49% of SARS-CoV-2 patients at the time of hospitalisation. These findings are coherent with the previous literature (Rodriguez-Morales et al., 2020), but are still biased by the high rate of included articles published in China. Indeed, in our meta-analysis the most prevalent comorbidity appears to be obesity, which was stated only by two included articles both issued in America with a pooled prevalence of 40.19% (95%CI 29.23;52.22). More articles from America, Africa and Europe with a structured research design are needed to fully comprehend how age, comorbidities and healthcare system disparities impact on positive SARS-COV-2 diagnosis.

At the timing of hospitalisation, SARS-CoV-2 patients present predominately fever and cough, coherently with previous findings (Rodriguez-Morales et al., 2020) and actual SARS-CoV-2 screening policy (WHO, 2020c). Cough has a 64.05% (95%CI 60.33;67.60) prevalence, which is a higher rate compared to those declared in a previous meta-analysis (Rodriguez-Morales et al., 2020), but a wide prediction interval (Table 2). Indeed, a recent Cochrane review (Struyf et al., 2020) highlighted how cough has a too poor specificity index to be considered a prominent diagnostic feature of SARS-CoV-2. Other respiratory symptoms, such as dyspnoea or pharyngalgia, are often reported in the included studies since ACE2 receptors appear to be the entry point for SARS-CoV-2 to into human cells, but both have an overall pooled prevalence lower than 30% with wide prediction intervals. Our estimated pooled prevalence for both dyspnoea and fatigue is lower than the one reported in Rodriguez-Morales et al. (2020) meta-analysis. However, we only included baseline data of SARS-CoV-2-positive patients at the time of hospitalisation in the pooled estimates and we considered articles from America and Europe, which Rodriguez-Morales et al. (2020) did not include. Further studies should clearly define the characteristic of SARS-CoV-2 cough (e.g. dry or wet) and whether it is more prevalent in mild or severe cases, older patients or associated to particular comorbidities. In Struyf et al work (2020), fever higher than 37.8° Celsius is one of the symptoms that increased the probability

of a SARS-CoV-2-positive diagnosis when present. However, in our review we found out then only 38.9% (95%CI 25.65;54.14) of the total sample had a temperature higher than 38° Celsius, and the temperature rate was only reported by six studies while its threshold by even fewer. Indeed, while diagnostic symptoms are commonly reported in the articles, diagnostic signs are often not stated, and this is an important evidence gap. Mean temperature, respiratory rate, heart rate and blood pressure were only reported by 4 included studies, and more evidences are needed to fully define SARS-CoV-2-positive patients. Further research should improve the reporting of SARS-CoV-2-positive patient signs at the time of hospitalisation and investigate whether mean age or disease severity (e.g. mild or severe patients) changes the prevalence or the mean value of diagnostic signs and reported symptoms. As previously suggested by Rodriguez-Morales et al. (2020), we confirm that even if diarrhoea is still a commonly reported gastrointestinal symptom of SARS-CoV-2-positive patients at the time of hospitalisation, it has a pretty low pooled prevalence. Instead, anorexia which is another uncommonly reported symptom showed a pooled prevalence almost as high as myalgia and higher than headache, both of which are considered to be possible red flags for a SARS-CoV-2-positive diagnosis (Struyf et al., 2020). SARS-CoV-2 diagnostic features are still unclear and may be slightly different in different populations. Further studies should improve the completeness and clearness of their reported symptoms, stating clear definitions of them in the methods sessions and reporting even unusual symptoms such loss of taste or smell or anorexia. Moreover, further studies need to assess multiple variable for their possible confounding effect on the summary estimates such as respiratory pathogens (seasonality), time since infection, disease severity or age.

The WHO firstly called SARS-CoV-2 a 'novel coronavirus-infected pneumonia', since many image characteristics at first appeared to be consistent with viral pneumonia. The use of CT as a primary screening tool is discouraged, since it has a very low specificity (Kim et al., 2020). However, in resource-constrained environments, imaging is still indicated for triage of patient with suspected SARS-CoV-2 and we chose to report the main commonly reported image characteristic or lesion regions provided by the included studies in this rapid review. GGO (38.25%) and 'generic' patchy shadows (58.34%) are the most prevalent images characteristics in CT of positive SARS-CoV-2 patients at the time of hospitalisation, and our findings are consistent with Bao et al. (2020) meta-analysis. However, in our meta-analysis consolidation has a consistently lower pooled proportion than the one stated by Bao et al. (2020), and this could be probably due to the overall low reporting accuracy of the included articles. Most of the included articles were not accurate in the reporting of CT findings, providing more a generic description rather than a clear definition, especially the ones recently published or issued in America (Table 3). Bilateral lung is the prevalent lesion distribution region with a pooled estimate of 65.22% (95%CI 49.45;77.62), while we chose not to estimate peripheral distribution since it was only stated in 3 included articles. Future studies should deepen the relationship between clinical features and CT scan image characteristics of the SARS-CoV-2 patients at the time of hospitalisation to speed up the diagnostic process.

The predominantly altered laboratory findings are lymphocytes, prothrombin time, LDH, inflammatory markers and the indices of liver function (Table 2). Instead, the indices of kidney function are not frequently reported as altered in SARS-CoV-2-positive patients at the time of hospitalisation. Lymphopenia is present in 50% of the SARS-CoV-2-positive patients across 10 studies with an overall sample of 2918 patients, and this finding suggests SARS-CoV-2 affects lymphocytes with a higher prevalence than that implied in a Rodriguez-Morales et al. (2020) meta-analysis. Previous studies suggested that inflammatory markers can be strong predictors of the progression of SARS-CoV-2 infection (Kermalia et al., 2020; Zeng et al., 2020), and CRP is increased in nearly 50% of our sample at the time of hospitalisation. However, other inflammatory markers such interleukin or procalcitonin were not reported as altered in the included studies. Liver function values, such as ALT, AST and total bilirubin, are increased in at least the 15% of the overall samples. These results are coherent with other recent studies showing liver as the most frequently damaged organ outside the respiratory system (Samidoust et al., 2020; Xu et al., 2020). Future studies should investigate whether high liver function values in SARS-CoV-2 patients at the time of hospitalisation could help define a diagnosis of severe SARS-CoV-2. Both D-Dimer and LDH were significantly increased in SARS-CoV-2 patients at the time of hospitalisation, with the LDH pooled prevalence second only to the one of CRP (Table 2). Necrosis of the cell membrane and lung damage is a trigger of LDH secretion and previous studies found abnormal levels of LDH in ICU patients, suggesting that LDH could be a predictive biomarker of disease severity (Kermalia et al., 2020; Zeng et al., 2020). However, if the laboratory finding changes, given different stages of illness, comorbidities or age at the time of hospitalisation are still not stated in the included studies and should investigate it further. Moreover, often the laboratory findings were reported in the included studies without a threshold reference or not in the adequate international unit of measure.

Limits of the review are due to the type and quality of the included articles, which are often case series. Even if updated, our review still includes few articles issued in Europe or America compared to those issued in China, and this could have led to an overestimation or an underestimation of some SARS-CoV-2 diagnostic features at the time of hospitalisation. Moreover, only articles in English or Chinese were included and this could have led to the loss of some meaningful articles. More detailed patient information, particularly regarding diagnostic signs, comorbidities and possible confounding variables are needed.

6 | CONCLUSION

This review provides an up-to-date synthesis of main diagnostic features of SARS-CoV-2-positive patients at the time of hospitalisation. The prevalence of obesity in SARS-CoV-2-hospitalised patients

and its implications should be investigated further. Future research should improve the completeness and clearness of their reported SARS-CoV-2 patients' signs and symptoms, reporting their characteristic signs at the time of hospitalisation and unusual symptoms such loss of taste or smell or anorexia. Moreover, future research should investigate whether abnormal laboratory findings such as lymphopenia, increased inflammatory markers and higher liver function values, could be associated with disease severity. Additionally, more studies from European and American Countries are needed to provide more comprehensive and generalisable results.

7 | RELEVANCE TO CLINICAL PRACTICE

As the number of reported COVID-19 cases keeps rising globally, especially in the United States, nurses and clinicians' knowledge of the disease is also gradually increasing thanks to ongoing research and clinical practice experience. Our findings could provide guidance for nurses and clinicians to early identification of positive patients at the time of the hospitalisation through a complete updated definition of main clinical features, laboratory and CT findings.

ACKNOWLEDGEMENTS

We thank Miss Annalisa Dorbolò and Dr Barbara Pala for the advices.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of these articles.

AUTHOR CONTRIBUTIONS

GA, DC and MLR involved in conceptualization. GD, MZ, FD and AC involved in data curation. AC, GA, MLR and DC involved in formal analysis. AG, DC, AC, FD and MLR involved in investigation. MLR, GA, DC, GD and AC involved in methodology. MLR, GA, DC and FD involved in project administration. GA, MLR and GD involved in supervision. GA, DC, AC, MZ, MLR and MZ involved in visualization. GA, DC, MLR and FD wrote the original draft. MLR, GA, GD and MZ involved in writing, reviewing and editing.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

How to cite this article: Anderson G, Casasanta D, Cocchieri A, et al. **Diagnostic features of sars-covid-2-positive patients: a rapid review and meta-analysis.** *J Clin Nurs*. 2021;30:1826–1837. https://doi.org/10.1111/jocn.15688