Article published online: 2022-07-14

Original Article

Hematologic, Biochemical, and Infection Biomarker Abnormalities Associated with COVID-19: A Systematic Review and Meta-Analysis

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Abstract

Objectives: We aimed to analyze the laboratory data of coronavirus disease 2019 (COVID-19) patients for clinical help, to overcome the vulnerabilities of reverse transcription–polymerase chain reaction testing for diagnosing COVID-19, and to reduce the number of negative results when diagnosing, particularly in global regions which are recognized to have limited resources. **Materials and Methods:** Following Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, the authors performed a systematic literature review, using three databases to assess laboratory data of COVID-19-confirmed cases, and the articles that described significant laboratory irregularities were ultimately chosen. Crosschecking was performed on the references of these articles in order to identify further studies. The statistical software R version 3.6.1 was used for meta-analysis of COVID-19 studies. **Results:** A total of 13 relevant articles were included. They yielded a total of 2662 individuals who tested positive for COVID-19. The analysis results demonstrated that male patients comprised a more substantial proportion, accounting for 57.9% of the total. The principal laboratory findings of the COVID-19 patients indicated that they commonly had lymphocytopenia 0.943 (confidence interval [CI]: 0.857–1.03), high D-dimer 0.459 (CI: 0.237–0.6808), high procalcitonin 0.089 (CI: 0.066–0.111), high C-reactive protein 17.203 (CI: 6.520–27.886), and high lactate dehydrogenase 278.265 (CI: 238.995–317.535). **Conclusions:** Infection with COVID-19 is associated with significant laboratory irregularities. The increased focus must be applied to laboratory parameters to quickly identify a large number of infected patients and asymptomatic carriers, prevent virus transmission, and assure timely treatment of patients, particularly in regions characterized by limited resources.

Keywords: A systematic review, coronavirus disease 2019, laboratory findings

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Submitted: 06-May-2020 **Revised:** 23-Jul-2020
Accepted: 30-Jul-2020 **Published:** 26-Sep-2020

Access this article online

Quick Response Code:

Website: www.ijmbs.org

DOI: 10.4103/ijmbs.ijmbs_47_20

How to cite this article: Abdulla SA, Elamami AH, Elawamy H, Muhammed AA. Hematologic, biochemical, and infection biomarker abnormalities associated with COVID-19: A systematic review and meta-analysis. Ibnosina J Med Biomed Sci 2020;12:185-94.

Introduction

An episode of a group of pneumonia instances of unknown etiology that began in Wuhan, China, has continued since December 2019. The pandemic proven to cause a tsunami inclinical practice, education and research.[1] Clinically, the disease is characterized by fever, dry cough, fatigue, and dyspnea. Upper respiratory tract manifestations are not distinguished, but diarrhea was accounted for by some patients. Pulmonary imaging has demonstrated multiple ground glass and infiltrative shadows in both lungs. Some cases have progressed to develop acute respiratory distress syndrome and sepsis.

On January 7, 2020, scientists successfully isolated the pathogen that causes pneumonia, a new type of β-coronavirus.[2] Subsequently, the WHO named it (coronavirus disease 2019 [COVID-19]) coronavirus disease. An epidemiological survey demonstrated that the first appearance of COVID-19 patients tightly concerned with a seafood market in the south of China. Due to the "Spring Festival Movement" (known as the "yearly migration of the populace in China"), COVID-19 quickly spread through the nation, and the number of tainted individuals slowly expanded. COVID-19 was spread among individuals who have been confirmed to take place through multiple channels, such as aerosols, mouth mucus membranes, droplets, and feces.[2]

As a result of meta-analysis, it has been determined that real-time reverse transcription–polymerase chain reaction (RT-PCR) has increased effectiveness in the diagnosis of novel coronavirus compared to smear-dyeing inspection, and culture identification is now considered the first option for diagnosing coronavirus infections.[3] However, recent data have indicated that RT-PCR tests' diagnostic precision for the detection of COVID-19 could be less than optimal. For example, the findings of computed tomography (CT) generated negative RT-PCR results from samples taken from throat swabs. The ramifications of a false-negative diagnosis can be very serious, particularly during this phase of the pandemic. This would enable the infection to spread further through infected individuals, which would be detrimental to the activities aimed at containing the spread of the virus.

On March 24, 2020, Libya reported the first infected COVID-19, who exhibited symptoms of a dry cough, elevated temperature, and dyspnea and had previously traveled to Saudi Arabia via Tunisia. The diagnosis was made using real-time PCR and a clear image produced by a CT scan. As of April 6, 2020, 18 cases of COVID-19 were reported in Libya, confirmed using throat swab samples by real-time RT-PCR. We conducted this study in order to focus on laboratory parameters, to quickly identify a significant number of infected patients and asymptomatic carriers to prevent virus transmission and assure timely treatment of patients, to overcome the vulnerabilities of RT-PCR testing for diagnosing COVID-19, and to reduce the number of false negatives when diagnosing.

Materials and Methods

Literature search and selection

A literature search was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses process. The Medline (PubMed interface), Scopus, and Web of Science databases were searched electronically utilizing the keywords "COVID-19" or "2019-nCoV" with no date (i.e., until April 6, 2020). The authors examined the titles, abstracts, and full text (where applicable) for each of the articles returned based on the search criteria above, and the articles that described major laboratory irregularities for individuals diagnosed with severe COVID-19 infections were ultimately chosen. Crosschecking was performed on the references of these articles in order to identify further studies.

Research selection and quality assessment

All articles were tested for their eligibility with strict inclusion criteria. These stipulated that the article should (a) collect patients with confirmed COVID-19 disease by RT-PCR, (b) have full text available, the patients' number should be more than 10, and (c) have mentioned most of the laboratory data quantitatively not qualitatively. Furthermore, the characteristics and demographic information of the patients included in the studies were as follows:

the year, country, amount of patients, median age, and sex.

Statistical analysis

Microsoft Excel database was used to record all available laboratory data. The R statistical software (version 3.6.1) Research Computing Center, The University of Chicago, Chicago IL, USA) was used for meta-analysis of COVID-19 studies. We first unified all units of variables and, then, expressed classified variables as percentages and expressed continuous variables as median and interquartile range (IQR). Most of the used studies had skewed data. Therefore, median and IQR were used as parameters to avoid disordering data. The pooled median and 95% confidence interval [CI] were calculated using a random-effects model.

Results

Sources

A total of 800 articles were retrieved. After deleting duplicates, 400 studies remained, of which 290 were excluded based on the title or abstract and 43 were eliminated after reading the full text. Finally, 48 case study and 6 descriptive analyses were eliminated after reading the full text. A total of 2662 patients from 13 studies were included in this systematic review [Figure 1].[1,4-15]

Demographical characteristics

The analysis results demonstrated that a more substantial proportion of male patients were diagnosed with COVID-19, accounting for 57.9% of the overall total, while females (42.1%). The mean age across all the studies was 50.9 years. The age range was reported in 11 studies. Most of the patients were above 20 years, and the maximum age was 95 years. A single study reported a 1-year-old patient [Table 1].

Hematological parameters

Hematological parameters in confirmed patients of COVID19 showed a mean (median) of leukocyte count, neutrophil count), Lymphocyte count, platelet count and hemoglobin level [5.2 (2.98-10.5) × 10^9/L, 3.5 (1.62- 8.1) × 10^9/L, 0.85 (0.6-1.46)× 10^9/L, 138.4 (123-284)10^9/L, 115.7 (118- 152) g/L] alternatively [Table 2]. "APTT" was reported in only (4/13) studies, with a mean (median) of 28.4 (24.2–34.1)s. "PT" was reported in 6/13 studies and its mean for total 11.7 (10.1- 13.7)s However, D-dimer was reported in seven studies mean (median) 0.46 (0.1- 3.2) µg/L [Table 3].

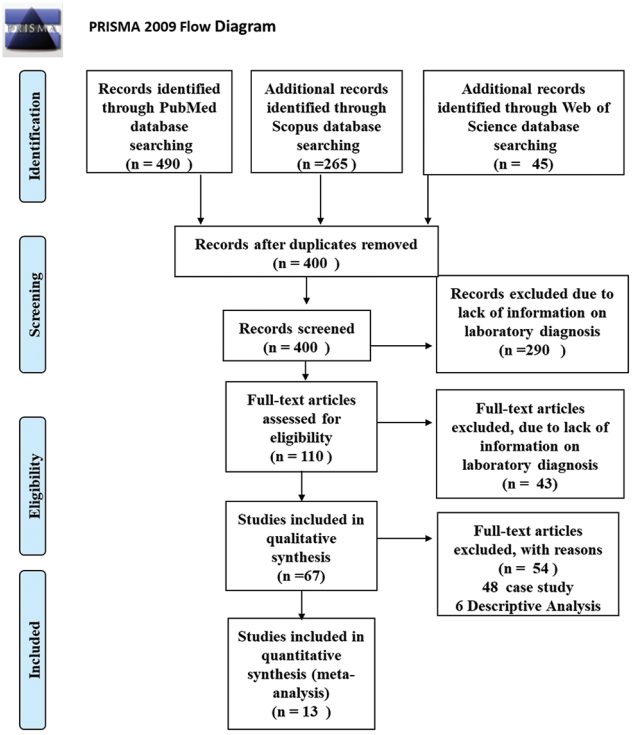

Figure 1: Flow diagram of the study selection process for the systemic review

Infection-related biomarkers

Of note, many studies did not report the infection-related biomarkers. For instance, interleukin-6 (IL-6), "erythrocyte sedimentation rate (ESR)," and serum ferritin were reported clearly in one study each and were slightly high (IL-6 = 7.9 pg/mL, normal range: 0.0–7; ESR = 49.9 mm/h, normal range: 0.0–15; and serum ferritin – mean: 722 ng/m, normal range: 21.0–274.7), whereas procalcitonin was reported in 10 studies, seven of which the mean (median) was 0.08(0.03-0.16) ng/mL. C-reactive protein (CRP) was reported and significantly high in seven studies, with an overall mean of 30.9 mg/L (normal range, 0.0–5) [Table 4].

Biochemical parameters

The liver function tests during infection with COVID-19 were reported in many studies, and the overall mean for alanine aminotransferase, aspartate aminotransferase (AST), albumin, and

Table 1: The demographic characteristics of the included studies

Authors	Cases*	Female (%)	Male (%)	Age**	References
Huang *et al*., 2020	41	11 (27)	30 (73)	49 (41-58)	[1]
Chen *et al*., 2020	99	32 (32)	67 (68)	51.5 (21-82)	[4]
Zhang *et al*., 2020	140	69 (49.3)	71 (50.7)	56 (25-87)	[5]
Zhou *et al*., 2020	191	72 (38)	119 (62)	56 (46-67)	[6]
Wan *et al*., 2020	135	63 (46.7)	72 (53.3)	47 (36-55)	[7]
Wang *et al*., 2020	69	37 (54)	32 (46)	42 (35-62)	[8]
Wang *et al*., 2020	138	63 (45.7)	75 (54.3)	56 (42-68)	[9]
Cao *et al*., 2020	199	79 (39.7)	120 (60.3)	58 (49-68)	[10]
Liu *et al*., 2020	61	30 (49.2)	31 (50.8)	40 (1-86)	[11]
Guan *et al*., 2020	1099	459 (41.9)	640 (58.1)	47 (35-58)	[12]
Shi *et al*., 2020	416	211 (50.7)	205 (49.3)	64 (21-95)	[13]
Xu *et al*., 2020	62	27 (44)	35 (33)	41(N/R)***	[14]
Liu *et al*., 2020	12	4 (33)	8 (66.7)	54 (N/R)***	[15]

*All cases reported from China, **Mean (range), ***N/R: Not clearly reported

Table 2: The hematological parameters of the included studies

Authors	Variables and reference range					References
	Leukocytes	Neutrophils	Lymphocytes	Platelets	Hemoglobin	
	3.5-9.5 $\times 10^9$/L	1.8-6.3 $\times 10^9$/L	1.1-3.2 $\times 10^9$/L	125-350 $\times 10^9$/L	130-175 g/L	
Huang *et al*., 2020	6.2 (4.1-10.5)	5.0 (3.3-8.9)	0.8 (0.6-1.1)	164.5 (131.5-263)	126 (118-140)	[1]
Chen *et al*., 2020	7.5 (3.6)	5.0 (3.3-8.1)	0.9 (0.5)	213.5 (79.1)	129.8	[4]
Zhang *et al*., 2020	4.7 (3.7-6.7)	N/R	0.8 (0.6-1.1)	N/R	N/R	[5]
Zhou *et al*., 2020	6.2 (4.5-9.5	N/R	1.0 (0.6-1.3)	206 (155-262)	128 (119-140)	[6]
Wan *et al*., 2020	5.4 (4.1-7.8)	3.5 (2.6-4.4)	1.1 (0.7-1.5)	158 (131-230)	133 (122-147)	[7]
Wang *et al*., 2019	3.82 (2.98-5.57)	2.35 (1.62-3.67)	1.15 (0.82-1.46)	171 (142-211)	130 (118-140)	[8]
Wang *et al*., 2020	4.5 (3.3-6.2)	3.0 (2.0-4.9)	0.8 (0.6-1.1)	163 (123-191)	N/R	[9]
Cao *et al*., 2020	7.0 (5.1-9.4)	N/R	0.9 (0.6-1.2)	207.0 (158-284)	N/R	[10]
Liu *et al*., 2020	4.3 (3.5-5.1)	2.5 (2.1-3.5)	1.0 (0.8-1.4)	164 (135-219.5)	138 (127-150)	[11]
Guan *et al*., 2020	4.7 (3.5-6.0)	N/R	1.0	0.168	134 (119-148)	[12]
Shi *et al*., 2020	5.8 (4.3-8.3)	N/R	0.9	207 (153-265)	124	[13]
Xu *et al*., 2020	4.7 (3.5-5.8)	2.9 (2.0-3.7)	1.0 (0.8-1.5)	176.0 (135.8-215.5)	137 (129-152)	[14]
Liu *et al*., 2020	5.9	4.05	1.3	164	N/R	[15]

N/R: Not clearly reported

Table 3: The coagulation tests of the included studies

Authors	Variables and normal range			References
	APTT	PT	D-dimer	
	21-37 s	10.5-13.5 s	0.0-1.5 μg/L	
Huang *et al*., 2020	27 (24.2-34.1)	11.1 (10.1-12.4)	0.5 (0.3-1.3)	[1]
Chen *et al*., 2020	27.3 (10.2)	11.3 (1.9)	0.9 (0.5-2.8)	[4]
Zhang *et al*., 2020	N/R	N/R	0.2 (0.1-0.5)	[5]
Zhou *et al*., 2020	N/R	11.6 (10.6-13.0)	0.8 (0.4-3.2)	[6]
Wan *et al*., 2020	26.9 (24.7-29)	10.9 (10.5-11.4)	0.4 (0.2-0.6)	[7]
Wang *et al*., 2019	N/R	N/R	N/R	[8]
Wang *et al*., 2020	31.4 (29.4-33.5)	13.0 (12.3-13.7)	0.203 (0.121-0.403)	[9]
Cao *et al*., 2020	N/R	N/R	N/R	[10]
Liu *et al*., 2020	N/R	12.0 (11.1-13.1)	N/R	[11]
Guan *et al*., 2020	N/R	N/R	0.26	[12]
Shi *et al*., 2020	N/R	N/R	N/R	[13]
Xu *et al*., 2020	N/R	N/R	0.2 (0.2-0.5)	[14]
Liu *et al*., 2020	N/R	N/R	N/R	[15]

APTT: Activated partial thromboplastin time, PT: Prothrombin time

total bilirubin was 27.6 U/L, 31.3 U/L, 36.7 g/L, and 10.8 μmol/L, respectively. These results show that the most affected parameter during infection with COVID-19 was reduced albumin level, whereas liver enzymes were mostly normal or marginally raised [Table 5]. Notably, in most studies, serum creatinine was measured and reported more than blood urea nitrogen. The overall mean for both indices was normal (70.8 μmol/L, 5 mmol/L). Serum glucose was mentioned in only two studies and was normal [Table 5]. The overall mean for the other parameters during infection with COVID-19 was higher for lactate dehydrogenase (LDH) (264.6 U/L) and normal creatine kinase (CK) (86.4 U/L), while myoglobin was reported in only two studies and was normal [Table 6].

Meta-analysis results

Lymphopenia 0.943 (CI: 0.857–1.03), high D-dimer 0.459 (CI: 0.237–0.6808), high procalcitonin 0.089 (CI: 0.066–0.111), high CRP 17.2 (CI: 6.5–27.9), and high LDH 278 (CI: 239–318) were the most prevalent laboratory results [Table 7 and Figures 2-6].

Discussion

Based on recently published data, numerous RT-PCR tests' diagnostic precision could be less than optimal. The ramifications of false-negative diagnoses can be severe, particularly during this phase of the pandemic, as they would enable the infection to spread via infected patients, thus hindering the activities aimed at containing the virus spread.

Recently published research revealed that significant laboratory irregularities were detected in the blood tests of patients diagnosed with COVID-19. This study showed that COVID-19 is more common in males accounting for 56.5% of the overall number. Other researchers have shown that more males were infected by MERS-CoV and SARS-CoV compared to females.[16,17] The fact that females are less susceptible to viral infections could be due to the protection afforded by X chromosome and sex hormones, which are critical factors in innate and adaptive immunity.[17] However, males should ensure that they focus more on taking suitable precautions. Further studies are required to determine the specific factors behind this.

This review also showed that most of the affected patients were above the age of 20, and very rarely, children are clinically affected by the virus. The cause behind this is still obscured. However, maybe the immune system is still not developed well, and so they are less likely to have cytokine storm, which is one of the main pathophysiological mechanisms proposed for the damage caused by COVID-19 infection.

Laboratory findings indicate that frequent observations included lymphocytopenia, a rise in LDH, and leukocytopenia. In general, these factors all corresponded with a respiratory virus infection. Lymphocytopenia could be utilized as

Table 4: The markers of infection measured in coronavirus disease 2019 patients in the included studies

Author	Biomarkers and reference range					References
	IL-6	ESR	Procalcitonin	CRP	Serum ferritin	
	0.0-7 (pg/mL)	0.0-15 (mm/h)	0.0-5 (ng/mL)	0.0-5 (mg/L)	21-274.7 (ng/mL)	
Huang *et al*., 2020	N/R	N/R	0.1 (0.1-0.1)	N/R	N/R	[1]
Chen *et al*., 2020	7.9 (6.1-10.6)	49.9 (23.4)	N/R	N/R	N/R	[4]
Zhang *et al*., 2020	N/R	N/R	0.07 (0.04-0.1)	34.2 (12.5-67.4)	N/R	[5]
Zhou *et al*., 2020	N/R	N/R	0.1 (0.1-0.1)	N/R	722 (377-1435)	[6]
Wan *et al*., 2020	N/R	N/R	0.11 (0.08-0.16)	10.5 (2.7-51.2)	N/R	[7]
Wang *et al*., 2019	N/R	N/R	0.13 (0.13-0.15)	13.2 (6.8-49.0)	N/R	[8]
Wang *et al*., 2020	N/R	N/R	49 (35.5)	N/R	N/R	[9]
Cao *et al*., 2020	N/R	N/R	N/R	N/R	N/R	[10]
Liu *et al*., 2020	N/R	N/R	N/R	12.0 (3.7-27.8)	N/R	[11]
Guan *et al*., 2020	N/R	N/R	5.5	60.7	N/R	[12]
Shi *et al*., 2020	N/R	N/R	0.07 (0.04-0.15)	45	N/R	[13]
Xu *et al*., 2020	N/R	N/R	0.04 (0.03-0.06)	41.1	N/R	[14]
Liu *et al*., 2020	N/R	N/R	1.08	N/R	N/R	[15]

N/R: Not clearly reported, IL-6: Interleukin-6, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein

Table 5: The blood biochemistry parameters (liver function test, renal function test, and glucose) of the included studies

Author	Albumin (g/L; normal range, 40-55)	ALT (U/L; normal range, 9.0-50.0)	AST (U/L; normal range, 15.0-40.0)	Total bilirubin (μmol/L; normal range, 0.0-21.0)	BUN (mmol/L; normal range, 3.6-9.5)	Serum creatinine (μmol/L; normal range, 57.0-111.0)	Glucose	Reference
Huang *et al*., 2020	31.4 (28.9-36)	32 (21-50)	34.0 (26.0-48)	11.7 (9.5-13.9)	N/R	74.2 (57.5-85.7)	N/R	[1]
Chen *et al*., 2020	31.6 (4.0)	39.0 (22.0-53.0)	34.0 (26.0-48)	15.1 (7.3)	5.9 (2.6)	75.6 (25.0)	7.4 (3.4)	[4]
Zhang *et al*., 2020	N/R	N/R	N/R	N/R	N/R	N/R	N/R	[5]
Zhou *et al*., 2020	32.3 (29.1-35.8)	30 (17-46)	N/R	N/R	N/R	>133	N/R	[6]
Wan *et al*., 2020	40.5 (37-43.4)	26 (12.9-33.15)	33.4 (27.8-43.7)	8.6 (5.9-13.7)	N/R	66 (57.8-74.5)	N/R	[7]
Wang *et al*., 2019	N/R	25 (17-40)	28.0 (22-42)	N/R	N/R	66.35 (58-79.65)	N/R	[8]
Wang *et al*., 2020	N/R	24 (16-40)	31 (24-51)	9.8 (8.4-14.1)	4.4 (3.4-5.8)	72 (60-87)	N/R	[9]
Cao *et al*., 2020	N/R	33.0 (22-55)	34.0 (26-45)	N/R	N/R	69.5 (57.2-82.5)	N/R	[10]
Liu *et al*., 2020	44 (40.5-47)	19.0 (14-33.5)	N/R	N/R	4.3 (3.5-5.6)	60 (47-69.5)	6.1 (5.5-6.9)	[11]
Guan *et al*., 2020	N/R	21.3	22.2	10.5	N/R	1.6	N/R	[12]
Shi *et al*., 2020	36	28 (18-46)	30 (22-43)	N/R	N/R	59.2 (48.6-71.6)	N/R	[13]
Xu *et al*., 2020	N/R	22 (14-34)	26 (20-32)	N/R	N/R	72.0 (61-84)	N/R	[14]
Liu *et al*., 2020	40.9	31.6	40.02	8.9	5.4	85.56	N/R	[15]

N/R: Not clearly reported, BUN: Blood urea nitrogen, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase

Table 6: The blood biochemistry parameters of muscle markers (creatine kinase, lactate dehydrogenase, and myoglobin) of the included studies

Author	CK (U/L; normal range, 50.0-310.0)	LDH (U/L; normal range, 120.0-250.0)	Myoglobin (ng/mL; normal range, 0.0-146.9)	References
Huang *et al*., 2020	132.5 (62.0-219.0)	28 (242-408)	N/R	[1]
Chen *et al*., 2020	85 (51-184)	336 (260-447)	49.5 (32.2-99.8)	[4]
Zhang *et al*., 2020	72.5 (52.2-115)	N/R	N/R	[5]
Zhou *et al*., 2020	21.5 (13-72.4)	300	N/R	[6]
Wan *et al*., 2020	82.2 (56.3-146.3)	320.5 (248.5-385.3)	N/R	[7]
Wang *et al*., 2019	N/R	224 (183-291)	N/R	[8]
Wang *et al*., 2020	92 (56-130)	261 (182-403)	N/R	[9]
Cao *et al*., 2020	69 (44-115)	325 (245-433)	N/R	[10]
Liu *et al*., 2020	93 (57-137)	N/R	N/R	[11]
Guan *et al*., 2020	13.7	41	N/R	[12]
Shi *et al*., 2020	N/R	N/R	N/R	[13]
Xu *et al*., 2020	69 (40.5-101)	205 (184-260.5)	N/R	[14]
Liu *et al*., 2020	219.6	605.3	67.87	[15]

N/R: Not clearly reported, CK: Creatine kinase, LDH: Lactate dehydrogenase

a reference index for diagnosing patients with coronavirus infections in the clinic. Data indicated that the number of inflammatory cytokines could be associated with disease severity,[1] which is therefore anticipated to signal the severity of the disease. Higher D-dimer concentration indicates the presence of a hypercoagulable state and secondary hyperfibrinolysis *in vivo*.

Increased levels of CRP, ferritin, IL-6, and LDH are also reflective of the severity of the infection, which is linked to increased intensity and duration of the treatment, including glucocorticoids, human immunoglobulin, more powerful antibiotics, high-flow oxygen therapy, and mechanical ventilation. Liu *et al*. demonstrated a significant decrease in CRP, ferritin, IL-6, and LDH after recovery.[18] In association with disease progression, IL-6 increased to a further degree, suggesting that IL-6 might be a valuable candidate for monitoring severe type COVID-19.[18] Higher leukocyte count and procalcitonin may also be due to secondary bacterial infection, whereby serum procalcitonin levels are typically normal in patients with viral infections (or viral sepsis). The measurement of other innovative sepsis biomarkers, for example, presepsin, for instance, would likely assistance in expanding the exactness in the finding of COVID-19 severe cases, just as for improving the present methodology utilized for mortality risk prediction.[19]

Extra caution should be taken in patients with high serum CK, which may be caused by direct effect of the virus or indirect effect of hypoxia.[19] Procalcitonin and coagulation tests deserve a special mention. Li *et al*. developed a rapid COVID-19 IgG–IgM combined antibody test utilizing lateral flow immune assay techniques. Results take <15 min to be available and determine whether there are recent COVID-19 infections. This test cannot affirm virus presence, only provides evidence of recent infection, but it provides essential immunological evidence for physicians to make the correct diagnosis along with other tests and to start treatment of patients.[20] Concerning prognostic laboratory data, which may be even more vital for the timely identification of patients at more significant risk of adverse outcomes,

Table 7: Meta-analysis results of the incidence of laboratory tests

Variable	n^a	Estimate	95% CI	n^b	SEM	*P*	t^2	*Q*	P^c	I^2 (%)
Leukocytes	11	5.158	4.58-5.73	2551	0.292	<0.0001	0.839	135.42	<0.0001	95.15
Neutrophils	7	3.339	2.60-4.07	605	0.376	<0.0001	0.875	56.54	<0.0001	94.69
Lymphocytes	9	0.943	0.857-1.03	1036	0.044	<0.0001	0.0139	44.78	<0.0001	83.38
Platelets	9	180.69	166.47-194.91	1312	7.256	<0.0001	393.906	74.71	<0.0001	87.61
Hemoglobin	7	132.279	129.24-135.32	1658	1.549	<0.0001	11.939	25.32	0.0003	78.45
APTT	3	28.555	25.51-31.60	314	1.555	<0.0001	6.584	93.12	<0.0001	96.95
PT	5	11.73	10.98-12.48	566	0.382	<0.0001	0.690	258.40	<0.0001	97.25
D-dimer	6	0.459	0.237-0.6808	668	0.113	<0.0001	0.0655	51.17	<0.0001	96.42
Procalcitonin	7	0.089	0.066-0.111	1054	0.0114	<0.0001	0.0009	544.27	<0.0001	99.92
CRP	4	17.203	6.520-27.886	405	5.451	0.0016	107.134	25.59	<0.0001	90.95
Albumin	4	37.063	31.017-43.109	428	3.084	<0.0001	37.537	267.50	<0.0001	98.97
ALT	10	27.585	24.089-31.081	1411	1.784	<0.0001	26.445	49.87	<0.0001	86.44
AST	8	31.182	28.966-33.368	1159	1.131	<0.0001	7.064	27.794	0.0002	74.91
Total bilirubin	3	10.020	8.298-11.743	314	0.879	<0.0001	1.988	12.477	0.0020	86.12
BUN	2	4.364	4.069-4.658	199	0.150	<0.0001	0	0.102	0.749	0
Serum creatinine	8	67.045	63.240-70.849	1121	1.941	<0.0001	24.822	63.524	<0.0001	87.61
CK	9	76.705	59.122-94.288	1066	8.971	<0.0001	25.371	199.987	<0.0001	94.53
LDH	7	278.265	238.995-317.535	743	20.036	<0.0001	2577.676	122.96	<0.0001	93.75

[a]Number of studies, [b]Number of patients, [c]Heterogeneity *P* value. SEM: Standard error of the mean, BUN: Blood urea nitrogen, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, PT: Prothrombin time, APPT: Activated partial thromboplastin time, CK: Creatine kinase; LDH: Lactate dehydrogenase, CRP: C-reactive protein, CI: Confidence interval

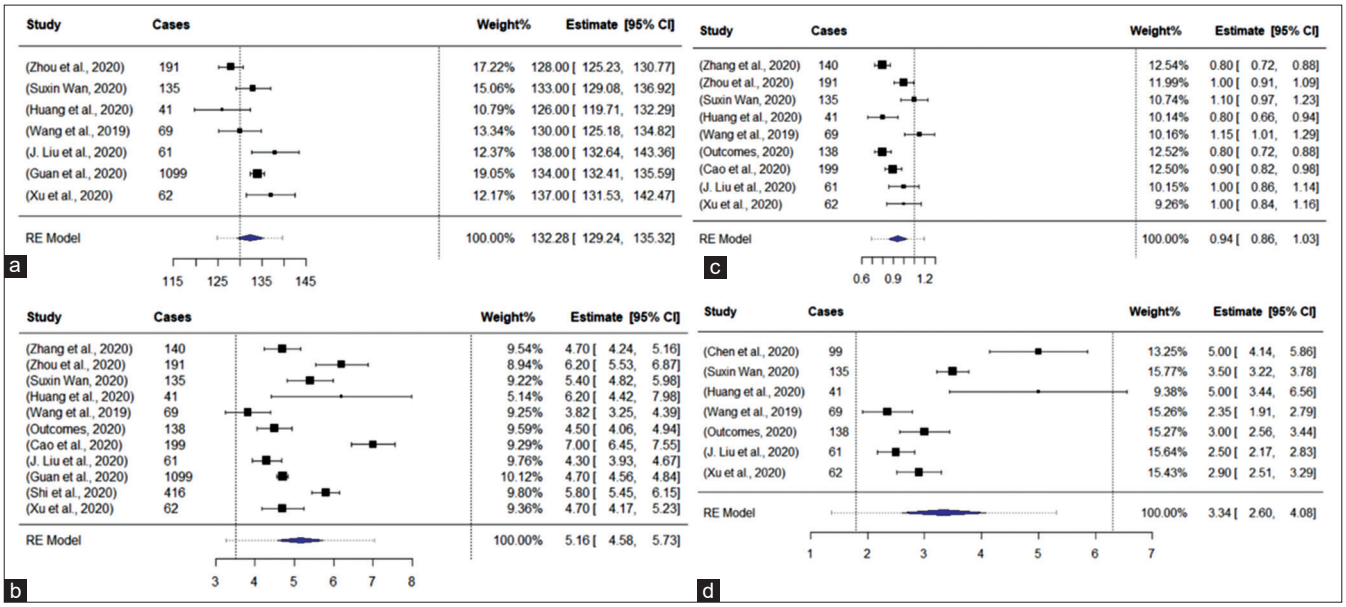

Figure 2: The forest plots of the incidence of basic hematological parameters: Hemoglobin (a), leukocytes (b), lymphocytes (c), and neutrophils (d). References are identical to those cited in Tables 1-6

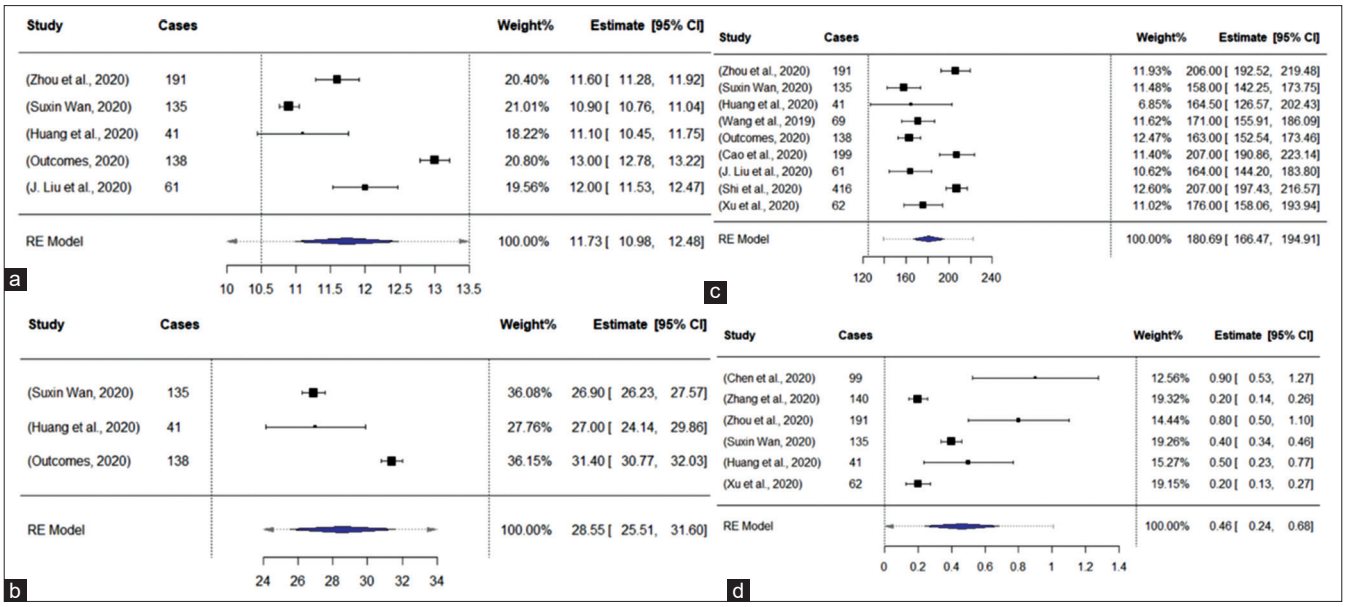

Figure 3: The forest plots of the incidence of thrombosis and hemostasis markers: (a) Prothrombin time, (b) activated partial thromboplastin time, platelet count (c), and D-dimer concentration (d). References are identical to those cited in Tables 1-6

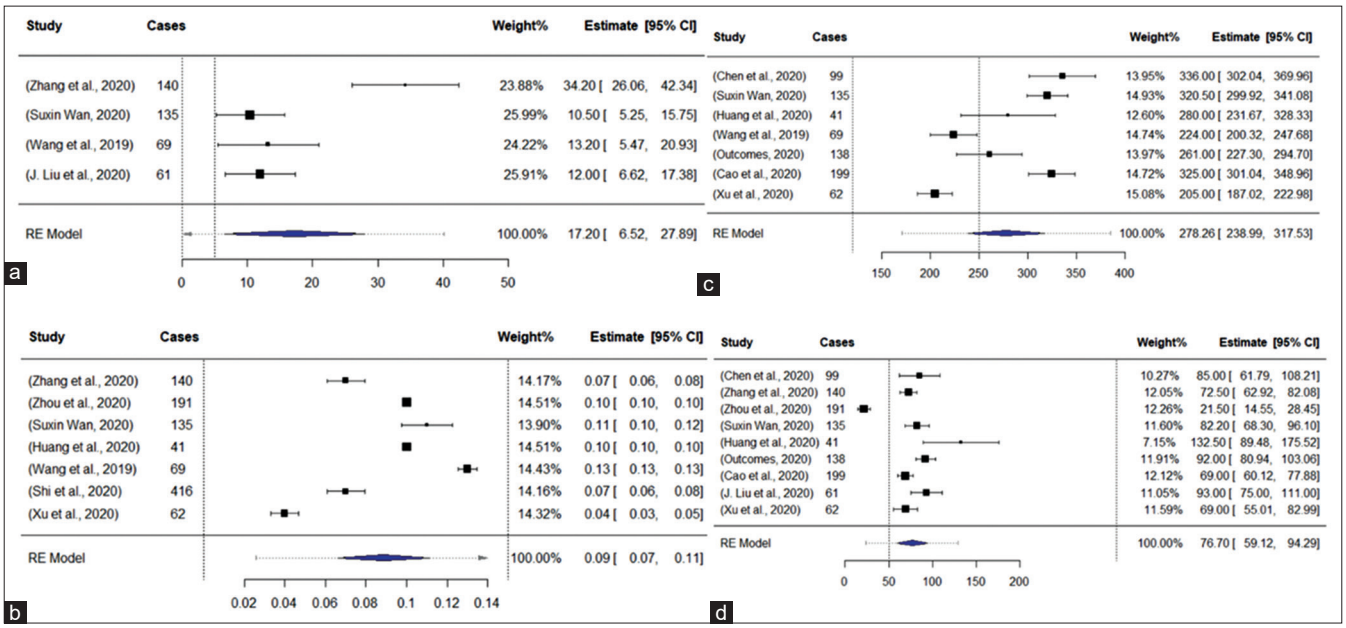

Figure 4: The forest plots of the incidence of inflammatory markers and other laboratory tests: C-reactive protein (a) procalcitonin (b), serum lactate dehydrogenase (c), and serum creatinine kinase (d). References are identical to those cited in Tables 1-6

a separate review will be published by our team nearly.

Conclusions

Infection with COVID-19 is associated with significant laboratory irregularities. Although the RT-PCR test has become the standard method for the diagnosis of COVID-19 infection, these real-time PCR test kits have many limitations. Since frequent significant laboratory irregularities were detected in the blood tests of patients diagnosed with COVID-19, an increased focus must be applied to laboratory parameters. This should enable quick identification of a large number of infected patients and asymptomatic carriers, to prevent virus transmission and assure timely treatment of patients, particularly in regions which are characterized by limited resources.

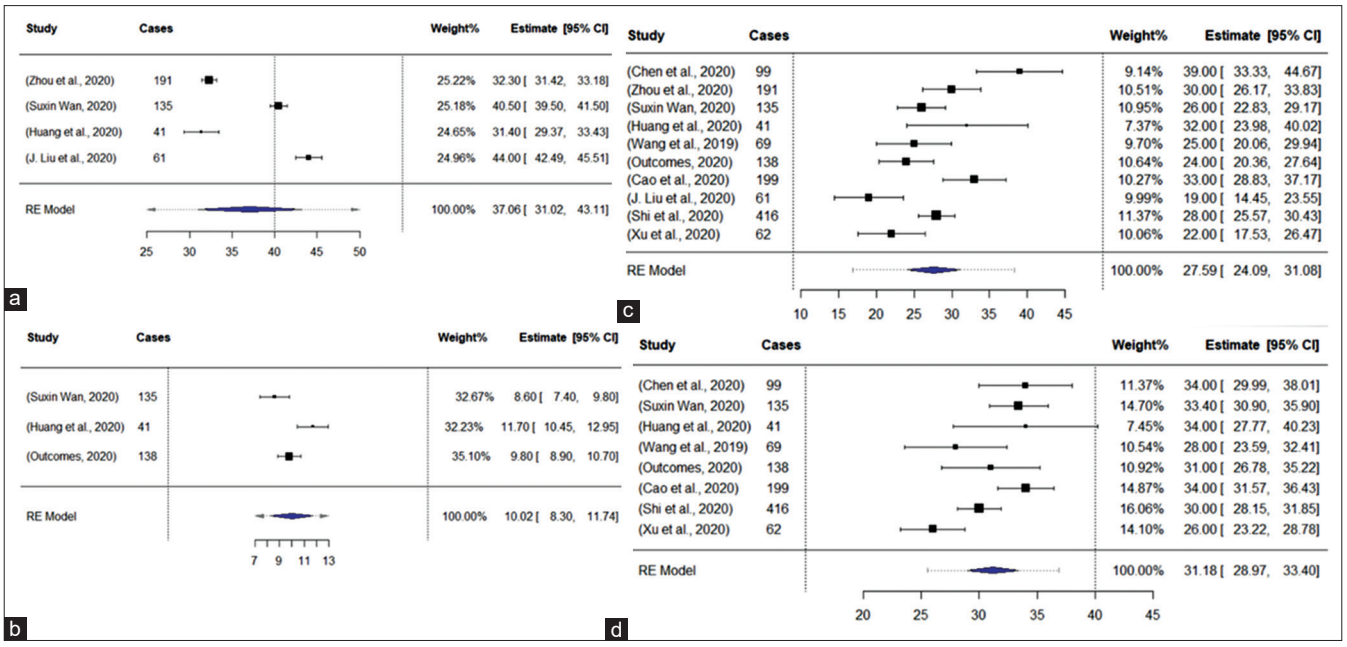

Figure 5: The forest plots of the incidence of laboratory hepatic function tests: Plasma albumin (a), serum total bilirubin (b), and the two transaminases: Alanine aminotransferase (c) and aspartate aminotransferase (d). References are identical to those cited in Tables 1-6

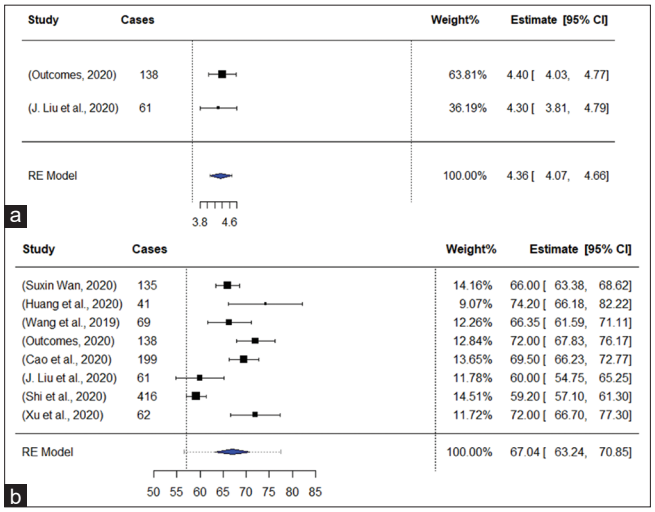

Figure 6: The forest plots of the incidence of laboratory tests of renal functions: Features: Blood urea nitrogen (a) and serum creatinine (b). References are identical to those cited in Tables 1-6

Acknowledgment

The authors are grateful to the support of Mr. Ahmed Miftah, Department of Civil Engineering, Cyprus International University, and all staff of the Department of Biochemistry, Faculty of Medicine, University of Benghazi, Benghazi, Libya.

Authors' contributions

SA, AE, and HE performed database research. HE reviewed the conflicts in the databases obtained by SA and AE. SA drafted the manuscript. SA and AE reviewed the manuscript critically for contents. AM reviewed the manuscript. All authors agree with the content of the manuscript and approved its final version.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Compliance with ethical principles

Not applicable. None of the authors reported human or animal studies of their own.

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