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# Acute kidney injury is associated with severe infection and fatality in patients with COVID-19: A systematic review and meta-analysis of 40 studies and 24,527 patients

Mengjiao Shao<sup>a,b,1</sup>, XiaoMei Li<sup>a,b,1</sup>, Fen Liu<sup>b</sup>, Ting Tian<sup>a,b</sup>, Junyi Luo<sup>a,b,\*</sup>, Yining Yang<sup>a,b,\*</sup>

<sup>a</sup> Department of Cardiology, The First Affiliated Hospital of Xinjiang Medical University, Urumqi, 830054, China

<sup>b</sup> Xinjiang Key Laboratory of Cardiovascular Disease Research, Clinical Medical Research Institute of First Affiliated Hospital of Xinjiang Medical University, Urumqi, China

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## ABSTRACT

Currently, coronavirus disease 2019 (COVID-19) is spreading rapidly around the world. This study aimed to investigate whether the presence of acute kidney injury (AKI) might increase the risk of severe infection and fatality in COVID-19 patients. We searched the PubMed, Web of Science, ScienceDirect, MedRxiv and COVID-19 academic research communication platforms for studies reporting severe infection rates and case-fatality rates in COVID-19 patients with and without AKI up to June 20, 2020. The main outcomes were the comparisons of the severe infection rates and fatality rates in COVID-19 patients with and without AKI and the estimation of the odds ratio (OR) and its 95 % confidence interval (CI) for severe infection and mortality. Statistical analyses were performed with R statistical software. A total of 40 studies involving 24,527 patients with COVID-19 were included in our meta-analysis. The incidence of AKI was 10 % (95 % CI 8%–13 %) in COVID-19 patients. The patients had higher severe infection and fatality rates (55.6 % vs. 17.7 % and 63.1 % vs. 12.9 %, respectively, all  $P < 0.01$ ) with COVID-19. AKI was a predictor of fatality (OR = 14.63, 95 % CI: 9.94–21.51,  $P < 0.00001$ ) and severe infection (OR = 8.11, 95 % CI: 5.01–13.13,  $P < 0.00001$ ) in patients with COVID-19. Higher levels of serum creatinine (Scr) and blood urea nitrogen (BUN) were associated with a significant increase in fatality [Scr: mean difference (MD): 20.19  $\mu\text{mol/L}$ , 95 % CI: 14.96–25.42,  $P < 0.001$ ; BUN: MD: 4.07 mmol/L, 95 % CI: 3.33–4.81,  $P < 0.001$ ] and severe infection (Scr: MD: 7.78  $\mu\text{mol/L}$ , 95 % CI: 4.43–11.14,  $P < 0.00001$ , BUN: MD: 2.12 mmol/L, 95 % CI: 1.74–2.50,  $P < 0.00001$ ) in COVID-19 patients.

In conclusion, AKI is associated with severe infection and higher fatality rates in patients with COVID-19. Clinicians should pay more attention to the monitoring and treatment of COVID-19 patients with AKI.

## 1. Introduction

Novel coronavirus disease 2019 (COVID-19), which emerged in Wuhan, China, in December 2019, has not only swept across China but also rapidly spread to almost all countries and regions around the world [1,2]. The World Health Organization (WHO) named pneumonia caused by infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) COVID-19 and declared it a global pandemic [3]. As of June 20, 2020, approximately 8,525,042 cases have been confirmed worldwide, and 456,973 deaths have occurred [4].

The main manifestation of COVID-19 is acute respiratory infection, and the renal, cardiovascular, digestive, blood and nervous systems may be simultaneously involved [5,6]. According to a report from the

Chinese Center for Disease Control and Prevention, the case-fatality rate was 2.3 % in 44,672 patients with confirmed cases of COVID-19, and all cases of death involved critical patients [7]. Therefore, the identification of predictors of severe infection and mortality is essential for guiding clinical treatment and intervention.

Acute kidney injury (AKI) is one of the most important complications of COVID-19 [8]. According to the definition of AKI by the Kidney Disease: Improving Global Outcomes (KDIGO) criteria, the incidence of AKI in hospitalized Chinese adults was 11.6 % and rose to 50 % for those in the intensive care unit (ICU), indicating that the incidence of COVID-19-induced AKI is highly variable to date [9–11]. Currently, several studies have shown that the fatality rate of COVID-19 patients with AKI is incredibly high, ranging from 8% to 23 % [12,13]. A

\* Corresponding authors at: Department of Cardiology, The First Affiliated Hospital of Xinjiang Medical University, No.137, South Liyushan Road, Xinshi Zone, Urumqi, Xinjiang, China.

E-mail addresses: [luojunyi3130@126.com](mailto:luojunyi3130@126.com) (J. Luo), [yangyn5126@163.com](mailto:yangyn5126@163.com) (Y. Yang).

<sup>1</sup> The first two authors contributed equally to this work.

previous study indicated that 6.7 % of patients with SARS might develop AKI, and the mortality rate of those with AKI is 91.7 % [14,15]. This finding indicates that clinicians must pay more attention to COVID-19 patients complicated with AKI. The development of AKI in COVID-19 patients is a critical prognostic factor for survival, but, unlike other known prognostic factors, AKI is possibly curable by interventions. In this article, we performed a systematic review and meta-analysis to explore the correlation between AKI and disease severity and fatality in patients with COVID-19 and to provide reliable evidence for improving the treatment and control of COVID-19.

## 2. Methods

Our systematic literature search was performed according to the Meta-Analysis of Observational Studies in Epidemiology (MOOSE) guidelines [16] and was conducted using a predetermined protocol according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [17].

### 2.1. Search strategy

The PubMed, Web of Science, ScienceDirect, MedRxiv and COVID-19 academic research communication platforms (articles in Chinese, <http://medjournals.cn/2019NCP/index.do>) were used to search for articles published up until June 20, 2020, without applying language restrictions.

The following keywords were used alone and in combination: (“coronavirus disease 2019” OR “COVID-19” OR “novel coronavirus pneumonia” OR “2019-nCoV” OR “SARS-CoV-2”) and (“kidney” OR “renal”) and (“clinical characteristics” OR “clinical features” OR “clinical outcome” OR “epidemiological characteristics”). The titles, abstracts and full texts of all documents identified with the search criteria were assessed, and those reporting AKI in COVID-19 patients with and without fatality and/or disease severity were included in this meta-analysis. The reference lists of all studies were also analyzed to identify additional eligible studies.

### 2.2. Study selection

Two investigators (MJS and JYL) independently scanned all the titles and abstracts to identify studies that met the inclusion criteria, and they extracted data from these studies. Any discrepancies between the reviewers were resolved by discussion with a third reviewer (FL). Studies were regarded as eligible for inclusion in this meta-analysis if they reported AKI in adult laboratory-confirmed COVID-19 patients, with and without fatality and/or disease severity data. The definition of severe COVID-19 refers to the guidelines on the diagnosis and treatment of novel coronavirus pneumonia (trial seventh edition) [18]. AKI was identified and classified based on the highest serum creatinine (Scr) level according to the KDIGO definition and staging system [19].

### 2.3. Data collection

The two investigators (MJS and JYL) who performed the literature search also independently extracted the data from the included studies. Any disagreements were resolved with a third investigator (FL) or by consensus. Data were collected and entered into a spreadsheet. We extracted the following variables: author, study period, location, age, sex, number of participants categorized as severe or non-severe, fatality rate, and the prevalence of clinical symptoms and comorbidities.

### 2.4. Statistical analysis

A meta-analysis was performed on the retrievable data, and the odds ratio (OR) and its 95 % confidence interval (CI) were estimated for AKI in COVID-19 patients with or without severe infection or fatality.

The meta-analysis was performed using R version 3.6.3 (R Foundation for Statistical Computing, Vienna, Austria). The Mantel-Haenszel method (statistical method) and a random-effects model (analysis model) were used to assess the outcomes. The incidence of AKI is expressed as a proportion and 95 % CI using a random-effects model, and the restricted maximum-likelihood estimator.

Heterogeneity was evaluated using the chi-squared test and the  $I^2$  statistic. For the chi-squared test, significant heterogeneity among studies was indicated with a Cochran's Q p-value of  $< 0.10$ .  $I^2$  values of 25 %, 25–50 %, or 50 % indicated low, moderate, or high heterogeneity, respectively [20]. If there was high heterogeneity, several sensitivity analyses were conducted to inspect the influence of individual studies by removing each trial independently using a random effects model (leave-one-out approach) [21]. If only the median and interquartile range (Q25, Q75) were reported, we used simple and elementary inequalities to estimate the mean and variance for the trials [22].

Publication bias was evaluated qualitatively by the asymmetry of the funnel plot and quantitatively by Egger's test, and the significance of asymmetry was explored using visual inspection and tested with a rank correlation test based on Kendall's  $\tau$ . We used the Newcastle-Ottawa Scale (NOS) to further evaluate the quality of the observational studies, and an NOS score  $> 7$  was considered good quality [23].

## 3. Results

The flow of studies through the analysis is presented in Fig. 1. A total of 40 eligible studies involving 24,527 patients were ultimately enrolled in our study. The characteristics of the included studies are described in Table 1, and the treatment and clinical outcome of the patients are described in Table 2. All articles included in the meta-analysis were high-quality according to the NOS tool.

### 3.1. Incidence of AKI

In this meta-analysis, there were 40 studies with 24,377 patients used to assess the incidence of AKI in COVID-19 patients [5,13,24–61]. We found that the incidence of AKI was 10 % (95 % CI 8%–13 %) in COVID-19 patients, but there was evidence of statistical heterogeneity among the studies, with  $I^2 = 98$  %. The meta-analysis also showed that the incidence of AKI was 15 % (95 % CI 9–24 %) and 9 % (95 % CI 7–11 %) internationally and in China, respectively (Fig. 2A). The funnel plot including all studies according to their weights almost showed symmetry, indicating a high risk of publication bias ( $\tau = -5.194$ ,  $P < 0.01$ , Fig. 2B).

The sensitivity analyses for the incidence of AKI produced trivial changes after the removal of each study individually. The incidence of AKI in the remaining studies was approximately 10 %, and the meta-analysis results were still robust (Supplementary material Fig. 1).

### 3.2. Risk of fatality

#### 3.2.1. Fatality rate

In this meta-analysis, there were 20 studies with 9,806 patients used to assess the fatality rate in COVID-19 patients with or without AKI, as shown in Fig. 3A. The overall fatality rate was 20.3 %.

Compared with patients with AKI, patients without AKI had a considerably lower fatality rate (12.9 % vs. 63.1 %,  $P < 0.01$ ), and AKI was significantly associated with increased fatality in patients with COVID-19 (OR = 14.63, 95 % CI: 9.94–21.51,  $P < 0.00001$ ,  $I^2 = 77$  %,  $P < 0.01$ ). The funnel plot including all studies according to their weights showed symmetry, indicating a low risk of publication bias ( $\tau = 0.3489$ ,  $P = 0.73$ , Fig. 3B).

The sensitivity analyses for the fatality rate in COVID-19 patients with or without AKI produced trivial changes after removal of each study individually, and the meta-analysis results were still robust

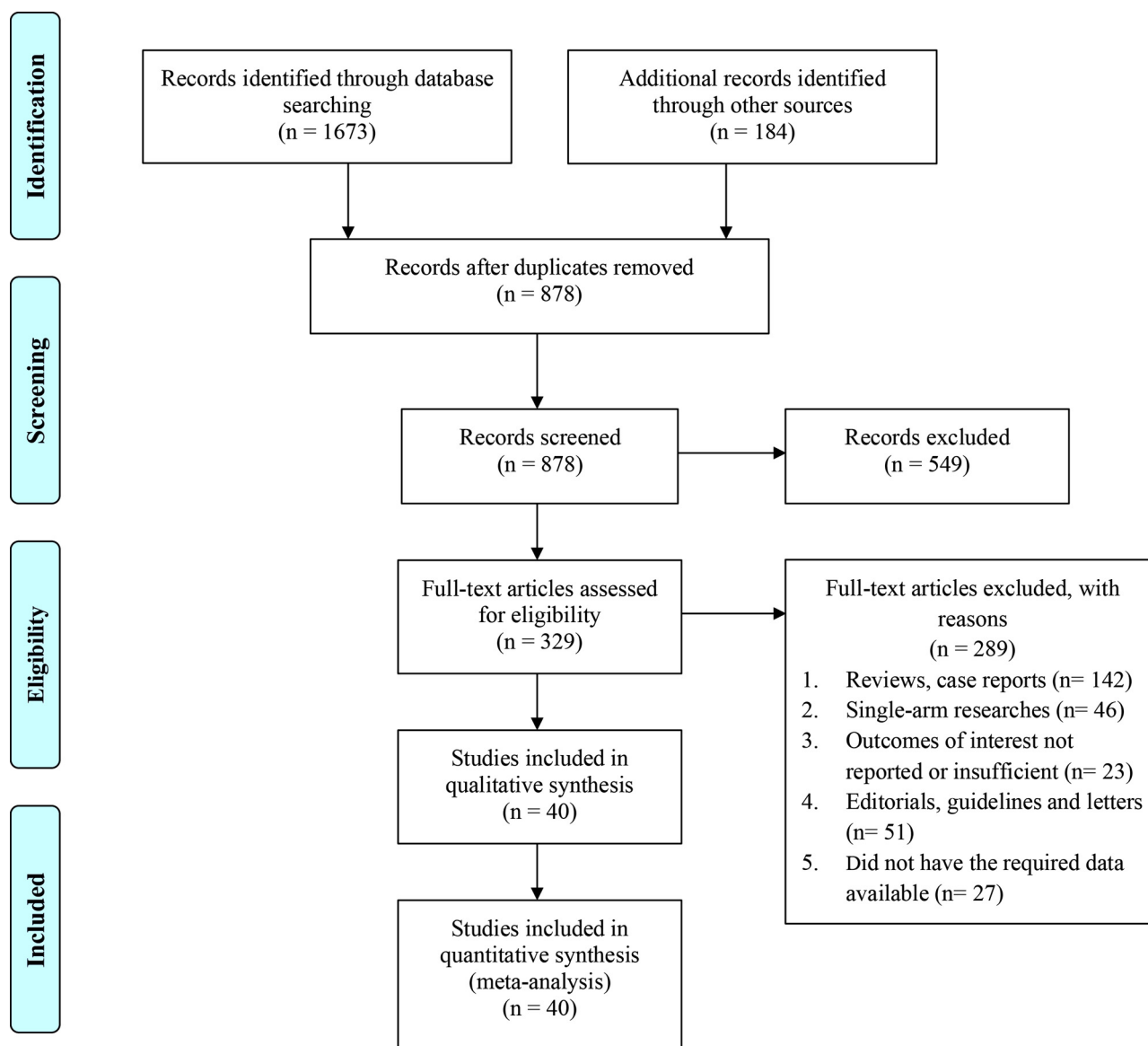


Fig. 1. Flow diagram of literature selection.

(Supplementary material Fig. 2).

### 3.2.2. Serum levels of Scr and BUN in the fatality of COVID-19 infection

A total of 8 studies including 2,138 COVID-19-infected patients (608 patients in the fatality group and 1,530 in the non-fatality group) were used to assess the relationship between Scr levels and fatality. Compared with the non-fatality group, the fatality group showed higher levels of Scr [mean difference (MD): 20.19  $\mu\text{mol/L}$ , 95 % CI: 14.96–25.42,  $P < 0.00001$ ,  $I^2 = 55$  %, Cochran's  $Q$ ,  $P = 0.03$ ] (Fig. 4A). The funnel plot including all studies according to their weights showed symmetry, indicating a low risk of publication bias ( $\tau = 0.3915$ ,  $P = 0.77$ , Fig. 4B).

A total of 5 studies including 1,458 COVID-19-infected patients (367 patients in the fatality group and 1,091 in the non-fatality group) were used to assess the relationship between serum blood urea nitrogen (BUN) levels and fatality. Compared with the non-fatality group, the fatality group had higher serum levels of BUN [MD: 4.07  $\text{mmol/L}$ , 95 % CI: 3.33–4.81,  $P < 0.00001$ ,  $I^2 = 46$  %, Cochran's  $Q$ ,  $P = 0.12$ ] (Fig. 4C). The funnel plot including all studies according to their weights showed symmetry, indicating a high risk of publication bias ( $\tau = -1.1917$ ,  $P = 0.32$ , Fig. 4D).

### 3.3. Risk of severe infection

#### 3.3.1. Severity rate

A meta-analysis with 12,557 patients from 24 published observational studies was performed for the rate of severe infection in COVID-19 patients with or without AKI (Fig. 5A). In our study, the overall severity rate was 26.4 %.

Compared with patients without AKI, patients with AKI had a considerably higher severity rate (55.6 % vs. 17.7 %,  $P < 0.01$ ), and AKI was found to be associated with a nearly 8.11-fold significantly increased risk of severe infection in COVID-19 patients (OR = 8.11, 95 % CI: 5.01–13.13,  $P < 0.00001$ ,  $I^2 = 88$  %,  $P < 0.01$ ). The funnel plot including all studies according to their weights showed symmetry, indicating a low risk of publication bias ( $\tau = -0.2904$ ,  $P = 0.77$ , Fig. 5B).

The sensitivity analyses for the rate of severe infection in COVID-19 patients with or without AKI produced trivial changes after removal of each study individually, and the meta-analysis results were still robust (Supplementary material Fig. 3).

#### 3.3.2. Serum levels of Scr and BUN in severe COVID-19 infection

A total of 12 studies including 1,968 COVID-19-infected patients

**Table 1**  
Characteristics of the 40 studies included in the meta-analysis.

Study	Study period	Location	Outcome	NOS score	No. of patients	Age	Male (n, %)	Comorbidity (n, %)					
								CKD	Hypertension	Diabetes	COPD	CVD	Cancer
Wang L et al. [24]	Jan 1 ~ Feb 6, 2020	Renmin Hospital of Wuhan University	Fatality	8	339	69 (65,76)	166 (49.0)	13 (3.8)	138 (40.8)	54 (16.0)	21 (6.2)	53 (15.7)	15 (4.4)
Yang X et al. [25]	Dec 24, 2019 ~ Jan 26, 2020	Wuhan Jin Yin-Tan Hospital	Fatality	8	52	59.7 ± 13.3	35 (67)	NA	NA	9 (17)	4 (8)	5 (10)	2 (4)
Zhou F et al. [26]	Dec 29, 2019 ~ Jan 31, 2020	Wuhan Jin Yin-Tan Hospital and Pulmonary Hospital	Fatality	8	191	56 (46,67)	119 (62)	2 (1)	58 (30)	36 (19)	6 (3)	23 (8)	2 (1)
Chen T et al. [27]	Jan 13 ~ Feb 28, 2020	Tongji Hospital	Fatality	8	274	62 (44,70)	171 (62)	4 (1)	93 (34)	47 (17)	18 (7)	24 (9)	7 (3)
Luo X et al. [28]	Jan 30 ~ Feb 25, 2020	Eastern Campus of Renmin Hospital of Wuhan University	Fatality	8	403	56 (39,68)	193 (47.9)	7 (1.7)	113 (28.0)	57 (14.1)	28 (6.9)	75 (18.6)	NA
Xiao G et al. [29]	Jan 5 ~ Mar 8, 2020	Nan Fang Hospital	Fatality	8	287	62 (51,70)	160 (55.7)	5 (2)	87 (30)	45 (16)	16 (6)	33 (12)	8 (3)
Deng Y et al. [30]	Jan 1 ~ Feb 21, 2020	Two tertiary hospitals in Wuhan	Fatality	7	225	69 (62,74)	124 (55.1)	NA	58 (25.8)	26 (11.6)	25 (11.1)	17 (7.6)	8 (3.6)
Safiya R et al. [31]	Mar 5 ~ Apr 8, 2020	New York City	Fatality	7	5700	63 (52,75)	3437 (60.3)	268 (5)	3026 (56.6)	1808 (33.8)	287 (5.4)	595 (11.1)	320 (6)
Peng Z et al. [32]	Jan 1 ~ Feb 10, 2020	Xishui People's Hospital	Fatality	7	107	51 (36,65)	57 (53.3)	3 (2.8)	26 (24.3)	11 (10.3)	3 (2.8)	13 (12.1)	NA
Alberto M et al. [33]	Feb 25 ~ Apr 19, 2020	La Paz University of Spain the Hospital	Fatality	7	2226	61 (46,78)	1074 (48.2)	174 (7.8)	920 (41.3)	381 (17.1)	153 (6.9)	429 (19.3)	133 (6.0)
Wang Y et al. [34]	Jan 25 ~ Feb 25, 2020	Tongji hospital	Fatality	7	344	64 (52,72)	179 (52.0)	NA	141 (41.0)	64 (18.6)	16 (4.7)	40 (11.6)	NA
Cao J et al. [35]	Jan 3 ~ Feb 1, 2020	Wuhan University Zhong nan Hospital	Fatality	7	102	54(37,67)	49 (48.0)	4 (3.9)	28 (27.5)	11 (10.8)	10 (9.8)	5 (4.9)	4 (3.9)
Zhang J et al. [36]	Jan 1 ~ Feb 1, 2020	Wuhan Fourth Hospital	Fatality	7	394	56 (42,67)	186 (47.2)	NA	115 (29.2)	47 (11.9)	23 (5.8)	38 (9.6)	24 (6.1)
Chen F et al. [37]	Jan 1 ~ Feb 15, 2020	Central Hospital of Wuhan	Fatality	7	660	55 (34,68)	295 (44.7)	NA	230 (34.8)	114 (17.3)	43 (6.5)	67 (10.2)	NA
Jerald P et al. [38]	NA	African American patients from underserved socioeconomic groups.	Fatality	7	223	65.9 ± 14.9	115 (52)	39 (17.5)	180 (72)	104 (47)	27 (12.1)	35 (11.2)	NA
Jeong Hoon et al. [61]	Feb 17 ~ Mar 22, 2020	The Kyungpook National University Hospital Daegu, South Korea	Fatality	7	160	67 (24,92)	86 (53.8)	NA	77 (48.1)	50 (31.2)	16 (10)	21 (13.1)	26 (16.3)
Pei G et al. [40]	Jan 28 ~ Feb 9, 2020	Tongji Hospital of Sino-French New City District	Non-severe/severe, Fatality	7	333	56.3 ± 13.4	182 (54.7)	NA	107 (32.2)	76 (22.9)	NA	NA	NA
Xu S et al. [41]	Jan 1 ~ Feb 20, 2020	The Second Affiliated Hospital of Anhui Medical University	Non-severe/severe, Fatality	7	355	NA	193 (54.4)	NA	125 (35.2)	147 (41.4)	NA	NA	NA
Jamie S et al. [42]	Mar 1 ~ Apr 5, 2020	13 Northwell Health hospitals	Non-severe/severe	8	5449	64 (52, 75)	3317 (60.9)	NA	3037 (55.7)	1797 (33.0)	296 (5.4)	600 (11.0)	327 (6.0)
Abdullah A et al. [43]	Feb 24 ~ May 24, 2020	Jaber Al-Ahmad Hospital, Kuwait.	Non-severe/severe, Fatality	8	417	45.4 ± 17.2	262 (63)	14 (3.4)	123 (29.5)	97 (23.3)	1 (0.2)	39 (9.4)	12 (2.9)
Sinan T et al. [44]	Mar 15 ~ May 1, 2020	Cerrahpasa Medical Faculty, Turkey	Non-severe/severe, Fatality	7	336	55.0 ± 15.9	192 (57.1)	NA	120 (35.7)	63 (18.8)	19 (5.7)	NA	31 (10.1)
Li X et al. [45]	Jan 26 ~ Feb 5, 2020	Sino-French New City Branch of Tongji Hospital	Non-severe/severe	8	548	60 (48, 69)	279 (50.9)	10 (1.8)	166 (30.3)	83 (15.1)	17 (3.1)	34 (6.2)	24 (4.7)
Cheng Y et al. [13]	Jan 28 ~ Feb 11, 2020	Tongji Hospital	Non-severe/severe	7	701	63 (50,71)	367 (52.4)	14 of 698 (2.0)	233 of 698 (33.4)	100 of 698 (14.3)	13 of 698 (1.9)	NA	32 of 698 (4.6)
Wan S et al. [46]	Jan 23 ~ Feb 8, 2020	Three Gorges Central Hospital	Non-severe/severe	8	135	47 (36, 55)	72 (53.3)	NA	13 (9.6)	12 (8.9)	1 (0.7)	7 (5.2)	4(3.0)
Huang C et al. [5]	Dec 16, 2019 ~ Jan 2, 2020.	Wuhan Jin Yin-tan hospital	Non-severe/severe	8	41	49 (41,58)	30 (73)	NA	6 (15)	8 (20)	1 (2)	6 (15)	1 (2)
Guan W et al. [47]	Dec 11, 2019 ~ Jan 31, 2020	cases outside Hubei province of Wuhan Jin Yin-Tan Hospital	Non-severe/severe	8	1099	47 (35,58)	610(58.1)	8 (0.7)	165 (15.0)	81 (7.4)	12 (1.1)	27 (2.5)	10 (0.9)

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Table 1 (continued)

Study	Study period	Location	Outcome	NOS score	No. of patients	Age	Male (n, %)	Comorbidity (n, %)					
								CKD	Hypertension	Diabetes	COPD	CVD	Cancer
Yan S et al. [48]	Jan 22 ~ Mar 14, 2020	Hainan province	Non-severe/severe	8	168	51 (36,62)	81 (48.2)	1 (0.6)	24 (14.3)	12 (7.1)	2 (1.2)	12 (7.1)	2 (1.2)
Zhao W et al. [49]	Jan 21 ~ Feb 8, 2020	Beijing YouAn Hospital, Beijing,	Non-severe/severe	7	77	52 ± 20	34 (44.2)	5 (6.5)	16 (20.8)	6 (7.8)	6 (7.8)	9 (11.7)	4 (5.2)
Wang D et al. [50]	Jan 1 ~ Jan 28, 2020	Zhongnan Hospital of Wuhan	Non-severe/severe	8	138	56 (42,68)	75 (54.3)	4 (2.9)	43 (31.2)	14 (10.1)	4 (2.9)	20 (14.5)	10 (7.2)
Zhang G et al. [51]	Jan 28 ~ Feb 20, 2020	Zhongnan Hospital of Wuhan	Non-severe/severe	8	221	55 (39,67)	108 (48.9)	6 (2.7)	54 (24.4)	22 (10.0)	6 (2.7)	22 (10.0)	9 (4.1)
Hu L et al. [52]	Jan 8 ~ Mar 10, 2020	Tianyou Hospital, Affiliated to Wuhan University of Science and Technology	Non-severe/severe	7	323	61 (23,91)	166 (51.4)	7 (2.2)	105 (32.5)	47 (14.6)	6 (1.9)	41 (12.7)	5 (1.5)
Shi P et al. [53]	Jan 27 ~ Mar 7, 2020	9 cities of Shanxi province	Non-severe/severe	7	134	46 (34,58)	65 (48.5)	0	20 (14.9)	9 (6.7)	5 (3.7)	6 (4.5)	5 (3.7)
Li Z et al. [54]	Jan 6 ~ Feb 21, 2020	4 hospitals in Hubei province and Chongqing city	Non-severe/severe	8	193	57 (46,67)	95 (49)	10 (5)	NA	NA	27 (14)	70 (36)	NA
Li Q et al. [55]	Jan 20 ~ Feb 29, 2020	Shanghai Public Health Clinical Center	Non-severe/severe	7	325	51 (36,64)	167 (51.4)	4 (1.2)	78 (24)	30 (9.2)	4 (1.2)	18 (5.5)	3 (0.9)
Zhao XY et al. [56]	Jan 16 ~ Feb 10, 2020	Jingzhou Central Hospital	Non-severe/severe	8	91	46	49 (53.8)	1 (1)	18 (19.8)	3 (3.3)	1(1)	NA	3 (3.3)
Yang L et al. [57]	Jan 30 ~ Feb 8, 2020	Yichang Central People's Hospital	Non-severe/severe	7	200	55.0 ± 17.1	98 (49)	3 (1.5)	45 (22.5)	21 (10.5)	7 (3.5)	11 (5.5)	4 (2)
Yang Q et al. [58]	Jan 28 ~ Feb 12, 2020	Wuhan Third Hospital	Non-severe/severe	7	136	56 (44,64)	66 (48.5)	4 (2.9)	36 (27.1)	20 (147)	NA	9 (6.6)	4 (2.9)
Michael G et al. [59]	Mar 11 ~ Apr 6, 2020	NYP/CUIMC electronic health record	Non-severe/severe	8	1000	63 (50,75)	596 (59.6)	137 (13.7)	601 (60.1)	372 (37.2)	66 (6.6)	131 (13.1)	67 (6.7)
Antoni S et al. [60]	Feb 20 ~ Apr 20, 2020	three urban primary healthcare centers, Barcelona, Spain	Non-severe/severe	7	322	56.7 ± 17.8	161 (50)	31 (9.6)	109 (33.9)	46 (14.3)	19 (5.9)	25 (7.8)	37 (11.5)
Kyung Soo et al. [39]	Up to March 29, 2020	Yeungnam University Medical Center, Daegu, Korea	Non-severe/severe	8	98	55.4 ± 17.1	38 (38.8)	NA	30 (30.6)	9 (9.2)	3 (3.1)	11 (11.2)	4 (4.1)

Data are presented as means ± SD, n (%) or median (interquartile range). No. of patients, number of COVID-19 confirmed patients; NOS, the Newcastle-Ottawa Scale; COPD, chronic obstructive pulmonary disease; CVD, Cardiovascular diseases; CKD, chronic kidney disease; NA, data not available.

**Table 2**  
Treatment and clinical outcome of patients with COVID-19 in the meta-analysis.

Study	AKI (n, %)	CSR (n, %)	CFR (n, %)	Treatment (n, %)							Laboratory findings				
				Antiviral	Glucocorticoids	Oxygen inhalation	NIV	IMV	ECMO	CRRT	BUN, mmol/L	Scr, $\mu$ mol/L	Proteinuria (n, %)	Hematuria (n, %)	UA, $\mu$ mol/L
Wang L et al. [24]	27 (8.1)	239 (70.5)	65 (19.2)	NA	NA	NA	NA	NA	NA	NA	5.5 (4.0,8.0)	61.0 (50.0, 76.0)	NA	NA	NA
Yang X et al. [25]	15 (28.8)	52 (100)	32 (61.5)	23 (44)	30 (58)	33 (63.5)	29 (56)	22 (42)	6 (11.5)	9 (17)	NA	76.3 $\pm$ 27.4	NA	NA	NA
Zhou F et al. [26]	28 (14.7)	66 (35)	54 (28)	41 (21)	57 (30)	41 (21)	26 (14)	32 (17)	3 (2)	10 (5)	NA	> 133 $\mu$ mol/L (4%)	NA	NA	NA
Chen T et al. [27]	29 (11.7)	NA	113 (41.2)	236 (86)	217 (79)	251 (92)	102 (37)	17 (6)	1 (0.4)	3 (1)	4.9 (3.5, 7.9)	76.0 (58.0,94.0)	100 of 166 (60)	84 of 166 (51)	NA
Luo X et al. [28]	57 (14.1)	205 (50.9)	100 (24.8)	394 (97.8)	166 (41.2)	106 (26.3)	56 (13.9)	23 (5.7)	NA	39 (9.7)	NA	69.0 (60.0, 86.0)	NA	NA	NA
Xiao G et al. [29]	55 (19.2)	124 (43)	19 (6.6)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Deng Y et al. [30]	20 (8.9)	104 (46.2)	109 (48.4)	185 (82.2)	88 (39.1)	115 (51.1)	68 (30.2)	21 (9.3)	2 (0.9)	NA	NA	NA	NA	NA	NA
Safiya R et al. [31]	523 (22.2)	373 (14.2)	553 (21)	NA	NA	NA	320 (12.2)	NA	NA	81 (3.2)	NA	NA	NA	NA	NA
Peng Z et al. [32]	14 (13.1)	11 (10.3)	19 (17.8)	105 (98.1)	62 (57.9)	80 (74.8)	7 (6.5)	17 (15.9)	3 (2.8)	NA	4.2 (3.2, 5.6)	71 (60,86)	NA	NA	NA
Alberto M et al. [33]	173 (7.8)	237 (7.6)	460 (14.7)	NA	NA	NA	NA	NA	NA	NA	NA	0.89 (0.8, 1) mg/dL	NA	NA	NA
Wang Y et al. [34]	86 (25.0)	133 (38.7)	344 (100)	283 (82.3)	225 (65.4)	35 (10.2)	34 (9.9)	100 (29.1)	2 (0.6)	9 (2.6)	5.3 (3.8,8.3)	74 (58,93)	NA	NA	NA
Cao J et al. [35]	20 (19.6)	18 (17.6)	17(16.7)	100 (98.0)	51 (50.0)	76 (74.5)	5 (4.9)	14 (13.7)	3 (2.9)	6 (5.9)	4.33 (3.45,5.46)	NA	NA	NA	269 (228,347)
Zhang J et al. [36]	37 (9.5)	NA	22 (5.6)	NA	NA	NA	NA	NA	NA	NA	4.35 (3.45,5.68)	69.0 (55.6,83.0)	NA	NA	NA
Chen F et al. [37]	36 (5.5)	151/643 (23.5)	82 (12.4)	NA	NA	NA	NA	NA	NA	NA	4.2 (3.3,5.6)	65.1 (52.0,79.5)	NA	NA	NA
Jerald P et al. [38]	110 (49.3)	NA	44 (19.7)	NA	49 (22.0)	NA	NA	48 (21.5)	NA	18 (8)	NA	NA	NA	NA	NA
Jeong Hoon et al. [61]	30 (18.8)	20/30 (66.7)	44 (27.5)	29/30 (96.7)	18/30 (60.0)	29/30 (96.7)	NA	16/30 (53.3)	1/30 (3.3)	5/30 (16.7)	23.7 (15.7,32.0)/30 mg/dL	1.1 (0.8,1.6) /30 mg/dL	NA	NA	NA
Pei G et al. [40]	35 (10.5)	56 (16.8)	29 (8.7)	NA	NA	NA	NA	NA	NA	NA	4.7 (3.5, 5.9)	74.0 (61.0, 89.0)	177 (89.4)	109 (55.0)	NA
Xu S et al. [41]	56 (15.8)	32 (9.0)	32 (9.0)	NA	NA	NA	NA	NA	NA	NA	4.9 (1.1, 37.5)	72.4 (32.0, 355.0)	NA	NA	259.7 (29.07, 677.07)
Jamie S et al. [42]	1993 (36.6)	1395 (25.6)	888 (16.3)	NA	NA	NA	NA	NA	10 (0.2)	NA	NA	1.01 (0.8,1.3) mg/dL	NA	NA	NA
Abdullah A et al. [43]	41 (9.8)	82 (19.7)	60 (14.6)	100 (24.0)	6 (1.4)	NA	NA	NA	3 (0.7)	NA	3.33 (2.83–4.03)	61.46 (51.5–75.86)	NA	NA	NA
Sinan T et al. [44]	61 (18.2)	59 (17.6)	43 (12.8)	NA	21 (6.3)	NA	NA	NA	NA	NA	37.6 $\pm$ 31.0 mg/dL	1.2 $\pm$ 1.2 mg/dL	NA	NA	5.1 $\pm$ 2.0 mg/dL
Li X et al. [45]	95 (17.3)	269 (49.1)	90 (16.5)	NA	341 (62.2)	355 (64.8)	78 (14.2)	25 (4.6)	NA	2 (0.4)	> 7.5 mmol/L 85 of 539 (15.8%)	> 85 $\mu$ mol/L 146 of 539 (27.1%)	200/300 (60.6)	NA	NA
Cheng Y et al. [13]	101 (14.4)	297 (42.4)	113 (16.1)	658 (93.9)	387 (55.2)	NA	NA	97 (13.4)	NA	NA	5.7 $\pm$ 3.9	77 $\pm$ 31	194 of 442(43.9 %)	118 of 442 (26.7 %)	NA
Wan S et al. [46]	10 (7.4)	40 (29.6)	1 (0.7)	135 (100)	36 (26.7)	90 (66.7)	34 (25.2)	1 (0.7)	0	5 (3.7)	NA	66(57.8,74.5)	NA	NA	NA
Huang C et al. [5]	3 (7.3)	13 (31.7)	6 (15)	38 (93)	9 (22)	27 (66)	10 (24)	2 (5)	2 (5)	3 (7)	NA	74.2 (57.5,85.7)	NA	NA	NA

(continued on next page)

Table 2 (continued)

Study	AKI (n, %)	CSR (n, %)	CFR (n, %)	Treatment (n, %)							Laboratory findings				
				Antiviral	Glucocorticoids	Oxygen inhalation	NIV	IMV	ECMO	CRRT	BUN, mmol/L	Scr, $\mu$ mol/L	Proteinuria (n, %)	Hematuria (n, %)	UA, $\mu$ mol/L
Guan W et al. [47]	6 (0.5)	173 (15.7)	55 (5.0)	393 (35.8)	204 (18.6)	454 (41.3)	56 (5.1)	25 (2.3)	5 (0.5)	9 (0.8)	NA	> 133 $\mu$ mol/L 12 of 752(1.6 %)	NA	NA	NA
Yan S et al. [48]	6 (3.6)	36 (21.4)	6 (3.6)	155 (92.3)	27 (16.1)	97 (57.7)	13 (7.7)	10 (6)	NA	NA	3.7 (2.9,4.5)	62 (49,75.1)	NA	NA	NA
Zhao W et al. [49]	2 (2.6)	20 (26)	16 (20.8)	NA	NA	NA	NA	NA	NA	NA	NA	64 (54,78)	NA	NA	NA
Wang D et al. [50]	5 (3.6)	36 (26.1)	6 (4.3)	124 (89.9)	62 (44.9)	106 (76.81)	15 (10.9)	17 (12.3)	4 (2.9)	2 (1.45)	4.4 (3.4,5.8)	72 (60,87)	NA	NA	NA
Zhang G et al. [51]	10 (4.5)	55 (24.9)	12 (5.4)	196 (88.7)	115 (52.0)	NA	27 (12.2)	16 (7.2)	10 (4.5)	5 (2.3)	4.3 (3.4,5.6)	69 (56,84)	NA	NA	NA
Hu L et al. [52]	17 (5.3)	172 (53.3)	NA	NA	196 (60.7)	NA	105 (32.5)	34 (10.5)	NA	72 (22.3)	> 8 mmol/L 72 (22.3)	> 144 $\mu$ mol/L 7 (2.2)	NA	NA	NA
Shi P et al. [53]	3 (2.2)	46 (34.2)	1 (0.7)	129 (96.3)	41 (30.6)	91 (67.9)	2 (1.5)	1 (0.7)	1 (0.7)	1 (0.7)	3.6 (3.0, 4.5)	60.0 (50.4, 73.0)	NA	NA	NA
Li Z et al. [54]	55 (28.5)	65 (33.7)	32 (17)	187 (98)	119 (62)	182 (94)	50 (26)	33 (17)	3 (2)	7 (4)	4.4 (3.22,6.44)	66 (54,82)	76 (59)	57 (44)	237 (185,302)
Li Q et al. [55]	19 (5.8)	3 (0.9)	26 (8)	296 (91.1)	69 (21.2)	NA	11 (3.4)	15 (4.6)	7 (2.2)	3 (0.9)	4.41 (3.55,5.45)	63 (51,75)	NA	NA	NA
Zhao XY et al. [56]	5 (5.5)	30 (33)	2 (2.2)	81 (89)	79 (86.8)	29 (31.9)	NA	NA	NA	3 (3.3)	NA	> 97 $\mu$ mol/L 5 (5.5)	NA	NA	> 417 $\mu$ mol/L 5 (5.5)
Yang L et al. [57]	24 (12)	29 (14.5)	15 (7.5)	199 (99.5)	112 (56)	158 (79)	35 (17.5)	16 (8)	NA	2 (1)	NA	64 (52.5,83.1)	NA	NA	NA
Yang Q et al. [58]	4 (2.9)	33 (24.3)	23 (16.9)	NA	NA	66 (48.5)	NA	25 (18.4)	NA	NA	4 (3.2,5.4)	67.9 (54.8,81.2)	NA	NA	NA
Michael G et al. [59]	288/850 (33.9)	236 (23.6)	211 (21.1)	NA	178/850 (20.9)	NA	NA	NA	5/850 (0.6)	NA	NA	NA	NA	NA	NA
Antoni S et al. [60]	8 (2.5)	56 (17.4)	NA	131 (40.7)	34 (10.6)	86 (26.7)	NA	NA	NA	NA	NA	NA	NA	NA	NA
Kyung Soo et al. [39]	9 (9.2)	13 (13.3)	5 (5.1)	97 (99)	18 (18.4)	37 (37.8)	12 (12.2)	11 (11.2)	4 (4.1)	3 (3.1)	15.3 $\pm$ 9.5 mg/dL	0.9 $\pm$ 0.5 mg/dL	NA	NA	NA

Data are presented as means  $\pm$  SD, n (%) or median (interquartile range). AKI, Acute kidney injury; CFR, case fatality rate; CSR, case severity rate; NA, data not available; NIV, non-invasive ventilation; IMV, invasive mechanical ventilation; ECMO: extracorporeal membrane oxygenation; CRRT, continuous renal replacement therapy; UA, Uric acid; BUN, Blood urea nitrogen; Scr, Serum creatinine.



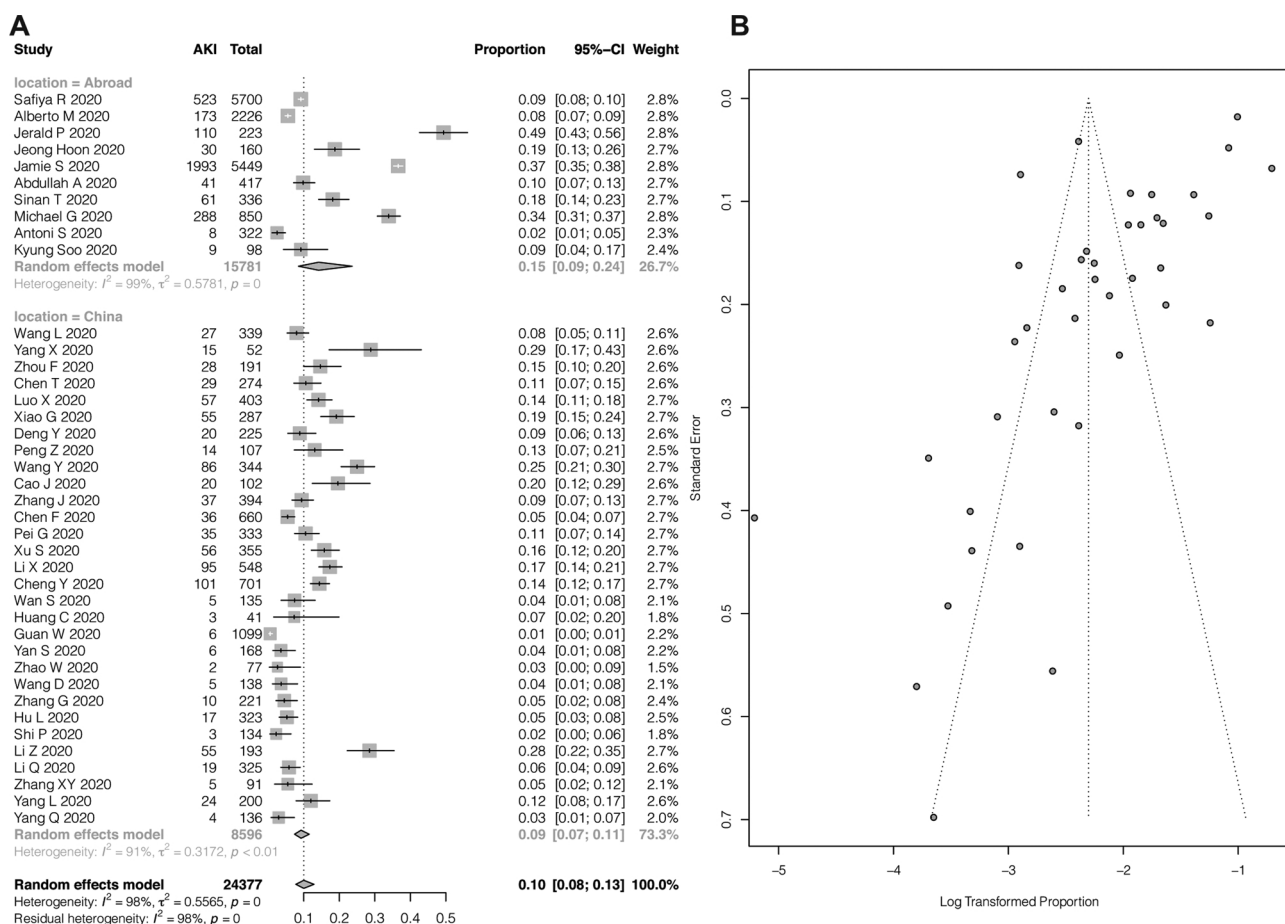


Fig. 2. Meta-analysis of incidence of AKI in COVID-19 infection.

- A. Forest plot of incidence of AKI in COVID-19 infection.
- B. Funnel plot of incidence of AKI in COVID-19 infection of publication bias.

(551 patients in the severe group and 1417 in the non-severe group) were used to assess the relationship between the severity of infection and the levels of Scr. Compared with the non-severe group, the severe group had higher serum levels of Scr [MD: 7.78  $\mu\text{mol/L}$ , 95 % CI: 4.43–11.14,  $P < 0.00001$ ,  $I^2 = 34\%$ , Cochran's  $Q$ ,  $P = 0.12$ ] (Fig. 6A).

The funnel plot including all studies according to their weights showed symmetry, indicating a low risk of publication bias ( $\tau = 2.4416$ ,  $P = 0.03$ , Fig. 6B).

A total of 7 studies including 1,445 COVID-19-infected patients (303 patients in the severe group and 1,142 in the non-severe group) was

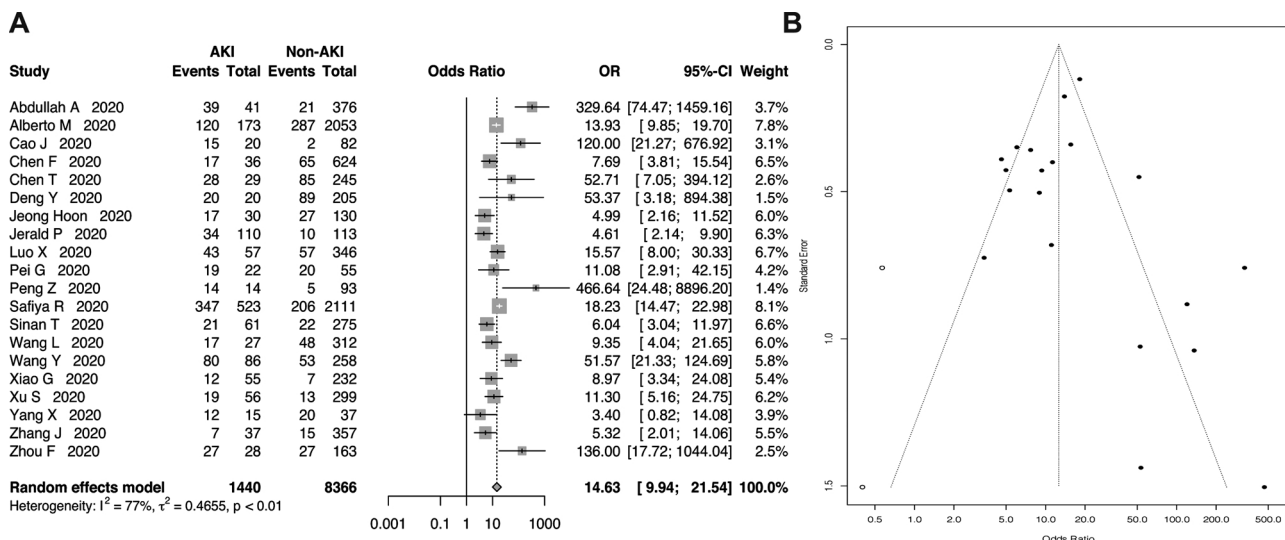


Fig. 3. Meta-analysis of fatality in COVID-19 patients with or without AKI.

- A. Forest plot of fatality in COVID-19 patients with or without AKI.
- B. Funnel plot of fatality for the assessment of publication bias.

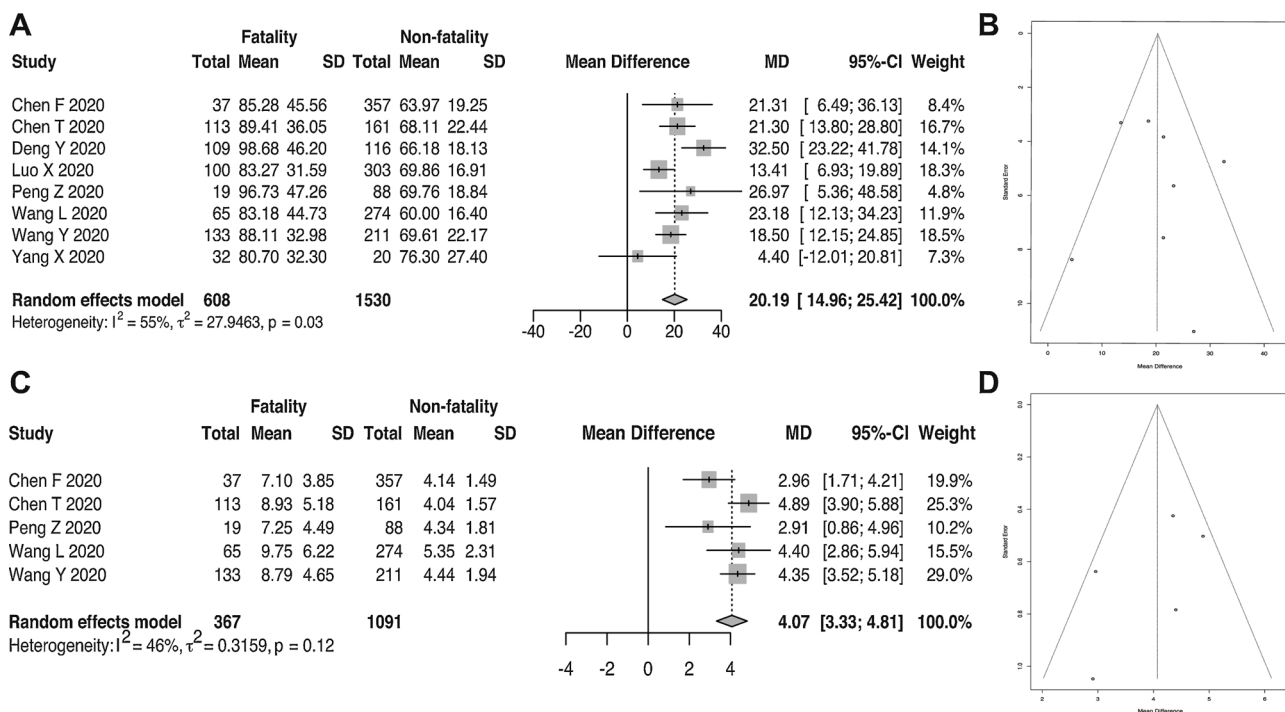


Fig. 4. Meta-analysis of the association between Scr and BUN levels and fatality in COVID-19 patients.

- A. Forest plot of the association between levels of Scr and fatality in COVID-19 patients.
- B. Funnel plot of Scr levels and fatality for the assessment of publication bias.
- C. Forest plot for the association between serum levels of BUN and fatality in COVID-19 patients.
- D. Funnel plot of BUN serum levels and fatality for the assessment of publication bias.

used to assess the relationship between the severity of infection and the serum BUN levels. Compared with the non-severe group, the severe group had higher serum BUN levels [MD: 2.12 mmol/L, 95 % CI: 1.74–2.50,  $P < 0.00001$ ,  $I^2 = 0%$ , Cochran's Q,  $P = 0.55$ ] (Fig. 6C). The funnel plot including all studies according to their weights showed symmetry, indicating a low risk of publication bias ( $\tau = -0.3816$ ,  $P = 0.72$ , Fig. 6D).

4. Discussion

Based on our meta-analysis of some early and preliminarily available data, COVID-19 patients with AKI had higher severe infection and case-fatality rates, and AKI was a risk factor associated with severe

infection and fatality in patients with COVID-19. To our knowledge, this study is the first systematic review and meta-analysis to assess the association between AKI and the risk of severe disease and death in COVID-19 patients. Our study has shown that the incidence of AKI in COVID-19 patients was 10 %, mainly indicated by elevated Scr and BUN levels. We found that the BUN and Scr levels were significantly higher in severe infection patients than in non-severe patients, and these factors were significantly associated with the death of COVID-19 patients. This finding is consistent with results from previous studies, which confirmed that elevated Scr and BUN levels were independent risk factors for in-hospital death [13,62,63].

In our meta-analysis, the overall fatality rate was 20.3 %, and the severity rate was 26.4 %, which are much higher than the values of 3.1

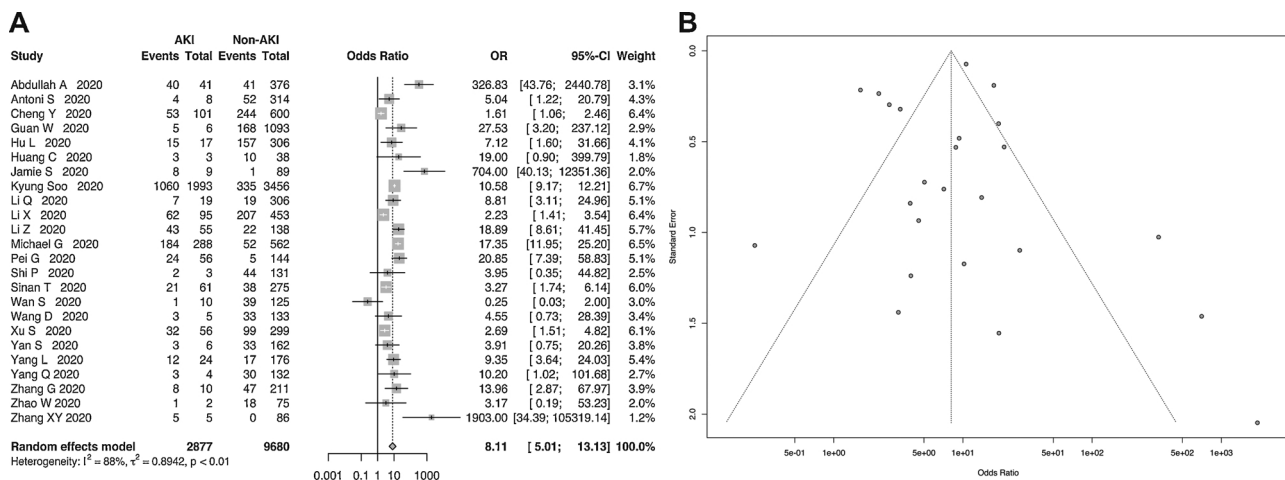
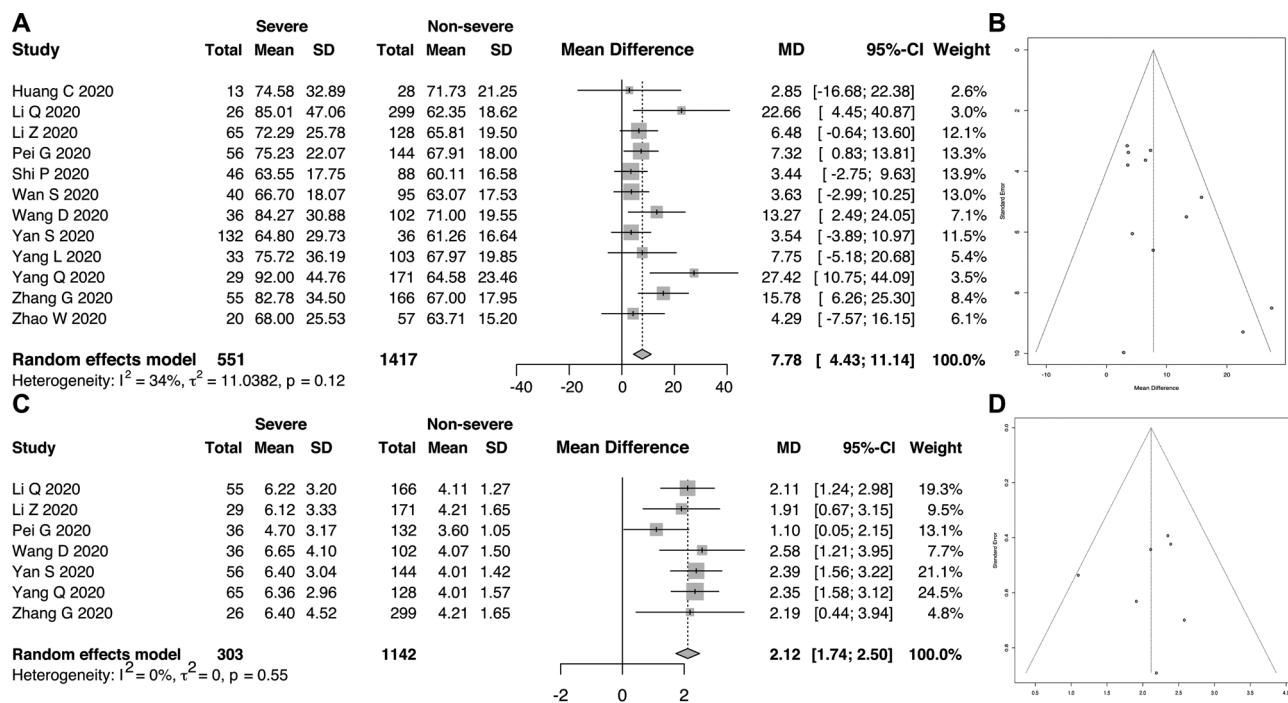


Fig. 5. Meta-analysis of severe infection in COVID-19 patients with or without AKI.

- A. Forest plot of severe infection in COVID-19 patients with or without AKI.
- B. Funnel plot of severe infection for the assessment of publication bias.



**Fig. 6.** Meta-analysis of the association between Scr and BUN levels and severe infection in COVID-19 patients. A. Forest plot of the association between serum levels of creatinine and severe infection in COVID-19 patients. B. Funnel plot of serum creatinine levels and severe infection for the assessment of publication bias. C. Forest plot of the association between serum blood urea nitrogen levels and severe infection in COVID-19 patients. D. Funnel plot of serum blood urea nitrogen levels and severe infection for the assessment of publication bias.

% and 20.2 % reported in a recent meta-analysis including 53,000 patients, with COVID-19 is the largest sample size so far. So, this study should be largely representative of the rate of severe infection and fatality at large in COVID-19 patients [64]. A possible reason for the high fatality rate is that the included studies had a high proportion of severely infected patients. This large sample size report also showed that the case-fatality rate was associated with disease severity, as all cases of death involved critical patients [7]. Another possible reason is different from study's searching strategy. Our study focuses on severe infection and fatality of acute kidney injury in COVID-19, It could overestimate the rate of severe infection and fatality. According to a recent study, AKI in COVID-19 patients was associated with a higher risk of death even after adjustment for potential confounders [13]. Therefore, the existence of AKI should be regarded as an important index in the risk stratification of disease severity and death for COVID-19 patients, and risk screening contributes to early intervention to reduce the incidence or progression of AKI.

#### 4.1. Pathophysiology of AKI

The detailed pathophysiologic relationship between COVID-19 and AKI remains unclear. SARS-CoV-2 causes kidney injury through direct and indirect pathogenic pathways [65]. First, the novel coronavirus may exert direct cytopathic effects on kidney tissue [66]. Online datasets and bioinformatic analyses identified that angiotensin-converting enzyme 2 (ACE2), one of the major receptors of SARS-CoV-2, is highly expressed in renal cells, particularly in tubular cells [67,68]. A recent report analyzed the histology of renal tissues from autopsies and found acute renal tubular damage in six COVID-19 cases, and human tissue RNA-sequencing data demonstrated that ACE2 expression in the kidney was nearly 100-fold higher than that in the lung [69,70]. Therefore, SARS-CoV-2 could enter renal tubular cells by binding to ACE2, which induces cytotoxicity and leads to abnormal renal function [54,67]. Second, SARS-CoV-2 infection may also cause kidney injury through

overactivation of the immune system, with the release of a large number of cytokines and cytokine storms [71]. Third, COVID-19 patients with severe infections often have low blood pressure, dehydration, hypoxemia, electrolyte acid-base imbalances, acute heart failure and viremia, which have all been implicated in AKI [8]. In addition, most COVID-19 patients with AKI are older and have frequent comorbidities such as hypertension or diabetes mellitus; these factors are well-known factors of renal vulnerability [72]. Nephrotoxic drugs can also be influential in AKI development, especially antibiotics, antiviral medications and traditional medicines. However, these factors have been poorly investigated in COVID-19 patients.

#### 4.2. Treatment of COVID-19-induced AKI

Based on these results, we should focus more attention on kidney damage at the early stage when patients are confirmed to be infected by COVID-19. Clinicians should longitudinally and dynamically measure kidney damage biomarkers, such as the fluctuation of Scr and BUN levels with respect to volume and hemodynamic status, during in-hospital SARS-CoV-2 infection, which may help to identify a subset of patients with AKI, especially in elderly patients, in combination with noting whether the patient has a past history of hypertension, coronary heart disease and chronic kidney disease; moreover, these measures should also be taken in patients admitted to the intensive care unit. Risk screening could predict the progression of COVID-19 to minimize patients' in-hospital fatality and improve their long-term prognosis.

To date, there is no specific treatment for COVID-19-induced AKI. The treatment of AKI is aimed at addressing the underlying causes of AKI. Therefore, antiviral drugs and immunomodulatory drugs are the primary modes of management for AKI in COVID-19 [72]. However, several older drugs, such as diuretics, acetylcysteine and sodium bicarbonate, are used to treat AKI in COVID-19 [73]. Alternatively, traditional Chinese medications (Bailing Granules) and Chinese herbal medicine are also used to treat AKI in COVID-19 [74]. If conservative

management fails, CRRT should be considered in patients with volume overload, especially those with refractory hypoxemia. For COVID-19 patients with a high risk, blood volume and hemodynamics should be optimized to ensure adequate, effective renal perfusion pressure, and the use of nephrotoxic drugs should be avoided. In the event of signs of AKI, potential interventions, including continuous renal replacement therapy, should be used to protect renal function as early as possible [10].

#### 4.3. Limitations

This study has several limitations. First, the COVID-19 patients in our meta-analysis had a high case-fatality rate, which may be due to them being early reports from early stages of the outbreak and involving a higher proportion of severely ill patients. Therefore, the relationship between AKI and fatality risk in mildly ill patients still needs to be evaluated. Second, most studies were not adjusted for various confounding factors, which might have caused bias in the results. Third, all included studies were retrospective, and there was a risk of bias in the data collected. At the same time, the quality of different studies varied, which might lead to bias. As the disease spreads around the world, it is hoped that other countries affected by COVID-19 will report more clinical data to verify our results. Finally, we have diligently and carefully tried to go through each included article's study setting and author list to avoid overlapping patient data. However, in our large meta-analysis of 24,527 patients, the small overlapping patient data of the same centers of Wuhan, China is inevitable and inconsequential.

#### 5. Conclusion

In conclusion, AKI is a crucial complication in patients with COVID-19, and it may be related to a higher risk of severe infection and poor prognosis. Special care and monitoring are needed in COVID-19 patients with AKI to reduce the risk of severe infection and improve prognosis.

#### Author contributions

Mengjiao Shao and Junyi Luo: literature research and selection, data extraction.

Mengjiao Shao, Junyi Luo and Fen Liu statistical analysis and interpretation.

All authors interpreted the results and contributed to critical review of the manuscript.

Yining Yang: funds collection, conception and design of the study and revised manuscript.

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#### Declaration of Competing Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

#### Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.phrs.2020.105107>.

#### References

- [1] N. Zhu, D. Zhang, W. Wang, X. Li, B. Yang, J. Song, X. Zhao, B. Huang, W. Shi, R. Lu, P. Niu, F. Zhan, X. Ma, D. Wang, W. Xu, G. Wu, G.F. Gao, W. Tan, A novel coronavirus from patients with pneumonia in China, 2019, *N. Engl. J. Med.* 382 (8) (2020) 727–733, <https://doi.org/10.1056/NEJMoa2001017>.
- [2] D.G. Ahn, H.J. Shin, M.H. Kim, S. Lee, H.S. Kim, J. Myoung, B.T. Kim, S.J. Kim, Current status of epidemiology, diagnosis, therapeutics, and vaccines for novel coronavirus disease 2019 (COVID-19), *J. Microbiol. Biotechnol.* 30 (3) (2020) 313–324, <https://doi.org/10.4014/jmb.2003.03011>.
- [3] D. Cucinotta, M. Vanelli, WHO declares COVID-19 a pandemic, *Acta Biomed.* 91 (1) (2020) 157–160, <https://doi.org/10.23750/abm.v91i1.9397>.
- [4] World-Health-Organization, Coronavirus Disease (COVID-2019) Situation Report - 107, (2020) <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports/>.
- [5] C. Huang, Y. Wang, X. Li, L. Ren, J. Zhao, Y. Hu, L. Zhang, G. Fan, J. Xu, X. Gu, Z. Cheng, T. Yu, J. Xia, Y. Wei, W. Wu, X. Xie, W. Yin, H. Li, M. Liu, Y. Xiao, H. Gao, L. Guo, J. Xie, G. Wang, R. Jiang, Z. Gao, Q. Jin, J. Wang, B. Cao, Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China, *Lancet* 395 (10223) (2020) 497–506, [https://doi.org/10.1016/s0140-6736\(20\)30183-3](https://doi.org/10.1016/s0140-6736(20)30183-3).
- [6] M.J. Shao, L.X. Shang, J.Y. Luo, J. Shi, Y. Zhao, X.M. Li, Y.N. Yang, Myocardial injury is associated with higher mortality in patients with coronavirus disease 2019: a meta-analysis, *J. Geriatr. Cardiol.* 17 (4) (2020) 224–228, <https://doi.org/10.11909/j.issn.1671-5411.2020.04.009>.
- [7] Z. Wu, J.M. McGoogan, Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72314 cases from the Chinese center for disease control and prevention, *Jama* 323 (12) (2020) 1239–1246, <https://doi.org/10.1001/jama.2020.2648>.
- [8] X.H. Yang, R.H. Sun, D.C. Chen, [Diagnosis and treatment of COVID-19: acute kidney injury cannot be ignored], *Zhonghua Yi Xue Za Zhi* 100 (16) (2020) 1205–1208, <https://doi.org/10.3760/cma.j.cn.112137-20200229-00520>.
- [9] H. Rabb, Kidney diseases in the time of COVID-19: major challenges to patient care, *J. Clin. Invest.* Jun 1;130 (6) (2020) 2749–2751, <https://doi.org/10.1172/jci138871>.
- [10] J.J. Ng, Y. Luo, K. Phua, A. Choong, Acute kidney injury in hospitalized patients with coronavirus disease 2019 (COVID-19): a meta-analysis, *J. Infect.* May 8;S0163-4453 (20) (2020), <https://doi.org/10.1016/j.jinf.2020.05.009>.
- [11] X. Xu, S. Nie, Z. Liu, C. Chen, G. Xu, Y. Zha, J. Qian, B. Liu, S. Han, A. Xu, X. Xu, F.F. Hou, Epidemiology and clinical correlates of AKI in Chinese hospitalized adults, *Clin. J. Am. Soc. Nephrol.* 10 (9) (2015) 1510–1518, <https://doi.org/10.2215/cjn.02140215>.
- [12] Z. Mou, X. Zhang, AKI during COVID-19 infection: low incidence, high risk of death, medRxiv 04.29.20079038 (2020), <https://doi.org/10.1101/2020.04.29.20079038>.
- [13] Y. Cheng, R. Luo, K. Wang, M. Zhang, Z. Wang, L. Dong, J. Li, Y. Yao, S. Ge, G. Xu, Kidney disease is associated with in-hospital death of patients with COVID-19, *Kidney Int.* 97 (5) (2020) 829–838, <https://doi.org/10.1016/j.kint.2020.03.005>.
- [14] K.H. Chu, W.K. Tsang, C.S. Tang, M.F. Lam, F.M. Lai, K.F. To, K.S. Fung, H.L. Tang, W.W. Yan, H.W. Chan, T.S. Lai, K.L. Tong, K.N. Lai, Acute renal impairment in coronavirus-associated severe acute respiratory syndrome, *Kidney Int.* 67 (2) (2005) 698–705, <https://doi.org/10.1111/j.1523-1755.2005.67130.x>.
- [15] F. Pacciarini, S. Ghezzi, F. Canducci, A. Sims, M. Sampaolo, E. Ferioli, M. Clementi, G. Poli, P.G. Conaldi, R. Baric, E. Vicenzi, Persistent replication of severe acute respiratory syndrome coronavirus in human tubular kidney cells selects for adaptive mutations in the membrane protein, *J. Virol.* 82 (11) (2008) 5137–5144, <https://doi.org/10.1128/jvi.00096-08>.
- [16] D.F. Stroup, J.A. Berlin, S.C. Morton, I. Olkin, G.D. Williamson, D. Rennie, D. Moher, B.J. Becker, T.A. Sipe, S.B. Thacker, Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group, *Jama* 283 (15) (2000) 2008–2012, <https://doi.org/10.1001/jama.283.15.2008>.
- [17] D. Moher, A. Liberati, J. Tetzlaff, D.G. Altman, Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement, *Bmj* 339 (2009) b2535, <https://doi.org/10.1136/bmj.b2535>.
- [18] N. C., Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (7rd Interim Edition), (2020) <http://www.nhc.gov.cn/zygj/s7653p/202003/46c9294a7dfe4cef80dc7f5912eb1989/files/ce3e6945832a438eae415350a8ce964>.
- [19] J.A. Kellum, N. Lameire, Diagnosis, evaluation, and management of acute kidney injury: a KDIGO summary (Part 1), *Crit Care* 17 (1) (2013) 204, <https://doi.org/10.1186/cc11454>.
- [20] J.P. Higgins, S.G. Thompson, J.J. Deeks, D.G. Altman, Measuring inconsistency in meta-analyses, *Bmj* 327 (7414) (2003) 557–560, <https://doi.org/10.1136/bmj.327.7414.557>.
- [21] W. Viechtbauer, M.W. Cheung, Outlier and influence diagnostics for meta-analysis, *Res. Synth. Methods* 1 (2) (2010) 112–125, <https://doi.org/10.1002/jrsm.11>.
- [22] D. Luo, X. Wan, J. Liu, T. Tong, Optimally estimating the sample mean from the sample size, median, mid-range, and/or mid-quartile range, *Stat. Methods Med. Res.* 27 (6) (2018) 1785–1805, <https://doi.org/10.1177/0962280216669183>.
- [23] B.S.G.A. Wells, D. O'Connell, J. Peterson, V. Welch, M. Losos, P. Tugwell, The Newcastle-Ottawa Scale (NOS) for Assessing the Quality of Nonrandomized Studies in Meta-analyses: Ottawa Hospital Research Institute, (2000) [http://www.ohri.ca/programs/clinical\\_epidemiology/oxford.asp](http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp).
- [24] L. Wang, W. He, X. Yu, D. Hu, M. Bao, H. Liu, J. Zhou, H. Jiang, Coronavirus disease 2019 in elderly patients: characteristics and prognostic factors based on 4-week follow-up, *J. Infect.* 80 (6) (2020) 639–645, <https://doi.org/10.1016/j.jinf.2020>.

- 03.019.
- [25] X. Yang, Y. Yu, J. Xu, H. Shu, J. Xia, H. Liu, Y. Wu, L. Zhang, Z. Yu, M. Fang, T. Yu, Y. Wang, S. Pan, X. Zou, S. Yuan, Y. Shang, Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study, *Lancet Respir. Med.* 8 (5) (2020) 475–481, [https://doi.org/10.1016/s2213-2600\(20\)30079-5](https://doi.org/10.1016/s2213-2600(20)30079-5).
- [26] F. Zhou, T. Yu, R. Du, G. Fan, Y. Liu, Z. Liu, J. Xiang, Y. Wang, B. Song, X. Gu, L. Guan, Y. Wei, H. Li, X. Wu, J. Xu, S. Tu, Y. Zhang, H. Chen, B. Cao, Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study, *Lancet* 395 (10229) (2020) 1054–1062, [https://doi.org/10.1016/s0140-6736\(20\)30566-3](https://doi.org/10.1016/s0140-6736(20)30566-3).
- [27] T. Chen, D. Wu, H. Chen, W. Yan, D. Yang, G. Chen, K. Ma, D. Xu, H. Yu, H. Wang, T. Zhang, W. Guo, J. Chen, C. Ding, X. Zhang, J. Huang, M. Han, S. Li, X. Luo, J. Zhao, Q. Ning, Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study, *Bmj* 368 (2020) m1091, <https://doi.org/10.1136/bmj.m1091>.
- [28] X. Luo, H. Xia, W. Yang, B. Wang, T. Guo, J. Xiong, Z. Jiang, Y. Liu, X. Yan, W. Zhou, L. Ye, B. Zhang, Characteristics of patients with COVID-19 during epidemic ongoing outbreak in Wuhan, China, *medRxiv* 03.19 (20033175) (2020), <https://doi.org/10.1101/2020.03.19.20033175>.
- [29] G. Xiao, H. Hu, F. Wu, T. Sha, Q. Huang, H. Li, J. Han, W. Song, Z. Chen, Z. Zeng, Acute kidney injury in patients hospitalized with COVID-19 in Wuhan, China: a single-center retrospective observational study, *medRxiv* 04.06 (20055194) (2020), <https://doi.org/10.1101/2020.04.06.20055194>.
- [30] Y. Deng, W. Liu, K. Liu, Y.Y. Fang, J. Shang, L. Zhou, K. Wang, F. Leng, S. Wei, L. Chen, H.G. Liu, Clinical characteristics of fatal and recovered cases of coronavirus disease 2019 (COVID-19) in Wuhan, China: a retrospective study, *Chin. Med. J. (Engl.)* Jun 5; 133(11) (2020) 1261–1267, <https://doi.org/10.1097/cm9.0000000000000824>.
- [31] S. Richardson, J.S. Hirsch, M. Narasimhan, J.M. Crawford, T. McGinn, K.W. Davidson, D.P. Barnaby, L.B. Becker, J.D. Chelico, S.L. Cohen, J. Cookingham, K. Coppa, M.A. Diefenbach, A.J. Dominello, J. Duer-Hefele, L. Falzon, J. Gitlin, N. Hajizadeh, T.G. Harvin, D.A. Hirschwerk, E.J. Kim, Z.M. Kozel, L.M. Marrast, J.N. Mogavero, G.A. Osorio, M. Qiu, T.P. Zanos, Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area, *Jama* May 26; 323 (20) (2020) 2052–2059, <https://doi.org/10.1001/jama.2020.6775>.
- [32] D. Wang, Y. Yin, C. Hu, X. Liu, X. Zhang, S. Zhou, M. Jian, H. Xu, J. Prowle, B. Hu, Y. Li, Z. Peng, Clinical course and outcome of 107 patients infected with the novel coronavirus, SARS-CoV-2, discharged from two hospitals in Wuhan, China, *Crit. Care* 24 (1) (2020) 188, <https://doi.org/10.1186/s13054-020-02895-02896>.
- [33] A.M. Borobia, A.J. Carcas, F. Arnalich, R. Alvarez-Sala, J. Monserrat, M. Quintana, et al., A cohort of patients with COVID-19 in a major teaching hospital in Europe, *J. Clin. Med.* 9 (6) (2020) 1733, <https://doi.org/10.3390/jcm9061733>.
- [34] Y. Wang, X. Lu, Y. Li, H. Chen, T. Chen, N. Su, F. Huang, J. Zhou, B. Zhang, F. Yan, J. Wang, Clinical course and outcomes of 344 intensive care patients with COVID-19, *Am. J. Respir. Crit. Care Med.* 201 (11) (2020) 1430–1434, <https://doi.org/10.1164/rccm.202003-0736LE>.
- [35] J. Cao, W.J. Tu, W. Cheng, L. Yu, Y.K. Liu, X. Hu, Q. Liu, Clinical Features and Short-term Outcomes of 102 Patients with Corona Virus Disease 2019 in Wuhan, China, *Clin. Infect. Dis.* 71 (15) (2020) 748–755, <https://doi.org/10.1093/cid/ciaa243>.
- [36] J. Zhang, J. Li, L. Su, J. Yang, X. Jiang, N. Jiang, Y. Lei, L. He, Q. Lu, S. Shen, F. Chen, Z. Peng, [Clinical characteristics and risk factors of acute kidney injury in coronavirus disease 2019], *Zhonghua Wei Zhong Bing Ji Jiu Yi Xue* 32 (4) (2020) 407–411, <https://doi.org/10.3760/cma.j.cn1121430-20200302-00198>.
- [37] F. Chen, W. Sun, S. Sun, Z. Li, Z. Wang, L. Yu, Clinical characteristics and risk factors for mortality among inpatients with COVID-19 in Wuhan, China, *Clin. Transl. Med.* Jun (04) (2020), <https://doi.org/10.1002/ctm.2.40>.
- [38] J. Pelayo, K.B. Lo, R. Bhargava, F. Gul, E. Peterson, R. DeJoy Iii, G.F. Salacup, J. Albano, A. Gopalakrishnan, Z. Azmaiparashvili, G. Patarroyo-Aponte, J. Rangaswami, Clinical characteristics and outcomes of community- and hospital-acquired acute kidney injury with COVID-19 in a US inner city hospital system, *Cardioresenal Med.* 10 (4) (2020) 223–231, <https://doi.org/10.1159/000509182>.
- [39] K.S. Hong, K.H. Lee, J.H. Chung, K.C. Shin, E.Y. Choi, H.J. Jin, J.G. Jang, W. Lee, J.H. Ahn, Clinical features and outcomes of 98 patients hospitalized with SARS-CoV-2 infection in Daegu, South Korea: a brief descriptive study, *Yonsei Med. J.* 61 (5) (2020) 431–437, <https://doi.org/10.3349/ymj.2020.61.5.431>.
- [40] G. Pei, Z. Zhang, J. Peng, L. Liu, C. Zhang, C. Yu, Z. Ma, Y. Huang, W. Liu, Y. Yao, R. Zeng, G. Xu, Renal involvement and early prognosis in patients with COVID-19 pneumonia, *J. Am. Soc. Nephrol.* Jun;31 (6) (2020) 1157–1165, <https://doi.org/10.1681/asn.2020030276>.
- [41] S. Xu, L. Fu, J. Fei, H.-X. Xiang, Y. Xiang, Z.-X. Tan, M.-D. Li, F.-F. Liu, Y. Li, M.-F. Han, X.-Y. Li, D.-X. Yu, H. Zhao, D.-X. Xu, Acute kidney injury at early stage as a negative prognostic indicator of patients with COVID-19: a hospital-based retrospective analysis, *medRxiv* 03.24.20042408 (2020), <https://doi.org/10.1101/2020.03.24.20042408>.
- [42] J.S. Hirsch, J.H. Ng, D.W. Ross, P. Sharma, H.H. Shah, R.L. Barnett, A.D. Hazzan, S. Fishbane, K.D. Jhaveri, Acute kidney injury in patients hospitalized with COVID-19, *Kidney Int.* 98 (1) (2020) 209–218, <https://doi.org/10.1016/j.kint.2020.05.006>.
- [43] A. Alshukry, H. Ali, Y. Ali, T. Al-Taweel, M. Abu-farha, J. AbuBaker, S. Devarajan, A.A. Dashti, A. Bandar, H. Taleb, A. Al Bader, N.Y. Aly, E. Al-Ozairi, F. Al-Mulla, M. Bu Abbas, Clinical characteristics of Coronavirus Disease 2019 (COVID-19) patients in Kuwait, *medRxiv* 06.14.20131045 (2020), <https://doi.org/10.1101/2020.06.14.20131045>.
- [44] S. Trabulus, C. Karaca, I.I. Balkan, M.T. Dincer, A. Murt, S.G. Ozcan, R. Karaali, B. Mete, A. Bakir, M.A. Kuskucu, M.R. Altıparmak, F. Tabak, N. Seyahi, Kidney function on admission predicts in-hospital mortality in COVID-19, *medRxiv* 06.18.20134627 (2020), <https://doi.org/10.1101/2020.06.18.20134627>.
- [45] X. Li, S. Xu, M. Yu, K. Wang, Y. Tao, Y. Zhou, J. Shi, M. Zhou, B. Wu, Z. Yang, C. Zhang, J. Yue, Z. Zhang, H. Renz, X. Liu, J. Xie, M. Xie, J. Zhao, Risk factors for severity and mortality in adult COVID-19 inpatients in Wuhan, *J. Allergy Clin. Immunol.* Jul;146 (1) (2020) 110–118, <https://doi.org/10.1016/j.jaci.2020.04.006>.
- [46] S. Wan, Y. Xiang, W. Fang, Y. Zheng, B. Li, Y. Hu, C. Lang, D. Huang, Q. Sun, Y. Xiong, X. Huang, J. Lv, Y. Luo, L. Shen, H. Yang, G. Huang, R. Yang, Clinical features and treatment of COVID-19 patients in northeast Chongqing, *J. Med. Virol.* Jul;92 (7) (2020) 797–806, <https://doi.org/10.1002/jmv.25783>.
- [47] W.J. Guan, Z.Y. Ni, Y. Hu, W.H. Liang, C.Q. Ou, J.X. He, L. Liu, H. Shan, C.L. Lei, D.S.C. Hui, B. Du, L.J. Li, G. Zeng, K.Y. Yuen, R.C. Chen, C.L. Tang, T. Wang, P.Y. Chen, J. Xiang, S.Y. Li, J.L. Wang, Z.J. Liang, Y.X. Peng, L. Wei, Y. Liu, Y.H. Hu, P. Peng, J.M. Wang, J.Y. Liu, Z. Chen, G. Li, Z.J. Zheng, S.Q. Qiu, J. Luo, C.J. Ye, S.Y. Zhu, N.S. Zhong, Clinical characteristics of coronavirus disease 2019 in China, *N. Engl. J. Med.* 382 (18) (2020) 1708–1720, <https://doi.org/10.1056/NEJMoa2002032>.
- [48] S. Yan, X. Song, F. Lin, H. Zhu, X. Wang, M. Li, et al., Clinical characteristics of coronavirus disease 2019 in Hainan, China, *medRxiv* 03.19.20038539 (2020), <https://doi.org/10.1101/2020.03.19.20038539>.
- [49] W. Zhao, S. Yu, X. Zha, N. Wang, Q. Pang, T. Li, A. Li, Clinical characteristics and durations of hospitalized patients with COVID-19 in Beijing: a retrospective cohort study, *medRxiv* 03.13.20035436 (2020), <https://doi.org/10.1101/2020.03.13.20035436>.
- [50] D. Wang, B. Hu, C. Hu, F. Zhu, X. Liu, J. Zhang, B. Wang, H. Xiang, Z. Cheng, Y. Xiong, Y. Zhao, Y. Li, X. Wang, Z. Peng, Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China, *Jama* Mar 17; 323 (11) (2020) 1061–1069, <https://doi.org/10.1001/jama.2020.1585>.
- [51] G. Zhang, C. Hu, L. Luo, F. Fang, Y. Chen, J. Li, Z. Peng, H. Pan, Clinical features and short-term outcomes of 221 patients with COVID-19 in Wuhan, China, *J. Clin. Virol.* 127 (2020) 104364, <https://doi.org/10.1016/j.jcv.2020.104364>.
- [52] L. Hu, S. Chen, Y. Fu, Z. Gao, H. Long, H.-w. Ren, et al., Risk factors associated with clinical outcomes in 323 COVID-19 patients in Wuhan, China, *Clin Infect Dis.* May 3 (ciaa539) (2020), <https://doi.org/10.1093/cid/ciaa539>.
- [53] P. Shi, G. Ren, J. Yang, Z. Li, S. Deng, M. Li, S. Wang, X. Xu, F. Chen, Y. Li, C. Li, X. Yang, Z. Xie, Z. Wu, M. Chen, Clinical characteristics of imported and second-generation COVID-19 cases outside Wuhan, China: a multicenter retrospective study, *medRxiv* 04.19.20071472 (2020), <https://doi.org/10.1101/2020.04.19.20071472>.
- [54] Z. Li, M. Wu, J. Yao, J. Guo, X. Liao, S. Song, J. Li, G. Duan, Y. Zhou, X. Wu, Z. Zhou, T. Wang, M. Hu, X. Chen, Y. Fu, C. Lei, H. Dong, C. Xu, Y. Hu, M. Han, Y. Zhou, H. Jia, X. Chen, J. Yan, Caution on kidney dysfunctions of COVID-19 patients, *medRxiv* 02.08.20021212 (2020), <https://doi.org/10.1101/2020.02.08.20021212>.
- [55] Y.L. Qiang Li, Jianliang Zhang, Weixia Li, Xiaoyu Zhang, Yinpeng Jin, Li Li, Qingchun Fu, Yuxian Huang, Hongzhou Lu, Liang Chen, Clinical Characteristics of SARS-CoV-2 Infections Involving 325 Hospitalized Patients outside Wuhan, *Research Square* 24 March, (2020), <https://doi.org/10.21203/rs.3.rs-18699/v1>.
- [56] X.Y. Zhao, X.X. Xu, H.S. Yin, Q.M. Hu, T. Xiong, Y.Y. Tang, A.Y. Yang, B.P. Yu, Z.P. Huang, Clinical characteristics of patients with 2019 coronavirus disease in a non-Wuhan area of Hubei Province, China: a retrospective study, *BMC Infect. Dis.* 20 (1) (2020) 311, <https://doi.org/10.1186/s12879-020-05010-w>.
- [57] L. Yang, J. Liu, R. Zhang, M. Li, Z. Li, X. Zhou, C. Hu, F. Tian, F. Zhou, Y. Lei, Epidemiological and clinical features of 200 hospitalized patients with corona virus disease 2019 outside Wuhan, China: a descriptive study, *J. Clin. Virol.* 129 (2020) 104475, <https://doi.org/10.1016/j.jcv.2020.104475>.
- [58] Q. Yang, L. Xie, W. Zhang, L. Zhao, H. Wu, J. Jiang, J. Zou, J. Liu, J. Wu, Y. Chen, J. Wu, Analysis of the clinical characteristics, drug treatments and prognoses of 136 patients with coronavirus disease 2019, *J. Clin. Pharm. Ther.* 45 (4) (2020) 609–616, <https://doi.org/10.1111/jcpt.13170>.
- [59] M.G. Argenziano, S.L. Bruce, C.L. Slater, J.R. Tiao, M.R. Baldwin, R.G. Barr, B.P. Chang, K.H. Chau, J.J. Choi, N. Gavin, P. Goyal, A.M. Mills, A.A. Patel, M.S. Romney, M.M. Safford, N.W. Schluger, S. Sengupta, M.E. Sobieszczyk, J.E. Zucker, P.A. Asadourian, F.M. Bell, R. Boyd, M.F. Cohen, M.I. Colquhoun, L.A. Colville, J.H. de Jonge, L.B. Dershowitz, S.A. Dey, K.A. Eisman, Z.P. Girvin, D.T. Goni, A.A. Harb, N. Herzik, S. Householder, L.E. Karaaslan, H. Lee, E. Lieberman, A. Ling, R. Lu, A.Y. Shou, A.C. Sisti, Z.E. Snow, C.P. Sperring, Y. Xiong, H.W. Zhou, K. Natarajan, G. Hripscak, R. Chen, Characterization and clinical course of 1000 patients with coronavirus disease 2019 in New York: retrospective case series, *Bmj* 369 (2020) m1996, <https://doi.org/10.1136/bmj.m1996>.
- [60] A. Sisó-Almirall, B. Kostov, M. Mas-Heredia, S. Vilanova-Rotllan, E. Sequeira-Aymar, M. Sans-Corrales, E. Sant-Arderiu, L. Cayuelas-Redondo, A. Martínez-Pérez, N. García Plana, A. Anguita-Guimet, J. Benavent-Àreu, Prognostic factors in Spanish COVID-19 patients: a case series from Barcelona, *medRxiv* 06.18.20134510 (2020), <https://doi.org/10.1101/2020.06.18.20134510>.
- [61] J.H. Lim, S.H. Park, Y. Jeon, J.H. Cho, H.Y. Jung, J.Y. Choi, C.D. Kim, Y.H. Lee, H. Seo, J. Lee, K.T. Kwon, S.W. Kim, H.H. Chang, Y.L. Kim, Fatal outcomes of COVID-19 in patients with severe acute kidney injury, *J. Clin. Med.* 9 (6) (2020), <https://doi.org/10.3390/jcm9061718>.
- [62] Y.-F. Liu, Z. Zhang, X.-L. Pan, G.-L. Xing, Y. Zhang, Z.-S. Liu, S.-H. Tu, The chronic kidney disease and acute kidney injury involvement in COVID-19 pandemic: a systematic review and meta-analysis, *medRxiv* 04.28.20083113 (2020), <https://doi.org/10.1101/2020.04.28.20083113>.

- [doi.org/10.1101/2020.04.28.20083113](https://doi.org/10.1101/2020.04.28.20083113).
- [63] N. Chen, M. Zhou, X. Dong, J. Qu, F. Gong, Y. Han, Y. Qiu, J. Wang, Y. Liu, Y. Wei, J. Xia, T. Yu, X. Zhang, L. Zhang, Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study, *Lancet* 395 (10223) (2020) 507–513, [https://doi.org/10.1016/s0140-6736\(20\)30211-30217](https://doi.org/10.1016/s0140-6736(20)30211-30217).
- [64] X. Zhao, B. Zhang, P. Li, C. Ma, J. Gu, P. Hou, Z. Guo, H. Wu, Y. Bai, Incidence, clinical characteristics and prognostic factor of patients with COVID-19: a systematic review and meta-analysis, *medRxiv* 03.17.20037572 (2020), <https://doi.org/10.1101/2020.03.17.20037572>.
- [65] V. Fanelli, M. Fiorentino, V. Cantaluppi, L. Gesualdo, G. Stallone, C. Ronco, G. Castellano, Acute kidney injury in SARS-CoV-2 infected patients, *Crit Care* 24 (1) (2020) 155, <https://doi.org/10.1186/s13054-020-02872-z>.
- [66] P. Zhou, X.L. Yang, X.G. Wang, B. Hu, L. Zhang, W. Zhang, H.R. Si, Y. Zhu, B. Li, C.L. Huang, H.D. Chen, J. Chen, Y. Luo, H. Guo, R.D. Jiang, M.Q. Liu, Y. Chen, X.R. Shen, X. Wang, X.S. Zheng, K. Zhao, Q.J. Chen, F. Deng, L.L. Liu, B. Yan, F.X. Zhan, Y.Y. Wang, G.F. Xiao, Z.L. Shi, A pneumonia outbreak associated with a new coronavirus of probable bat origin, *Nature* 579 (7798) (2020) 270–273, <https://doi.org/10.1038/s41586-020-2012-2017>.
- [67] C. Fan, K. Li, Y. Ding, W.L. Lu, J. Wang, ACE2 expression in kidney and testis may cause kidney and testis damage after 2019-nCoV infection, *medRxiv* 02.12.20022418 (2020), <https://doi.org/10.1101/2020.02.12.20022418>.
- [68] B. Diao, C. Wang, R. Wang, Z. Feng, Y. Tan, H. Wang, C. Wang, L. Liu, Y. Liu, Y. Liu, G. Wang, Z. Yuan, L. Ren, Y. Wu, Y. Chen, Human kidney is a target for novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, *medRxiv* 03.04.20031120 (2020), <https://doi.org/10.1101/2020.03.04.20031120>.
- [69] X.W. Pan, D. Xu, H. Zhang, W. Zhou, L.H. Wang, X.G. Cui, Identification of a potential mechanism of acute kidney injury during the COVID-19 outbreak: a study based on single-cell transcriptome analysis, *Intensive Care Med.* Jun;46 (6) (2020) 1114–1116, <https://doi.org/10.1007/s00134-020-06026-1>.
- [70] H. Su, M. Yang, C. Wan, L.X. Yi, F. Tang, H.Y. Zhu, F. Yi, H.C. Yang, A.B. Fogo, X. Nie, C. Zhang, Renal histopathological analysis of 26 postmortem findings of patients with COVID-19 in China, *Kidney Int.* Jul;98 (1) (2020) 219–227, <https://doi.org/10.1016/j.kint.2020.04.003>.
- [71] K. Singbartl, C.L. Formeck, J.A. Kellum, Kidney-immune system crosstalk in AKI, *Semin. Nephrol.* 39 (1) (2019) 96–106, <https://doi.org/10.1016/j.semnephrol.2018.10.007>.
- [72] P. Gabarre, G. Dumas, T. Dupont, M. Darmon, E. Azoulay, L. Zafrani, Acute kidney injury in critically ill patients with COVID-19, *Intensive Care Med.* 46 (7) (2020) 1339–1348, <https://doi.org/10.1007/s00134-020-06153-06159>.
- [73] D. Hertzberg, L. Rydén, J.W. Pickering, U. Sartipy, M.J. Holzmänn, Acute kidney injury—an overview of diagnostic methods and clinical management, *Clin. Kidney J.* 10 (3) (2017) 323–331, <https://doi.org/10.1093/ckj/sfx003>.
- [74] S.S. Jean, P.I. Lee, P.R. Hsueh, Treatment options for COVID-19: the reality and challenges, *J. Microbiol. Immunol. Infect.* 53 (3) (2020) 436–443, <https://doi.org/10.1016/j.jmii.2020.03.034>.