



Risk Factors for Acute Kidney Injury in Adult Patients With COVID-19: A Systematic Review and Meta-Analysis

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Background and Objective: Since December 2019, coronavirus disease 2019 (COVID-19) has spread rapidly around the world. Studies found that the incidence of acute kidney injury (AKI) in COVID-19 patients was more than double the incidence of AKI in non-COVID-19 patients. Some findings confirmed that AKI is a strong independent risk factor for mortality in patients with COVID-19 and is associated with a three-fold increase in the odds of in-hospital mortality. However, little information is available about AKI in COVID-19 patients. This study aimed to analyse the risk factors for AKI in adult patients with COVID-19.

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Cai X, Wu G, Zhang J and Yang L (2021) Risk Factors for Acute Kidney Injury in Adult Patients With COVID-19: A Systematic Review and Meta-Analysis. Front. Med. 8:719472. doi: 10.3389/fmed.2021.719472 **Methods:** A systematic literature search was conducted in PubMed, EMBASE, Web of Science, the Cochrane Library, CNKI, VIP and WanFang Data from 1 December 2019 to 30 January 2021. We extracted data from eligible studies to compare the effects of age, sex, chronic diseases and potential risk factors for AKI on the prognosis of adult patients with COVID-19.

Results: In total, 38 studies with 42,779 patients were included in this analysis. The meta-analysis showed that male sex (OR = 1.37), older age (MD = 5.63), smoking (OR = 1.23), obesity (OR = 1.12), hypertension (OR=1.85), diabetes (OR=1.71), pneumopathy (OR = 1.36), cardiovascular disease (OR = 1.98), cancer (OR = 1.26), chronic kidney disease (CKD) (OR = 4.56), mechanical ventilation (OR = 8.61) and the use of vasopressors (OR = 8.33) were significant risk factors for AKI (P < 0.05).

Conclusions: AKI is a common and serious complication of COVID-19. Overall, male sex, age, smoking, obesity, hypertension, diabetes, pneumopathy, cardiovascular disease, cancer, CKD, mechanical ventilation and the use of vasopressors were independent risk factors for AKI in adult patients with COVID-19. Clinicians need to be aware of these risk factors to reduce the incidence of AKI.

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Keywords: risk factor, acute kidney injury, COVID-19, systematic review, meta-analysis

INTRODUCTION

Since December 2019, a novel coronavirus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused an international outbreak of respiratory illness described as coronavirus disease 2019 (COVID-19). As of 30 January 2021, approximately 102,638,000 cases have been confirmed worldwide, and 2,216,546 deaths have occurred.

The main manifestation of COVID-19 is acute respiratory infection, and the renal, cardiovascular, digestive, blood and nervous systems may be simultaneously involved (1, 2). Acute kidney injury (AKI) is a common condition in critically ill patients, particularly in those with serious infections, and has been found to be associated with substantial morbidity and mortality (3). Current evidence suggests four broad mechanisms of renal injury: hypovolaemia, acute respiratory distress syndrome (ARDS), cytokine storms and direct viral invasion, as seen on renal findings during autopsies (4). Most patients have significant insensible fluid loss due to high-grade pyrexia and tachypnoea on presentation (5). These patients are particularly prone to developing pre-renal AKI. Impaired gaseous exchange with hypercapnia leads to a reduction in the renal vasodilatory response and renal blood flow, with altered diuresis and increased oxygen utilisation in the proximal tubule. Severe hypoxemia also causes a reduction in renal blood flow with possible activation of the hypoxia-inducible factor system, influencing lung and kidney outcomes (6). Observational data from a subgroup of patients with COVID-19 suggested the development of features consistent with cytokine storm syndrome triggered by SARS-CoV-2 and characterised by high serum ferritin, D-dimer, lactate dehydrogenase, and IL-6 levels; cytopenia; ARDS; acute cardiac injury; abnormal liver function test results; and coagulation abnormalities (7). In addition, this hyperinflammatory state could cause AKI.

Recently, several clinical studies have demonstrated that AKI is one of the most common complications in patients with COVID-19, and several studies have shown that the mortality rate of COVID-19 patients with AKI is incredibly high, ranging from 8 to 23% (8). It has also been reported that the incidence rate of AKI in COVID-19 patients ranges from 0.5 to 29% depending on disease severity. The AKI incidence rate was found to be 0.1-2% in patients with for mild cases, 3-3.2% in those with severe cases, and up to 8.3-29% in critically ill patients who needed to be admitted to the ICU (9). AKI prolongs the length of hospital stay, increases the cost of hospitalisation, and even increases the risk of death. Therefore, if we can identify the risk factors for AKI in patients with COVID-19 early and initiate preventive measures, we could improve the prognosis of patients. In this article, we performed a systematic review and meta-analysis to explore the characteristics of high-risk groups to provide reliable evidence that can be used to guide clinical practice.

METHODS

Inclusion and Exclusion Criteria

Make inclusion and exclusion criteria according to PECOS principles.

TABLE 1 | Search strategy.

Databases	PubMed, EMBASE, Web of Science, Cochrane, CNKI, VIP, and WanFang Data
Data	1 December 2019 to 30 January 2021
#1	"2019-nCoV" or "SARS-CoV-2" or "COVID-19" or "coronavirus disease 2019"
#2	"acute kidney injury" or "acute kidney failure" or "acute renal failure" or "acute renal injury" or "AKI"
#3	"risk factor" or "influence factor"
Search	#1 and #2 and #3

Inclusion criteria:

Population = patients age > 16 years old with confirmed Covid-19 through any detection methods.

Exposure = patients with one of the following conditions: smoking, obesity, hypertension, diabetes, pneumopathy, cardiovascular disease, cancer, chronic kidney disease (CKD), mechanical ventilation and the use of vasopressors.

Comparison/Control = patients without these following conditions: smoking, obesity, hypertension, diabetes, pneumopathy, cardiovascular disease, cancer, chronic kidney disease (CKD), mechanical ventilation, and the use of vasopressors.

Outcomes = the prevalence of acute kidney injury (AKI) in both group. AKI was diagnosed by using 2012 Kidney Disease Improving Global Outcomes (KDIGO) guidelines.

Study Design = The study types were randomised controlled trials or non-randomised studies (horizontal cross-sectional studies, case-control studies, and cohort studies).

Exclusion criteria: Studies were excluded if the subjects were not representative of the general population, the diagnostic criteria for COVID-19 were not defined, the diagnostic criteria for AKI were not defined, and there was no control group. Studies that were unpublished or duplicate reports and those with incomplete information or logical errors were excluded. Reviews, case reports, conference abstracts, animal studies and basic research were also excluded.

Search Strategy

A systematic literature search was conducted in PubMed, EMBASE, Web of Science, Cochrane, CNKI, VIP, and WanFang Data from 1 December 2019 to 30 January 2021. The following Medical Subject Heading terms and free words were used, as shown in **Table 1**: "2019-nCoV" or "SARS-CoV-2" or "COVID-19" or "coronavirus disease 2019" and "acute kidney injury" or "acute kidney failure" or "acute renal failure" or "acute renal injury" or "AKI" and "risk factor" or "influence factor."

Study Selection and Data Collection

Two investigators independently scanned all the titles and abstracts to identify studies that met the inclusion criteria, and they extracted the relevant data from those studies. Any discrepancies between the reviewers were resolved by discussion with a third reviewer. The titles, abstracts and full texts of all initially identified documents were assessed, and those reporting AKI in COVID-19 patients were included in this analysis. The reference lists of all identified studies were also analysed to identify additional eligible studies. Data were collected and entered into a spreadsheet. We extracted the following variables: author, study period, location, and patient age, sex and clinical characteristics. The Newcastle-Ottawa Scale (NOS) was used as a bias assessment tool for cohort studies and case-control studies, and a score \geq 7 indicated good quality. We performed sensitivity analyses to identify which studies caused the observed heterogeneity. The exclusion of each study one at a time did not significantly alter the results for each factor or the heterogeneity.

Statistical Analysis

The meta-analysis was performed using RevMan 5.4. Mantel-Haenszel was used for statistical method of dichotomous, and Inverse Variance was used for continuous. The mean differences (MDs) and 95% confidence intervals (CIs) were calculated for continuous data. The odds ratios (ORs) and 95% CIs were calculated for dichotomous data. The I² statistic was used to assess the statistical heterogeneity. If I² \leq 50%, there is little heterogeneity. Otherwise, it can be considered that there is large heterogeneity. Since the included studies were not RCT study, random-effects model was used for analyses. Potential study bias was assessed using funnel plots.

RESULTS

Search Results and Characteristics of the Included Studies

The flow of studies through the analysis is presented in **Figure 1**. A total of 38 eligible studies involving 42,779 patients were ultimately enrolled in our study, including 18 studies from Asia, 8 studies from Europe and 12 studies from America. The characteristics of the included studies and bias risk assessment results are described in **Table 2**. About 33 studies scored \geq 7 by using NOS tool. This indicated that most studies are good quality and the risk of bias assessment is low.

Analysis of Risk Factors for AKI in COVID-19 Patients General Risk Factors

All studies analysed the relationship between sex and the development of AKI in COVID-19 patients, and 36 studies were included after the sensitivity analysis. The I² test showed I² = 40%, indicating that no heterogeneity existed among the studies. The random-effects model was used to pool the data, yielding an OR of 1.37 (95% CI 1.25–1.49, Z = 7.1, P < 0.00001), suggesting that male sex is a risk factor for AKI (**Figure 2A**).

Thirty-two studies analysed the relationship between age and the development of AKI in COVID-19 patients, and 27 studies were included after the sensitivity analysis. The I² test showed I² = 80%, indicating that a high degree of heterogeneity existed among the studies. Therefore, the studies were analysed in subgroups stratified by region. The I² statistic was <50% in all subgroups. The random-effects model was used to pool the data

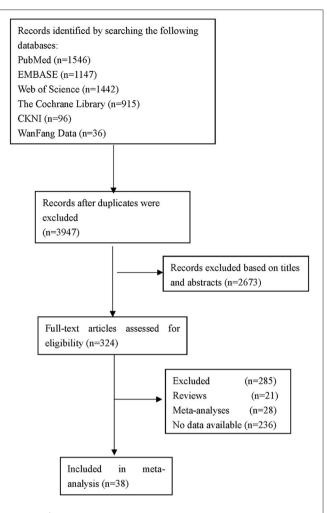


FIGURE 1 | Flow diagram of the selection of studies.

(**Figure 2B**). The MD was 8.17 in the Americas (95% CI 7.53–8.81, Z = 25.06, P < 0.00001), 3.31 in Europe (95% CI 1.42–5.2, Z = 3.43, P = 0.0006), and 3.7 in Asia (95% CI 2.56–4.84, Z = 6.36, P < 0.00001), suggesting that age is a risk factor for AKI; the older the patient is, the higher the risk of AKI.

Only 10 studies analysed the relationship between smoking and the development of AKI in COVID-19 patients. The I² test showed I² = 34%, indicating that no heterogeneity existed among the studies. The random-effects model was used to pool the data, yielding an OR of 1.23 (95% CI 1.07–1.42, Z = 2.85, P = 0.004), suggesting that smoking is a risk factor for AKI (**Figure 2C**).

Ten studies analysed the relationship between obesity and the development of AKI in COVID-19 patients. The I² test showed I² = 42%, indicating slight heterogeneity among the studies. The random-effects model was used to pool the data, yielding an OR of 1.12 (95% CI 1.01–1.25, Z = 2.15, P = 0.03), suggesting that obesity is a risk factor for AKI (**Figure 2D**).

Comorbidities

Thirty-four studies analysed the relationship between hypertension and the development of AKI in COVID-19

TABLE 2 | Characteristics of the 39 studies included in the meta-analysis.

References	Country	Type of study	NOS score	AKI	Non-AKI	Age	Male (n, %)	CKD (%)	Hypertension (%)	Diabetes (%)	COPD (%)	CVD (%)	Cancer (%)
Xu et al. (10)	China	Case-control	5	18	44	62.9 ± 15.3	39 (62.9)	2 (3.2)	26 (41.9)	9 (14.5)	5 (8.1)	11 (17.7)	3 (4.8)
Doher et al. (11)	Brazil	Cohort	8	101	100	64 (52,80)	123 (61.2)	NA	98 (48.8)	64 (31.8)	19 (9.5)	16 (8.0)	NA
Kolhe et al. (12)	England	Cohort	7	304	857	NA	657 (56.6)	224 (19.3)	NA	255 (22.0)	311 (26.8)	117 (10.1)	102 (8.8)
Li et al. (13)	China	Cohort	7	48	59	70	69 (64.5)	5 (4.7)	73 (68.2)	22 (20.6)	23 (21.5)	33 (30.8)	NA
Bowe et al. (14)	United States	Cohort	8	1,655	3,561	70 (61,76)	4,908 (94)	NA	3,985 (76)	2,537 (49)	1,302 (25)	1,588 (30)	799 (15)
Zahid et al. (15)	United States	Cohort	8	128	341	66 (55,75)	268 (57.1)	50 (10.7)	323 (68.9)	219 (46.7)	34 (7.3)	74 (15.8)	31 (6.6)
Taher et al. (16)	Bahrain	Cohort	7	29	44	54.3 ± 13.5	44 (60.3)	6 (8.2)	31 (42.5)	33 (45.2)	NA	9 (12.3)	5 (6.8)
Chan et al. (17)	United States	Case-control	7	1,406	1,829	66.5 (55.6,77.8)	1,868(57.7)	323 (10)	1,193 (36.9)	800 (24.7)	NA	281 (8.7)	NA
Hirsch et al. (18)	United States	Cohort	8	1,993	3,456	64.0 (52.0, 75.0)	3,317 (60.9)	NA	3,037 (55.7)	1,797 (33.0)	296 (5.4)	600 (11.0)	327 (6.0)
Joseph et al. (19)	France	Cohort	7	81	19	59 (53,67)	70 (70.0)	29 (29.0)	56 (56.0)	30 (30.0)	2 (2.0)	15 (15)	NA
Cui et al. (20)	China	Case-control	7	21	95	NA	66(56.9)	5(4.3)	38 (32.8)	28 (24.1)	14 (12.1)	48 (41.4)	NA
Louis et al. (21)	France	Case-control	7	80	101	NA	127 (70.0)	13 (7.2)	132 (73.0)	54 (30.0)	22 (12.0)	52 (29.0)	22(12.0)
Yan et al. (22)	China	Cohort	8	115	767	71 (68,77)	440(49.9)	83(9.4)	NA	277 (31.4)	86 (9.8)	515 (58.2)	41(4.7)
Chan et al. (23)	United States	Case-control	8	1,835	2,158	64 (56,78)	2,289 (57.3)	420 (11.0)	1,527 (38.0)	1,019 (26.0)	NA	396 (10.0)	NA
Tan et al. (24)	China	Cohort	8	40	377	45.2 ± 17.7	198 (47.3)	NA	55 (13.2)	19 (4.6)	16 (3.8)	26 (6.2)	6 (1.4)
Hamilton et al. (25)	England	Case-control	7	210	822	71 (56,83)	569 (55.1)	144 (14.0)	NA	134(13.0)	259 (25.1)	129 (12.5)	72 (7.0)
Lee et al. (26)	United States	Cohort	8	294	708	66 (53,76)	619 (62.0)	138 (14.0)	597 (60.0)	378 (38.0)	81 (8.0)	131 (13.0)	NA
Rubin et al. (27)	France	Cohort	8	57	14	61.2±12.2	55 (77.0)	NA	43 (61.0)	21 (30.0)	8 (11.0)	17 (24.0)	NA
Xu et al. (28)	China	Cohort	7	263	408	65 (56,73)	434 (65.0)	NA	287 (43.0)	131 (20.0)	37 (6.0)	87 (13.0)	20 (3.0)
Pelayo et al. (29)	United States	Case-control	7	110	113	NA	115(51.6)	NA	180 (80.7)	104 (46.6)	27 (12.1)	59 (26.5)	NA
Li et al. (30)	China	Cohort	7	48	59	70 (64,78)	69 (64.5)	5 (4.7)	73 (68.2)	22 (20.6)	23 (21.5)	33 (30.8)	NA
Xia et al. (31)	China	Cohort	8	41	40	66.6±11.4	54 (66.7)	3 (3.7)	43 (53.1)	19 (23.5)	NA	17 (21.0)	NA
Luther et al. (32)	Sweden	Case-control	6	51	6	NA	44(77.2)	NA	30 (52.6)	16 (28.1)	14 (24.6)	6 (10.5)	4(7.0)
Peng et al. (33)	China	Case-control	6	285	3,735	61 (50,69)	1,912 (47.6)	100 (2.5)	852 (21.2)	424 (10.5)	NA	270 (6.7)	NA
Wang et al. (34)	China	Case-control	7	136	139	69 (62,77)	161 (58.4)	16 (5.8)	150 (54.5)	62 (22.5)	37 (13.5)	35 (12.7)	NA
Lim et al. (35)	Korea	Case-control	8	30	130	NA	86(53.8)	NA	77 (48.1)	50 (31.3)	16 (10.0)	31 (19.4)	26(16.3)
Wang et al. (36)	China	Cohort	7	12	104	62 (55,69)	62 (53.4)	NA	47 (40.5)	20 (17.2)	3 (2.6)	12 (10.3)	10 (8.6)
Nimkar et al. (37)	United States	Case-control	8	179	148	71 (59,82)	182 (55.7)	40 (12.2)	209 (63.9)	139 (42.5)	44 (13.5)	98 (29.9)	66(20.2)
Hectors et al. (38)	United States	Case-control	7	16	29	65 (24,97)	23 (51.0)	NA	26 (57.8)	13 (28.9)	NA	11 (24.4)	NA
Ng et al. (39)	United States	Cohort	8	3,854	5,803	NA	5,747 (59.5)	492 (5.1)	5,730 (59.3)	3,469 (35.9)	610 (6.3)	2,040 (21.1)	754(7.8)
Fominskiy et al. (40)	Italy	Case-control	8	72	24	NA	80 (83.3)	6 (6.3)	42 (43.8)	16 (16.7)	7 (7.3)	13 (13.5)	3(3.1)
Hansrivijit et al. (41)	United States	Cohort	8	115	168	64.1 ± 15.9	159 (56.2)	66 (23.3)	189 (66.8)	108 (38.2)	73 (25.8)	53 (18.7)	NA
Paek et al. (42)	Korea	Case-control	6	28	676	NA	210 (29.8)	NA	226 (32.1)	123 (17.5)	NA	NA	NA
Chaibi et al. (43)	European	Case-control	7	55	156	60.0 ± 11.0	163 (77.0)	18 (8.0)	107 (51.0)	78 (37.0)	NA	28 (13.0)	NA
Sang et al. (44)	China	Case-control	8	92	118	64 (56,71)	131 (62.4)	10 (4.8)	98 (46.7)	44 (21.0)	5 (2.4)	23 (11.0)	14 (6.7)
Cheng et al. (45)	China	Cohort	8	99	1239	63 (50,71)	711 (51.0)	21 (2.0)	499 (36.0)	241 (17.0)	77 (6.0)	NA	62 (5.0)
Lin et al. (46)	China	Case-control	6	6	27	59.9 ± 12.8	23 (69.7)	3 (9.1)	15 (45.5)	6 (18.2)	NA	2 (6.1)	3 (9.1)
Zhang et al. (47)	China	Cohort	7	37	357	56 (42,67)	186 (47.2)	NA	115 (29.2)	47 (11.9)	23 (5.8)	38 (9.6)	24 (6.1)

Data are presented as the means ± SD, n (%) or median (interquartile range). COPD, chronic obstructive pulmonary disease; CVD, cardiovascular diseases; CKD, chronic kidney disease; NA, data not available.

patients, and 31 studies were included after the sensitivity analysis. The I² test showed I² = 39%, indicating that no heterogeneity existed among the studies. The random-effects model was used to pool the data, yielding an OR of 1.85 (95% CI 1.70–2.02, Z = 14.23, P < 0.00001), suggesting that hypertension is a risk factor for AKI (**Figure 3A**).

Thirty-seven studies analysed the relationship between diabetes and the development of AKI in COVID-19 patients. The I^2 test showed $I^2 = 26\%$, indicating that no heterogeneity existed among the studies. The random-effects model was used

to pool the data, yielding an OR of 1.71 (95% CI 1.59–1.84, Z = 14.61, P < 0.00001), suggesting that diabetes is a risk factor for AKI (**Figure 3B**). Twenty-eight studies analysed the relationship between pneumopathy and the development of AKI in COVID-19 patients, and 27 studies were included after the sensitivity analysis. The I² test showed I² = 47%, indicating that slight heterogeneity existed among the studies. The random-effects model was used to pool the data, yielding an OR of 1.36 (95% CI 1.16–1.6), Z = 3.85, P = 0.00001), suggesting that pneumopathy is a risk factor for AKI (**Figure 3C**).

	male		fema			Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% C	M-H, Random, 95% Cl
Bowe.B2020	1608	4908	47	308		Not estimable	
Chaibi.K2020	45	163	10	48	1.1%	1.45 [0.67, 3.15]	
Chan.L.L2020	827	1868	579	1367	9.2%	1.08 [0.94, 1.24]	
Chan.L.L2021	1101	2289	734	1704	9.6%	1.22 [1.08, 1.39]	*
Cheng.Y.C2020	67	711	32	681	3.0%	2.11 [1.37, 3.26]	
Cui.X.Y2020	12	66	9	50	0.8%	1.01 [0.39, 2.63]	
Doher.M.P2020	67	123	34	78	1.9%	1.55 [0.87, 2.74]	
Fominskiy.E.V2020	59	80	13	16	0.4%	0.65 [0.17, 2.50]	
Hamilton.P2020	131	569	79	463	4.7%	1.45 [1.07, 1.98]	
Hansrivijit.P2021	73	159	42	124	2.5%	1.66 [1.02, 2.69]	
Hectors.S.J2020	6	23	10	24	0.5%	0.49 [0.14, 1.70]	
Hirsch.J.S2020	1270	3317	723	2132	10.0%	1.21 [1.08, 1.35]	-
Joseph.A2020	59	70	22	30	0.7%	1.95 [0.69, 5.49]	
Kolhe.N.V2020	179	657	125	504	5.6%	1.14 [0.87, 1.48]	+-
Lee.J.R2020	208	619	86	383	5.1%	1.75 [1.30, 2.34]	-
Li.Q.L2020	32	69	16	38	1.1%	1.19 [0.53, 2.64]	
Li.Q2020	19	56	7	29	0.7%	1.61 [0.59, 4.45]	
Lim.J.H2020	20	66	10	64	0.9%	2.35 [1.00, 5.52]	
Lin.L2020	5	23	1	10	0.1%	2.50 [0.25, 24.72]	
Louis.G2020	61	127	19	54	1.5%	1.70 [0.88, 3.29]	<u> </u>
Luther.T2020	40	44	11	13	0.2%	1.82 [0.29, 11.26]	
Ng.J.H2020	2381	5747	1473	3910	10.9%	1.17 [1.08, 1.27]	-
Nimkar A2020	101	182	78	145	2.9%	1.07 [0.69, 1.66]	—
Paek.J.H2020	16	210	12	494	1.1%	3.31 [1.54, 7.13]	
Pelayo.J2020	60	115	50	108	2.2%	1.27 [0.75, 2.14]	
Peng.S.Y2020	161	1912	124	2108	6.2%	1.47 [1.15, 1.88]	-
Rubin.S2020	46	55	11	16	0.4%	2.32 [0.65, 8.32]	
Sang.L2020	62	131	30	79	1.9%	1.47 [0.83, 2.59]	<u> </u>
Taher.A2020	21	44	8	29	0.7%	2.40 [0.88, 6.56]	<u> </u>
Tan.L.S2020	26	198	14	219	1.4%	2.21 [1.12, 4.37]	
Wang.F.L2020	81	161	55	114	2.5%	1.09 [0.67, 1.76]	
Wang.J2020	10	62	2	54	0.3%	5.00 [1.04, 23.94]	
Xia.P2020	30	54	11	27	0.3%		
						1.82 [0.71, 4.64]	_
Xu.J.Y2020	173	434 39	90	237	4.4%	1.08 [0.78, 1.50]	
Xu.S2020	15 86		3	23	0.4%	4.17 [1.05, 16.47]	
Yan.Q2020		440	29	442	2 00/	Not estimable	
Zahid.U2020	89	268	39	201	3.0%	2.07 [1.34, 3.18]	
Zhang.J.H2020	24	186	13	208	1.3%	2.22 [1.10, 4.50]	
Total (95% CI)		20897		15784	100.0%	1.37 [1.25, 1.49]	•
Total events	7577		4575				
Heterogeneity: Tau ² =	0.02; Chi ²	= 57.92	, df = 35 (P = 0.00	09); l² = 40	%	0.01 0.1 1 10 100
Test for overall effect:	Z = 7.10 (F	P < 0.00	001)				male female

Thirty-five studies analysed the relationship between cardiovascular disease and the development of AKI in COVID-19 patients. The I² test showed I² = 65%, indicating that a high degree of heterogeneity existed among the studies. Therefore, the studies were analysed in subgroups stratified by study type. I² was <50% in all subgroups. The random-effects model was used to pool the data (**Figure 3D**). Coronary heart disease was associated with an OR of 1.77 (95% CI 1.50–2.10, Z = 6.69, P < 0.00001), and heart failure was associated with

an OR of 2.41 (95% CI 2.08–2.79, Z = 11.7, P < 0.00001). Other cardiovascular disease, including other types of heart disease and types not described were associated with an OR of 1.72 (95% CI 1.38–2.15, Z = 4.87, P < 0.00001). The results suggested that cardiovascular disease is a risk factor for AKI.

Twenty-three studies analysed the relationship between cancer and the development of AKI in COVID-19 patients. The I^2 test showed $I^2 = 8\%$, indicating that no heterogeneity

		AKI			NAKI			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random, 95% CI	IV. Random, 95% Cl
2.1.1 America									
3owe.B2020	72	9.6	1655	69	12.6	3561		Not estimable	
Chan.L.L2020	71	13.8	1406	62	17	1829	6.3%	9.00 [7.94, 10.06]	•
Chan.L.L2021	71	14.8	1835	63	17.8	2158	6.3%	8.00 [6.99, 9.01]	
Ooher.M.P2020	73	20.7	101	60	20.1	100	2.7%	13.00 [7.36, 18.64]	
lansrivijit.P2021	68.8	14	115	60.8	16.4	168	4.2%	8.00 [4.44, 11.56]	-
lectors.S.J2020	72	39.3	16	61	54.1	29	0.2%	11.00 [-16.54, 38.54]	_
lirsch.J.S2020	69	14.8	1993	61	16.3	3456	6.4%	8.00 [7.15, 8.85]	•
ee.J.R2020	69	14.8	294	63	17.8	708	5.5%	6.00 [3.86, 8.14]	*
Nimkar A2020	75	16.3	179	67	18.1	148	4.0%	8.00 [4.23, 11.77]	-
Pelayo.J2020		12.18	110	61.6	16.15	113	4.0%	8.73 [4.98, 12.48]	-
Zahid.U2020	67	15.6	128	65	14.1	341		Not estimable	
Subtotal (95% CI)			6049			8709	39.6%	8.17 [7.53, 8.81]	•
leterogeneity: Tau ² =	0 15 Ch	$ni^2 = 9.5$		8(P = 0)	30)· l ² =				
Test for overall effect:						1070			
	2 - 20.0	0(1 1		<i>,</i>					
2.1.2 Europe									
Chaibi.K2020	63	10	55	60	11	156	4.6%	3 00 1.0 16 6 161	–
Fominskiy.E.V2020	63	8.5	55 72	54.5	15	24	4.6% 2.4%	3.00 [-0.16, 6.16] 8.50 [2.19, 14.81]	
· · · · · · · · · · · · · · · · · · ·									Ļ
Hamilton.P2020	71.5	17	210	71	20	822	5.0%	0.50 [-2.18, 3.18]	L
loseph.A2020	60	10.4	81	54	11.9	19	2.6%	6.00 [0.19, 11.81]	
Kolhe.N.V2020	74.9	12.8	304	71.1	17	857	5.7%	3.80 [1.97, 5.63]	
Rubin.S2020	61.7	11.4	57	59.1	15	14	1.6%	2.60 [-5.80, 11.00]	A
Subtotal (95% CI)			779			1892	21.8%	3.31 [1.42, 5.20]	•
leterogeneity: Tau ² =				5 (P = 0	.16); I ² =	= 37%			
Test for overall effect:	Z = 3.43	6 (P = U.	00061						
		· · ·	,						
13 Asia			,						
2.1.3 Asia	61.05			59 59	14.6	95	2 4%	2 47 [2 78 9 72]	-
Cui.X.Y2020	61.05	12.9	21		14.6	95	2.4%	2.47 [-3.78, 8.72]	
Cui.X.Y2020 .i.Q.L2020	73	12.9 10.4	21 48	68	8.9	59	4.1%	5.00 [1.28, 8.72]	-
Cui.X.Y2020 .i.Q.L2020 .im.J.H2020	73 75	12.9 10.4 28.1	21 48 30	68 67	8.9 50.4	59 130	4.1% 0.7%	5.00 [1.28, 8.72] 8.00 [-5.27, 21.27]	
Cui.X.Y2020 .i.Q.L2020 .im.J.H2020 .in.L2020	73 75 71.83	12.9 10.4 28.1 13.2	21 48 30 6	68 67 57.3	8.9 50.4 11.26	59 130 27	4.1%	5.00 [1.28, 8.72] 8.00 [-5.27, 21.27] 14.53 [3.15, 25.91]	
Cui.X.Y2020 .i.Q.L2020 .im.J.H2020 .in.L2020 Paek.J.H2020	73 75 71.83 74.3	12.9 10.4 28.1 13.2 12.1	21 48 30 6 28	68 67 57.3 57	8.9 50.4 11.26 17.4	59 130 27 676	4.1% 0.7% 1.0%	5.00 [1.28, 8.72] 8.00 [-5.27, 21.27] 14.53 [3.15, 25.91] Not estimable	-
Cui, X. Y2020 .i.Q. L2020 .im.J. H2020 .in. L2020 Paek. J. H2020 Sang. L2020	73 75 71.83 74.3 65	12.9 10.4 28.1 13.2 12.1 10.4	21 48 30 6 28 92	68 67 57.3 57 62	8.9 50.4 11.26 17.4 11.9	59 130 27 676 118	4.1% 0.7% 1.0% 4.7%	5.00 [1.28, 8.72] 8.00 [-5.27, 21.27] 14.53 [3.15, 25.91] Not estimable 3.00 [-0.02, 6.02]	
Cui.X.Y2020 .i.Q.L2020 .im.J.H2020 .in.L2020 Paek.J.H2020 Sang.L2020 Faher.A2020	73 75 71.83 74.3 65 57.5	12.9 10.4 28.1 13.2 12.1 10.4 13.7	21 48 30 6 28 92 29	68 67 57.3 57 62 52.2	8.9 50.4 11.26 17.4 11.9 13.1	59 130 27 676 118 44	4.1% 0.7% 1.0%	5.00 [1.28, 8.72] 8.00 [-5.27, 21.27] 14.53 [3.15, 25.91] Not estimable 3.00 [-0.02, 6.02] 5.30 [-1.01, 11.61]	
Cui.X.Y2020 .i.Q.L2020 .im.J.H2020 .in.L2020 Paek.J.H2020 Sang.L2020 Faher.A2020 Faner.A2020	73 75 71.83 74.3 65 57.5 60.1	12.9 10.4 28.1 13.2 12.1 10.4 13.7 12.5	21 48 30 6 28 92 29 40	68 67 57.3 57 62 52.2 43.7	8.9 50.4 11.26 17.4 11.9 13.1 17.4	59 130 27 676 118 44 377	4.1% 0.7% 1.0% 4.7% 2.4%	5.00 [1.28, 8.72] 8.00 [-5.27, 21.27] 14.53 [3.15, 25.91] Not estimable 3.00 [-0.02, 6.02] 5.30 [-1.01, 11.61] Not estimable	
Cui, X. Y2020 .i. Q. L2020 .im. J. H2020 .in. L2020 Paek. J. H2020 Sang. L2020 Faher. A2020 Fan. L. S2020 Wang. F. L2020	73 75 71.83 74.3 65 57.5 60.1 70	12.9 10.4 28.1 13.2 12.1 10.4 13.7 12.5 10.4	21 48 30 6 28 92 29 40 136	68 67 57.3 57 62 52.2 43.7 68	8.9 50.4 11.26 17.4 11.9 13.1 17.4 11.9	59 130 27 676 118 44 377 139	4.1% 0.7% 1.0% 4.7% 2.4% 5.0%	5.00 [1.28, 8.72] 8.00 [-5.27, 21.27] 14.53 [3.15, 25.91] Not estimable 3.00 [-0.02, 6.02] 5.30 [-1.01, 11.61] Not estimable 2.00 [-0.64, 4.64]	
Cui.X.Y2020 i.Q.L2020 i.m.J.H2020 i.m.L2020 Paek.J.H2020 Sang.L2020 Faher.A2020 Faher.A2020 Vang.F.L2020 Vang.J2020	73 75 71.83 74.3 65 57.5 60.1 70 66	12.9 10.4 28.1 13.2 12.1 10.4 13.7 12.5 10.4 12	21 48 30 6 28 92 29 40 136 12	68 67 57.3 57 62 52.2 43.7 68 62	8.9 50.4 11.26 17.4 11.9 13.1 17.4 11.9 10.4	59 130 27 676 118 44 377 139 104	4.1% 0.7% 1.0% 4.7% 2.4% 5.0% 2.0%	5.00 [1.28, 8.72] 8.00 [-5.27, 21.27] 14.53 [3.15, 25.91] Not estimable 3.00 [-0.02, 6.02] 5.30 [-1.01, 11.61] Not estimable 2.00 [-0.64, 4.64] 4.00 [-3.08, 11.08]	
Cui.X.Y2020 i.Q.L2020 i.m.J.H2020 i.n.L2020 Paek.J.H2020 Sang.L2020 Faher.A2020 Faher.A2020 Fan.L.S2020 Wang.F.L2020 Wang.J2020 Kia.P2020	73 75 71.83 74.3 65 57.5 60.1 70 66 69.6	12.9 10.4 28.1 13.2 12.1 10.4 13.7 12.5 10.4 12 9.3	21 48 30 6 28 92 29 40 136 12 41	68 67 57.3 57 62 52.2 43.7 68 62 63.6	8.9 50.4 11.26 17.4 11.9 13.1 17.4 11.9 10.4 12.7	59 130 27 676 118 44 377 139 104 40	4.1% 0.7% 1.0% 4.7% 2.4% 5.0% 2.0% 3.2%	5.00 [1.28, 8.72] 8.00 [-5.27, 21.27] 14.53 [3.15, 25.91] Not estimable 3.00 [-0.02, 6.02] 5.30 [-1.01, 11.61] Not estimable 2.00 [-0.64, 4.64]	
Cui.X.Y2020 .i.Q.L2020 .im.J.H2020	73 75 71.83 74.3 65 57.5 60.1 70 66	12.9 10.4 28.1 13.2 12.1 10.4 13.7 12.5 10.4 12	21 48 30 6 28 92 29 40 136 12	68 67 57.3 57 62 52.2 43.7 68 62	8.9 50.4 11.26 17.4 11.9 13.1 17.4 11.9 10.4	59 130 27 676 118 44 377 139 104	4.1% 0.7% 1.0% 4.7% 2.4% 5.0% 2.0%	5.00 [1.28, 8.72] 8.00 [-5.27, 21.27] 14.53 [3.15, 25.91] Not estimable 3.00 [-0.02, 6.02] 5.30 [-1.01, 11.61] Not estimable 2.00 [-0.64, 4.64] 4.00 [-3.08, 11.08]	
Cui.X.Y2020 i.Q.L2020 i.m.J.H2020 i.n.L2020 Paek.J.H2020 Sang.L2020 Faher.A2020 Faher.A2020 Fan.L.S2020 Wang.F.L2020 Wang.J2020 Kia.P2020	73 75 71.83 74.3 65 57.5 60.1 70 66 69.6	12.9 10.4 28.1 13.2 12.1 10.4 13.7 12.5 10.4 12 9.3	21 48 30 6 28 92 29 40 136 12 41	68 67 57.3 57 62 52.2 43.7 68 62 63.6	8.9 50.4 11.26 17.4 11.9 13.1 17.4 11.9 10.4 12.7	59 130 27 676 118 44 377 139 104 40	4.1% 0.7% 1.0% 4.7% 2.4% 5.0% 2.0% 3.2%	5.00 [1.28, 8.72] 8.00 [-5.27, 21.27] 14.53 [3.15, 25.91] Not estimable 3.00 [-0.02, 6.02] 5.30 [-1.01, 11.61] Not estimable 2.00 [-0.64, 4.64] 4.00 [-3.08, 11.08] 6.00 [1.14, 10.86]	
Cui.X.Y2020 i.Q.L2020 i.m.J.H2020 aek.J.H2020 Sang.L2020 Faher.A2020 Faher.A2020 FanL.S2020 Wang.F.L2020 Wang.J2020 Ku.J.Y2020	73 75 71.83 74.3 65 57.5 60.1 70 66 69.6 69.6 66	12.9 10.4 28.1 13.2 12.1 10.4 13.7 12.5 10.4 12 9.3 11.1	21 48 30 6 28 92 29 40 136 12 41 263	68 67 57.3 57 62 52.2 43.7 68 62 63.6 64	8.9 50.4 11.26 17.4 11.9 13.1 17.4 11.9 10.4 12.7 13.3	59 130 27 676 118 44 377 139 104 40 408	4.1% 0.7% 1.0% 4.7% 2.4% 5.0% 2.0% 3.2% 5.7%	5.00 [1.28, 8.72] 8.00 [-5.27, 21.27] 14.53 [3.15, 25.91] Not estimable 3.00 [-0.02, 6.02] 5.30 [-1.01, 11.61] Not estimable 2.00 [-0.64, 4.64] 4.00 [-3.08, 11.08] 6.00 [1.14, 10.86] 2.00 [0.14, 3.86]	
Cui.X.Y2020 i.Q.L2020 i.m.J.H2020 Paek.J.H2020 Paek.J.H2020 Gang.L2020 Faher.A2020 Faher.A2020 Wang.F.L2020 Wang.J2020 Ku.J.Y2020 Ku.S2020	73 75 71.83 74.3 65 57.5 60.1 70 66 69.6 69.6 66 65.3	12.9 10.4 28.1 13.2 12.1 10.4 13.7 12.5 10.4 12 9.3 11.1 16.1	21 48 30 6 28 92 29 40 136 12 41 263 18	68 67 57.3 57 62 52.2 43.7 68 62 63.6 64 61.9	8.9 50.4 11.26 17.4 11.9 13.1 17.4 11.9 10.4 12.7 13.3 15.6	59 130 27 676 118 44 377 139 104 40 408 44	4.1% 0.7% 1.0% 4.7% 2.4% 5.0% 2.0% 3.2% 5.7% 1.5%	5.00 [1.28, 8.72] 8.00 [-5.27, 21.27] 14.53 [3.15, 25.91] Not estimable 3.00 [-0.02, 6.02] 5.30 [-1.01, 11.61] Not estimable 2.00 [-0.64, 4.64] 4.00 [-3.08, 11.08] 6.00 [1.14, 10.86] 2.00 [0.14, 3.86] 3.40 [-5.35, 12.15]	
Cui, X. Y2020 i. Q. L2020 i.m. J. H2020 Paek. J. H2020 Paek. J. H2020 Sang. L2020 Faher. A2020 Fan. L. S2020 Wang. J. L2020 Ku. J. Y2020 Ku. S2020 Yan. Q2020 Zhang. J. H2020	73 75 71.83 74.3 65 57.5 60.1 70 66 69.6 69.6 65.3 75	12.9 10.4 28.1 13.2 12.1 10.4 13.7 12.5 10.4 12.9 3 11.1 16.1 8.9	21 48 30 6 28 92 29 40 136 12 41 263 18 115	68 67 57.3 57 62 52.2 43.7 68 62 63.6 64 61.9 70	8.9 50.4 11.26 17.4 11.9 13.1 17.4 11.9 10.4 12.7 13.3 15.6 5.9	59 130 27 676 118 44 377 139 104 40 408 44 767	4.1% 0.7% 1.0% 4.7% 2.4% 5.0% 2.0% 3.2% 5.7% 1.5%	5.00 [1.28, 8.72] 8.00 [-5.27, 21.27] 14.53 [3.15, 25.91] Not estimable 3.00 [-0.02, 6.02] 5.30 [-1.01, 11.61] Not estimable 2.00 [-0.64, 4.64] 4.00 [-3.08, 11.08] 6.00 [1.14, 10.86] 2.00 [0.14, 3.86] 3.40 [-5.35, 12.15] 5.00 [3.32, 6.68]	
Cui.X.Y2020 i.Q.L2020 i.m.J.H2020 2aek.J.H2020 2aek.J.H2020 5ang.L2020 Faher.A2020 Faher.A2020 Vang.F.L2020 Vang.F.L2020 Vang.J2020 Ku.J.Y2020 Ku.S2020 Yan.Q2020	73 75 71.83 74.3 65 57.5 60.1 70 66 69.6 69.6 65.3 75 71	12.9 10.4 28.1 13.2 12.1 10.4 13.7 12.5 10.4 2 9.3 11.1 16.1 8.9 17	21 48 30 6 28 92 29 40 136 12 41 263 18 115 37 811	68 67 57.3 57 62 52.2 43.7 68 62 63.6 64 61.9 70 55	8.9 50.4 11.26 17.4 11.9 13.1 17.4 11.9 10.4 12.7 13.3 15.6 5.9 17	59 130 27 676 118 44 377 139 104 40 408 44 767 357 1975	4.1% 0.7% 1.0% 4.7% 2.4% 5.0% 3.2% 5.7% 1.5% 5.9% 38.5%	5.00 [1.28, 8.72] 8.00 [-5.27, 21.27] 14.53 [3.15, 25.91] Not estimable 3.00 [-0.02, 6.02] 5.30 [-1.01, 11.61] Not estimable 2.00 [-0.64, 4.64] 4.00 [-3.08, 11.08] 6.00 [1.14, 10.86] 2.00 [0.14, 3.86] 3.40 [-5.35, 12.15] 5.00 [3.32, 6.68] Not estimable	
Cui.X.Y2020 .i.Q.L2020 .im.J.H2020 Paek.J.H2020 Paek.J.H2020 Sang.L2020 Faher.A2020 Fan.L.S2020 Vang.J.2020 Vang.J2020 Ku.J.Y2020 Ku.J.Y2020 Ku.S2020 Fan.Q2020 Chang.J.H2020 Subtotal (95% CI) Heterogeneity: Tau ² =	73 75 71.83 74.3 65 57.5 60.1 70 66 69.6 69.6 65.3 75 71 0.57; Ch	12.9 10.4 28.1 13.2 12.1 10.4 13.7 12.5 10.4 12.9 .3 11.1 16.1 8.9 17 17	21 48 30 6 28 92 29 40 136 12 41 263 115 37 811 92, df =	68 67 57.3 57 62 52.2 43.7 68 62 63.6 64 61.9 70 55 = 11 (P =	8.9 50.4 11.26 17.4 11.9 13.1 17.4 11.9 10.4 12.7 13.3 15.6 5.9 17	59 130 27 676 118 44 377 139 104 40 408 44 767 357 1975	4.1% 0.7% 1.0% 4.7% 2.4% 5.0% 3.2% 5.7% 1.5% 5.9% 38.5%	5.00 [1.28, 8.72] 8.00 [-5.27, 21.27] 14.53 [3.15, 25.91] Not estimable 3.00 [-0.02, 6.02] 5.30 [-1.01, 11.61] Not estimable 2.00 [-0.64, 4.64] 4.00 [-3.08, 11.08] 6.00 [1.14, 10.86] 2.00 [0.14, 3.86] 3.40 [-5.35, 12.15] 5.00 [3.32, 6.68] Not estimable	
Cui.X.Y2020 i.Q.L2020 i.m.J.H2020 Paek.J.H2020 Paek.J.H2020 Gaher.A2020 Fant.S2020 Vang.J.2020 Vang.J2020 Ku.S2020 Ku.S2020 Ku.S2020 Can.Q2020 Chang.J.H2020 Subtotal (95% CI)	73 75 71.83 74.3 65 57.5 60.1 70 66 69.6 69.6 65.3 75 71 0.57; Ch	12.9 10.4 28.1 13.2 12.1 10.4 13.7 12.5 10.4 12.9 .3 11.1 16.1 8.9 17 17	21 48 30 6 28 92 29 40 136 12 41 263 115 37 811 92, df =	68 67 57.3 57 62 52.2 43.7 68 62 63.6 64 61.9 70 55 = 11 (P =	8.9 50.4 11.26 17.4 11.9 13.1 17.4 11.9 10.4 12.7 13.3 15.6 5.9 17	59 130 27 676 118 44 377 139 104 40 408 44 767 357 1975	4.1% 0.7% 1.0% 4.7% 2.4% 5.0% 3.2% 5.7% 1.5% 5.9% 38.5%	5.00 [1.28, 8.72] 8.00 [-5.27, 21.27] 14.53 [3.15, 25.91] Not estimable 3.00 [-0.02, 6.02] 5.30 [-1.01, 11.61] Not estimable 2.00 [-0.64, 4.64] 4.00 [-3.08, 11.08] 6.00 [1.14, 10.86] 2.00 [0.14, 3.86] 3.40 [-5.35, 12.15] 5.00 [3.32, 6.68] Not estimable	
Cui.X.Y2020 i.Q.L2020 i.m.J.H2020 Paek.J.H2020 Paek.J.H2020 Paher.A2020 Faher.A2020 Faher.A2020 Vang.F.L2020 Vang.J.2020 Vang.J2020 Vang.J.Y2020 Vang.J.H2020 Subtotal (95% CI) Heterogeneity: Tau ² = Fest for overall effect:	73 75 71.83 74.3 65 57.5 60.1 70 66 69.6 69.6 65.3 75 71 0.57; Ch	12.9 10.4 28.1 13.2 12.1 10.4 13.7 12.5 10.4 12.9 .3 11.1 16.1 8.9 17 17	21 48 30 6 28 92 29 40 136 12 41 263 115 37 811 92, df =	68 67 57.3 57 62 52.2 43.7 68 62 63.6 64 61.9 70 55 = 11 (P =	8.9 50.4 11.26 17.4 11.9 13.1 17.4 11.9 10.4 12.7 13.3 15.6 5.9 17 = 0.30);	59 130 27 676 118 44 377 139 104 408 44 408 44 767 357 1975 1 ² = 15%	4.1% 0.7% 1.0% 4.7% 2.4% 5.0% 3.2% 5.7% 1.5% 5.9% 38.5%	5.00 [1.28, 8.72] 8.00 [-5.27, 21.27] 14.53 [3.15, 25.91] Not estimable 3.00 [-0.02, 6.02] 5.30 [-1.01, 11.61] Not estimable 2.00 [-0.64, 4.64] 4.00 [-3.08, 11.08] 6.00 [1.14, 10.86] 2.00 [0.14, 3.86] 3.40 [-5.35, 12.15] 5.00 [3.32, 6.68] Not estimable	
Cui.X.Y2020 i.Q.L2020 i.m.J.H2020 Paek.J.H2020 Sang.L2020 Faher.A2020 Faher.A2020 FanL.S2020 Vang.F.L2020 Vang.J2020 Ku.J.Y2020 Ku.S2020 Chang.J.H2020 Subtotal (95% Cl) Test for overall effect: Fotal (95% Cl)	73 75 71.83 74.3 65 57.5 60.1 70 66 69.6 66 65.3 75 71 0.57; Ch Z = 6.36	$12.9 \\ 10.4 \\ 28.1 \\ 13.2 \\ 12.1 \\ 10.4 \\ 13.7 \\ 12.5 \\ 10.4 \\ 12 \\ 9.3 \\ 11.1 \\ 16.1 \\ 8.9 \\ 17 \\ 16 \\ 17 \\ 16 \\ (P < 0.1 \\ (P < $	21 48 30 6 28 92 29 40 136 12 41 263 18 115 37 811 92, df = 00001) 7639	68 67 57.3 57 62 52.2 43.7 68 62 63.6 64 61.9 70 55 55	8.9 50.4 11.26 17.4 11.9 13.1 17.4 11.9 10.4 12.7 13.3 15.6 5.9 17 = 0.30);	59 130 27 676 118 44 377 139 104 40 408 44 767 357 1975 12 = 15%	4.1% 0.7% 1.0% 4.7% 2.4% 5.0% 2.0% 3.2% 5.7% 1.5% 5.9% 38.5% 6 100.0%	5.00 [1.28, 8.72] 8.00 [-5.27, 21.27] 14.53 [3.15, 25.91] Not estimable 3.00 [-0.02, 6.02] 5.30 [-1.01, 11.61] Not estimable 2.00 [-0.64, 4.64] 4.00 [-3.08, 11.08] 6.00 [1.14, 10.86] 2.00 [0.14, 3.86] 3.40 [-5.35, 12.15] 5.00 [3.32, 6.68] Not estimable 3.70 [2.56, 4.84]	
Cui.X.Y2020 .i.Q.L2020 .im.J.H2020 Paek.J.H2020 Paek.J.H2020 Sang.L2020 Faher.A2020 Fan.L.S2020 Vang.J.2020 Vang.J2020 Ku.J.Y2020 Ku.J.Y2020 Ku.S2020 Fan.Q2020 Chang.J.H2020 Subtotal (95% CI) Heterogeneity: Tau ² =	73 75 71.83 74.3 65 57.5 60.1 70 66 69.6 66 65.3 75 71 0.57; Ch Z = 6.36	$12.9 \\ 10.4 \\ 28.1 \\ 13.2 \\ 12.1 \\ 10.4 \\ 13.7 \\ 12.5 \\ 10.4 \\ 12 \\ 9.3 \\ 11.1 \\ 16.1 \\ 8.9 \\ 17 \\ 17 \\ 16^2 = 12 \\ (P < 0.1 \\ n)^2 = 12 \\ n)^2 = 12$	21 48 30 6 28 92 29 40 136 12 41 263 18 115 37 811 92, df = 00001) 7639 9.77, df	68 67 57.3 57 62 52.2 43.7 68 62 63.6 64 61.9 70 55 = 11 (P =	8.9 50.4 11.26 17.4 11.9 13.1 17.4 11.9 10.4 12.7 13.3 15.6 5.9 17 = 0.30);	59 130 27 676 118 44 377 139 104 40 408 44 767 357 1975 12 = 15%	4.1% 0.7% 1.0% 4.7% 2.4% 5.0% 2.0% 3.2% 5.7% 1.5% 5.9% 38.5% 6 100.0%	5.00 [1.28, 8.72] 8.00 [-5.27, 21.27] 14.53 [3.15, 25.91] Not estimable 3.00 [-0.02, 6.02] 5.30 [-1.01, 11.61] Not estimable 2.00 [-0.64, 4.64] 4.00 [-3.08, 11.08] 6.00 [1.14, 10.86] 2.00 [0.14, 3.86] 3.40 [-5.35, 12.15] 5.00 [3.32, 6.68] Not estimable 3.70 [2.56, 4.84]	
Cui.X.Y2020 i.Q.L2020 i.m.J.H2020 Paek.J.H2020 Paek.J.H2020 Gang.L2020 Faher.A2020 FanL.S2020 Wang.F.L2020 Wang.J2020 Ku.S2020 Yan.Q2020 Chang.J.H2020 Subtotal (95% Cl) Heterogeneity: Tau ² = Fest for overall effect: Fotal (95% Cl) Heterogeneity: Tau ² =	73 75 71.83 74.3 65 57.5 60.1 70 66 69.6 69.6 65.3 75 71 0.57; Cr Z = 6.36 5.76; Cr Z = 9.13	$12.9 \\ 10.4 \\ 28.1 \\ 13.2 \\ 12.1 \\ 10.4 \\ 13.7 \\ 12.5 \\ 10.4 \\ 12 \\ 9.3 \\ 11.1 \\ 16.1 \\ 8.9 \\ 17 \\ 16^2 = 12. \\ 6 (P < 0. \\ 0.1 \\ $	21 48 30 6 28 92 29 40 136 12 41 263 18 115 37 811 92, df = 00001) 7639 9.77, df 00001)	68 67 57.3 57 62 52.2 43.7 68 62 63.6 64 61.9 70 55 = 11 (P =	8.9 50.4 11.26 17.4 11.9 13.1 17.4 11.9 10.4 12.7 13.3 15.6 5.9 17 = 0.30);	59 130 27 676 118 44 377 139 104 40 408 44 767 357 1975 1 ² = 15% 12576 001); 1 ² =	4.1% 0.7% 1.0% 4.7% 2.4% 5.0% 2.0% 3.2% 5.7% 1.5% 5.9% 38.5% 6 100.0% = 80%	5.00 [1.28, 8.72] 8.00 [-5.27, 21.27] 14.53 [3.15, 25.91] Not estimable 3.00 [-0.02, 6.02] 5.30 [-1.01, 11.61] Not estimable 2.00 [-0.64, 4.64] 4.00 [-3.08, 11.08] 6.00 [1.14, 10.86] 2.00 [0.14, 3.86] 3.40 [-5.35, 12.15] 5.00 [3.32, 6.68] Not estimable 3.70 [2.56, 4.84]	-100 -50 0 50 100 AKI NAKI

	smoki	-	non-sm			Odds Ratio	Odds Ratio
Study or Subgroup			Events		Weight	M-H, Random, 95% Cl	M-H. Random, 95% Cl
Bowe.B2020	781	2323	874	2893	35.5%	1.17 [1.04, 1.32]	
Cheng.Y.C2020	12	83	87	1309	4.4%	2.37 [1.24, 4.54]	
Doher.M.P2020	2	6	99	195	0.7%	0.48 [0.09, 2.71]	
Fominskiy.E.V2020	3	5	69	91	0.6%	0.48 [0.08, 3.05]	
Hansrivijit.P2021	45	109	70	174	7.3%	1.04 [0.64, 1.70]	
Ng.J.H2020	871	1962	2983	7695	37.9%	1.26 [1.14, 1.39]	-
Nimkar A2020	29	56	150	271	5.5%	0.87 [0.49, 1.54]	
Xia.P2020	7	12	34	69	1.3%	1.44 [0.42, 4.98]	
Zahid.U2020	18	38	189	431	4.3%	1.15 [0.59, 2.24]	
Zhang.J.H2020	8	36	29	358	2.6%	3.24 [1.35, 7.76]	
Total (95% CI)		4630		13486	100.0%	1.23 [1.07, 1.42]	♦
Total events	1776		4584				
				D 040	1. 12 - 3/0/		
	0.01; Chi ²	= 13.69	9, df = 9 (P = 0.13	/, I = 04 /	0	0.01 0.1 1 10 100
Heterogeneity: Tau ² = Test for overall effect:				P = 0.13	y, 1 – 34 /		0.01 0.1 1 10 100 smoking non-smoking
Heterogeneity: Tau ² =				P = 0.13	y, 1 – 34 /		
Heterogeneity: Tau² = Test for overall effect: .	Z = 2.85 (i obesi	P = 0.00)4) norm		<i>),</i> 1 – 34 /	Odds Ratio	smoking non-smoking Odds Ratio
Heterogeneity: Tau ² =	Z = 2.85 (i obesi	P = 0.00 ty Total	ý)4)	al	Weight		smoking non-smoking
Heterogeneity: Tau² = Test for overall effect: .	Z = 2.85 (i obesi	P = 0.00 ty <u>Total</u> 2679)4) norm	al	Weight 25.0%	Odds Ratio	smoking non-smoking Odds Ratio
Heterogeneity: Tau ² = Test for overall effect: : <u>Study or Subgroup</u>	Z = 2.85 (obesi Events	P = 0.00 ty Total	norm Events	al Total	Weight	Odds Ratio M-H. Random, 95% Cl	smoking non-smoking Odds Ratio
Heterogeneity: Tau ² = Test for overall effect: : Study or Subgroup Bowe.B2020	Z = 2.85 (obesi <u>Events</u> 908	P = 0.00 ty <u>Total</u> 2679	norm <u>Events</u> 747	al <u>Total</u> 2537	Weight 25.0%	Odds Ratio <u>M-H. Random. 95% Cl</u> 1.23 [1.09, 1.38]	smoking non-smoking Odds Ratio
Heterogeneity: Tau ² = Test for overall effect: ; Study or Subgroup Bowe.B2020 Fominskiy.E.V2020	Z = 2.85 (obesi <u>Events</u> 908 16	P = 0.00 ty <u>Total</u> 2679 22	norm <u>Events</u> 747 56	al <u>Total</u> 2537 74	Weight 25.0% 1.0%	Odds Ratio <u>M-H. Random. 95% Cl</u> 1.23 [1.09, 1.38] 0.86 [0.29, 2.52]	smoking non-smoking Odds Ratio
Heterogeneity: Tau ² = Test for overall effect: ; Study or Subgroup Bowe.B2020 Fominskiy.E.V2020 Hansrivijit.P2021	Z = 2.85 (obesi <u>Events</u> 908 16 54	P = 0.00 ty <u>Total</u> 2679 22 132	norm <u>Events</u> 747 56 61	al <u>Total</u> 2537 74 151	Weight 25.0% 1.0% 4.4%	Odds Ratio <u>M-H. Random. 95% Cl</u> 1.23 [1.09, 1.38] 0.86 [0.29, 2.52] 1.02 [0.63, 1.64]	smoking non-smoking Odds Ratio
Heterogeneity: Tau ² = Test for overall effect: Study or Subgroup Bowe.B2020 Fominskiy.E.V2020 Hansrivijit.P2021 Hirsch.J.S2020	Z = 2.85 (obesi Events 908 16 54 559 18 71	P = 0.00 ty <u>Total</u> 2679 22 132 1475	norm Events 747 56 61 1434	al <u>Total</u> 2537 74 151 3974	Weight 25.0% 1.0% 4.4% 24.2%	Odds Ratio <u>M-H. Random. 95% Cl</u> 1.23 [1.09, 1.38] 0.86 [0.29, 2.52] 1.02 [0.63, 1.64] 1.08 [0.96, 1.22]	smoking non-smoking Odds Ratio
Heterogeneity: Tau ² = Test for overall effect: Study or Subgroup Bowe.B2020 Fominskiy.E.V2020 Hansrivijit.P2021 Hirsch.J.S2020 Joseph.A2020	Z = 2.85 (obesi Events 908 16 54 559 18	P = 0.00 ty <u>Total</u> 2679 22 132 1475 21	norm Events 747 56 61 1434 63	Total 2537 74 151 3974 79	Weight 25.0% 1.0% 4.4% 24.2% 0.6%	Odds Ratio <u>M-H. Random. 95% Cl</u> 1.23 [1.09, 1.38] 0.86 [0.29, 2.52] 1.02 [0.63, 1.64] 1.08 [0.96, 1.22] 1.52 [0.40, 5.82]	smoking non-smoking Odds Ratio
Heterogeneity: Tau ² = Test for overall effect: Study or Subgroup Bowe.B2020 Fominskiy.E.V2020 Hansrivijit.P2021 Hirsch.J.S2020 Joseph.A2020 Lee.J.R2020	Z = 2.85 (obesi Events 908 16 54 559 18 71	P = 0.00 ty <u>Total</u> 2679 22 132 1475 21 184	norm Events 747 56 61 1434 63 223	al <u>Total</u> 2537 74 151 3974 79 818	Weight 25.0% 1.0% 4.4% 24.2% 0.6% 7.9%	Odds Ratio <u>M-H. Random. 95% Cl</u> 1.23 [1.09, 1.38] 0.86 [0.29, 2.52] 1.02 [0.63, 1.64] 1.08 [0.96, 1.22] 1.52 [0.40, 5.82] 1.68 [1.20, 2.34]	smoking non-smoking Odds Ratio
Heterogeneity: Tau ² = Test for overall effect: Study or Subgroup Bowe.B2020 Fominskiy.E.V2020 Hansrivijit.P2021 Hirsch.J.S2020 Joseph.A2020 Lee.J.R2020 Louis.G2020	Z = 2.85 (obesi <u>Events</u> 908 16 54 559 18 71 29	P = 0.00 ty <u>Total</u> 2679 22 132 1475 21 184 68	norm Events 747 56 61 1434 63 223 51	al <u>Total</u> 2537 74 151 3974 79 818 113	Weight 25.0% 1.0% 4.4% 24.2% 0.6% 7.9% 2.8%	Odds Ratio <u>M-H. Random. 95% Cl</u> 1.23 [1.09, 1.38] 0.86 [0.29, 2.52] 1.02 [0.63, 1.64] 1.08 [0.96, 1.22] 1.52 [0.40, 5.82] 1.68 [1.20, 2.34] 0.90 [0.49, 1.66]	smoking non-smoking Odds Ratio
Heterogeneity: Tau ² = Test for overall effect: 3 Study or Subgroup Bowe.B2020 Fominskiy.E.V2020 Hansrivijit.P2021 Hirsch.J.S2020 Joseph.A2020 Lee.J.R2020 Louis.G2020 Ng.J.H2020	Z = 2.85 (obesi <u>Events</u> 908 16 54 559 18 71 29 1329	P = 0.00 ty <u>Total</u> 2679 22 132 1475 21 184 68 3323	norm Events 747 56 61 1434 63 223 51 2525	al 2537 74 151 3974 79 818 113 6334	Weight 25.0% 1.0% 4.4% 24.2% 0.6% 7.9% 2.8% 29.1%	Odds Ratio <u>M-H. Random. 95% CI</u> 1.23 [1.09, 1.38] 0.86 [0.29, 2.52] 1.02 [0.63, 1.64] 1.08 [0.96, 1.22] 1.52 [0.40, 5.82] 1.68 [1.20, 2.34] 0.90 [0.49, 1.66] 1.01 [0.92, 1.10]	smoking non-smoking Odds Ratio
Heterogeneity: Tau ² = Test for overall effect: 3 Study or Subgroup Bowe.B2020 Fominskiy.E.V2020 Hansrivijit.P2021 Hirsch.J.S2020 Joseph.A2020 Lee.J.R2020 Louis.G2020 Ng.J.H2020 Nimkar A2020	Z = 2.85 (obesi <u>Events</u> 908 16 54 559 18 71 29 1329 63	P = 0.00 ty <u>Total</u> 2679 22 132 1475 21 184 68 3323 113	norm Events 747 56 61 1434 63 223 51 2525 116	aal Total 2537 74 151 3974 79 818 113 6334 214	Weight 25.0% 1.0% 4.4% 24.2% 0.6% 7.9% 2.8% 29.1% 4.7%	Odds Ratio <u>M-H. Random. 95% Cl</u> 1.23 [1.09, 1.38] 0.86 [0.29, 2.52] 1.02 [0.63, 1.64] 1.08 [0.96, 1.22] 1.52 [0.40, 5.82] 1.68 [1.20, 2.34] 0.90 [0.49, 1.66] 1.01 [0.92, 1.10] 1.06 [0.67, 1.68]	smoking non-smoking Odds Ratio
Heterogeneity: Tau ² = Test for overall effect: 3 Bowe.B2020 Fominskiy.E.V2020 Hansrivijit.P2021 Hirsch.J.S2020 Joseph.A2020 Lee.J.R2020 Louis.G2020 Ng.J.H2020 Nimkar A2020 Taher.A2020	Z = 2.85 (obesi <u>Events</u> 908 16 54 559 18 71 29 1329 63	P = 0.00 ty <u>Total</u> 2679 22 132 1475 21 184 68 3323 113 3	norm Events 747 56 61 1434 63 223 51 2525 116	al Total 2537 74 151 3974 79 818 113 6334 214 70	Weight 25.0% 1.0% 4.4% 24.2% 0.6% 7.9% 2.8% 29.1% 4.7% 0.2%	Odds Ratio M-H. Random. 95% Cl 1.23 [1.09, 1.38] 0.86 [0.29, 2.52] 1.02 [0.63, 1.64] 1.08 [0.96, 1.22] 1.52 [0.40, 5.82] 1.68 [1.20, 2.34] 0.90 [0.49, 1.66] 1.01 [0.92, 1.10] 1.06 [0.67, 1.68] 3.19 [0.28, 36.85]	smoking non-smoking Odds Ratio
Heterogeneity: Tau ² = Test for overall effect: 3 Bowe.B2020 Fominskiy.E.V2020 Hansrivijit.P2021 Hirsch.J.S2020 Joseph.A2020 Lee.J.R2020 Louis.G2020 Ng.J.H2020 Nimkar A2020 Taher.A2020 Total (95% CI)	Z = 2.85 (obesi <u>Events</u> 908 16 54 559 18 71 29 1329 63 2 3049	P = 0.00 ty <u>Total</u> 2679 22 132 1475 21 184 68 3323 113 3 8020	norm <u>Events</u> 747 56 61 1434 63 223 51 2525 116 27 5303	al <u>Total</u> 2537 74 151 3974 79 818 113 6334 214 70 14364	Weight 25.0% 1.0% 4.4% 24.2% 0.6% 7.9% 2.8% 29.1% 4.7% 0.2% 100.0%	Odds Ratio M-H. Random. 95% Cl 1.23 [1.09, 1.38] 0.86 [0.29, 2.52] 1.02 [0.63, 1.64] 1.08 [0.96, 1.22] 1.52 [0.40, 5.82] 1.68 [1.20, 2.34] 0.90 [0.49, 1.66] 1.01 [0.92, 1.10] 1.06 [0.67, 1.68] 3.19 [0.28, 36.85] 1.12 [1.01, 1.25]	smoking non-smoking Odds Ratio

FIGURE 2 | (A) Forest plot showing the relationship between sex and AKI in COVID-19 patients. (B) Forest plot showing the relationship between age and AKI in COVID-19 patients. (C) Forest plot showing the relationship between smoking and AKI in COVID-19 patients. (D) Forest plot showing the relationship between obesity and AKI in COVID-19 patients.

existed among the studies. The random-effects model was used to pool the data, yielding an OR of 1.26 (95% CI 1.13–1.40), Z = 4.12, P < 0.00001), suggesting that cancer is a risk factor for AKI (**Figure 3E**).

Twenty-four studies analysed the relationship between CKD and the development of AKI in COVID-19 patients. The I² test showed I² = 61%, indicating that a high degree of heterogeneity existed among the studies. The random-effects model was used to pool the data, yielding an OR of 4.56 (95% CI 3.63–5.73, Z = 13.04, P < 0.00001), suggesting that CKD is a risk factor for AKI (**Figure 3F**).

Supportive Treatment

Twenty-five studies analysed the relationship between mechanical ventilation and the development of AKI in COVID-19 patients. The I^2 test showed $I^2 = 96\%$, indicating that a high degree of heterogeneity existed among the

studies. A sensitivity analysis and subgroup analysis were performed, but the heterogeneity could not be reduced. The random-effects model was used to pool the data, yielding an OR of 8.61 (95% CI 5.63–13.17, Z = 9.94, P < 0.00001), suggesting that mechanical ventilation is a risk factor for AKI (**Figure 4A**).

Fifteen studies analysed the relationship between the use of vasopressors and the development of AKI in COVID-19 patients. The I^2 test showed $I^2 = 96\%$, indicating that a high degree of heterogeneity existed among the studies. The random-effects model was used to pool the data, yielding an OR of 8.33 (95% CI 4.72–14.72), Z = 7.31, P < 0.00001), suggesting that the use of vasopressors is a risk factor for AKI (**Figure 4B**).

Bias Assessment

Finally, funnel plots were constructed to qualitatively analyse the publication bias among the included studies. The relationship

between diabetes and AKI in COVID-19 patients was used as an example. The funnel plots displayed symmetrical distributions, with no obvious publication bias (**Figure 5**).

DISCUSSION

Our study included 42,779 subjects in 38 studies and explored the risk factors for AKI in adult patients with COVID-19. To our knowledge, this study had the largest number of included studies and the largest sample size. Although research has investigated the clinical characteristics, pathobiology, treatment methods and other related factors, means of improving the prognosis of AKI remain to be identified, and further research is needed to reduce the adverse consequences for patients. Recently, Fisher et al. from New York reported higher rates of AKI in those with COVID-19 than in those who tested negative for

this disease (48). Currently, the mechanism underlying kidney injury in patients with COVID-19 is believed to involve SARS-CoV-2 directly attacking intrinsic renal cells. SARS-CoV-2 is a cytopathic virus that passes through the membrane protein ACE2 to enter host cells (49). The expression level of ACE2 in renal cells ranks 4th among the 55 tissue types and 6 blood cell types, with consistent standardised expression levels. Therefore, patients with COVID-19 have a relatively higher risk of developing AKI. Kidney histology in patients with COVID-19 has shown the presence of acute tubular necrosis, moderate-tosevere lymphocytic infiltration and collapsing glomerulopathy (50). Invasion by SARS-CoV-2 causes the T lymphocyte count to decrease, especially CD4+T cells and CD8+T cells, and the levels of IL-6, IL-10, IL-2, and interferon to increase (51). These inflammatory cytokine levels are increased due to the recruitment and infiltration of inflammatory cells and participate in tissue

	Hyperte	nsion	norm	al		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% C	M-H, Random, 95% Cl
Bowe.B2020	1416	3985	239	1231	9.7%	2.29 [1.96, 2.67]	-
Chaibi.K2020	32	107	23	104	1.7%	1.50 [0.81, 2.80]	
Chan.L.L2020	618	1193	788	2042	10.1%	1.71 [1.48, 1.98]	-
Chan.L.L2021	820	1527	1015	2466	10.8%	1.66 [1.46, 1.89]	
Cheng.Y.C2020	40	499	59	893	3.2%	1.23 [0.81, 1.87]	<u>+-</u>
Cui.X.Y2020	9	38	12	78	0.7%	1.71 [0.65, 4.50]	
Doher.M.P2020	59	98	42	103	2.0%	2.20 [1.25, 3.86]	
Fominskiy.E.V2020	34	42	38	54	0.7%	1.79 [0.68, 4.70]	
Hansrivijit.P2021	85	189	30	94	2.3%	1.74 [1.04, 2.93]	
Hectors.S.J2020	10	26	6	19	0.4%	1.35 [0.39, 4.72]	
Hirsch.J.S2020	1292	3037	701	2412	11.4%	1.81 [1.61, 2.02]	
Joseph.A2020	48	56	33	44	0.7%	2.00 [0.73, 5.51]	
Lee.J.R2020	211	597	83	405	5.3%	2.12 [1.58, 2.85]	
Li.Q.L2020	36	73	12	34	1.0%	1.78 [0.77, 4.13]	
Li.Q2020	36	73	12	34	1.0%	1.78 [0.77, 4.13]	
Lim.J.H2020	18	59	12	71	1.0%	2.16 [0.94, 4.96]	
Lin.L2020	5	15	1	18	0.1%	8.50 [0.87, 83.49]	· · · · · · · · · · · · · · · · · · ·
Louis.G2020	65	132	15	49	1.3%	2.20 [1.10, 4.41]	
Luther.T2020	29	31	22	26	0.2%	2.64 [0.44, 15.72]	
Ng.J.H2020	2613	5730	1241	3927	12.5%	1.81 [1.67, 1.98]	•
Nimkar A2020	126	209	53	118	2.8%	1.86 [1.18, 2.94]	
Paek.J.H2020	22	226	6	478	0.8%	8.48 [3.39, 21.24]	
Pelayo.J2020	104	180	6	43		Not estimable	
Peng.S.Y2020	95	852	190	3168	6.2%	1.97 [1.52, 2.55]	-
Sang.L2020	45	98	47	112	2.1%	1.17 [0.68, 2.03]	- -
Taher.A2020	15	31	14	42	0.8%	1.88 [0.72, 4.86]	+
Tan.L.S2020	15	55	25	362		Not estimable	
Wang.F.L2020	71	150	65	125		Not estimable	
Wang.J2020	7	47	5	69	0.5%	2.24 [0.67, 7.54]	
Xia.P2020	23	43	18	38	0.9%	1.28 [0.53, 3.06]	- <u>-</u> -
Xu.J.Y2020	121	287	142	384	4.9%	1.24 [0.91, 1.70]	
Xu.S2020	10	26	8	36	0.6%	2.19 [0.72, 6.67]	
Zahid.U2020	165	323	42	146	3.2%	2.59 [1.70, 3.93]	
Zhang.J.H2020	23	115	14	279	1.3%	4.73 [2.34, 9.58]	
Total (95% CI)		19764		18974	100.0%	1.85 [1.70, 2.02]	•
Total events	8128		4923				
Heterogeneity: Tau ² = Test for overall effect:				P = 0.02	?); I² = 39%	, 0	L L L L L L L L L L L L L L L L L L L

FIGURE 3 | Continued

damage and repair, resulting in cell, tissue and organ oedema and other injuries. SARS-CoV-2 can penetrate the proximal tubule by connecting ACE2 to CD147 and can also penetrate podocytes by linking ACE2 (52). Viruses can cause podocyte dysfunction, resulting in glomerular disease. SARS-CoV-2 results in an imbalance in renin-angiotensin system (RAS) activation and promotes the progression of glomerular dysfunction, fibrosis, vasoconstriction, and inflammation (53). Infection with SARS-CoV-2 can also activate the coagulation system, leading to renal vascular injury (54). AKI is considered a negative prognostic factor with regard to survival (55). Mortality was found to be significantly more common in patients with hospital-acquired AKI and patients with intrinsic AKI. Identifying the risk factors for AKI in these patients may help reduce mortality due to COVID-19.

Our study found that male sex, age, smoking, obesity, hypertension, diabetes, pneumopathy, cardiovascular disease, cancer, CKD, mechanical ventilation and use of vasopressors were independent risk factors for AKI in adult patients with COVID-19. Previous studies have confirmed increased severity of and mortality due to COVID-19 in elderly patients (56). A recent study comparing the clinical characteristics and results in COVID-19 patients of different ages showed that the symptoms in elderly patients were more atypical, and these patients had more comorbidities, secondary infections, organ injuries, immunodeficiencies and critical illness (57). Many comorbidities

	diabet	tes	norm	al		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	
Bowe.B2020	953	2537	702	2679	11.3%	1.69 [1.51, 1.91]	•
Chaibi.K2020	23	78	32	133	1.2%	1.32 [0.70, 2.47]	
Chan.L.L2020	434	800	972	2435	9.0%	1.78 [1.52, 2.10]	-
Chan.L.L2021	568	1019	1267	2974	9.9%	1.70 [1.47, 1.96]	· · · · · · · · · · · · · · · · · · ·
Cheng.Y.C2020	23	241	76	1151	1.9%	1.49 [0.92, 2.43]	
Cui.X.Y2020	2	28	19	88	0.2%	0.28 [0.06, 1.28]	
Doher.M.P2020	39	64	62	137	1.3%	1.89 [1.03, 3.45]	
Fominskiy.E.V2020	12	16	60	80	0.3%	1.00 [0.29, 3.45]	
Hamilton.P2020	59	273	151	759	3.5%	1.11 [0.79, 1.56]	+-
Hansrivijit.P2021	56	108	59	175	1.9%	2.12 [1.30, 3.46]	
Hectors.S.J2020	5	13	11	32	0.3%	1.19 [0.31, 4.53]	
Hirsch.J.S2020	830	1797	1163	3652	11.4%	1.84 [1.64, 2.06]	-
Joseph.A2020	27	30	54	70	0.3%	2.67 [0.71, 9.95]	+
Kolhe.N.V2020	75	255	229	906	4.1%	1.23 [0.91, 1.68]	t -
Lee.J.R2020	138	378	156	624	4.8%	1.73 [1.31, 2.28]	
Li.Q.L2020	12	22	36	85	0.6%	1.63 [0.64, 4.19]	
Li.Q2020	12	22	36	85	0.6%	1.63 [0.64, 4.19]	+
Lim.J.H2020	14	36	16	94	0.7%	3.10 [1.31, 7.33]	— ,
Lin.L2020	3	6	3	27	0.1%	8.00 [1.08, 59.13]	
Louis.G2020	31	54	49	127	1.2%	2.15 [1.12, 4.10]	
Luther.T2020	16	16	35	41	0.1%	6.04 [0.32, 113.74]	
Ng.J.H2020	1699	3469	2155	6188	13.3%	1.80 [1.65, 1.96]	
Nimkar A2020	87	139	92	188	2.2%	1.75 [1.12, 2.73]	
Paek.J.H2020	16	123	12	581	0.8%	7.09 [3.26, 15.41]	
Pelayo.J2020	58	104	52	119	1.7%	1.62 [0.96, 2.76]	
Peng.S.Y2020	45	424	240	3596	3.6%	1.66 [1.19, 2.32]	-
Sang.L2020	23	44	69	166	1.1%	1.54 [0.79, 3.00]	+
Taher.A2020	17	33	12	40	0.5%	2.48 [0.95, 6.48]	<u> </u>
Tan.L.S2020	5	19	35	398	0.4%	3.70 [1.26, 10.89]	· · · ·
Wang.F.L2020	30	62	106	213	1.5%	0.95 [0.54, 1.67]	
Wang.J2020	3	20	9	96	0.3%	1.71 [0.42, 6.96]	
Xia.P2020	11	19	30	62	0.5%	1.47 [0.52, 4.14]	- -
Xu.J.Y2020	62	131	201	540	2.9%	1.52 [1.03, 2.23]	<u>⊢</u>
Xu.S2020	3	9	15	53	0.2%	1.27 [0.28, 5.73]	— -
Yan.Q2020	46	227	69	655	2.6%	2.16 [1.43, 3.25]	
Zahid.U2020	114	219	93	250	3.1%	1.83 [1.27, 2.65]	
Zhang.J.H2020	7	47	30	347	0.6%	1.85 [0.76, 4.48]	<u>+</u>
Total (95% CI)		12882		29846	100.0%	1.71 [1.59, 1.84]	•
Total events	5558		8408				
Heterogeneity: Tau ² =	0.01; Chi ²	= 48.93	, df = 36 ((P = 0.0	7); l² = 26%	6	
Test for overall effect:							0.01 0.1 1 10 100 diabetes normal

FIGURE 3 | Continued

in the elderly population, such as hypertension, diabetes and CKD, are treated with ACE inhibitors (ACEIs) and angiotensin II receptor blockers (ARBs), which upregulate ACE2, thereby increasing the risks of SARS-CoV-2 infection and severe disease. The proliferative ability of stem cells, which play an important role in renal cell repair, gradually decreases with age (58). Our study showed that age was an independent risk factor for AKI; the older the patient was, the higher the risk of AKI. Another study (59) showed that advanced age was an independent risk factor for AKI, which was consistent with our conclusion.

Recently, chronic kidney disease (CKD) emerged as the most common risk factor for severe COVID-19, and alarmingly, after age, it is also the strongest risk factor for severe COVID-19 (60). The removal of CKD as a risk factor would decrease the percentage of the global population at increased risk of severe COVID-19 from 22 to 17% (61). Thus, CKD explains the increased risk of severe COVID-19 in approximately one in four individuals at high risk worldwide, which is equivalent to 5% of the global population or 86,530,000 persons. CKD has emerged not only as the most prevalent comorbidity that is associated with an increased risk for severe COVID-19 but also as the comorbidity that conveys the highest risk for severe COVID-19. The increased risk is evident even below the threshold for the estimated glomerular filtration rate (eGFR) that is used to define CKD, and the risk increases as the eGFR decreases, with the highest risk in patients on renal replacement therapy. Some research has demonstrated that patients with CKD, particularly those with end-stage kidney disease (ESKD), have immune dysregulation and increased susceptibility to infections (62). For many patients with CKD, renin-angiotensin-aldosterone system (RAAS) blockade is a mainstay of treatment. The potential detrimental effect of the ongoing use of ACEIs or ARBs is the upregulation of ACE2, which could increase the ability of the virus to enter the cells.

Some studies have shown that the protein expression level of ACE2 in smokers is significantly higher than that in nonsmokers. This may be evidence that a history of smoking is a risk factor for AKI in patients with COVID-19. We also found that hypertension, diabetes and cardiovascular disease were independent risk factors for AKI, and these

	Pneumo	-	norm			Odds Ratio	Odds Ratio
Study or Subgroup	Events		Events			M-H, Random, 95% C	M-H. Random, 95% Cl
Bowe.B2020	437	1302	1218	3914	12.0%	1.12 [0.98, 1.28]	
Cheng.Y.C2020	11	77	88	1315	3.9%	2.32 [1.18, 4.56]	
Cui.X.Y2020	4	14	17	102	1.4%	2.00 [0.56, 7.13]	
Doher.M.P2020	9	19	92	182	2.3%	0.88 [0.34, 2.27]	
Fominskiy.E.V2020	1	3	71	93	0.4%	0.15 [0.01, 1.79]	
Hamilton.P2020	45	259	165	773		Not estimable	
Hansrivijit.P2021	33	73	82	210	5.2%	1.29 [0.75, 2.21]	
Hirsch.J.S2020	147	296	1846	5153	10.2%	1.77 [1.40, 2.24]	-
Joseph.A2020	2	2	79	98	0.3%	1.23 [0.06, 26.59]	
Kolhe.N.V2020	85	311	219	850	9.0%	1.08 [0.81, 1.45]	+
Lee.J.R2020	36	81	258	921	6.2%	2.06 [1.30, 3.26]	
Li.Q.L2020	11	23	37	84	2.4%	1.16 [0.46, 2.94]	
Li.Q2020	11	23	37	84	2.4%	1.16 [0.46, 2.94]	
Lim.J.H2020	4	16	26	144	1.5%	1.51 [0.45, 5.07]	
Louis.G2020	13	22	67	159	2.5%	1.98 [0.80, 4.91]	
Luther.T2020	13	14	38	43	0.5%	1.71 [0.18, 16.03]	
Ng.J.H2020	310	610	3544	9047	11.5%	1.60 [1.36, 1.89]	•
Nimkar A2020	24	44	155	283	4.2%	0.99 [0.52, 1.88]	
Pelayo.J2020	12	27	98	196	3.0%	0.80 [0.36, 1.80]	
Sang.L2020	2	5	90	205	0.7%	0.85 [0.14, 5.21]	
Tan.L.S2020	5	16	35	401	1.8%	4.75 [1.56, 14.46]	
Wang.F.L2020	14	37	122	238	3.6%	0.58 [0.28, 1.18]	
Wang.J2020	1	3	11	113	0.4%	4.64 [0.39, 55.35]	
Xu.J.Y2020	16	37	247	634	3.9%	1.19 [0.61, 2.33]	
Xu.S2020	2	5	16	57	0.7%	1.71 [0.26, 11.20]	
Yan.Q2020	17	86	98	796	4.8%	1.75 [0.99, 3.11]	
Zahid.U2020	13	34	194	435	3.5%	0.77 [0.38, 1.58]	
Zhang.J.H2020	5	23	32	371	1.9%	2.94 [1.02, 8.45]	
Total (95% CI)		3203		26128	100.0%	1.36 [1.16, 1.60]	•
Total events	1238		8817				
Heterogeneity: Tau ² =	0.05; Chi ² :	= 49.52,	df = 26 (F	= 0.00	4); ² = 47%	6	
Test for overall effect:	Z = 3.85 (P	= 0.000)1) `				0.01 0.1 1 10 100
			,				Pneumopathy normal

FIGURE 3 | Continued

	Cardiovascular d	isease	norm	al		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H. Random, 95% CI	M-H. Random. 95% CI
8.1.1 Coronary heart							
Chaibi.K2020	8	19	47	192	1.3%	2.24 [0.85, 5.91]	+
Doher.M.P2020	13	16	88	185	0.8%	4.78 [1.32, 17.32]	
Fominskiy.E.V2020	5	6	67	90	0.3%	1.72 [0.19, 15.47]	<u> </u>
Hamilton.P2020	16	83	194	949	2.6%	0.93 [0.53, 1.64]	+
Hansrivijit.P2021	25	50	90	233	2.4%	1.59 [0.86, 2.94]	<u>+</u>
Hectors.S.J2020	3	6	13	39	0.5%	2.00 [0.35, 11.32]	
Hirsch.J.S2020	289	600	1704	4849	5.2%	1.72 [1.45, 2.03]	-
Kolhe.N.V2020	42	119	262	1042	3.6%	1.62 [1.09, 2.43]	-
Lim.J.H2020	5	21	25	139	1.1%	1.43 [0.48, 4.25]	- -
Lin.L2020	1	2	5	31	0.2%	5.20 [0.28, 97.62]	
Luther.T2020	44	44	7	13	0.2%	77.13 [3.92, 1516.56]	
Ng.J.H2020	650	1249	3204	8408	5.4%	1.76 [1.56, 1.99]	-
Pelayo.J2020	20	35	90	188	2.0%	1.45 [0.70, 3.01]	+
Tan.L.S2020	10	26	30	391	1.5%	7.52 [3.14, 18.01]	
Wang.F.L2020	19	35	117	240	2.0%	1.25 [0.61, 2.54]	
Wang.J2020	3	12	9	104	0.6%	3.52 [0.81, 15.37]	
Xia.P2020	8	17	33	64	1.1%	0.84 [0.29, 2.44]	
Xu.J.Y2020	44	87	219	584	3.3%	1.71 [1.08, 2.68]	
Xu.S2020	4	11	14	51	0.7%	1.51 [0.38, 5.97]	-
Zahid.U2020	46	74	161	395	2.9%	2.39 [1.43, 3.98]	
Subtotal (95% CI)		2512		18187	37.8%	1.77 [1.50, 2.10]	♦
Total events	1255		6379				
Heterogeneity: Tau ² =		df = 19 (P		² = 38%			
Test for overall effect:				_			
8.1.2 Heart failure							
Chaibi.K2020	4	9	51	202	0.8%	2.37 [0.61, 9.16]	+
Chan.L.L2020	165	281	1241	2954	4.7%	1.96 [1.53, 2.52]	-
Chan.L.L2021	244	396	1591	3597	4.9%	2.02 [1.64, 2.50]	-
Doher.M.P2020	13	17	88	184	1.0%	3.55 [1.11, 11.28]	
Hamilton.P2020	23	129	187	903		Not estimable	
Hansrivijit.P2021	26	53	89	230	2.5%	1.53 [0.84, 2.78]	+
Hectors.S.J2020	5	5	11	40	0.2%	28.22 [1.44, 552.30]	→
Hirsch.J.S2020	208	349	1785	5100	4.9%	2.74 [2.20, 3.42]	-
Joseph.A2020	15	15	66	85	0.2%	9.09 [0.52, 158.89]	+
Kolhe.N.V2020	81	207	223	954	4.2%	2.11 [1.54, 2.89]	~
Lee.J.R2020	67	131	227	871	3.8%	2.97 [2.04, 4.32]	
Lim.J.H2020	2	10	28	150	0.6%	1.09 [0.22, 5.41]	-+
Luther.T2020	14	14	37	43	0.2%	5.03 [0.27, 95.05]	
Ng.J.H2020	501	791	3353	8866	5.3%	2.84 [2.44, 3.30]	-
Pelayo.J2020	19	24	91	199	1.2%	4.51 [1.62, 12.55]	
Subtotal (95% CI)		2302		23475	34.2%	2.41 [2.08, 2.79]	•
Total events	1364		8881				
Heterogeneity: Tau ² =	0.02; Chi ² = 21.46, d	df = 13 (P	= 0.06); l ²	² = 39%			
Test for overall effect:	Z = 11.70 (P < 0.000	001)					
8.1.3 others							
Bowe.B2020	574	1588	1081	3628	5.4%	1.33 [1.18, 1.51]	*
Cui.X.Y2020	10	48	11	68	1.3%	1.36 [0.53, 3.52]	-
Fominskiy.E.V2020	7	7	65	89	0.2%	5.61 [0.31, 101.98]	
Li.Q.L2020	21	33	27	74	1.6%	3.05 [1.30, 7.15]	
Li.Q2020	21	33	27	74	1.6%	3.05 [1.30, 7.15]	
Louis.G2020	26	52	54	129	2.3%	1.39 [0.73, 2.65]	<u>+-</u>
Nimkar A2020	59	98	120	229	3.1%	1.37 [0.85, 2.22]	<u>†</u>
Pelayo.J2020	15	23	95	200	1.5%	2.07 [0.84, 5.11]	+
Peng.S.Y2020	35	270	250	3750	3.8%	2.09 [1.43, 3.04]	
Sang.L2020	9	23	87	187	1.5%	0.74 [0.30, 1.79]	-+-
Taher.A2020	6	9	23	64	0.6%	3.57 [0.81, 15.61]	+
Yan.Q2020	79	515	36	367	3.5%	1.67 [1.10, 2.53]	~
Zhang.J.H2020	9	38	28	356	1.6%	3.64 [1.57, 8.43]	
Subtotal (95% CI)	-	2737		9215	27.9%	1.72 [1.38, 2.15]	♦
Total events	871		1904				
Heterogeneity: Tau ² =		f = 12 (P		² = 44%			
Test for overall effect:			0.00/, 1	/ /0			
		.,					
Total (95% CI)		7551		50877	100.0%	1.98 [1.74, 2.24]	♦
Total events	3490		17164				
Heterogeneity: Tau ² =		df = 46 /F		01): l² =	65%		<u>+ + + + + + + + + + + + + + + + + + + </u>
			0.0000	,			0.005 0.1 1 10 200
Test for overall effect: Test for subaroup diffe			= 0.008)	2 = 70 4	5%	(Cardiovascular disease normal

comorbidities were associated with micro- and macrovascular complications, all of which affected the renal blood flow. Any minor haemodynamic or nephrotoxic insult can lead to substantial AKI in these patients. Due to the use of ACEIs, the expression of the ACE2 protein in hypertensive patients is higher than that in non-hypertensive patients (63). This increases the risk of COVID-19-associated AKI by increasing the sites for virus binding. Patients with underlying cardiovascular disease and hypertension have been reported to have significantly high-case fatality rates compared with patients without these underlying comorbidities (10.5 and 6% mortality, respectively, compared with 0.9% mortality without underlying comorbidities) (64). Our study have stated that diabetes and obesity as risk factors for AKI in Covid-19 patients, therefore controlling those factors with anti-diabetic drugs may help in reducing the burden from the disease and mortality rate. Several anti-diabetic drugs have shown beneficial and neutral effects towards Covid-19. Some preliminary data from retrospective studies have confirmed a reduction in death rates in metformin users compared with non-users in patients with T2DM hospitalised for COVID-19 (65). Patients with diabetes should be advised to continue taking metformin drugs despite COVID-19 infection status (66). One metaanalysis suggests that pre-admission use of GLP-1RA may offer beneficial effects on Covid-19 mortality in patients with diabetes mellitus (67).

One study showed that coronavirus pneumonia brought about a 24% mortality in individuals with cancer while a 3% mortality was observed with non-cancer patients (68). Related studies have reported that AKI is a common complication in patients with malignant tumours, and the incidence of AKI in such patients is as high as 30%, which may be attributed to the renal toxicity of anti-cancer regimens (69). The incidence of AKI is markedly elevated in mechanically ventilated patients. Our study also confirms that mechanical ventilation is a risk factor for AKI in adult patients with COVID-19. Mechanical ventilation can increase the pressure in the thoracic cavity, resulting in reduced venous return, decreased cardiac output and decreased renal perfusion. In addition, mechanical ventilation can also induce pro-inflammatory reactions, change the neuro-humoural system, affect glomerular filtration, and cause or promote the occurrence and development of AKI (70).

CONCLUSIONS

AKI is a common and serious complication of COVID-19. Our meta-analysis indicates that male sex, age, smoking, obesity,

	cance		norm			Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% C	M-H, Random, 95% Cl
Bowe.B2020	270	799	1385	4417	26.6%	1.12 [0.95, 1.31]	•
Cheng.Y.C2020	5	62	94	1330	1.3%	1.15 [0.45, 2.95]	_ _ _
Doher.M.P2020	13	19	88	182	1.2%	2.31 [0.84, 6.35]	<u>– </u>
Fominskiy.E.V2020	3	3	69	93	0.1%	2.47 [0.12, 49.50]	
Hamilton.P2020	20	72	190	960	3.9%	1.56 [0.91, 2.67]	
Hirsch.J.S2020	133	327	1860	5122	16.8%	1.20 [0.96, 1.51]	-
Kolhe.N.V2020	32	102	272	1059	5.6%	1.32 [0.85, 2.05]	
Lim.J.H2020	7	26	21	132	1.2%	1.95 [0.73, 5.21]	+
Lin.L2020	0	3	6	30	0.1%	0.54 [0.02, 11.80]	
Louis.G2020	11	22	69	159	1.5%	1.30 [0.53, 3.18]	- <u>-</u> -
Luther.T2020	26	26	25	31	0.1%	13.51 [0.72, 252.34]	
Ng.J.H2020	341	754	3513	8903	28.6%	1.27 [1.09, 1.47]	•
Nimkar A2020	36	66	143	261	3.8%	0.99 [0.58, 1.70]	+
Peng.S.Y2020	3	40	282	3980	0.8%	1.06 [0.33, 3.47]	
Sang.L2020	10	14	82	196	0.8%	3.48 [1.05, 11.47]	
Taher.A2020	3	5	26	68	0.3%	2.42 [0.38, 15.49]	
Tan.L.S2020	0	6	40	411	0.1%	0.71 [0.04, 12.76]	
Wang.J2020	1	10	11	106	0.3%	0.96 [0.11, 8.31]	
Xu.J.Y2020	8	20	255	650	1.4%	1.03 [0.42, 2.56]	
Xu.S2020	1	3	17	59	0.2%	1.24 [0.10, 14.54]	
Yan.Q2020	7	41	108	841	1.7%	1.40 [0.60, 3.23]	
Zahid.U2020	13	31	194	438	2.1%	0.91 [0.43, 1.90]	_
Zhang.J.H2020	8	24	29	370	1.4%	5.88 [2.32, 14.89]	
Total (95% Cl)		2475		29798	100.0%	1.26 [1.13, 1.40]	•
Total events	951		8779				
Heterogeneity: Tau ² =	•			(P = 0.3	85); ² = 8%	0	0.005 0.1 1 10 200
Test for overall effect: 2	Z = 4.12 (P < 0.0	001)				cancer normal

	CKE)	NCK	D		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H. Random, 95% Cl
Chaibi.K2020	11	18	44	193	3.6%	5.32 [1.95, 14.55]	
Chan.L.L2020	243	323	1163	2912	10.1%	4.57 [3.51, 5.94]	-
Chan.L.L2021	339	420	1496	3573	10.2%	5.81 [4.52, 7.47]	-
Cheng.Y.C2020	4	21	95	1371	3.1%	3.16 [1.04, 9.58]	
Cui.X.Y2020	1	5	20	111	0.9%	1.14 [0.12, 10.73]	
Fominskiy.E.V2020	6	6	66	90	0.6%	4.79 [0.26, 88.23]	
Hansrivijit.P2021	44	66	71	217	6.6%	4.11 [2.29, 7.38]	
Joseph.A2020	27	29	54	71	1.9%	4.25 [0.91, 19.75]	
Kolhe.N.V2020	104	224	200	937	9.6%	3.19 [2.35, 4.34]	-
Lee.J.R2020	66	138	228	864	8.9%	2.56 [1.77, 3.69]	-
Li.Q.L2020	5	5	43	102	0.6%	15.05 [0.81, 279.35]	
Li.Q2020	5	5	43	102	0.6%	15.05 [0.81, 279.35]	
Lin.L2020	3	3	3	30	0.5%	55.00 [2.32, 1302.98]	——
Louis.G2020	11	13	69	168	1.9%	7.89 [1.70, 36.72]	
Ng.J.H2020	323	492	3531	9165	10.7%	3.05 [2.52, 3.69]	-
Nimkar A2020	33	40	146	287	4.5%	4.55 [1.95, 10.63]	
Paek.J.H2020	16	68	12	636	4.8%	16.00 [7.19, 35.61]	
Peng.S.Y2020	28	100	257	3920	8.0%	5.54 [3.52, 8.73]	-
Sang.L2020	6	10	86	200	2.4%	1.99 [0.54, 7.26]	+
Taher.A2020	6	6	23	67	0.6%	24.62 [1.33, 456.22]	
Wang.F.L2020	15	16	121	259	1.1%	17.11 [2.23, 131.42]	
Xia.P2020	1	3	40	78	0.8%	0.47 [0.04, 5.46]	
Xu.S2020	1	2	17	60	0.6%	2.53 [0.15, 42.78]	
Yan.Q2020	37	83	78	799	7.5%	7.44 [4.55, 12.16]	
Total (95% Cl)		2096		26212	100.0%	4.56 [3.63, 5.73]	◆
Total events	1335		7906				
Heterogeneity: Tau ² =	0.12; Chi ²	= 58.9	0, df = 23	(P < 0.0	0001); l² =	61%	0.001 0.1 1 10 1000
Test for overall effect:	Z = 13.04	(P < 0.0	00001)				CKD NCKD

FIGURE 3 | (A) Forest plot showing the relationship between hypertension and AKI in COVID-19 patients. (B) Forest plot showing the relationship between diabetes and AKI in COVID-19 patients. (C) Forest plot showing the relationship between pneumopathy and AKI in COVID-19 patients. (D) Forest plot showing the relationship between cardiovascular disease and AKI in COVID-19 patients. (E) Forest plot showing the relationship between cancer and AKI in COVID-19 patients. (F) Forest plot showing the relationship between CKD and AKI in COVID-19 patients.

hypertension, diabetes, pneumopathy, cardiovascular disease, cancer, CKD, mechanical ventilation and the use of vasopressors were independent risk factors for AKI in adult patients with COVID-19. Clinicians need to be aware of these risk factors to reduce the incidence of AKI. Some anti-diabetic drugs may help in reducing the burden from the disease and mortality rate. Several anti-diabetic drugs have shown beneficial and neutral effects towards Covid-19, such as metformin, GLP-1RA, and DPP-4 inhibitor (65, 67, 71). If we use metformin, GLP-1RA as the drug of choice for the management of patients with type 2 diabetes during the COVID-19 pandemic, it may improve patient outcomes, especially those with cardiovascular risk factors.

The limitations of this study are as follows: there were differences in the ethnicities of the subjects, numbers of cases, research methodologies and regions among the studies included in this analysis, and there was heterogeneity after the combination of some risk factors. The sample sizes of the included patients were not large enough for some factors. Further studies are still needed. Although we identified 11 risk factors for AKI, we believe that there are more potential risk factors for AKI that need to be investigated in future studies. Early identification and early intervention can reduce the occurrence of AKI and further improve the prognosis of patients with COVID-19.

DATA AVAILABILITY STATEMENT

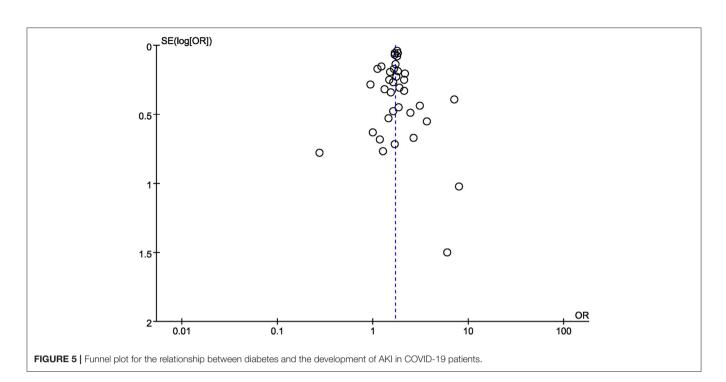
The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

AUTHOR CONTRIBUTIONS

XC: statistical analysis. XC and GW: literature research and selection, data extraction. XC, GW, and JZ: data analysis/interpretation. LY: funds collection, conception and design of the study, and revised manuscript. All authors interpreted the results and contributed to critical review of the manuscript.

	MV		Non-N	IV			Odds Ratio		Odds Ratio
Study or Subgrou	p Events	Total	Events	Total	Weigh	t M-	<u>H. Random, 95% Cl</u>	М-Н,	Random, 95% Cl
Bowe.B2020	585	863	1070	4353	4.8%	6	6.46 [5.51, 7.57]		
Cheng.Y.C2020	80	284	19	1108	4.5%	6 2	22.48 [13.34, 37.88]		
Cui.X.Y2020	8	23	13	93	3.7%	6	3.28 [1.16, 9.28]		
lamilton.P2020	63	124	147	908	4.6%	6	5.35 [3.61, 7.93]		
lansrivijit.P2021	47	58	68	225	4.2%	6	9.86 [4.82, 20.18]		
lirsch.J.S2020	1068	1190	925	4259	4.8%	6 3	31.55 [25.81, 38.58]		-
oseph.A2020	49	55	32	45	3.7%		3.32 [1.14, 9.62]		
Kolhe.N.V2020	50	81	254	1080	4.5%		5.25 [3.28, 8.39]		
.ee.J.R2020	179	261	115	742	4.7%		11.90 [8.57, 16.53]		
i.Q.L2020	41	67	7	40	3.9%		7.43 [2.87, 19.26]		
i.Q2020	41	67	7	40	3.9%		7.43 [2.87, 19.26]		
.ouis.G2020	79	149	,	32	2.3%		34.99 [4.65, 262.98]		
uther.T2020	9	9	42	48	1.4%		2.91 [0.15, 56.14]		
Ng.J.H2020	1897	2036	1957	7621	4.8%		39.50 [33.00, 47.28]		
Pelayo.J2020	37	48	73	175	4.2%		4.70 [2.25, 9.82]		
Peng.S.Y2020	38	708	53	3312	4.6%		3.49 [2.28, 5.33]		
Sang.L2020	80	118	12	92	4.2%		14.04 [6.84, 28.81]		
Taher.A2020	12	13	17	60	2.2%		30.35 [3.66, 251.83]		
「an.L.S2020	25	35	15	382	4.0%	661	1.17 [24.95, 149.97]		
Vang.F.L2020	119	223	17	52	4.3%	6	2.36 [1.25, 4.45]		
(ia.P2020	36	66	5	15	3.5%	6	2.40 [0.74, 7.79]		+
(u.J.Y2020	156	290	107	381	4.7%	6	2.98 [2.16, 4.11]		
(u.S2020	14	30	4	32	3.4%	6	6.13 [1.72, 21.80]		
(an.Q2020	75	172	40	710	4.6%	6	12.95 [8.35, 20.09]		
Zahid.U2020	68	100	60	369	4.5%	6	10.94 [6.62, 18.10]		-
「otal (95% CI)		7070		26174	100.0%	6	8.61 [5.63, 13.17]		•
Total events	4856		5060						
leterogeneity: Tau	2 = 0.97 Chi	= 537	07, df = 24	+ (P < 0	.00001)	; l ² = 9	6%		
	- 0.07, OIII							0.005 0.1	1 10 200
• •	· · · · ·							0.000 0.1	MAL March MAL
• •	· · · · ·							0.000	MV Non-MV
Test for overall effe	· · · · ·	P < 0.0		asopres	sors		Odds Ratio		Odds Ratio
est for overall effect	ct: Z = 9.94 (use of vasopre Events	P < 0.0	0001) unuse of v Even	S	Total V	-	M-H, Random, 95% Cl		
Test for overall effect tudy or Subgroup thaibi.K2020	ect: Z = 9.94 (use of vasopre Events 46	P < 0.0 essors <u>Total</u> 155	unuse of v Even	9	Total V 56	6.9%	M-H. Random, 95% Cl 2.20 [1.00, 4.87]		Odds Ratio
est for overall effect tudy or Subgroup haibi.K2020 heng.Y.C2020	ect: Z = 9.94 (use of vasopre <u>Events</u> 46 75	P < 0.0 essors Total 155 194	0001) unuse of v Even	9 4	Total V 56 1198	6.9% 7.5%	M-H. Random, 95% Cl 2.20 [1.00, 4.87] 30.83 [18.76, 50.67]		Odds Ratio
est for overall effect tudy or Subgroup haibi.K2020 heng.Y.C2020 ui.X.Y2020	use of vasopre <u>Events</u> 46 75 65	P < 0.0 essors Total 155 194 113	0001) unuse of v Even 2 1	9 4 5	Total V 56 1198 68	6.9% 7.5% 7.1%	M-H, Random, 95% Cl 2.20 [1.00, 4.87] 30.83 [18.76, 50.67] 4.78 [2.41, 9.48]		Odds Ratio
Test for overall effect tudy or Subgroup thabibi.K2020 theng.Y.C2020 tober.M.P2020	use of vasopre <u>Events</u> 46 75 65 11	P < 0.0 essors <u>Total</u> 155 194 113 13	unuse of v Even 2 1 9	9 4 5 0	Total V 56 1198 68 188	6.9% 7.5% 7.1% 5.0%	<u>M-H. Random, 95% Cl</u> 2.20 [1.00, 4.87] 30.83 [18.76, 50.67] 4.78 [2.41, 9.48] 5.99 [1.29, 27.76]		Odds Ratio
est for overall effect tudy or Subgroup haibi.K2020 heng.Y.C2020 oher.M.P2020 oher.M.P2020 ansrivijit.P2021	use of vasopre <u>Events</u> 46 75 65	P < 0.0 essors <u>Total</u> 155 194 113 13 53	0001) unuse of v Even 2 1 9 7	9 4 5 0 1	Total V 56 1198 68 188 230	6.9% 7.5% 7.1% 5.0% 6.9%	<u>M-H. Random, 95% Cl</u> 2.20 [1.00, 4.87] 30.83 [18.76, 50.67] 4.78 [2.41, 9.48] 5.99 [1.29, 27.76] 10.95 [5.07, 23.64]		Odds Ratio
est for overall effect tudy or Subgroup haibi.K2020 heng.Y.C2020 ui.X.Y2020 oher.M.P2020 ansrivijit.P2021 irsch.J.S2020	ect: Z = 9.94 (use of vasopre <u>Events</u> 46 75 65 11 44	P < 0.0 essors <u>Total</u> 155 194 113 13	0001) unuse of v Even 2 1 9 7 94	9 4 5 0 1	Total V 56 1198 68 188	6.9% 7.5% 7.1% 5.0%	<u>M-H. Random. 95% CI</u> 2.20 [1.00, 4.87] 30.83 [18.76, 50.67] 4.78 [2.41, 9.48] 5.99 [1.29, 27.76] 10.95 [5.07, 23.64] 31.16 [25.44, 38.17]		Odds Ratio
tudy or Subgroup haibi.K2020 heng.Y.C2020 ui.X.Y2020 oher.M.P2020 lansrivijit.P2021 lirsch.J.S2020 oseph.A2020	ect: Z = 9.94 (use of vasopre <u>Events</u> 46 75 65 11 44 1049	P < 0.04 essors Total 155 194 113 13 53 1168	0001) unuse of v Even 2 1 9 7 94	9 4 5 0 1 4 7	Total V 56 1198 68 188 230 4281	6.9% 7.5% 7.1% 5.0% 6.9% 7.8%	<u>M-H. Random, 95% Cl</u> 2.20 [1.00, 4.87] 30.83 [18.76, 50.67] 4.78 [2.41, 9.48] 5.99 [1.29, 27.76] 10.95 [5.07, 23.64]		Odds Ratio
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Test for overall effect tudy or Subgroup thaibi.K2020 theng.Y.C2020 toher.M.P2020 lansrivijit.P2021 lirsch.J.S2020 oseph.A2020 e.J.R2020 i.Q.L2020 i.Q2020	ect: Z = 9.94 (use of vasopre <u>Events</u> 46 75 65 11 44 1049 44 183	P < 0.0 sssors <u>Total</u> 155 194 113 13 53 1168 51 261	0001) unuse of v Even 2 1 9 7 94 3 11 1 1	9 9 4 5 0 1 4 7 1	Total V 56 1198 68 188 230 4281 49 741	6.9% 7.5% 7.1% 5.0% 6.9% 7.8% 6.3% 7.7%	<u>M-H. Random, 95% Cl</u> 2.20 [1.00, 4.87] 30.83 [18.76, 50.67] 4.78 [2.41, 9.48] 5.99 [1.29, 27.76] 10.95 [5.07, 23.64] 31.16 [25.44, 38.17] 2.04 [0.73, 5.71] 13.32 [9.54, 18.58]		Odds Ratio
Test for overall effect tudy or Subgroup thaibi.K2020 theng.Y.C2020 tui.X.Y2020 toher.M.P2020 lansrivijit.P2021 linsch.J.S2020 oseph.A2020 ee.J.R2020 i.Q.L2020 ti.Q.L2020 uther.T2020	ect: Z = 9.94 (use of vasopre <u>Events</u> 46 75 65 11 44 1049 44 183 29 29 9	P < 0.0 sssors <u>Total</u> 155 194 113 13 53 1168 51 261 38 38 38 9	0001) unuse of v Even 2 1 3 7 94 3 11 1 1 4	9 9 4 5 5 0 1 4 7 7 1 9 9 9 2	Total V 56 1198 68 8 188 230 4281 49 741 69 69 48	6.9% 7.5% 7.1% 5.0% 6.9% 7.8% 6.3% 7.7% 6.6% 6.6% 2.5%	<u>M-H. Random. 95% CI</u> 2.20 [1.00, 4.87] 30.83 [18.76, 50.67] 4.78 [2.41, 9.48] 10.95 [5.07, 23.64] 31.16 [25.44, 38.17] 2.04 [0.73, 5.71] 13.32 [9.54, 18.58] 8.48 [3.39, 21.18] 8.48 [3.39, 21.18] 2.91 [0.15, 56.14]		Odds Ratio
Test for overall effect tudy or Subgroup thaibi.K2020 theng.Y.C2020 tui.X.Y2020 oher.M.P2020 lansrivijit.P2021 linsch.J.S2020 oseph.A2020 ee.J.R2020 i.Q.12020 uther.T2020 lg.J.H2020	ect: Z = 9.94 (use of vasopre <u>Events</u> 46 75 65 11 44 1049 44 183 29 29 9 1938	P < 0.0 sssors <u>Total</u> 155 194 113 13 53 1168 51 261 38 38 38 9 2089	0001) unuse of v Even 2 1 9 4 3 11 1 1 4 4 191	9 9 4 5 5 0 1 4 7 1 9 9 9 2 6	Total V 56 1198 68 188 230 4281 49 741 69 69 48 7568	6.9% 7.5% 7.1% 5.0% 6.9% 7.8% 6.3% 7.7% 6.6% 6.6% 2.5% 7.9%	M-H. Random, 95% Cl 2.20 [1.00, 4.87] 30.83 [18.76, 50.67] 4.78 [2.41, 9.48] 5.99 [1.29, 27.76] 10.95 [5.07, 23.64] 31.16 [25.44, 38.17] 2.04 [0.73, 5.71] 13.32 [9.54, 18.58] 8.48 [3.39, 21.18] 8.48 [3.39, 21.18] 2.91 [0.15, 56.14] 37.86 [31.83, 45.03]		Odds Ratio
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Test for overall effer tudy or Subgroup thaibi.K2020 theng.Y.C2020 toher.M.P2020 toher.M.P2020 lansrivijit.P2021 lirsch.J.S2020 oseph.A2020 ee.J.R2020 i.Q.L2020 i.Q.L2020 g.J.H2020 lg.J.H2020 la.P2020 u.J.Y2020	ect: Z = 9.94 (use of vasopre Events 46 75 65 11 44 1049 44 183 29 29 9 1938 36 147	P < 0.0 sssors Total 155 194 113 13 53 1168 51 261 38 38 9 2089 63 277	0001) unuse of v Even 2 1 9 7 94 3 11 1 1 1 4 191	9 9 4 5 0 1 4 7 7 1 9 9 9 2 6 5 5 6	Total V 56 1198 68 188 230 4281 49 741 69 69 48 7568 18 394	6.9% 7.5% 7.1% 5.0% 6.9% 7.8% 6.3% 7.7% 6.6% 6.6% 2.5% 7.9% 6.0% 7.7%	<u>M-H. Random, 95% CI</u> 2.20 [1.00, 4.87] 30.83 [18.76, 50.67] 4.78 [2.41, 9.48] 5.99 [1.29, 27.76] 10.95 [5.07, 23.64] 31.16 [25.44, 38.17] 2.04 [0.73, 5.71] 13.32 [9.54, 18.58] 8.48 [3.39, 21.18] 8.48 [3.39, 21.18] 2.91 [0.15, 56.14] 37.86 [31.83, 45.03] 3.47 [1.10, 10.90] 2.71 [1.97, 3.73]		Odds Ratio
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Test for overall effect tudy or Subgroup thaibi.K2020 theng.Y.C2020 tui.X.Y2020 oher.M.P2020 lansrivijit.P2021 lirsch.J.S2020 oseph.A2020 ee.J.R2020 i.Q.L2020 Uther.T2020 Ig.J.H2020 Ja.P2020 u.J.Y2020 an.Q2020	ect: Z = 9.94 (use of vasopre Events 46 75 65 11 44 1049 44 183 29 29 9 1938 36 147	P < 0.0 sssors Total 155 194 113 13 53 1168 51 261 38 38 9 2089 63 277	0001) unuse of v Even 2 1 9 7 94 3 11 1 1 1 4 191	99 44 50 11 44 77 11 99 92 65 56 1	Total V 56 1198 68 188 230 4281 49 741 69 69 48 7568 18 394	6.9% 7.5% 7.1% 5.0% 6.9% 7.8% 6.3% 7.7% 6.6% 6.6% 2.5% 7.9% 6.0% 7.7% 7.6%	<u>M-H. Random, 95% CI</u> 2.20 [1.00, 4.87] 30.83 [18.76, 50.67] 4.78 [2.41, 9.48] 5.99 [1.29, 27.76] 10.95 [5.07, 23.64] 31.16 [25.44, 38.17] 2.04 [0.73, 5.71] 13.32 [9.54, 18.58] 8.48 [3.39, 21.18] 8.48 [3.39, 21.18] 2.91 [0.15, 56.14] 37.86 [31.83, 45.03] 3.47 [1.10, 10.90] 2.71 [1.97, 3.73]		Odds Ratio
Test for overall effer tudy or Subgroup thaibi.K2020 theng.Y.C2020 toher.W.P2020 lansrivijit.P2021 lirsch.J.S2020 oseph.A2020 ee.J.R2020 i.Q.2020 uther.T2020 ig.J.H2020 ia.P2020	ect: Z = 9.94 (use of vasopre Events 46 75 65 11 44 1049 44 183 29 29 9 1938 36 147	P < 0.0 sssors <u>Total</u> 155 194 113 13 53 1168 51 261 38 38 9 2089 63 277 178	0001) unuse of v Even 2 1 9 7 94 3 11 1 1 1 4 191	994500144500114477199926656611	Total V 56 1198 68 1198 68 188 2300 4281 49 741 69 69 48 7568 18 394 704	6.9% 7.5% 7.1% 5.0% 6.9% 7.8% 6.3% 7.7% 6.6% 6.6% 2.5% 7.9% 6.0% 7.7% 7.6%	M-H, Random, 95% CI 2.20 [1.00, 4.87] 30.83 [18.76, 50.67] 4.78 [2.41, 9.48] 5.99 [1.29, 27.76] 10.95 [5.07, 23.64] 31.16 [25.44, 38.17] 2.04 [0.73, 5.71] 13.32 [9.54, 18.58] 8.48 [3.39, 21.18] 8.48 [3.39, 21.18] 2.91 [0.15, 56.14] 37.86 [31.83, 45.03] 3.47 [1.10, 10.90] 2.71 [1.97, 3.73] 11.51 [7.46, 17.76]		Odds Ratio

FIGURE 4 | (A) Forest plot showing the relationship between mechanical ventilation and AKI in COVID-19 patients. (B) Forest plot showing the relationship between the use of vasopressors and AKI in COVID-19 patients.



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