A SYSTEMATIC REVIEW OF SYSTEMATIC REVIEWS ON THE INCIDENCE OF ACUTE KIDNEY INJURY IN COVID-19 PATIENTS

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ARTICLE INFO

Received: 11 May 2021
Received in revised form: 17 Aug 2021
Accepted: 19 Aug 2021
Available online: 28 Aug 2021

Keywords: COVID-19, Kidney disease, AKI, Systematic review, Renal failure

ABSTRACT

The recent COVID-19 pandemic has caused a lot of perturbation all around the globe. The risk of acute kidney injury (AKI) increases manifold during SARS-CoV-2 infection. This systematic review of systematic reviews aims to compile all the evidence on the incidence of AKI in COVID-19 patients, published in the form of systematic reviews. PRISMA guidelines were used to conduct this systematic review of systematic reviews. The comprehensive electronic search was conducted systematically on OVID, Cochrane library, EMBASE, ProQuest, PubMed, ScienceDirect, Scopus, and Web of Science databases up to the 17th of March 2021. Random effect meta-analysis was performed to assess the overall incidence of AKI in coronavirus patients as well as the associated mortality with 95% confidence of interval. After full-length analysis, only 15 systematic reviews with a total of 265162 coronavirus infected patients were included in the final study. The total sum of AKI patients in the systematic reviews was 24277 (9.15%). After applying the random effect model, it was observed that the overall incidence of AKI was 1 (95% CI: 1%-2%). Heterogeneity F2 < 1%, p < 0.001) and mortality associated with AKI in COVID-19 patients was 64 (95% CI: 44%-83%, Heterogeneity F2 = 99.32%, p < 0.001). Our study found that the incidence of AKI among COVID-19 patients was very common. Early and judicious clinical evaluation of AKI and the treatment of underlying causes of AKI should be one of the prime focuses of a clinician in the management of coronavirus-associated AKI.

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Introduction

Coronavirus belongs to the class of pathogens that are single-stranded RNA-viruses [1]. The recent COVID-19 pandemic has caused a lot of perturbation all around the globe [2]. Comparative analysis of clinical manifestations suggested that patients infected with this virus exhibit pneumonia-like symptoms with diffused alveolar injury which may cause ARDS (Acute Respiratory Distress Syndrome). However, common symptoms after the onset of SARS-CoV-2 infection include cough, fever, and fatigue, while some other symptoms are diarrhea, dyspnea, hemoptysis, sputum production, and lymphopenia [3]. Several reports claimed that SARS-CoV-2 is transmitted either directly through contact with the coronavirus infected person or indirectly by making a contact with droplets of an infected person released due to coughing and sneezing [4]. Another method

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of transmission of this virus is through intimate contact with surfaces containing a minimum dose of viral load that can cause infection [5]. Involvement of multiple organs including kidney, liver, and gastrointestinal tract have been reported in COVID-19 [6]. Obesity, old age, and the presence of various kinds of comorbidities may have also been associated with the increased rate of mortality [6]. People with low immunity like pregnant women, HIV patients, old, diabetic, and people on long-term immunosuppressant are more prone to the infection of coronavirus with associated multiple organ damage [7]. The risk of acute kidney injury (AKI) increases manifold during SARS-CoV-2 infection [8]. The exact mechanism of action of COVID-19 associated AKI is still unknown; however, it is believed to be associated with multi-organ shock and failure indicating acute tubular necrosis during AKI [8]. Elevated blood urea nitrogen (BUN), baseline serum creatinine, proteinuria, and hematuria are some of the representations of AKI during COVID-19 [9]. Renal replacement therapy (RRT) is often considered essential in severe cases of AKI, and it has been very successful in reducing the level of inflammatory cytokine levels [10].

Various studies have reported the development of acute kidney injury during the hospital stay of covid-19 patients and the injury was more common among critically ill patients or patients with other comorbid conditions. In a cohort study on 99 critically ill coronavirus patients, AKI was developed in 42.9% of patients and the majority of these patients had KDIGO stage III AKI [11]. A retrospective study conducted in hospitalized patients of New York city summarized that patients suffering from COVID-19 showed a higher incidence of AKI with increased requirement for mechanical ventilation, intensive care facility, and renal replacement therapy, as compared to patients without COVID-19 [12]. In clinical investigations of COVID-19, AKI is presented as an independent predisposing cause of mortality [13]. Studies have shown that critically ill AKI patients infected with coronavirus were at increased risk of mortality ranging from 8% to 23% [14, 15]. Some studies even showed an in-hospital mortality rate of 62%, 77%, and 80% among COVID-19 patients with Stage I, Stage II, and Stage III AKI, respectively [16].

Conducting a systematic review of systematic reviews provides the opportunity to present a broad view of already compiled evidence and highlight a wide range of issues related to the topic of interest [17, 18]. Reviews are fundamental to the evidence-based decision-making process because these are considered as high level of evidence in the compiled form [19, 20]. A large number of systematic reviews and general reviews are being published nowadays and they are becoming an essential part of routine research in the healthcare system [21]. However, this increasing phenomenon over the years has also created a problem of overloading of reviews in healthcare sciences and it has become very difficult for clinicians or policymakers to extract the relevant evidence from a compiled review [22-24]. Therefore, a review of systematic review is the need of the hour in extracting and compiling outcomes of interests from various reviews because many reviews on a particular topic have variability in their scope and quality. Thus, a single document that could represent and compare the results of multiple reviews can only be made by conducting a systematic review of various reviews on the topic of interest [17, 25].

There are various systematic reviews published on the incidence of AKI in coronavirus patients. However, to date, there is a need for comprehensive summative evidence that guides the clinicians to timely identify the symptoms and clinical variations that often led to renal failure among COVID-19 patients. The essential step at this stage is to conduct a systematic review of already published systematic reviews because there are already many systematic reviews published on the topic of interest. Keeping in view the aforementioned fact, the motivation behind this study is to synthesize a systematic review of systematic reviews. This systematic review of systematic reviews aims to compile all the evidence on the incidence of AKI in COVID-19 patients, published since the advent of the coronavirus pandemic. This systematic review of systematic reviews will provide healthcare decision-makers with the evidence they require in compiled form.

Materials and Methods

PRISMA guidelines (Preferred Reporting Items for Systematic reviews and Meta-analysis) were used to conduct this systematic review of systematic reviews [26].

Search Strategy


Data Extraction

Two authors independently extracted the data and a consensus was reached on the remaining data. Data extraction mainly focused on the incidence of AKI in COVID-19 patients. PICOS (Patient: Only coronavirus patients; Intervention: Requirement of renal replacement therapy [RRT]; Control: Those coronavirus patients who didn’t develop AKI; Outcome: Death due to AKI or survival; Study type: Systematic reviews with or without meta-analysis) algorithm was used to screen titles and abstracts to retrieve full-text articles for data extraction. Criteria for inclusion and exclusion were predefined.
Eligibility Criteria
Studies that were included consisted of systematic reviews on the incidence of acute kidney injury. All the letters, abstracts, interim reports, case reports, general reviews, and editorials were excluded. Studies that did not provide valuable clinical information on the incidence of AKI and those studies in which data extraction was difficult were excluded.

Quality Assessment
Included studies were qualitatively judged using A Measurement Tool to Assess Systematic Reviews 2 (AMSTAR-2) tool [27]. This tool utilized 16 questions that categorized the systematic reviews based on critical and non-critical domains. Overall confidence in the results was rated using these domains. The confidence on the systematic review was considered “high” if it had one or no non-critical weakness; confidence was considered “moderate” if it had no critical weakness, but more than one non-critical weakness; confidence was considered “low” if it had one critical weakness irrespective of the presence of non-critical weaknesses; confidence was considered “critically low” if it had more than one critical weaknesses irrespective of the presence of non-critical weaknesses.

Data Analysis
The descriptive method for analysis was the primary method exploited to compile the extracted data. Percentages and counts were used to describe categorical variables. Random effect meta-analysis was performed to assess the overall incidence of AKI in coronavirus patients as well as the associated mortality with 95% confidence of interval. I² statistics were performed to analyze the statistical heterogeneity among systematic reviews for the application of the random effect model and fixed effects model. Heterogeneity was considered insignificant if $I^2 < 25$%; heterogeneity was considered low if the value of $I^2$ falls between 25% to 50%; heterogeneity was considered moderate if the value of $I^2$ falls between 50% to 75%; and heterogeneity was considered high if the value of $I^2 > 75$% [28, 29]. So, the random effect model (REM) was utilized if the value of $I^2$ was more than 50% [29]. A $P$-value of 0.05 was considered as the threshold of a statistically significant level for this study.

Results and Discussion

Study Characteristics

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**Figure 1.** PRISMA chart showing selection criteria of systematic reviews on the incidence of AKI in COVID-19 patients
Table 1. General characteristic of the 15 systematic reviews on the incidence of AKI in COVID-19 patients

<table>
<thead>
<tr>
<th>Authors</th>
<th>Publication date</th>
<th>No. of articles</th>
<th>No. of patients</th>
<th>Study period</th>
<th>Types of studies</th>
<th>Comorbidities</th>
<th>Subgroup analysis</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fabrizio Fabrizi</td>
<td>15 December 2020</td>
<td>39</td>
<td>25566</td>
<td>1 December 2019 to 30 June 2020</td>
<td>Systematic review and meta-analysis</td>
<td>Yes</td>
<td>Yes</td>
<td>[30]</td>
</tr>
<tr>
<td>Hamza Bajwa</td>
<td>15 June 2020</td>
<td>5</td>
<td>1098</td>
<td>1 December 2019 to 13 April, 2020</td>
<td>Systematic review</td>
<td>Yes</td>
<td>Yes</td>
<td>[31]</td>
</tr>
<tr>
<td>Sadie Bennett</td>
<td>23 September 2020</td>
<td>45</td>
<td>14358</td>
<td></td>
<td>Systematic review</td>
<td>Yes</td>
<td>No</td>
<td>[32]</td>
</tr>
<tr>
<td>Vinson Wai-Shan Chan</td>
<td>27 May 2020</td>
<td>21</td>
<td>3714</td>
<td>Up to 8 April 2020</td>
<td>Systematic review and meta-analysis</td>
<td>No</td>
<td>No</td>
<td>[33]</td>
</tr>
<tr>
<td>Edouard L. Fu</td>
<td>2 September 2020</td>
<td>142</td>
<td>49048</td>
<td>1 December 2019 to 29 May 2020</td>
<td>Systematic review and meta-analysis</td>
<td>No</td>
<td>Yes</td>
<td>[34]</td>
</tr>
<tr>
<td>Ashraf Imam</td>
<td>24 July 2020</td>
<td>21</td>
<td>58</td>
<td>Up to 6 May 2020</td>
<td>Systematic review</td>
<td>Yes</td>
<td>No</td>
<td>[35]</td>
</tr>
<tr>
<td>Lirong Lin</td>
<td>10 November 2020</td>
<td>79</td>
<td>49692</td>
<td>1 January 2020 to 15 May 2020</td>
<td>Systematic review and meta-analysis</td>
<td>No</td>
<td>Yes</td>
<td>[36]</td>
</tr>
<tr>
<td>Camila Barbosa Oliveira</td>
<td>9 October 2020</td>
<td>21</td>
<td>15536</td>
<td>Up to 25 May 2020</td>
<td>Systematic review and meta-analysis</td>
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<td>Yes</td>
<td>[37]</td>
</tr>
<tr>
<td>Nicola Potere</td>
<td>2 July 2020</td>
<td>44</td>
<td>14866</td>
<td>Up to 20 April 2020</td>
<td>Systematic review and meta-analysis</td>
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<td>Yes</td>
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</tr>
<tr>
<td>Mengjiao Shao</td>
<td>31 July 2020</td>
<td>40</td>
<td>24527</td>
<td>Up to 20 June 2020</td>
<td>Systematic review and meta-analysis</td>
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<td>Yes</td>
<td>[39]</td>
</tr>
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<td>Zhenjian Xu</td>
<td>5 February 2021</td>
<td>22</td>
<td>16199</td>
<td>1 January 2020 to 1 June 2020</td>
<td>Systematic review and meta-analysis</td>
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<td>Yes</td>
<td>[40]</td>
</tr>
<tr>
<td>Xianghong Yang</td>
<td>18 June 2020</td>
<td>24</td>
<td>4963</td>
<td>December 2019 to May 2020</td>
<td>Systematic review and meta-analysis</td>
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<td>Yes</td>
<td>[41]</td>
</tr>
<tr>
<td>Xiaopeng Yang</td>
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<td>51</td>
<td>21531</td>
<td>Up to 25 July 2020</td>
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<td>No</td>
<td>Yes</td>
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</tr>
<tr>
<td>Xizi Zheng</td>
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<td>25</td>
<td>10554</td>
<td>Up to 30 July 2020</td>
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<td>Yes</td>
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<tr>
<td>Shoulian Zhou</td>
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<td>58</td>
<td>13452</td>
<td>Up to 16 June 2020</td>
<td>Systematic review and meta-analysis</td>
<td>No</td>
<td>Yes</td>
<td>[44]</td>
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</table>

Our search strategy (Figure 1) initially identified 3853 articles, of which only 71 articles were considered eligible for full-text analysis after the removal of duplicates and screening of titles and abstracts as shown in the PRISMA flow chart. After full-length analysis, only 15 systematic reviews (Table 1) with a total of 265162 coronavirus infected patients were included in the final study. These systematic reviews consisted of clinical trials, observational studies, retrospective cohort studies, case series, prospective cohort studies, case reports, and cross-sectional studies. Most of these systematic reviews were based on patients from China while only a few of these articles were based on patient data from other countries. These articles had conducted systematic reviews on the incidence of AKI in COVID-19 patients. There was a hundred percent agreement on all the included and excluded studies among authors based on already defined eligibility criteria.

Quality Assessment of the Included Systematic Reviews

The majority of the systematic reviews were placed under the “critically low” confidence category of the AMSTAR-2 tool because they had more than one critical weakness or flaw while addressing the critical domains of the study. Three studies were placed under the “low” confidence category because they failed to address only one critical domain. Only one study had a “high” overall confidence rating as it didn’t even miss a single critical and non-critical domain and its results were deemed comprehensive and accurate. Details of the quality assessment are further highlighted in Table 2.

Table 2. Quality ratings of the systematic reviews based on A Measurement Tool to Assess Systematic Reviews 2 (AMSTAR-2) tool

<table>
<thead>
<tr>
<th>Authors</th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>Q5</th>
<th>Q6</th>
<th>Q7</th>
<th>Q8</th>
<th>Q9</th>
<th>Q10</th>
<th>Q11</th>
<th>Q12</th>
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<th>Q14</th>
<th>Q15</th>
<th>Q16</th>
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</thead>
<tbody>
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<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Critically low</td>
</tr>
<tr>
<td>Hamza Bajwa</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>N/A</td>
<td>N/A</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Critically low</td>
</tr>
</tbody>
</table>

95
Clinical Characteristics of the Patients

Only three systematic reviews with total of 29282 provided information on the prevalent symptoms of the patients. Initial clinical presentation of the patients include fever (15691/29282 patients [53.58%]; 3 studies), cough (13551/29282 patients [46.27%]; 3 studies), fatigue (4300/14416 patients [29.28%]; 2 studies), anorexia (1130/14416 patients [7.83%]; 2 studies), shortness of breath (9130/29282 patients [31.17%]; 3 studies), expectoration (3460/14358 [24.09%]; 1 study), chills (184/14416 patients [12.86%]; 2 studies), myalgia (5624/14416 patients [39.01%]; 2 studies), diarrhea (6582/14416 patients [45.65%]; 2 studies), sore throat (5770/14416 patients [40.02%]; 2 studies), and nasal congestion (3334/14358 patients [23.22%]; 1 study). Detailed clinical characteristics from three systematic reviews are shown in Figure 2.

Figure 2. Clinical characteristics of COVID-19 patients

Co-morbidities among Patients

Data from seven systematic reviews suggested that hypertension (26039/96009 patients [27.12%]; 7 studies) and diabetes (16666/96009 patients [17.35%]; 5 studies) were the most prevalent comorbidities among patients. Cardiovascular diseases (12959/96009 patients [13.49%]; 5 studies) were the third most prevalent comorbidities in these studies. Heart failure,
myocardial injury, myocarditis, venous thrombosis, arrhythmia, and cardiogenic shock were the most common cardiovascular diseases reported. The rest of the comorbidities from these seven systematic reviews are highlighted in Figure 3.

Figure 3. Prevalence of comorbidities in COVID-19 patients

Acute Kidney Injury and Mortality among Patients

<table>
<thead>
<tr>
<th>Authors</th>
<th>No. of patients</th>
<th>Incidence of AKI</th>
<th>No. of AKI patients</th>
<th>Mortality with AKI</th>
<th>Overall Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fabrizio Fabrizi</td>
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<td>0.154</td>
<td>39</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
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<td>1098</td>
<td>6</td>
<td>66</td>
<td>62</td>
<td>234</td>
</tr>
<tr>
<td>Sadie Bennett</td>
<td>14358</td>
<td>12.6</td>
<td>1809</td>
<td>-</td>
<td>1177</td>
</tr>
<tr>
<td>Vinson Wai-Shun Chan</td>
<td>3714</td>
<td>7.58</td>
<td>282</td>
<td>61</td>
<td>-</td>
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<td>10.5</td>
<td>5150</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Ashraf Imam</td>
<td>58</td>
<td>34.1</td>
<td>18</td>
<td>-</td>
<td>11</td>
</tr>
<tr>
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<td>49692</td>
<td>10.6</td>
<td>5267</td>
<td>-</td>
<td>1403</td>
</tr>
<tr>
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<td>15536</td>
<td>12.3</td>
<td>1911</td>
<td>1280</td>
<td>-</td>
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<td>Nicola Potere</td>
<td>14866</td>
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<td>892</td>
<td>-</td>
<td>1687</td>
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<tr>
<td>Mengjiao Shao</td>
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<td>10</td>
<td>2453</td>
<td>-</td>
<td>1990</td>
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<tr>
<td>Zhenjian Xu</td>
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<td>10</td>
<td>1620</td>
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<td>-</td>
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<td>372</td>
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<td>-</td>
<td>-</td>
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<td>13452</td>
<td>9</td>
<td>1211</td>
<td>875</td>
<td>10882</td>
</tr>
</tbody>
</table>

The total sum of AKI patients in the systematic reviews was 24277 (9.15%) as shown in Table 3. After applying the random effect model, it was observed that the overall incidence of AKI was 1 (95% CI: 1%-2%, Heterogeneity $I^2 < 1\%$, $p < 0.001$) (Figure 4). Only four studies gave data on mortality associated with COVID-19 patients that suffered from AKI. The results of their findings revealed that 65.66% of patients (n=2278) died due to AKI. After the application of the random effect model, it was found that mortality associated with AKI in COVID-19 patients was 64 (95% CI: 44%-83%, Heterogeneity $I^2 = 99.32\%$, $p < 0.001$) (Figure 5). The highest incidence of AKI was 34.1 in a systematic review that consisted of only kidney transplant patients [35]. Similarly, the highest mortality associated with AKI was found 67.01% (n=1280) which was reported by one of the systematic reviews [37]. However, overall mortality (with or without AKI) was found to be 13.32% (n=20370) from eleven systematic reviews.
This systematic review of systematic review is the first of its kind on the incidence of AKI in COVID-19 patients that provide comprehensive evidence available so far, and it utilized fifteen systematic reviews on the topic of interest. Though most of the systematic reviews were of critically low quality, it is because AMSTAR-2 mainly focuses more on the quality of reporting system than on the quality of methodology [27, 45]. This instrument does not explore the logic or purpose of conducting a
systematic review and overemphasizes the reporting system like registration of protocol before conducting systematic review [27]. Therefore, we suggest that this quality rating should not diminish the confidence of readers in reviews included in this study.

Our study found that the incidence of AKI among COVID-19 patients was very common. The specific pathophysiological mechanism of incidence of AKI in coronavirus patients is still not discovered. However, it is believed that the existence of co-morbidities (especially hypertension, diabetes mellitus, and other cardiovascular diseases) and hypovolemic conditions, use of contrast media and nephrotoxic drugs, and subsequent pre-renal acute kidney injury significantly increase the risk of AKI in coronavirus patients [46]. ACE2 (Angiotensin Converting Enzyme-2) serves as a binding site for SARS-CoV-2, and its presence in multiple organs, especially in the kidney, suggests the multi-organ involvement of this virus. Cellular TMPRSSs (Transmembrane serine proteases) cleave the S-protein of coronavirus after its binding with ACE2 [47]. This co-expression of TMPRSSs and ACE2 in proximal tubule cells and podocytes eases the entry of this virus into the host kidney and this pathophysiological mechanism suggests that the kidney is one of the prime targets of coronavirus. Proximal tubule cells and podocytes have a very important role in the filtration, reabsorption, and excretion of urine from the kidneys. Studies suggest that podocytes are more vulnerable to the attacks of infectious agents than proximal tubule cells [48]. These cytopathic effects of coronavirus may be responsible for the development of AKI among patients. Another hypothesis suggests that microvascular thrombosis, hypoperfusion, and cytokine storm may also be responsible for AKI apart from the previously mentioned cytopathic mechanism [46]. Moreover, the presence of ARDS raised intra-thoracic pressure or severe hypoxemia in coronavirus infected patients has also been associated with the development of AKI because such mechanisms cause direct injury to the renal cells [49]. Additionally, the imbalance caused by the COVID-19 to the normal functioning of the RAAS system (renin-angiotensin-aldosterone system) leads to fibrosis, inflammation, and vasoconstriction at the renal level which may also have a role in the development of AKI [50].

Cough, fever, shortness of breath, and fatigue were the most common symptoms found in this review. These pneumonia-like symptoms could be very lethal for elderly patients, patients with multiple co-morbidities, or immunocompromised patients [51]. The majority of patients in this study had multiple comorbidities, especially hypertension, diabetes mellitus, and various other cardiovascular diseases. These patients are at the greater of COVID-19 associated mortality and the presence of high mortality in this study justifies that fact. Kidney transplant patients are considered the high-risk group because they utilize various immunosuppressive medications that compromise their immunity and made them succumb to multiple infections [52].

Though this study included very few systematic reviews, the mortality associated with AKI was found to be extremely high and this fact indicates the ominous unfolding of this pandemic, especially in AKI patients. The mortality rate (67%) associated with AKI in this review was similar to another systematic review by Oliveira CB, et al. [37].

This systematic review of systematic review indicated that the incidence of AKI was very common, and it was associated with the high mortality rate in COVID-19 patients. Our results suggest that manageable factors of AKI should be one of the prime focuses of a clinician through various diagnostic and treatment strategies. Such strategies should range from the avoidance of potentially nephrotoxic drugs to the management of hypoxic symptoms to COVID-19 patients. Moreover, full volume resuscitation in volume responsive patients coupled with vasopressor support should also be considered to counter fluid imbalance [53]. Additionally, early testing of urine and serum samples for the assessment of kidney functions at an early stage of coronavirus infection would be conducive to the improvement of treatment success rates and reduction in the development of AKI [36]. The specific treatment of AKI in COVID-19 is yet to be discovered; however, the available methods should be aimed at managing the underlying causes of the development of AKI. Keeping in view these baseline objectives, various immunomodulatory and antiviral drugs, that are not potentially nephrotoxic, can be used in the management of coronavirus-associated AKI [46]. Continuous Renal Replacement Therapy (CRRT) should be the next option for patients who remain unresponsive to the conservative management of AKI, especially for those who continue to present volume overload and refractory hypoxemia even after the utilization of conservative management [39]. Early optimization of hemodynamics and blood volume should be considered in the high-risk group of patients to ensure effective and adequate renal perfusion pressures [54].

This review is important for several reasons. Firstly, it compares the results of already published systematic reviews on the incidence of AKI. Secondly, it provides a ready assessment that the authors independently addressed similar questions as has been described in already published reviews. Thirdly, this review of reviews provides a summarization of existing evidence on the incidence of AKI and also highlights the absence of evidence where required. Fourthly, this review will serve as a guide to clinicians and urologists around the world in decision making and decision support systems. Fifthly, this review of reviews clearly states its objective and designed the review to answer that single question. Sixthly, in our opinion, it is the most appropriate and suitable step to highlight the overall incidence of AKI because there are already many reviews with heterogeneous results on the topic of interest. This review provides the readers with a compiled result on the incidence of AKI that is compared in the form of a single comprehensive document. This will help clinicians in addressing the challenge of AKI posted by COVID-19 by devising and implementing clinical interventions for the management of AKI.

The findings of this review should be translated under the light of certain limitations. Firstly, the number of systematic reviews included in this study is very small. We suggest more systematic reviews should be conducted to give a comprehensive picture of the conclusive unfolding of AKI in coronavirus patients. Secondly, the majority of reviews included in this study consisted of patient data from China and there may be different manifestations of COVID-19 concerning AKI in different parts of the world. Thirdly, there may be a chance of bias in the results as the included systematic reviews were not adjusted for various
confounding factors. Despite all these limitations, we still consider our study gives a comprehensive summary of the available systematic reviews published on COVID-19 associated AKI, and it will help clinicians and urologists in better management of AKI in coronavirus patients.

Conclusion

To conclude, AKI is a major complication associated with COVID-19 and it is one of the major factors of adverse outcomes in coronavirus patients. Our study found a high incidence of AKI in coronavirus patients and subsequent mortality with AKI was also very high. Early and judicious clinical evaluation of AKI and the treatment of underlying causes of AKI should be one of the prime focuses of a clinician in the management of coronavirus-associated AKI.

Acknowledgments: We would like to thank Dr. Maqbool Ali for his valuable input in this article and for reviewing the work.

Conflict of interest: None

Financial support: None

Ethics statement: None

References