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RESEARCH ARTICLE

ACUTE KIDNEY INJURY IN HOSPITALIZED PATIENTS WITH CORONAVIRUS DISEASE 2019 (COVID-19) AND LITERATURE REVIEW

Najoua Benothman, Latifa Oumaiouf and El Ouardi Youssef
Surgical Resuscitation Service, Hospital Ibn Tofail, CHU Mohamed VI Marrakech Morocco.

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Abstract

The coronavirus disease 2019 (COVID-19) outbreak has quickly become a global pandemic. Most patients with COVID-19 have mild symptoms, but develop severe symptoms as well, which can include acute respiratory distress syndrome, septic shock, and multiple organ failure. Renal involvement is common, with a clinical presentation ranging from mild proteinuria to progressive acute renal failure requiring renal replacement therapy (RRT). An understanding of the pathophysiology and mechanisms of kidney injury and ARI in the context of critical illness and COVID-19 We conducted a literature review to identify the impact of COVID 19 infection on the occurrence of acute renal failure. We specifically analyzed kidney functions in COVID-19 patients and their relationship to mortality. Only acute renal failure (ARI) directly linked to SARS-CoV 2 infection is considered; other causes of renal failure of hemodynamic, iatrogenic or other origin are excluded

Introduction:-

The coronavirus disease 2019 (COVID-19) outbreak has quickly become a global pandemic. Most patients with COVID-19 have mild symptoms, but develop severe symptoms as well, which can include acute respiratory distress syndrome, septic shock, and multiple organ failure. Renal involvement is common, with a clinical presentation ranging from mild proteinuria to progressive acute renal failure requiring renal replacement therapy (RRT). An understanding of the pathophysiology and mechanisms of kidney injury and ARIs in the context of severe disease and COVID-19 is emerging.to emerge, although further research isneeded to identify patients at risk for ARI and to guide management strategies [1]

To date, large amounts of epidemiological data and case studies have been available for coronavirus disease 2019 (COVID-19), suggesting that mortality was not solely related to respiratory complications [2]

Most articles published on COVID-19 have highlighted the lungs as the primary organ involved in the disease, while few articles have reported SARS-CoV-2 involvement in other organs, including the kidneys [3]

From a medical and scientific point of view, this pandemic is an opportunity to assess whether there is an interaction between SARS-CoV-2 and the kidney, likely to modify the epidemiology of acute renal failure (ARI). [4]

Corresponding Author:- Najoua Benothman
Address:- Surgical Resuscitation Service, Hospital Ibn Tofail, CHU Mohamed VI Marrakech Morocco.

Materials and Methods:-

We conducted a literature review to identify the impact of COVID 19 infection on the occurrence of acute renal failure.We searched the PubMed, science direct and medRxiv databases.

We then extracted the epidemiological, physiopathological data and compared the incidence of ARI according to the studies

Here, we specifically analyzed kidney functions in COVID-19 patients and their relationship to mortality.Only acute renal failure (ARI) directly related to SARS-CoV2 infection is considered; other causes of renal failure of hemodynamic, iatrogenic or other origin are excluded.

Epidemiology [5]

Novel coronavirus disease (COVID-19) is a newly discovered contagious disease caused by severe acute respiratory syndrome (SARS) - coronavirus virus (CoV)-2, manifesting primarily as an acute respiratory disease with interstitial and alveolar pneumonia, but it can affect several organs such as kidney, heart, digestive tract, blood and nervous system. This rapidly spreading outbreak emerged in Wuhan, Hubei Province, China in December 2019, and has since been declared a global pandemic by the World Health Organization. As of March 16, 2020, 167,511 of COVID-19 cases have been reported globally in 151 countries, 6606 deaths. In recent days, the number of cases has increased rapidly in South Korea, Japan, Europe, and the United States.

SARS-CoV-2 has been identified as a batorigin CoV. The full-length genome sequence of the COVID-19 virus shows a close relationship to the bat-like coronavirus SARS strain Bat Cov RaTG13 belonging to the genus Beta coronavirus.

SARS-CoV and the Middle East respiratory syndrome coronavirus (MERS-Co-V), have infected more than 10,000 people over the past two decades, mortality rates of 10% and 37% respectively.

Pathophysiology

The cause of renal involvement in COVID-19 is likely multifactorial, with cardiovascular comorbidity and predisposing factors (eg, sepsis, hypovolemia, and nephrotoxins).

Cardiorenal syndrome, particularly right ventricular failure secondary to COVID-19 pneumonia, could lead to renal congestion and subsequent AKI. Similarly, left ventricular dysfunction can lead to low cardiac output, arterial underfilling, and renal hypoperfusion.[1]

The AKI directly linked to Covid19 infection is mainly linked to this state which is called “the cytokine stormsyndrom” or cytokine storm syndrome.

The viral particles will spread through the respiratory mucosa and infect other cells, causing a massive release of inflammatory cytokines. At the same time, various anti-inflammatory mediators will also be produced in an attempt to attenuate the systemic effects of inflammatory cytokines, but on the other hand may facilitate immune depression and secondary infections. ARI may also be due to tubular cell damage directly related to viral invasion. It has also been demonstrated that converting enzyme 2 (EC2), which is the cellular receptor for SARS-CoV2, is widely expressed in tubular cells [6]

Additionally, SARS-CoV-2 can directly infect renal tubular epithelium and podocytes through an angiotensin-converting enzyme 2 (ACE2)-dependent pathway and cause mitochondrial dysfunction, and acute tubular necrosis. [1]

Recent evidence suggests that the new SARS-CoV-2 virus and the original SARS-CoV virus use the same cell entry receptor, the ACE2 protein, which is expressed at high levels on the surface of lung epithelial cells, cells myocardium, and arterial smooth muscle cells.

Ding et al. systematically examined the presence of SARS-CoV in the tissues of deceased SARS patients by immunohistochemistry and in situ hybridization; the authors found that SARS-CoV was present in the lungs, small

intestine, kidneys, liver, pancreas, brain and other tissues, indicating that organs expressing ACE2 may serve as direct targets of SARS-CoV. Additionally, SARS-CoV uses the ACE2 protein for cell entry and uses the cellular serine protease TMPRSS2 for viral spike protein priming.

A recent study confirmed that the closely related SARS-CoV-2 also uses both ACE2 and TMPRSS2. Additionally, other proteins such as CD147 can also be utilized by both SARS-CoV and SARS-CoV-2 during virus transmission.

Nonetheless, it is noteworthy that a subset of previously healthy and even relatively young COVID-19 patients were killed by SARS-CoV-2, suggesting that patient genomes for DNA variations could have an impact on the severity and mortality of the disease [5]

Entry of the coronavirus into host cells is mediated by the transmembrane spike (S) glycoprotein that forms the surface-protruding homotrimers.

S comprises two functional subunits responsible for binding to the host cell receptor (S1 subunit) and fusion of virus and cell membranes (S2 subunit). For many CoVs, S is cleaved at the boundary between the S1 and S2 subunits, which remain non-covalently bound in the prefusion conformation. The distal S1 subunit comprises the receptor binding domain(s) and contributes to stabilizing the prefusion state of the anchored membrane the S2 subunit containing the fusion machinery. For all CoVs, S is further cleaved by proteases at the so-called S2 site located immediately upstream of the peptide fusion.

This cleavage has been proposed to activate the protein for membrane fusion via large irreversible conformational changes.

Therefore, entry of the coronavirus into susceptible cells is a complex process that requires the concerted action of receptor binding and proteolytic processing of protein S to promote virus-cell fusion. [8]

TMPRSS2 inhibitor approved for clinical use blocked entry and could be a treatment [9]

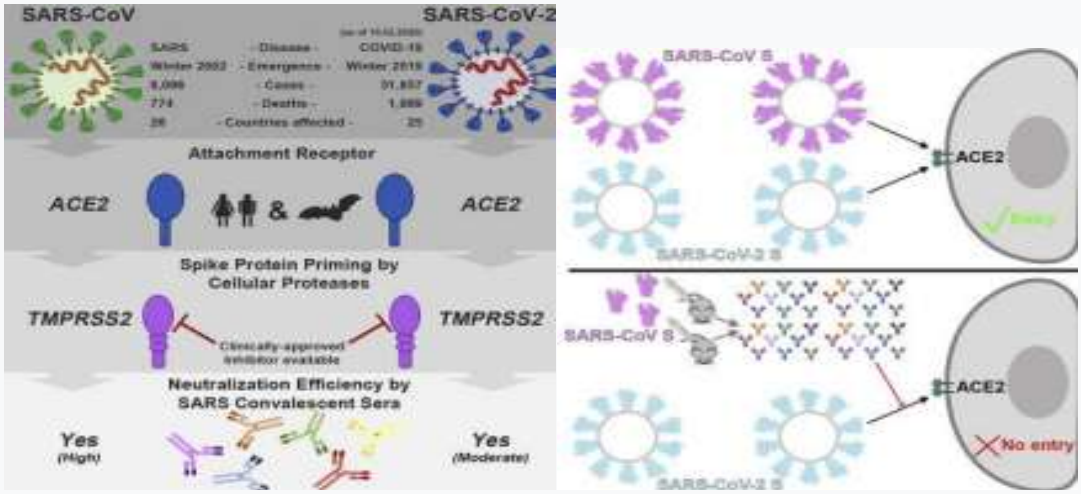

Figure 1:- Pathophysiology of'kidney damage during'SARS COV 2 infection.

Results:-

1-Kidney Damage During Covid-19

Regarding kidney damage, Chu et al. found that 6.7% of patients (36 of 536) with SARS developed AKI with a median interval of 20 days (range: 5-48 days) after onset of viral infection; strikingly, the vast majority of these 36 SARS patients with AKI (91.7%, or 33 patients) eventually died, compared to a mortality rate of only 8.8% in SARS patients without AKI. These results reinforce the idea that AKI may be a major risk factor contributing to the increased mortality rate in patients with SARS. Accordingly, renal function should be monitored in patients with COVID-19, thus providing a possible prognostic indicator of poor outcome [10]

During COVID-19 (coronavirus disease-19) the question arises of a possible singularity of renal damage In an early Chinese cohort of patients hospitalized with COVID-19, the incidence of AKI of all grades was by 5%. This incidence compares favorably with that of a representative "non-COVID-19" hospital population, around 8%.1 However, the mortality associated with COVID-19 is significantly influenced by the presence or the absence of renal insufficiency on admission (33.7 vs 13.2% respectively), or by the development of an ARI during the stay. An increase in serum creatinine (> 133 µmol/l on admission is observed more frequently (9.6 vs 1%) in patients who will experience an unfavorable hospital outcome such as admission to intensive care or death. After admission to intensive care, the need to resort to dialysis concerns about 5.5 to 11.9% of patients 3,4 and then confers a very high mortality. During the SARS-COV virus epidemic in 2003, mortality reached 92%5 and was largely due to the severity of the patient's medical condition. Mortality could be similar during the current pandemic. [4-11]

A recent clinical study of 59 patients with COVID-19 found that 32 of 51 patients (63%) had proteinuria, an indicator of kidney failure. Regarding other renal indicators, the authors also found that 19% and 27% of COVID-19 patients had elevated levels of plasma creatinine and urea nitrogen, respectively. Importantly, a separate study of 52 COVID-19 patients (with 20 survivors and 32 non-survivors) found that 15 patients (29%) had acute kidney failure. Additionally, Zhou et al. reported that 15% of patients infected with SARS-CoV-2 had AKI, compared to 50% in non-surviving patients. [7]

2-Characteristics of Kidney Damage During Covid-19

The pathogenesis of specific kidney injury during COVID-19, if proven, raises questions. In 2003 during the SARS-CoV epidemic, as currently with COVID-19, kidney biopsies performed in this context did not reveal specific lesions (in particular glomerular) attributable to the virus, but acute tubular necrosis. These lesions, observed almost exclusively on autopsies, are part of a multi-organ failure that could explain ischemic, even potentially septic or toxic, tubular lesions. Should we then consider that the tubular lesions during COVID-19 are not specific, but represent a variation of a process common to multi-organ failures whatever the cause?

In favor of the singularity of the AKI associated with COVID-19, many clinicians observe later episodes in the evolution of the disease and which sometimes occur in the absence of marked hemodynamic alterations. This suggests a direct toxicity of the virus for the kidney, which could sensitize the tubular cells to more classic attacks. [4]

Additionally, Cheng et al. reported that patients with acute kidney injury have a higher mortality rate than other patients [12]

COVID-19 patients can experience a wide range of symptoms. Although the majority of patients infected with SARS-CoV-2 experience relatively mild symptoms, a considerable number of patients develop severe disease.**[13-14]**

3-Management of Kidney Involvement in COVID-19 [1]

In the absence of specific anti-SARS-CoV-2 treatments, supportive care and the use of sequential extracorporeal therapies for critically ill patients with signs of renal impairment provide a vital bridge to recovery and increase the likelihood of a favorable result. The decision to use sequential extracorporeal therapies should consider the technical effort and dedicated skills of multidisciplinary personnel that are necessary for safe and effective therapy delivery. Careful patient selection for sequential extracorporeal therapies is needed because age and comorbidities appear to influence outcomes in critically ill patients with COVID-19.

Further research is needed to improve the understanding of AKI secondary to COVID-19, to obtain adequate evidence to support the clinical approaches discussed here, and to develop new surveillance and management approaches. Promoting an international collaborative and interdisciplinary research culture will be crucial to rigorously test therapies in clinical trials and rapidly identify patients with COVID-19 who are at risk for ACI and who will benefit from established and emerging therapeutic approaches. .

Conclusion:-

Taken together, these results indicate that renal function should be closely monitored when treating patients with COVID-19, especially patients with abnormal serum creatinine levels, blood urea nitrogen levels, or relevant CT results. [7]

Clinicians should consider any potential intervention to protect kidney functions in early stage disease and renal replacement therapies in critically ill patients, especially for those with strong inflammatory reactions or cytokine storm **[2].**

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