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Review Article

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MANAGING COVID-19 IN KIDNEY TRANSPLANT RECIPIENTS A CHALLENGING SITUATION: A REVIEW

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ABSTRACT

Coronavirus disease (COVID-19) originated by novel coronavirus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has recognized to be a rapidly spreading infection. This review aims to address the challenges and recommended therapy for managing the kidney transplant recipients (KTRs) with COVID-19. The database was obtained from PubMed, Science Direct, and Google scholar to identify relevant scientific article including case studies, case reports, trial studies and cohort studies to narrate the review. The current review at the end concludes awaking the physicians to modify therapy and management strategies for KTRs with COVID-19 infection.

KEYWORDS: - COVID-19, Kidney transplant recipients, Challenges in KTRs with COVID-19, Management therapy, Management strategies.

INTRODUCTION

Coronavirus disease (COVID-19) caused by novel corona virus known by the name severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has perceived to be a rapidly spreading infection.[1] This pandemic continues to seize the world in unpredicted ways with radiance speed mutation rates and host changing potential.[2] COVID 19 virus strike to respiratory system, causing pneumonia and lymphocytopenia in infected populations. Viral portions like nucleocapsid and spike proteins aggravates an immune reaction in the host to eradicate the virus.[3] The early manifestation of coronavirus disease such as pneumonia, acute respiratory distress syndrome and multiple organ failure are observed through the action of immune system.[4] Patients with kidney transplant are possibly at the first line of developing serious coronavirus disease 2019 (COVID-19) infection which is attributable to chronic immunosuppression.[5]

Notably kidney transplant recipient (KTR) suffers from immunosuppressed therapy along with chronic kidney disease (CKD) and especially endangered to acute kidney injury.[6] Even though the prevalence between KTR do not appear to vary from the general population, [7] the COVID-19- associated mortality reported in this group of victims ranges from 17.9% to 28%.[8] Particularly considering elderly KTR, present 50% short term fatality rate.[9]

Current review address about the challenges and potential therapy which might be safer in management of covid -19 in KTRs.

METHODS

A literature review was accomplished using PubMed, Science Direct and Google scholar to identify relevant scientific article including case studies, case reports, trial studies and cohort studies published from 1997 to 2022. Search terms included immunosuppression in KTR COVID-19 infection in KTR, KTR sensitivity to infections. Severity of COVID-19 infection in KTR. Renal consequences, impact of COVID-19 infection in KTRs, management therapy of KTRs with COVID-19. The search followed 44 original research articles reporting on patients who received inpatient and outpatient COVID-19 treatment those who were a kidney transplant recipient.

Immunosuppressive therapy boosting COVID-19 infection to critical side

Immunosuppressive therapy for a longer period is established risk factor for bacterial and viral infections and it is also decisive to prevent antiviral anti-inflammatory response.[10] basiliximab has antagonistic action on IL-2 receptor,[11,12] Before time use of alemtuxumab in KTR was linked with severe and persistent lymphocyte depletion. Efalizumab (once weekly subcutaneous injection), act as an immunosuppressive agent by sticking to the CD11a subunit of lymphocyte function-associated antigen 1 (LFA-1) and inhibiting white blood cell emigration.[13]

Recently developed Tofacitinib is a kinase inhibitor with immunosuppressive potential.[14] Long exposure to chronic immunosuppression critically destroys components of host immunity, such as natural killer cells, chronic antigen stimulation from transplanted organs, weakens the defensive capabilities of the immune system.[15] Coronavirus infection critically causes lymphocytopenia in infected individuals, viral spike protein and nucleocapsid proteins provoke an immunological response in host to eradicate the virus. B cells or major histocompatibility complex to the T cells recognize those viruses and stimulating antibody production. Cytolytic activity, increased cytokinin secretion in the acute phase of infection.[16]

KTR are subjected to T cell depleting therapy along with maintenance of immunosuppression which make alteration in viral response.[17] The probable risk of glucocorticoid therapy in COVID-19 sick person include immune suppression, weakened viral destruction and elevated plasma viral load and epithelial shedding.[18]

Renal load after infection

SARS-C0V-2 invade into human cells with the help of several proteins counting furin, TMPRSS2, and lysosomal proteases by sticking the receptor binding domain and which enables endocytosis, the activity results in impaired immune clearance of the virus.[19] Angiotensin converting enzyme (ACE2) is the target of SARS-CoV-2 in the host cell. Upon binding to the SARS-CoV-2, the ACE2 level is hampered and the Angiotensin II (Ang II) level rises, encouraging vasoconstriction, oxidative stress, inflammation, and cell apoptosis.[20] In some findings from a case series of 193 patients, it was reported 31% of patient had aggravated serum creatinine. It was also found that among 147 patients, 60% reported proteinuria and 48% noted with hematuria.[21]

In similar retrospective analysis of 333 patients, around 75% faced urine dipstick peculiarities or Acute kidney injury (AKI).[22] Further study of 701 patients among those 11.9 % noted with raised baseline creatinine caused AKI compared to 4,0% in patients with usual creatinine baseline. The mortality was significantly higher in patients aggravated hematuria, proteinuria, baseline creatinine and urea and AKI stage 2-3.[23] Infection could cause tubular damage through the crowd of forming MAC complex (the end process of the compliment cascade) on tubules and infiltration of CD68+ macrophages in the tubules.[24] In certain findings of Afro-American patients biopsies it was reported glomerulosclerosis with COVID-19 infection.[25,26]

Immunity in Kidney transplant Recipient and Impact of COVID-19 infection

Production of IgG antibodies against SARS-CoV-2 was delayed[27] Aggravated immunological response, can upshot tissue damage in COVID-19[28] Laboratory findings reported lymphopenia with hampered CD3, CD4, and CD8 T cells.[29] Thus delays the recovery from COVID-19.

Management therapy in KTR with COVID-19

The European Renal Association-European Dialysis and Transplant Association (ERA-EDTA) guidelines recommended that instead of discontinuing calcineurin inhibitors the reduction in doses of calcineurin inhibitors with discontinuing mycophenolate, azathioprine, or mTOR-inhibitors might be more significant option for COVID-19 patients without pneumonia.[30] Calcineurin inhibitors have been reported to show antiviral effects and both tacrolimus and cyclosporin A reported to inhibit the invitro replication of various coronavirus inclusive of SARS-CoV at small nontoxic concentrations.[31,32] Few Clinicians recommends that shifting from tacrolimus to cyclosporin might be a satisfactory option in COVID-19 infected KTRs.[33] In a case report the first organ transplant patient with malignant melanoma who received Ipilimumab followed by Nivolumab without experiencing a kidney allograft rejection.[34]

In severely ill patients, it is recommended not to discontinue immunosuppression instead converting those patients to Hydrocortisone/ Solumedrol. This could proceed towards boosting viral removal and could result in immune reconstruction. This approach may improve viral clearance but could lead to immune repair.[35,36]

Management of COVID-19 in Kidney transplant recipient

Findings recommends that a subgroup of victims with severe COVID-19 suffers through a cytokine storm condition indicated by elevated interleukins (IL)-1, IL-6, IL-7, interferon- γ inducible protein.[37,38] Few studies have reported the potential action of Tocilizumab, an IL-6 inhibitor, in managing and controlling cytokine cyclone in COVID-19 patients.[39] In a cohort monitoring study anti-cytokine therapy with Tocilizumab (42%), followed by Anakinra (12%), respiratory secondary infection and mortality was found to be avoided in KTRs with COVID-19, few of this anti cytokine therapy in KTRs reported to be clinically safe.[40]

In a case report a treatment therapy with Azithromycin, Hydrochloroquine, Mycophenolic acid, Tacrolimus reported to give satisfactory recovery of KTRs from COVID-19 infection journey.[41] Administering Remdesivir and Dexamethasone in severely ill patients, earlier may prevent the steroid related delay in knocking down of virus is proven in some studies.[42,43] It was reported that replacing high dose corticosteroids with calcineurin inhibitors and antiproliferative therapy skips the progression of COVID-19 infection.[44]

CONCLUSION

The current review at the end concludes the challenges and recommended therapy could aware the physicians to modify therapy and management strategies for KTRs with COVID-19 infection.

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