Outcome of COVID-19 Infection and the Impact of COVID-19 Vaccination in Chronic Kidney Disease Patients: A Single-Center Study

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Abstract

Introduction: Chronic kidney disease (CKD) patients have increased vulnerability to infections including Covid-19. There is limited availability of antiviral in CKD patients. All guidelines have prioritized vaccinations for CKD patients. The variability in immunogenic response is multifactorial in CKD group. We have tried to analyze the outcome of Covid-19 infection and the impact of COVID-19 vaccination [COVAXIN / COVISHIELD] in our cohort. **Materials Methods and Statistical Analysis:** In a retrospective observational study, 73 cases of Covid-19 positive CKD patients were selected, who were managed as per MOFHW guidelines. The data of first laboratory values and radiological findings were evaluated. Their treatment outcome and stay during hospitalization were studied. All data were later analyzed using STATA 16.1 software. **Results:** In this study, 73 cases of CKD with Covid-19 were included. There were 38 patients who were vaccinated with at least one dose of the Covid-19 vaccine, while there were 35 patients who were unvaccinated. Out of 38 patients, 20 were vaccinated with 2 doses of Covid-19 while 18 received only one dose. The unvaccinated group was having more hypoxia and raised inflammatory markers, and had more lung involvement [i.e. higher CT severity value] [p value for CTSS-0.0765]. There was a higher mortality rate observed in the unvaccinated group [i.e-65.71%] than the vaccinated group [39.47%] [p-value 0.0249]. Dialysis was needed in 57.50% of the study population either due to failure of conservative management for renal failure or due to maintenance dialysis. The mean duration of hospitalization was 11.47 days with a mortality rate of 52% which is much higher than the reported average data in CKD patients. **Conclusion:** Vaccination seems to be very helpful in combating the adverse effect of Covid-19 in CKD patients. It also reduces mortality significantly in Covid-19 infected CKD patients.

Keywords: Chronic kidney disease, COVID-19, COVID-19 vaccination

Résumé

Introduction: Il existe une différence entre les sexes dans les caractéristiques démographiques, cliniques et les résultats des patients atteints d'IRA associée à une chirurgie cardiaque et vasculaire. **Méthodes:** Cette étude rétrospective a eu un total de 88 participants pour lesquels les données socio-démographiques, cliniques et de laboratoire (électrolytes sériques, numération globulaire complète, analyse d'urine et volume d'urine, taux de créatinine et de filtration glomérulaire) des participants ont été prises avant et après l'opération. jours 1, 7 et 30. **Résultats:** Au total, 88 participants (66 hommes et 22 femmes) ont été étudiés. Les maladies des valves cardiaques étaient plus fréquentes chez les femmes que chez les hommes. L'âge moyen des participants était de 65,9 ± 6,9 ans, avec des hommes de 65,1 ± 7,6 ans et des femmes de 68,3 ± 8,4 ans, P = 0,02. Avant la chirurgie, une proportion significativement plus élevée de femmes avaient un dysfonctionnement rénal par rapport aux hommes, P = 0,003. La chirurgie valvulaire et le pontage coronarien étaient les chirurgies les plus courantes. La proportion de chirurgies d'urgence et d'admissions de moins de 7 jours était significativement plus élevée chez les femmes que chez les hommes, P = 0,04 et P = 0,02 respectivement. La récupération complète de

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l'IRA était significativement plus élevée chez les hommes, car la récupération partielle et la mort étaient significativement plus faibles chez eux, P = 0,02. Sur les 35 (39,8%) qui ont été dialysés, 85,7% se sont complètement rétablis, 5,7% sont devenus dépendants de la dialyse tandis que 8,6% sont décédés. **Conclusion:** Les hommes atteints d'IRA étaient plus jeunes que les femmes. Les chirurgies valvulaires étaient les plus courantes. Le dysfonctionnement rénal de base et l'âge avancé étaient des facteurs de risque d'IRA. Après l'opération, l'IRA était plus fréquente chez les hommes qui étaient plus susceptibles de récupérer une fonction rénale complète. L'optimisation de la préparation des patients pourrait réduire l'incidence de CVS-AKI.

Mots-clés: Chirurgie cardiaque et vasculaire associée insuffisance rénale aiguë, dialyse, récupération de la fonction rénale, chirurgie valvulaire

Introduction

The COVID-19 infection has a wide range of presentations in various clinical conditions. This COVID-19 pandemic has been associated with high rates of mortality and morbidity.[1] The outcome of COVID-19 infection depends on the severity of infection at the time of presentation, duration of symptoms, and underlying comorbid conditions. As there is a high chance of other comorbidities such as diabetes, hypertension, and cardiovascular comorbidities in chronic kidney disease (CKD) patients and these patients have more severe presentations. CKD patients have increased vulnerability to infections including COVID-19.

As there is limited availability of antiviral in CKD patients, all guidelines have prioritized vaccinations for CKD patients.[2] Vaccinations are considered an important strategy against infectious diseases.

However, studies of patients who are having multiple comorbidities have shown a tendency toward a lower immune response to vaccination (vaccine efficacy) in comparison to a normal healthy population (66.2% in patients with chronic medical disease vs. 93.4 for severe COVID-19 in healthy adults).[3] The variability in immunogenic response can be due to various immunosuppressive used in transplant groups or autoimmune causes or an inflammatory state associated with CKD.

There are various other valid reasons which force us to believe that CKD patients will have a less immunogenic response when vaccinated in comparison with the normal population. For example, the low erythropoietin level is associated with a low Th-1 response to antigen, thus leading to a poor immunogenic response.[4] Similarly, CKD patients are prone to Vitamin D deficiency which leads to a poor dendritic cell response to antigen and T-cell interaction.[5] Uremia also causes reduced signaling by impairing the expression of costimulatory molecule B7-2 on monocytes, leading to a decreased activation of T helper cells.[6]

Despite various hypotheses for low immune response to vaccination, CKD patients are being vaccinated with the hope to develop an immune response against COVID-19. After searching the database, we could not find any study for the comparison between the two groups of vaccinated versus unvaccinated. Here, we have tried to compare the immunogenic response to the COVID-19 vaccine (either Covaxin or Covidshield) versus unvaccinated status in CKD patients in terms of severity of illness, the outcome of the disease, and various other parameters.

Rationale

As there occurs a blunted immune response in CKD patients, it is not known how effective the vaccination status will be in preventing adverse outcomes in CKD patients infected with COVID-19.

Materials and Methods

This study was conducted at a tertiary care center at the time of the second COVID-19 wave in India. In this study, records of 3074 patients were accessed, in which 73 patients with CKD were selected. COVID-19 positivity (either by rapid antigen test or by reverse transcriptase-polymerase chain reaction) with CKD patients was used as inclusion criteria. While patients with an underlying lung disease such as COPD, bronchiectasis, past pulmonary tuberculosis, or patients on immunosuppressive drugs were excluded from this study.

The baseline values of serum urea, creatinine, C-reactive protein (CRP), D-dimer, complete blood count, and liver function test were recorded from files. Vaccination status regarding partial or complete vaccination and disease duration were collected through telemedicine from either patients or attendants (in the case where the patient died). All the details were recorded in the data sheet. Records of high-resolution computed tomography (HRCT) of the thorax were analyzed. The duration of hospital stay, requirements of dialysis, CT severity score; baseline saturation (Spo2), and oxygen requirements or ventilatory supports were noted. After going through all files, we found out that all patients were managed as per the COVID-19 guidelines of the Ministry of Health and Family Welfare.

Aims and objectives

Primary objective

The primary objective of this study was to study the relationship of vaccination status and their outcome in CKD with COVID-19 infection.

Secondary objective

The secondary objective of this study was to compare the outcome of COVID-19 infection in partially vaccinated and completely vaccinated CKD patients.

Statistical analysis

All the data were tabulated in an Excel chart and statistical analysis was done using SSP software. All continuous variables are presented as means with standard deviation (mean ± SD). We have expressed the categorical variables as frequencies and percentages. We have used Student's *t*-test for comparing the means of two different groups. Nominal categorical data between the two groups have been compared using the Chi-square test 2 × 2 calculator. A value of <0.05 has been considered statistically significant. The analysis was performed using Stata 16.1. General-purpose statistical software package developed by StataCorp LLC, Texas [USA].

Results

In a study group of 73 cases who had CKD and were hospitalized with COVID-19 were included. Out of 73 patients, 55 patients (75.34%) were male, whereas 18 patients (24.66%) were female. The mean age for males was 61.18 (SD 57.53 ± 64.84), whereas for females mean age was 57.50 (SD 48.64 ± 66.36). There were 38 patients who were vaccinated with at least one dose of the COVID-19 vaccine, whereas there were 35 patients who were not vaccinated at all. About 20 out of 38 patients were vaccinated with both doses of COVID-19, whereas 18 received only one dose.

Routine blood test parameters of the patients were recorded [Table 1]. HRCT of the thorax was done only in 55 cases. Their CT severity value was calculated out of 25 (out of 5 scores for each lobe). In the other 18 patients, HRCT of the thorax was not done as either they were hemodynamically unstable or they had very high fractional inspired oxygen requirements. All CKD patients had initially been tried for conservative management but dialysis was done in 57.50% of the study population either due to failure of conservative management or because they were already on dialysis support before hospitalization or had advanced stage of disease previously. The mean duration of hospitalization was 11.47% with a mortality rate of 52% which is much higher than the reported average data in CKD patients. A comparison of multiple variables between the vaccinated and unvaccinated populations was done [Table 2].

Table 1: Mean and standard deviation for different variables in the entire study population

Variables	Mean±SD at 95% CI
Age (years)	60.27±14.65
Serum urea (mg/dl)	140.700±69.274
Serum creatinine (mg/dl)	6.5167±4.6101
Oxygen support (%)	91.71±10.63
CRP (mg/ml)	94.3071±80.8940
D-dimer (mg/ml)	3.0238±2.5211
CT severity score (out of 25)	11.25±7.61
Days of hospitalization (days)	11.47±8.32
Duration of chronic kidney disease (years)	3.315±2.627
Dialysis requirement (%)	57.50
Mortality (%)	52.00
Ventilatory requirements (%)	50.60

SD=Standard deviation, CRP=C-reactive protein, CT=Computed tomography, CI=Confidence interval

There was no significant difference in age between the two groups. However, the unvaccinated group was having more hypoxia and raised inflammatory markers. The unvaccinated group had more lung involvement (i.e., higher CT severity value) and secondary infection (*P* value for CTSS-0.0765). There was a higher mortality rate observed in the unvaccinated group (i.e., -65.71%) much higher than the vaccinated group (39.47%) (*P* = 0.0249).

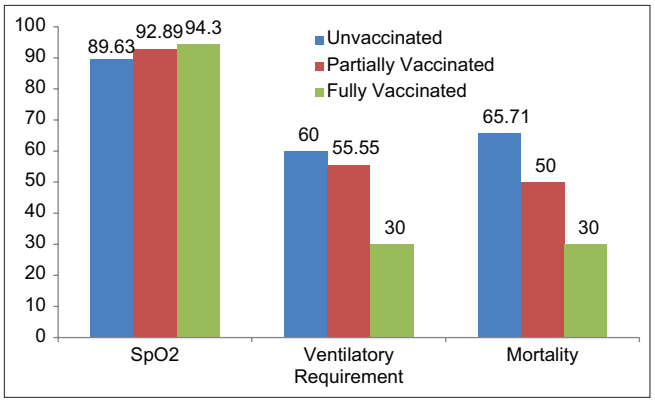
On comparing fully vaccinated with partially vaccinated, we found that there was less lung involvement in fully vaccinated COVID-19 infected patients with CKD but the difference failed to reach the level of statistical significance [Table 3]. The baselines Spo2 of both the partially and fully vaccinated patients were good and comparable without any statistically significant difference.

The CT severity score, duration of hospital stay, and mortality tend to be less in the fully vaccinated group in comparison to the partially vaccinated but failed to reach the level of statistical significance. Similarly, these benefits were also observed in those who are partially vaccinated in comparison to the nonvaccinated group [Graph 1].

Discussion

COVID-19 has shown to have high severity in patients who are suffering from immunosuppressive diseases or multiple comorbidities. The prevalence of 2.42% of CKD patients in our case study proves it true as the prevalence reported in other studies is 4.09%.[7]

The high prevalence of CKD in our study group may be due to the fact the institute served as the tertiary care center for all peripheral centers and was the first government-approved center in Bhubaneswar for all dialysis patients infected with COVID-19, especially for the first few months. There was a male dominance (75.34%) in CKD patients which is nearly



Graph 1: Comparison between Unvaccinated patients with partially and completely vaccinated patients [in %]

Table 2: Comparison of different variables between vaccinated and unvaccinated

Variables	Vaccinated (*n*=38)	Unvaccinated (*n*=35)	*P*
Age (years), mean±SD	60.61±11.47	59.91±17.64	0.8421
Baseline oxygen Spo2 (%), mean±SD	93.63±7.23	89.63±13.19	0.1086
Oxygen requirement (%)	50.00 (*n*=19)	68.57 (*n*=24)	0.1071
CRP (µg/ml), mean±SD	93.7739±95.09	94.8860±63.37	0.9537
D-dimer (µg/ml), mean±SD	3.0016±2.7397	3.0480±2.2001	0.9380
CT severity score (out of 25), mean±SD	9.94±7.77	13.09±7.15	0.0765
Days of hospitalization (days), mean±SD	11.92±8.76	10.97±7.91	0.6294
Dialysis requirement (%)	02.58 (*n*=30)	02.29 (*n*=19)	0.6967
TLC (cells×10^3), mean±SD	9742.89±5037.03	11537.71±5630.85	0.1550
Dialysis requirement (%)	60.50	54.20	0.2762
Ventilatory support requirement (%)	42.10	60.00	0.1265
Mortality (%)	39.47	65.71	0.0249

SD=Standard deviation, TLC=Total Leukocyte count, CRP=C-reactive protein, CT=Computed tomography

Table 3: Comparison of partially vaccinated with fully vaccinated

Variables	Single dose vaccinated (*n*=18)	Completely vaccinated (*n*=20)	*P*
SpO2 (%) at time of presentation, mean±SD	92.89±9.71	94.30±4.05	0.5553
CT severity score (out of 25), mean±SD	11.00±8.10	08.88±7.53	0.4480
Hospital stay (days), mean±SD	13.00±9.67	10.95±7.98	0.4789
CRP (µg/ml), mean±SD	93.3961±92.04	94.1140±100.14	0.9818
D-dimer (µg/ml), mean±SD	3.72±3.01	2.35±2.35	0.873
Mortality (%)	50	30	0.20
Ventilatory requirement (%)	55.55	30	0.111

SD=Standard deviation, CRP=C-reactive protein, CT=Computed tomography

similar to the reported national incidence of 70% for males versus 30% for females.[8] Since there were two different vaccines (Covishield and Covaxin), these patients had received different vaccines randomly. In our study, the mean age of presentation in the CKD group was 60.27 ± 14.65 in comparison to the reported national prevalence of (45.22 ± 15.2).[9]

A high mean for CRP, D-dimer, and CT severity score is suggestive of severe COVID-19 infection in the CKD population. Mortality was 52.00% overall in CKD patients. The mortality in severe COVID-19 was 69.76%, whereas inpatients who were mild category had a mortality of 26.66%. Studies have shown mortality of 27% of inpatients having no intensive care unit (ICU) requirement versus 56% of inpatients with end-stage renal disease requiring ICU care.[10]

On comparing with the vaccinated and unvaccinated groups, we found better oxygen saturation and low CT severity score in the vaccinated group. There were slightly high inflammatory markers such as CRP and D-dimer despite low lung involvement. After searching the entire database, we could not find any case reports or articles for the proposed mechanism of this inflammatory marker rise. Whether this phenomenon is due to a good humoral response toward COVID-19 virus due to vaccination or variation in infecting virus, remains unidentified. However, CRP is raised in CKD patients *per se* and a slight rise in D-dimer can also be seen in advanced CKD cases.

There was a statistically insignificant but a good trend of less requirement for ventilatory support in the vaccinated group (42.10%) in comparison to the unvaccinated (60.00%) (P = 0.1265) was observed. Compared with another study group, there was an up to a 4-fold increase in ventilatory requirement in CKD patients.

There was a statistically significant increase in mortality in the nonvaccinated group (65.71%) in comparison to the vaccinated group (39.47%) (P = 0.025). This mortality benefit indicates a protective immune response to vaccine in CKD patients despite an incompetent humoral immunity.

On comparing the two subgroups of partially vaccinated with complete vaccinated, there was a better SpO2 level in fully vaccinated. There was also a low CT severity value and fewer requirements for ventilatory support which indicates a milder degree of illness from the COVID-19 point of view. However, these failed to reach the level of statistical significance.

There was a high CRP value in the fully vaccinated group in comparison to the nonvaccinated group. This could be due to a faster cellular response to virus invasion in patients who are vaccinated with the COVID-19 vaccine. There was a low D-dimer in patients who are fully vaccinated which is contrary to claims of a prothrombotic state in the vaccinated group. There was statistically insignificant mortality in patients who are fully vaccinated versus those partially vaccinated (P = 0.20). In this study, it was found

that CKD patients have a high risk of mortality probably due to its association with multicomorbidities and probable combined effect of hypoxia and fluid overload state. There was a high need for ventilator support requirement possibly due to volume overload status, combined metabolic acidosis (secondary to CKD) and respiratory failure (secondary to COVID-19), or development of ARDS at an early stage or due to multiple comorbidities. There seems to be a low severity of COVID-19 pneumonia and mortality in vaccinated CKD patients despite a weak immune response to vaccines in CKD patients.

There are other similar studies who have proven an advantage of double dose over single-dose vaccination citing better immune response and protection.[11] However, still, there are studies which showed a rapid vaccination with single dose only to the large population may have better outcomes.[12] However, due to heterogeneity in infecting strains, it is difficult to draw a clear line between the efficacy of various dosing schedules and vaccines.[13] Thus, hereby, we have observed a distinct advantage in terms of mortality and morbidity in vaccinated CKD patients against nonvaccinated patients.

Limitation of the study

1. Small sample size
2. COVID-19 serology of CKD patients could not be evaluated
3. Retrospective study.

Conclusion

Vaccination seems to be very helpful in combating the adverse effect of COVID-19 in CKD patients like less need for ventilators. It also reduces mortality significantly in COVID-19-infected CKD patients. A double dose of vaccinations appears to be more efficacious than a single dose of vaccination.

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Conflicts of interest

There are no conflicts of interest.

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