Scholars Journal of Applied Medical Sciences
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Nephrology

Assessment of Antibody Titers after Vaccination against SARS-COV-2 in Patients with CKD stage 4, 5 and CKD 5d

Dr. Md. Farucul Hasan[1*], Dr. Mst. Arifa Afroz[2], Dr. Kamruzzaman Abne Taz[3], Prof. Dr. A. B. M. Mobasher Alam[4] Dr. Syed Anisuzzaman[5], Dr. Sushanta Kumar Barman[6], Dr. Md. Abdus Sabur Khan[7], Dr. Md. Shahinur Rahman[8], Dr. Mehedi Hasan[9]

[1]MBBS, BCS (Health), MD (Nephrology), MCPS (Medicine), MACP (America), CCD (Diabetic) (Birdem), Medical Officer, Rangpur Medical College and Hospital, Rangpur, Rangpur- Dinajpur Highway, Cantt, Near Central Jail, Rangpur 5400, Bangladesh
[2]MBBS, BCS (Health), M. phil (Biochemistry), Lecturer, Microbiology Department, Rangpur Medical College, Rangpur, Rangpur- Dinajpur Highway, Cantt, Near Central Jail, Rangpur 5400, Bangladesh
[3]MBBS, BCS (Health), M.Phil. (Microbiology), Chief Health Officer (Attachment), Rangpur City Corporation, Rangpur, Rangpur- Dinajpur Highway, Cantt, Near Central Jail, Rangpur 5400, Bangladesh
[4]MBBS, MD (Nephrology) FRCP (Edin, UK) FRCP (Glasgow), FASN (Fellow American Society of Nephrology), Professor & Head, Department of Nephrology, Rangpur Medical College and Hospital, Rangpur, Rangpur- Dinajpur Highway, Cantt, Near Central Jail, Rangpur 5400, Bangladesh
[5]MBBS, BCS (Health), MD (Nephrology), Associate Professor, Rangpur Medical College & Hospital, Rangpur, Rangpur- Dinajpur Highway, Cantt, Near Central Jail, Rangpur 5400, Bangladesh
[6]MBBS, BCS (Health), MD (Nephrology), IMO, Rangpur Medical College and Hospital, Rangpur, Rangpur- Dinajpur Highway, Cantt, Near Central Jail, Rangpur 5400, Bangladesh
[7]MBBS, BCS (Health), MD (Nephrology), Registrar, Rangpur Medical College and Hospital, Rangpur, Rangpur- Dinajpur Highway, Cantt, Near Central Jail, Rangpur 5400, Bangladesh
[8]MBBS, MS (Pediatric Surgery), IMO, Department of Pediatric Surgery, Rangpur Medical College Hospital, Rangpur, Rangpur- Dinajpur Highway, Cantt, Near Central Jail, Rangpur 5400, Bangladesh
[9]MBBS, MD (Cardiology), Dialysis Medical Officer & Medical Officer (Nephrology), Rangpur Medical College Hospital, Rangpur, Rangpur- Dinajpur Highway, Cantt, Near Central Jail, Rangpur 5400, Bangladesh

DOI: 10.36347/sjams.2024.v12i05.026 | **Received:** 18.02.2024 | **Accepted:** 01.04.2024 | **Published:** 29.05.2024

***Corresponding author:** Dr. Md. Farucul Hasan
MBBS, BCS (Health), MD (Nephrology), MCPS (Medicine), MACP (America), CCD (Diabetic) (Birdem), Medical Officer, Rangpur Medical College and Hospital, Rangpur, Rangpur- Dinajpur Highway, Cantt, Near Central Jail, Rangpur 5400, Bangladesh

Abstract

Original Research Article

Background: Since the pandemic of COVID-19 started from December 2019, remarkable numbers of infections and deaths associated with COVID-19 have been recorded worldwide. Chronic kidney disease patients are particularly at high risk of infections due to impairments in the innate and adaptive immune systems. Adequate humoral (antibody) and cellular (T cell-driven) immunity are required to minimize pathogen entry and promote pathogen clearance to enable infection control. Vaccination can generate cellular and humoral immunity against this specific pathogen. COVID-19 prevention through successful vaccination is therefore paramount in chronic kidney disease population. But vaccination efficacy is diminished in these patients because premature ageing of the immune system and chronic systemic low-grade inflammation are the main causes of immune alteration in these patients. Therefore, it is urgently necessary to establish a different vaccination strategy for chronic kidney disease and dialysis patient in terms of the dose and administration time. ***Aims:*** This study aimed to the assessment of antibody titers after vaccination against SARS-COV-2 in patients with chronic kidney disease stages 4, 5 on conservative management and maintenance haemodialysis. ***Methods:*** This prospective observational comparative study was conducted in the Nephrology department of Dhaka Medical College Hospital. The selection of patients was done by purposive sampling according to inclusion and exclusion criteria. A total 135 patients were distributed in three groups: 45 patients of chronic kidney disease (CKD) stage 4, 5 on conservative management, 45 patients on maintenance haemodialysis (MHD) and 45 healthy controls were approached for the study who were receiving SARS-COV-2 vaccination. Demographic, clinical and laboratory data were collected initially. At first, a pre vaccination sample or 1st sample was taken for antibody measurement. Then participants from all groups were given 2 doses MODERNA vaccine containing 100 µg in 0.5 ml each in 28 days apart. Then after 14 days of 1st dose of vaccination the 2nd samples were taken. Study populations were subdivided into two groups according to pre-vaccination SARS-COV-2 antibody titer; seropositive- positive response before vaccination and seronegative- negative response before vaccination. They were also divided into two groups according to quantitative antibody response; positive response- values ≥10 DU/mL were positive Negative response- values of <10 DU/mL were negative. ***Result:***

The seroconversion rate was around 20% among study participants before vaccination. 14 days after the 1st dose of vaccination, 90.04% of patients had positive immune responses in CKD stages 4, and 5 on conservative management group whereas in the MHD group 84.82% responded to vaccination and the immune response in the control group was 100%. Immune response is 100% among all the groups after 14 days of 2nd dose of vaccination but the concentration of antibody differs significantly among the study groups. Antibody response after 6 months completion of 2nd dose of vaccination reveals that, among CKD stage 4, 5 on the conservative management group 80.3% of patients had immune response whereas in MHD group 67.2% responded to vaccination but the immune response in the control group was 100%. Responders were comparatively younger with normal BMI. ***Conclusion:*** Haemodialysis patients as well as patients with chronic kidney disease stages 4, and 5 on conservative management showed a favorable but profoundly lower early antibody response, which decreased substantially during follow-up measurement mainly 6 months after vaccination compared to controls, supports the need for booster vaccinations to foster a stronger and more persistent antibody response.

Keywords: Covid-19, Corona virus, CKD, MHD.

INTRODUCTION

Coronaviruses were described for the first time in 1966 by Tyrell and Bynoe, who cultivated the viruses from patients with common colds. They are enveloped, positive, single-stranded large RNA viruses that not only infect humans but also a wide range of animals (bats, pangolins, cats, pigs and birds, among others) (Tyrrell *et al*., 1966). Coronavirus disease 2019 (COVID-19) is defined as illness caused by a novel coronavirus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; formerly called 2019-nCoV), which was first identified amid an outbreak of respiratory illness cases in Wuhan City, Hubei Province, China (Centers for Disease Control and Prevention, 2020).

The clinical spectrum of COVID-19 infection is very variable, ranging from asymptomatic infection, anosmia, ageusia or minor upper respiratory tract illness to severe pneumonia with respiratory failure and even death (Zhou *et al*., 2020). Diarrhoea and cutaneous and thrombotic manifestations were also described. More severe cases with higher rates of mortality have been reported in older patients and in those with chronic illness such as cardiovascular disease, hypertension, diabetes and kidney failure patient (Tang *et al*., 2020).

Chronic kidney disease (CKD) constitutes a serious global health problem. According to the Global Burden of Disease study, incidence of CKD reached 9.1% in 2017, resulting in 697.5 million cases worldwide (Bikbov *et al*., 2020). A marked increase in the mortality rate associated with CKD was also noted, which accounted for 4.6% of global deaths and thereby placed CKD as 12th leading cause of death globally in 2017 (Cockwell and Fisher, 2020). Progressive declines in renal function eventually result in end-stage kidney disease (ESKD), with 2.5 million patients who require renal replacement therapies, such as kidney transplantation or dialysis, and this number is expected to double by 2030 with huge sanitary costs (Liyanage *et al*., 2015). Renal failure and dialysis treatment are associated with disorders of the innate and adaptive immune system, contributing to the increase of infection rate (Kato *et al*., 2008). Indeed, infectious disease is the second most common cause of death after cardiovascular disease in patients with CKD (Reddy, Chitturi and Yee, 2019).

The COVID-19 pandemic has disproportionately affected patients with chronic kidney disease and on dialysis. Although SARS-CoV-2 seroprevalence among patients on dialysis is similar to the general population (Bajema *et al*., 2021). Immune dysregulation caused by uremia is characterized not only by immune depression that makes this patient group prone to acquiring COVID-19 during their hospital visits but also by immune activation that predisposes to cardiovascular diseases, placing an additional risk for severe COVID-19 disease (Yen *et al*., 2021).

A 20-30-fold higher mortality rate compared with the general population seen in patient with CKD. More recent data continue to show mortality rates in this population in excess of 15% (Hsu *et al*., 2021). Hospitalization rates have been 3-to-4 fold higher than other Medicare beneficiaries (Centers for Medicare & Medicaid Services, 2020). Nearly one-third of patients receiving dialysis died after hospitalization with COVID-19 (Ng *et al*., 2020).

Control measures such as the use of masks, physical distancing, testing of exposed or symptomatic persons, contact tracing and isolation have helped limit the transmission where they have been rigorously applied; however, these actions have been variably implemented and have proved insufficient in impeding the spread of coronavirus disease 2019 (Covid-19). Vaccines are needed to reduce the morbidity and mortality associated with Covid-19 and multiple platforms have been involved in the rapid development of vaccine candidates (Ramasamy *et al*., 2020).

Several vaccines have been approved for SARS-CoV-2 infection. Live attenuated vaccines generally should be avoided in patients on maintenance HD due to their dysregulated immune system. Both the mRNA vaccines BNT162b2 (Pfizer-BioNTech) and

mRNA-1273 (Moderna) and the replication-defective viral-vectored vaccines, such as ChAdOx1 nCoV-19 (Oxford-AstraZeneca) and an inactivated virus COVID-19 vaccines (Sinopharm COVID-19 vaccine) are considered safe for use in patients treated with maintenance HD (Windpessl *et al*., 2021). The mRNA vaccine platform has advantages as a pandemic-response strategy, given its flexibility and efficiency in immunogenic design and manufacturing. Earlier work had suggested that the spike protein of the coronavirus responsible for the 2002 SARS outbreak was a suitable target for protective immunity **(**He *et al*., 2006).

Our study result indicated that the placebo group had 14,164 participants with 769 SARS-CoV-2 infection cases, while the mRNA-1273 group comprised 14,287 subjects with 56 COVID-19 incidents. The vaccine efficacy rose steadily to a peak of 94.1% on day 120, successive to 92.6% 40 days following the initial dose. At around 120 days, the vaccine efficacy began to decline, and it had fallen to 89.6% by 200 days (Pouwels *et al*., 2021).

In this regard, patients on dialysis for vaccination have been at the forefront of SARS-CoV-2 vaccination programs internationally. Response to vaccination can be considerably lower in patients with severely impaired kidney function due to the immunosuppressive effect of uremia and specific medications. This has been shown for vaccination against hepatitis B, influenza, and Streptococcus pneumonia (Sanders., 2022). Chronic kidney disease impairs both natural and adaptive immune response, which might be the culprit for the lower seroconversion rates seen in dialysis patients (Alcázar-Arroyo *et al.*, 2021).

MATERIAL & METHODS

This Prospective observational comparative study was conducted in the Department of Nephrology, Dhaka Medical College and Hospital, Bangladesh from January 2021 to July 2022. After informed written consent from parents/guardians, a total number of 120 chronic kidney disease stage 4, 5 on conservative management and maintenance hemodialysis (MHD) patients who were receiving the SARS-CoV-2 vaccine were included in the study. Individuals with COVID-19-related clinical signs, e.g., fever, coughing, runny nose, sore throat, dyspnea, shortness of breath, aches and pain at the time of sample collection, malignancy, history of organ transplantation, taking immunosuppressive medications (including cytotoxic agents and systemic corticosteroids), HIV/AIDS infection, Pregnancy and Age <18 years were not considered for enrollment in the study. Detailed history and all clinical examination were done focusing on age, gender, medications, weight, height and body mass index (BMI). KDIGO 2012 clinical practice guideline for chronic kidney disease (CKD) was utilized for diagnosis and staging of CKD. CKD 4, 5 patients were withdrawn from the study if their renal function had deteriorated to the point that dialysis was needed. All Data was collected in a pre-tested questionnaire by taking history, examining the patients clinically, laboratory finding and patient outcomes. All data was recorded systematically in preformed data collection form. Data were analyzed by Statistical Package of Social Science (SPSS) version 26.

RESULTS

This study was conducted in department of Nephrology, DMCH. After completion of two doses of SARS-COV-2 vaccination, antibody titer was measured before and 14 days after 1st dose of vaccination. The study subjects were divided into two groups according to pre vaccination antibody level- seropositive and seronegative. Different demographic, clinical and biochemical variables were compared among these groups. The results are presented by the following tables:

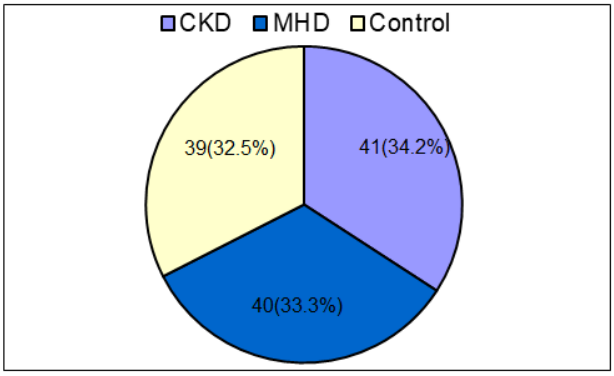

Figure 1: Pie chart shows the CKD, MHD and control status of study patients (n=120)

Pie chart shows the CKD, MHD and control status of study patients. It was observed that more than one third (34.2%) of patients were found CKD followed by 40 (33.3%) were MHD and 39 (32.5%) were control.

Table I: Comparison of demographic profile with study groups (n=120)

Demographic profile	CKD stage 4, 5 (n=41)		MHD (n=40)		Control (n=39)		*p* value
	n	%	n	%	n	%	
Age (years)							
≤50	23	56.1	22	55.0	30	76.9	
51-60	8	19.5	8	20.0	7	18.0	
>60	10	24.4	10	25.0	2	5.1	
Mean ± SD	49.71± 12.99		48.65± 14.61		45.08± 15.17		[a]0.085[ns]
Range (min-max)	27-76		24-78		23-63		
Sex							
Male	21	51.2	21	52.5	25	64.1	[b]0.445[ns]
Female	20	48.8	19	47.5	14	35.9	

ns= not significant
[a]p value reached from Kruskal Wallis test
[b]p value reached from Chi-square test
CKD= Chronic kidney disease MHD= Maintenance hemodialysis

Table I shows the comparison of demographic profile with study groups. It was observed that more than half (56.1%) of patients belonged to age was ≤50 years in CKD, 22 (55.0%) in MHD and 30 (76.9%) in control. The mean age was 49.71±12.99 years in CKD, 48.65±14.61 years in MHD and 40.08±11.17 years in control. More than half (51.2%) of patients were male in CKD, 21 (52.5%) in MHD and 25 (64.1%) in control. The differences of age were statistically significant ($p<0.05$) among three groups.

Table II: Comparison of BMI with study groups (N=120)

BMI (kg/m^2)	CKD stage- 4, 5 (n=41)		MHD (n=40)		Control (n=39)		*p* value
	n	%	n	%	n	%	
Underweight	5	12.2	6	15.0	0	0.0	
Normal	19	46.3	16	40.0	29	74.4	
Overweight	12	29.3	15	37.5	6	15.3	
Obese	5	12.2	3	7.5	4	10.3	
Mean ± SD	23.0±3.2		22.1±2.1		24.3±3.7		[a]0.007[s]

s= significant ns= not significant
[a]p value reached from ANOVA test
[b]p value reached from Chi-square test
BMI= Body mass index CKD= Chronic kidney disease
MHD= Maintenance hemodialysis

Table II shows the comparison of BMI with study groups. It was observed that almost half (46.3%) of patients who belonged to BMI were normal in CKD, 16 (40.0%) in MHD and 29 (74.4%) in control. The mean BMI was 23.0±3.2 kg/m^2 in CKD, 22.1±2.1 kg/m^2 in MHD and 24.3±3.7 kg/m^2 in control. The differences of BMI were statistically significant ($p<0.05$) among three groups.

Table III: Comparison of causes of CKD with study groups (N=120)

Cause of CKD	CKD stage- 4, 5 (n=41)		MHD (n=40)		Control (n=39)		*p* value
	n	%	n	%	n	%	
Glomerulonephritis	14	34.1	12	30.0	0	0.0	0.001[s]
Diabetes mellitus	15	36.6	14	35.0	0	0.0	0.001[s]
Hypertension	5	12.2	6	15.0	0	0.0	0.049[s]
Others	4	9.8	5	12.5	0	0.0	0.086[ns]
Unknown	3	7.3	4	10.0	0	0.0	0.152[ns]

s= significant
ns= not significant
p value reached from Chi-square test

Table III shows the comparison of cause of CKD with study groups. Glomerulonephritis, diabetes mellitus and hypertension were statistically significant ($p<0.05$) among three groups.

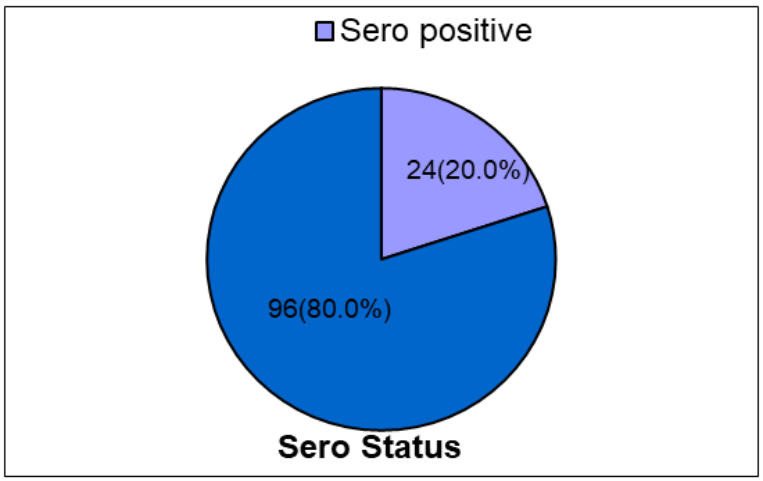

Figure 2: Pie chart shows the pre vaccination seroconversion status of study population (n=120)

Pie chart shows the pre-vaccination seroconversion status of study population. It was observed that about one-fourth (20.0%) of patients was seropositive and 96 (80.0%) were seronegative.

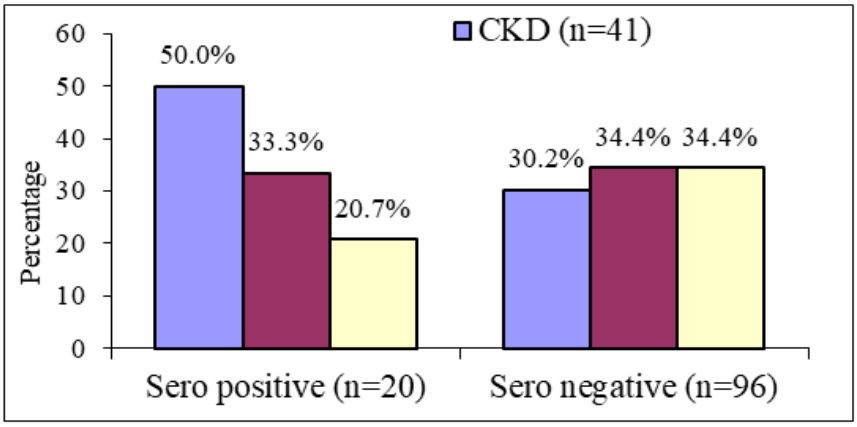

Figure 3: Bar diagram shows the Comparison of pre vaccination seroconversion with CKD, MHD & control patients (n=120)

CKD= Chronic kidney disease MHD= Maintenance hemodialysis

Bar diagram shows the Comparison of pre vaccination seroconversion status with CKD, MHD & control groups. In seropositive, it was observed that half 11 (50.0%) of patients had CKD followed by 8 (33.3%) had MHD and 5 (20.8%) were control. In seronegative, 29 (30.2%) patients had CKD, 33 (34.4%) had MHD and 34 (35.4%) were control.

Table IV: Comparison of antibody titers with pre vaccination seroconversion status (N=120)

Anti-body level (DU/ml)	**Seropositive (n=24)**	**Seronegative (n=96)**	***p* value**
	Mean± SD	**Mean± SD**	
2nd sample (14 days after 1st dose	341.42±41.67	223.86±46.35	0.001^s

s= significant ns= not significant

p value reached from Unpaired-t test

Table IV shows the comparison of pre vaccination seroconversion status with Anti-body titers. The mean 2nd sample was 341.42±41.67 in seropositive and 223.86±46.35 in seronegative. The mean 3rd sample was 469.36±127.77 in seropositive and 291.46±96.16 in seronegative. The mean 4th sample was 243.37±61.89 in

seropositive and 121.59±46.81 in seronegative. The differences of the 2nd sample, 3rd sample, and 4th sample were statistically significant (p<0.05) with pre-vaccination seroconversion status.

Table V: Comparison of antibody titers with study groups (N=120)

Anti-body level (DU/ml)	CKD stage- 4, 5 (n=41)	MHD (n=40)	Control (n=39)	*p* value
	Mean ± SD	Mean ± SD	Mean ± SD	
1st sample (pre vaccination)	31.5± 26.41	29.48± 23.79	43.21±41.61	0.298ns
2nd sample (14 days after 1st dose)	227.66± 225.82	168.27± 165.73	334.07±54.35	0.001s

s= significant
ns= not significant
p value reached from ANOVA test
CKD= Chronic kidney disease MHD= Maintenance hemodialysis

Table V shows the comparison of Anti-body titers with study groups. The mean 1st sample (pre vaccination) was 31.5±26.41 in CKD, 29.48±23.79 in MHD and 43.21±41.61 in control. The mean 2nd sample was 227.66±225.82 in CKD, 168.27±165.73 in MHD and 334.07±54.35 in control. The mean 3rd sample was 396.02±93.24 in CKD, 318.84±54.49 in MHD and 604.29±150.28 in control. The mean 4th sample was 187.81±180.86 in CKD, 126.03±117.8 in MHD and 388.33±70.11 in control. The differences of 2nd, 3rd and 4th sample mean were statistically significant (p<0.05) among three groups.

Table VI: Comparison of antibody titers with CKD stage 4, 5 on conservative management (N=120)

Anti-body level (DU/ml)	CKD stage- 4 (n=20)	CKD stage- 5 (n=21)	*p* value
	Mean ± SD	Mean ± SD	
1st sample (pre vaccination)	30.5± 27.41	29.18± 17.08	0.298ns
2nd sample (14 days after 1st dose)	220.66± 215.62	203.78± 195.73	0.241s

s= significant
ns= not significant
p value reached from ANOVA test
CKD= Chronic kidney disease

Table VI shows the comparison of Anti-body titers with CKD- 4,5. The mean 1st sample (pre vaccination) was 30.5±27.41 in CKD and 29.18±17.08 in CKD-5. The mean 2nd sample was 220.66±215.62 in CKD-4 and 203.78±195.73 in CKD-5. The mean 3rd sample was 380.52±74.24 in CKD-4 and 365.84±56.49 in CKD-5. The mean 4th sample was 180.81±175.86 in CKD-4 and156.03±150.8 in CKD-5. The differences of 2nd, 3rd and 4th sample mean were not statistically significant (p<0.05).

Table VII: Antibody titers after 14 days of completion of 1st dose of vaccination (2nd sample) in in study groups (N=120)

Anti-body level (DU/ml)	CKD stage- 4, 5 (n=41)	MHD (n=40)	CONTROL (n=39)	p value
Responder (108) (≥10 DU/ml)	36 (90.04%)	33 (84.82%)	39(100%)	0.046s
Non- Responder (12) (<10 DU/ml)	5 (12.19%)	7 (21.21%)	0	
Antibody titer (DU/ml) (Mean ± SD)	227.66± 225.82	168.27± 165.73	334.07± 54.35	0.001s

s= significant p value reached from ANOVA test
CKD= Chronic kidney disease MHD= Maintenance hemodialysis

Table VII shows the antibody titers after 14 days of completion of 1st dose of vaccination. Among CKD stage 4-5 (ND) group 90.04% patients had immune response whereas in MHD group 84.82% responded to vaccination and immune response in control group was 100%. Difference of immune response and antibody titer were significant among three groups (p < 0.05).

Table VIII: Antibody titers after 14 days of completion of 2nd dose of vaccination (3rd sample) in study groups (N=120)

Anti-body level (DU/ml)	CKD stage- 4, 5 (n=41)	MHD (n=40)	CONTROL (n=39)	*p* value
Responder (120) (≥10 DU/ml)	41 (100%)	40 (100%)	39 (100%)	----
Non-Responder (0) (<10 DU/ml)	0	0	0	
Antibody titer (DU/ml) (Mean ± SD)	396.02± 93.24	318.84± 54.49	604.29±150.28	[b]0.001[s]

s= significant [a]p value reached from Chi-square test
[b]p value reached from Kruskal Wallis test

Table VIII shows the antibody titers after 14 days of completion of 2nd dose of vaccination. Immune response is 100% among all the groups after vaccination. Difference of antibody titers were significant among study groups ($p < 0.05$).

Table IX: Antibody titers after 6 months completion of 2nd dose of vaccination (4th sample) in CKD stage 4, 5 and MHD patients (N=120)

Anti-body level (DU/ml)	CKD stage- 4-5 (n=41)	MHD (n=40)	CONTROL (n=39)	*p* value
Responder (62) (≥10 DU/ml)	33 (80.3%)	27 (67.2%)	39 (100%)	[a]0.001[s]
Non-Responder (31) (<10 DU/ml)	8 (19.7%)	13 (32.8%)	0	
Antibody titer (DU/ml) (Mean ± SD)	187.81± 80.86	126.03± 47.8	388.33± 70.11	[b]0.001[s]

s= significant [a]p value reached from Chi-square test [b]p value reached from Kruskal Wallis test

Table IX shows the Antibody titers after 6 months completion of 2nd dose of vaccination. Among CKD stage 4, 5 group 80.3% patients had immune response whereas in MHD group 67.2% responded to vaccination but immune response in control group was 100%. Difference of immune response and antibody titers were significant between two groups ($p < 0.05$).

Table X: Comparison of immune response according to age of study population (n=120)

Age in years	1st sample (pre vaccination)	2nd sample (14 days after 1st dose	P value
	Mean±SD	Mean±SD	
≤50 years	30.65±41.39	324.6±47.48	0.001[s]
51–70 years	30.06±44.7	322.63±43.77	0.001[s]
> 70 years	15.42±41.34	238.22±44.18	0.001[s]

s= significant
P value reached from Kendall's W Test

Table X shows the association between age with anti-body titers. The ages level of ≤50 years, 51-70 years and > 70 years were statistically significant ($p<0.05$) with anti-body collection groups.

Table XI: Comparison of immune response in relation to BMI (N=120)

Variables	Responder (≥10 DU/ml)	Non-Responder (<10 DU/ml)	*p* value
BMI (Kg/m^2)			
Underweight (11)	-	(30.3%)	
Normal (64)	(75.8%)	(44.8%)	
Overweight (33)	(24.2%)	(21.3%)	
Obese (12)	-	(3.6%)	
Mean ± SD	23.1±3.1	20.0±3.2	[a]0.018[s]

s= significant ns= not significant [a]p value reached from Unpaired-t test.

DISCUSSION

This study was carried out with an aim to observe the antibody response of SARS-COV-2 vaccines in healthy individuals and patients with chronic kidney disease stage 4, 5 on conservative management and on maintenance haemodialysis and measure the post-vaccination antibody titers in those three groups. This was a prospective observational comparative study consisting of 45 patients with CKD stage 4, 5 on conservative treatment, another 45 haemodialysis patients and 45 healthy controls fulfilling the selection criteria. Antibody titer of Covid-19 vaccine was measured before and 14 days after 1st dose of vaccination.

In this present study, the mean age was 49.71±12.99 years in CKD 4, 5 on conservative treatment, 48.65±14.61 years in MHD and 40.08±11.17 years in control. More than half of the patients were male in both groups, which is consistent with a study done by Shahin *et al*., (2009). It was observed that more than half (56.1%) of patients belonged to age was ≤50 years in CKD, 22(55.0%) in MHD and 30(76.9%) in control.

Regarding the comparison of BMI with study groups, it was observed that almost half (46.3%) of patients belonged to BMI was normal in CKD 4, 5 on conservative treatment, 16(40.0%) in MHD and 29 (74.4%) in control (Table II). The Similar range of BMI in these group of patients was observed by Kataoka *et al*., (2019) and Ahmed *et al*., (2021). The differences of BMI were statistically significant ($p<0.05$) among three groups and it was less in CKD 4, 5 on conservative treatment and MHD groups than in controls group. This may be due to wasting is prevalent among patients with chronic kidney disease and this was thought to be the direct consequence of inadequate nutrition intake or malnutrition. Other factors including systemic inflammation, influence of appetite-controlling hormones from reduced renal clearance, aberrant neuropeptide signaling, insulin and insulin-like growth factor resistance and metabolic acidosis (Tu, Cheung and Mak, 2016).

The present study showed that around 20% study participants were seropositive before vaccination. These findings were supported by Das *et al*., (2021), where seroconversion rate was 20.02% before vaccination, but less than that of results from Jahan *et al*., (2021), where seroconversion rate was 22.7% which was slightly higher than our findings. Regarding the comparison of pre vaccination seroconversion status with CKD 4, 5 on conservative treatment, MHD & control patients, it was observed that half 11 (50.0%) of patients had CKD followed by 8 (33.3%) had MHD and 5(20.8%) control were seropositive. In seronegative, 29(30.2%) patients had CKD 4, 5 on conservative treatment, 33 (34.4%) had MHD and 34 (35.4%) control (figure 3). It was observed that more participants with CKD 4, 5 on conservative treatment and MHD become seropositive than controls although they were asymptomatic. On top of that, the vast majority of these vulnerable patients are treated with in-center haemodialysis. This means an increased risk of exposure to COVID-19 due to frequent contacts with potentially infected patients, healthcare professionals or transport personnel (Baden *et al*., 2021). Also, these patients have several conditions that make them a target population for the virus, i.e., an older age, comorbidities and a frail immunological system (Vivanco-Hidalgo *et al*., 2020).

When stratified by clinical and laboratory variables, this current study showed a lower response in older adults, obese, advanced CKD patients specially on dialysis. It was observed that when comparing the groups and data within groups, age is a substantial factor in determining the level of response. Following increasing age, there was significant decrease of antibody levels in all samples. Similar findings were observed by Grupper *et al*., (2021). Where they observed older age was associated with antibody response in the lower quartile. This can partially be explained by a reduction in immunologic memory with increasing age as aged T cells produce short lived inflammatory effector T-cells instead of memory or follicular helper T cells (Akyol *et al*., 2021). As degeneration of bone marrow occurs with aging, impairment of humoral and cellular immune response occurs. As a result, there is less seroconversion following vaccination in old age (Asan *et al*., 2017).

Regarding observation of BMI in relation to immune response, it was found that patients having BMI either underweight or obese had lower immune response than normal. In the current study, three fourth (75.8%) of patients who had adequate response had normal range of BMI. Patients with BMI either underweight & obese did not achieve adequate response, there were more non responders. The differences of BMI were statistically significant ($P<0.05$) within different immune response groups (Table VIII). Al Saran *et al*., (2021) stated that there was no significant difference in BMI among response groups, which did not support our study. But Asan *et al*., (2022) stated that BMI ≥30 kg/m² has a significant association with non-response to SARS-COV-2 vaccination. There may be multiple reasons behind this reduced immune response in obese - the amount of SARS-COV-2 in the vaccine may be too low in relation to body mass, suboptimal immune dysfunction in obese population due to hyperinsulinemia and hyperlipidemia and may be needles were too short to reach the muscle (Meier and Berger, 2020). This present study showed malnutrition was also associated with poor immune response and among MHD patients there were more underweight patients than CKD.

In comparison to pre vaccination antibody titers with post vaccination antibody titers among the study groups, the mean 2nd sample was 341.42±41.67 in

seropositive and 313.86±46.35 in seronegative. The differences of 2nd sample were statistically significant ($p<0.05$). Regarding immune response in seropositive populations revealed that antibody levels are more in seropositive than in seronegative patients in 2nd sample and there is a significant difference among the antibody levels. These findings were supported by Talaei *et al*., (2022), who showed that there was increasing trend of antibody titers in pre vaccination seropositive patients. The increasing trend of antibodies may be due to asymptomatic infection. Another study suggested that a previous SARS-CoV-2 infection had a booster effect on the intensity of antibody response (in high responder). They showed that an initial encounter with the virus helps trigger a secondary broad immune response to the antigen which makes a link between seroconversion rate and the IgG levels (Bachelet *et al*., 2021).

CONCLUSION

This study showed that the early and long-term antibody response is highly variable both in quantity and duration. Even if vaccination was followed by a seroconversion, the antibody concentration was significantly lower in patients with CKD 4, and 5 on conservative management and MHD than in control subjects. As a result, most of them remain unprotected despite having scheduled vaccination.

LIMITATIONS

There were a number of limitations of this study which include following:

- All patients received the same mRNA vaccine, which precludes conclusions about the response to other types of vaccines.
- This was a small, single-center study, limiting our ability to fully assess all factors associated with immune response.
- We could not evaluate cellular immunity (especially memory T cells), which contributes importantly to the longevity of immunity against SARS-CoV-2
- Regarding the measurement of follow-up antibody titers 6 months after the second vaccination, since CKD stage progression was observed in some patients in chronic kidney disease stage 4, 5 on conservative management.
- Genetic analysis could not be done.

REFERENCE

- Abbott Core Laboratory: SARS-CoV-2 Immunoassays: Advancing diagnostics of COVID-19. Availableat: corelaboratory.abbott/ int/en/ offerings/ segments/infectiousdisease/ sars-cov-2. Accessed April 1, 2021
- Agur, T., Ben-Dor, N., Herman-Edelstein, M., Steinmetz, T., Lichtenberg, S., Schneider, S., Yahav, D., Rozen-Zvi, B. and Zingerman, B., 2022. Longevity of Humoral Response Six Months Following BNT162b2 Vaccine in Dialysis Patients. Frontiers in Medicine, 9, p.781888.
- Akyol, M., Çevik, E., Ucku, D., Tanrıöver, C., Afşar, B., Kanbay, A., Covic, A., Ortiz, A., Basile, C. and Kanbay, M., 2021. Immunogenicity of SARS-CoV-2 mRNA vaccine in dialysis and kidney transplant patients: A systematic review. Tuberkuloz ve Toraks, 69(4), pp.547-560.
- Akomea-Frimpong, I., Jin, X., Osei-Kyei, R. and Tumpa, R.J., 2022. A critical review of public–private partnerships in the COVID-19 pandemic: key themes and future research agenda. Smart and Sustainable Built Environment, (ahead-of-print).
- Al Kaabi, N., Zhang, Y., Xia, S., Yang, Y., Al Qahtani, M.M., Abdulrazzaq, N., Al Nusair, M., Hassany, M., Jawad, J.S., Abdalla, J. and Hussein, S.E., 2021. Effect of 2 Inactivated SARS-CoV-2 Vaccines on Symptomatic COVID-19 Infection in Adults: A Randomized Clinical Trial. Jama.
- Alonso del Barrio, D. and Gatica-Pérez, D., 2022, June. How Did Europe's Press Cover Covid-19 Vaccination News? A Five-Country Analysis. In Proceedings of the 1st International Workshop on Multimedia AI against Disinformation (pp. 35-43).
- Amoutzias, G.D., Nikolaidis, M., Tryfonopoulou, E., Chlichlia, K., Markoulatos, P. and Oliver, S.G., 2022. The remarkable evolutionary plasticity of coronaviruses by mutation and recombination: insights for the COVID-19 pandemic and the future evolutionary paths of SARS-CoV-2. Viruses, 14(1), p.78.
- Anand, S., Montez-Rath, M.E., Han, J., Garcia, P., Cadden, L., Hunsader, P., Kerschmann, R., Beyer, P., Dittrich, M., Block, G.A. and Boyd, S.D., 2021. Antibody response to COVID-19 vaccination in patients receiving dialysis. Journal of the American Society of Nephrology, 32(10), pp.2435-2438.
- Ara, J., Islam, M.S., Kader, M.T.U., Das, A., Hasib, F.Y., Islam, M.S., Rahman, T., Das, S., Chowdhury, M.H., Das, G.B. and Chowdhury, S., 2022. Sero-prevalence of anti-SARS-CoV-2 antibodies in Chattogram Metropolitan Area, Bangladesh. medRxiv.
- Bachelet, T., Bourdenx, J.P., Martinez, C., Mucha, S., Martin-Dupont, P., Perier, V. and Pommereau, A., 2021. Humoral response after SARS-CoV-2 mRNA vaccines in dialysis patients: Integrating anti-SARS-CoV-2 Spike-Protein-RBD antibody monitoring to manage dialysis centers in pandemic times. PLoS One, 16(10), p.e 0257646.
- Baden, L.R., El Sahly, H.M., Essink, B., Kotloff, K., Frey, S., Novak, R., Diemert, D., Spector, S.A., Rouphael, N., Creech, C.B. and McGettigan, J., 2021. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. New England Journal of Medicine, 384(5), pp.403-416
- Beaumont, P., 2020. Covid-19 vaccine: who are countries prioritising for first doses. The Guardian, 18.

- Berar-Yanay, N., Freiman, S., Shapira, M., Saffoury, A., Elemy, A., Hamze, M., Elhaj, M., Zaher, M., Matanis, L. and Armaly, Z.A., 2021. Waning humoral response 3 to 6 months after vaccination with the SARS-COV-2 BNT162b2 mRNA vaccine in dialysis patients. Journal of Clinical Medicine, 11(1), p.64.
- Bikbov, B., Purcell, C.A., Levey, A.S., Smith, M., Abdoli, A., Abebe, M., Adebayo, O.M., Afarideh, M., Agarwal, S.K., Agudelo-Botero, M. and Ahmadian, E., 2020. Global, regional, and national burden of chronic kidney disease, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. The lancet, 395(10225), pp.709-733.
- Billany, R.E., Selvaskandan, H., Adenwalla, S.F., Hull, K.I., March, D.S., Burton, J.O., Bishop, N.C., Carr, E.J., Beale, R., Tang, J.W. and Bird, P.W., 2021. Seroprevalence of antibody to S1 spike protein following vaccination against COVID-19 in patients on hemodialysis: a call to arms. Kidney international.
- Buti, M., Viladomiu, L., Jardi, R., Olmos, A., Rodriguez, J.A., Bartolome, J., Esteban, R. and Guardia, J., 1992. Long-term immunogenicity and efficacy of hepatitis B vaccine in hemodialysis patients. American journal of nephrology, 12(3), pp.144-147
- Cavanagh, D., 2003. Severe acute respiratory syndrome vaccine development: experiences of vaccination against avian infectious bronchitis coronavirus. Avian pathology, 32(6), pp.567-582.
- Butler, D., 2012. SARS veterans tackle coronavirus. Nature, 490(7418), p.20.
- CDC COVID-19 Response Team, CDC COVID-19 Response Team, CDC COVID-19 Response Team, Chow, N., Fleming-Dutra, K., Gierke, R., Hall, A., Hughes, M., Pilishvili, T., Ritchey, M. and Roguski, K., 2020. Preliminary estimates of the prevalence of selected underlying health conditions among patients with coronavirus disease 2019—United States, February 12–March 28, 2020. Morbidity and Mortality Weekly Report, 69(13), pp.382-386
- Chen, J.J., Lee, T.H., Tian, Y.C., Lee, C.C., Fan, P.C. and Chang, C.H., 2021. Immunogenicity rates after SARS-CoV-2 vaccination in people with end-stage kidney disease: a systematic review and meta-analysis. JAMA network open, 4(10), pp.e2131749-e2131749.
- Clark, A.N., 2022. Christian Nationalists and Their Initial Response to the Death of George Floyd: Select Churches and Organizations in Southern California, Nevada, and Arizona (Doctoral dissertation, Youngstown State University).
- Cockwell, P. and Fisher, L.A., 2020. The global burden of chronic kidney disease. The Lancet, 395(10225), pp.662-664.
- Corbett, R.W., Blakey, S., Nitsch, D., Loucaidou, M., McLean, A., Duncan, N. and Ashby, D.R., 2020. Epidemiology of COVID-19 in an urban dialysis center. Journal of the American Society of Nephrology, 31(8), pp.1815-1823.
- Dan, J.M., Mateus, J., Kato, Y., Hastie, K.M., Yu, E.D., Faliti, C.E., Grifoni, A., Ramirez, S.I., Haupt, S., Frazier, A. and Nakao, C., 2021. Immunological memory to SARS-CoV-2 assessed for up to 8 months after infection. Science, 371(6529), p.eabf4063.
- Das, S., Singh, J., Shaman, H., Singh, B., Anantharaj, A., Sharanabasava, P., Pandey, R., Lodha, R., Pandey, A.K. and Medigeshi, G.R., 2022. Pre-existing antibody levels negatively correlate with antibody titers after a single dose of BBV152 vaccination.
- Degarege, A., Naveed, Z., Kabayundo, J. and Brett-Major, D., 2020. Risk factors for severe illness and death in COVID-19: a systematic review and meta-analysis. MedRxiv.
- Eknoyan, G., Lameire, N., Eckardt, K., Kasiske, B., Wheeler, D., Levin, A., Stevens, PE, Bilous, RW, Lamb, EJ, Coresh, J. and Levey, AS, 2013. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int , 3 (1), pp. 5-14.
- Eslahtalab, A., Mahvelati Feyzabadi, M., Jajarmi Khayyat, H., Tohidipour, Z., Mohammadi, B., Mirzaei, M. and Fazeli, F., 2021. A Reflection on the Types of COVID-19 Vaccines with Emphasis on the Side Effects of Vaccines; A Review. Medical Education Bulletin, 2(2), pp.183-198.
- Fehr, A.R. and Perlman, S., 2015. Coronaviruses: an overview of their replication and pathogenesis. Coronaviruses, pp.1-23.
- Francis, A., Baigent, C., Ikizler, T.A., Cockwell, P. and Jha, V., 2021. The urgent need to vaccinate dialysis patients against severe acute respiratory syndrome coronavirus 2: a call to action. Kidney international, 99(4), pp.791-793
- Fucci, A., Giacobbe, S., Guerriero, I., Suzumoto, Y., D'Andrea, E.L., Scrima, M., Nolli, M.L., Iervolino, A., Chiuchiolo, L.A., Salvatore, E. and Renzulli, R., 2022. The DiaCoVAb study in South Italy: immune response to Sars-CoV-2 vaccination in dialysis patients. Kidney and Blood Pressure Research, pp.1-8.
- Gates, B., 2020. The vaccine race explained: What you need to know about the COVID-19 vaccine. The Gates Notes. Archived from the original on, 14.
- Greenberger, L.M., Saltzman, L.A., Senefeld, J.W., Johnson, P.W., DeGennaro, L.J. and Nichols, G.L., 2021. Antibody response to SARS-CoV-2 vaccines in patients with hematologic malignancies. Cancer cell, 39(8), pp.1031-1033.
- Grupper, A., Sharon, N., Finn, T., Cohen, R., Israel, M., Agbaria, A., Rechavi, Y., Schwartz, I.F., Schwartz, D., Lellouch, Y. and Shashar, M., 2021. Humoral response to the Pfizer BNT162b2 vaccine in patients undergoing maintenance

hemodialysis. Clinical Journal of the American Society of Nephrology.

- Harikrishnan, S., Jeemon, P., Mini, G.K., Thankappan, K.R. and Sylaja, P., 2018. GBD 2017 causes of death collaborators. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980-2017: a systematic analysis for the global burden of disease study 2017.
- Hicks, S.R., 2021. Rotten with Prediction (Doctoral dissertation, University of Nevada, Las Vegas).
- Hilbrands, L.B., Duivenvoorden, R., Vart, P., Franssen, C.F., Hemmelder, M.H., Jager, K.J., Kieneker, L.M., Noordzij, M., Pena, M.J., Vries, H.D. and Arroyo, D., 2020. COVID-19-related mortality in kidney transplant and dialysis patients: results of the ERACODA collaboration. Nephrology Dialysis Transplantation, 35(11), pp.1973-1983
- Hill, N.R., Fatoba, S.T., Oke, J.L., Hirst, J.A., O'Callaghan, C.A., Lasserson, D.S. and Hobbs, F.R., 2016. Global prevalence of chronic kidney disease–a systematic review and meta-analysis. PloS one, 11(7), p.e0158765.
- Holman, N., Knighton, P., Kar, P., O'Keefe, J., Curley, M., Weaver, A., Barron, E., Bakhai, C., Khunti, K., Wareham, N.J. and Sattar, N., 2020. Risk factors for COVID-19-related mortality in people with type 1 and type 2 diabetes in England: a population-based cohort study. The lancet Diabetes & endocrinology, 8(10), pp.823-833.
- Hombach, J., Solomon, T., Kurane, I., Jacobson, J. and Wood, D., 2005. Report on a WHO consultation on immunological endpoints for evaluation of new Japanese encephalitis vaccines, WHO, Geneva, 2–3 September, 2004. Vaccine, 23(45), pp.5205-5211
- Hsu, C.M., Weiner, D.E., Aweh, G., Miskulin, D.C., Manley, H.J., Stewart, C., Ladik, V., Hosford, J., Lacson, E.C., Johnson, D.S. and Lacson Jr, E., 2021. COVID-19 among US dialysis patients: risk factors and outcomes from a national dialysis provider. American Journal of Kidney Diseases, 77(5), pp.748-756.
- Huang, Z., Su, Y., Zhang, T. and Xia, N., 2022. A review of the safety and efficacy of current COVID-19 vaccines. Frontiers of Medicine, pp.1-17.
- Jager, K.J., Kramer, A., Chesnaye, N.C., Couchoud, C., Sánchez-Álvarez, J.E., Garneata, L., Collart, F., Hemmelder, M.H., Ambühl, P., Kerschbaum, J. and Legeai, C., 2020. Results from the ERA-EDTA Registry indicate a high mortality due to COVID-19 in dialysis patients and kidney transplant recipients across Europe. Kidney international, 98(6), pp.1540-1548.
- Jahan, N., Brahma, A., Kumar, M.S., Bagepally, B.S., Ponnaiah, M., Bhatnagar, T. and Murhekar, M.V., 2021. Seroprevalence of IgG antibodies against SARS-CoV-2 in India, March 2020-August 2021: a systematic review and meta-analysis. International Journal of Infectious Diseases.Nature communications, 13(1)
- Kato, S., Chmielewski, M., Honda, H., Pecoits-Filho, R., Matsuo, S., Yuzawa, Y., Tranaeus, A., Stenvinkel, P. and Lindholm, B., 2008. Aspects of immune dysfunction in end-stage renal disease. Clinical Journal of the American Society of Nephrology, 3(5), pp.1526-1533.
- Keech C, Albert G, Cho I. Phase 1–2 trial of a SARS-CoV-2 recombinant spike protein nanoparticle vaccine. N Engl J Med 2020;383:2320-2332
- Kennedy, N.A., Goodhand, J.R., Bewshea, C., Nice, R., Chee, D., Lin, S., Chanchlani, N., Butterworth, J., Cooney, R., Croft, N.M. and Hart, A.L., 2021. Anti-SARS-CoV-2 antibody responses are attenuated in patients with IBD treated with infliximab. Gut, 70(5), pp.865-875.
- VDI, C., 2020. Coronavirus disease 2019 (COVID-19).
- *Kirsten, Vannice; Marti, Melanie (2021-04-29)*. "Evidence Assessment: Sinopharm/BBIBP COVID-19 vaccine"
- Liu, J., Mao, Q., Wu, X., He, Q., Bian, L., Bai, Y., Wang, Z., Wang, Q., Zhang, J., Liang, Z. and Xu, M., 2022. Considerations for the Feasibility of Neutralizing Antibodies as a Surrogate Endpoint for COVID-19 Vaccines. Frontiers in Immunology, 13.
- Liyanage, T., Ninomiya, T., Jha, V., Neal, B., Patrice, H.M., Okpechi, I., Zhao, M.H., Lv, J., Garg, A.X., Knight, J. and Rodgers, A., 2015. Worldwide access to treatment for end-stage kidney disease: a systematic review. The Lancet, 385(9981), pp.1975-1982.
- Mallano, A., Ascione, A. and Flego, M., 2022. Antibody Response against SARS-CoV-2 Infection: Implications for Diagnosis, Treatment and Vaccine Development. International Reviews of Immunology, 41(4), pp.393-413.
- Mallucci, L., McIntosh, K. and Tyrrell, D., 1968. Virology: coronaviruses. Nature, 220, p.650.
- Matsunami, M., Suzuki, T., Fukuda, J., Terao, T., Ukai, K., Sugihara, S., Toishi, T., Nagaoka, K., Nakata, M., Ohara, M. and Yashima, J., 2022. Comparison of antibody response following the second dose of SARS-CoV-2 mRNA vaccine in elderly patients with late-stage chronic kidney disease. Renal replacement therapy, 8(1), pp.1-5.odialysis. Vaccines, 10(2), p.327
- Mills, K.T., Xu, Y., Zhang, W., Bundy, J.D., Chen, C.S., Kelly, T.N., Chen, J. and He, J., 2015. A systematic analysis of worldwide population-based data on the global burden of chronic kidney disease in 2010. Kidney international, 88(5), pp.950-957.
- Neuman, B.W., Kiss, G., Kunding, A.H., Bhella, D., Baksh, M.F., Connelly, S., Droese, B., Klaus, J.P., Makino, S., Sawicki, S.G. and Siddell, S.G., 2011. A structural analysis of M protein in coronavirus

assembly and morphology. Journal of structural biology, 174(1), pp.11-22.

- Ng, J.H., Hirsch, J.S., Wanchoo, R., Sachdeva, M., Sakhiya, V., Hong, S., Jhaveri, K.D., Fishbane, S., Abate, M., Andrade, H.P. and Barnett, R.L., 2020. Outcomes of patients with end-stage kidney disease hospitalized with COVID-19. Kidney international, 98(6), pp.1530-1539.
- Paal, M., Arend, F.M., Lau, T., Hasmann, S., Soreth-Rieke, D., Sorodoc-Otto, J., Beuthien, W., Krappe, J., Toepfer, M., Gersdorff, G.V. and Thaller, N., 2021. Antibody response to mRNA SARS-CoV-2 vaccines in haemodialysis patients. Clinical kidney journal, 14(10), pp.2234-2238.
- Palmenberg, A.C., Spiro, D., Kuzmickas, R., Wang, S., Djikeng, A., Rathe, J.A., Fraser-Liggett, C.M. and Liggett, S.B., 2009. Sequencing and analyses of all known human rhinovirus genomes reveal structure and evolution. Science, 324(5923), pp.55-59.
- Polack, F.P., Thomas, S.J., Kitchin, N., Absalon, J., Gurtman, A., Lockhart, S., Perez, J.L., Pérez Marc, G., Moreira, E.D., Zerbini, C. and Bailey, R., 2020. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. New England Journal of Medicine, 383(27), pp.2603-2615
- Pranata, R., Supriyadi, R., Huang, I., Permana, H., Lim, M.A., Yonas, E., Soetedjo, N.N.M. and Lukito, A.A., 2020. The association between chronic kidney disease and new onset renal replacement therapy on the outcome of COVID-19 patients: a meta-analysis. Clinical Medicine Insights: Circulatory, Respiratory and Pulmonary Medicine, 14, p.1179548420959165.
- Ramasamy, M.N., Minassian, A.M., Ewer, K.J., Flaxman, A.L., Folegatti, P.M., Owens, D.R., Voysey, M., Aley, P.K., Angus, B., Babbage, G. and Belij-Rammerstorfer, S., 2020. Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV002): a single-blind, randomised, controlled, phase 2/3 trial. The Lancet, 396(10267), pp.1979-1993.
- Reddy, S., Chitturi, C. and Yee, J., 2019. Vaccination in chronic kidney disease. Advances in chronic kidney disease, 26(1), pp.72-78. (33) Yen JS, Wang IK, Yen TH. COVID-19 vaccination & dialysis patients: Why the variable response. QJM 2021 Nov 5; 114(7): 440-4.
- Rentsch, C.T., Kidwai-Khan, F., Tate, J.P., Park, L.S., King Jr, J.T., Skanderson, M., Hauser, R.G., Schultze, A., Jarvis, C.I., Holodniy, M. and Lo Re III, V., 2020. Patterns of COVID-19 testing and mortality by race and ethnicity among United States veterans: A nationwide cohort study. PLoS medicine, 17(9), p.e1003379.
- Saco, T.V., Strauss, A.T. and Ledford, D.K., 2018. Hepatitis B vaccine nonresponders: Possible mechanisms and solutions. Annals of Allergy, Asthma & Immunology, 121(3), pp.320-327.
- Subbarao, K., 2021. The success of SARS-CoV-2 vaccines and challenges ahead. Cell host & microbe, 29(7), pp.1111-1123.
- Tang, N., Bai, H., Chen, X., Gong, J., Li, D. and Sun, Z., 2020. Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy. Journal of thrombosis and haemostasis, 18(5), pp.1094-1099.
- Tyrrell, D.A.J. and Bynoe, M.L., 1966. Cultivation of viruses from a high proportion of patients with colds. Lancet, pp.76-7.
- Vergano, D., 2021. COVID-19 Vaccines Work Way Better Than We Had Ever Expected. Scientists Are Still Figuring Out Why. BuzzFeed News.
- Verbeke, R., Lentacker, I., De Smedt, S.C. and Dewitte, H., 2019. Three decades of messenger RNA vaccine development. Nano Today, 28, p.100766.
- Vestergaard, S.V., Christiansen, C.F., Thomsen, R.W., Birn, H. and Heide-Jørgensen, U., 2021. Identification of patients with CKD in medical databases: a comparison of different algorithms. Clinical Journal of the American Society of Nephrology, 16(4), pp.543-551.
- Villalobos, N.V.F., Ott, J.J., Klett-Tammen, C.J., Bockey, A., Vanella, P., Krause, G. and Lange, B., 2020. Quantification of the association between predisposing health conditions, demographic, and behavioural factors with hospitalisation, intensive care unit admission, and death from COVID-19: a systematic review and meta-analysis. medRxiv.
- Vivanco-Hidalgo, R.M., Vela-Vallespín, E., Clèries, M. and Monterde, D., 2020. Informe sobre les característiques sociodemogràfiques, clíniques i els factors pronòstics dels pacients amb el diagnòstic de COVID-19 a Catalunya: resum executiu.
- Wertheim, J.O., Chu, D.K., Peiris, J.S., Kosakovsky Pond, S.L. and Poon, L.L., 2013. A case for the ancient origin of coronaviruses. Journal of Virology, 87(12), pp.7039-7045.
- Williamson, E.J., Walker, A.J., Bhaskaran, K., Bacon, S., Bates, C., Morton, C.E., Curtis, H.J., Mehrkar, A., Evans, D., Inglesby, P. and Cockburn, J., 2020. Open SAFELY: factors associated with COVID-19 death in 17 million patients. Nature.
- Windpessl, M., Bruchfeld, A., Anders, H.J., Kramer, H., Waldman, M., Renia, L., Ng, L.F.P., Xing, Z. and Kronbichler, A., COVID-19 vaccines and kidney disease [published online ahead of print February 8, 2021]. Nat Rev Nephrol, 10.
- Yau, K., Abe, K.T., Naimark, D., Oliver, M.J., Perl, J., Leis, J.A., Bolotin, S., Tran, V., Mullin, S.I., Shadowitz, E. and Gonzalez, A., 2021. Evaluation of the SARS-CoV-2 antibody response to the BNT162b2 vaccine in patients undergoing hemodialysis. JAMA network open, 4(9), pp.e2123622-e2123622.

- Yuan, M., Wu, N.C., Zhu, X., Lee, C.C.D., So, R.T., Lv, H., Mok, C.K. and Wilson, I.A., 2020. A highly conserved cryptic epitope in the receptor binding domains of SARS-CoV-2 and SARS-CoV. Science, 368(6491), pp.630-633.
- Zhou, F., Yu, T., Du, R., Fan, G., Liu, Y., Liu, Z., Xiang, J., Wang, Y., Song, B., Gu, X. and Guan, L., 2020. Clinical course and risk factors for mortality of adult in patients with COVID-19 in Wuhan, China: a retrospective cohort study. The lancet, 395(10229), pp.1054.