

# Comparison of Factors Affecting the Immune Response to Hepatitis B Vaccination in Patients with Stage 5 Chronic Kidney Disease-haemodialysis and Predialysis



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## Abstract:

**Aim:** To evaluate the factors that affect the immune response to Hepatitis B vaccination in the Stage 5 chronic kidney disease population (Haemodialysis and Predialysis).

**Methods:** Eligible Stage 5 chronic kidney disease patients on haemodialysis (Cohort A: N= 39) and Predialysis (Cohort B: N=56) in an outer metropolitan renal service in Western Australia with no prior Hepatitis B infection or vaccination between Jan 2015 to Dec 2021 were involved in this retrospective cohort study. Serological response to Hepatitis B vaccination (H-B-VAX<sup>®</sup> 40 mcg intramuscularly at 0, 1 and 6 months) was evaluated six-eight weeks post-vaccination. Factors such as age, gender, diabetes mellites, cardiovascular disease, hypertension, chronic obstructive airway disease, serum albumin, and erythropoietin stimulating agent dependence were studied for their influence on immune responses in these cohorts.

**Results:** There were 95 eligible respondents in the study. Cohort B (Predialysis) showed a significantly higher response than Cohort A (Haemodialysis) (66.1% vs 53.8%) ( $p=0.003$ ). Different factors affecting the vaccine response were identified in the two cohorts. Serum albumin  $<35\text{g/L}$  was associated with negative response in 61.1% ( $p=0.0023$ ) Cohort A HD patients. In the Predialysis Cohort B, 84.2% ( $p=0.026$ ) were male gender, 63.2% ( $p=0.028$ ) with the presence of cardiovascular disease, and 57.9% ( $p=0.001$ ) who were Erythropoietin dependent showed a negative response to the vaccine.

**Conclusion:** This study showed that the Hepatitis B vaccine response was lower in HD patients than in Predialysis patients with stage 5 chronic kidney disease. Clinical factors of serum albumin, cardiovascular disease, and patient factors of gender and erythropoietin dependence were identified as factors that affected vaccine response in these two cohorts. We postulate these factors to be considered in the hepatitis B vaccination management to enhance immunological response strategies and extend to earlier stages of chronic kidney failure.

**Keywords:** Haemodialysis, Hepatitis B virus, Immune response, Stage 5 chronic kidney disease, Vaccination, Predialysis.

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Cite as: Light C, Heslop K, Kulkarni H. Comparison of Factors Affecting the Immune Response to Hepatitis B Vaccination in Patients with Stage 5 Chronic Kidney Disease-haemodialysis and Predialysis. Open Urol Nephrol J, 2024; 17: e1874303X304324. <http://dx.doi.org/10.2174/011874303X304324240529133609>



Received: February 24, 2024

Revised: May 18, 2024

Accepted: May 21, 2024

Published: June 05, 2024



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## 1. INTRODUCTION

Chronic Kidney Disease (CKD) is a leading global

public health epidemic disease, with estimated prevalence reported to be 13.4% in 2019 [1].

Kidney function stage	GFR (mL/min/1.73m <sup>2</sup> )	Albuminuria stage		
		Normal (urine ACR mg/mmol) Male: <2.5 Female: <3.5	Microalbuminuria (urine ACR mg/mmol) Male: <2.5-25 Female: <3.5-35	Macroalbuminuria (urine ACR mg/mmol) Male: >25 Female: >35
1	≥90	Not CKD unless haematuria, structural or pathological abnormalities present		
2	60-89			
3a	45-59			
3b	30-44			
4	15-29			
5	<15 or on dialysis			

**Fig. (1).** Classification of chronic kidney disease. ACR, albumin-to-creatinine ratio; CKD, chronic kidney disease; GFR, glomerular filtration rate. Reproduced with permission from Kidney Health Australia, Chronic kidney disease (CKD) management in primary care, 4th edn, Melbourne, Vic: Kidney Health Australia, 2020.

In Australia, the Australian Institute of Health and Welfare (AIHW) reported an estimated 1.7 million Australians aged over 18 years had CKD in 2020 [2].

CKD is defined as a decline in kidney function caused by structural damage. The level of kidney function can be determined by the estimated glomerular filtration rate (eGFR) using the Modification of Diet in Renal Disease (MDRD) method [3] or the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula [4].

CKD is classified into 5 stages according to the degree of kidney damage, as shown in Fig. (1) (Kidney Health Australia, 2020).

Infection is a major cause of morbidity and mortality in chronic kidney disease (CKD) [5, 6]. Hepatitis B virus (HBV) causes serious diseases such as acute hepatitis, liver fibrosis and liver cancer [7, 8]. Since its use in 1982, vaccination remains the most effective way to minimise the effects of Hepatitis B infection [9].

Hepatitis B vaccination is a standard of care in patients with advanced chronic kidney disease (CKD) in particular, the haemodialysis (HD) population who are at potentially high risk due to exposure to blood and blood products within haemodialysis equipment, breaching of skin integrity, frequent surgeries, and hospitalisation. Advanced CKD is associated with suboptimal immune responses to infections or vaccinations due to immune suppression related to uraemia impacting CD3<sup>+</sup>, CD4<sup>+</sup>, CD8<sup>+</sup> T and B lymphocytes [10, 11]. Thereby, a complex process involving an intact innate and adaptive immune system is required for the immune response to the vaccination [12]. Besides the immunological impact, many patient-associated factors have been associated with the suboptimal response in the CKD and HD population

[13-15]. This study explored these factors on patients with stage 5 CKD on Haemodialysis and those who were not yet started on dialysis (Predialysis).

**1.1. Aim**

To evaluate the factors that affect the immune response to Hepatitis B vaccination in the Stage 5 chronic kidney disease population (Haemodialysis and Predialysis).

**1.2. Hypothesis**

We hypothesised clinical and patient-related factors influence the immunological response to Hepatitis B vaccination in dialysis and predialysis dependent stage 5 chronic kidney disease.

**2. METHODS**

In order to determine the factors that influence the response to Hepatitis B vaccination in stage 5 CKD patients, this study employed the “Retrospective Study” design to examine data collected from the medical records of the following two groups of patients.

Hepatitis B naïve and seronegative for Anti HBsAb (no prior Hepatitis B infection or vaccination) patients on maintenance haemodialysis (Cohort A: n =39) and Stage 5 CKD not yet on dialysis, ie predialysis (Cohort B: n =56) within an outer metropolitan renal service in Western Australia between Jan 2015 to Dec 2021 were included in the study, after excluding 10 immune (HBsAb >10 mIU/mL) and seven deceased patients. Patients with active advanced malignancy, known immune deficiency or immunosuppressants were also excluded at the initial screening.

Current guidelines recommend that patients with advanced CKD and those on dialysis should receive active

vaccination against the hepatitis B virus [16]. Variations in vaccination regimes are available for three or four doses over a six-month regime [17]. In this study, we have adapted the recommendation of three doses over a six-month regime for our clinical practice.

The hepatitis B vaccine used in this study was the Australian Therapeutic Goods Administration (TGA) approved H-B-VAX® II hepatitis B recombinant 40 µg in 1 mL (Dialysis formulation), given intramuscularly as per product instruction. The serological response was evaluated six to eight weeks after the completion of this single course of hepatitis B vaccine, which was given intramuscularly at 0, 1, and 6 months. Serology results of HBsAb > 10mIU/mL denote a positive seroconversion [18]. Thus, patients with HBsAb > 10mIU/mL were classified as “Responders” and “Non-responders” for those with HBsAb < 10 mIU/mL in this study.

Serology and biochemical results and information relevant to the study population were obtained from the institution's medical records and electronic laboratory database.

Factors explored for their effects on the immune response were age (years.), gender (M=male, F=female), diabetes mellitus (DM), cardiovascular disease (CVD), hypertension (HT), chronic obstructive airway disease (COAD), serum albumin (SA), and erythropoietin stimulating agents (ESA) dependence (Yes/No) at the entry were studied.

Albumin is the most abundant human serum protein and has been used as an indicator of malnutrition [19]. In this study, we used serum albumin <35 g/L as the biomarker, as other studies have shown adverse effects of its indication of malnutrition [19, 20].

### 2.1. Statistics

Descriptive statistics were used to analyse demographic data (Mean / Standard Deviation (SD)).

An independent samples t-test was used to test the significance of the difference in values in the continuous variable, such as age and serum albumin.

The chi-square  $\chi^2$  test was used for categorical variables in gender, DM, CVD, HT, COPD and ESA dependence, as well as serum albumin < 35g/L, which were presented as frequencies and percentages. A *p*-value of <0.05 is considered as statistically significant. Analyses were performed using the statistical package SPSS, version 28, for Windows (IBM, Corporation, Armonk, NY, USA).

### 2.2. Ethics Considerations

Ethics approval for the study was granted by the East Metropolitan Health Service Human Research Ethics Committee, protocol number GS0000005290 and reciprocal ethic approval through the Curtin University Human Research Ethics Committee, protocol number HRE2022-0378.

Eligible adult patients attending the HD unit and Renal Clinic at the centre and available for the study duration were evaluated and consented to the study.

Waiver of Consent was approved for participants who were uncontactable due to natural attrition or relocation to a different address. This followed the criteria set out in Section 2.3.10 of the National Statement of Ethical Conduct in Human Research 2007 -updated 2018 [21].

### 3. RESULTS

112 Stage 5 CKD patients eligible for the study attended the haemodialysis unit (N = 51) and Predialysis Nurse Practitioner Clinic (n = 61) between Jan 2015 and Dec 2021. Of these, 10 patients (nine HD patients and one Predialysis patient) had HBsAb titres > 10 mIU/mL, and seven patients (3 in HD and 4 in Predialysis CKD cohorts) who died prior to completion of the vaccination schedule were excluded.

Thus, the final 95 patients who had completed the vaccination course at 0, 1 and 6 months, defined as Cohort A (HD; n = 39) and Cohort B (Predialysis; n= 56), were included in the study. The detailed demographics of the Cohort A and Cohort B patients, together with the co-morbidities of DM, CVD, HT, COPD, S Albumin <35 g/L and ESA dependence, are represented in Table 1.

**Table 1. Demographics and co-morbidities of Cohort A and Cohort B patients.**

Parameters	Cohort A Haemodialysis (HD) Patients (n=39)	Cohort B Pre -dialysis Patients (n=56)
Mean Age, years (SD)	65.0 (± 17.0)	68.6 (± 13.4)
Gender male, n (%)	21 (53.8)	36 (64.3%)
Gender female, n (%)	18 (46.2)	20 (35.7%)
DM, n (%)	21 (53.8)	35 (62.5)
CVD, n (%)	16 (41.0)	24 (42.9)
HT, n (%)	17(43.6)	32 (57.1)
COPD, n (%)	8 (20.5)	14 (25.0)
S ALB <35 g/L, n (%)	14 (35.9)	10 (17.8)
ESA dependence, n (%)	9 (23.1)	13 (23.2)

**Abbreviations:** DM Diabetes Mellitus, CVD cardiovascular disease, HT hypertension, COPD chronic obstructive pulmonary disease, S Alb serum albumin, ESA Erythropoietin stimulating agents.

**Table 2. Response to hepatitis B vaccine for Cohort A and Cohort B patients.**

Parameters	Cohort A Haemodialysis (HD) (n=39)	Cohort B Predialysis Patients (n=56)
“Non-Responders” (HBsAb<10mIU/mL)	18 (46.2%)	19 (33.9%)
“Responders” (HBsAb>10mIU/mL)	21 (53.8%)	37 (66.1%) (p=0.003)
Results of “Responders”		
Min	16.9	14.1
Max	1000	1000
Quartile 1	39	35.7
(Median) Quartile 2	183.3	139.1
Quartile 3	663.2	483.65
Interquartile ranges (IQR)	479.9	344.55
Range	983.1	985.9

Our results showed that 46.2% (n=18) Cohort A patients and 33.9%(n=19) Cohort B patients did not respond to the vaccine (HBsAb < 10 mIU/mL), while the Predialysis patients (Cohort A) had a higher serological response (HBsAb >10 mIU/mL) than the Cohort B Haemodialysis patients (66.1% versus 53.8%) (P=0.003). The range, median, and Interquartile Range (IQR) of the “Responders” of both Cohort A and Cohort B are further detailed in Table 2.

### 3.1. Characteristics and Vaccine Response in both Cohorts

Tables 3a and 3b detail the study data in HD and Predialysis cohorts, respectively.

Data in Table 3a demonstrate that serum albumin <

35g/L was significantly associated with non-response versus response in the Haemodialysis Cohort (61.1% Vs 14.3%) (p=0.0023), but this was not observed in the Predialysis CKD Cohort (p=0.054) as in Table 3b.

Similarly, ESA dependence was associated with a significant negative influence in the Predialysis CKD cohort (p =0.001) but not in the Haemodialysis cohort.

Male Gender (84.2% males vs 15.8% females) (p =0.026) CVD (63.2%) (p =0.028) were also associated with suboptimal vaccine response in Predialysis Stage 5 CKD patients.

Other factors, such as age and individual co-morbidities (DM, HT, COPD), had no significant impact on the vaccine response in either the Haemodialysis or Predialysis CKD cohort (p >0.05).

**Table 3a. Cohort A HD patients - characteristics and vaccine response.**

Cohort A HD Patients N=39						
-	Non-Responders (n=18, 46.2%)		Responders (n=21, 53.8%)		-	-
Categoric Data	n	%	n	%	χ <sup>2</sup> (df)	P value
<b>Gender</b>						
Male	10	55.6	11	52.4	0.039 (1)	0.843
Female	8	44.4	10	47.6		
<b>DM</b>						
Yes	8	44.4	13	61.9	1.189 (1)	0.276
No	10	55.6	8	38.1		
<b>CVD</b>						
Yes	9	50	7	33.3	1.113 (1)	0.291
No	9	50	14	66.7		
<b>HT</b>						
Yes	7	38.9	10	47.6	0.300 (1)	0.548
No	11	61.1	11	52.4		
<b>COPD</b>						
Yes	5	27.8	3	14.3	1.082 (1)	0.298
No	13	72.2	18	85.7		
<b>ESA Dependent</b>						
Yes	5	27.8	4	19.1	0.416 (1)	0.519
No	13	72.2	17	80.9		
<b>S Alb &lt;35g/L</b>						
Yes	11	61.1	3	14.3	9.235(1)	0.0023*
No	7	38.9	18	85.7		

(Table 3) contd....

Cohort A HD Patients N=39						
-	Non-Responders (n=18, 46.2%)		Responders (n=21, 53.8%)		-	-
Categoric Data	n	%	n	%	$\chi^2$ (df)	P value
Numerical data	Mean	$\pm$ SD	Mean	$\pm$ SD	t (df)	p-value
S Alb	33.22	5.140	36.57	5.437	-1.966 (37)	0.027*
-	-	-	-	-	-	-
Age	67.33	15.699	62.67	17.539	0.869 (37)	0.390
-	-	-	-	-	-	-

**Abbreviations:** DM: Diabetes Mellites; CVD, cardiovascular disease; HT, hypertension; COPD, chronic obstructive pulmonary disease; ESA, erythropoietin stimulating agents; S Alb, Serum Albumin; SD, standard deviation.

Note for P values: Chi-square tests used for categoric variables: Gender, DM, CVD, HT, COPD, ESA Dependent, S Alb <35 g/L

t-test, Independent Samples t test used for numerical data for S Alb, Age

\* P <0.05, statistically significant.

Table 3b. Cohort B Predialysis patients - characteristics and vaccine response.

Cohort B Predialysis patients N=56						
-	Non-Responders (n=19, 33.9%)		Responders (n=37, 66.1%)		-	-
Categoric Data	n	%	n	%	$\chi^2$ (df)	P value
<b>Gender</b>						
Male	16	84.2	20	54.1	4.912 (1)	0.026*
Female	3	15.8	17	45.9		
<b>DM</b>						
Yes	12	63.1	23	62.2	0.005 (1)	0.942
No	7	36.9	14	37.8		
<b>CVD</b>						
Yes	12	63.2	12	32.4	4.839 (1)	0.028*
No	7	36.8	25	67.6		
<b>HT</b>						
Yes	10	52.6	22	59.5	0.239 (1)	0.625
No	9	47.4	15	40.5		
<b>COPD</b>						
Yes	3	15.8	11	29.7	1.301 (1)	0.254
No	16	84.2	26	70.3		
<b>ESA Dependent</b>						
Yes	11	57.9	2	5.4	19.403 (1)	0.001*
No	8	42.1	35	94.6		
<b>S Alb &lt;35g/L</b>						
Yes	6	31.6	4	10.8	3.691 (1)	0.054
No	13	68.4	33	89.1		
<b>Numerical data</b>	<b>Mean</b>	<b><math>\pm</math>SD</b>	<b>Mean</b>	<b><math>\pm</math>SD</b>	<b>t (df)</b>	<b>p-value</b>
S Alb	37.58	4.623	39.30	3.423	-1.576 (54)	0.121
-	-	-	-	-	-	-
Age	71.21	12.268	67.24	13.861	1.053 (54)	0.297
-	-	-	-	-	-	-

**Abbreviations:** DM: Diabetes Mellites; CVD, cardiovascular disease; HT, hypertension; COPD, chronic obstructive pulmonary disease; ESA, erythropoietin stimulating agents; S Alb, Serum Albumin; SD standard deviation.

Note for P values: Chi-square tests used for categoric variables: Gender, DM, CVD, HT, COPD, ESA Dependent, S Alb <35 g/L

t-test, Independent Samples t test used for numerical data for S Alb, Age

\* P <0.05, statistically significant.

4. DISCUSSION

Morbidity and mortality due to vaccine-preventable illnesses, such as hepatitis B, influenza, COVID-19, and Streptococcus pneumoniae pneumonia, is higher among patients with advanced chronic kidney disease compared with the general population [12]. Vaccinations against

these illnesses are recommended for patients with advanced CKD by most major national and international medical societies despite knowing the concerns about vaccine efficacy, safety, and appropriate timing. Various attempts to improve the immunogenicity of the vaccines have been made, including the dose, frequency, route of

administration, change of adjuvant and others, with limited success [12]. Thus, the role of non-modifiable patient-related factors was also explored in various studies in the dialysis population [13-15]. We aimed to study these factors in Stage 5 CKD, including those not yet on dialysis. We are not aware of any such reported comparative study evaluating patient-related non-modifiable factors. Limitations of the retrospective design of the study and small population size are acknowledged.

In our study, hypoalbuminemia in the haemodialysis cohort (serum albumin <35g/L, as a surrogate marker of nutritional state [14, 19, 22]) and ESA dependence in the Predialysis cohort were associated with significant negative vaccination response in specific patient groups while male gender and presence of CVD were associated with moderate negative impact in this cohort. Such a differential response warrants further studies in a larger cohort and a prospectively designed trial.

Serum albumin is considered a surrogate biochemical marker for nutrition in CKD [14, 19, 22]. Hypoalbuminemia may relate to increased catabolism, protein loss on dialysis and worsening nutrition in the dialysis cohort. The effect of hypoalbuminemia hampering the differentiation of monocyte-derived cells of the immune system was postulated by Fabrizi *et al.* [14]. The similar negative impact of malnutrition in the CKD population was also reflected in a meta-analysis conducted by Fabrizi *et al.* [14]. It is unclear at this stage whether correction of malnutrition will improve the vaccination response in the dialysis cohort. However, improving nutritional status as a strategy to enhance vaccine response in hepatitis B vaccination may be considered in the clinical practice guidelines.

In our study, ESA dependence was a striking factor associated with poor vaccination response in the Predialysis cohort. All previous studies linking it to vaccination response to ESA were done exclusively in the dialysis population, including that by Fabrizi *et al.* [15] and Afsar [23]. Afsar [23] showed Erythropoietin (EPO) resistance inversely influenced response to the hepatitis B vaccine in 97 HD patients, using the ESA hypo-responsiveness index by dividing weekly EPO dose per kg body weight by haemoglobin level, while Fabrizi *et al.* [15] found no link between ESA dependence and hepatitis B vaccine response in a meta-analysis of 11 studies in haemodialysis patients.

EPO resistance calculation was unable to be retrieved in this retrospective study. Thus, ESA dependence was studied instead. EPO therapy is a standard treatment for anaemia of chronic kidney failure, and anaemia is common in this population due to EPO secretion deficiency related to the degree of renal failure [24]. The findings of ESA dependence in our predialysis cohort highlighted the factors that warrant EPO, which may also contribute to impaired immune response.

The role of gender (males) with suboptimal response in the Predialysis cohort was explored earlier with the postulation of inhibitory effects of testosterone on

immunoglobulin production, as well as restrained production on IL-6 from monocytes described by Kanda *et al.* [25] as cited in Yang *et al.* [26]. This gender difference was further supported in a meta-analysis by Khedmat *et al.* [27] involving 19 clinical trials in the haemodialysis population, showing males significantly respond less to the Hepatitis B vaccine. A similar gender difference was demonstrated in our Predialysis cohort.

On other factors investigated in the current paper, such as age, DM, HT and COAD, we found no significant impact on vaccination response in both Cohort A and Cohort B. Sit *et al.* [28] and Zitt *et al.* [16] noted that age has a negative influence on the vaccine response in dialysis patients due to impaired humoral and cellular responses in the elderly patients with bone marrow depression in the ageing process. We did not find that factors such as age, DM, HT, and COAD had any impact on either cohort.

Although we demonstrated CVD negatively influences the vaccine response ( $P=0.028$ ) in Predialysis patients, there was limited literature on the relationships between CVD and hepatitis B vaccine response.

In a 12-month study on 144 HD patients, Al Saran *et al.* [29] showed that DM, HT and COAD had no impact on the vaccine response. However, a meta-analysis of 12 studies by Fabrizi *et al.* [13] demonstrated impaired response in HD patients with DM. The current study involving the predialysis patient cohort showed an unclear role of the DM and provided indication for further studies to investigate the vaccine response affected by the presence of DM in earlier predialysis CKD state.

## CONCLUSION

Results of the study showed a statistically significant low vaccine response rate in HD patients as compared to Predialysis patients (53.8% v/s 66.1%) ( $p=0.003$ ).

Hypoalbuminemia (serum albumin < 35g/L) in the HD cohort and gender (male), CVD and ESA dependence in the Predialysis cohort were associated with poor response in our study.

The definitive role of these factors should be considered for enhanced immunological response strategies for hepatitis B vaccination management and extend to earlier stages of chronic kidney failure.

## AUTHORS' CONTRIBUTION

CL: main author, design of the study, manuscript writing, data analysis and interpretation of result; KH, HK: Statistic analysis, review and revise the manuscript critically.

All authors read and approved the manuscript and met the criteria for authorship.

## LIST OF ABBREVIATIONS

AIHW	= Australian Institute of Health and Welfare
CKD	= Chronic Kidney Disease

CKD-EPI	=	Chronic Kidney Disease Epidemiology Collaboration
COPD	=	Chronic Obstructive Pulmonary Disease
CVD	=	Cardio-vascular Disease
DM	=	Diabetes Mellitus
eGFR	=	Estimated Glomerular Filtration Rate
EPO	=	Erythropoietin
ESA	=	Erythropoietin Stimulating Agents
HBsAb	=	Hepatitis B surface Antibodies
HBV	=	Hepatitis B virus
HD	=	Haemodialysis
HT	=	Hypertension
MDRD	=	Modification of Diet in Renal Disease
S ALB	=	Serum Albumin
SD	=	Standard Deviation

## ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study has received ethical approvals from the East Metropolitan Health Service Human Research Ethics Committee in Western Australia, protocol number GS0000005290 and reciprocal ethic approval through the Curtin University of Western Australia, Human Research Ethics Committee, protocol number HRE2022-0378.

## HUMAN AND ANIMAL RIGHTS

All procedures performed in studies involving human participants were in accordance with the ethical standards of institutional and/or research committees and with the 1975 Declaration of Helsinki, as revised in 2013.

## CONSENT FOR PUBLICATION

Waiver of Consent was approved for participants who were uncontactable due to natural attrition or relocation to a different address. This followed the criteria set out in Section 2.3.10 of the National Statement of Ethical Conduct in Human Research 2007 -updated 2018.

## STANDARDS OF REPORTING

STROBE guidelines and methodologies were followed.

## AVAILABILITY OF DATA AND MATERIALS

The data and supportive information are available within the article.

## FUNDING

None.

## CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

## ACKNOWLEDGEMENTS

Declared none.

## REFERENCES

- [1] Lv JC, Zhang LX. Prevalence and disease burden of chronic kidney disease. *Adv Exp Med Biol* 2019; 1165: 3-15. [http://dx.doi.org/10.1007/978-981-13-8871-2\\_1](http://dx.doi.org/10.1007/978-981-13-8871-2_1) PMID: 31399958
- [2] Chronic kidney disease overview- Australian institute of health and welfare. 2020. Available from: <http://www.aihw.gov.au/reports-data/health-conditions-disability-deaths/chronic-kidney-disease/overview>
- [3] Levey AS, Coresh J, Greene T, *et al.* Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. *Ann Intern Med* 2006; 145(4): 247-54. <http://dx.doi.org/10.7326/0003-4819-145-4-200608150-00004> PMID: 16908915
- [4] Levey AS, Stevens LA, Schmid CH, *et al.* A new equation to estimate glomerular filtration rate. *Ann Intern Med* 2009; 150(9): 604-12. <http://dx.doi.org/10.7326/0003-4819-150-9-200905050-00006> PMID: 19414839
- [5] Reddy S, Chitturi C, Yee J. Vaccination in chronic kidney disease. *Adv Chronic Kidney Dis* 2019; 26(1): 72-8. <http://dx.doi.org/10.1053/j.ackd.2018.10.002> PMID: 30876620
- [6] Fabrizi F, Dixit V, Messa P, Martin P. Transmission of hepatitis B virus in dialysis units: A systematic review of reports on outbreaks. *Int J Artif Organs* 2015; 38(1): 1-7. <http://dx.doi.org/10.5301/ijao.5000376> PMID: 25633894
- [7] Hettenbaugh J, Mullane R, Gillispie G, *et al.* Hepatitis B vaccination in advanced chronic kidney disease: A quality improvement project at a veteran affairs chronic kidney disease clinic. *Infect Dis Rep* 2021; 13(4): 1036-42. <http://dx.doi.org/10.3390/idr13040094> PMID: 34940404
- [8] Mysore P, Khinkar RM, McLaughlin D, *et al.* Improving hepatitis B vaccination rates for advanced chronic kidney disease patients: A quality improvement initiative. *Clin Exp Nephrol* 2021; 25(5): 501-8. <http://dx.doi.org/10.1007/s10157-020-02013-4> PMID: 33411114
- [9] Krueger KM, Ison MG, Ghossein C. Practical guide to vaccination in all stages of CKD, including patients treated by dialysis or kidney transplantation. *Am J Kidney Dis* 2020; 75(3): 417-25. <http://dx.doi.org/10.1053/j.ajkd.2019.06.014> PMID: 31585683
- [10] Betjes MGH. Immune cell dysfunction and inflammation in end-stage renal disease. *Nat Rev Nephrol* 2013; 9(5): 255-65. <http://dx.doi.org/10.1038/nrneph.2013.44> PMID: 23507826
- [11] Haddiya I. Current knowledge of vaccinations in chronic kidney disease patients. *Int J Nephrol Renovasc Dis* 2020; 13: 179-85. <http://dx.doi.org/10.2147/IJNRD.S231142> PMID: 32801834
- [12] Ma BM, Yap DYH, Yip TPS, Hung IFN, Tang SCW, Chan TM. Vaccination in patients with chronic kidney disease—Review of current recommendations and recent advances. *Nephrology* 2021; 26(1): 5-11. <http://dx.doi.org/10.1111/nep.13741> PMID: 32524684
- [13] Fabrizi F, Dixit V, Martin P, Messa P. Meta-analysis: The impact of diabetes mellitus on the immunological response to hepatitis B virus vaccine in dialysis patients. *Aliment Pharmacol Ther* 2011; 33(7): 815-21. <http://dx.doi.org/10.1111/j.1365-2036.2011.04589.x> PMID: 21281319
- [14] Fabrizi F, Dixit V, Martin P, Jadoul M, Messa P. Meta-analysis: The impact of nutritional status on the immune response to hepatitis B virus vaccine in chronic kidney disease. *Dig Dis Sci* 2012; 57(5): 1366-72. <http://dx.doi.org/10.1007/s10620-011-1987-1> PMID: 22143368
- [15] Fabrizi F, Dixit V, Martin P, Messa P. Erythropoietin use and immunogenicity of hepatitis B virus vaccine in chronic kidney disease patients: A meta-analysis. *Kidney Blood Press Res* 2012; 35(6): 504-10. <http://dx.doi.org/10.1159/000335956> PMID: 22813903
- [16] Zitt E, Hafner-Giessauf H, Wimmer B, *et al.* Response to active hepatitis B vaccination and mortality in incident dialysis patients.

- Vaccine 2017; 35(5): 814-20.  
<http://dx.doi.org/10.1016/j.vaccine.2016.12.032> PMID: 28049587
- [17] Gasim GI, Bella A, Adam I. Immune response to hepatitis B vaccine among patients on hemodialysis. *World J Hepatol* 2014; 7(2): 270-5.  
<http://dx.doi.org/10.4254/wjh.v7.i2.270> PMID: 25729482
- [18] Eleftheriadis T, Pissas G, Antoniadi G, Liakopoulos V, Stefanidis I. Factors affecting effectiveness of vaccination against hepatitis B virus in hemodialysis patients. *World J Gastroenterol* 2014; 20(34): 12018-25.  
<http://dx.doi.org/10.3748/wjg.v20.i34.12018> PMID: 25232238
- [19] Cabrerizo S, Cuadras D, Gomez-Busto F, Artaza-Artabe I, Marín-Ciancas F, Malafarina V. Serum albumin and health in older people: Review and meta analysis. *Maturitas* 2015; 81(1): 17-27.  
<http://dx.doi.org/10.1016/j.maturitas.2015.02.009> PMID: 25782627
- [20] Chen Z, Shao Y, Wang K, *et al.* Prognostic role of pretreatment serum albumin in renal cell carcinoma: A systematic review and meta-analysis. *OncoTargets Ther* 2016; 9: 6701-10.  
<http://dx.doi.org/10.2147/OTT.S108469> PMID: 27822073
- [21] National statement on ethical conduct in human research. 2018. Available from:  
<http://www.nhmrc.gov.au/about-us/publications/national-statement-ethical-conduct-human-research-2007-updated-2018>
- [22] Gama-Axelsson T, Heimbürger O, Stenvinkel P, Bárány P, Lindholm B, Qureshi AR. Serum albumin as predictor of nutritional status in patients with ESRD. *Clin J Am Soc Nephrol* 2012; 7(9): 1446-53.  
<http://dx.doi.org/10.2215/CJN.10251011> PMID: 22723451
- [23] Afsar B. The relationship between erythropoietin resistance and antibody response to hepatitis B vaccine in hemodialysis patients. *Nephrourol Mon* 2013; 5(3): 806-12.  
<http://dx.doi.org/10.5812/numonthly.8919> PMID: 24282790
- [24] Mikhail A, Brown C, Williams JA, *et al.* Renal association clinical practice guideline on anaemia of chronic kidney disease. *BMC Nephrol* 2017; 18(1): 345.  
<http://dx.doi.org/10.1186/s12882-017-0688-1> PMID: 29191165
- [25] Kanda N, Tsuchida T, Tamaki K. Testosterone inhibits immunoglobulin production by human peripheral blood mononuclear cells. *Clin Exp Immunol* 2003; 106(2): 410-5.  
<http://dx.doi.org/10.1046/j.1365-2249.1996.d01-842.x> PMID: 8918592
- [26] Yang S, Tian G, Cui Y, *et al.* Factors influencing immunologic response to hepatitis B vaccine in adults. *Sci Rep* 2016; 6(1): 27251-1.  
<http://dx.doi.org/10.1038/srep27251> PMID: 27324884
- [27] Khedmat H. Sex bias in response to hepatitis B vaccination in end-stage renal disease patients: Meta-analysis. *World J Nephrol* 2021; 5(1): 115-24.
- [28] Sit D, Esen B, Atay AE, Kayabaşı H. Is hemodialysis a reason for unresponsiveness to hepatitis B vaccine? Hepatitis B virus and dialysis therapy. *World J Hepatol* 2015; 7(5): 761-8.  
<http://dx.doi.org/10.4254/wjh.v7.i5.761> PMID: 25914776
- [29] Al Saran K, Sabry A, Al Halawany Z, Ismail M. Factors affecting response to hepatitis b vaccine among hemodialysis patients in a large Saudi hemodialysis center. *Saudi J Kidney Dis Transpl* 2014; 25(1): 185-91.  
<http://dx.doi.org/10.4103/1319-2442.124572> PMID: 24434410