Section: Nephrology

Original Research Article

FACTORS AFFECTING IMMUNOGENICITY OF RECOMBINANT HEPATITIS B VACCINATION IN PATIENTS WITH CHRONIC KIDNEY DISEASE IN SOUTH INDIA

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Abstract

Background: This study aimed at determining the factors affecting immunogenicity of recombinant Hepatitis B vaccination in patients with chronic kidney disease. **Materials and Methods:** This was a single centre prospective cohort study without control, conducted in patients with chronic kidney disease in a tertiary care centre in South India from October 2017 to September 2018. Relevant data was collected using a predesigned questionnaire. 25 hydroxy vitamin D levels and serum levels of intact parathormone were measured. Nutritional assessment was done using anthropometry and laboratory values. They were vaccinated with second generation Hepatitis B vaccine double dose intramuscularly in 0,1, 2, 6 monthly schedules. AntiHBs titres were checked,2 months after completion of their schedule and a titre ≥10 milli international units(mIU/ml) was considered as a marker of seroconversion. **Result:** The total seroconversion rate of the study group was 84.8%, whereas it was 83.7% in patients on dialysis. Females had a significantly better seroconversion rate than males (88.6 %vs 70.8%, p value 0.037). The seroconversion rate was low in those with hypoalbuminemia when compared to those without. (74% vs 90.4 %, p value= 0.02). The seroconversion rate was low in those with diabetes mellitus when compared to those without diabetes. (77.7 vs 94%, p value=0.002). There was no significant difference in seroconversion rate in those patients with vitamin D deficiency, hyperparathyroidism or history of erythropoietin use, when compared to those without. **Conclusion:** Male sex, diabetes mellitus and hypoalbuminemia were found to be significantly associated with low antiHBs titre following hepatitis b vaccination in patients with chronic kidney disease.

INTRODUCTION

Infection with hepatitis B Virus (HBV) poses a major public health issue all over the world, with the burden of chronic carrier state approaching around 150 million. The prevalence of HBV is greater among dialyzed patients compared to the general population, due to the need for repeated transfusions with blood products, along with the jeopardy posed by contaminated hemodialysis tools and devices.[1] Also, if infected, patients on maintenance dialysis are at considerable risk of becoming chronic carriers due to poor cellular and humoral immune responses.[2] To prevent transmission of HBV in hemodialysis (HD) settings, the recommended measures include the periodic screening of blood for HBV surface antigen (HBsAg), minimising the use of blood and blood products, the implementation of universal precautions in dialysis rooms,[3] and vaccination of patients and health care professionals working in dialysis unit against HBV. Immunisation with HBV vaccine is recommended in all patients after diagnosis of CKD, irrespective of the stage of the disease.[4] and is the most important intervention in preventing infection with HBV.

It Is recommended that patients with chronic kidney disease should receive four doses of hepatitis B vaccine as early in the course of disease as possible

with recombinant hepatitis B vaccine.[5] Use special formulations of vaccine (40 mcg/ml) or two 1 ml 20 mcg doses given at one site. Dose schedule should be 0, 1, 2, and 6 months given intramuscular in deltoid regions. Assess antibody titer to hepatitis B surface antigen (anti-HBs) 1-2 months after the primary course is completed and annually thereafter.[5]

A titer of antibodies to surface antigen of hepatitis B virus (anti-HBs) ≥ 10mIU/L is commonly considered as a marker of seroconversion to anti-HBs positivity after vaccination in both non-dialyzed and dialyzed patients.[6] When compared to a response rate of over 90% in the general population,[7] it is often less than 90% in patients with CKD,[6,8] and only 50 to 85% of patients on dialysis achieve antibody levels conferring protection following hepatitis B vaccination even with an enhanced schedule.[9-11]

Numerous inherited and/or acquired factors are implicated in diminished immunization following hepatitis B vaccination. A very well-established negative factor of immunization failure is increasing age.[12] Seroconversion rate to anti-HBs positivity after vaccination was 84% in HD patients below 40 years and only 33% in those ≥ 60 years.[12] The impaired response to hepatitis B vaccine in dialysis patients has been also attributed to male gender,[13] poor nutritional status, mainly low serum albumin concentration,[14] serological positivity for hepatitis C virus (HCV),[15] or human immunodeficiency virus (HIV),[16] and diabetes mellitus.[17] Vitamin D deficiency is also found to be associated with a poor antibody formation upon hepatitis B vaccination in stage 3-5D CKD patients.[18] However, there is a paucity of data on the factors affecting seroconversion following hepatitis b vaccination in CKD patients in Indian population.

MATERIALS AND METHODS

This study aimed to assess the seroconversion rate after double dose recombinant hepatitis B vaccination in 0,1,2,6 monthly schedules in patients with chronic kidney disease and to determine the factors affecting immunogenicity of recombinant Hepatitis B vaccination in these patients. A single centre prospective cohort study without control, this was conducted in patients having chronic kidney disease with eGFR (as defined by CKD-EPI Creatinine 2009 equation) less 60ml/minute of age between 18 and 70 years in a tertiary care centre in South India between October 2017 and September 2018. Patients who were HBsAg positive and those who were already vaccinated with at least one dose of hepatitis b vaccination were excluded. The relevant data including name, age, sex, history of use of erythropoietin, history of diabetes mellitus, infection with HIV or Hepatitis C were collected using a predesigned questionnaire. 25-hydroxyvitamin D (25(OH)D) levels were measured by chemiluminescence immunoassays. Vitamin D deficiency was defined as a serum 25 hydroxy Vitamin D [25(OH)D] concentration below <12 ng/ml. Patients having 25(OH)D levels between 12 ng/ml and 20ng/ml we said to have inadequate stores and those with levels above 20ng/ml were said to have adequate stores.[19] Intact parathormone levels were measured using chemiluminescent microparticle immunoassay. Hyperparathyroidism was diagnosed based on plasma intact PTH target levels mentioned as per KDOQI guidelines.[20] Nutritional statuses of the patients were assayed by parameters of weight, body mass index, serum albumin and total cholesterol. A body mass index of less than 18.5 kg/m2, hypoalbuminemia as defined by a serum albumin level of less than 3.5 g/dL and a serum total cholesterol level of less than 150 mg/dL were considered as markers of malnutrition. They were vaccinated with second generation Hepatitis B vaccine double dose intramuscularly in 0,1, 2, 6 monthly schedules. In the 8th month anti HBs titre of these patients was measured by VIDAS immunoassay analyser. An anti HBs titre ≥10 IU/ml was considered as a marker of seroconversion,[6] and was treated as a categorical variable. Those who developed an anti-HBs titre between 10 and 100 IU/L are referred to as low responders while those with a titre>100mIU/ml are referred to as good responders.[6] The variables were analysed using Statistical Package for the Social Sciences, version 15.0 (SPSS Inc., Chicago, IL) software. Chi square test was used to compare baseline characteristics (discrete variables) between seroconverters and nonconverters and odds ratio was calculated. P value less than 0.05 was taken as significant.

RESULTS

Baseline demographic characteristics: The mean age of the study group was 51.27 ± 12.857 with a male to female ratio of 11:3. 28 patients were in the age group 18-45 years, 61 patients in the age group 46-60 years, and 23 in the age group 61-70 years.

The baseline demographic characteristics are given in [Table 1]. Out of 112 participants, non-responders to Hepatitis B vaccine (anti HBS titre <10 mIU/ml) was 17 in number (15.1%), 32 patients (28.5%) were low responders (had a titre between 10 and 100mIU/ml) while 63 of them(56.25%) were good responders with a titre >100 mIU/ml. see [Figure 1] The total seroconversion rate of the study group was 84.8% (95 out of 112 participants), whereas it was 83.7% in patients on dialysis (31 out of 37 participants). 40% of the patients were diabetic and they had a seroconversion rate of 71.1%. 75% of the study group had inadequate vitamin D stores ie 25 (OH)Vitamin D levels below 20ng/ml, while only 22 % had Vitamin D deficiency which was defined as a serum 25 hydroxy Vitamin D concentration below <12 ng/ml. However, those with Vitamin D deficiency had a seroconversion rate of 80%. Only 6

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patients had a body mass index of less than 18.5 kg/m2 and all of them had an anti HBS titre ≥10 mIU/ml.46 patients had a serum cholesterol level below 150 mg/dL and they had a seroconversion rate of 78.2%. 39 patients had hypoalbuminemia and they had a seroconversion rate of 74.3%. 83 patients had hyperparathyroidism, as per KDOQI guidelines and they had a seroconversion rate of 82.8 %. 77 patients were on erythropoietin injections, and they had an 83.1%serconversion rate. Only one patient had co-existent HCV infection, but she was on haemodialysis and had good anti HBs titre. None had HIV infection. None were currently on immunosuppressants.

Factors affecting seroconversion after hepatitis B vaccination.

The relationship between the variables and response to Hepatitis b vaccination was analysed. Odds ratio and p value were found out for both non responders and responders, the results of which are summarised in [Tables 2-4].

Age, gender, and seroconversion rate: There was no significant decrease in seroconversion rate following vaccination in the older age group 46-70 years, when compared to those in the age group below 45 years. However, it was found that males had a significantly better seroconversion rate, in our study group when compared to females. (88.6 %vs 70.8%, p value 0.037). See [Table 2]

Dialysis and seroconversion rate: Although seroconversion rate was slightly lower in dialytic population no significant difference was observed between dialytic and predialytic patients. (83.7% vs 85.3%, p value 0.82). See [Table 2]

Malnutrition and seroconversion rate: There was no significant difference in the seroconversion rates between patients with a body mass index of less than 18.5 kg/m2 and those having a BMI greater than 18.5 kg/m2, however the seroconversion rate was found to be significantly low in those patients with hypoalbuminemia when compared to those without. (74% vs 90.4 %, p value= 0.02). Also, it was found the seroconversion rate was higher (89.3%) in patients with a total cholesterol level of 150 mg/dL and above, when compared to patients having a level below 150mg/dL (78.2%), but this difference was not found to be statistically significant. (p value 0.11) see [Table 3].

Diabetes mellitus and seroconversion rate: The seroconversion rate was low in those with diabetes mellitus when compared to those without diabetes and the difference was found to be statistically significant (71.1% vs 94%, p value=0.002). See [Table 4].

Hyperparathyroidism and seroconversion rate: The seroconversion rate in patients with hyperparathyroidism was lower (80%), when compared to those without hyperparathyroidism (89.6%) but the difference was not found to be statistically significant (p value = 0.26). See [Table 4].

History of erythropoietin use and seroconversion rate: Patients on erythropoietin had a seroconversion rate of 83.1%, which was lower than in patients those not on erythropoietin 88.5%, but the difference was not found to be statistically significant (p value 0.2). See [Table 4].

Vitamin D deficiency and seroconversion rate: The seroconversion rate in patients with severe vitamin D deficiency was lower (80%), when compared to those without vitamin D deficiency (86.2%) but the difference was not found to be statistically significant (p value = 0.44). Also no significant difference in seroconversion rate was found between those having inadequate vitamin D stores ,that is vitamin D levels 20 ng/mmol and below and those having higher values. See [Table 5]

Hence it was concluded that while males had a significantly better seroconversion rate when compared to females in our study group. Presence of diabetes mellitus and hypoalbuminemia were found to be significantly associated with a low antiHBs titre.

Table 1: Baseline demographic characteristics.

Mean age(years)	**51.27 ± 12.857**
Sex	n(%)
Male	88(78.57)
Female	24(21.42)
BMI	
Less than 18.5	6(5.2%)
18.5 and above	106(94.6)
KDIGO CKD stage	n(%)
3	25(22.3)
4	15(13.3)
5	35(31.2)
5D	37(33)
Presence of diabetes mellitus	
Yes	45(40.1)
No	67(59.8)
Vitamin D levels	
<12 ng/ml	25(22.3)
12 ng/ml and above	87(77.6)
Serum albumin levels	
<4 g/dL	64(57.1)
4 g/dL and above	48(42.8)

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Fasting Cholesterol level	
150 mg/dL	46(41)
150 mg/dL and above	66(59)
Hyperparathyroidism	
Yes	83(74.1)
No	29(25.8)

Table 2: Association of age, gender and dialysis with seroconversion rate

Response and age			
Age	**Total No**	**Anti HBs**	
		<10	**>=10**
18-45	28	3	25
46-70	84	14	70
Odds ratio	1.6667		
95 % CI:	0.4417 to 6.2889		
z statistic	0.754		
Significance level	P = 0.4509		
Response and Gender			
Gender	**Total No**	**Anti HBs**	
		<10	**>=10**
Male	88	10	78
Female	24	7	17
Odds ratio	3.2118		
95 % CI:	1.0700 to 9.6407		
z statistic	2.081		
Significance level	P = 0.0375		
Response & Stage 5D CKD			
Stage 5D CKD	**Total No**	**Anti HBs**	
		<10	**>=10**
Yes	37	6	31
No	75	11	64
Odds ratio	0.888		
95 % CI:	0.3006 to 2.6235		
z statistic	0.215		
Significance level	P = 0.8299		

Table 3: Malnutrition and seroconversion rate

Response and low BMI			
Low BMI	**Total No**	**Anti HBs**	
		<10	**>=10**
Yes	6	0	6
No	106	17	89
Odds ratio	2.5419		
95 % CI:	0.1369 to 47.2129		
z statistic	0.626		
Significance level	P = 0.5314		
Response & Hypoalbuminemia			
Hypoalbuminemia	**Total No**	**Anti HBs**	
		<10	**>=10**
Yes	39	10	29
No	73	7	66
Odds ratio	0.3076		
95 % CI:	0.1066 to 0.8878		
z statistic	2.18		
Significance level	P = 0.0293		
Response & Low Serum Cholesterol			
Low Serum Cholesterol	**Total No**	**Anti HBs**	
		<10	**>=10**
Yes	46	10	36
No	66	7	59
Odds ratio	0.4271		
95 % CI:	0.1493 to 1.2219		
z statistic	1.586		
Significance level	P = 0.1127		

BMI: Body mass index

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Table 4: Association of Diabetes mellitus, hyperparathyroidism and erythropoietin use with seroconversion rate

Response & Diabetes			
Diabetes Mellitus	**Total No**	**Anti HBs**	
		<10	**>=10**
Yes	45	13	32
No	67	4	63
Odds ratio	0.1563		
95 % CI:	0.0471 to 0.5182		
z statistic	3.035		
Significance level	P = 0.0024		
Response & Hyperparathyroidism			
Hyperparathyroidism	**Total No**	**Anti HBs**	
		<10	**>=10**
Yes	94	14	80
No	18	3	15
Odds ratio	1.1429		
95 % CI:	0.2923 to 4.4683		
z statistic	0.192		
Significance level	P = 0.8478		
Response and Erythropoetin use			
Hyperparathyroidism	**Total No**	**Anti HBs**	
		<10	**>=10**
Yes	77	13	64
No	35	4	31
Odds ratio	0.6352		
95 % CI:	0.1913 to 2.1089		
z statistic	0.741		
Significance level	P = 0.4586		

Table 5: Vitamin D levels and seroconversion rate

Response & Severe Vitamin D Deficiency			
Severe Vitamin D Deficiency Vitamin D level less than 12	**Total No**	**Anti HBs**	
		<10	**>=10**
Yes	25	5	20
No	87	12	75
Odds ratio	1.5625		
95 % CI:	0.4928 to 4.9545		
z statistic	0.758		
Significance level	P = 0.4485		
Response &Vitamin D Deficiency			
Vitamin D Deficiency Vitamin D level 20 and below	**Total No**	**Anti HBs**	
		<10	**>=10**
Yes	84	11	73
No	28	6	22
Odds ratio	1.8099		
95 % CI:	0.6006 to 5.4540		
z statistic	1.054		
Significance level	P = 0.2918		

DISCUSSION

The total seroconversion rate of the study group was 84.8%, with a seroconversion rate of 85.35% in the predialytic population, whereas it was 83.7% in patients on haemodialysis. When compared to various international studies the seroconversion rate in our study group was similar in predialytic population but somewhat higher in the dialytic population. Da Rosa et al,[9] showed that the efficacy of HBV vaccination decreases as CKD progresses, with reported seroconversion rates of over 95% in healthy adults and infants, up to 90% in patients at CKD stage 3 or 4, and between 40% and 50% in patients with ESRD. In the study by Cordova et al.[21] the seroconversion rate in the dialytic population was 77%. In a study by Ghadiani et al,[22] the seroconversion rate in the predialytic population was 89.7% with a much lower rate of 44.3% in the dialytic population. However a recent study by Fabrizi et al,[23] showed that the seroprotection rate was 95% and 82% in pre-dialysis and dialysis patients, respectively, one month after completing vaccine schedule with, however they used an adjuvanted recombinant (HBV-AS04) vaccine .Also a study by Hashemi et al,[11] showed that the level of HBV antibody after HBV vaccination did not reveal a statistically significant difference across different stages of CKD. A recent study from the northern part of India showed a seroconversion rate of 63.3 % in the dialytic population.[24] The higher immunogenicity in our population in the dialytic group may be due to factors such as genetic predisposition, nutritional factors and adequacy of dialysis, which needs further research.

In our study there was no significant difference in seroconversion rate across different age groups,

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however surprisingly males had a significantly better seroconversion rate when compared to females. This contrasts with the studies by Ghadiani et al,[22] and Ali asan et al,[25] which showed a reduced seroconversion rate in the elderly age group while gender had no impact on seroconversion rates. Previous studies on healthy adults have showed reduced immunogenicity to hepatitis b vaccination in males, explained by the inhibiting effect of testosterone in the production of IgG and IgM from B-lymphocytes.[26]

Hypoalbuminemia was found to be significantly associated with a low immunogenicity following hepatitis vaccination. This finding is in consensus with previous studies which showed an impaired vaccine response among chronic kidney disease patients having poor nutrition status as mostly detected by serum albumin levels.[27]

In addition to erythropoiesis, erythropoietin can bind the tissue-protective receptor on innate and adaptive immune cells and plays an important role immune regulation.[28] In our study although a reduced immune response was noted among patients on erythropoietin when compared to those not on, no statistically significant response was found, as in a previous meta-analysis.[29]

The cells of the immune system express the vitamin D receptor, also monocytes/macrophages and dendritic cells possess 1α-hydroxylase, the enzyme that activates 25(OH)D to calcitriol.[18] Hence vitamin D deficiency is said to be associated with reduced immune response. Previous studies,[18,24] have demonstrated conflicting results in seroconversion rates in those with vitamin D deficiency however no significant difference in immune response was observed in our patient population in those with vitamin D deficiency and inadequate vitamin D stores when compared to those without.

Our study found out that diabetic patients had a significantly low seroconversion rate after hepatitis B vaccination when compared to the non-diabetic patients similar to the findings obtained in a previous meta-analysis.[17] The presence of DR3 and DR7 human leukocyte antigen (HLA) alleles in diabetic patients, and increased tolerance to stimulation and reduced cytokine secretions of peripheral blood mononuclear cells (PBMCs) are proposed as mechanisms that underlie this impaired immunological response.[17]

Secondary hyperparathyroidism in ESRD patients has been studied as a possible factor in the development of an acquired immune dysfunction in CKD. However, in our study although seroconversion rates were lower in patients with hyperparathyroidism when compared to those without, but the difference was not found to be statistically significant.

Limitations of the study

This was a single centre study with a small sample size. The baselines values prior to hepatitis B vaccination were taken on a single occasion.

CONCLUSION

To conclude male sex, diabetes mellitus and hypoalbuminemia were found to be significantly associated with low antiHBs titre following hepatitis b vaccination in patients with chronic kidney disease. Vitamin D deficiency, Hyperparathyroidism and history of erythropoietin use were found to be not associated with low seroconversion after hepatitis B vaccination in patients with CKD.

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REFERENCES

1. Gasim GI, Bella A, Adam I. Immune response to hepatitis B vaccine among patients on hemodialysis. World J Hepatol. 2015;7(2):270-275. doi:10.4254/wjh.v7.i2.270
2. Fabrizi F, Martin P: Hepatitis B virus infection in dialysis patients. Am J Nephrol 2000; 20:1–11.
3. Centers for Disease Control and Prevention: Recommendations for preventing transmission of infections among chronic haemodialysis patients. MMWR 2001;50:1–43.
4. Centers for Disease Control. Hepatitis B Vaccination Recommendations for Adults. MMWR. 2006:55 (RR–16). .
5. Guidelines for vaccination in patients with chronic kidney disease. Indian J Nephrol. 2016;26(Suppl 1):S15-S18.
6. Grzegorzewska AE. Hepatitis B vaccination in chronic kidney disease: review of evidence in non-dialyzed patients. Hepat Mon. 2012 Nov;12(11):e7359. doi: 10.5812/hepatmon.7359. Epub 2012 Nov 14. PMID: 23326280; PMCID: PMC3546461.
7. Shakhgil'dian IV, Khukhlovich PA, Savin EA, Kuzin SN, Anan'ev VA, Sergeeva NA, Khasanova VA, Shostka GD, Vu Z, Vasil'ev AN, et al.Risk of infection with hepatitis B and C viruses of medical workers, patients in the hemodialysis ward, and vaccine prophylaxis of hepatitis B infection in these populations]. Vopr Virusol. 1994 Sep-Oct;39(5):226-9. Russian. PMID: 7716909
8. McNulty CA, Bowen JK, Williams AJ. Hepatitis B vaccination in predialysis chronic renal failure patients a comparison of two vaccination schedules. Vaccine. 2005 Jul 14;23(32):4142-7. doi: 10.1016/j.vaccine.2005.03.020. PMID: 15913854.
9. DaRoza G, Loewen A, Djurdjev O, Love J, Kempston C, Burnett S, Kiaii M, Taylor PA, Levin A. Stage of chronic kidney disease predicts seroconversion after hepatitis B immunization: earlier is better. Am J Kidney Dis. 2003 Dec;42(6):1184-92. doi: 10.1053/j.ajkd.2003.08.019. PMID: 14655190.
10. European Best Practice Guidelines.Prevention and management of HBV, HCV and HIV in HD patients. Nephrol Dial Transplant. 2002;17:72-87
11. Hashemi B, Mahdavi-Mazdeh M, Abbasi M, Hosseini-Moghaddam SM, Zinat NH, Ahmadi F. Efficacy of HBV vaccination in various stages of chronic kidney disease: is earlier better? Hepat Mon. 2011 Oct;11(10):816-20. doi: 10.5812/kowsar.1735143X.751. PMID: 22224080; PMCID: PMC3234577.
12. Shatat HZ, Kotkat AM, Farghaly AG. Immune response to hepatitis B vaccine in haemodialysis patients. J Egypt Public Health Assoc. 2000;75(3-4):257-75.
13. Stevens C, Alter H, Taylor P, Zang E, Harley E, Szmuness W. The Dialysis Vaccine Trial Study Group: Hepatitis B vaccine in patients receiving hemodialysis. N Engl J Med. 1984;311:496-501.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

14. Brown CM, Donlon S, O'Kelly P, Casey AM, Collier C, Conlon PJ, et al. A prospective study of hepatitis B vaccination - a comparison of responders versus nonresponders. Ren Fail. 2011;33(3):276-9.
15. Navarro JF, Teruel JL, Mateos ML, Marcen R, Ortuno J. Antibody level after hepatitis B vaccination in hemodialysis patients: influence of hepatitis C virus infection. Am J Nephrol. 1996;16(2):95-7.
16. Ahuja TS, Kumar S, Mansoury H, Rodriguez H, Kuo YF. Hepatitis B vaccination in human immunodeficiency virus-infected adults receiving hemodialysis. Kidney Int. 2005;67(3):1136-41.
17. Alavian SM, Tabatabaei SV. The effect of diabetes mellitus on immunological response to hepatitis B virus vaccine in individuals with chronic kidney disease: A meta-analysis of current literature. Vaccine. 2010;28(22):3773-7
18. Zitt E, Sprenger-Mahr H, Knoll F, Neyer U, Lhotta K. Vitamin D deficiency is associated with poor response to active hepatitis B immunisation in patients with chronic kidney disease. Vaccine. 2012;30(5):931-5
19. Amrein, K., Scherkl, M., Hoffmann, M. et al. Vitamin D deficiency 2.0: an update on the current status worldwide. Eur J Clin Nutr 74, 1498–1513 (2020).
20. National Kidney Foundation. K/DOQI clinical practice guidelines for bone metabolism and disease in chronic kidney disease. Am J Kidney Dis. 2003 Oct;42(4 Suppl 3):S1-201. PMID: 14520607.
21. Cordova E, Miglia I, Festuccia F, Sarlo MG, Scornavacca G, Punzo G, Menè P, Fofi C. Hepatitis B vaccination in haemodialysis patients: an underestimated problem. Factors influencing immune responses in ten years of observation in an Italian haemodialysis centre and literature review. Ann Ig. 2017 Jan-Feb;29(1):27-37. doi: 10.7416/ai.2017.2129. PMID: 28067935.
22. Ghadiani MH, Besharati S, Mousavinasab N, Jalalzadeh M. Response rates to HB vaccine in CKD stages 3-4 and hemodialysis patients. J Res Med Sci. 2012;17(6):527-533.
23. Fabrizi F, Cerutti R, Dixit V, Ridruejo E. Hepatitis B virus vaccine and chronic kidney disease. The advances. Nefrologia (Engl Ed). 2021 Mar-Apr;41(2):115-122. English, Spanish. doi: 10.1016/j.nefro.2020.08.016. Epub 2021 Jan 7. PMID: 33423842.
24. Jhorawat R, Jain S, Pal A, Nijhawan S, Beniwal P, Agarwal D, Malhotra V. Effect of vitamin D level on the immunogenicity to hepatitis B vaccination in dialysis patients. Indian J Gastroenterol. 2016 Jan;35(1):67-71. doi: 10.1007/s12664-016-0621-8. Epub 2016 Feb 15. PMID: 26876961.
25. Asan A, Demirhan H, Sorkun HÇ, Özkan S, Aydın M, Akın D, Tatar B, Çatak B, Şener A, Köse Ş. Factors affecting responsiveness to hepatitis B immunization in dialysis patients. Int Urol Nephrol. 2017 Oct;49(10):1845-1850. doi: 10.1007/s11255-017-1616-9. Epub 2017 Jun 15. PMID: 28620716.
26. Yang S, Tian G, Cui Y, Ding C, Deng M, Yu C, Xu K, Ren J, Yao J, Li Y, Cao Q, Chen P, Xie T, Wang C, Wang B, Mao C, Ruan B, Jiang T, Li L. Factors influencing immunologic response to hepatitis B vaccine in adults. Sci Rep. 2016 Jun 21;6:27251. doi: 10.1038/srep27251. PMID: 27324884; PMCID: PMC4914839.
27. 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 May;57(5):1366-72. doi: 10.1007/s10620-011-1987-1. Epub 2011 Dec 6. PMID: 22143368.
28. Peng B, Kong G, Yang C, Ming Y. Erythropoietin and its derivatives: from tissue protection to immune regulation. Cell Death Dis. 2020 Feb 3;11(2):79. doi: 10.1038/s41419-020-2276-8. PMID: 32015330; PMCID: PMC6997384.
29. 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. doi: 10.1159/000335956. Epub 2012 Jul 14. PMID: 22813903.

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