

# Vaccination rates and the causes of vaccine hesitancy among patients with end stage renal disease

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## ABSTRACT

**Aim:** Chronic kidney disease creates a tendency to infections, and infections are the second most common reason for mortality following cardiovascular events in chronic kidney disease. Health authorities recommend vaccination against hepatitis B, annual influenza, pneumonia, zoster, tetanus, and new coronavirus disease for people with end-stage kidney disease. Vaccine-preventable diseases cause mortality in the adult population with chronic diseases.

The primary purpose of this study is to investigate vaccination rates and awareness about vaccination among end-stage renal disease patients who were on renal replacement therapies in a single tertiary center in Turkey.

**Material and Method:** 86 hemodialysis patients were included in this cross-sectional study. A questionnaire was used to investigate whether the patients were aware of the immunization schedule or not and whether they were vaccinated against hepatitis B virus, seasonal influenza virus, pneumonia, herpes zoster, tetanus, and SARS-CoV-2 or not.

**Results:** Fifty-eight (67.4%) patients were vaccinated against SARS CoV2. 48(55.8%) patients were vaccinated against the Hepatitis B virus. 31 (36%) patients were vaccinated against Pneumococcus pneumonia. 48 (55.8%) patients have been vaccinated against the influenza virus annually. Only 14 (16.3%) patients were vaccinated against tetanus during the previous 10 years, and only 1 (1.2%) patient was vaccinated against Herpes zoster. Influenza vaccination rates were found to be higher in patients with a longer duration of hemodialysis when compared to the other group( $p=0.03$ ). SARS-CoV 2 vaccination rates were higher in patients who were older than 59 years of age when compared to the younger patients( $p=0.03$ ).

**Conclusion:** Vaccination rates are far from the targets in patients with end-stage kidney disease. The most common reason to be unvaccinated is a lack of enough knowledge about the subject.

**Keywords:** End-stage kidney disease, adult vaccination, vaccine hesitancy

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## INTRODUCTION

Chronic kidney disease (CKD) creates a tendency to infections, and infections are among the most important reasons for mortality following cardiovascular events in chronic kidney disease (1,2). Prevention from infections is easier, cheaper, and safer than their treatment. Active immunization is the key point of prevention from various bacterial and viral infectious diseases not only in the pediatric group but also in adults. Advisory Committee on Immunization Practice (ACIP) recommends immunization against influenza, hepatitis B, pneumococcal pneumonia, herpes zoster, varicella-zoster, tetanus, diphtheria, pertussis, measles-mumps-rubella, and human papillomavirus for chronic kidney disease patients (3). Unfortunately, vaccine-preventable disease-related deaths

are not rare in the adult population, especially in patients with comorbidities (4). Furthermore, the vaccination coverage rate of patients with comorbidities is far from the target. For example, pneumococcal vaccination coverage for adults in the United States was 65.2% in people older than 65 years of age, while it was 20.1% for the high-risk group younger than 65 years of age (5).

The Adult Vaccination Campaign in Europe (ADVICE) was developed in 2012, to increase awareness about immunization in adults (6). This goal may be achieved in various ways, one of which is to define the properties of regions. According to ADVICE, major barriers against immunization are organizational, health care provider-related, health care system-related, and patient-related (6).

We don't have enough knowledge either about vaccine hesitancy rates or vaccine awareness among adult CKD patients in Turkey. Because vaccine hesitancy rates are increasing day by day, it is important to find out the main reasons for this subject. Unvaccinated persons transmit infectious diseases easily to the main population (7).

The primary purpose of this study is to investigate immunization rates and awareness about vaccination among end-stage renal disease (ESRD) patients who were on renal replacement therapies in a single tertiary center in Turkey. The secondary purpose is to find out the vaccine hesitancy rates among this patient group and to define the reasons for vaccine hesitancy.

**MATERIAL AND METHOD**

The study was carried out with the permission of Samsun University Training and Research Hospital Non-interventional Clinical Researches Ethics Committee (Date: 01.05.2021, Decision No: GOKA/2021/9/9) and all participants gave written informed consent. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

**Study Design**

This is a cross-sectional questionnaire-based study. The patients were selected among adult end-stage renal failure patients who were on a hemodialysis program in Samsun Training and Research Hospital. 86 hemodialysis patients who accepted to join the study were included.

**Participants' Eligibility and Recruitment**

Hemodialysis patients who were taking renal replacement therapy at our center were included in the study. All patients who were older than 18 years of age and who were willing to attend were included.

**Questionnaire**

A questionnaire was created to investigate whether the patients were aware of the immunization schedule or not and whether they were vaccinated against hepatitis B virus, seasonal influenza virus, pneumonia, herpes zoster, tetanus, and SARS-CoV-2 or not. A literature search was done for optimal question selection and the authors form the questionnaire based on the current literature (8-10). For each question there were three answers Likert scale including "yes", "no", and "I can't remember". For the answers indicating that the patient was not vaccinated against the specific microorganism, a new question was formed with eleven distinct answers. These answers were related to the reasons for vaccine refusal or deprivation. The patient could mark more than one reason. The questions and the summary of the questionnaire were shown in **Table 1**.

Table 1. The questionnaire form		
<b>Demographical properties</b>		
Age		
Gender		
Educational status		
The duration of chronic kidney disease		
The duration of dialysis		
<b>Vaccination status</b>		
Have you ever been vaccinated against Hepatitis B?	Yes	No
<b>If your answer is "No", please mark all the appropriate answers for you.</b>		
a. I'm afraid of the side effects of the vaccines.		
b. I don't believe that the vaccines can prevent diseases.		
c. I have previous history of adverse vaccine reaction.		
d. I think that the alternative and complementary medicine has more effective and less harming than vaccines.		
e. I don't think that I am in the risk group for this disease.		
f. I refuse vaccination because of my religious belief.		
g. I'm not vaccinated because of the news on media.		
h. I did not know that I should get vaccinated.		
i. I did not have enough knowledge about the vaccine.		
j. My practitioner did not recommend, if he/she would recomend I would.		
k. No idea		
Have you ever been vaccinated against Pnomococcus (pneumonia)?	Yes	No
If your answer is "No", please mark all the appropriate answers for you.	Same as the above 11 answers	
Are you vaccinated against seasonal influenza virus (flu)?	Yes	No
If your answer is "No", please mark all the appropriate answers for you.	Same as the above 11 answers	
Have you get vaccinated againts tetanus in the previous 10 years?	Yes	No
If your answer is "No", please mark all the appropriate answers for you.	Same as the above 11 answers	
Have you ever get vaccinated against herpes zoster?	Yes	No
If your answer is "No", please mark all the appropriate answers for you.	Same as the above 11 answers	
Are you vaccinated against new coronavirus disease (COVID 19)?	Yes	No
If your answer is "No", please mark all the appropriate answers for you.	Same as the above 11 answers	

**Statistical analysis**

Statistical Package for the Social Sciences (SPSS) Programme Version 22.0 was used for statistical analysis. Normally distributed continuous variables were expressed as mean ± standard deviation (SD) whereas non-normal distributed continuous variables were expressed as median (min-max). Categorical variables were expressed as numbers and percentages (%). The Chi-square test was used for the comparison of categorical variables. The p-value < 0.05 was accepted as statistically significant.

## RESULTS

86 patients, 52 (60.5%) male, and 34 (39.5%) female, with end-stage chronic kidney disease were included in this study. The mean age was 59.1 (23-81; SD 12.28). The median duration of hemodialysis was 41 months (2-291 months). The educational status of 78 (90.7%) patients was elementary school while 8 (9.3%) of them were high school.

Vaccination status against each recommended infection was summarized in **Table 2**. The hepatitis B status of the patients was also recorded. There were 38 people who were not vaccinated against hepatitis B. Of these 38 people, 34 either had chronic hepatitis B infection (positive hepatitis B surface antigen more than 6 months) or had positive antibody hepatitis B surface antigen. So only four patients were not vaccinated against Hepatitis B despite recommendation. For each vaccine, the patients without any vaccination history were asked to answer eleven questions, and these answers were analyzed separately for each vaccine. The results were shown in **Table 3**.

Type of vaccine	Vaccinated patients n (%)	Unvaccinated patients n (%)
Hepatitis B	48 (55.8)	4 (4.6)
Pneumonia	31 (36)	55 (64)
Influenza annually	48 (55.8)	8 (44.2)
Tetanus in the previous 10 years	14 (16.3)	72 (83.7)
Zoster	1 (1.2)	85 (98.8)
SARS CoV2	58 (67.4)	28 (32.6)

For hepatitis B vaccine, pneumococcal vaccine, tetanus vaccine, and herpes zoster vaccine we did not find any significant difference between the two groups according to age, gender, duration of hemodialysis, and educational status ( $p > 0.05$ ) (**Table 4**). Influenza vaccination rates were found to be higher in patients with a longer duration of hemodialysis when compared to the other group ( $p = 0.03$ ). But there was no statistically significant difference between groups according to age, gender, or educational status for influenza vaccination ( $p > 0.05$ ).

SARS-CoV 2 vaccination rates were higher in patients who were older than 59 years of age when compared to the younger patients ( $p = 0.03$ ).

A univariate analysis was performed to demonstrate whether age, gender, duration of hemodialysis, and educational status have an impact on overall the study population (**Table 4**).

	n (%)	n (%)	p value
Age	<59 years-old	≥59 years-old	
Hepatitis B	17 (45.9)	20 (54.1)	0.992
Pneumococcus	28 (51.9)	26 (48.1)	0.145
Tetanus	31 (43.7)	40 (56.3)	0.355
Herpes zoster	38 (45.2)	46 (54.6)	0.459
Influenza	20 (54.1)	17 (45.9)	0.184
SARS-CoV-2	17 (63.0)	10 (37.0)	0.031
Gender	Female	Male	
Hepatitis B	14 (36.8)	24 (63.2)	0.650
Pneumococcus	23 (41.8)	32 (58.2)	0.514
Tetanus	31 (43.1)	41 (56.9)	0.130
Herpes zoster	34 (40.0)	51 (60.0)	1.000
Influenza	13 (34.2)	25 (65.8)	0.369
SARS-CoV-2	11 (39.3)	17 (60.7)	0.974
Hemodialysis duration	< 41 months	≥ 41 months	
Hepatitis B	19 (50)	19 (50)	1.000
Pneumococcus	29 (52.7)	21 (47.3)	0.500
Tetanus	36 (50)	36 (50)	1.000
Herpes zoster	43 (50.6)	42 (49.4)	1.000
Influenza	24 (63.2)	14 (36.8)	0.030
SARS-CoV-2	13 (46.4)	15 (53.6)	0.645
Educational status	Primary and secondary school	High school and above	
Hepatitis B	36 (94.7)	2 (5.3)	0.293
Pneumococcus	51 (92.7)	4 (7.3)	0.451
Tetanus	67 (93.1)	5 (6.9)	0.118
Herpes zoster	77 (90.6)	8 (9.4)	1.000
Influenza	36 (94.7)	2 (5.3)	0.293
SARS-CoV-2	25 (89.3)	3 (10.7)	0.712

Causes of vaccine refusal	Type of vaccine				
	SARS CoV2	Pneumonia	Influenza	Tetanus	Zoster
a. I'm afraid of the side effects of the vaccines.	14 (50)	14 (25.5)	5 (13.2)	8 (11.1)	8 (9.4)
b. I don't believe that the vaccines can prevent diseases.	7 (25)	4 (7.3)	4 (10.5)	5 (6.9)	5 (5.9)
c. I have previous history of adverse vaccine reaction.	4 (14.3)	3 (5.5)	1 (2.6)	4 (5.6)	4 (4.7)
d. I think that the alternative and complementary medicine has more effective and less harming than vaccines.	7 (25)	3 (5.5)	4 (10.5)	5 (6.9)	6 (7.1)
e. I don't think that I am in the risk group for this disease.	7 (25)	3 (5.5)	3 (7.9)	7 (9.7)	12 (14.1)
f. I refuse vaccination because of my religious belief.	2 (7.1)	1 (1.8)	2 (5.3)	5 (6.9)	3 (3.5)
g. I'm not vaccinated because of the news on media.	7 (25)	1 (1.8)	2 (5.3)	7 (9.7)	3 (3.5)
h. I did not know that I should get vaccinated.	7 (25)	12 (21.8)	13 (34.2)	30 (41.7)	30 (35.3)
i. I did not have enough knowledge about the vaccine.	12 (42.9)	26 (47.3)	16 (42.1)	37 (51.4)	47 (55.3)
j. My practitioner did not recommend, if he/she would recommend I would.	11 (39.3)	30 (54.5)	20 (52.6)	34 (47.2)	42 (49.4)
k. No idea	18 (64.3)	44 (80)	27 (71.1)	38 (52.8)	56 (65.9)

## DISCUSSION

Chronic kidney disease patients are advised to be vaccinated against Hepatitis B virus, Pneumococcus pneumonia, influenza, Herpes zoster, tetanus, and SARS CoV2 according to the Turkey Health Ministry vaccination recommendations (11). Our study indicates that vaccination hesitancy is still common among hemodialysis patients .

Because hepatitis viruses can be transmitted between patients through hemodialysis systems, these viruses are well evaluated. Screening of hepatitis B virus in patients undergoing hemodialysis and providing immunization against this virus with vaccination are topics that have been studied for many years. It is recommended that all patients undergoing hemodialysis be vaccinated against hepatitis B (3,12-13). In a study evaluating the general immunization status of ESRD patients, the rate of hepatitis B vaccination within the first 3 years after starting dialysis was found to be 77% (14). In another study, the rate of vaccination against hepatitis B in ESRD patients was determined as 73% (15). Our results show that only 4 patients have not been vaccinated despite recommendation. We think that vaccination and immunization rates for hepatitis B virus in our study are compatible with the literature.

Our study showed that 55.8% of hemodialysis patients were vaccinated against the influenza virus in the previous year. There are different results in the literature about influenza vaccination rates among ESRD patients. A recent study showed that the influenza vaccination rate for the previous year was 24% among 95 hemodialysis patients (16). 62.5% of these patients thought that they were in the high-risk group for influenza infection (16). This result may be affected by various factors rather than the lack of awareness for immunization. Two other study results showed that the influenza vaccination rate was 71% and 73% in ESRD patients (14,15). The influenza vaccination rate of our patient group was lower than that of the literature. The most common reason for influenza vaccine hesitancy was lack of enough knowledge about the vaccine. Nearly half of the patients who did not get vaccinated answer "yes" to the question "My practitioner did not recommend if he/she would recommend I would." This ratio was found to be 54.5% for the pneumococcal vaccine.

Pneumococcal pneumonia has a higher mortality rate in hemodialysis patients when compared to the general population (17). There are conflicting data in the literature about the pneumococcal vaccination rates of ESRD patients. For example, in one study, the rate of pneumococcal vaccination within the first 3 years of starting hemodialysis was found to be 53% (14). In another study, the pneumococcal vaccination rate of ESRD patients was found to be 44% (15). In our study, the rate of pneumococcal vaccination in patients undergoing

hemodialysis was 36%, and it was found to be lower than the aforementioned sources. However, compared to the study that found the pneumococcal vaccination rate of 25% in ESRD patients, it can be said that there was a higher vaccination rate in our study (18).

In a study in which half of the patients diagnosed with ESRD and had shingles were followed up for two years, 51% of the patients died and the mean time from the diagnosis of shingles to death was 8.1 months (19). However, we could not find data on zoster vaccination of ESRD patients in the literature. In our study, only one patient was vaccinated against zoster. The reasons for zoster vaccine hesitancy were similar to that of the other vaccines. But we think that another reason for the low vaccination rate against zoster is that vaccine is out of insurance. The lack of the question "I am not vaccinated because of payment." in the questionnaire is a limitation of our study.

We found that the second-highest vaccination rates were for SARS CoV-2 vaccines following hepatitis B. We think that this result is a consequence of the global pandemic. 28 patients refuse vaccination, but the vaccine hesitancy reason was different from the other vaccines. Half of the patients refuse vaccination because they were afraid of the side effects of SARS COV2 vaccines. This result is compatible with the literature (20).

The majority of the patients who were not vaccinated answered "yes" to the question "I have no idea". In general, for each vaccine except SARS-CoV2, insufficient knowledge about vaccines was the most common real reason for vaccine hesitancy. It was shown in the previous studies that vaccine hesitancy increases when the educational status of the people improves (21). According to this study, the high educational status of the parents was correlated with the high levels of vaccine hesitancy. We did not find any significant difference between the groups according to educational status or gender.

We showed that the patients were more vaccinated against SARS COV2 by increasing age. The high mortality rates of new coronavirus disease among the elderly might direct the patients for vaccination in this group. We showed that the longer duration of dialysis is related to the higher levels of vaccination against influenza. This may be related to the accumulated experience of the patients. But this hypothesis may not be true because it was not get verified for the other vaccines.

Another key point is the awareness of healthcare professionals about adult vaccination. For example, nephrology practitioners were asked about adult vaccination awareness for patients with chronic kidney disease in a study (22). While all 32 consultants told that CKD patients should have a vaccine against the Hepatitis B virus, only 19 of them agree with this for the influenza

virus and only 22 of them agree with pneumococcus vaccination (22). However, we think that there is a need for more comprehensive studies on this subject.

The literature search showed that religious beliefs and some news on media may affect the vaccine refusal rates (23). But our study showed that these reasons for vaccine hesitancy were rarely seen in patients with end-stage renal failure disease. Most of the studies about vaccine hesitancy were done in pediatric patient groups by asking their parents. Unfortunately, evidence about adult vaccine hesitancy and its reasons is lacking. More epidemiological studies are needed to determine the rates and reasons for vaccine hesitancy among adults.

## CONCLUSION

This study found out that vaccination rates for end-stage renal disease patients were low in our center. Study results showed that the most common reason for vaccine hesitancy is a lack of knowledge about the subject. Our study emphasizes the importance of the education of patients on adult vaccination. We think that our study elucidates methods to handle this public health problem.

## ETHICAL DECLARATIONS

**Ethics Committee Approval:** The study was carried out with the permission of Samsun University Training and Research Hospital, Non-interventional Clinical Researches Ethics Committee (Date: 01.05.2021, Decision No: GOKA/2021/9/9).

**Informed Consent:** All patients signed the free and informed consent form.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

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