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Depression and Cognitive Impairment in Patients on Hemodialysis: A cross-sectional study

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Abstract
Depression and cognitive impairment are the most common complications of patients on hemodialysis. The objective of this study is to identify contributing factors to depression and cognitive impairment in hemodialysis patients. This is a cross-sectional study involving 110 hemodialysis patients in Hospital Kuala Lumpur. The samples were recruited through universal sampling. Patients were assessed with the Beck Depression Inventory and Montreal Cognitive Assessment. This study found that 18.2% of patients had depression, and 48.2% had cognitive impairment. Factors associated with depression were unmarried status, low education level, and cognitive impairment. Factors associated with cognitive impairment were low education level, depression, and unemployment.

Keywords: hemodialysis, depression, cognitive, ESRD

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1.0 Introduction

Chronic Kidney Disease (CKD), including end stage renal disease (ESRD), has become a worldwide pandemic. This disease is one of the leading causes of hospitalization and death globally (Goh, Ong, and Lim 2014). It occurs when the kidney has been damaged or loses its ability to excrete waste from the body. According to the Malaysian National Clinical Practice Guidelines, ESRD occurs when the kidney no longer functions for three months or more (Goh, Ong, and Lim 2014). Hemodialysis is a type of renal replacement therapy. It helps the patient with ESRD to live longer, but it does not cure the disease.

The prevalence of CKD has been increasing over the years, with an estimated prevalence of 16.8% in America and 12.1% to 17.5% in Asian countries. According to the 21st Report of The Malaysian Dialysis & Transplant Registry, the number of new dialysis patients has increased linearly over the past decade (Goh, Ong, and Lim 2014). Most of this is due to the increasing incidence of Diabetic Kidney Disease. This steep increase has affected people and the healthcare system of Malaysia (Goh B.L., 2014). Depression and cognitive impairment give rise to change in behavior and need changes to the environment to suit the psychobiological dynamics in the body.

There is still a lack of local studies investigating depression and cognitive impairment among dialysis patients. It is important to view health-related outcomes from patients who are either depressed or cognitively impaired, including treatment adherence, quality of life, and social burden. The purpose of this study is to identify the relationship between depression and cognitive impairment in hemodialysis

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patients. This study aims to investigate factors contributing to depression and cognitive impairment among hemodialysis patients in Hospital Kuala Lumpur

2.0 Literature Review

2.1 Dialysis and Depression

Patients with CKD do experience depression, and dialysis patients with depression have a lower quality of life, more functional impairments, greater occurrence of co-morbid conditions and psychopathologic states, lower adherence to drug treatment, and an increased likelihood of long-term body pain (Cukor et al. 2009; Kutner et al. 2007). Prevalence of depression among hemodialysis patients in western countries ranges from 19% to 47% as measured by the Beck Depression Inventory (BDI) (Smith, Hong, and Robson 1985; Watnick et al. 2003). Moreover, in Malaysia, depression among dialysis patients ranges around 21.1% (N. Ibrahim, Chiew-Thong, Desa, & Razali, 2013). Studies have identified important risk factors associated with depression in ESRD dialysis patients over the past decades. These include having a history of depression, female gender, less than 24 months of dialysis, younger age, living alone, and unemployment (Craven, Rodin, and Littlefield 1988; Drayer et al. (2006). Malaysian data have also suggested low diastolic blood pressure, positive history of ischemic heart disease, and stroke as risk factors of depression in ESRD patients (Othman, Ismail, Saring, & Jamaluddin, 2014). A prospective study in Hospital Universiti Sains Malaysia in 2017 found a worsening of depression over time in hemodialysis patients. There is a linear increase in depression prevalence from baseline (Khan, Khan, Adnan, Sulaiman, & Mushtaq, 2019). Given all these shreds of evidence, depression has been a prevalent occurrence among hemodialysis patients. It warrants an immediate understanding of its contributing factors, especially in Klang Valley, where living standards are high, and survival through this demand is an obstacle when one has a chronic physical illness. In particular, the presence and absence of social support need to be identified. It could be key to prevention and intervention plans for managing depression in dialysis patients (Ratti et al., 2017).

2.2 Dialysis and Cognitive Impairment

Cognitive impairment in the dialysis population has also been prevalent, ranging from 30% to 60% (Sehgal, O'Rourke, & Snyder, 1997). Memory and language were the most severely impaired domains in the mild cognitive impairment group. Attention and visuospatial function domains were the most serious impaired domains in the major cognitive impairment group (Luo et al., 2020). Research on ESRD patients and cognitive impairment found few risk factors. Being elderly is a risk factor, and having uremia worsens cognitive function (Chikotas, Gunderman, & Oman, 2006; Meyer & Hostetter, 2007; Raff, Meyer, & Hostetter, 2008; Vanholder et al., 2008). Additionally, uremic states also reduce concentration, worsen memory, and intellectual functioning (Bae & Park, 2008; Pliskin, Yurk, Ho, & Umans, 1996). Another prevalent condition in patients going through dialysis is anemia. It reduces oxygen and thus increases the chance of cerebrovascular diseases, leading to the worsening of cognitive impairment (Bae & Park, 2008). Furthermore, ESRD patients are commonly diagnosed with hypertension and diabetes, impairing cognitive function, and leading to vascular dementia (Saczynski et al., 2008). A better understanding of the nature of depression and cognitive impairment can contribute to preventing its common occurrences. These steps would improve health benefits and help reduce the total human, economic, and social burden to the medical field and caregivers.

3.0 Methodology

3.1 Sampling

This is a cross-sectional, convenient sampling study. Convenient sampling was used given a limited number of hemodialysis patients at the hemodialysis unit that consented to join the study. The study was conducted from 28th July 2015 until 31st October 2015. The sample size was calculated based on the prevalence of depression among hemodialysis patients, estimated to be 8% (Ibrahim, N., Desa, A., & Kong, N. (2011)). The calculated sample size with a confidence interval at 95% and absolute precision at 5% was 124. The sample was only taken in Hospital Kuala Lumpur as it was a national referral center.

3.2 Inclusion Criteria

Those who met the inclusion criteria were screened and signed the informed consent. The inclusion criteria included: patients aged 18 to 70 years old, those who have been undergoing hemodialysis for a minimum of 3 months before the study began, patients who have given informed consent, and patients who can answer the questionnaire independently or with assistance. Exclusion criteria included previously diagnosed with dementia or delirium, patients with profound or severe mental retardation, those who refused to give consent, patients who are unable to communicate in English or Malay, the onset of any new major medical illnesses diagnosed in the last 2 weeks of recruitment which required admission to the hospital, i.e., stroke, heart disease, pneumonia, etc.

3.3 Questionnaires

Socio-demographic data included age, sex, marital status, smoking status, number of children, employment, education level, caretaker type, year of ESRD diagnosis, months on hemodialysis, cause of end-stage renal failure. We used the validated Malay version of the Beck Depression Inventory (BDI). The recommended optimal cut-off score for BDI in patients undergoing dialysis is 16 or more, with a specificity of 87.1% and sensitivity of 88.9% (Chilcot, Wellsted, and Farrington 2008). Hence, according to Chilcot, Wellsted, and

Farrington (2008), the suggested cut-off points are: normal: 0-9, mild depression: 10-15, moderate depression: 16-23, severe depression: >24. The validated Malay version of Montreal Cognitive Assessment (MOCA-BM) was used to assess cognitive impairment. Furthermore, 1 point was added to the total MOCA score if the patients had 12 or fewer formal education years. In our study, the cut-off point of 24 or lower indicated cognitive impairment in patients undergoing dialysis (Tiffin-Richards et al., 2014).

3.4 Analysis

The socio-demographic data, the severity of depression, the prevalence of depression, and prevalence of cognitive impairment were analyzed using descriptive statistics. Chi-square test was used to measure the association between these characteristics and having depression and cognitive impairment.

4.0 FIndings

4.1 Socio-demographic variables

Of 124 patients, only 110 patients were recruited in the study due to exclusion criteria such as no consent given, age more than 70 years old, deaths before questionnaires were filled up, and medical illnesses that warrant ward admission. The response rate was 89%.

Table 1. Socio-Demographic Variables

Characteristics	N (%)	Median (IQR)	Mean (SD)
Age			48 (13)
Age			
19-29	13 (11.8)		
30-39	17 (15.5)		
40-49	24 (21.8)		
50-59	31 (28.2)		
60-69	25 (22.7)		
Gender			
Male	65 (59.1)		
Female	45 (40.9)		
Race			
Malay	46 (41.8)		
Chinese	45 (40.9)		
Indian	15 (13.6)		
Other	4 (3.6)		
Smoking status	13 (11.8)		
Smoker	95 (86.4)		
Non-smoker			
Education			
Low: Primary level	34 (31.2)		
High: Secondary level and more	75 (68.8)		
Marital status			
Ever married	68 (61.8)		
Never married	42 (38.2)		
Employment			
Unemployed	70 (63.6)		
Pensioner	5 (4.5)		
Professional	29 (26.4)		
Teacher	3 (2.7)		
Driver	3 (2.7)		
Carers			
Alone	15 (13.8)		
Family	91 (83.5)		
Welfare	3 (2.8)		
Number of children		1 (2.25)	
Cause of renal failure			
Unknown	43 (39.4)		
Hypertension	35 (32.1)		
IgA Nephropathy	4 (3.7)		
Polycystic Kidney Disease	3 (2.8)		
Nephrotic Syndrome	7 (6.4)		
Renal Tubular Acidosis	1 (0.9)		
MGN-mononephritis syndrome	1 (0.9)		
SLE nephropathy			
Gout	3 (2.8)		
Diabetes Mellitus	1 (0.9)		
Trauma	8 (7.3)		
Renal Stone	2 (1.8)		

	1 (0.9)

Table 1 shows that there was a total of 110 patients, from which more than half (59.1%) are males and less than half (45%) are females. The mean (SD) age of patients is 48 (13) years old. Malays and Chinese have an almost similar percentage of 41.8% and 40.9%, respectively, followed by a smaller group of Indians (13.6%) and Others (3.6%). Most of the patients are non-smokers at the time of the interview (86.4%), while smokers are 11.8%. Most of the patients received education at the secondary level or more (68.8%) than a smaller group of patients who received education up to primary level or less (31.2%).
More than half (61.8%) of the patients have ever been married, and 38.2% are those who were never married. The majority of patients are unemployed (63.6%), and a large majority (83.5%) of patients stays with their family as their carers. The median number of children among ever-married patients is 1 child. The most common cause of renal failure is unknown (39.4%), followed by Hypertension (32.1%).

4.2 Depression and cognitive impairments

Table 2. Prevalence Of Depression And Cognitive Impairment

	N	%
Depression	20	18.2
No Depression	90	81.8
Cognitive Impairment	53	48.2
No Cognitive Impairment	57	51.8

In Table 2 based on cut - off BDI score of ≥16 is considered as clinical depression (Chilcot, Wellsted, and Farrington, 2008). Hence, the prevalence of depression among hemodialysis patients in Hospital Kuala Lumpur is 18.2%.

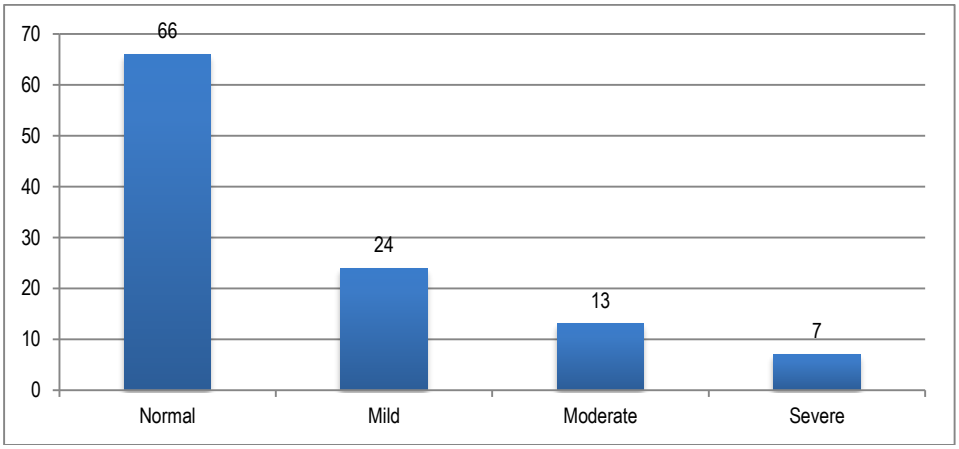

Figure 1. Severity of Depression with Beck Depression Inventory

In Figure 1, based on BDI, it was found that 66 patients (60%) have no depressive symptoms (score= 0-10), 24 patients (21.8%) have mild depression (score=10-15), 13 patients (11.8%) have moderate depression (score=16-23) and 7 patients (6.4%) have severe depression (score= 24-63). Based on cut-off score from Tiffin-Richards et al. (2014), MOCA scores of 24 or less are considered to be cognitively impaired. 53 patients (48.2%) have cognitive impairment while 57 (51.8%) has no cognitive impairment.

Table 3. Factors associated with Depression

Items	Depression n (%)		X^2	p value	OR	95% CI
	Yes	No				
Gender						
Male	10(15.4%)	55 (84.6%)	0.84	0.36[a]	0.64	0.24, 1.68
Female	10 (22.2%)	35 (77.8%)				
Age group (years)						
Less than 50	9 (16.7%)	45 (83.3%)	0.43	0.84[a]	0.9	0.33, 2.42
More than 50	10 (18.2%)	45 (81.8%)				
Race						
Malay	6 (13.0%)	40 (87%)	1.66	0.44[a]		
Chinese	9 (20.0%)	36 (80%)				
Indian	4 (26.7%)	11 (73.3%)				
Marital Status						
Unmarried	13 (31%)	29 (69%)	7.45	0.01[a]	3.90	1.41, 10.83
Ever married	7 (10.3%)	61 (89.7%)				

Employment						
Unemployed	14 (20%)	56 (80%)	0.43	0.51[a]	1.41	0.49, 4.03
Employed	6 (15%)	34 (85%)				
Education						
Up to Primary	10 (29.4%)	24 (70.6%)	4.93	0.03[a]	3.06	1.11, 8.43
Secondary and above	9 (12%)	66 (88%)				
Carer						
Non-family	5 (27.8%)	13 (72.7%)	1.60	0.30[b]	2.12	0.65, 6.88
Family	14 (15.4%)	77 (84.6%)				
Cognition						
Cognitive impairment	13 (24.5%)	40 (75.5%)	2.77	0.096[a]	2.32	0.85, 6.36
No cognitive impairment	7 (12.3%)	50 (87.7%)				

a= Pearson Chi Square Test, p<0.05
b= Fisher's exact test, p<0.05

Table 3 shows the univariate analysis of factors associated with depression in hemodialysis patients. For unmarried patients, there was a significant association with depression. Whereby they have almost 4-times the risk of getting depression compared to those who are ever married (OR=3.90, CI=1.41-10.83,

P value = 0.01). Moreover, patients who received education up to primary level or less were 3 times more likely to developed depression while on hemodialysis (OR=3.06, CI=1.11, 8.43, P value=0.03). Furthermore, patients with cognitive impairment have twice the risk of having depression than those with no cognitive impairment (OR 2.32, CI=0.85, 6.36, P value=0.096).

4.3 Factors associated with cognitive impairment

Table 4. Factors associated with Cognitive Impairment

Items	Cognitive Impairment n (%)		X^2	p value	OR	95% CI
	Yes	No				
Gender						
Male	30 (46.2%)	35 (53.8%)	0.26	0.61[a]	0.82	0.38, 1.76
Female	23 (51.1%)	22 (48.9%)				
Age group (years)						
Less than 50						
More than 50	24 (44.4%)	30 (55.6%)	0.46	0.57[b]	0.78	0.36, 1.64
	28 (50.9%)	27 (49.1%)				
Race						
Malay	19 (41.3%)	27 (58.7%)	1.51	0.47[a]		
Chinese	24 (53.3%)	21 (46.7%)				
Indian	8 (53.3%)	7 (46.7%)				
Marital Status						
Never married	19 (45.2%)	23 (54.8%)	0.24	0.63[a]	0.83	0.38, 1.79
Ever married	34 (50%)	34 (50%)				
Employment						
Unemployed	41 (58.6%)	29 (41.4%)	8.32	<0.01[a]	3.30	1.44, 7.54
Employed	12 (30%)	28 (70%)				
Education	27 (79.4%)	7 (20.6%)	19.91	<0.01[a]	7.71	2.95, 20.15
Low	25 (33.3%)	50 (66.7%)				
High						
Smoking Status						
Non-smoker	44 (46.3%)	51 (53.7%)	2.4	0.12[a]	0.38	0.11, 1.33
Smoker	9 (69.2%)	4 (30.8%)				
Carer						
Non-family	11 (61.1%)	7 (38.9%)	1.55	0.21[a]	1.91	0.68, 5.39
Family	41 (45.1%)	50 (54.9%)				
BDI						
Depressed	13 (65%)	7 (35%)	2.77	0.096a	2.32	0.85, 6.36
Not depressed	40 (44.4%)	50 (55.6%)				

a= Pearson Chi Square, p<0.05

Table 4 shows the univariate analysis of factors associated with cognitive impairment in hemodialysis patients. For unemployed patients, 41 (58.6%) were found to be cognitively impaired compared to only 12 (30%) in those who are employed who are cognitively impaired. There is a significant association between patients who are unemployed with cognitive impairment. They have almost 3-times the risk of having cognitive impairment than those employed (OR=3.30, CI=1.44-7.54, P value<0.01). Moreover, patients who only attended school up to primary level or less, 27 (79.4%) were found to have cognitive impairment compared to 25 (33.3%) in those who attended school up to secondary level or more. This association was significant, whereby those who attended school up to primary level

or less were almost 8 times more likely to developed cognitive impairment while on hemodialysis (OR=7.71, CI=2.95-20.15, P value=0.096). Depression patients had twice the risk of getting cognitive impairment in hemodialysis patients (OR=2.32; CI=0.85-6.36; p value=0.096).

5.0 Discussion

5.1 Dialysis and Depression

This study was conducted at the hemodialysis unit at Hospital Kuala Lumpur. Of the 124 patients approached, 110 completed all questionnaires. Of those excluded, 2 patients did not consent to participate in the study, 4 patients were more than 70 years old. In comparison, another 2 patients were admitted to the medical ward for acute medical illness related to underlying CKD. Six patients died before they were able to give consent. The total response rate was 89%. Our study may have achieved a high response rate due to universal sampling.

In this study, the prevalence of depression in hemodialysis patients was 18.2% (Table 2) using the BDI (cut-off point of 16). The prevalence is very similar to previous studies conducted in Malaysia, which reported 21.1% of mixed hemodialysis and Continuous Ambulatory Peritoneal Dialysis (CAPD) patients (N. Ibrahim et al., 2013) and 36.3% in a multi-centered study in Peninsular Malaysia (Bujang et al., 2015). Othman et al. (2014) used the BDI with a cut-off point of 11, which is similar to the general population, while N. Ibrahim et al. (2013) used a cut-off point of 14. Bujang et al. (2015) used Depression Anxiety and Stress Scale (DASS) to assess the prevalence of depression in their sample.

The prevalence of depression in dialysis in neighboring countries was 32% in Taiwan (Wang, Chan, Chang, Chen, & Tsai, 2013), 52% in China (Dong et al., 2016), 31.3% in South Korea (Jeon et al., 2012) and 40% in Japan (Fukuhara et al., 2006). Hence, the prevalence of depression among dialysis patients in Asian countries seems to be on the rise and definitely much higher than that of the general population. In this study, 60% of patients had no depression, 21.8% had mild depression, 11.8% had moderate depression, and 6.4% had severe depression (Table 2). These results were comparable to other studies done in Peninsular Malaysia: 14.2% with moderate depression and 6.7% with severe depression (N. Ibrahim et al., 2013). Although the prevalence of severe depression was much lower than the less severe, it is important to routinely screen depression in all patients on hemodialysis as ESRD is a chronic illness requiring a high commitment to treatment adherence (Fukuhara et al., 2006).

Screening for the symptoms would aid diagnosis of depression and ultimately lead to proper treatment. This study found a significant association between unmarried patients and those with a primary education level or lower. The odds of having depression in unmarried patients compared to the ever-married group of patients were 3.9 times higher (OR=3.90, CI=1.41-10.83, P value=0.01). In previous studies, spousal social support was a buffer against the patient's level of depression. This may explain our findings that being married is protective against depression. If the patient-perceived high levels of spousal social support, there would be less risk of progression of their depressive affect and linked to longer survival of patients with and without renal disease.

In this study, the percentage of patients with low education level, i.e., education up to primary level or less, was 31%. In contrast, the others had education up to secondary level or more. Those with a low education level had 3 times the risk of developing depression (OR=3.06, CI=1.11-8.43, P value=0.03). We found that those with a high education level were less likely to develop depression than low level; this was by a study done in Saudi Arabia by AlDukhayel (2015), who found that depression was more likely in those with a lower education level. He found that low education level, together with lower monthly income, were contributing factors to depression. Similarly, this study's participants are similar in terms of expected education levels. Hospital Kuala Lumpur is a government hospital, and medical treatment is free hence more participants from lower education and lower economic background attends Hospital Kuala Lumpur.

5.2 Dialysis and cognitive Impairment

On the other hand, this study found that cognitively impaired patients have twice the risk of developing depression (OR=2.32; CI=0.85-6.36; P value=0.096). Those with an MOCA score of less than 24 reported more depressive symptoms than those with no cognitive impairment. Those on hemodialysis carry vascular risk factors putting them at risk of white matter lesions and, in the state of uremia, can lead to cognitive impairment and depression. Cognitive impairment has been found to lower Quality of Life (QoL) in hemodialysis patients, which may be one of the causes of depression (Jung et al., 2013). It is estimated that about 30% to 70% of ESRD patients on maintenance hemodialysis are cognitively impaired (Bugnicourt, Godefroy, Chillon, Choukroun, & Massy, 2013; Griva et al., 2010; Kurella, Chertow, Luan, & Yaffe, 2004; Murray et al., 2006; Sehgal et al., 1997). In this study, the prevalence of cognitive impairment was found to be 48% when assessed with MOCA (Table 2).

This study showed those with education levels up to primary level or less had nearly 8 times the risk of developing cognitive impairment compared to those patients with education up to secondary level or more (OR=7.71, CI=2.95-20.15, P value=0.096). On top of vascular changes in the brain leading to cerebrovascular disease in CKD patients, other factors that increase the risk of cognitive impairment in CKD include education level, depression, and psychiatric diseases (Drew et al. 2015). Participants in this study have lower educational backgrounds; hence it may have affected their understanding of the importance of a healthy lifestyle. It includes the prevention of more vascular insults to the brain structure. A study in China found that mild cognitive impairment has a higher risk of turning into major cognitive impairment in hemodialysis patients (Pei et al., 2018).

Form Table 4, about 65% of depressed patients in the study had cognitive impairment, and they had twice the risk of developing cognitive impairment (OR=2.32; CI=0.85-6.36; P value=0.096). cognitive impairment and dementia in dialysis patients (Agganis et al., 2010; Dong et al., 2016; Kalirao et al., 2011; Murray, 2008). Depression in dialysis patients is comparable to those with late-life depression because the effect is more prominent on executive function and becomes a risk factor for cognitive impairment (Agganis et al. 2010). Since depression can be treated, it becomes a modifiable risk factor for patients on dialysis to prevent or halt further progression of cognitive impairment. Depression if screened early and consistently on top of screening for cognitive impairment, may help reduce the risk of cognitive impairment.

6.0 Conclusion & Recommendation

This study contributes to understanding the contributing factors of depression and cognitive function among patients on hemodialysis. Further research in a local setting is needed to head towards understanding the reciprocal relationship between depression and cognitive impairment in hemodialysis patients. It is important to understand that depression and cognitive impairment are two complicated issues in hemodialysis patients. Both conditions are underdiagnosed and undertreated. These two conditions, independently, lead to many other complications in patients on maintenance hemodialysis.

Nephrologists treating this group of patients should conduct routine and periodic screening for depression and cognitive function and subsequently refer the suspected patients with co-morbid depression or cognitive impairment to appropriate mental health professionals, psychiatrists, geriatricians, or neurologists for further management. It is important to have a multi-disciplinary approach towards managing patients with chronic illnesses such as hemodialysis.

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Paper Contribution to Related Field of Study

This paper's finding contributes to the care and wellbeing of patients on hemodialysis.

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