

Prevalence of stroke among patients with chronic kidney disease, Taif, Saudi Arabia

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ABSTRACT

الأهداف: لتقييم مدى انتشار الجلطات الدماغية بين مرضى الفشل الكلوي المزمن (CKD) في مدينة الطائف، المملكة العربية السعودية.

المنهجية: تم إجراء هذه الدراسة بأثر رجعي من مايو 2021م حتى أغسطس 2022م على 1857 مريض فشل كلوي مزمن، يبلغون من العمر 18 عاماً أو أكبر ويتم علاجهم في أربع مراكز غسيل كلوي في مدينة الطائف. جميع البيانات أخذت من الملفات الطبية لهؤلاء المرضى.

النتائج: أظهرت دراستنا وجود ضعف شديد في معدل الترشيح الكبيبي الكلوي (GFR) لدى 98.3% من عينة الدراسة. منهم 49.1% يخضعون للغسيل الكلوي بنوعيه الدموي والبريتوني، منهم (87.2%) يخضعون لنوع الغسيل الدموي. تم الإبلاغ عن مدى انتشار الجلطات الدماغية بنسبة 8.3% بين المرضى. معظم الجلطات الدماغية كانت من النوع الاقناري التجلطي مع اختلاف نوع الانتشار بين المرضى بناءً على نوع الغسيل الكلوي، حيث ارتبطت الجلطات الاقنارية بنوع الغسيل الدموي بينما الجلطات النزفية بنوع الغسيل البريتوني. لم تظهر دراستنا علاقة ارتباط بين مدى التعرض للجلطات الدماغية وبين حدة القصور الكلوي أو مدة الخضوع لجلسات الغسيل الكلوي بالسنتين.

الخلاصة: مدى انتشار الجلطة الدماغية بين عينة الدراسة هو 8.3%، معظمها من النوع الاقناري التجلطي. مع عدم وجود علاقة ارتباط بين مدى الانتشار ومدى حدة القصور الكلوي.

كانت السكتات الدماغية أكثر تواتراً في مرضى غسيل الكلى البريتوني، في حين حدثت السكتات الدماغية النزفية بشكل متكرر أكثر في مرضى غسيل الكلى مع وجود ارتباط يعد به إحصائياً.

Objectives: To evaluate the prevalence of stroke among chronic kidney disease (CKD) patients in Taif, Saudi Arabia.

Methods: A multicentric retrospective study was carried out from May 2021 to August 2022 on 4 dialysis centers in Taif, Saudi Arabia. With a total of 1857 CKD patients (aged ≥ 18 years old) participated in this study. Data were collected by reviewing patients' files.

Results: Approximately 98.3% of the participants had severely decreased glomerular filtration rate. Approximately 49.1% of them were on dialysis; the majority of them (87.2%) underwent hemodialysis.

The prevalence of stroke in these CKD patients was 8.3%. Ischemic stroke was the most frequently reported issue (81.2%). Ischemic stroke was comparatively more frequently observed in peritoneal dialysis patients (12.1%); whereas hemorrhagic stroke was more on hemodialysis patients with statistically significant association ($p=0.029$). However, there was no significant association between the prevalence of stroke and stages of CKD.

Conclusion: The prevalence of stroke in our cohort was 8.3%, and the majority of cases were ischemic strokes. Furthermore, ischemic strokes were more frequent in peritoneal dialysis patients, whereas hemorrhagic strokes occurred more frequently in hemodialysis patients with a statistically significant association.

Keywords: prevalence, chronic kidney disease, renal failure, end-stage renal disease, glomerular filtration, cerebrovascular disease, stroke

Saudi Med J 2023; Vol. 44 (11): 1139-1144
doi: 10.15537/smj.2023.44.11.20230206

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Received 2nd September 2023. Accepted 5th October 2023.

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Chronic kidney disease (CKD) is an irreversible change in the function or structure of the kidneys. An adult patient is diagnosed to have CKD when the glomerular filtration rate (GFR) is less than 60 ml/min/1.73 m² for 3 months or more. There are 5 stages of CKD according to GFR, in end-stage renal disease (ESRD) the patient needs to be in maintenance dialysis.¹ The prevalence of CKD has been increasing in the last few years. Chronic kidney disease is estimated to affect approximately 1.72 million people in Saudi Arabia.² It is associated with many complications such as cardiovascular disease (CVD), cognitive dysfunction, and hospitalization, which may increase mortality and morbidity rates.³

Stroke is one of the major public health concerns worldwide in CKD patients; a meta-analysis of studies involving more than 2 million patients found a clear correlation between a declining renal function and a higher risk of stroke.⁴ Furthermore, reduced glomerular filtration levels increases the risk of stroke by approximately 40%, while proteinuria raises the risk by approximately 70%, according to cohort studies and trials.⁵

Patients on dialysis for ESRD have an 8-10 times higher risk of stroke than the general population, with rates ranging from 10-33 per 1,000 patient in reported studies.⁶ Wang et al⁷ showed that the incidence of ischemic and hemorrhagic strokes is higher in patients on peritoneal dialysis (PD) or hemodialysis (HD) in comparison to the general population.

Moreover, Ozelsancak et al⁸ reported in their study that out of 139 patients in hemodialysis, 65 (24.62%) had ischemic stroke and 25 (9.47%) had a hemorrhagic stroke. Peritoneal dialysis was associated with a 16% lower risk of hemorrhagic stroke compared to HD.⁹

Until now, the prevalence of stroke in CKD in Saudi Arabia is uncertain. Our aim in this study is to evaluate the prevalence of stroke among CKD patients in Taif, Saudi Arabia.

Methods. This is a multicentric retrospective study aimed to investigate the prevalence of stroke among CKD patients and compare stroke prevalence between patients on HD and PD. This study was carried out in May 2021 - August 2022 (with a sample size of 1857) at 4 dialysis centers (King Abdulaziz Specialist Hospital, King Faisal Medical Complex, Prince Mansour Military

Hospital, and Alhada Armed Forced hospital) in Taif, Saudi Arabia. Ethical approval was obtained from the ethical committee of Health Affairs in Taif, Saudi Arabia. All procedures were carried out according to principles of Helsinki Declaration.

Inclusion criteria were all CKD patients aged ≥ 18 years old and who agreed to participate. Exclusion criteria were all those people not CKD, less than 18, and who refuse to participate.

Information was collected from the medical record of all CKD patients who met our inclusion criteria. Our data include information on demographics (age, gender, nationality, marital status, level of education, and body mass index), and the presence of any comorbidities (namely, hypertension, diabetes mellitus, CVD, dementia, hematological disorders, malignant disorders, and more). Specific information regarding CKD was obtained (namely, duration of illness, stage, and GFR). Dialysis status includes dialysis type and treatment duration. Information on the presence of stroke was obtained; if present, further information was collected regarding the type, whether it was hemorrhagic or ischemic, and duration of stroke.

Statistical analysis. Data was analyzed using the Statistical Package for the Social Sciences, version 23 for Windows (IBM Corp., Armonk, NY, USA). Descriptive statistics were used in the form of frequencies and percentages. Mean and standard deviation was used for representing the continuous variables. Pearson's Chi-square test was used to assess the relationship between categorical variables. A multivariate regression model was carried out to analyze the risk factors for stroke in CKD patients. A *p*-value of <0.05 was considered significant.

Results. Our analysis included CKD patients' data from 4 tertiary care hospitals in Taif, Saudi Arabia. The mean age of the patients was 60.3 ± 18.9 years. The socio-demographic data showed that 66.2% of the patients were over 55 years old, 59.3% were males, 50.4% were married, 6.3% had a primary school education level or were illiterate, and 19.4% were obese (Table 1). The most commonly reported comorbidity was hypertension (78.9%), followed by diabetes (41.5%), and ischemic heart disease (25.1%).

The clinical characteristics of the CKD patients showed that approximately 1010 (54.4%) had end-stage renal disease (ESRD) and remaining had CKD. The GFR was found to be severely decreased in 98.3% of the patients, where it was significantly higher among ESRD patients compared to CKD patients ($p < 0.01$).

Disclosure. Authors have no conflict of interests, and the work was not supported or funded by any drug company.

Table 1 - Sociodemographic details.

Variables	n (%)
<i>Hospital's name</i>	
Al-Hada	964 (51.9)
King Abdulaziz	328 (17.7)
King Faisal	457 (24.6)
Prince Mansour	108 (5.8)
<i>Age (years)</i>	
≤25	101 (5.4)
26-35	127 (6.8)
36-45	168 (9.0)
46-55	232 (12.5)
>55	1229 (66.2)
<i>Gender</i>	
Female	756 (40.7)
Male	1101 (59.3)
<i>Marital status</i>	
Single	169 (9.1)
Married	935 (50.4)
Divorced or widowed	40 (2.2)
Not recorded	713 (38.4)
<i>Educational qualification</i>	
Primary school or illiterate	118 (6.3)
Secondary (high school)	42 (2.3)
Collage and above	68 (3.7)
Not recorded	1629 (87.7)
<i>Body mass index</i>	
Underweight	56 (3.0)
Normal	226 (12.2)
Overweight	251 (13.5)
Obese	361 (19.4)
Not recorded	963 (51.9)

Values are presented as numbers and percentages (%).

The total of patients who were on dialysis were 911 (49.1%), where the majority (95.3%) were in ESRD ($p<0.01$).

The majority of patients who were on dialysis underwent hemodialysis (87.2%), where 95% of those were ESRD patients and approximately 76.1% of those who had PD were CKD patients ($p<0.01$). In our cohort, 9 patients were on dialysis for more than 10 years and all of them were ESRD patients ($p<0.01$, [Table 2](#)).

The prevalence of stroke in these CKD patients was found to be 8.3%. Approximately 48.7% of these 154 patients had a stroke in less than one year, and 7.8% had its onset for more than 10 years. Ischemic stroke was the most reported stroke among these patients (81.2%, [Table 3](#)).

When we assessed the relationship between the prevalence of stroke with stages of CKD, duration of dialysis, and type of dialysis, no statistically significant association was observed ($p>0.05$, [Table 4](#)). There was also no statistical significance observed between the

Table 2 - Clinical characteristics related to chronic kidney disease.

Characteristics	n (%)	P-values
<i>Type of CKD</i>		
CKD	847 (45.6)	
ESRD	1010 (54.4)	
<i>GFR</i>		
<i>CKD</i>		
Mildly to moderately decreased	11 (1.3)	
Moderately to severely decreased	20 (2.4)	
Severely decreased	816 (96.3)	<0.001
<i>ESRD</i>		
Moderately to severely decreased	1 (0.1)	
Severely decreased	1009 (99.9)	
<i>Dialysis</i>		
<i>CKD</i>		
No	804 (94.9)	
Yes	43 (5.1)	<0.001
<i>ESRD</i>		
No	142 (14.1)	
Yes	868 (85.9)	
<i>Type of dialysis (n=911)</i>		
<i>CKD</i>		
Hemodialysis	38 (88.4)	
Peritoneal dialysis	5 (11.6)	<0.001
<i>ESRD</i>		
Hemodialysis	756 (87.1)	
Peritoneal dialysis	112 (12.9)	
<i>Duration of dialysis (n=911)</i>		
<i>CKD</i>		
<1 years	18 (41.9)	
1-2 years	11 (25.6)	
3-5 years	10 (23.3)	
6-10 years	4 (9.3)	
<i>ESRD</i>		
<1 years	359 (41.4)	<0.001
1-2 years	264 (30.4)	
3-5 years	182 (21.0)	
6-10 years	55 (6.3)	
>10 years	8 (0.9)	

Values are presented as numbers and percentages (%).
CKD: chronic kidney disease, GFR: glomerular filtration rate,
ESRD: end stage renal disease

duration of dialysis and the type of stroke ($p>0.05$). However, ischemic stroke was comparatively more frequent in the patients on PD (12.1%), whereas hemorrhagic stroke was more frequent in the patients on HD; this result showed a statistically significant association ($p=0.029$, [Table 5](#)).

A multivariate logistic regression model was carried out to assess the risk factors for stroke among CKD patients. It was found that age above 55 years (odds ratio [OR]=3.30, 95% confidence interval [CI]: [1.86-5.86], $p<0.001$), being married (OR=1.27, 95% CI: [0.82-2.60], $p=0.001$), hypertension (OR=3.11, 95% CI: [1.58-6.12], $p=0.001$), and ischemic heart disease (OR=1.38, 95% CI: [0.95-2.00], $p=0.043$) were independently associated with stroke ([Table 6](#)).

Table 3 - Prevalence of stroke and its characteristics.

Characteristics	n (%)
Diagnosed with stroke	154 (8.3)
<i>Duration of onset kidney disease (n=154)</i>	
<1 year	75 (48.7)
1-2 years	36 (23.4)
3-5 years	19 (12.3)
6-10 years	12 (7.8)
>10 years	12 (7.8)
<i>Stroke (n=154)</i>	
Hemorrhagic stroke	29 (18.8)
Ischemic stroke	125 (81.2)

Values are presented as numbers and percentages (%).

Table 4 - Relationship of stroke with chronic kidney disease and dialysis.

Variables	Stroke			P-values
	No	Yes	Total	
<i>Stages of CKD</i>				
0	105 (89.7)	12 (10.3)	117 (100)	0.238
1	57 (89.1)	7 (10.9)	64 (100)	
2	200 (90.5)	21 (9.5)	221 (100)	
3	291 (94.2)	18 (5.8)	309 (100)	
4	96 (96.0)	4 (4.0)	100 (100)	
5	922 (91.3)	88 (8.7)	1010 (100)	
<i>Duration of dialysis</i>				
<1 years	1212 (91.8)	108 (8.2)	1320 (100)	0.769
1-2 years	257 (92.8)	20 (7.2)	277 (100)	
3-5 years	174 (90.6)	18 (9.4)	192 (100)	
6-10 years	52 (88.1)	7 (11.9)	59 (100)	
>10 years	8 (88.9)	1 (11.1)	9 (100)	
<i>Type of dialysis</i>				
Hemodialysis	725 (91.0)	72 (9.0)	797 (100)	0.315
Peritoneal dialysis	978 (92.3)	82 (7.7)	1060 (100)	

Values are presented as numbers and percentages (%). CKD: chronic kidney disease

Discussion. Chronic kidney disease is a well-known highly prevalent medical issue associated with many complications (namely, cerebrovascular disease, cognitive dysfunction, and hospitalization), which may increase mortality and morbidity rates.¹⁰ Stroke is considered to be one of the major public health concerns in CKD patients; therefore, in this study, we aimed to evaluate the prevalence of stroke among CKD patients.

When we assessed the severity of GFR among the CKD patients, we found that 98.3% of them could be classified as having severely decreased GFR. The observed percentage is very high, which prompted us to more carefully evaluate the patients with mild to moderate decrease in GFR to prevent the progression to the severe stage. Moreover, another study on 778 patients showed that among the 639 patients with brain ischemia, 22% of them had severely decreased GFR.¹¹

In addition, 49.1% of the patients who participated in our study were on dialysis, and most of them were on HD (87.2%). In another study on 148 participants with ESRD, the percentage of the patients on HD was 85.1%, which is comparable to our results.¹²

Furthermore, we noticed that the duration of dialysis in our study was mostly less than one year, which may indicate that most of the patients (especially those with a stroke) presented later in the course of their CKD. A study carried out on elderly patients on dialysis showed that the peak of stroke occurred during the first 30 days of initiating dialysis.¹⁰

In our study, the prevalence of stroke among CKD patients was 8.3%, which is higher compared to that in a study carried out in the United States that reported a prevalence of 6.1%.¹³ This discrepancy may be due to the ethnicity effect.¹⁴ However, 81.2% of our stroke

Table 5 - Relationship between type of stroke and dialysis.

Variables	Type stroke			P-values
	Hemorrhagic	Ischemic	Total	
<i>Duration of dialysis</i>				
<1 years	1166 (88.3)	154 (11.7)	1320 (100)	0.234
1-2 years	257 (92.8)	20 (7.2)	277 (100)	
3-5 years	175 (91.1)	17 (8.9)	192 (100)	
6-10 years	52 (88.1)	7 (11.9)	59 (100)	
>10 years	8 (88.9)	1 (11.1)	9 (100)	
<i>Type of dialysis</i>				
Hemodialysis	726 (91.1)	71 (8.9)	797 (100)	0.029
Peritoneal dialysis	932 (87.9)	128 (12.1)	1060 (100)	

Values are presented as numbers and percentages (%).

Table 6 - Multivariate logistic regression model (independent variable = stroke).

Variables	OR	95% CI		P-values
		Lower	Upper	
Age above 55 years	3.30	1.86	5.86	<0.001
Gender	0.76	0.52	1.12	0.166
Marital status (married)	1.27	0.82	2.60	0.001
Education level	0.24	0.04	1.34	0.103
BMI of >25	0.90	0.78	1.04	0.152
Hypertension	3.11	1.58	6.12	0.001
Diabetes	0.83	0.57	1.21	0.331
Acute kidney injury	2.30	0.71	7.41	0.163
Benign prostatic hyperplasia	1.35	0.61	3.00	0.466
Chronic obstructive pulmonary disease	1.96	0.79	4.85	0.148
Hyperlipidemia	3.18	0.33	30.87	0.318
Ischemic heart disease	1.38	0.95	2.00	0.043
Urinary tract infection	1.15	0.42	3.17	0.786
Hypothyroidism	1.32	0.74	2.37	0.346
On dialysis	0.99	0.64	1.55	0.975
On dialysis for >5 years	1.13	0.89	1.44	0.327
Constant	0.09			0.001

OR: odds ratio, CI: confidence interval, BMI: body mass index

patients had an ischemic stroke, which is comparable to the results reported by Ohasam et al,¹⁵ who stated that 70.5% of their CKD patients developed an ischemic stroke.

This well-known association between declined renal function and ischemic stroke has been investigated and explained in many studies. In the literature, the pathogenesis has been explained by several factors such as deterioration of the vascular endothelial system, accumulation of indoxyl sulfate, and alteration of prothrombotic mechanisms.^{4,16} Our study found no association between stages of CKD and the prevalence of stroke. However, a meta-analysis of 21 articles (with 14 of them assessing ESRD patients with an eGFR value of <60 ml/min/1.73 m², found an increased prevalence

of stroke in stages III-IV and among ESRD patients. In our cohort, only 49.1% were ESRD patients; among those, 41.4% underwent dialysis for a period that was less than one year, which may explain the discrepancy.¹⁷ In addition, our study revealed no relationship between stroke prevalence and the type of dialysis, which agrees with the study by Murray et al.¹⁰

Furthermore, a systemic review found that there was no significant association between the type of dialysis and the type of stroke, which contradicts our results.¹⁸ This discrepancy can be explained by the difference in the types of carried out studies. Furthermore, the above-mentioned study reported a low risk of hemorrhagic stroke in PD patients, which matches our results.¹⁸ However, the high bleeding tendency in HD patients

has been reported in many studies, which may be due to hemodynamic instability.^{19,20}

Overall, age above 55 years, hypertension, and CVD are independently related to stroke. Another study has also reported that older age, diabetes, and CVD are independently associated with stroke.²¹ A previous study showed that patients with CKD and hypertension may experience unfavorable cardiovascular outcomes, especially stroke.⁵ Moreover, the mainstay of both primary and secondary stroke prevention is controlling hypertension.⁶ However, patients with CKD are a high-risk population for stroke and, thus, should receive clinical priority.⁵

Study limitations. In this study, the data were obtained from medical records; however, not all records were fully informative regarding the CKD stage or GFR, which may prone our cohort to misclassification. We recommend that future studies should include serum creatinine levels in the data collection process to calculate eGFR.

In conclusion, our study showed that ischemic stroke is more prevalent among patients with CKD. Furthermore, a statistically significant association between ischemic stroke with PD and hemorrhagic stroke with HD was evident. Stroke prevalence was neither associated with the stage or duration of CKD nor with the type of dialysis. These results identify CKD patients as a high-risk population for stroke regardless of their disease course and type of dialysis.

Acknowledgment. *The authors gratefully acknowledge Dr. Muhanna J. Altalbi, Dr. Ahmed H. Alsubaymi, Dr. Qussi H. Omer, Dr. Razan A. Almakki, Dr. Mrooj A. Suwayyid, Dr. Abdullah S. Alkhtani, and Dr. Muhanna A. Albusayni for their valuable contribution in the data collection process. The authors also would like to thank Falcon Scientific Editing for their English language editing.*

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