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Prevalence of Chronic Kidney Disease in Patients Presenting with Acute Stroke

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Abstract

Introduction: Stroke is the brain equivalent of a heart attack. Stroke does not stop at the individual, but it extends to their family as a burden economically and socially. The high rates of disability and mortality due to stroke are determined not only by the neurological deficits but also by the associated medical co- morbidities as cardiovascular disease, hypertension, diabetes and renal dysfunction. The high prevalence of CVD found in patients starting dialysis treatment suggests that CVD begins in the early stages of CKD. The risk for CVD increases with a decline in kidney function. This study was conducted to determine the prevalence of chronic kidney disease in patients presenting with acute stroke and its association with disease severity.

Materials and methods: This hospital based cross-sectional study was carried out during September, 2017 and August, 2019 among 200 patients diagnosed with acute stroke. Stroke was diagnosed based on neurological examination and admission computed tomography scan. Descriptive statistics like proportions, mean and standard deviation were used. Chi-square test and ANOVA were used to check for associations of CKD with other variable of interest.

Results: The study population included 82 females and 118 males. Around 28% of the participants were from the age group of 71 to 80 years followed by 51 to 60 years (23%) and 61 to 70 years (19%). Minimum cases (0.5%) were from the age group 30-40 years. The prevalence of CKD was 34% (68). CKD (eGFR< 60ml/min/1.73m2) was significantly ($p<0.05$) associated with higher age group and Atrial fibrillation. Gender, smoking, coronary artery disease and dyslipidemia, were not associated with CKD.

Conclusion: CKD has a high prevalence in a population with acute stroke. Therefore, all patients with stroke should be considered at risk of CKD and be aggressively managed for CKD prevention. Moreover, the high prevalence of CKD in population with acute stroke prompts the need for greater public awareness about risks of CKD.

Keywords: risk factors, cardiovascular disease, prevalence, chronic kidney disease, acute stroke

Introduction

Stroke is the brain equivalent of a heart attack. Blood must flow to and through the brain for it to function. If its flow is obstructed, by a blood clot moving to the brain, or by narrowing or bursting of blood vessels, the brain losses its energy supply, causing damage to tissue leading to stroke. Stroke does not stop at the individual, but it extends to their family as a burden economically and socially. Only 8% of the published cardiovascular research is from developing countries, although low and middle income countries shoulder 80% of the disease [1].

The high rates of disability and mortality due to stroke are determined not only by the neurological deficits but also by the associated medical co-morbidities as cardiovascular disease, hypertension, diabetes and renal dysfunction. Renal function impairment has also been associated with a high prevalence of cardiovascular disease (CVD) [2]. Patients with reduced renal function are at high risk for the subsequent development of CVD disease including stroke [3].

Renal dysfunction carries a substantial risk for cardiovascular morbidity and mortality and this was first shown in patients with end stage renal disease. Nowadays it is known that the prevalence of coronary artery disease in patients with end stage renal disease is approximately 40% and mortality due to cardiovascular disease (CVD) in these patients is up to 20 times higher than in the general population. The high prevalence of CVD found in patients starting dialysis treatment suggests that CVD begins in the early stages of CKD. The risk for CVD increases with a decline in kidney function. The hazard ratio for incident CVD was elevated for both markers of renal dysfunction (GFR and albuminuria), independently of each other. Furthermore, the patients with CKD are more likely to die of CVD than to start with replacement therapy because of end stage

Despite atherosclerosis being a systemic disease, attention has centered mainly on cardiac aspects and manifestations. Less is known about the association of renal dysfunction and stroke. In 1998, the National Kidney Foundation convened a Task Force on Cardiovascular Disease in Chronic Renal Disease, members reviewed evidence linking CKD and CVD. They were unable to draw any conclusions about cerebrovascular disease because the literature was scant [6,7].

During the last few decades, clinical and epidemiological studies have indicated that lower glomerular filtration rate (GFR), a marker of chronic kidney disease, is associated with risk of stroke [8]. Evaluating CKD risk in individuals with stroke involves much the same process as in other populations because of the same risk factors [9].a

In population based studies conflicting results have been reported about the association between stroke and CKD before replacement therapy. However, in high risk patients, defined by the presence of either cardiovascular disease or cardiovascular risk factors, different stages of CKD are clearly associated with subsequent stroke. In patients with stroke, the exact prevalence of renal dysfunction is not known. Reported prevalence from a few published studies is up to 38% and it is higher than that in age-matched control groups. Thus, this study was undertaken to determine the prevalence of chronic kidney disease in patients presenting with acute stroke in our setting. Furthermore, in patients suffering from stroke, renal dysfunction is associated with short and long term mortality [10].

Materials And Methods

It was a cross sectional study conducted in a tertiary hospital in Imphal, Manipur during September, 2017 and August, 2019. Acute stroke (both ischemic and haemorrhagic) patient admitted in Medicine Ward of RIMS, Imphal were taken in the study. The exclusion criteria were transient ischemic attack, tumour, head trauma, patients with acute kidney injury and patients unwilling to participate. Stroke was diagnosed based on neurological examination and admission computed tomography scan. (Phillips Brilliance 64 slices CT Axial Scanning with orbital view with slice thickness 3mm, 120 kvp, 250 mA, rotation time 0.8sec). Serum creatinine was measured on admission and during hospitalization (within 48 hours and the last before discharge). (Jaffe's method)

The assessment of renal function was based on the GFR estimated by MDRD equation, where, GFR (mL/min/1.73 m^2) = 186.3× (serum creatinine(mg/dl))-1.154 × (Age)-0.203 × (0.742 if female) × (1.212 if African American)

All cases underwent a comprehensive clinical work up with special emphasis on nephrological problem, relevant laboratory investigations: kidney function test, complete hemogram, liver function test, lipid profile, urinalysis, chest X-ray, electrocardiography, ultrasonography of abdomen, etc. A stroke or cerebrovascular accident is defined as an abrupt onset of a neurological deficit that is attributable to a focal vascular cause. The definition of TIA requires that all neurologic signs and symptoms resolve within 24 hours without evidence of brain infarction on imaging. Stroke has occurred if the neurologic signs and symptoms last for > 24 hours or brain infarction is demonstrated. Chronic Kidney Disease is defined

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as kidney damage (generally ascertained from albuminuria, but also including abnormalities in urine sediment, pathology or imaging studies, acid-base and electrolyte disorders due to tubular disorders, or history of kidney transplantation) or estimated glomerular filtration rate (GFR) less than 60ml/min/1.73m2 for 3 months or more, irrespective of cause and classified into stages according to the level of GFR.

Kidney Disease Improving Global Outcome (KDIGO) classification of CKD:

GFR categories; G1: Normal or high, GFR≥ 90 (ml/min/1.73m2); G2: Mildly decreased, 60- 89 (ml/min/1.73m2); G3a: Mildly to moderately decreased, 45- 59 (ml/min/1.73m2); G3b: Moderately to severely decreased, 30- 44 (ml/min/1.73m2); G4: Severely decreased, 15- 29 (ml/min/1.73m2); G5: Kidney Failure <15 (ml/min/1.73m2). Patients with eGFR< 60ml/min/1.73m2 were labelled as having chronic kidney disease.

Ethics

Approval of the Research Ethics Board of the institute where the study was carried out was taken and informed consent from the participants were obtained. Privacy and confidentiality were maintained.

Statistical Analysis

The data was tabulated in MS Excel and statistical analysis was carried out using SPSS software version 21. Descriptive statistics like mean, standard deviation and proportions were used. Chi-square test and ANOVA were done to check for associations of CKD with other variable of interest. P value less than 0.05 was taken

Results

A total of 200 acute stroke patients admitted in Medicine ward were included in the study. Around 28% of the participants were from the age group of 71 to 80 years followed by 51 to 60 years (23%) and 61 to 70 years (19%). Minimum cases (0.5%) were from the age group 30-40 years. Males were 59% of the cases. 77% of the cases were Hindu followed by 15% Christian. Infarct was the major type of CVA among the patients which constituted 65% of cases. The characteristics of the participants are shown in table *1*.

Table No. 1: Characteristics of the patients with acute stroke (N=200)

Characteristics		Frequency	Percentage
Age in years	30-40	10	0.5
	41-50	26	13.0
	51-60	46	23.0
	61-70	38	19.0
	71-80	56	28.0
	81-90	24	12.0
	Mean ± Standard Deviation		65.2±13.3
Gender	Male	118	59.0
	Female	82	41.0
Religion	Hindu	154	77.0
	Christian		
	Muslim		

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				30	15.0
				16	8.0
Type of CVA		Infarct	130	65.0	
		ICH	70	35.0	
	Total		200	100	

Around 43.5% of the cases were in stage G2, followed by 34% of cases with CKD (eGFR< 60ml/min/1.73m2) and G1 with 22.5%. Among the CKD patients most of them had mildly to moderately decreased GFR (IIIa) followed by moderately to severely decreased GFR (IIIb) and kidney failure (V) as shown in table 2.

Table No. 2: Distribution of the respondents by stages of CKD (N=200)

Sl.no.	Stages of CKD (GFR in ml/min/1.73m2)		Frequency		Percentage	
1.	G1 (≥90)	G1 (GFR ≥90)	45	45	22.5	22.5
2.	G2(60-89)	G2(GFR 60-89)	87	87	43.5	43.5
3.		G3a(GFR 45-59)	26		13.0	
4.		G3b (GFR 30-44)	18		9.0	
5.		G4 (GFR 15-29)	6		3.0	
6.	CKD (GFR<60)	G5 (GFR <15)	18	68	9.0	34.0
7.	Total		200		100.0	

Table 3 shows CKD significantly (p<0.05) associated with higher age group. Gender, smoking, coronary artery disease and dyslipidemia, were not associated with CKD. Hypertension and diabetes were more among patients with GFR ≥60 ml/min/1.73m2 group. Patients with both hypertension and diabetes were seen more in GFR<60 ml/min/1.73m2 group but it was not significant. Collagen vascular disease and alcohol history were more associated with GFR ≥60ml/min/m2 and it was statistically significant. CKD (eGFR< 60ml/min/1.73m2) was significantly associated with atrial fibrillation.

Table No. 3: Demographic, risk factors and clinical characteristics of the patients according to eGFR and their association

Demographic variables	GFR<60 n(%)/ mean±SD	GFR≥60-89 n(%)/ mean±SD	GFR≥90 n(%)/ mean±SD	Total N(%)	p-value
Age (years)	68.97±11.01	66.91±12.7	56.31±14.2	-	0.000
		Sex			
Male	34 (50.0)	55(63.2)	29(64.4)	118(59.0)	

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Female	34(50.0)	32(36.8)	16(35.6)	82(41.0)	0.170
History of					
Hypertension	24(35.3)	53(60.9)	19(42.2)	96(48.0)	0.004
Diabetes	4(5.0)	2(2.3)	4(8.9)	10(5.0)	0.020
Hypertension+ Diabetes	10(14.7)	4(4.6)	4(8.9)	18(9.0)	0.050
Dyslipidemia	26(38.2)	21(24.1)	15(33.3)	62(31.0)	0.158
CAD	8(11.8)	6(6.9)	2(4.4)	16(8.0)	0.32
Collagen vascular disease	2(2.9)	2(2.3)	6(13.3)	10(5.0)	0.014
Smoking	32(47.1)	40(46.0)	24(53.3)	96(48.0)	0.711
Alcohol consumption	30(44.1)	22(44.1)	22(48.9)	74(37.0)	0.009
Clinical presentation					
Infarct	56(82.4)	48(55.2)	26(57.8)	130(65.0)	0.001
ICH	12(17.6)	39(44.8)	19(42.2)	70(35.0)	
Presence of atrial fibrillation					
Yes	22(52.4)	14(16.1)	6(13.3)	42(21.0)	0.017
Total	68(100)	87(100)	45(100.0)	200(100.0)	

Table 4 shows that haemoglobin was lower among CKD group and also statistically significant. TLC, platelet count, triglyceride, cholesterol, LDL and HDL level, serum albumin, blood sugar and serum potassium were not associated with CKD. Serum urea and creatinine were significantly ($p<0.05$) higher among CKD patient. Serum sodium was significantly reduced in CKD patient.

Table No. 4: Distribution of various laboratory findings according to eGFR (N=200)

Investigations	GFR<60 ml/min/1.73m2, mean±SD	GFR 60-89 ml/min/1.73m2 , mean±SD	GFR≥90 ml/min/1.73m2, mean±SD	p- value
Haemoglobin (g/dl)	12.2±2.24	12.4±2.3	13.4±1.6	0.010
Total Leucocyte Count (per microliter)	9115±7133.5	8786.4±2799	8445.6±2862	0.761
Platelet count (lakhs per microliter)	2.1±1.0	2.2±0.6	2.5±0.5	0.059
Urea (mg/dl)	78.8±64.6	29.6±9.6	26.7±9.4	0.000

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Creatinine (mg/dl)	3.05±3.2	0.98±0.13	0.79±0.16	0.000
Cholesterol (mg/dl)	168.2±46.6	161.9±39.7	161.4±41.6	0.600
Triglyceride (mg/dl)	107.1±54.7	88.6±41.6	92.2±49.4	0.053
Low Density Lipoprotein (mg/dl)	108.8±42.0	102.2±39.5	102.2±38.5	0.541
High Density Lipoprotein (mg/dl)	44.11±13.6	45.4±12.7	41.8±13.6	0.313
Serum sodium (mmol/L)	132.8±6.4	135.5±4.2	135.8±3.5	0.002
Serum potassium (mmol/L)	6.8±10.4	4.9±6.4	5.7±8.2	0.361
Fasting blood glucose (mg/dl)	90.3±7.2	104.5±13.2	102.0±0.0	0.079
Blood glucose (Post Prandial) (mg/dl)	128.7±53.7	134.6±40.8	125.5±31.9	0.291
Serum albumin (g/dl)	3.8±4.0	3.2±0.6	2.8±0.5	0.064

Table 5 shows that patient with CKD (GFR<60) was more among infarct group than ICH group and this finding was found to be statistically significant (p<0.05).

Table No. 5: Relation between various stages of CKD with types of CVA (N=200)

Sl.no.	CKD stages	Infarct n(%)	ICH n(%)	N (%)	p-value
1.	G1 and G2	74(56.9)	58(82.9)	132(66.0)	0.000
2.	CKD (G3a, G3b, G4, G5)	56(43.1)	12(17.1)	68(44.0)	
3.	Total	130(100.0)	70(100.0)	200(100.0)	

It is shown in table 6, that 10 cases (5%) was on renal replacement therapy and among the ICH patients, 8.6% had RRT in comparison to 3.1% of inarct patient, but the finding was not significant (p>0.05).

Table No. 6: Association between types of Cerebro Vascular Accident and Renal Replacement Therapy (N=200)

Types of CVA	RRT		Total, N(%)	p-value
	Yes, n(%)	No, n(%)		
Infarct	4(3.1)	126(96.9)	130(100.0)	0.089
ICH	6(8.6)	64(91.4)	70(100.0)	
Total	10(5.0)	190(95.0)	200(100.0)	

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Table 7 shows that, those with GFR< 60ml/min/1.73m2 stayed longer in hospital than higher GFR groups (47% vs. 29.9% vs. 22.2%) and the finding was found to be statistically significant (p<0.05).

Table No. 7: Association between duration of hospital stay and eGFR (N=200)

Duration of hospital stay	GFR<60 ml/min/1.73m2, n(%)	GFR 60-89 ml/min/1.73m2, n(%)	GFR≥90 ml/min/1.73m2, n(%)	Total, N(%)	p value
Upto 7 days	36(52.9)	61(70.1)	35(77.8)	132(66.0)	0.014
>7 days	32(47.1)	26(29.9)	10(22.2)	68(34.0)	
Total	68(100.0)	42(100.0)	90(100.0)	200 (100.0)	

As shown in table 8, among patients with GFR <60ml/min/m2, mortality was more among ICH (33.3% vs. 17.9%) and also in those with GFR 60-89 ml/min/1.73m2 and ≥90 ml/min/m2. The findings were found to be significant (p<0.05). Similarly among infarct patient mortality was more among CKD patient (GFR<60ml/min/m2) and was statistically significant (p-0.01).

Table No. 8: Relation between outcome and eGFR stratified by types of stroke

Outcome	GFR<60 ml/min/1.73m2		GFR 60-89 ml/min/1.73m2		GFR ≥90 ml/min/1.73m2	
	Infarct n(%)	ICH n(%)	Infarct n(%)	ICH n(%)	Infarct n(%)	ICH n(%)
Discharge	40(71.4)	2(16.7)	34(70.8)	19(48.7)	22(84.6)	9(47.4)
Death/mortality	10(17.9)	4(33.3)	0(0.0)	12(30.8)	2(7.7)	6(31.6)
LAMA	6(10.7)	6(50.0)	14(29.2)	8(20.5)	2(7.7)	4(21.1)
Total	56(100.0)	12(100.0)	48(100.0)	39(100.0)	26(100.0)	19(100.0)
p value	0.001		0.000		0.006	

Discussion

Out of the 200 acute stroke patients enrolled in the study, 68 (34%) were having CKD. This finding is similar to the study by Yahalom G et al [11], where CKD was present in 36% of patients based on MDRD equation and 18% based on Mayo Clinic quadratic equation. Tsagalis G et al [3] also found that 28.08% of acute stroke patients presented with moderate or severe renal dysfunction estimated by eGFR. In a study by Chwojnicki et al [12], the prevalence of CKD in post-stroke patients was 40.38%. Thus, CKD is common among acute stroke patient.

On comparing the baseline characteristics of acute stroke patients in this study, patients with CKD was significantly associated more with higher age group. The increasing prevalence of CKD with advanced age has already been reported, and age might reflect

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the progressive development of atherosclerosis. Recent study has shown that advanced age was a major risk factor for CKD and stroke [13]. On further evaluation in this study, mean age of the patients with acute stroke was 65.2 years. In a study by Yahalom et al [11], mean age was 67.6 years. Kissela et al [14] found that mean age at stroke was 69.2 years. These findings suggest that mean age at stroke has declined in recent years. This is of great public health significance because strokes in younger patients carry the potential for greater lifetime burden of disability and more over some potential contributors identified for this trend are modifiable [15]. Males were predominant with 59% of cases compared to females (41%) in this study. Obviagele et al [16] found that prevalence of stroke was 24% to 30% higher in men. This may be due to presence of more risk factors of stroke like hypertension and alcohol consumption in males [17].

It was found from the study that infarct was the major type of CVA among the patients which constituted 65% of cases. ICH was present in 35% of the patients. ICH was more common (71.4% vs. 52.3%) among males and infarct among females (47.7% vs. 28.6%). Although smoking increases the risk of atherosclerotic events in the general population and renal atherosclerotic damage result in a serial decline in renal function, this study fails to show significance of association between smoking and CKD in the patients with stroke. This may be due to the fact that smoking was already a risk factor for stroke and detailed smoking history in terms of quantity and quality were not considered in this study. This study has shown that dyslipidemia was present more in patients with CKD. Results of this study are consistent with those of several other previous studies [18]. As a risk factor, dyslipidemia participate in the process of stroke. Therefore, dyslipidemia which promotes accelerated atherosclerosis is a common risk factor for CKD and stroke. Significant reduction in haemoglobin level was seen in CKD group. TLC, platelet count, Triglyceride, cholesterol, LDL and HDL level, serum albumin, blood sugar and serum potassium were not associated with CKD. Serum urea and creatinine were significantly ($p<0.05$) higher among CKD group. Similarly serum sodium was also significantly reduced in CKD.

In this study, reduced GFR was significantly associated with atrial fibrillation. Yahalom G et al [11] and Tsagalis G et al [3] also found a significant association of chronic kidney disease with atrial fibrillation. Potential mechanisms for the higher burden of AF in CKD include augmented sympathetic tone, activation of the renin-angiotensin-aldosterone system and myocardial remodeling. AF confers an increased risk for both stroke and overall mortality in the CKD population [3].

It was shown that 10 cases (5%) was on renal replacement therapy and more patients on RRT had ICH (8.6%) than infarct (3.1%) but it was insignificant ($p>0.05$). Stroke patient with GFR<60 ml/min/1.73m2 had more mortality than those with GFR 60-89 and GFR≥90 but it was not insignificant ($p>0.05$). LAMA was more in patients with GFR 60-89(25.3%) and GFR <60(17.6%) and lesser in those with GFR≥90ml/min/1.73m2 (13.3%). Those with GFR< 60ml/min/1.73m2 tend to stay longer in the hospital than higher GFR groups (47% vs. 29.9% vs. 22.2%) and the finding is found to be statistically significant ($p<0.05$).

Tsagalis G et al [3] have shown that even a moderate reduction in renal function appeared to be an independent and clinically relevant risk factor for the overall mortality, which was similar to the results of this study. Yahalom et al [11] also indicated that chronic kidney disease in patients with acute stroke was an independent factor for 1-year mortality and an independent predictor for poor outcomes. Husseini NE et al [19] found that among patients hospitalized for stroke, presence of renal dysfunction at admission was associated with increased risks of inpatient mortality and were less likely to be discharged home. Co- existence of adverse conditions, such as anemia, oxidative stress, platelet dysfunction, electrolyte imbalance and hyperhomocysteinemia in patients with CKD have been implicated as the reason why these patients have poorer outcomes compared to the normal population.

In a study conducted by Hao Z et al [20], renal dysfunction was an independent risk factor for death/disability, a further analysis based on different types of stroke indicated that reduced eGFR was an independent predictor of death/disability at the end of 12th month in patients with hemorrhagic stroke. The reasons are unclear and may be opportunistic or due to the role of other confounding factors. It is worth noting that in patients with ICH, the use of mannitol

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to lower intracranial pressure is widely practiced. The dehydrating agent will increase the burden on the kidneys, which suggests that the use of dehydrating agents should strictly be limited in patients with ICH.

This study has some limitations. First of all, this study was cross sectional, and long-term prognosis of patients could not be analysed. A prospective study on the development of CKD in the population with stroke may warrant the results. Secondly, proteinuria is not included in the definition of CKD and patients are assigned to the definition of CKD according to eGFR only. It may be interesting to analyse problem about changes of proteinuria in the population with stroke in the future study. Despite these limitations, those results report the prevalence of CKD according to eGFR stage and show characteristics of risk factors for CKD in the population with acute stroke. Moreover, results have shown the importance of monitoring of renal function and eliminating the risk factors for CKD and decreasing the incidence of CKD in the patients with stroke.

Conclusions

CKD has a high prevalence in a population with acute stroke. Because of the overlap of several risk factors for stroke and CKD, the patients with acute stroke have increased risk of CKD. Therefore, all patients with stroke should be considered at risk of CKD and be aggressively managed for CKD prevention. Moreover, the high prevalence of CKD in population with acute stroke prompts the need for greater public awareness about risks of CKD.

Additional Information

Disclosures

Human subjects: Consent was obtained or waived by all participants in this study. Research Ethics Board, Regional Institute of Medical Sciences issued approval A/206/REB-Comm(SP)/RIMS/2015/289/32/2017.

Approval certificate was obtained before the study and it can be submitted whenever required. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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