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ORIGINAL ARTICLE

Predictors of Ischemic Stroke Among the Patients with end-Stage Renal Disease: A Single Centric Study of Local Population

MUHAMMAD USMAN[1], YASIR HUSSAIN[2], SAJAD AHMAD[3], MUHAMMAD WASIF BAIG[4], TALHA MUNIR[5]
[1]Senior Registrar Nephrology, FMU/DHQ Hospital Faisalabad
[2]Senior Registrar Nephrology, Amiruddin Medical College Lahore General Hospital
[3]Assistant Professor, Fatima Jinnah Medical University, Sir Ganga Ram Hospital, Lahore
[4]Assistant Professor, University Medical and Dental College, Madina Teaching Hospital Faisalabad
[5]Senior Registrar Medicine, Medical Unit 5 FMU/DHQ Hospital Faisalabad
Correspondence to: Muhammad Usman, Email: dr.usmanke@gmail.com, Cell: 03336556415

ABSTRACT

Objective: The incidence of stroke is greater in patients with end-stage renal disease (ESRD) as compared to the general population. It is thought that there may be a few extra risk factors in ESRD patients suffering from stroke as compared to ESRD patients without stroke. This study aims to better understand the risk factors for stroke that are unique to patients with ESRD.

Methods: In order to find out the different causative factors influencing the production of ischemic stroke (IS) in patients with ESRD, we carried out this retrospective study at the DHQ hospital in Faisalabad. In this study total of sixty patients were recruited and further divided into two groups. The first group consisted of 30 patients with ESRD with a history of ischemic stroke, while 30 patients with stroke-free dialysis were selected as the age and gender control group. Patients with and without ischemic stroke were compared in terms of demographic characteristics, stroke risk factors, and lab results.

Results: Patients with acute ischemic stroke had an average age of 56.70 ± 8.87 years with 52% male whereas the non-ischemic stroke group had an average age of 58.9 ± 9.20 years. Small vascular obstruction was found to be the most common subtype of IS (42%), followed by atherosclerosis of large vessels (28%). Compared with patients who did not have a stroke, patients who had a stroke had significantly higher rates of hypertension (HTN), higher systolic (SBP) and diastolic blood pressure (DBP) at admission. The group with a stroke had significantly lower total cholesterol and LDL cholesterol. Lower levels of low-density lipoprotein (LDL) and higher systolic blood pressure were found to be the independent risk factor for an ischemic stroke in a multivariate analysis (OR=1.025, 95% CI p=0.045 and OR=1.458, 95% CI, P=0.03 respectively).

Conclusion: According to the findings of our study, ESRD patients with hypertension and diabetes have a higher chance of ischemic stroke and the lower LDL levels and higher systolic blood pressure were the independent predictors of ischemic stroke.

Keywords: Hemodialysis, Ischemic stroke, risk factors, Hypertension, end stage renal disease,

INTRODUCTION

Stroke is considered one of the debilitating diseases with severe socio-economic consequences (1). In developing countries like Pakistan with limited resources stroke is one of the leading causes of mortality along with cardiovascular disorders and cancer (2). The pathophysiology of chronic renal disease (CKD) shares many common vascular risk factors with that of stroke but involves a different type of terminal artery. As a result, stroke is more likely to occur in CKD patients, especially those with end-stage renal disease (ESRD) (3). Several studies have revealed a 5 to 10 times greater risk of stroke in dialysis patients (4-6). There are several reasons why these CKD patients have an abnormally elevated risk of stroke. The well know contributory risk factors for stroke, such as diabetes (DM), ischemic heart disease (IHD), hypertension (HTN), and previous history of strokes, are much more common found in patients with dialysis than in the general population, as per past research (7). Conventional risk factors appear to explain much, but not all, of the increased incidence of stroke in these individuals.

Atherosclerotic vascular disease, which is caused by uremia itself, may also contribute to rising rates of stroke, and ESRD may also play a role (8). Some stroke risk variables in the ESRD show specific patterns of participation at the onset of stroke. The most significant risk factor for stroke in recent studies is reported hypertension (9, 10). In individuals with ESRD, there is still no definitive evidence about the impact of lipids on stroke. Atorvastatin was not reliable in preventing strokes in patients undergoing hemodialysis (HD). Although dialysis patients have a greater incidence of stroke than the general population, the risk factor unique to this population is not fully recognized (11, 12). Compared to stroke-free ESRD patients, those with a stroke may have additional risk factors. Furthermore, it is well documented that individuals with ESRD who experience strokes have unusual clinical characteristics and laboratory results (11).

The purpose of this study was to determine the association of risk factors with stroke in hemodialysis patients. By identifying risk factors, we can prevent a stroke from occurring by controlling the modifiable risk factors.

METHODOLOGY

This retrospective case-control study included a total of sixty patients. The study was conducted at the nephrology ward of DHQ hospital Faisalabad for a period of two years from September 2019 to August 2021 after the approval of the ethical review board of the hospital. The sixty participants were divided into two groups. The first group (Group IS) consisted of diagnosed patients with ischemic stroke (IS) undergoing maintenance dialysis. In the second control group (Group C) thirty age and sex-matched patients were recruited who were on dialysis but did not have a history of stroke. Magnetic resonance imaging (MRI) was used to get the IS diagnosis. More than one neurologist was involved in the diagnosis, classification, and assessment of the neurological severity of IS. Computed tomography (CT) was employed when MRI was not recommended. The clinical diagnosis was made correctly by neurological symptoms and the exclusion of other disorders if the MRI and CT scans were weak or negative.

Both groups' anthropometric characteristics, laboratory findings, clinical characteristics (retinal disease cause, medication and length of dialysis) along with other measurements, including BMI, haemoglobin, albumin levels, creatinine, blood urea nitrogen, lipid profiles and initial blood pressure, were assessed.

The mean, standard deviation and median were used for all data. Chi-square and the independent t-test were used to evaluate the significance of the variance. In order to identify the distinct causes of stroke evolution in patients with ESRD, we also performed logistic regression analysis. P values less than 0.05 or lower were assessed as significant.

RESULTS

A total of 298 hemodialysis patients were screened during the recruitment period. Thirty of them suffered an acute ischemic stroke with ESRD. Every patient with ESRD had been receiving hemodialysis (HD). In the control group, thirty ESRD patients were selected who had no stroke and were on maintenance HD.

Table 1 displays the demographic characteristics of the two ESRD groups (stroke vs. non-stroke). Males made up 52 percent

of the stroke group, with a mean age of 56.70 ± 8.87 years (range: 48-64 years).

Table 1: Demographic variables of both groups:

Variables	Group IS (N=30	Group C (N=30)	P-Value
Age (Years)	56.70 ± 8.87	58.9 ± 9.20	0.54
Age >60 Years (%)	13 (43)	14 (46)	0.09
Male Gender (%)	19 (62)	18 (59)	0.62
Duration Of Dialysis (Years)	3.8±2.10	2.90±2.60	0.89
Weight (Kg)	71.58±6.82	59.84±7.21	0.19
BMI (Kg/m2)	24.21±2.78	22.68±3.21	0.22
SBP At Admission (mm Hg)	162.20±28.50	142.60±22.85	0.01*
DBP At Admission (mm Hg)	92.5±21.00	84.20±8.50	0.003*
Smoking (%)	4 (13)	5 (16)	0.64
Hypertension (%)	28 (94)	22 (74)	0.012*
Diabetes Mellitus (%)	23 (76)	16 (52)	0.03*
Dyslipidemia (%)	13 (42)	14 (46)	0.82
Cardiac Embolism (%)	2 (6)	0 (0)	0.077

The presence of both hypertension and diabetes (n=17) was the most frequent factor identified in the IS group, followed by hypertension (n=11) and diabetes (n=6). Analysis revealed that the proportion of diabetic and hypertensive individuals in the IS group was considerably higher (p=0.012 and 0.03 respectively). Percentage of patients who received aspirin, statins and other antihypertensive medications did not differ between the groups. (Figure 1).

Systolic and diastolic blood pressure at baseline and history of hypertension were statistically different between the two groups. Systolic and diastolic blood pressure was higher in patients with a stroke at the time of admission to the hospital than in patients without a stroke (p=0.01 and 0.003, respectively).

Total serum cholesterol levels (p=0.03) and serum low density lipoprotein (LDL) values were also considerably lower in the ischemic stroke group (p=0.002). Other laboratory variables did not produce any notable variations (Table 2).

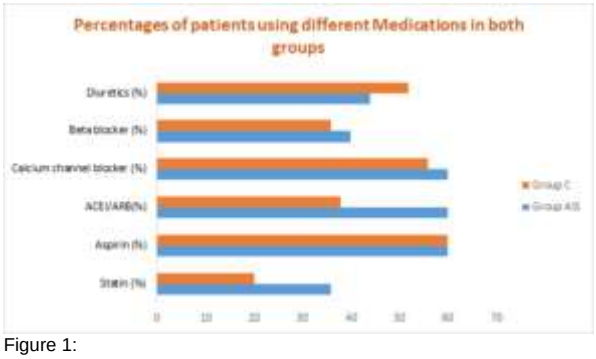

Figure 1:

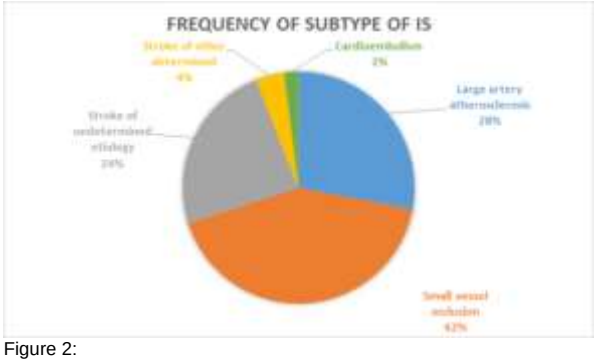

Figure 2:

To examine the association between different ESRD features and the likelihood of developing a stroke, we employed multivariate logistic regression analysis. The risk variables for stroke incidence were higher systolic blood pressure and lower LDL cholesterol levels (OR=1.025, 95 percent CI, p=0.045 and OR=1.458, 95 percent CI, p=0.03, respectively) (Table 3).

It showed a reverse link between the likelihood of stroke and LDL cholesterol levels when compared to the general population, even if the connection's minor statistical significance lessened its therapeutic value. The radiological characteristics of infarctions in ESRD are shown in Figure 2. Small vascular occlusion (42 percent) and big vessels atherosclerosis were the two most prevalent subtypes of ischemic stroke (28 percent)

Table 2: Comparison of lab data between ESRD patients with and without ischemic stroke.

	Group IS (N=30)	Group C (N=30)	P-Value
WBC (x 10^3mm^3)	8.4±3.2	7.9±3.6	0.59
Hb (g/dL)	9.65±1.24	9.89±1.10	0.62
Hematocrit (%)	29.09±3.96	28.62±3.15	0.26
Total calcium levels (mg/dl)	7.8±2.12	7.6±1.98	0.51
Total cholesterol (mg/dL)	154.53±28.50	189.28±41.55	0.03*
HDL-cholesterol (mg/dL)	33.21±11.42	35.90±12.02	0.95
Triglyceride (mg/dL)	142.20±54.26	145.57±94.25	0.82
LDL-cholesterol (mg/dL)	67.54±28.69	101.12±32.54	0.002*
aPTT (sec)	36.84±5.46	34.21±7.28	0.81
INR	1.21±0.09	1.02±0.11	0.23
FBS (mg/dL)	144.62±47.56	164.54±62.60	0.092
HbA1C (%)	6.96±1.22	6.45±1.68	0.28
Albumin levels (g/dL)	3.24±0.44	3.78±0.74	0.48
Total protein/TP(g/dL)	6.68±0.47	6.46±0.42	0.77
BUN (mg/dL)	68.89±49.42	72.26±39.69	0.11
Creatinine (mg/dL)	6.88±4.78	7.12±3.78	0.86
WBC= White blood cell, INR= International Normalizing Ratio, FBS=Fasting blood sugar, BUN= Blood urea nitrogen, Hb= Hemoglobin			

Table-3: Multivariate logistic regression:

Variables	Odds ratio	(95% CI)	p value
Age >60 (years)	1.005	(0.326-4.238)	0.49
Duration of dialysis	1.234	(1.225-1.545)	0.064
SBP at admission	1.458	(0.548-1.568)	0.03*
DBP at admission	0.965	(0.689-5.214)	0.52
Total cholesterol	0.854	(0.425-1.102)	0.124
LDL-cholesterol	1.025	(0.758-0.998)	0.045*

DISCUSSION

The medical data from the nephrology division at the DHQ Faisalabad Hospital served as the basis for this investigation. Despite the fact that earlier studies on HD patients have focused on their greater percentage of stroke, compared to the general population, including cerebral hemorrhage. In addition to trying to identify the independent variables that may influence the onset of an ischemic stroke in ESRD patients, we looked at the risk factors for cerebral infarction in those individuals. Since various factors are recognized that can contribute in the development of stroke regardless of the nature of stroke i,e either ischemic or hemorrhagic in nature. In the current analyses we only included ischemic stroke patients with ESRD.

In the present study, stroke patients had higher entry systolic/diastolic blood pressure and a substantially more common history of elevated blood pressure. Although stroke itself may be the reason for the higher initial blood pressure among stroke patients. The common history of high blood pressure in the stroke group suggests that high blood pressure is an important factor for ischemic stroke in ESRD patients (13). This is in line with statistics from the general population, which have demonstrated a link between high blood pressure and an increased risk of stroke (14). Our study's statistical analysis also revealed that the ischemic group had much more hypertension than the nonischemic group.

Our findings show that they are distinct from earlier publications and overlap with them. According to the CHOICE

research, prior strokes, diabetes, concomitant illnesses, age, and race all raised the risk of cerebrovascular events (15).

According to a Japanese study, assaults on the vertebrate basilar system are far more common (16). Contrary to Japanese research that claimed a considerably greater incidence of strokes in the vertebrobasilar system, our examination found that stroke events were more common in the areas serviced by the anterior circulation. The HSR showed that posterior circulation ischemic strokes were less frequent in the general population (39.8%) (17).

Contrary to the overall population result of the HSR, SVO was the most common subtype of stroke. The LAA and SVO varieties were the two that were most common in the HSR. As was previously indicated, ESRD patients' small arteries may have undergone microinflammatory changes as a result of malnutrition, which might account for this gap (17).

In our study, persons who experienced ischemic strokes had lower total and LDL cholesterol levels. This goes against conventional population studies. According to various studies, low LDL cholesterol may be connected to the emergence of cerebral hemorrhage, whereas high LDL cholesterol may be related to an increased risk of ischemic stroke (18, 19). Therefore, the basic mechanism is still unclear.

Because low cholesterol likely compromises the integrity of endothelial cells in the microscopic brain capillaries, hemorrhagic strokes can occur more often (20). Low LDL cholesterol in dialyzed individuals has no known connection to ischemic stroke. Malnutrition and persistent inflammation affect a significant portion of ESRD patients (21). The relationship between malnutrition and stroke seen in the current study might thus be explained by the same mechanism that causes inflammation and stroke in the general population as well as those who get dialysis. In contrast, none of the inflammatory symptoms were linked in the CHOICE study to an increased risk of stroke (17).

The positive correlation between blood pressure and ischemic stroke must be interpreted with caution. The use of anti-hypertensive drugs may have obscured the effects of blood pressure (22). However, in our study, both patient groups received regular dialysis and shared comparable perspectives on how to manage hypertension. Elevated systolic and diastolic blood bp in the stroke group may be due to the stroke itself, but when analyzing the relationship between high blood pressure and ischemic stroke in ESRD patients, a more recurrent history of hypertension could be more important. Risk factors should be addressed in all people that have had an ischemic stroke.

According to the 2011 American Heart Association/American Stroke Association guidelines, ischemic stroke patients should take statins, antiplatelet drugs, and decrease their blood pressure. In persons with hyperlipidemia, treatment with statins lowers their risk of stroke, although high cholesterol on its own is not a significant risk factor for stroke (23). Therefore, it is possible that statins' protective effects are brought about less by their ability to decrease cholesterol and more by their capacity to prevent atherothrombosis (24). Other methods include quitting smoking, giving myocardial embolism patients oral anticoagulation, controlling their blood sugar levels if they have diabetes, and having an endarterectomy if they have carotid artery stenosis. The prevention of stroke in those with chronic renal disease is not advised, nevertheless (25). Due to a higher risk of hemorrhagic stroke, warfarin should be used with extreme caution, especially in hemodialysis patients (16).

Our investigation has several limitations. We were unable to conduct a well-controlled blind trial due to the survey's retrospective approach. In addition, the limited patient sample size may preclude the conclusion that LDL cholesterol protects against stroke in patients with ESRD. In addition, we have not evaluated inflammatory biomarkers such as interleukin 6 and high sensitivity C-reactive protein. To arrive at more relevant findings in the future, well-controlled prospective research with a large population of subjects should be conducted.

CONCLUSION

We discovered that individuals with ESRD who have a history of hypertension and have greater systolic/diastolic blood pressure significantly increase their risk of developing an ischemic stroke. Specifically, the independent risk factor for ischemic stroke was low in LDL and total cholesterol. In our ESRD patients, the stroke subtype categorization also favors small vessel disease, displaying a distinct pattern from the general population.

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