Association of Atrial Fibrillation with Age, Gender, Hypertension, and Diabetes Mellitus in Cases of Ischemic Stroke

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ABSTRACT

Objective: To determine the frequency of atrial fibrillation in patients presenting with ischemic stroke and explore association of atrial fibrillation with age, gender, diabetes mellitus, and hypertension.

Study Design: Cross-sectional analytical study

Place and Duration of Study: Department of Internal Medicine, Pak-Emirates Military Hospital, Rawalpindi Pakistan, from Jan to Sep 2018.

Methodology: All patients diagnosed with ischemic strokes as per the World Health Organization guidelines presenting to the department were included. Information was gathered regarding age, gender, hypertension, and diabetes mellitus and electrocardiogram was recorded for each patient within 24 hours of presentation to check for atrial fibrillation. Computed tomographic scans of the sampled individuals were evaluated to exclude patients with intracerebral bleed, sub-arachnoid hemorrhage or brain tumors.

Results: Ninety-five patients (mean age: 46.8±15.5 years) with ischemic stroke were included. Sixty (63.2%) patients were male and 35(36.8%) were female. Atrial fibrillation was present in 35(36.8%) patients. It was significantly more common in patients with diabetes and patients with hypertension (p=0.001 and p=0.004 respectively). No significant association of atrial fibrillation with gender or age of the patient was observed (p=0.086 and p=0.057 respectively)

Conclusion: Atrial fibrillation was quite high in our sampled patients with ischemic stroke. The frequency was more common in patients with diabetes and patients with hypertension.

Keywords: Age-dependence, Atrial fibrillation, Diabetes mellitus, Electrocardiogram, Hypertension, Ischemic stroke, Risk factors.

INTRODUCTION

Stroke comes in the second place among the diseases that are responsible for death of humankind around the globe.[1] Around 5.5 million people die of stroke every year.[1] Among the people who survive a stroke event, nearly half of them end up in permanent disability. Thus, stroke is a public health concern of huge importance with everlasting physical, functional, financial, and social consequences. The public health burden of stroke is anticipated to increase over future decades due to increasing incidence of risk factors related to stroke development, particularly in developing countries.[2]

Most strokes are caused by occlusion of blood vessels supplying blood to the brain parenchyma. This occlusion can be a result of local thrombosis or embolization from heart or carotid vessels. As expected, stasis of blood in heart chambers like the one occurring in atrial fibrillation (AF) can lead to thrombus formation and these thrombi can then dislodge and act as emboli for the cerebral blood vessels.[3]

Atrial fibrillation gets the major chunk of attention amongst cardiac arrhythmias primarily because of its common occurrence in clinical practice. This commonly occurring arrhythmia is a consequence of electrical discharge from multiple excitatory foci in the atria, which lead to erratic and incomplete contraction of atrial chambers, thus leading to stasis and irregular rhythm of the heart.[4] Not surprisingly, this abnormal rhythm of the heart is often implicated in the occlusion of cerebral blood vessels leading to what we know as cerebrovascular accident or stroke. AF is thus one of the major risk factors leading to ischemic strokes.[5-7] The presence of AF in stroke patients has been linked with many risk factors including hypertension, diabetes mellitus (DM), age, and gender.[8]

There are few studies in Pakistan that have explored the prevalence of AF in patients presenting with ischemic stroke. In one of the studies, AF was reported

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in 41.5% of the elderly patients of stroke whereas another study reported AF in 5% cases of ischemic stroke.[5,9] However, the data regarding risk factors in the presence of AF in stroke patients is deficient. Only one study has explored the risk factors associated with AF in stroke patients.[5] The purpose of this study was to find the percentage of patients in whom AF is implicated in the development of first ischemic stroke and discover implications of age, gender, and comorbidities like DM and hypertension on the frequency of AF. With this study, the association of risk factors with stroke in presence of AF could be truly appreciated in our health care setups and this would help in giving recommendations regarding screening for AF and earlier mentioned risk factors in specific patients with stroke.

METHODOLOGY

The cross-sectional analytical study was carried out at the Department of Internal Medicine, Pak-Emirates Military Hospital, Rawalpindi Pakistan, from January to September 2018. A minimum sample of 73 was calculated according to the World Health Organization (WHO) sample size calculator. The anticipated population proportion was taken as 0.059 and the confidence level was kept at 95%.

Inclusion Criteria: Patients of age 12-80 years belonging to both genders diagnosed with ischemic stroke were included.

Exclusion Criteria: Patients having evidence or history of structural/valvular heart disease were excluded. All patients underwent computed tomographic scan of the brain without contrast. The scans were reviewed by a consultant radiologist. After the scan, all patients with evidence of intracerebral bleed, sub-arachnoid hemorrhage or brain tumors were excluded.

Permission from the ethical review committee (Ltr no: 8039/2/2017) was taken. The diagnosis of stroke was made based on the definition given by WHO that defines stroke as a rapidly progressing focal or global disturbance of cerebral function rooting from vascular problems lasting for ≥ 24 hours or leading to death.[1] Study participants or their next of kin were informed about the purpose, procedures, and importance of the study. Written consent was taken from each participant and/or the next of kin. Ninety-nine patients who fulfilled the inclusion criteria were enrolled in the study. Relevant history was documented along with all valid medical record and demographic data like age and gender. Computed tomographic scans were carried out in the Diagnostic Radiology Department of Pak Emirates Military Hospital or any other radiology center and evaluated by a consultant radiologist for exclusion criteria. Four patients were excluded after exclusion through computed tomographic scan. Electrocardiogram was recorded for each patient within 24 hours of presentation through a standard and calibrated machine and presence of AF was confirmed and reported by an internal medicine consultant. Patients were considered to have hypertension if they either had a blood pressure measurement of ≥140mmHg systolic and ≥90mmHg diastolic at two separate occasions, or were currently using antihypertensive medications.[10] DM was diagnosed if fasting blood glucose was ≥126mg/dL (7.0mmol/L) or 2 hours post load glucose was ≥200mg/dL (11.1mmol/L) during an Oral Glucose Tolerance Test, or the patient was currently using anti-diabetic medications.[10] The whole information was recorded on a pre-designed proforma.

Statistical package for Social Sciences (SPSS version 21) was used to record and analyze the gathered data. Means and standard deviations were calculated for age. Frequencies were calculated for AF, gender, hypertension, and DM. Based on age, two groups were generated i.e. age ≤50 years and age >50 years. Chi-square test was applied and p-value ≤0.05 was taken as significant.

RESULTS

Table: correlation of different target variables with atrial fibrillation (n=95)

Variables	Atrial fibrillations		p-value
	Present n(%)	Absent n(%)	
Age group			
Age ≤50 years	17(17.89%)	41(43.15%)	0.057
Age >50 years	18(18.94%)	19(20%)	
Gender			
Male	26(27.36%)	34(35.78%)	0.086
Female	9(9.47%)	26(27.36%)	
Diabetes Mellitus			
Yes	23(24.21%)	19(20%)	0.001
No	12(12.63%)	41(43.15%)	
Hypertension			
Yes	24(24.48%)	23(23.46%)	0.004
No	11(11.57%)	37(38.94%)	

Ninety-five patients with ischemic stroke were finally selected to conduct this study. Sixty patients (63.2%) were male and 35(36.8%) patients were female. The mean age was 46.8±15.5 years (range 18-70 years). Fifty-eight (61.1%) patients were ≤50 years of age while 37(38.9%) were >50 years of age. Forty-two (44.2%) patients had DM and 47(49.5%) patients had hypertension. AF on electrocardiogram was present in 35 (36.8%) patients. Evaluation of AF in relation to age

group, gender, DM, and hypertension revealed that AF was significantly more common in patients with diabetes and patients with hypertension (p=0.001 and p=0.004 respectively, shown in abve mentioned Table). No significant association of AF with gender or age of the patient was observed (p=0.086 and p=0.057 respectively).

DISCUSSION

The stroke in Pakistan has an incidence of 95 per 100,000 persons per year adjusted for age and gender.[11] Studies in Pakistan have also tried to identify and quantify the risk factors linked with development of stroke. Atrial fibrillation is one of the major risk factors associated with ischemic strokes identified in some Pakistani studies. The frequency of AF shows a variation when different localities in Pakistan are studied. From Sindh province, Aquil *et al.* and Taj *et al.* have reported a frequency of 5% and 7.6% in acute ischemic strokes.[9,10] Three studies from Khyber Pakhtunkhwa have reported prevalence of 4.8%, 22%, and 3.31%,[4,6,12] respectively representing population groups from Peshawar. From Islamabad, a study has reported a frequency of 13.1%,[13] and from Azad Jammu and Kashmir; the reported prevalence is 11.2%.[14] This variation probably has resulted from varied sampling techniques. Internationally also, there is a variation in the prevalence of AF across different geographical regions. An American study observed a prevalence of 18.2% in 930010 patients admitted with acute ischemic stroke across 45 states from 2003 to 2014.[15] An Indian study noticed a prevalence of 25.2%,[16] while a systematic review of the epidemiology of AF in regions outside North America and Europe reported a prevalence of AF in a range of 2.8%-14% in different hospital based studies.[17]

Regarding the other common risk factors, we found that 44.2% of our cohort had DM and 49.5% had hypertension. Other Pakistani studies have found a prevalence of 16.6%, 40.3%, 32.7%, 38.6%, and 49% respectively for DM and a prevalence of 76%, 78%, 55.45%, 62.7%, and 85% respectively for hypertension in their sampled individuals.[9,10,12-14] Hypertension can increase the risk of stroke by two folds whereas as a 1.7 fold increase has been associated with DM for stroke development.[8] Hypertension and DM are not only the independent risk factors for development of stroke,[18] they also fortify the pathological process of stroke through promotion of AF. In one study, hypertension and DM were observed to independently increase the chances of stroke by 1.5–3.0% and 2.0–3.5% per year in

a cohort of AF patients that did not receive any anticoagulant.[18] Another study identified hypertension and DM as the common risk factors for AF besides advanced age, obesity, hyperthyroidism, smoking, obstructive sleep apnea, and abuse of alcohol or drugs.[19] We also observed hypertension and DM to be strongly associated with AF in stroke patients. DM is believed to exert its negative effect through acceleration of atherosclerosis resulting in structural, electrical, and autonomic remodeling ultimately increasing arrhythmogenicity.[18]

Advanced age is an effective independent risk factor for stroke in AF patients. In a systematic review, eight of thirteen studies found increasing age to be significantly associated with stroke.[8] The risk of stroke increased by 1.5-fold every decade for patients with AF.[8] A designed study with AF as a lone risk factor for stroke development found that the stroke incidence significantly increased with age especially after 60 years.[18] An earlier Pakistani study,[5] has documented that AF in stroke survivors is independently associated with age and the incidence is directly proportion to the advancing age. The statistical analysis of AF with advanced age though did not yield significant results in our study. Supporting our study, a review of Pakistani studies notified that the studies showing a higher percentage of AF (41.5%, 13.3%, and 11.2% respectively) had sampled patients with mean ages (age >50 years, 60±11 years, and 63.8±10 years respectively),[5,6,8] that were not significantly different from studies that recruited patients with similar or relatively older mean age patients (66.74 years, 63.4%, and 60 years respectively) but showed a smaller percentage of AF i.e. 4.8%, 5%, and 3.3% respectively.[4,9,12] Thus, based on Pakistani data of stroke survivors, advancing age alone cannot be attributed as independent risk factor for stroke development in Pakistani patients with AF.

Female gender is considered an independent risk factor in AF patients for the development of stroke.[8] In a systematic review, half of the studies evaluating gender as a potential risk factor for stroke endorsed female gender as a probable vulnerability.[20] This threat is more evident after menopause, when estrogen levels drop in blood. The estrogen deficiency affects lipid metabolism, promotes inflammatory % pro-coagulant markers, remodels left ventricle, and accelerates development of hypertension and thromboembolism,[18] all contributing to stroke progress. In our study, quite the opposite, we could not find any association of gender with AF frequency. Similar observation was made by an earlier Pakistani study.[7]

Stroke may be the first indicator of previously undetected AF, and the risk of stroke remains the same in presence or absence of AF symptoms.[21] Therefore, all patients with stroke must undergo electrocardiography as a screening tool for AF. Sometimes, the AF has a paroxysmal course and is missed during routine electrocardiography. In such circumstances, more meticulous monitoring of heart rhythm with ambulatory devices such as Holter monitor, Zio patch or insertable loop recorder is recommended.[22] After the confirmation of AF, echocardiography, chest radiographs, and estimation of cardiac biomarkers and B-type natriuretic peptide is suggested to look for other cardiac diseases associated with AF e.g. ischemic heart disease, valvular heart disease, and cardiomyopathy.[21] Chest radiographs, may not diagnose AF, but may show evidence of congestive heart failure, aside from signs of lung or vascular pathology (e.g. chronic obstructive pulmonary disease, pneumonia, and pulmonary embolism,). Additional testing for non-cardiac diseases associated with AF such as hyperthyroidism, may be suggested by the presence of risk factors and associated comorbidities.

Once diagnosed, AF needs prompt treatment. People without treatment or with inadequate treatment usually land up in hospitals with some thromboembolic potentially life-threatening complication the most important being stroke and heart failure. Treatment of AF thus is the most important preventive strategy to save life of the affected individual. The goals of treatment in AF are management of abnormal heart rate or rhythm and reduction in clotting ability of blood.[22] Anticoagulants or antiplatelets used for the treatment purpose are very helpful but may increase the risk of bleeding and significant disability or death may ensue. These complications are avoided by intelligent decision making through risk stratification for both stroke and bleeding.[23] Stroke risk stratification tools include the CHADS2 and the CHA2DS2-VASc scores,[24] while HAS-BLED,[22,23] is a bleeding risk stratification scoring system. There are some non-pharmacological approaches that may also help in prevention. Regular exercise, eating heart healthy foods, maintaining optimal body mass index, and avoidance of smoking and alcohol are the time-tested approaches.

Cardioembolic strokes are associated with high morbidity and mortality because they involve larger or multiple cerebral vascular territories.[25] The risk of early secondary hemorrhage is also very high. The findings of the present study endorse essential screening of stroke patients for AF. Furthermore, this study also reinforces the importance of DM and hypertension in risk stratification for AF in stroke patients.

CONCLUSION

AF frequency was quite high in our sampled patients with ischemic stroke. The frequency was more common in patients with DM and patients with hypertension. No association with gender or age of the patient was observed.

Conflict of Interest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

AP: Study design, drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

SBA: Data acquisition, data analysis, approval of the final version to be published.

MA: Critical review, concept, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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