

ATRIAL FIBRILLATION & STROKE; HAS ANTITHROMBOTIC PROPHYLAXIS CHANGED THE MODE OF PRESENTATION FROM ISCHAEMIC TO HEMORRHAGIC ?

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ABSTRACT

Background: Both atrial fibrillation and stroke are common disorders. Untreated AF can complicate ischaemic stroke. Prophylactic antithrombotics for AF has the potential of causing haemorrhagic strokes.

Aim & Objective: To determine the frequency of the type of stroke in patients with atrial fibrillation on/not on antithrombotic prophylaxis.

Place and Duration: Medical A Unit, Hayatabad Medical Complex, Peshawar, Pakistan, from 8th Feb 2011 to 8th Feb 2012.

Subjects & Methods: This descriptive study was conducted on admitted pts from both genders above age 18 who had atrial fibrillation and stroke. After obtaining a detailed history and conducting a thorough clinical examination, a long lead ECG and CT Scan were advised to all those who clinically had AF and features of stroke whether on antithrombotic prophylaxis or not on such measures. All these informations were entered in a printed proforma which later on was analysed through spss.

Results: A total of 78 patients with AF and stroke irrespective of whether on or off antithrombotic agents were studied for the type of stroke (hemorrhagic or non hemorrhagic). Fourteen {14(17.4%)} had hemorrhagic strokes and 64(82.5%) had nonhemorrhagic strokes. Twentyeight {28(35.89%)} were on antithrombotics while 50(64.1%) had no h/o intake of antithrombotic agents. Out of 14 pts with hemorrhagic stroke 7 were on antithrombotic agents while 7 had no such a history. Out of 64 pts with nonhemorrhagic stroke 21 were on antithrombotic agents while 43 were not on such agents.

Conclusion: Overall still in patients with atrial fibrillation the frequency of ischemic strokes is more than the hemorrhagic strokes even if antithrombotic prophylaxis with its tendency to cause hemorrhagic phenomena is taken into consideration.

INTRODUCTION

Stroke is the third commonest cause of death and the first leading cause of disability in developed and developing countries¹. Ischaemic strokes are most common as about 70-80 percent of strokes are due to blood clots. Clots can form in the arteries supplying the brain, or can come from some other part of the body. Most of the clots that come from other parts of the body are formed during atrial fibrillation². Each year, about 700,000 people have a stroke in the U.S., with about 500,000 being first attacks³. About every 45 seconds someone in the U.S. has a stroke³.

About 35% of AF patients will have a stroke during their lifetime⁴. AF increases with age, doubling each decade after age 55⁴. Over 90% of strokes due to blood clots originating in other parts of the body come from clots formed in the left atrial appendage⁵.

According to World Health Organization estimates, 5.5 million people died of stroke in 2002, and

roughly 20% of these deaths occurred in South Asia⁶. The incidence of the disease in the Western population has decreased but the burden of the disease in South Asian countries (India, Pakistan, Bangladesh, and Sri Lanka) has increased and is expected to rise⁷.

The true incidence of stroke in Pakistan is not known as large scale epidemiological studies are not available. Estimated annual incidence is 250/100,000, translating to 350,000 new cases every year⁸. At a major University hospital with a busy Neurology service in Karachi, 519 patients with stroke were admitted over a 22 month period⁹. In a retrospective analysis of patients admitted with stroke in two major hospitals over an 8 years period, 796/12,454 (6.4%) of consecutive cases admitted in medical units had stroke¹⁰. A community survey in Kolkata, carried out by the Indian Council of Medical Research, showed the average annual incidence of stroke as 145 per 100,000 persons per year¹¹. In China, the total average age-adjusted incidence of first-ever stroke ranged from 116 to 219 per 100 000 per year¹².

Rheumatic heart disease is an important cause of embolic vascular events including strokes in developing countries. In a community based study from rural Pakistan, a prevalence of approximately 6/1000 was observed¹⁶.

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In hospital-based studies, 22-31% of patients had intracerebral haemorrhage (ICH).^{9,10,14,15,17} A higher figure is reported in young stroke patients (32-43%)¹³. Khealani et al reported that in hypertensive patients, diabetes mellitus and ischaemic heart disease are independent predictors of ischaemic stroke¹⁸.

One study reported ischaemic stroke subtypes in patients prospectively enrolled in the Aga Khan University acute stroke data bank. The ischaemic stroke group comprised of lacunar 168/393 (42.7%); large artery atherosclerosis 106/393 (26.9%); cardioembolic 24/393 (6.1%); undetermined 80/393 (20.3%); and other determined types 15/393 (3.8%)⁹.

Atrial fibrillation carries a substantial mortality and morbidity from stroke, thromboembolism, and heart failure, and a significant impairment of quality of life¹⁹⁻²⁰. The prevalence of AF increases markedly with older age²¹⁻²², about 5% of people over 65 years and 10% of people age \geq 80 years suffer from AF²².

AF is a major risk factor for stroke, increasing the risk of ischemic stroke by approximately 5-fold, with approximately 15% of all strokes in the U.S. being attributable to AF²³. As mentioned already age is also a risk factor for stroke, with the lifetime probability of suffering a stroke increasing steadily with age, from 5.9% at 55 to 59 years, to 22.3% at 80 to 84 years in men, and from 3.0% to 23.9% over this age range in women¹⁹. Therefore, the combination of increasing age and AF means that stroke prevention in elderly people with AF must be a priority.

Stroke prevention in pts with AF certainly needs attention but unmonitored antithrombotic agents can result in cerebral haemorrhage. Who should be advised these agents and who should not be, depends not only on the presence of AF but other factors also need consideration. Scoring systems eg CHAD SS can provide a guideline in such situations.

Since in our set up lab facilities for monitoring INR are insufficient physicians are reluctant to advise oral anticoagulants. Where lab facilities are available physicians do advise OAC and with this the number of pts on these agents are increasing. With these changing trends it needs to be known whether such practices have reduced the frequency of ischemic strokes or has increased the frequency of hemorrhagic strokes or otherwise.

Exclusion criteria; All those cases having intracranial space occupying lesion, myeloproliferative disorders, aplastic anemia, acute leukemia, bleeding and clotting disorders (not antiplatelets and or anticoagulants induced) head trauma and stroke without AF were excluded.

Inclusion criteria; Pts having stroke and AF, between age 18 and above and not having the above exclusion criteria were included.

Study setting; Hayat Abad Medical Complex Medical A Unit

Duration Of Study; 1 year (from 8th Feb 2011 to 8th Feb 2012).

RESULTS

A total of 78 pts with AF and stroke irrespective of whether on or off antithrombotic agents were studied for the frequency of the type of stroke (hemorrhagic or non hemorrhagic).

Data was analyzed through SPSS 16.

Table 1 shows the statistics regarding age with a Mean age of 56.29 years. A histogram is also given in figure 1.

Statistics of CT scan brain findings are given in Table 2 and bar chart 1.

Table 3 shows the frequencies and percentages of the antithrombotic agents.

Table 4 and 5 shows the summarized forms of percentages of the type of stroke and the type of antithrombotic agents respectively.

Table 6 shows the CT brain findings in different age groups.

DISCUSSION

Seventy eight (78) patients presenting to medical A unit with stroke and atrial fibrillation irrespective of antithrombotic agents were studied for the frequency of the type of stroke (hemorrhagic or non hemorrhagic). The minimum age was 18 years and maximum 90 years, with a mean age of 56.29 years. Atrial fibrillation is of diverse etiology, with some causes more common in one age group and some in other. Whatever is the cause of AF it predisposes to thromboembolic phenomena. In our study pts from all age groups were represented. 9 pts were below age 40 and in all of them only non hemorrhagic stroke was observed. All 14 pts with hemorrhagic strokes were above 40.

Of the total 78 pts, 14 (17.94%) were found to have hemorrhagic stroke with half of them already on antithrombotic agents while the rest half were not on any such agent. Among pts on antithrombotic agents, four (4) were on warfarin and three (3) on aspirin. Thus from the data it is clear that AF pts on antithrombotic agents can present with both types of stroke.

Sixty four (82.05%) of our pts had non hemorrhagic stroke. Overall the frequency of ischaemic stroke is more than hemorrhagic stroke and the same was observed in our study. However we included pts on antithrombotic agents in our study & thus were expecting more cases of hemorrhagic strokes. One possible explanation for finding more ischemic strokes than hemorrhagic in our study was the small number of pts

Table 1-A: Frequencies Statistics

Age		
N	Valid	78
	Missing	0
Mean		56.2949
Median		58.5000
Mode		49.00
Std. Deviation		1.57827E1

Table-1 B: Descriptive Statistics

	N	Mini- mum	Maxi- mum	Mean	Std. Devi- ation
Age	78	18.00	90.00	56.2949	15.78270
Valid N (list- wise)	78				

Table 2: Statistics CT Scan findings

N	Valid	78
	Missing	0

		Fre- quency	Per- cent	Valid Per- cent	Cumu- lative Percent
Valid	Hemor- rhage	14	17.9	17.9	17.9
	Infract	40	51.3	51.3	69.2
	Atrophy	12	15.4	15.4	84.6
	Normal	12	15.4	15.4	100.0
	Total	78	100.0	100.0	

Table 3: Statistics Antithrombotic drugs

N	Valid	78
	Missing	0

		Fre- quency	Per- cent	Valid Per- cent	Cumu- lative Percent
Valid	Aspirin	12	15.4	15.4	15.4
	Warfarin	7	9.0	9.0	24.4
	Clopidogrel	3	3.8	3.8	28.2
	Aspirin plus warfarin	6	7.7	7.7	
	None	50	64.1	64.1	100.0
	Total	78	100.0	100.0	

Table 4: Percentage of patients with stroke type

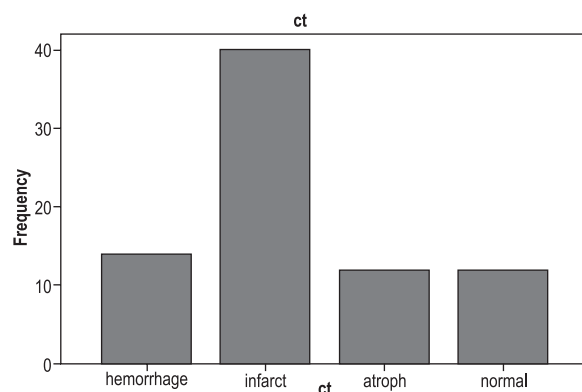
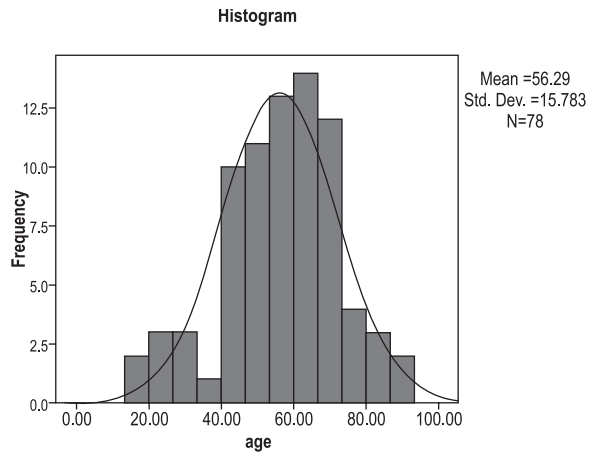
Type of stroke	No. of pts	%age
Hemorrhagic	14	17.94
Non hemorrhagic	64	82.05
Total	78	99.99

Table 5: Percentage of patients on anticoagulants / and or antiplatelets or none

Type of stroke	No. of pts	%age
Anticoagulant /and or antiplatelet	28	35.89
None	50	64.10
Total	78	99.99

Table 6: Age range and CT scan findings of patients with stroke and Atrial Fibrillation

CT scan findings	Age in years			
	<40	40-59	60-80	>80
Infarct	8	14	15	3
Normal		9	3	
Hemorrhage		8	5	1
Cerebral atrophy	1	1	9	1
Total	9	32	32	5



on antithrombotic agents {28(35.89%)} compared to those not on such agents {50 (64.10%)}. A well designed study exclusively on hemorrhagic strokes in AF pts on antithrombotic agents will address the issues of frequency of the type of stroke in a better way. Similarly we did not exclude diabetics or hypertensives from our study and how much were they contributing to the etiology of stroke independently of the status of AF or its treatment, was beyond the scope of this study.

Only 28(35.89%) pts in our study were taking antithrombotics which might be a reason why we had small number of hemorrhagic strokes than ischaemic. Studies have shown that age and AF independently increase stroke risk, elderly people with AF are less likely to receive oral anticoagulant therapy despite standing to receive the greatest benefit from such treatment.²⁴

Sixty four (64) pts in our study had nonhemorrhagic stroke. Twenty one (21) were on antithrombotic agents while forty three (43) were not on such agents. Forty (40) had infarct on CT, 12 had findings consistent with cerebral atrophy and 12 had normal CTs. Out of 40 pts with cerebral infarcts 3 were on warfarin, 9 on aspirin, 3 on clopidogrel, 3 on both antiplatelets and anticoagulants but 22 were not on such agents. The 12 pts with normal CT had no h/o intake of anticoagulant, and or antiplatelet agent. Cerebral infarct in presence of AF in pts without antithrombotic agents is understandable but why pts who were on such agents had developed nonhemorrhagic stroke, reasons were not completely known. Inadequate anticoagulation however was a contributing factor.

Out of total 78 pts with AF and stroke, only 28 were on one or the other antithrombotic agent but the remaining 50 were not on any such agent. As a result in our study more pts with AF and non hemorrhagic strokes were seen than those with hemorrhagic stroke on anticoagulants.

Evidence supports that prevalence of AF increases markedly with older age.²¹⁻²² About 5% of people over 65 years and 10% of people age \geq 80 years suffer from AF²². Although AF in any particular group was not our selection criteria and all pts above age 15 years with AF were included in our study, however it was found that most of our pts were elderly. Sixty four (64) were in the age range of 40-80 years, 5 were above 80 and 9 were below 40 years of age. In pts under age 40 years hemorrhagic stroke was not found. The maximum number of infarcts (15) were observed in 60-80 years range while the number of hemorrhages were more (8) in 40-59 years age range.

Eight pts with cerebral infarcts had age less than 40 years. One out of them had thyrotoxic AF while the rest had valvular heart disease. Out of 5 pts above age 80 years, four had ischaemic and only one had hemorrhagic stroke. While attributing cerebral hemorrhages to anticoagulants care must be taken as elderly pts

with AF have more chances of fall and can develop traumatic intracranial bleed²⁵, which infact are not due to antithrombotic agents.

Out of the total 14 pts with hemorrhagic stroke maximum (8) number of pts were in the age range of 40-59 years. Since more pts in this age group were on antithrombotic agents there is a possibility of antithrombotic induced hemorrhagic stroke. These results also show the trends of prescribing antithrombotic agents more in this age group.

Conclusion; Irrespective of prophylactic antithrombotic agents overall the frequency of ischemic strokes is still more than the hemorrhagic strokes in pts with atrial fibrillation. Well designed studies exclusively performed on pts presenting with hemorrhagic or ischemic stroke already on prophylactic antithrombotics for AF can further clear the issues.

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