**J Cardiovasc Disease Res., 2018; 9(1):5-8.**
A Multifaceted Peer Reviewed Journal in the field of Cardiology
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*Original Article*

# Atrial Fibrillation, Clinical Profile and Adherence to Guidelines

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## ABSTRACT

**Background:** Even in developed countries suboptimal anticoagulation and low adherence to guidelines is frequently observed in Atrial fibrillation (AF) patients. There is no data from our regional population and very scarce Indian data about the utilization patterns and adherence to guidelines for stroke prevention in AF. **Aims and Objectives:** To characterize clinical profile and assess adherence to guidelines in stroke prevention in AF in north Indian population. **Material and Methods:** It was a single centre observational study. All patients presenting to outpatient department or admitted in cardiology wards from May 2014 to April 2016 with AF were included. Detailed history, examination and relevant investigations were carried out .$CHADS_2$ score was used for risk stratifying and prescribing oral anticoagulants in nonvalvular AF. The effectiveness of oral anticoagulant was assessed by INR. **Result:** Total of 446 patients were included. Mean age of our patients was 60.83±16.86 years. 48% were males and 52% were females. Rheumatic heart disease was most common (37.2%) ethology followed by hypertensive cardiovascular disease (18.2%). Mean $CHADS_2$ score was 2.63±1.5 in non valvular AF. Out of 446 patients, 409(92%) patients were found to have indication for prescription of OAC as per guidelines, out of which only 290 (71%) patients actually received OAC. OAC prescription was significantly higher in valvular vs. non valvular AF ( p=0.0001).The rates of OAC prescription in our patients in age group, ≤65, 66-75, >75 years were 84.4%, 65% and 60.2% respectively Out of 290 patients who were eligible for OAC ,only 102(25%) patients were optimally anti-coagulated. **Conclusion:** Discordance between guidelines and practice was found regarding prescription of OACs and maintenance of optimal anticoagulation for stroke prevention in our population. Optimal anticoagulation needs to be emphasized on both patients as well as physicians to prevent strokes and achieve better outcomes.
**Key words:** Oral Anticoagulants, International normalized ratio, $CHADS_2$ score, Valvular heart disease.

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**Submission Date:** 31-10-2017;
**Revision Date:** 10-12-2017;
**Accepted Date:** 18-12-2017.
**DOI :** 10.5530/jcdr.2018.1.2

## INTRODUCTION

Atrial fibrillation (AF) is the most common cardiac rhythm disturbance associated with frequent emergency department visits, hospitalizations, morbidity, mortality and serious economic consequences.[1] The prevalence of AF is estimated at 1-2% in general population increasing with age[2,3] and as many as 9% of people older than 80 years are affected. AF accounts for 34.5% of patients hospitalized with a cardiac rhythm disturbances.[4] The age adjusted prevalence is higher in men.[5] The total mortality rate is approximately double in patients with AF compared with patients with normal sinus rhythm and is linked to the severity of underlying heart disease.[6] The risk of ischemic stroke among patients with non-rheumatic AF averages 5 % per year which is 2 to 7 times more than in people without AF. One out of six strokes occurs in patients with AF.[7] Prevention of thromboembolism is the main tenet of AF management and should begin with individual risk assessment of each patient. Chronic oral anti-coagulation is currently the most effective therapy for attenuating the risk of stroke associated with atrial fibrillation Studies have shown that even in developed countries suboptimal anticoagulation is frequently observed[8, 9,10,11] and adherence to guidelines[12] for prevention of stroke is poor. There is hardly any data from our regional population which has addressed this problem. There is very little Indian data .Small studies like CRAFT[13] from India have focused on treatment of Rheumatic AF only. This study was designed to meet this unmet need to assess to what extent our AF population is being prescribed appropriate stroke preventive measures and how successfully the present guidelines are being applied in this context.

## AIMS AND OBJECTIVES

1. To study the clinical , etiological profile of AF
2. To assess whether anticoagulation for stroke prevention in AF is adhered to the current guidelines

## MATERIAL AND METHODS

All patients with atrial fibrillation presenting to outpatient department or admitted in cardiology or medical wards of the Sher-I-Kashmir Institute of Medical Sciences, Soura from May 2014 to April 2016 for period of two years patients were studied. Work up of the patients included detailed medical history with particular emphasis on possible etiological factors like hypertension, coronary artery disease (CAD), valvular heart disease, cardiomyopathy, chronic obstructive pulmonary disease(COPD), thyroid disease etc. Detailed drug history especially the use of anti-arrhythmic, anti-platelets, anticoagulant, and the frequency of prescription com-pliance was obtained from all patients. Physical examination included assessment of pulse, heart rate, blood pressure, evidence of heart failure such as raised JVP, pedal oedema, S3, crepts, hepatomegaly and cardiac murmurs. Investigative work up constituted estimation of blood sugar, lipid profile, blood urea, serum creatinine, thyroid function, ECG, chest X-ray 24hrs Holter recording and echocardiography. Patients presenting for the first time with new onset atrial fibrillation were reassessed on follow up for categorization of atrial fibrillation. Patients with non-valvular atrial fibrillation were stratified for need of oral anticoagulation to prevent thrombo-embolic phenomenon by $CHADS_2$ score. For compliance of treatment and anticoagulated state, International normalized ratio (INR) was taken into account. Guideline adherence was based on compliance with anti-thrombotic recommendations for AF stroke prevention according to the CHADS2 score. Guideline-adherent was defined as the following: (1) For AF patients with a CHADS2 score of 0 no anti-thrombotic drug was necessary. (2) For AF patients with

CHADS2 of 1 only aspirin was necessary. (3) For those with CHADS2 with score of more than or equal to 2, OACs was necessary.

### Statistical analysis

Continuous variables were expressed as mean± standard deviation and categorical variables as percentages. Differences in continuous variables between the two groups were evaluated with unpaired *t* test and differences in categorical variable, were evaluated using Fisher's exact test. A p-value of less than 0.05 was considered as statistically significant. Data analysis was done using SPSS 20 version software.

## RESULTS

The mean age of our patient cohort was 60.83±16.86 years (range of 16 to 90). The median age was 65 years. Of total 446 patients who had atrial fibrillation, 48% (214) were males and 52% (232) were females. Males were older than the females and this difference was statistically significant (62.84±17.8 vs 58.97±15.7, p value 0.015). In our study, rheumatic heart disease (RHD) was the most common etiology (37.2 %) followed by hypertensive cardiovascular disease (HTCVD) (18.2%), CAD in 15.9%, dilated cardiomyopathy in 12.8% (Table 1). Prevalence of RHD was significantly higher in females as compared to the males (41.8% vs 32.2%, p value 0.037). Whereas prevalence of CAD (19.6% vs 12.5%, p value 0.04) and COPD (4.7% vs 0.9%, p value 0.03) was significantly higher in males compared to females. When studying the associated risk factors in our patients, we found that 63.9 % (285) of our patients were hypertensive, 33% (147) were smokers and both these factors were significantly more commonly seen in males. Diabetes mellitus was present in 15% (67) patients and 7.2% (32) had renal dysfunction associated (Table 2). Systolic LV dysfunction (LVEF<50%) was documented in 16.5% (73) patients. 67.5% (301) of our total patients were seen to have left atrial( LA) size more than 4cm while 33.9% (151) patients had LA size more than 5.0 cm. The mean LA size of our patient population was 4.7±1.3 cm. Out of total 446 patients, valvular AF (rheumatic and non- rheumatic) was seen in 179 (40%) patients. Rest of 267(60%) patients had a non-valvular etiology for their AF. These 267 patients were risk stratified for stroke risk using $CHADS_2$ score. Figure 1 show the $CHADS_2$ score ranging from 0 to 6. Majority of patients had a score of 2 and 3 which accounted for 63.3% of total non-valvular AF patients (Figure1). Mean $CHADS_2$ score was 2.63±1.5. Out of these 267 patients, 230 (86.14%) patients had $CHADS_2$ score of ≥2 thereby implying the need for oral anticoagulants as the preferred modality for stroke prevention .Overall, 23.3% (104) of our patients received anti-platelets. 49.6% (221) patients received oral anticoagulants ( OAC) and 19.1% (85) received both OAC and anti-platelets. Significantly, 8.1% (36) patients did not receive any form of stroke prevention therapy-neither aspirin nor OAC (Table 3). Out of 446, 409 (91.7%) patients in our study population had indication for receiving OAC and 37 (8.3%) patients did not have indication for OAC according to current guidelines .Of total 409 patients having indication for OAC, 290 (70.9%) received OAC whereas 119 (29.1%) did not receive it despite being eligible. Of 37 patients who had no indication for OAC, 16 patients received OAC. A total of 306 patients received OAC. Out of 306 patients who received OAC, 61.4% patients were found to be inadequately anticoagulated whereas 35.6% were optimally anticoagulated, rest of the patients were over anticoagulated. Of 306 patients who received OACs, 260(84.9%) were on warfarin, while as 46(46.03%) were on acenocoumarol. The mean dose of warfarin was 4.9 ±1.3 mg while as mean dose of acenocoumarol was 2.6 ±1.2 mg We also tried to study the factors influencing OAC prescription. On subgroup analysis of OAC requiring patients adherence to guidelines was seen in 91.6 % of patients with valvular AF while as in those with non valvular AF with CHADS2≥ 2 only 54.8% of patients received OACS (p=0.0001) The rates of OAC prescription in our patients in age group, ≤65, 66-75, >75 years were 84.4%, 65% and 60.2% respectively. Frequency of OAC prescription decreased from 70% in those who did not have stroke to 60 % in those who had stroke.73% of patients with LA > 4cm were on OACS while as 86.8% with LA > 5cm received OAC.

Of total 409 patients having indication for OAC, 290 (70.9%) received OAC whereas 119 (29.1%) did not receive it despite being eligible. The mean age of this population who did not receive OACs was 65± 15 years. Males were 61(51%) while as females were 58(49%).Of these 119 patients 95 patients (79.8%) had one or more than one from of contraindication to OAC. The various contraindications included poor compliance [48 (50.5%)], limited life expectancy[12 (12.63%)] ,patient refusal of warfarin, [10 (10.52%)] severe psychological disorder including dementia [10(10.52%)], history of major bleeding [5(5.26%)], blood dyspraxia [4(4.21%)], bleeding secondary to warfarin[3(3.15%)], Intracranial hemorrhage[3(3.15%)]. Of these patients 60 ( 63.15%) received aspirin However in 24(20.16%) patients no contraindication was found. In these patients 14(58.3%) received aspirin.

**Table 1: Table showing etiological profile in AF patients**

| ETIOLOGY | TOTAL n(%) 446(100) | MALE n(%) 214(48) | FEMALE n(%) 232(52) | *p* value |
|---|---|---|---|---|
| RHD | 166(37.2) | 69(32.2) | 97(41.8) | 0.037* |
| HTCVD | 81(18.2) | 31(14.5) | 50(21.6) | 0.053 |
| CAD | 71(15.9) | 42(19.6) | 29(12.5) | 0.04* |
| DCM | 57(12.8) | 32(15.0) | 25(10.8) | 0.18 |
| IDIOPATHIC | 24(5.4) | 13(6.1) | 11(4.7) | 0.53 |
| NONRHEUMATIC | 13(2.9) | 4(1.9) | 9(3.91) | 0.21 |
| COPD | 12(2.7) | 10(4.7) | 2(0.9) | 0.013* |
| CHD | 10(2.2) | 3(1.4) | 7(3.0) | 0.25 |
| PAH | 7(1.6) | 5(2.3) | 2(0.9) | 0.21 |
| HCM | 2(0.4) | 2(0.4) | 0(0) | 0.14 |
| ARVD | 2(0.4) | 2(0.4) | 0(0) | 0.14 |

* Statistically significant

**Table 2: Table showing associated risk factors in AF patients**

| RISK FACTORS | TOTAL n(%) 446(100) | MALES n(%) 214(48) | FEMALES n(%) 232(52) | p VALUE |
|---|---|---|---|---|
| Hypertension | 285(63.9) | 150(70.1) | 135(58.2) | 0.009* |
| Smoking | 147(33.0) | 115(53.7) | 32(13.8) | 0.000* |
| LV dysfunction | 73(16.4) | 40(18.7) | 33(14.2) | 0.203 |
| Diabetes | 67(15.0) | 34(15.9) | 33(14.2) | 0.620 |
| Renal dysfunction | 32(7.2) | 23(10.7) | 9(3.9) | 0.005* |
| LA size >4cm | 301(67.5) | 138(64.5) | 163(70.3) | 0.194 |
| LA size >5cm | 151(33.9) | 63(29.4) | 88(37.9) | 0.058 |

*Statistically significant

**Table 3: Table showing prescription of antithrombotic prophylaxis**

| | Total n (%) | Male n (%) | Female n(%) |
|---|---|---|---|
| Aspirin only | 104(23.3) | 58(55.8) | 46(44.2) |
| OAC only | 221(49.6) | 93(42.1) | 128(57.9) |
| Both | 85(19.1) | 45(52.9) | 40(47.1) |
| None | 36(8.1) | 18(50.0) | 18(50.0) |
| Total | 446(100) | | |

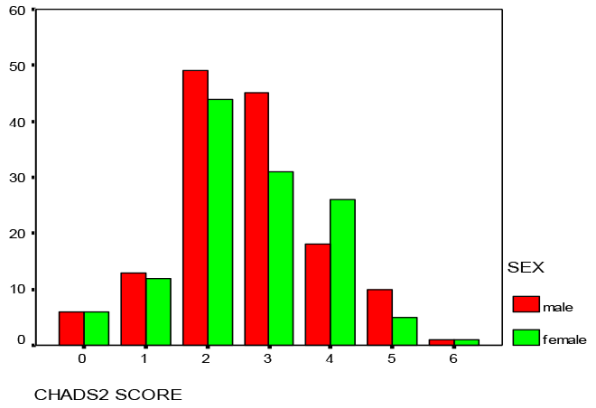


**Figure 1:** Bar diagram showing frequency of CHADS2 score with respect to sex.

## DISCUSSION

The present study is the first prospective study assessing clinical profile of the patients with AF and adherence to guidelines for stroke prevention in our region. We noted that females formed 52% of AF cohort which is in accordance with, (56.4% females )[14] and (51.04% females).[15] However in various other studies prevalence of AF was higher in males.[16,17] Mean age of our patient population was 60.83±16.86 years. Males were significantly older than females (62.84±17.84 vs 58.97±15.71 p=0.015). Mean age of presentation of AF was higher in our population as compared to in various other studies but is comparable with (69.8±11.8 years)[17] and (65 years).[18]

In our study 403 (90.35%) out of 446 patients had underlying cardiac disorder. Valvular heart disease (40.1%) including both rheumatic (37.2%) as well as non-rheumatic(2.9%) was the most common etiological factor in our patient population followed by hypertensive cardiovascular disease (HTCVD) (18.1%), coronary artery disease (CAD) (15.9%), dilated cardiomyopathy (DCM) (12.8%) and Idiopathic (lone AF) accounted for 5.4% . Our study is in contrast to various studies[16,17,20] in which HTCVD is the most common etiology and rheumatic valvular disease comes much lower down. This reflects the increased prevalence of RHD in our population. Similar results were found in a study done in rural Bihar in which RHD accounted for 51.5% of patient.

The risk factors which were associated with AF in our study included hypertension 285(63.9%), smoking 147(33%), LV dysfunction 73(16.4%), diabetes 67(15%) and renal insufficiency 32(7.2%). LA size >4cm was seen in 301 (67.5%) patients. Mean LA size was 4.7±1.3cm. Hypertension was the most common associated condition as seen in various other studies.[14,15,17,21]

Prevention of thromboembolism is the main tenet of AF management and should begin with individual risk assessment of each patient. We used $CHADS_2$ score to risk stratify the patients with non-valvular AF. Of 446 patients, 267 patients had non-valvular cause of AF. Mean $CHADS_2$ score in our non-valvular patient population was 2.61±1.2. 95.5% (255) of 267 patients had $CHADS_2$ score ≥1 while 86.1% (230) patients had $CHADS_2$ score of ≥ 2. The mean $CHADS_2$ score varied from 1.9±1.1 to 1.33±1.24 in various studies.[14,17,22]

Out of 446, 409 (91.7%) patients in our study population had indication for receiving OAC (oral anticoagulation) while 37 (8.3%) patients did not have indication for OAC according to current guidelines. The rate of prescription (71.9%) of OAC to our patients was considerably higher in our study as compared to other studies.[14,15,16] However it was more in agreement with 67% [18] and 60% [23] In a study by,[17] among patients with an indication for OAC, 88% (403/458) effectively received it.[17] This study had one of highest rate of OAC prescriptions. A higher and good rate of OAC prescription in our study population may be due to the fact that in our hospital all AF patients are followed and treated by experienced cardiologists.

We also found that our OAC prescription decreased as age increased. The rates of OAC prescription in our patients in age group, ≤65, 66-75, >75 years were 84.4%, 65% and 60.2% respectively which was in stark contrast to study done by Meiltz et al in which the rate increased from 72% in ≤65 years group to 87% in >75 years group. However, this negative effect of age on rate of OAC prescription has been seen in many other studies by.[23,24,25] The fact of the matter is that chances of stroke increase with increasing age and it is this population of elderly people who derive the maximum benefits of stroke prevention with OAC. However, the results of our and various other studies reflect the mindset and fear of bleeding in elderly which needs to be corrected to pass on the full benefits to this high risk group of patients. We also found that OAC prescription was significantly higher in valvular vs. non valvular AF ($p$=0.0001).This may reflect poor application of $CHADS_2$ score in risk stratifying patients by the treating physicians.

In our study a total of 306 patients (of which 16 patients were not actually eligible) received OAC. Out of 306 patients who received OAC, 61.4% patients were found to be inadequately anticoagulated whereas 35.6% were optimally anticoagulated, rest of the patients were over anticoagulated. We noted that overall only one fourth (24.9%, 102/409) of our population were optimally anticoagulated various large randomized trials have evaluated the status of anticoagulant therapy in their patient population. In SPAF III, SPORTIF III, SPORTIF V, ACTIVE W trials only 61%, 66%, 68%, 69% patients respectively had INR in therapeutic range.[26,27,28.29] These rates are higher than what we have observed in our study. The above mentioned studies were randomized trials in which lot of attention and close follow up is given to patients and despite that optimal anticoagulation was seen in 60-69% patients. The various reasons of suboptimal anticoagulation in our patients could be lack of proper education, awareness among our patients as well as economic reasons for regular monitoring of INR.

### Limitations

This study was a single center observational study with small sample size so extrapolation of these results to general population requires further validation from prospective multicenter studies.

## CONCLUSION

Discordance between guidelines and practice was found regarding prescription of OACs and maintenance of optimal anticoagulation for stroke prevention in our population. Optimal anticoagulation needs to be emphasized on both patients as well as physicians to prevent strokes and achieve better outcomes.

## CONFLICT OF INTEREST

NIL

## ABBREVIATION USED

**CAD:** coronary artery disease; **RHD:** Rheumatic heart disease; **HTN:** Hypertensio; **AF:** Atrial fibrillation; **OAC:** Oral anticoagulation.

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**Cite this article :** Mukesh, Rashid A, Iqbal S, hafeez I, Ione A, Aslam K. Atrial Fibrillation, Clinical Profile and Adherence to Guidelines. J Cardiovasc Disease Res. 2018; 9(1):5-8.