

ANTICOAGULATION CONTROL AMONG PATIENTS WITH ATRIAL FIBRILLATION

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ABSTRACT

Objective: To assess adequacy of anticoagulation in Warfarin treated patients with atrial fibrillation

Study Design: Prospective observational study.

Place and Duration of Study: Armed Forces Institute of Cardiology/National Institute of Heart Diseases, Rawalpindi, from Nov 2019 to Apr 2020.

Methodology: All individuals fulfilling the inclusion criteria were enrolled in the study after their consent. Based upon their serial International Normalized Ratio (INR) values, Time in Therapeutic Range (TTR) was calculated using Rosendaal method. A TTR>70% was a marker of adequate anticoagulation. Factors associated with TTR <70% were identified.

Results: Total 70 participants were included in the study. Mean age (\pm SD) was 51.43 (\pm 11.27) years. Thirty four (48.6%) were males and 36 (51.4%) were females. Twenty four (34.3%) had valvular atrial fibrillation while 46 (65.7%) had non-valvular atrial fibrillation. Overall, TTR>70% was observed in 29 (41.4%) of study participants. Poly-pharmacy and multiple co-morbidities were identified as statistically significant factors associated with sub-therapeutic anticoagulation (TTR<70%).

Conclusion: Determined TTR of study population indicates poor anticoagulation control in majority of patients being anticoagulated with Warfarin in highlighting the need for focused interventions such as dedicated anticoagulation clinics and patient education.

Keywords: Anticoagulants, Atrial Fibrillation, Warfarin.

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INTRODUCTION

Atrial Fibrillation is the most common rhythm disorder encountered in clinical practice¹. It is expected that atrial fibrillation will affect around 6-12 Million people in USA by year 2050². Atrial fibrillation poses a public health challenge because it is associated with significant morbidity and mortality³. Patients with atrial fibrillation have a five fold higher risk of developing stroke compared to age matched individuals in sinus rhythm⁴. Warfarin has been used as the main anticoagulant for prevention of thromboembolic complications associated with atrial fibrillation. It is very effective in reducing the risk of stroke as shown by meta-analysis of several clinical trials reporting a 64% reduction in risk of stroke among patients with Non-valvular atrial fibrillation treated with warfarin^{4,5}. Despite its advantages, the level of anticoagulation with warfarin is

unpredictable owing to narrow therapeutic index and various drug and food interactions. In order to ensure that level of anticoagulation is adequate, the dose of warfarin is monitored through international normalized ratio (INR) the value of which should lie in a particular range to minimize the risk of bleeding or thromboembolic complications associated with supra or sub-therapeutic INR⁶⁻⁹. Time in therapeutic range (TTR) refers to the time, INR of the patients treated with warfarin remains within therapeutic range^{10,11}. A high TTR (>70%) is required for patients on warfarin to accrue maximum benefit. TTR>70% reduces not only the risk of thromboembolic events but also major bleeding^{11,12}. Time in therapeutic range (TTR) is calculated based upon various INR values of the patient, using linear interpolation method of Rosendaal¹³. Data from international randomized trials indicate that optimum TTR threshold is reached in only about 60% of the patients¹⁴. Data on adequacy of anticoagulation in patients with atrial fibrillation in Pakistan is

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lacking we therefore undertook this study to assess the adequacy of anticoagulation in this patient population.

METHODOLOGY

This prospective, cross sectional study was conducted at Armed Forces Institute of Cardiology/National Institute of Heart Diseases from 1st November, 2019 to 30th April, 2020. Diagnosed patients with atrial fibrillation, irrespective of the gender between the age of 18 to 85 years, who had been on warfarin for at least three months were included in the study. Patients with three or fewer INR values were excluded. A total of 70 patients were enrolled in the study using non-probability consecutive sampling. The patient data and serial INR values were recorded during the six months follow-up period. At the end of the study, time in therapeutic range (TTR) was calculated for each patient using Rosendaal method with the help of template prepared and made freely available by INR Pro. Statistical analysis was performed using statistical software SPSS 23. Mean and standard deviation was calculated for quantitative variable, while frequency and percentage were calculated for qualitative variable. Chi-square test was used for the comparison between two qualitative variables. A *p*-value less than 0.05 was considered statistically significant.

RESULTS

There were total 70 participants in our study. The mean age of the study population was 51.43 ± 11.273 years out of which 34 (48.6%) were males and 36 (51.4%) were females. Thirty six (51.4%) participants were non-smokers while 34 (48.6%) were smokers. In terms of level of education, 26 (37.1%) had attained secondary level of education, 28 (40%) had acquired higher secondary level and 16 (22.9%) were graduates. While studying frequencies of different co-morbidities, it was revealed that frequency of hypertension was 24 (34.3%), that of diabetes, obesity, ischemic heart disease and chronic kidney disease was 25 (35.7%), 16 (22.9%), 12 (17.1%), and 5 (7.1%) respectively.

In terms of type of atrial fibrillation, 24 (34.3%) had valvular atrial fibrillation while

Table-I: Demographic characteristics.

S. No.	Variable	Mean \pm SD / n (%)
1.	Age	51.43 \pm 11.273
2.	Gender	
	Male	34 (48.6%)
	Female	36 (51.4%)
3.	Smoking Status	
	Smoker	34 (48.6%)
	Non-Smoker	36 (51.4%)
4.	Education level	
	Secondary	26 (37.1%)
	Higher Secondary	28 (40%)
	Graduate	16 (22.9%)
5.	Hypertension	
	Yes	24 (34.3%)
	No	46 (65.7%)
6.	Diabetes mellitus	
	Yes	25 (35.7%)
	No	45 (64.3%)
7.	Obesity	
	Yes	16 (22.9%)
	No	54 (77.1%)
8.	Ischemic Heart Disease	
	Yes	12 (17.1%)
	No	58 (82.9%)
9.	Chronic Kidney Disease	
	Yes	5 (7.1%)
	No	65 (92.9%)

Table-II: Clinical characteristics.

S. No.	Variable	Mean \pm SD/ n (%) Range
1.	Type of AF	
	Valvular AF	24 (34.3%)
	Non-Valvular AF	46 (65.7%)
2.	Time in Therapeutic range (TTR) >70%	
	Yes	29 (41.4%)
	No	41 (58.6%)
3.	CHADVASC Score	Range: 3
4.	HAS-BLED Score	Range :3
5.	Anemia	
	Yes	6 (8.6%)
	No	64 (91.4%)

Table-III: Association of clinical parameters.

S. No	Variable	<i>p</i> -value
1.	TTR < 70 & No. of Medicines	0.001
2.	TTR<70 & No. of Co-morbids	0.001

46 (65.7%) had non-valvular atrial fibrillation. Mean CHA₂DS₂-VASc score was 2.59 ± 0.734 with range of 3 and mean HASBLED score was 1.21 ± 0.700 with range of 3. Overall, adequate anti-coagulation based upon TTR value of >70% was recorded in 29 (41.4%) of study participants.

Further analysis revealed a statistically significant association between TTR <70% and number of medicine (polypharmacy) (p -value 0.000). There was also significant association between TTR<70% and number of comorbidities (p -value 0.000).

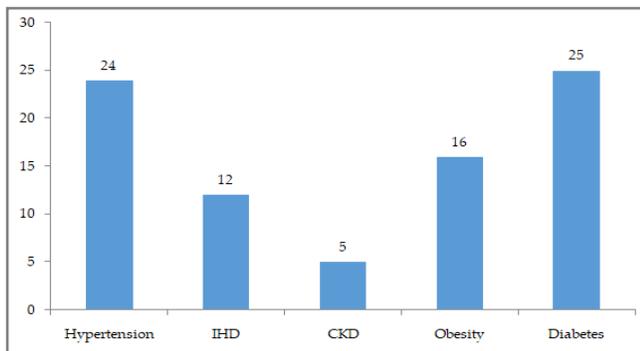


Figure: Co-morbidities in study population.

DISCUSSION

This prospective study was performed to assess the adequacy of anticoagulation in those patients with atrial fibrillation who are anticoagulated with warfarin. Atrial fibrillation is the most common arrhythmia affecting general population and is associated with increased risk of thromboembolic complications. Good quality anti-coagulation can mitigate the risk of stroke and other thromboembolic complications. The problem with use of warfarin is its narrow therapeutic index and various drug and food interactions because of which regular monitoring is imperative. While other studies have assessed quality of anticoagulation in their respective populations, such a study in Pakistani population was lacking. We assessed quality of anticoagulation in terms of Time in Therapeutic Range (TTR) using method of Rosendaal *et al*¹³. Additionally, our study tried to determine factors associated with poor anticoagulation control in patients treated with Warfarin. TTR value of more than 70% was

considered as evidence of adequate anticoagulation, which meant that about 70% of the time during the study period, INR of the patient remained within therapeutic range. Poor anticoagulation control was more common in patients receiving polypharmacy and having multiple comorbidities.

Overall, Adequate anticoagulation (TTR >70%) was observed in 29 (41.4%) of the patients. This figure is lower than what has generally been reported in other international studies. For example, in a single center study from Qatar, adequate anticoagulation was observed in 65.1% of the patients¹⁵, while a Swiss study reported anticoagulation adequacy in 61% of the patients¹⁶. These findings indicate a generally poor level of anti-coagulation in our study population. Detailed analysis revealed a relationship between TTR <70% and number of medicine i.e. polypharmacy ($p=0.000$). It is well established that intake of multiple medications increases the risk of drug interactions, reduction in cognitive and functional capacity and promote non-adherence which inturn can lead to sub-therapeutic INR values¹⁷. This observation is consistent with findings by Shaban *et al*¹⁵.

In addition to polypharmacy, we found as association between TTR<70% and number of comorbidities ($p=0.000$). It may be more challenging to achieve adequate anticoagulation in patients with multiple co-morbidities. Nelson *et al*¹⁸ demonstrated that heart failure, diabetes and history of stroke were associated with higher likelihood of lower TTR. We believe that since patients with multiple co-morbidities are likely to receive multiple medicines, they are more likely to suffer from drug-drug interactions and poor compliance with medical advice, thus culminating in suboptimal anticoagulation. These findings support affording special attention to such high risk populations such as patients with polypharmacy and multiple co-morbidities to accrue maximum benefit from anticoagulation.

Our study highlights the current state of anticoagulation control in Pakistani patients with

atrial fibrillation. Lower rate of adequate anticoagulation demands establishment of special anticoagulation clinics aimed at improving patient education, compliance and monitoring. In future, a larger, multi-center prospective study is recommended to study the overall adequacy of anticoagulation and its main associations to get a more comprehensive data on this important issue.

CONCLUSION

Determined TTR of study population indicates poor anticoagulation control in majority of patients being anti coagulated with Warfarin highlighting the need for focused interventions such as dedicated anticoagulation clinics and patient education.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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