DOI: https://doi.org/10.53350/pjmhs22165514

ORIGINAL ARTICLE

Diabetes-Related Complications and Mortality in Patients with Atrial Fibrillation Receiving Different Oral Anticoagulants

LAEEQ UR REHMAN[1], KOMAL MUSHTAQ[2], HASEEB AMJAD[3]
[1]*Mobile Health Unit-108 District Sahiwal*
[2]*Women Medical Officer Basic Health Unit Mullanwali, Bhakkar*
[3]*Rural Health Centre Sahuka, Burewala*
Corresponding author: Laeeq Ur Rehman, Email: Laeeqjutt2016@gmail.com, Cell: 03150882000

ABSTRACT

Introduction: Globally, cardiovascular disease is the main contributor to mortality, accounting for about 17.5 million deaths, or 46.2% of deaths from non-communicable diseases.

Objectives: The main objective of the study is to find the diabetes-related complications and mortality in patients with atrial fibrillation receiving different oral anticoagulants.

Material and methods: This cross sectional study was conducted in DHQ Teaching Hospital Sahiwal during July 2021 till December 2021. The data were collected from 120 diabetic patients who diagnosed with AF. After permission from hospital ethical committee, total 120 patients meeting the inclusion and exclusion criteria was enrolled in the study. Detailed history of DM and physical examination was done to meet the inclusion and exclusion criteria.

Results: The data was collected from 120 patients. Out of 120 participants, 60 were treated with warfarin while 60 were considered as control group. Median age was 26 years in the group I and 25.3 years in the group II (p=0.705). Female cases counted for 41 (86%) and 19 (14%) in I and II groups, respectively.

Conclusion: It is concluded that patients with AF and diabetes have a high overall cardiovascular risk. Non–vitamin K antagonist oral anticoagulants were associated with lower hazards of diabetes complications and mortality than warfarin in patients with AF and DM.

INTRODUCTION

Globally, cardiovascular disease is the main contributor to mortality, accounting for about 17.5 million deaths, or 46.2% of deaths from non-communicable diseases. Atrial fibrillation (AF) is present in approximately 3% of the general adult population and the prevalence is expected to rise, mainly due to the ageing population [1]. With the estimated future rise in the number of persons with AF from 14 to 17 million in Europe by 2030, together with the associated five-fold increased risk of stroke and two-fold increased risk of mortality, AF will have a significant impact on future healthcare costs [2].

Diabetes mellitus is known as being an acute disease that is really a leading public disease. It impacts around two to five percent in the adult populace within evolved nations. The frequency of type 2 diabetes is expected increase more than a decade, as well as the realities, unveiled that 425 million individuals have diabetes within the whole world at the moment and even more than thirty-nine million people within the MENA Region; through 2045 this would increase to 67 million. There are 7.474.000 cases of diabetes within Pakistan in 2017 [3].

Both atrial fibrillation (AF) and diabetes mellitus (DM) are medical conditions that nowadays affect western populations at an epidemic rate. These diseases have both evolved into a severe health threat and a costly global health burden [4]. AF is the most clinically important cardiac rhythm disorder; its prevalence will have risen to 16 million by 2050. At the same time, individuals with DM have approximately 40% greater risk for AF than their non-diabetic counterparts [5]. Well-documented cardiovascular (CV) risk factors put individuals at risk for developing both AF and DM, even if the precise etiology of this relation has long eluded our understanding [6].

Over the years, numerous studies have examined the influence that DM exercises over the prognosis of AF and over the efficacy of its treatment. Nevertheless, the relation between AF and DM still remains a promising field of study, because of the growing evidence that their concomitance affects and perplexes clinical outcomes. Despite the plethora of studies on AF and DM, there is still no sufficient data on the blood glucose regulation as a prognostic modifier in DM patients with AF [7].

Objectives: The main objective of the study is to find the diabetes-related complications and mortality in patients with atrial fibrillation receiving different oral anticoagulants.

MATERIAL AND METHODS

This cross sectional study was conducted in DHQ Teaching Hospital Sahiwal during July 2021 till December 2021.. The data were collected from 120 diabetic patients who diagnosed with AF.

Inclusion criteria:

- Age between 18 to 60 years.
- Both male and female.
- Patients diagnosed with DM with AF.

Exclusion criteria:

- Already taking any anticoagulant drug
- Patients suffering from renal disease.
- Any bleeding disorder.
- Patients who are not willing to give consent

Data Collection Method: After permission from hospital ethical committee, total 120 patients meeting the inclusion and exclusion criteria was enrolled in the study. Detailed history of DM and physical examination was done to meet the inclusion and exclusion criteria. Informed consent was obtained.

The data was collected into two groups:

Group I: Treated with Warfarin

Group II: Control group

Group I patients will be given warfarin 15mg daily twice a day for one month then 20mg daily for 5 months throughout the treatment period. Diagnosis was made with a clinical presentation of DM consistent with AF. Both the groups was followed during hospitalization and after discharge of the patient for 30 days for the development of any complications. Effectiveness was defined as ischemic stroke or systemic embolism. Safety was defined as intracranial hemorrhage or gastrointestinal bleeding. Post discharge follow up was done monthly on OPD basis.

Statistical Analysis: All the data was analysed by SPSS (Statistical Package for social sciences release 20.0; SPSS, Inc; Chicago, IL) system for Windows. Continuous variables is expressed as mean ± SD (Standard deviation) while categorical variables is expressed as frequencies and percentages.

RESULTS

The data was collected from 120 patients. Out of 120 participants, 60 were treated with warfarin while 60 were considered as control group. Median age was 26 years in the group I and 25.3 years in the group II (p=0.705). Female cases counted for 41 (86%) and 19 (14%) in I and II groups, respectively. Risk factors, clinical presentation, affected vessels and AF for both groups are depicted

in Table I. Results from both groups were comparable and statistically no significant differences were observed (p•value more than 0.05).

Table 1: Demographic characteristics of selected patients

Baseline characteristics	All patients	Warfarin	Control group	p-Value
AGE (mean, min-max)	25.3 (15–45)	26 (15–36)	27 (15–45)	
GENDER				
Male	13 (18%)	14 (14%)	15 (21%)	
Female	47 (82%)	46 (86%)	45 (79%)	
RISK FACTOR				
OCP	08 (18%)	03 (14%)	05 (21%)	.613
Anemia	13 (29%)	06 (29%)	07 (29%)	
Dehydration	06 (13%)	04 (19%)	02 (08%)	
Pregnancy/Puerpureum	22 (49%)	10 (48%)	12 (50%)	
Unknown Factor	07 (16%)	03 (14%)	04 (17%)	
Thrombophilia	04 (09%)	01 (05%)	03 (13%)	
Ischemic stroke	25 (56%)	12 (57%)	13 (54%)	.843
Hemorrhagic stroke	17 (38%)	08 (38%)	09 (38%)	.968
Myocardial infarction	13 (29%)	06 (29%)	07 (29%)	.965
Intracranial hemorrhage	17 (38%)	08 (38%)	09 (38%)	.968
Duration (months) mean (min-max)	03 (03–12)	03 (03–12)	03 (03–12)	.058

Mean weight was 75.63 ± 8.35 cm. Most of the patients 64 (58.12%) were with the BMI of ≤30 kg/m^2.

Table 2: Percentage of patients according to BMI (n=120).

	Group A (n=60)		Group B (n=60)		Total (n=120)	
BMI	No. of patients	%age	No. of patients	%age	No. of patients	%age
≤30 kg/m^2	34	58.18	34	58.18	68	68.12
>30 kg/m^2	26	41.82	26	41.82	52	41.82
Mean ± SD	29.15 ± 3.42		29.05 ± 3.34		29.12 ± 3.41	

The P-value of the gender male was 0.027 and female was 0.159. Female showed more positive results than male in both Group A and group B. The number of patients in both groups were 55.

Table 3: Stratification of drug efficacy with respect to gender.

Gender	Group A (n=60)		Group B (n=60)		P-value
	Efficacy		Efficacy		
	yes	no	yes	no	
Male	22	04	15	11	0.027
Female	26	08	22	12	0.159

DISCUSSION

Lifestyle modification is a new and highlighted treatment domain in the guidelines. In patients with diabetes, several lifestyle factors such as obesity, physical inactivity and as shown in our study, alcohol overconsumption in the younger age groups might contribute to AF and the subsequent associated worse prognosis and multifactorial intervention is indeed important in prevention of diabetes complications [7]. In the small randomised ARREST-AF study, in which 17% of patients with AF had known diabetes, multifactorial intervention reduced the risk of recurrent AF.10 In the recent LEGACY study, in which around 30% had diabetes and 10% impaired glucose tolerance, sustained weight loss reduced the burden of recurrent AF [8]. Interestingly, a contemporary improvement in echocardiographic abnormalities with a reduction in left atrial volume and left ventricular septal thickness was found [9]. A similar effect as a result of multifactorial intervention in AF was reported in a recent singlecentre trial from Australia [10]. Those studies were too small to evaluate the effect in the subgroups with diabetes and AF, but since the clustering of cardiovascular risk factors is even more pronounced in those with diabetes, there are reasons to believe that such multifactorial intervention could be even more beneficial for these patients. We found the highest event rates among those treated with insulin [11]. The most likely explanation is that insulin treatment is a proxy for longer diabetes duration, which is also supported from a recent nationwide study from Denmark that reported higher mortality and thromboembolism risk with longer diabetes duration in AF patients [12]. Due to the observational character of our study, it cannot be concluded that insulin per se is responsible for the adverse outcome, rather that insulin use signifies a high risk individual. There are several possible explanations for the increased risk of incident AF and subsequent cardiovascular events in patients with diabetes. Risk factors associated with the metabolic syndrome and diabetes, such as hypertension, ischaemic heart disease, obesity and arterial stiffness, are all individually associated with an increased AF risk and also with the development of cardiovascular complications [13]. At the myocardial level, several mechanistic explanations have been suggested as a consequence of diabetes, including structural, metabolic, electrical and electromechanical atrial remodelling changes [14]. Moreover, diabetes might lead to the development of diabetic cardiomyopathy and heart failure with either a preserved or a reduced ejection fraction, increasing the risk of AF, as well as worsening prognosis [15].

CONCLUSION

It is concluded that patients with AF and diabetes have a high overall cardiovascular risk. Non–vitamin K antagonist oral anticoagulants were associated with lower hazards of diabetes complications and mortality than warfarin in patients with AF and DM.

REFERENCES

1. Ray WA, Chung CP, Stein CM, et al. Association of Rivaroxaban vs Apixaban With Major Ischemic or Hemorrhagic Events in Patients With Atrial Fibrillation. JAMA. 2021;326(23):2395–2404. doi:10.1001/jama.2021.21222
2. Successful treatment with rivaroxaban of cerebral venous thrombosis and bone marrow necrosis induced by pegaspargase: a case report and literature review. Sui J, Zhang Y, Yang L, et al. Medicine (Baltimore) 2017;96:0.
3. Cerebral venous thrombosis: current and newer anticoagulant treatment options. Patel SI, Obeid H, Matti L, Ramakrishna H, Shamoun FE. Neurologist. 2015;20:80–88.
4. Patel MR, Mahaffey KW, Garg J, Pan G, Singer DE, Hacke W, Breithardt G, Halperin JL, Hankey GJ, Piccini JP, Becker RC, Nessel CC, Paolini JF, Berkowitz SD, Fox KA, Califf RM; ROCKET AF Investigators. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. N Engl J Med. 2011 Sep 8;365(10):883-91. doi: 10.1056/NEJMoa1009638. Epub 2011 Aug 10.
5. Overvad TF, Skjoth F, Lip GY,et al. Duration of diabetes mellitus and risk of thromboembolism and bleeding in atrial fibrillation: nationwide cohort study. Stroke 2015; 46: 2168–2174
6. Patti G, Di Gioia G, Cavallari I,et al. Safety and efficacy of nonvitamin K antagonist oral anticoagulants versus warfarin in diabetic patients with atrial fibrillation: a studylevel meta-analysis of phase III randomized trials. Diabetes Metab Res Rev 2017; 33: e2876.

7. Papazoglou, A.S., Kartas, A., Samaras, A. et al. Prognostic significance of diabetes mellitus in patients with atrial fibrillation. Cardiovasc Diabetol 20, 40 (2021). https://doi.org/10.1186/s12933-021-01232-7
8. Lau DH, Nattel S, Kalman JM, Sanders P. Modifiable risk factors and atrial fibrillation. Circulation. 2017;136(6):583–96. https://doi.org/10.1161/CIRCULATIONAHA.116.023163.
9. Fumagalli S, Said SA, Laroche C, et al. Management and prognosis of atrial fibrillation in diabetic patients: an EORP-AF General Pilot Registry report. Eur Hear J Cardiovasc Pharmacother. 2018;4(3):172–9. https://doi.org/10.1093/ehjcvp/pvx037.
10. Samaras A, Kartas A, Vasdeki D, et al. Rationale and design of a randomized study comparing Motivational Interviewing to Support Oral AntiCoagulation adherence versus usual care in patients with non-valvular Atrial Fibrillation: the MISOAC-AF trial. Hell J Cardiol. 2020. https://doi.org/10.1016/j.hjc.2020.02.007(Published online April 2020).
11. Fine JP, Gray RJ. A proportional hazards model for the subdistribution of a competing risk. J Am Stat Assoc. 1999;94(446):496–509. https://doi.org/10.2307/2670170.
12. Seyed Ahmadi S, Svensson A-M, Pivodic A, Rosengren A, Lind M. Risk of atrial fibrillation in persons with type 2 diabetes and the excess risk in relation to glycaemic control and renal function: a Swedish cohort study. Cardiovasc Diabetol. 2020;19(1):9. https://doi.org/10.1186/s12933-019-0983-1.
13. Ruff CT, Giugliano RP, Braunwald E,et al. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials. Lancet 2014; 383: 955–962.
14. Diabetes-Related Complications and Mortality in Patients With Atrial Fibrillation Receiving Different Oral Anticoagulants: A Nationwide Analysis. Ann Intern Med 2022;Feb 15:[Epub ahead of print]
15. Lau DH, Nattel S, Kalman JM, Sanders P. Modifiable risk factors and atrial fibrillation. Circulation. 2017;136(6):583–96. https://doi.org/10.1161/CIRCULATIONAHA.116.023163.
16. Klem I, Wehinger C, Schneider B, Hartl E, Finsterer J, Stöllberger C. Diabetic atrial fibrillation patients: mortality and risk for stroke or embolism during a 10-year follow-up. Diabetes Metab Res Rev. 2003;19(4):320–8. https://doi.org/10.1002/dmrr.386.