

Low aspirin use in Diabetics

Daad H. Akbar, FRCP, Arab Board, Maimona M. Ahmed, FRCP, Arab Board, Aisha M. Siddique, FRCP.

ABSTRACT

Objective: To determine the percentage of adult diabetics with cardiovascular disease, or risk factors for cardiovascular disease who are using aspirin, and to report on any differences between males and females, or Saudis and non-Saudis.

Method: Medical records of diabetics seen at King Abdulaziz University Hospital during the period January 1998 through to December 2000 were analyzed. The following data were collected: patients age, sex, nationality, body mass index, duration of diabetes, history of cardiovascular disease, risk factors for cardiovascular disease (hypertension, hyperlipidemia, obesity, smoking, family history of ischemic heart disease) and aspirin use.

Results: A total of 550 patients were studied with a mean age of 53 years and male: female ratio 1.1:1. Saudis constitute 260/550 (47%) of the study group. In patients with cardiovascular disease 110/174 (63%) were using

aspirin versus 64/174 (37%) (p 0.001). In patients with one or more risk factors for cardiovascular disease but no cardiovascular disease, aspirin was used in 27/223 (12%) versus 195/223 (88%) (p 0.0001). Aspirin was used by 85/291 (29%) male versus 56/259 (22%) females (p 0.2). Sixty-three of 260 (24%) Saudis used aspirin versus 77/290 (27%) non-Saudis (p 0.7).

Conclusion: Aspirin use is low in diabetics with cardiovascular disease and one or more risk factor of cardiovascular disease, with no significant difference between males and females, or Saudis and non-Saudis. Physicians should be encouraged to use aspirin more in diabetics for both primary and secondary prevention of cardiovascular disease.

Keywords: Aspirin, diabetics, cardiovascular diseases.

Saudi Med J 2002; Vol. 23 (4): 457-460

Diabetic patients have a 2-4 fold increased risk of developing cardiovascular diseases (CVD).¹⁻³ The cardiovascular risk for a person with type-2 diabetes who has not had a recognized myocardial infarction is the same as a non-diabetic individual who has already had a heart attack.³ Diabetic patients have platelets that are hypersensitive to aggregating agents and there is increased thromboxane production that is blocked by low dose aspirin.⁴ Colwell⁵ and others⁶⁻⁹ have demonstrated that aspirin has a primary and secondary preventive role for cardiovascular events in diabetics. In 1997 the American Diabetes Association (ADA) recommended low-dose aspirin therapy as a primary and secondary prevention strategy in people with diabetes mellitus (DM).¹⁰ The aim of our work is to

determine the percentage of adults diabetics with CVD or risk factors for CVD who are using aspirin and to report on any differences between males and females or Saudis and non-Saudis.

Methods. During the period beginning January 1998 through to December 2000, medical records of diabetic patients seen at King Abdulaziz University Hospital (KAUH), Jeddah, Kingdom of Saudi Arabia (KSA), were studied. Patients age, sex, nationality, body mass index (BMI), duration of DM, history of CVD (ischemic heart disease angina or myocardial infarction, stroke, lower, extremities claudication) were recorded as well as aspirin use (those who use aspirin for 6 months or more were defined aspirin users). Risk factors for CVD as defined by the ADA

From the Department of Medicine, King Abdulaziz University Hospital, Jeddah, Kingdom of Saudi Arabia.

Received 5th November 2001. Accepted for publication in final form 26th January 2002.

Address correspondence and reprint request to: Dr. Daad H. Akbar, Associate Professor/Consultant Physician, PO Box 18298, Jeddah 21415, Kingdom of Saudi Arabia. Fax. +966 (2) 6944857. E-mail: daadakb@yahoo.com

guidelines,⁸ hypertension defined as elevated blood pressure (systolic >140 mmHg or diastolic >90 mmHg) or ever prescribed medication for hypertension, hyperlipidemia defined as high density lipoprotein level (HDL) <1.1 mmol/l in males or <1.5 mmol/l in females. Low density lipoprotein level (LDL) >2.6 mmol/l or fasting triglyceride >2.28 mmol/l, and obesity defined as BMI >27.8 kg/m² for males and >27.3 kg/m² for females were retrieved as was history of smoking and family history of ischemic heart disease (IHD). Aspirin use was calculated in patients with CVD and CVD risk factors. Also a comparison was made between males and females, and Saudis and non-Saudis.

Statistical analysis. The data were entered into an statistical package for social sciences (SPSS) database program and statistical analysis was performed. Mean ± standard deviation (SD) was determined for quantitative data and frequency for categorical variables. Student t test was used when comparing continuous variables and the Chi-square test for categorical variables. P value <0.05 was considered significant.

Results. A total of 550 patients were studied. The mean age was 53.19 ± 19.7 years and male: female ratio 291:259 (1.1:1). Saudis constitute 260/550 (47%) while non-Saudis 290/550 (53%). Ischemic heart disease was the most frequent CVD while hypertension constitutes the most common CVD risk factor (**Table 1**). In those >30 years, aspirin was used in 140/505 (28%) compared to 365/505 (72%) (p 0.003) while its use increased in those, >60 years 74/225 (33%) versus 150/225 (67%) (p 0.004). In 174/550 (32%) patients with CVD, aspirin

Table 1 - Frequency of cardiovascular disease and cardiovascular disease risk factors.

Variable	N patients Total = 550 N (%)
Ischemic heart disease	148 (27)
Stroke	33 (6)
Lower extremities claudication	21 (4)
Hypertension	201 (37)
Hyperlipidemia	133 (24)
Obesity	115 (21)
Smoking	125 (23)
Family history of ischemic heart disease	20 (4)
N - number	

Table 2 - Prevalence of aspirin use in different groups of patients.

Variable	Aspirin used N (%)	N Aspirin used N (%)	P value
Ischemic heart disease N=148	103 (70)	45 (30)	<0.001
Stroke N=33	15 (45)	18 (55)	<0.001
Lower extremities claudication N=21	12 (57)	9 (43)	<0.001
Hypertension N=201	84 (42)	117 (58)	<0.001
Hyperlipidemia N=133	53 (40)	80 (60)	<0.001
Obesity N=115	31 (27)	84 (73)	<0.001
Smoking N=125	43 (34)	82 (66)	0.04
Family history of ischemic heart disease N=20	9 (45)	11 (55)	<0.001
Males:females 291:259	85:56 (29:22)	206:203 (71:88)	0.2
Saudis:non-Saudis 260:290	63:77 (24:27)	197:213 (76:73)	0.7
N - number			

was used in 110/174 (63%) versus 64/174 (37%) (p.0.001). In patients with one or more CVD risk factors but no CVD, aspirin was used in 27/223 (12%) versus 195/223 (88%) (p 0.001). Aspirin use was low in patients with CVD and CVD risk factors. There was no significant difference in aspirin use between males and females or Saudis and non-Saudis (**Table 2**). Aspirin was used more in diabetics with long duration of DM 9.5 ± 7.6 years versus 7.2 ± 6.2 years (p<0.001).

Discussion. It is well recognized that the most frequent chronic complication of DM is atherosclerotic CVD.^{11,12} Ischemic heart disease and stroke account for half of the total mortality among individuals with diabetes.¹³ Ischemic heart disease was seen in 27% of diabetics seen in our institute. Cardiovascular disease (including angina, myocardial infarction, stroke and lower extremities claudication) was seen in 32% of patients, which is not far from what had been reported by others.¹⁴ Aspirin was used by 63% of them (as secondary prevention) which is close to Harpaz et al¹⁵ findings (52%) but more than what had been reported by Rolka et al (37%).¹⁴ In the 3rd National Health and Nutrition Examination

Survey (NHANES III) which was conducted in 1988-1994, more than 99% of adults with diagnosed diabetes had CVD or at least one CVD risk factor.¹⁶ Two prospective trials, the Early Treatment Diabetic Retinopathy Study (ETDRS)⁷ and the Hypertension Optimal Treatment (HOT) study¹⁷ had shown significant reduction in the risk for the first myocardial infarction with aspirin therapy. Hypertension is a major CVD risk factor in diabetics as well as non-diabetics¹⁸ and it is twice frequent in diabetics as in non-diabetics.¹⁹ Its prevalence in diabetics varies from 39%-46%.²⁰⁻²² It is the most frequent risk factor found in our study followed by hyperlipidemia. Elevated serum lipids are associated with a higher risk of CVD for diabetics as they are for non-diabetics.²³ Aspirin use was low in diabetics with one or more CVD risk factor but no CVD (primary prevention). It is reported by Rolka et al¹⁴ to be 13% which is similar to our findings.

It is clear that women with type-2 DM are at high risk for cardiovascular events. Recent studies of NHANES I cohort have shown a 23% increase in cardiovascular mortality in diabetic women in comparison with a decrease of 27% in non-diabetic women between 1971 and 1984.²⁴ It has been reported that aspirin was less likely to be used by women than men and by black, Mexican and American than non Hispanic whites.^{14,25-28} Our study did not show any significant difference in aspirin use between males and females or Saudis and non-Saudis. Older diabetics and those with long duration of diabetics were more likely to use aspirin, which could be explained by the higher rate of cardiovascular complications in this group of patients.

The low rate of aspirin use among people with DM observed in our study and others could be explained by the fear of the treating physicians from the risk of aspirin therapy particularly those with hypertension and retinopathy, but studies did not show significant increase in the risk of severe complications^{7,17} or poor patients compliance. Physicians patients should be encouraged to use aspirin according to the ADA guidelines.^{8,10} 1. Aspirin to be used for secondary prevention in men and women with evidence of large vessel disease (myocardial infarction, vascular bypass procedure, stroke, transient ischemic attack, or angina) and 2. Be considered for primary prevention in adults who have one or more risk factors for CVD (family history or coronary heart disease, hypertension, hyperlipidemia, smoking, obesity, albuminuria) or who are >30 years. It's beneficial effects, low cost, ready availability, and lack of severe complications makes it practical for wide spread use in diabetics.

References

1. Stmler J, Vaccaro O, Neaton JD, Wentworth D. Multiple Risk Factors Intervention Trial Research Group: Diabetes, other risk factors and 12-year cardiovascular mortality for screened in the Multiple Risk Factors Intervention Trial. *Diabetes Care* 1993; 16: 434-444.
2. Assamann G, Schulte H. The Prospective Cardiovascular Munster (PROCAM) Study: prevalence of hyperlipidemia in persons with hypertension and/or diabetes mellitus and the relationship to coronary heart disease. *Am Heart J* 1988; 116: 1713-1724.
3. Haffner SM, Lehto S, Ronnema T, Pyorala K, Laakso M. Mortality from coronary heart disease in subjects with type-2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. *N Engl J Med* 1998; 339: 229-234.
4. Davi G, Catalano I, Averna T. Thromboxane biosynthesis and platelets function in type-2 diabetes mellitus. *N Engl J Med* 1990; 322: 1769-1774.
5. Colwell JA. Aspirin therapy in diabetes mellitus (Technical Review). *Diabetes Care* 1997; 20: 1767-1771.
6. Antiplatelets TRIALS' Collaboration: Collaborative overview of randomized trials of antiplatelets therapy I. Prevention of death, myocardial infarction, and stroke by prolonged antiplatelets therapy in various categories of patients. *BMJ* 1994; 308: 81-106.
7. ETDRS Investigators: Aspirin effects on mortality and morbidity in patients with diabetes mellitus. *JAMA*; 1992; 268: 1292-1300.
8. American Diabetes Association: Aspirin therapy in diabetes (position statement). *Diabetes Care* 2000; 23 Suppl 1: 61-62.
9. Hennekens CH. Update on aspirin in the treatment and prevention of cardiovascular disease. *Am Heart J* 1999; 137: 9-13.
10. American Diabetes Association: Aspirin therapy in Diabetes (position statement). *Diabetes Care* 1997; 20: 1772-1773.
11. Steiner G. Atherosclerosis, the major complication of diabetes. In: Vranic M, Hollenberg CH, Steiner F, editors. Comparison of type 1 and 2 diabetes. New York (NY): Plenum; 1985. p. 20-32.
12. Hamsten A, Steiner G. Non-insulin dependent diabetes mellitus and atherosclerosis: a lipoprotein perspective (editorial). *J Intern Med Suppl* 1994; 736: 1-3.
13. Geiss LS, Herman WH, Smith PJ. Mortality in non-insulin dependent diabetes mellitus. In: National Diabetes Data Group, editors. Diabetes in America. 2nd ed. Washington (DC): US Govt printing Office; 1995. p. 233-257
14. Rolka D, Campagna AF, Narayan KV. Aspirin use among adults with diabetes. *Diabetes Care* 2001; 24: 197-201.
15. Gottlieb S, Graff E, Boyko V, Kishon Y, Behar S. Effects of aspirin treatment on survival in non-insulin dependent diabetic patients with coronary artery disease. *Am J Med* 1998; 105: 494-499.
16. National Center for Health Statistics: Plan and operation of the Third National Health and Nutrition Examination Survey, 1988-1994. *Vital Health Stat 1* 1994; 32: 1-407.
17. Hasson L, Zanchetti A, Carruthers SG, Dahlof B, Elmfdet D, Julius S et al. Effect of intensive blood pressure lowering and low dose aspirin in patients with hypertension: principle results of the Hypertension Optimal Treatment (HOT) randomized trial. *Lancet* 1998; 351: 1755-1762.
18. The National High Blood Pressure Education Program Working Group: report on hypertension in diabetics. *Hypertension* 1994; 23: 145-158.
19. Stein B, Weintraub WS, Gebbart S. Influence of diabetes mellitus on early and late outcome after percutaneous transluminal coronary angioplasty. *Circulation* 1995; 91: 979-989.
20. Wokoma FS. Hypertension in non-insulin dependent diabetic Nigerians: a comparative analysis of normotensive and hypertensive subgroups. *Diabetes International Journal* 1999; 9: 57-58.
21. The Hypertension in Diabetes Study Group. Hypertension in Diabetes Study (HDS): 1. Prevalence of hypertension in newly presenting type-2 diabetic patients and the association with risk factors for cardiovascular and diabetic complications: II. Increased risk of cardiovascular complications in hypertensive type-2 diabetic patients. *J Hypertens* 1993; 11: 309-319.

22. Akbar D. Is hypertension common in hospitalized type-2 diabetic patients? *Saudi Med J* 2001; 22: 139-141.
23. Lehto S, Ronnema T, Haffner SM, Pyorala K, Kallio V, Laakso M. Dyslipidemia and hyperglycemia predict coronary heart disease events in middle-aged patients with NIDDM. *Diabetes* 1997; 46: 1354-1359.
24. Gu K, Cowie CC, Harris MI. Diabetes and decline in heart disease mortality in US adults. *JAMA* 1999; 281: 1291-1297.
25. Shahar E, Folsom AR, Romm FJ, Bisgard KM, Metcalf PA, Grum L et al. Patterns of aspirin use in middle-aged adults: the atherosclerosis risk in communities (ARIC) Study. *Am Heart J* 1996; 131: 915-922.
26. McCormick D, Gurwitz JH, Lessard D, Yarzebski J, Gore JM, Goldberg RJ. Use of aspirin, beta blockers and lipid lowering medications before recurrent acute myocardial infarction: missed opportunities for prevention? *Arch Intern Med* 1999; 159: 561-567.
27. Stafford RS. Aspirin use is low among United States outpatients with coronary artery disease. *Circulation* 2000; 101: 1097-1101
28. Leape LL, Hilborne LH, Bell R, Kamberg C, Brook RH. Under use of cardiac procedures: do women, ethnic minorities, and the uninsured fail to receive needed revascularization? *Ann Intern Med* 1999; 130: 183-192.