Original

ISSN 0946-1965

DOI 10.5414/CP201574
e-pub: ■■■

Antiplatelet therapy in diabetic ischemic stroke patients: associated factors and outcomes

Y. Hassan[1], S.W. Al-Jabi[2,3], N. Abd Aziz[1], I. Looi[4] and S.H. Zyoud[3,5]

[1]Department of Pharmacy Practice, Faculty of Pharmacy, Universiti Teknologi MARA (UiTM), Puncak Alam Campus, Bandar Puncak Alam, Selangor Darul Ehsan, [2]Clinical Pharmacy Program, School of Pharmaceutical Sciences, Universiti Sains Malaysia (USM), Penang, Malaysia, [3]Faculty of pharmacy, An-Najah National University, Nablus, Palestine, [4]Clinical Research Center, Hospital Pulau Pinang, and [5]National Poison Center, Universiti Sains Malaysia (USM), Penang, Malaysia

Key words
antiplatelet therapy – acute ischemic stroke – diabetes mellitus – outcomes – prevalence

Abstract. Background: Patients with diabetes mellitus (DM) are more prone to develop atherosclerotic complications including stroke. Moreover, as a primary and secondary prevention of stroke, antiplatelet therapy is recommended by clinical guidelines for patients with DM. Aims: This study aimed to determine the prevalence of antiplatelet therapy use prior to current stroke in diabetic ischemic stroke patients, to examine the factors associated with the use of this important therapy and to assess the impact of the previous use of antiplatelet therapy on ischemic stroke outcomes. Methods: An observational study of diabetic acute ischemic stroke patients attending a Malaysian hospital during a 1-year period was carried out. Demographic information, risk factors, previous antiplatelet use and variables used to assess stroke outcomes were collected from medical records. Results: Overall, 295 diabetic stroke patients were analyzed. The prevalence of previous antiplatelet use among diabetic patients was 38.3%. The independent variables associated with the previous use of antiplatelet medication were previous stroke attack ($p < 0.001$) and ischemic heart disease ($p < 0.001$). Better outcomes as measured by a minor Glasgow Coma Scale at admission ($p = 0.032$), and a higher Modified Barthel index at discharge ($p = 0.027$) were observed among patients on previous antiplatelet therapy. Conclusion: Our data suggest that antiplatelet therapy is under prescribed among such diabetic stroke patients, particularly in primary prevention. Effective methods to increase antiplatelet use and to enhance the adherence of clinical practice guidelines should be considered at the national and community level.

Received
March 19, 2011;
accepted
July 21, 2011

Correspondence to
Y. Hassan, PhD
Professor of Clinical Pharmacy, Department of Pharmacy Practice, Faculty of Pharmacy, Universiti Teknologi MARA (UiTM), Puncak Alam Campus, Bandar Puncak Alam 42300, Selangor Darul Ehsan, Malaysia
dryahaya2909@puncakalam.uitm.edu.my

Introduction

Stroke is one of the leading causes of significant disability and mortality worldwide [1]. Patients with diabetes mellitus (DM) are more prone to develop atherosclerotic complications including cerebrovascular disease, with previous studies confirming an independent effect of DM on ischemic stroke in both males and females, with an increased relative risk in diabetic patients ranging from 1.8- to nearly 6-fold [2].

Diabetes mellitus not only significantly increases the risk of stroke, but also affects the outcomes following ischemic stroke. Some studies reported higher mortality rates from stroke among diabetics, compared to non-diabetic patients [3, 4]. Moreover, DM may affect the rate of recovery from neurologic dysfunction after stroke, and patients with DM recovered more slowly than non-diabetic patients [3]. Some researchers have linked this increase in mortality rate and morbidity to the size of the cerebral infarct [5].

One of the abnormalities of the hemostatic system among diabetic patients is the hyperreactivity of platelets [6]. Therefore, antiplatelet therapy, as a primary and secondary prevention of vascular events including stroke, is recommended by the American Diabetes Association for diabetic patients, especially those who are over 50 y old, or who have at least one additional risk factor, such as a family history of vascular disease, hypertension, smoking, dyslipidemia or albuminuria [7]. Some studies have reported that patients who have an ischemic stroke while taking aspirin have less severe strokes than those not on such pretreatment, resulting in more favorable outcomes [8, 9], but others have suggested that aspirin has no effect on stroke severity or its outcomes [10, 11].

Most previous observational studies have focused on the prevalence of aspirin as the

main antiplatelet agent among diabetic patients [12, 13, 14]. But none have considered the prevalence of previous use of aspirin and other antiplatelet agents among diabetic ischemic stroke patients. Furthermore, none have considered the effect of antiplatelet therapy on ischemic stroke outcomes among this group of patients.

The goal of the current study was to determine the prevalence of antiplatelet therapy use (aspirin and newer platelet aggregation inhibitors) prior to the current stroke attack for both primary and secondary prevention in diabetic ischemic stroke patients, and to examine the patient characteristics and risk factors that are associated with the use of this important therapy. Moreover, particular consideration was given to assess the impact of the previous use of antiplatelet therapy on stroke outcomes among diabetic ischemic stroke patients.

Methods

Patients, study design and setting

We retrospectively surveyed the medical files of all acute ischemic stroke patients who were attending a 1,090-bed hospital located in northern Malaysia, over a 1-year period between 1 April 2008 and 31 March 2009. Permission from the local health authorities and medical ethics committee regarding access to and use of patient clinical information was obtained before starting the study.

Patients were identified using a computer-generated list obtained from the hospital record office. The study cases were confirmed according to the International Classification of Diseases Tenth revision (ICD-10). Patients with diagnostic codes I63.0 – I63.9 (acute ischemic stroke) were included in the study. Case ascertainment was supplemented by records from medical wards and intensive care units. Source documentation used for validation included emergency room records, the admission database, physical examinations and neurology consultations [15]. For stroke attacks, definitive computerized tomography (CT) scans or magnetic resonance imaging (MRI) were used as confirmation of diagnosis. Acute ischemic stroke was defined as a measurable neurological deficit present for more than 24 h due to presumed ischemic etiology [16].

The current study focused on ischemic stroke patients with DM. Both Type 1 and Type 2 DM were included, with no differentiation between the two types because this difference is not clinically important when recommending antiplatelet medication. Furthermore, DM was determined based on the concentration of fasting blood glucose > 6.3 mmol/l, or a history of diet-controlled, oral hypoglycemic-treated or insulin-treated disease [17]. These diabetic ischemic stroke patients were divided into two groups based on their antiplatelet utilization prior to hospital admission. Antiplatelet therapy use was defined as the use of aspirin, clopidogrel, ticlopidine or dipyridamole, or a combination of any of these drugs.

Data collection: demographic and risk factors

A specially designed data collection form was used to collect data from the medical records, including demographic information and risk factors. The main risk factors considered in this study were previous stroke attack, hypertension, dyslipidemia, atrial fibrillation (AF), ischemic heart disease (IHD), renal impairment and heart failure (HF). Recurrent stroke was defined as a previous history of ischemic attacks. Hypertension was defined as systolic blood pressure > 140 mmHg or diastolic blood pressure > 90 mmHg, a physician's diagnosis of hypertension or when a patient was on antihypertensive therapy. Dyslipidemia was defined by the presence of one or more abnormal serum lipid concentrations. A previous history of AF was noted in addition to screening for AF by the hospital physician from an electrocardiogram performed either during the patient's hospital stay or from previous evaluation. Ischemic heart disease was defined as a history of angina or myocardial infarction [17, 18]. Serum creatinine concentrations ≥ 150 μmol/l or at least 50% higher than baseline were selected as indicators of renal impairment [19].

Data collection: ischemic stroke classification and clinical outcomes

Acute ischemic stroke was classified using the Oxfordshire Community Stroke Project (OCSP) classification system, which is based on the signs and symptoms present at the time of maximal deficit after stroke attack, and determined without referring to brain imaging findings. This classification includes total anterior circulation infarct (TACI), partial anterior circulation infarct (PACI), lacunar infarct (LACI), posterior circulation infarct (POCI) and unclassified type [20].

The Glasgow Coma Scale (GCS) was used to assess the level of consciousness of all diabetic stroke patients at the time of admission. GCS scale is a 15-point measure of neurological dysfunction, with lower scores indicating more severe impairment. It is composed of independent observations of three aspects of behavior: eye opening (on a scale of 1 – 4), motor responsiveness (1 – 6), and verbal responsiveness (1 – 5), which when summed give an overall score between 3 and 15. In the current study, GCS was divided into three stages: minor (total score ≥ 13), moderate (total score 9 – 12), and severe (total score ≤ 8) [21].

Both in-hospital mortality and the Modified Barthel Index (MBI) score were compared between the previous antiplatelet users and nonusers after excluding those patients who discharged against medical advice and who were discharged to another hospital. The MBI evaluated ten basic everyday-life activities with a maximal value of 100 (full independence) and a minimal value of 0 (completely dependent). The results of patients who died were assigned with the lowest possible score (0) in the MBI. Moreover, a score of 100 does not necessarily mean normality, but only that the patient should manage without assistant care [22]. In the current study, a score > 75 corresponded to mild or no disability [23].

The other outcomes analyzed for the two groups of previous antiplatelet user and nonuser diabetic stroke patients were the ambulatory status at discharge and the length of hospital stay (LOS). For better estimation of these two outcomes, we included only the live cases. Also, patients who discharged against medical advice and who were discharged to another hospital were excluded from the analysis. Patients were considered ambulant when they were able to walk by themselves or with some means of aid or support, and nonambulant if they were wheelchair bound or bedbound. LOS was measured in hours and calculated as the hour of discharge minus the hour of admission, and the median LOS was compared between the antiplatelet users and nonusers.

Statistical analysis

Analysis of the two groups of antiplatelet users and nonusers and the effect of previous antiplatelet therapy on patients' outcome was carried using the Statistical Package for Social Sciences program version 15 (SPSS). Data were expressed as frequency (%) for categorical variables and mean ± SD for continuous variables. Variables that were not normally distributed were expressed as median (lower upper quartiles). The χ^2- or Fisher's exact tests were used, as appropriate, to test for significance between categorical variables. An independent Student's t-test was used to compare the means of continuous variables. If assumptions of the equality of variance and normality (assumed for the t-test) were not met, the Mann-Whitney U-test was performed as appropriate. A p-value less than 0.05 was considered significant.

Multiple logistic regression was used to assess the factors associated with the use of antiplatelet medication prior acute ischemic stroke. Variables included in the regression were those with p-values < 0.1 in the univariate analysis. The proportion of patients who previously used antiplatelet medication was expressed as a prevalence rate with a 95% confidence interval (95% CI). The association between the previous use of antiplatelet and the variables of interest was evaluated by calculating the odds ratio (OR) with the corresponding 95% confidence interval (CI).

Results

604 patients were diagnosed with acute ischemic stroke during the study period. Of those, 295 (48.8%) patients were diabetic.

Table 1. Demographic information, risk factors and clinical characteristics of diabetic ischemic stroke patients admitted to the hospital during the study period (n = 295).

Variable	Total n = 295	With previous antiplatelet use n = 113	Without previous antiplatelet use n = 182	Odds ratio (95% CI for odds ratio)	p-value
Age	64.5 ± 11.3	63.9 ± 11.5	64.9 ± 11.2	0.99 (0.97 – 1.0)	0.459[a]
Gender					
Male	174 (59%)	74 (65.5%)	100 (54.9%)	Reference	0.074
Female	121 (41%)	39 (34.5%)	82 (45.1%)	0.6 (0.4 – 1.1)	
Ethnic group					
Malay	86 (29.2%)	35 (31%)	51 (28%)	Reference	0.164
Chinese	150 (50.8%)	49 (43.4%)	101 (55.5%)	0.7 (0.4 – 1.2)	0.216
Indian	57 (19.3%)	28 (24.8%)	29 (15.9%)	1.4 (0.7 – 2.8)	0.321
Other	2 (0.7%)	1 (0.9%)	1 (0.5%)	1.5 (0.1 – 4.1)	0.793
Stroke event					
First ever	186 (63.1%)	51 (45.1%)	135 (74.2%)	Reference	< 0.001
Recurrent	109 (36.9%)	62 (54.9%)	47 (25.8%)	3.5 (2.1 – 5.7)	
Hypertension					
Present	272 (92.2%)	108 (95.6%)	164 (90.1%)	2.4 (0.9 – 6.6)	0.089[b]
Absent	23 (7.8%)	5 (4.4%)	18 (9.9%)	Reference	
Dyslipidemia					
Present	130 (44.1%)	58 (51.3%)	72 (39.6%)	1.6 (1.1 – 2.6)	0.048
Absent	165 (55.9%)	55 (48.7%)	110 (60.4%)	Reference	
Atrial fibrillation					
Present	23 (7.8%)	13 (11.5%)	10 (5.5%)	2.2 (0.9 – 5.3)	0.061
Absent	272 (92.2%)	100 (88.5%)	172 (94.5%)	Reference	
Ischemic heart disease					
Present	72 (24.2%)	50 (44.2%)	22 (12.1%)	5.8 (3.2 – 10.3)	< 0.001
Absent	223 (75.8%)	63 (55.8%)	160 (87.9%)	Reference	
Renal impairment					
Present	54 (18.3%)	25 (22.1%)	29 (15.9%)	1.5 (0.8 – 2.7)	0.181
Absent	241 (81.7%)	88 (77.9%)	153 (84.1%)	Reference	
Heart failure					
Present	9 (3.1%)	6 (5.3%)	3 (1.6%)	3.3 (0.8 – 13.6)	0.075[b]
Absent	286 (96.9%)	107 (94.7%)	179 (98.4%)	Reference	

CI = confidence interval. [a]Significance of differences estimated with Student's t-test; [b]significance of differences estimated with Fisher's exact test.

Among the 604 ischemic stroke patients, 185 patients were identified as previous antiplatelet users, representing a 1-year period prevalence of 30,629 per 100,000 individuals. The prevalence of previous antiplatelet use among diabetic patients was 38.3% (113/295), compared to 23.3% (72/309) among nondiabetic patients. Therefore, there was a significant difference in the prevalence of previous antiplatelet use between diabetic and nondiabetic patients ($p < 0.001$).

Of the total 113 diabetic stroke patients on antiplatelet drugs, 79 (69.9%) were on aspirin, 14 (12.4%) on ticlopidine, 6 (5.3%) on clopidogrel, 3 (2.7%) on dipyridamole, 7 (6.2%) on aspirin and dipyridamole, and 4 (3.5%) on aspirin and clopidogrel.

The univariate analysis of the demographic characteristics and the risk factors of the 295 ischemic stroke patients with DM are shown in Table 1. The 295 patients had a mean ± SD age of 64.5 ± 11.3 y, and there were 174 (59%) males. There were no differences between the previous antiplatelet users and nonusers in terms of age, gender, incidence of hypertension, AF, renal impairment or HF. However, diabetic stroke patients on antiplatelet therapy before admission were more likely to have a previous stroke attack compared to patients without previous antiplatelet use (54.9% vs. 25.8%, OR = 3.5; CI = 2.1 – 5.7; $p < 0.001$). IHD was associated with more than a 3-fold increase in antiplatelet use (OR = 3.8; CI = 3.2 – 10.3; $p < 0.001$). Moreover, diabetic stroke patients who were

Table 2. Independent factors associated with previous use of antiplatelet medication among diabetic ischemic stroke patients.

Variables	β	S.E.	Wald[a]	p value	Odds ratio (95% CI for odds ratio)
Gender	–0.24	0.28	0.72	0.397	0.79 (0.45 – 1.37)
Stroke event (Recurrent)	1.31	0.28	22.01	0.000	3.72 (2.15 – 6.44)
Hypertension	0.64	0.57	1.26	0.262	1.90 (0.62 – 5.86)
Dyslipidemia	0.36	0.27	1.71	0.191	1.43 (0.84 – 2.45)
Atrial fibrillation	0.42	0.51	0.68	0.411	1.53 (0.56 – 4.18)
Ischemic heart disease	1.67	0.32	27.36	0.000	5.29 (2.84 – 9.88)
Heart failure	1.20	0.85	1.99	0.158	3.32 (0.63 – 17.57)

β = the coefficient of the predictor variables; CI = confidence interval; S.E = standard error. [a]Wald = a parametric statistical test was used to test the statistical significance of each coefficient (β) in the model (i.e., predictors contribution).

Table 3. Clinical outcomes of diabetic ischemic stroke patients admitted to the hospital during the study period (n = 295).

Variable	Total n = 295	With previous antiplatelet use n = 113	Without previous antiplatelet use n = 182	p-value
OCSP classification of ischemic stroke				
TACI	23 (7.8%)	6 (5.3%)	17 (9.3%)	0.209
PACI	57 (19.3%)	20 (17.7%)	37 (20.3%)	0.578
LACI	155 (52.5%)	62 (54.9%)	93 (51.1%)	0.529
POCI	26 (8.8%)	11 (9.7%)	15 (8.2%)	0.660
Unclassified	34 (11.6%)	14 (12.4%)	20 (11%)	0.674
Glasgow Coma Scale				
Minor	217 (73.6%)	91 (80.5%)	126 (69.2%)	0.032
Moderate	47 (15.9%)	12 (10.6%)	35 (19.3%)	0.049
Severe	31 (10.5%)	10 (8.8%)	21 (11.5%)	0.464
Status at discharge[a]				
Alive	229 (81.8%)	91 (85.8%)	138 (79.3%)	0.169
Dead	51 (18.2%)	15 (14.2%)	36 (20.7%)	
MBI[a]				
≥ 75	127 (45.4%)	57 (53.8%)	70 (40.2%)	0.027
< 75	153 (54.6%)	49 (46.2%)	104 (59.8%)	
Ambulatory status at discharge[b]				
Ambulant	128 (55.9%)	59 (64.8%)	69 (50%)	0.027
Wheelchair bound	73 (31.9%)	23 (25.3%)	50 (36.2%)	0.082
Bedbound	28 (12.2%)	9 (9.9%)	19 (13.8%)	0.381
Length of hospital stay[b,c]	72 (46 – 117)	71 (41 – 112)	73 (48 – 120)	0.170

LACI = lacunar infarct; LS group = long hospital stay; MBI = Modified Barthel Index; PACI = partial anterior circulation infarct; OCSP = Oxfordshire Community Stroke Project; POCI = posterior circulation infarct; TACI = total anterior circulation infarct. [a]Total of patients included = 280, patients discharged against medical advice or discharged to another hospital (15 patients) were excluded from the analysis; [b]total of patients included = 229, dead patients and patients discharged against medical advice or discharged to another hospital (66 patients) were excluded from the analysis; [c]significance of differences estimated with Mann-Whitney U-test.

on previous antiplatelet use were significantly more likely to have dyslipidemia as a risk factor (OR = 1.6; CI = 1.1 – 2.6; p = 0.048) (Table 1).

Regarding AF patients, 56.5% (13/23) patients were on antiplatelet medication before the current stroke attack, compared to 43.5% (10/23) who did not use antiplatelet medication before (p = 0.061). On the other hand, only 3 patients (13%) of those having AF were on anticoagulant medication before the currents ischemic stroke attack.

The multiple logistic regression analysis of variables associated with the use of antiplatelet among diabetic patients before ischemic stroke is shown in Table 2. All the variables

that have p-value < 0.1 were included in the analysis. The results showed that the previous use of antiplatelet among diabetic ischemic stroke patients were previous stroke attack and IHD. The odds of the use of antiplatelet before ischemic stroke attack are increased by 3.72 (CI = 2.15 – 6.44; p < 0.001) in previous stroke attack, and increased by 5.29 (CI = 2.84 – 9.88; p < 0.001) in the presence of IHD as ischemic stroke risk factor.

Table 3 illustrates the clinical outcomes of diabetic ischemic stroke patients with and without previous antiplatelet use. Both OCSP ischemic stroke classification and GCS were evaluated on admission. There were no significant differences between the two groups of patients in terms of ischemic stroke subtypes. However, minor and moderate GCS were significantly affected by previous antiplatelet use. Previous antiplatelet users were admitted with minor GCS compared to antiplatelet nonusers (p = 0.032), whereas patients without previous antiplatelet use were admitted with moderate GCS compared to antiplatelet users (p = 0.049).

Both status at discharge in terms of in-hospital mortality and the MBI score were compared between the previous antiplatelet users and nonusers after excluding 15 patients, 8 of them discharged against medical advice and 7 of them were discharged to another hospital. During the hospital stay, there was no significant difference in terms of in-hospital mortality in the antiplatelet user group and the nonuser group (14.2 vs. 20.7%, p = 0.169). However, diabetic stroke patients who were using antiplatelet agents prior to the current stroke had significantly better activity of daily living as measured by a higher MBI score compared to nonusers (p = 0.027).

We then analyzed the impact of previous antiplatelet use on the ambulatory status at discharge and the LOS. For better estimation of these factors, 66 of the 295 diabetic stroke patients studied were excluded; of these, 51 died, 8 were discharged against medical advice and 7 were discharged to another hospital. Previous antiplatelet users were discharged in an ambulant status more significantly than previous antiplatelet nonusers (64.5 vs. 50%, p = 0.027). Moreover, regarding the LOS, there was no significant association between the LOS and previous antiplatelet use among diabetic stroke patients (p = 0.170).

On the other hand, in comparing diabetic and nondiabetic patients according to vital status at discharge, and after excluding patients who discharged against medical advice and patients who were discharged to another hospital, 83 patients died during hospitalization. Among them, 51 (61.4%) were diabetic compared to 32 (38.6%) who were not diabetic (p = 0.011).

Discussion

To the best of our knowledge, this study is the first of its kind to obtain initial data regarding the prevalence rate of antiplatelet therapy use (aspirin and newer platelet aggregation inhibitors) prior to the current stroke attack in diabetic ischemic stroke patients in Malaysia, and to assess the impact of previous use of antiplatelet therapy on ischemic stroke outcomes among this group of patients. The prevalence of previous antiplatelet use before the current stroke attack among diabetic patients was 38.3%, with most (69.9%) on aspirin as monotherapy. This prevalence was lower than that reported in some studies that included all diabetic patients from the US (54%), the UK (52%), India (100%), and in diabetic patients with cardiovascular disease from Palestine (56.9%) [12, 13, 14, 24].

In the current study, the use of antiplatelet therapy was mainly as a secondary prevention rather than a primary one. The results of multiple logistic regression shows that diabetic patients who used antiplatelet therapy before the current stroke attack were more likely to have a previous stroke attack (p < 0.001) and IHD (p < 0.001).

Despite the consensus guidelines that recommend the use of antiplatelets for diabetic patients who are over 50 y old, or who have at least one additional risk factor [7], our diabetic patients were not widely using the highly available, inexpensive and proven effective aspirin therapy, especially for primary prevention. Some practitioners may doubt the role of antiplatelet therapy especially in the primary prevention of stroke in diabetic patients; this doubt stems from studies that resulted in smaller and not statistically significant benefits from antiplatelet use in cardiovascular disease prevention

[25]. Moreover, some studies have observed that previous aspirin use among the patients studied had no effect on stroke severity or outcomes [10, 11]. In addition, several reasons for inadequate use of antiplatelet therapy in diabetic patients have been mentioned by some prescribers and include: difficulties in applying guidelines to individuals, patient resistance or contraindication to taking aspirin, risk of hemorrhagic stroke and gastrointestinal bleeding, and prioritization of other issues and medication, especially in cases of patient noncompliance [26].

In the current study, 56.5% among AF patients were on antiplatelet medication before the current stroke attack, and only 13% patients of those having AF were on anticoagulant medication. Clinical guidelines have recommended the use of warfarin in patients with AF for ischemic stroke prevention, especially in the presence of an additional risk factor to develop stroke [27]. In these patients, warfarin significantly reduces the relative risk of stroke by 62%, whereas aspirin affords a 22% relative risk reduction [28]. Despite that, previous studies found only 32 – 54% of patients with AF with no contraindications to oral anticoagulants receive warfarin [29]. A number of potential barriers to warfarin use including: age, history of recent major bleeding, history of falls, ability to comply with therapy and risk of warfarinization [29].

Although the current study showed a significant relationship between DM as a risk factor for stroke and mortality after stroke attack, we found that previous treatment with an antiplatelet agent was associated with a small but not significant reduction in in-hospital mortality in diabetic stroke patients. This finding is compatible with the results of previous reports that studied the effect of aspirin use among all patients admitted with acute ischemic stroke [11, 30]. However, it contrasts with another study that found a lower mortality rate 4 weeks after the stroke attack in all ischemic stroke subtypes, but not among patients with strokes due to small vessel occlusion ($p = 0.8$) [31]. In the current study, nearly half of the cases were diagnosed with a lacunar infarct.

Antiplatelet agents may lessen the severity of stroke and improve outcome by reducing the size of emboli, by preventing platelet aggregation in the microcirculation, reducing thromboxane A2-mediated vasoconstriction in the ischemic brain area, and via their antioxidant properties [32].

The GCS is a useful severity-of-illness measure for ischemic stroke patients, and is a good predictor of the outcome of these patients on the basis of their level of consciousness at the time of assessment [21]. In the present study, diabetic stroke patients on antiplatelet therapy before admission had a significantly lower GCS score at the time of admission; moreover, those patients not on previous antiplatelet therapy had a moderate GCS score. This result clarifies the association between previous antiplatelet use and improving stroke outcome. A previous study showed that the increase in GCS was correlated with improved functional outcome as measured by independence in activities of daily living, as well as being a predictor of survival after stroke attack [33].

In the current study, the outcome for patients sustaining an ischemic stroke appeared to be better when they received antiplatelet therapy prior to their stroke, as measured by the MBI score that evaluates the dependency in activities of daily living and patients' functional status, at the time of discharge. Previous studies have given conflicting results [8, 34]. In a large prospective study, there was no evidence of any association of previous aspirin use with baseline stroke severity as measured by observed outcome (death or dependency at 6 months) [34]. Moreover, in the current study, there were no significant differences between the antiplatelet users and nonusers in terms of OCSP classification, taking into consideration that OCSP classification provides a simple assessment of stroke severity, with TACI classes having the worst prognosis [20]. These conflicting results regarding the outcomes may be due to the different strategies used in evaluating stroke severity and outcomes, the small sample size, and the presence of factors that influence aspirin use and may also affect clinical stroke severity.

Although this study is the first of its type in Malaysia, its limitations include the fact that we were unable to analyze the duration of antiplatelet therapy before the current attack, and were dependent on patients' compliance as recorded by the physician

or the pharmacist from the patients or their families. Furthermore, the beneficial effects of the adjunctive cardiac drug were not assessed in this study.

Conclusion

Despite clinical practice guidelines that recommend the use of antiplatelet therapy for patients with diabetes as primary and secondary prevention against ischemic stroke, our data suggest that antiplatelet therapy is under prescribed among these diabetic stroke patients, particularly in primary prevention. Among diabetic stroke patients, a higher prevalence of previous antiplatelet use was associated with the presence of previous stroke attack, IHD and dyslipidemia as risk factors. Prior use of antiplatelet therapy among diabetic patients may be associated with an improvement of GCS on admission and ischemic stroke outcome as measured by the MBI score at the time of discharge. Effective methods to increase antiplatelet use and to enhance the adherence of clinical practice guidelines should be considered at the national and community level.

Acknowledgments

The authors would like to thank the Universiti Sains Malaysia (USM) for the financial support provided for their research. The assistance of the medical and record office staff is gratefully acknowledged.

References

[1] *Rothwell PM, Coull AJ, Silver LE, Fairhead JF, Giles MF, Lovelock CE, Redgrave JN, Bull LM, Welch SJ, Cuthbertson FC, Binney LE, Gutnikov SA, Anslow P, Banning AP, Mant D, Mehta Z; Oxford Vascular Study.* Population-based study of event-rate, incidence, case fatality, and mortality for all acute vascular events in all arterial territories (Oxford Vascular Study). Lancet. 2005; *366:* 1773-1783.

[2] *Goldstein LB, Adams R, Becker K, Furberg CD, Gorelick PB, Hademenos G, Hill M, Howard G, Howard VJ, Jacobs B, Levine SR, Mosca L, Sacco RL, Sherman DG, Wolf PA, del Zoppo GJ.* Primary prevention of ischemic stroke: A statement for healthcare professionals from the Stroke Council of the American Heart Association. Circulation. 2001; *103:* 163-182.

[3] *Jørgensen H, Nakayama H, Raaschou HO, Olsen TS.* Stroke in patients with diabetes. The Copenhagen Stroke Study. Stroke. 1994; *25:* 1977-1984.

[4] *Laing SP, Swerdlow AJ, Carpenter LM, Slater SD, Burden AC, Botha JL, Morris AD, Waugh NR, Gatling W, Gale EA, Patterson CC, Qiao Z, Keen H.* Mortality from cerebrovascular disease in a cohort of 23 000 patients with insulin-treated diabetes. Stroke. 2003; *34:* 418-421.

[5] *Kent TA, Soukup VM, Fabian RH.* Heterogeneity affecting outcome from acute stroke therapy: making reperfusion worse. Stroke. 2001; *32:* 2318-2327.

[6] *Vinik AI, Erbas T, Park TS, Nolan R, Pittenger GL.* Platelet dysfunction in type 2 diabetes. Diabetes Care. 2001; *24:* 1476-1485.

[7] *American Diabetes Association.* Standards of medical care in diabetes--2010. Diabetes Care. 2010; *33 (Suppl 1):* S11-S61.

[8] *Wilterdink JL, Bendixen B, Adams HP Jr, Woolson RF, Clarke WR, Hansen MD.* Effect of prior aspirin use on stroke severity in the trial of Org 10172 in acute stroke treatment (TOAST). Stroke. 2001; *32:* 2836-2840.

[9] *Shook SGR, Vora N, Shumecher C, Tievsky D.* Pretreatment with antiplatelets is associated with smaller diffusion-weighted volume in middle cerebral artery territory infarcts. Stroke. 2005; *36:* 416.

[10] *Sivenius J, Cunha L, Diener HC, Forbes C, Laakso M, Lowenthal A, Smets P, Riekkinen P Sr.* Antiplatelet treatment does not reduce the severity of subsequent stroke. European Stroke Prevention Study 2 Working Group. Neurology. 1999; *53:* 825-829.

[11] *Sharma J, Fletcher S, Vassallo M, Ross I.* Prior aspirin therapy, subsequent stroke severity and mortality and relationship with cardiovascular risk factors in patients admitted to hospital with acute stroke. HeartDrug. 2000; *2:* 221-227.

[12] *Miller SR, Littenberg B, MacLean CD.* Prevalence of antiplatelet therapy in patients with diabetes. Cardiovasc Diabetol. 2005; *4:* 18

[13] *Woodward A, Bayley D, Overend L, Gill G.* Antiplatelet drug use in a diabetic clinic. QJM. 2007; *100:* 547-550.

[14] *Sweileh W.* Anti-platelet therapy in diabetic hypertensive patients with and without cardiovascular diseases in Palestine, from 2003 to 2008. CVD Prev Contr. 2009; *4:* 157-162.

[15] *Morgenstern LB, Smith MA, Lisabeth LD, Risser JM, Uchino K, Garcia N, Longwell PJ, McFarling DA, Akuwumi O, Al-Wabil A, Al-Senani F, Brown DL, Moyé LA.* Excess stroke in Mexican Americans compared with non-Hispanic Whites: the Brain Attack Surveillance in Corpus Christi Project. Am J Epidemiol. 2004; *160:* 376-383.

[16] *Warlow C, Sudlow C, Dennis M, Wardlaw J, Sandercock P.* Stroke. Lancet. 2003; *362:* 1211-1224.

[17] *Hajat C, Dundas R, Stewart JA, Lawrence E, Rudd AG, Howard R, Wolfe CD.* Cerebrovascular risk factors and stroke subtypes: differences between ethnic groups. Stroke. 2001; *32:* 37-42.

[18] *Pinto A, Tuttolomondo A, Di Raimondo D, Fernandez P, Licata G.* Cerebrovascular risk factors and clinical classification of strokes. Semin Vasc Med. 2004; *4:* 287-303.

[19] *Kellum JA, Levin N, Bouman C, Lameire N.* Developing a consensus classification system for acute renal failure. Curr Opin Crit Care. 2002; *8:* 509-514.

[20] *Bamford J, Sandercock P, Dennis M, Burn J, Warlow C.* Classification and natural history of clinically identifiable subtypes of cerebral infarction. Lancet. 1991; *337:* 1521-1526.
[21] *Prasad K.* The Glasgow Coma Scale: a critical appraisal of its clinimetric properties. J Clin Epidemiol. 1996; *49:* 755-763.
[22] *Hacke W, Kaste M, Fieschi C, Toni D, Lesaffre E, von Kummer R, Boysen G, Bluhmki E, Höxter G, Mahagne MH et al; The European Cooperative Acute Stroke Study (ECASS).* Intravenous thrombolysis with recombinant tissue plasminogen activator for acute hemispheric stroke. JAMA. 1995; *274:* 1017-1025.
[23] *Taub NA, Wolfe CD, Richardson E, Burney PG.* Predicting the disability of first-time stroke sufferers at 1 year. 12-month follow-up of a population-based cohort in southeast England. Stroke. 1994; *25:* 352-357.
[24] *Sabitha P, Kamath A, Adhikari PM.* Prescription of Aspirin for adults with Diabetes. Int J Diabetes Dev Ctries. 2008; *28:* 51-53.
[25] *Sacco M, Pellegrini F, Roncaglioni MC, Avanzini F, Tognoni G, Nicolucci A; PPP Collaborative Group.* Primary prevention of cardiovascular events with low-dose aspirin and vitamin E in type 2 diabetic patients: results of the Primary Prevention Project (PPP) trial. Diabetes Care. 2003; *26:* 3264-3272.
[26] *Short D, Frischer M, Bashford J, Ashcroft D.* Why are eligible patients not prescribed aspirin in primary care? A qualitative study indicating measures for improvement. BMC Fam Pract. 2003; *4:* 9.
[27] *Singer DE, Albers GW, Dalen JE, Fang MC, Go AS, Halperin JL, Lip GY, Manning WJ; American College of Chest Physicians.* Antithrombotic therapy in atrial fibrillation: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest. 2008; *133 (Suppl):* 546S-592S.
[28] *Wolf PA, Abbott RD, Kannel WB.* Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. Stroke. 1991; *22:* 983-988.
[29] *Partington SL, Abid S, Teo K, Oczkowski W, O'Donnell MJ.* Pre-admission warfarin use in patients with acute ischemic stroke and atrial fibrillation: The appropriate use and barriers to oral anticoagulant therapy. Thromb Res. 2007; *120:* 663-669.
[30] *De Keyser J, Herroelen L, De Klippel N.* Early outcome in acute ischemic stroke is not influenced by the prophylactic use of low-dose aspirin. J Neurol Sci. 1997; *145:* 93-96.
[31] *Kalra L, Perez I, Smithard DG, Sulch D.* Does prior use of aspirin affect outcome in ischemic stroke? Am J Med. 2000; *108:* 205-209.
[32] *Pongrácz E, Káposzta Z.* Antiplatelet therapy in ischemic stroke. Expert Rev Neurother. 2005; *5:* 541-549.
[33] *Bushnell CD, Phillips-Bute BG, Laskowitz DT, Lynch JR, Chilukuri V, Borel CO.* Survival and outcome after endotracheal intubation for acute stroke. Neurology. 1999; *52:* 1374-1381.
[34] *Ricci S, Lewis S, Sandercock P; IST Collaborative Group.* Previous use of aspirin and baseline stroke severity: an analysis of 17,850 patients in the International Stroke Trial. Stroke. 2006; *37:* 1737-1740.