[1] College of Pharmacy, An-Najah National University, Nablus, Palestine
[2] Poison Control and Drug Information Center (PCDIC), An-Najah National University, Nablus, Palestine

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CLINICAL CHARACTERISTICS, SEX DIFFERENCES AND IN-HOSPITAL MORTALITY AMONG STROKE PATIENTS WITH AND WITHOUT DIABETES MELLITUS

Waleed M. Sweileh[1], Sa'ed H. Zyoud[2], Ansam F. Sawalha[1], Samah W. Al-Jabi[2], Adham S. Abu-Taha[1]

Key words: stroke, diabetes mellitus, hemorrhage, hospital

SUMMARY

The aim of the study was to investigate and compare clinical characteristics, sex differences and in-hospital mortality between stroke patients with and without diabetes mellitus (DM). All patients admitted to Al-Watani Governmental Hospital for 12 consecutive months and diagnosed with acute stroke were included in the study. Demographic data, clinical characteristics and in-hospital mortality were compared between diabetic and nondiabetic stroke patients. Pearson χ^2-test and Student's t-test were used on univariate analysis. Data were analyzed using SPSS 16. There were 186 stroke patients, mean age 69.09±0.9 years, with positive DM history recorded in 48.9% of male and 45.2% of female patients. Diabetic stroke patients were significantly younger (66.8±10.99 vs. *71±10.52 years;* P=*0.009) and had a higher proportion of ischemic heart disease (11.9%* vs. *3.9%;* P=*0.04) compared to nondiabetic stroke patients. In-hospital mortality accounted for 39 (21%) patients, including 23 (27.4%) diabetic and 16 (15.7%) nondiabetic stroke patients (*P=*0.051). Univariate analysis of diabetic stroke patients based on sex showed male patients to have significantly more hemorrhagic strokes (*P=*0.04), recurrent strokes (*P=*0.003) and in-hospital mortality (*P=*0.034) compared to female patients. There was no sex difference in nondiabetic stroke patients. Analysis of diabetic stroke patients based on vital status indicated that in-hospital mortality was significantly associated with sex (*P=*0.034), type of stroke (*P=*0.006) and recurrent stroke (*P=*0.01). None of the variables was significantly associated with mortality in nondiabetic stroke patients. In conclusion, diabetic patients have different clinical characteristics, show sex differences and in-hospital mortality differences compared to nondiabetic patients after acute stroke.*

INTRODUCTION

Stroke is one of the leading causes of morbidity and mortality worldwide (1,2). There are several modifiable risk factors for stroke. Diabetes mellitus (DM) is one of the well-known risk factors for stroke (3). In addition, it has been suggested that stroke patients with DM have higher in-hospital mortality

Corresponding author: Assoc. Professor Waleed M. Sweileh, PhD, Clinical Pharmacology, College of Pharmacy, An-Najah National University, Nablus, Palestine
E-mail: waleedsweileh@najah.edu; waleedsweileh@yahoo.com

rates and poorer outcome than those without diabetes (3-10). Therefore, screening and better glycemic control is believed to reduce the risk of death after acute stroke (11).

To improve our knowledge of stroke in diabetic patients, we carried out this one-year, hospital-based study with the following objectives: to compare clinical characteristics; to determine sex differences, if any; and to identify variables associated with in-hospital mortality in stroke patients with and without DM. The knowledge of such factors might help reduce mortality after stroke by implementing specific therapeutic and management strategies to high-risk patients.

PATIENTS AND METHODS

This one-year, hospital-based study was conducted in 2007 at the Intensive Care Unit (ICU), Al-Watani Governmental Hospital in Nablus, Palestine. All patients with acute stroke admitted to Al-Watani Hospital were included in the study. The diagnosis of

Table 1. **Clinical characteristics of diabetic and nondiabetic stroke patients**

Variable	Diabetic stroke patients n=84 (45.2%)	Nondiabetic stroke patients n=102 (54.8%)	*P*
Age# (yrs)	66.8±10.99	71±10.52	0.009
Sex			
Male	39 (46.4%)	52 (51%)	0.64
Female	45 (53.6%)	50 (49%)	
CrCl at admission# (mL/ min)	93.2±63.4	94.2±55	0.86
Type of stroke			
Ischemic	70 (83.3%)	83 (81.4%)	0.88
Hemorrhagic	14 (16.7%)	19 (18.6%)	
Hypertension			
Present	61 (72.6%)	69 (67.6%)	0.57
Absent	23 (27.4%)	33 (32.4%)	
Congestive heart failure			
Present	7 (8.3%)	16 (15.7%)	0.2
Absent	77 (91.7%)	86 (84.3%)	
Atrial fibrillation			
Present	10 (11.9%)	16 (15.7%)	0.6
Absent	74 (88.1%)	86 (84.3%)	
Ischemic heart disease			
Present	10 (11.9%)	4 (3.9%)	0.04
Absent	74 (88.1%)	98 (96.1%)	
Recurrent stroke			
Present	37 (44%)	37 (36.3%)	0.35
Absent	47 (56%)	65 (63.7%)	
Obesity			
Present	17 (20.2%)	14 (13.7%)	0.32
Absent	67 (79.8%)	88 (86.3%)	
Death at hospital			
Present	23 (27.4%)	16 (15.7%)	0.05
Absent	61 (72.6%)	86 (84.3%)	

Categorical variables were expressed as frequency and percentage. Continuous variables (#) were expressed using mean ± standard deviation (SD). All variables were tested using χ^2-test except for continuous variables, which were tested by independent Student's t-test. Yates correction factor was used with χ^2-test.

stroke was made and confirmed by computed tomography (CT) scan and clinical evaluation (12). Patients with no definitive CT scan results or those suspected to have transient ischemic attacks were excluded from the study. Data collection was performed by clinical pharmacists and authorized by hospital administration and supervising physicians. Data for the study were obtained from patient medical files. The information on the presence of diabetes was extracted from medical records. Patients were regarded as diabetic if their medical records contained the diagnosis of DM or if they were current users of insulin or oral hypoglycemic medications. Since we were not able to differentiate whether patients on insulin treatment had type 1 or type 2 DM, we combined all diabetic patients into one group.

For each patient, demographic data, type of stroke, risk factors, clinical variables and outcome were recorded. Demographic variables included age and sex. Types of stroke included ischemic and hemorrhage. Risk factors included a history of hypertension (HTN), DM, ischemic heart disease (IHD), congestive heart failure (CHF), atrial fibrillation (AF), smoking, previous stroke, obesity, and elderly (>65 years). Obesity was defined based on the body mass index (BMI) value; males and females with BMI >30 were considered to be obese. Clinical variables considered as post-stroke complications included infection, constipation, limb pain, anxiety and seizure. Patient outcome included vital status at discharge (alive or dead).

Statistical analysis

Data analysis was carried out using the Statistical Program for Social Science (SPSS) for Windows version 16.0 (SPSS Inc., Chicago, IL, USA). Descriptive analysis included mean ± SD and frequency. Univariate analysis for each variable in relation to differences in the frequency of demographic characteristics, risk factors, and vital status at discharge between stroke patients with and without diabetes was assessed with the independent Student's *t*-test and Pearson χ^2-test. Statistical significance was set at $P<0.05$.

RESULTS

During the study period, 186 stroke patients were admitted to Al-Watani Hospital. Forty-nine per cent of stroke patients were males and 51% were females, giving a male to female ratio of 0.96:1. The mean age of stroke patients was 69.09±10.9 years and there was no significant difference in mean age between male (69.8 years) and female (68.5 years) patients. Ischemic stroke was found in 153 (82.3%) and hemorrhagic stroke in 33 (17.7%) cases. Seventy-four (39.8%) patients had previous stroke attacks, while 112 (60.2%) had first-ever stroke. Of all stroke patients, 84 (45.2%) had a positive history of DM, while the rest (54.8%) had no history of DM. In the present study, diabetic stroke patients were significantly younger (66.8±10.99 *vs*. 71±10.52 years; $P=0.009$) and had a higher proportion of ischemic heart disease ($P=0.04$) compared to nondiabetic stroke patients (Table 1).

Univariate analysis of diabetic stroke patients based on sex indicated that males had significantly more hemorrhagic attacks ($P=0.04$), previous stroke ($P=0.003$) and in-hospital mortality ($P=0.034$) compared to females (Table 2). In nondiabetic stroke patients, there were no significant sex differences in any of the study variables (Table 2). Of all stroke patients, 39 (21%) patients died during their hospital stay (64% male and 36% female). Most of in-hospital mortality occurred in diabetic stroke patients compared to nondiabetic stroke patients (59% *vs*. 41%). The difference in in-hospital mortality between diabetic and nondiabetic stroke patients was at the border of significance ($P=0.051$).

Univariate analysis of diabetic stroke patients based on vital status at discharge indicated that sex ($P=0.034$), type of stroke ($P=0.006$), number of post-stroke complications ($P=0.001$) and previous stroke attacks ($P=0.01$) were significantly associated with in-hospital mortality (Table 3). However, univariate analysis in nondiabetic stroke patients showed that none of the variables was significantly associated with in-hospital mortality.

Table 2. **Clinical characteristics of stroke patients with and without diabetes according to sex differences**

	Stroke patients with diabetes n=84			Stroke patients without diabetes n=102		
Risk factor	Male n=39 (46.4%)	Female n=45 (53.6%)	*P*	Male n=52 (51%)	Female n=50 (49%)	*P*
Age* (mean)	65.97±11.28	67.53±10.8	0.52	72.07±9.6	69.8±11.34	0.28
Type of stroke						
Ischemic	29 (74.4)	41 (91.1)	0.04	41 (78.8)	42 (84)	0.5
Hemorrhagic	10 (25.6)	4 (8.9)		11 (21.2)	8 (16)	
Hypertension						
Present	32 (82.1)	29 (64.4)	0.07	34 (65.4)	35 (70)	0.61
Absent	7 (17.9)	16 (35.6)		18 (34.6)	15 (30)	
Congestive heart failure						
Present	1 (2.6)	6 (13.3)	0.07	5 (9.6)	11 (22)	0.08
Absent	38 (94.4)	39 (86.7)		47 (90.4)	39 (78)	
Atrial fibrillation						
Present	4 (10.3)	6 (13.3)	0.66	7 (13.5)	9 (18)	0.52
Absent	35 (89.7)	39 (86.7)		45 (86.5)	41 (82)	
Ischemic heart disease						
Present	5 (12.8)	5 (11.1)	0.8	3 (5.8)	1 (2)	0.32
Absent	34 (87.2)	40 (88.9)		49 (94.2)	49(98)	
Previous stroke						
Present	24 (61.5)	13 (28.9)	0.003	19 (36.5)	18 (36)	0.95
Absent	15 (38.5)	32 (71.1)		33 (63.5)	32 (64)	
Obesity						
Present	7 (17.9)	10 (22.2)	0.62	5 (9.6)	9 (18)	0.23
Absent	32 (82.1)	35 (77.8)		47 (90.4)	41 (82)	
Number of post-stroke complications#	1±1	1.1±1.1	0.58	1.06±0.89	1.18±1.11	0.54
Death at hospital						
Present	15 (38.5)	8 (17.8)	0.034	10 (19.2)	6 (12)	0.31
Absent	24 (61.5)	37 (82.2)		42 (80.8)	44 (88)	

Categorical variables were expressed as frequency and percentage. Continuous variables (#) were expressed using mean ± SD. All variables were tested using χ^2-test except for continuous variables, which are tested by independent T test.

DISCUSSION

In the present study, we investigated clinical characteristics, sex differences and in-hospital mortality in 186 consecutive diabetic and nondiabetic patients with acute stroke. According to our data, the prevalence of diabetes among stroke patients was 45.2%. This is similar and within the range of what has been reported in stroke patients in other countries (5,13-16). The finding that diabetic stroke patients were younger and had a higher proportion of ischemic heart disease than nondiabetic stroke patients was expected. It is well known that chronic DM leads to microvascular and macrovascular complications including cerbrovascular and coronary atherosclerosis (17). This might explain the significant association between IHD and diabetic stroke but not nondiabetic stroke. Such an association has been previously reported (18-20).

In this study, differences in in-hospital mortality between diabetic and nondiabetic stroke patients were at the border of significance. Different findings are reported in the literature regarding the impact of DM on mortality among stroke patients. The German Stroke Study found DM to have a significant impact

Table 3. **Risk for in-hospital mortality in stroke patients with and without diabetes mellitus**

	Stroke patients with diabetes n=84				Stroke patients without diabetes n=102			
Variable	Total n=84 (%)	Died n=23 (%)	Survived n=61 (%)	*P*	Total n=102 (%)	Died n=16 (%)	Survived n=86 (%)	*P*
Age* (mean)	66.8±10.99	69±10.67	65.98±11.08	0.26	71±10.52	74.06±11.84	70.4±10.23	0.203
Sex								
Male	39 (46.4)	15 (65.2)	24 (39.3)	0.034	52 (51)	10 (62.5)	42 (48.8)	0.31
Female	45 (53.6)	8 (34.8)	37 (60.7)		50 (49)	6 (37.5)	44 (51.2)	
Type of stroke								
Ischemic	70 (83.3)	15 (65.2)	55 (90.2)	0.006	83 (81.4)	11 (68.8)	72 (83.7)	0.15
Hemorrhagic	14 (16.7)	8 (34.8)	6 (9.8)		19 (18.6)	5 (31.3)	14 (16.3)	
Hypertension								
Present	61 (72.6)	18 (78.3)	43 (70.5)	0.47	69 (67.6)	12 (75)	57 (66.3)	0.49
Absent	23 (27.4)	5 (21.7)	18 (29.5)		33 (32.4)	4 (25)	29 (33.7)	
Congestive heart failure								
Present	7 (8.3)	0 (0)	7 (11.5)	0.09	16 (15.7)	3 (18.8)	13 (15.1)	0.71
Absent	77 (91.7)	23 (100)	54 (70.1)		86 (84.3)	13 (81.3)	73 (84.9)	
Atrial fibrillation								
Present	10 (11.9)	4 (17.4)	6 (9.8)	0.34	16 (15.7)	0 (0)	16 (18.6)	0.06
Absent	74 (88.1)	19 (82)	55 (90.2)		86 (53.8)	16 (100)	70 (81.4)	
Ischemic heart disease								
Present	10 (11.9)	2 (8.7)	8 (13.1)	0.577	4 (3.9)	1 (6.3)	3 (3.5)	0.6
Absent	74 (88.1)	21 (91.3)	53 (86.9)		98 (96.1)	15 (93.8)	83 (96.5)	
Previous stroke								
Present	37 (44)	15 (65.2)	22 (59.5)	0.01	37 (36.3)	9 (56.3)	28 (32.6)	0.07
Absent	47 (56)	8 (34.8)	39 (63.9)		65 (63.7)	7 (43.8)	58 (67.4)	
Obesity								
Present	17 (20.2)	3 (13)	14 (23)	0.34	14 (13.7)	4 (25)	10 (11.6)	0.15
Absent	67 (79.8)	20 (87)	47 (77)		88 (86.3)	12 (75)	76 (88.4)	
Number of post-stroke complications	1.1±1.0	1.74±1.1	0.85±0.96	0.001	1.1±1.0	1.44±0.96	1.05±1.01	0.168

on early outcome (21). However, a Polish study suggested that diabetes had no effect on the course and outcome of ischemic stroke (22). In the present study, in-hospital mortality among diabetic stroke patients was sex-dependent, with males having higher in-hospital mortality than females. In contrast, in-hospital mortality among nondiabetic stroke patients was not sex-dependent. The impact of sex on diabetic stroke patients could be attributed to the significant association of male sex with clinical characteristics considered to be more fatal such as hemorrhagic stroke, and recurrent stroke compared to females. These findings were in agreement with those obtained by Sasaki *et al*., who found that male diabetic stroke patients had higher in-hospital mortality than female diabetic stroke patients (23).

Patients having hemorrhagic stroke had a higher risk of mortality than those diagnosed with ischemic stroke. Diabetic patients with hemorrhagic stroke had a larger hematoma size than patients without diabetes (24). In different studies, hemorrhage volume was the best predictor of mortality for all locations of spontaneous intracerebral hemorrhage (25,26). Diabetes is known to produce deleterious effects on microvasculature, which may result in an increased risk of bleeding (27). Recently, in the European

BIOMED stroke project, the case-fatality rate was independently associated with hemorrhage in stroke patients (13).

In conclusion, this study showed that diabetic stroke patients were younger and had a higher proportions of IHD; their clinical characteristics were sex-dependent; and finally, the type of stroke and number of post-stroke complications were independent predictors of mortality compared to nondiabetic stroke patients. These results suggest that better glycemic control is important, especially among male patients, to decrease the risk of mortality after acute stroke.

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