



# SEX DIFFERENCES IN PATIENTS WITH ACUTE ISCHEMIC STROKE IN TUZLA REGION, BOSNIA AND HERZEGOVINA

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## ABSTRACT

Although many aspects of stroke are similar at both sexes, however, there are some differences and characteristics as well. The aim of this study was to analyze sex differences in patients with acute ischemic stroke (IS) regarding to risk factors, subtypes, stroke severity and outcome.

From January 1<sup>st</sup> 2001 to December 31<sup>st</sup> 2005 at the Department of Neurology Tuzla 2833 patients were admitted with acute ischemic stroke (IS). We were analyzed risk factors, subtypes, stroke severity (Scandinavian Stroke Scale), and thirty-day outcome.

There were 1484 (52,3%) female, and they were older than male ( $67,8 \pm 10,6$  vs.  $65,7 \pm 10,5$ ,  $p < 0,0001$ ). Hypertension (78% vs. 67%,  $p < 0,0001$ ), heart diseases (50% vs. 45%,  $p = 0,009$ ), atrial fibrillation (22% vs. 14%,  $p < 0,0001$ ) and diabetes mellitus (33% vs. 21%,  $p < 0,0001$ ) were frequently in female, while smoking (45% vs. 14%) and alcohol overuse (18% vs. 0,6%) in male ( $p < 0,0001$ ). Atherothrombotic type of ischemic stroke was frequently in male (37,4% vs. 31,6%,  $p = 0,0013$ ) and cardioembolic in female (21,7% vs. 15,5%,  $p < 0,0001$ ). At admission female had lower SS (SS  $31,0 \pm 15$  vs.  $34,0 \pm 15$ ,  $p < 0,0001$ ). Thirty-day mortality was significantly higher in female (23,3% vs. 18,4%,  $p = 0,0015$ ), and favourable outcome within one month (Rankin Scale  $\leq 2$ ) had 58% male and 51% female ( $p = 0,001$ ).

The frequency of ischemic stroke is higher in female who are older than male. There are some sex differences according to the distribution of risk factors and subtypes of ischemic stroke. Stroke severity at admission, thirty-day mortality, and disability are higher in female.

KEY WORDS: ischemic stroke, risk factors, sex

## INTRODUCTION

Stroke is a leading cause of death and disability in industrialized countries and is common in female and male (1). Although, many aspects of stroke, particularly with regard to epidemiology, clinical presentation, neuroimaging, management and prevention, are well described in many studies, stroke is still very interesting for medical sciences. One of interesting topics in stroke is sex differences. Several studies have reported sex differences in the management of patients with cardiovascular disease (2). When compare with male, female were more likely to receive, in the acute phase, a less aggressive therapy and, in general, a reduced amount of diagnostic and therapeutic procedures. In contrast, the literature on stroke and sex differences is not as comprehensive. The greater prevalence of stroke in male is well known, but recent issues emphasize the importance of stroke in female (3). Stroke has a greater effect on female than male owing to the fact that female have more stroke events and are less likely to recover. Age-specific stroke rates higher in male; however, because of female's longer life expectancy and the much higher incidence of stroke at older ages (4). Recent studies in our region, in a post-war period, show higher frequency of stroke in female (5, 6) which differs from similar studies in the other regions (1, 7).

After the war in our country, we did not perform detailed analysis regarding sex differences in patients with acute stroke. Therefore, the aim of this study was to analyze sex differences in patients with acute ischemic stroke (IS) in Tuzla region, Bosnia and Herzegovina, regarding to the risk factors, subtypes, stroke severity and early outcome.

## MATERIALS AND METHODS

From January 1st 2001 to December 31st 2005, at the Department of Neurology Tuzla were admitted 2833 patients with acute ischemic stroke, which seemed 73,3% of the total number of hospitalized patients with stroke.

The medical history and stroke risk factors information of each patient were obtained. We were analyzed the following risk factors: sex, age, hypertension, heart diseases, atrial fibrillation, diabetes mellitus, hyperlipoproteinemia, cigarette smoking and alcohol consumption. Risk factors were included even if they were present before or after a stroke diagnose. Hypertension was defined as being present when the patient was previously

diagnosed with hypertension by a clinician or systolic blood pressure was higher than 140 mmHg and/or diastolic blood pressure was higher than 90 mmHg. The heart diseases group consisted of heart diseases such as angina pectoris, cardiomyopathy, hypertensive heart diseases and heart rhythm disorders. Atrial fibrillation was considered as a separate risk factor. The diagnoses of heart diseases and heart rhythm disorders were confirmed by electrocardiogram, and examination by specialists of internal medicine (7). Diabetes mellitus was diagnosed according to the National Institutes of Health (revised criteria, 1980) (8, 9). Hyperlipoproteinemia was defined as the total serum cholesterol higher than 5,0 mmol/l, low density lipoprotein (LDL) higher than 3,0 mmol/l and triglycerides higher than 2,0 mmol/l. Patients were considered to be smokers if they smoked active or passive (7). Alcohol consumption was represented by the frequency of consumption during the past two months, 100g per day (or higher), and/or acute alcohol intoxication 24 hours before the onset of disease (10).

The diagnosis of stroke subtypes was performed on clinical and cerebral imaging. Etiology of IS was made according to the TOAST criteria (Trial of Org 10172 in Acute Stroke Treatment) (11), and stroke was confirmed by computed tomography (CT) on the SIEMENS EMOTION 6 (Erlangen, Germany). Stroke severity was estimated with Scandinavian Stroke Scale (SS) (12), and stroke disability with Rankin Scale (13). SS ranges from 0 to 58, and Rankin Scale from 0 to 5. Patients with higher score SS reflecting milder stroke, while score Rankin scale >2 reflecting harder stroke. Both scales were evaluated twice, on admission and at discharge.

An inclusion criteria was acute ischemic stroke confirmed by CT, while an exclusion criteria was recurrent ischemic stroke.

### *Statistical analysis*

For statistical analyses of data used by the ARCUS QUICKSTAT program, and significance was estimated by Chi-square test. A value of  $p < 0,05$  was considered to be significant. The study was approved by the Ethical Committee of the University Clinical Centre Tuzla.

## RESULTS

There were 1484 (52,3%) female of average  $67,8 \pm 10,6$  years, while the age for male was  $65,7 \pm 10,5$  years ( $p < 0,0001$ ). Hypertension, heart diseases, atrial fibrillation and diabetes mellitus were

Variable	Female (n=1484)		Male (n=1349)		P
	N	%	N	%	
Age, Mean, SD	67,8	±10,6	65,7	±10,5	<0,0001
Hypertension	1163	78,40	904	67,0	<0,0001
Heart diseases	742	50,00	609	45,14	0,009
Atrial fibrillation	329	22,16	190	14,08	<0,0001
Diabetes mellitus	492	33,15	284	21,05	<0,0001
Hyperlipoproteinaemia	197	13,27	190	14,08	0,5
Smoking	215	14,48	607	45,0	<0,0001
Alcohol overuse	9	0,60	247	18,3	<0,0001
SS, Mean, SD	31	±15	34	±15	<0,0001

SS – Scandinavian Stroke Scale; SD - standard deviation p-value obtained with chi-square test

TABLE 1. General characteristics and risk factors in the patients with ischemic stroke according to sex

Subtypes IS	Female (n=1484)		Male (n=1349)		Total (n=2833)		p
	N	%	N	%	N	%	
Atherothrombotic	469	31,6	504	37,4	973	34,3	0,0013
Cardioembolic	323	21,7	210	15,5	533	18,8	<0,0001
Lacunar	493	33,2	443	32,8	936	33,0	0,8
Other etiology	16	1,1	25	1,8	41	1,4	0,08
Unknown etiology	183	12,3	167	12,3	350	12,3	1

IS – ischemic stroke p-value obtained with chi-square test

TABLE 2. Distribution of patients with ischemic stroke according to subtypes and sex

Outcome	Female (n=1484)		Male (n=1349)		P
	N	%	N	%	
Died, n, %	346	23,3	249	18,4	0,0015
Rankin Scale ≤2	583	51,2	641	58,2	0,001
Rankin Scale, Mean, SD	2,63	±1,4	2,45	±1,3	0,0005

SD - standard deviation p-value obtained with chi-square test

TABLE 3. Rankin Scale and outcome in the patients with ischemic stroke according to sex

significantly more common in female, while smoking and alcohol overuse in male (Table 1).

Atherothrombotic subtype of IS was more common in male, while cardioembolic in female, which can be attributed to the distribution of stroke risk factors. Distribution of the other subtypes of IS (lacunar, other and unknown etiology) was similar in both sexes, without statistical significance (Table 2).

Thirty-day mortality was higher in female. Favourable outcome within one month had 58% of male and 51% of female ( $p=0,001$ ). The male had significantly lower Rankin Scale compared to female ( $p=0,0005$ ) (Table 3).

## DISCUSSION

Ischemic stroke (IS) takes two-thirds of all strokes at our Department, and it is present in a greater number in female, but without statistical significance. In the study of Niewada et al. (14) female are represented in the same percent (52%) as well as in our study. We also found that females are significantly older than

males, which is similar to the study of Arboix et al. (15). The risk factors profile according to our results varies depending on sex (Table 1). These findings are similar with the results of other studies (15, 16), but Sharma et al. (17) didn't found sex differences in risk factors. Vuković et al. (18) in their review showed that the distribution of risk factors such as hypertension, diabetes and hyperlipidemia between genders is inconsistent. We founded that hypertension, atrial fibrillation, diabetes mellitus and heart diseases are more frequent in female, while smoking and alcohol consumption in male, which is similar in the study of Morin-Martin et al. (16). Sex distribution of risk factors is different in the study of Di Carlo et al. (19) comparing with our results. In this study, sex distribution of atrial fibrillation (20,8% female vs. 15,2% male) and cigarette smoking (18,4% female vs. 57,3% male) is approximately the same as in our study, while the frequency of hypertension is lower (50,7% female vs. 46,7% male) than in our study. The frequency of diabetes mellitus in male (21,3%) is similar as in our study (21%), while in female is lower (20,5%). In the mention study, alcohol overuse presented in higher percent in both sexes (47,9% male

vs. 21,2% female), than in our study (19). In the study of Dikanović et al. (20) distribution some of risk factors, such as hypertension (77,69%), heart diseases (46,15%), atrial fibrillation (16,92%), and smoking (28,46%), is similar as in our study (72,9%, 47,6%, 18,3%, 29%, respectively).

The frequency of subtypes of IS are different between sexes, which can be attributed to the distribution of risk factors. In our study, as well as in the other studies (16, 21) male were more affected by atherothrombotic strokes, while female suffered more by cardioembolic. Other subtypes of IS are equally represented in both sexes. Unfortunately, our data were based on hospital register and it was one of the limitation of this study. Official stroke register hasn't yet been formed in our region.

## CONCLUSION

We can conclude that the frequency of ischemic stroke is higher in female and they are older than male. Hypertension, atrial fibrillation, diabetes mellitus and heart diseases are significantly more common in female, while cigarette smoking and alcohol intake in male. Atherothrombotic type of ischemic stroke is more frequent in male and cardioembolic in female. Stroke severity at admission, mortality and disability within the first month are higher in female.

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