

STROKE AT A YOUNGER AGE

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SUMMARY – Stroke is a suddenly developing disorder, caused by focal disturbance of cerebral circulation, followed by neurologic deficits of varying intensity with duration longer than 1 hour; it mostly occurs in old and middle age, and rarely at a younger age. The aim of the study was to analyze the occurrence of stroke at a younger age (18–49 years). We analyzed all stroke patients aged 18–49 treated at University Department of Neurology in Sarajevo during 2009, including analysis of their risk factors. During the one-year period, there were 820 stroke patients in total, 132 (18.5%) of them aged 18–49, male to female ratio 51.35%:48.65%. The majority of strokes were of ischemic type (94.59%), with only 5.41% of hemorrhagic stroke. The following risk factors were confirmed in study patients: hypertension (64.86%), smoking (57.76%), dyslipidemia (48.65%), ischemic heart disease (43.32%), psychological stress (29.73%), diabetes mellitus type 2 (24.43%), previous stroke including transient ischemic attack (21.62%), and others. During the one-month follow-up, 27.03% of patients achieved complete recovery, whereas mild neurologic signs were retained in 54.05%, signs of severe deficit requiring assistance in 13.51%, and 5.41% of patients died. In conclusion, stroke occurs even at a younger age in certain percentage. Along with smoking, diabetes, dyslipidemia and stress, hypertension is one of the leading risk factors for stroke also at a younger age. Timely and appropriate treatment contributes to faster recovery and shorter hospital stay, while reducing overall stroke sequels. The best prevention is primary, i.e. fighting risk factors and healthy lifestyle.

Key words: *Stroke; Age factors; Risk factors*

Introduction

Hippocrates, the father of medicine, was the first to recognize the symptoms of stroke more than 2400 years ago¹. Stroke (stroke, cerebral apoplexy, cerebrovascular accident) is a disease of the brain parenchyma, which is caused by inadequate cerebral circulation, compromised or complete interruption of blood flow to an area, regardless of whether it results from disturbance in the brain or it is the result of impaired cerebral circulation caused by diseases of other organs or organ systems and influenced by the actions of different physical and chemical agents².

Stroke is defined as a disorder with abrupt onset, followed by neurological deficit of varying intensity,

caused by focal disturbance of cerebral circulation, with a duration of deficit for more than 24 hours, which can lead to lethal outcome. Even with diagnostic and therapeutic advances in medicine, stroke is now the third leading cause of mortality in the world (after cancer and cardiovascular disease), the second leading cause of disability (after trauma), and the second leading cause of dementia (after Alzheimer's disease). Therefore, stroke is a major health, social and community problem.

The aim of the study was to determine the total number of patients suffering stroke at a younger age (18–49 years) during a one-year period (from January 1 to December 31, 2009), with special reference to the presence of risk factors in these patients.

Patients and Methods

The study was conducted at University Department of Neurology, Sarajevo University Clinical Center in

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Received December 2, 2010, accepted July 8, 2011

Sarajevo in 2009. It included all patients aged 18-49 diagnosed with stroke. Patients diagnosed with transient ischemic attack (TIA) were not included. The diagnosis of stroke was confirmed by history, clinical examination, computed tomography scan of the brain, and laboratory tests, with special reference to the presence of hypertension, diabetes, hyperlipidemia, smoking, AV malformations, use of contraceptives, etc. Additional electrocardiography and cardiologic tests were performed as appropriate.

Results

From January 1 to December 31, 2009, a total of 820 patients diagnosed with stroke were hospitalized at University Department of Neurology, Sarajevo University Clinical Center. There were 132 (18.5%) patients aged 18-49, defined as a younger age group, female 48.65% and male 51.35%.

In order to accurately analyze and determine correlation between the occurrence of stroke and patient age, the younger age male and female patients were divided into three age groups as follows: group 1 aged 18-30, group 2 aged 31-40 and group 3 aged 41-49 years. The percentage of female and male patients was as follows: group 1 (aged 18-30) 8.12% and 2.70%; group 2 (aged 31-40) 8.12% and 18.91%; and group 3 (aged 41-49) 32.43% and 29.72%, respectively. According to educational level, there were 29.72% of patients with primary education, 53.24% of patients with secondary education, and 17.0% of patients with university education. At baseline, ischemic stroke was diagnosed in 94.59% and hemorrhagic stroke in 5.41% of study patients. In the majority of patients (n=125),

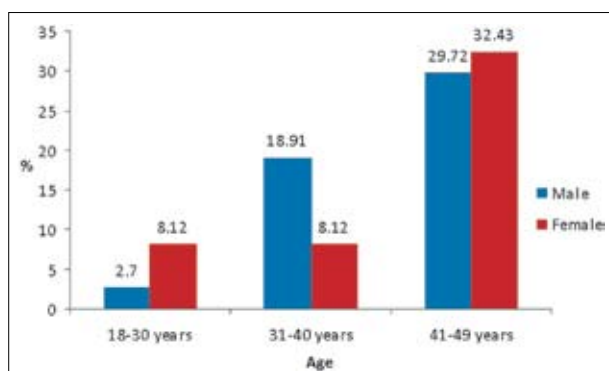


Fig. 1. Age and sex distribution of study patients

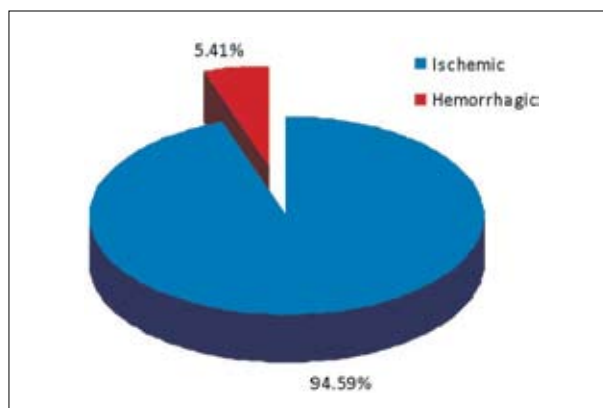


Fig. 2. Distribution of stroke types

the mean length of hospital stay was 16.78 (range 7-32 days), i.e. mode=16, standard deviation 6.16 days or average linear deviation from the mean 6.12 days.

Out of 132 patients, 128 survived stroke and four patients died. Complete recovery was achieved in 27.03%, persistence of minor neurologic signs (hemiparesis or mild dysphasia) or gradual improvement in the course of disease was recorded in 51.05% and full symptom persistence in 13.51% of study patients, whereas 5.41% of patients did not survive the insult.

The presence of the following risk factors was recorded:

- hypertension (64.85%),
- dyslipidemia (48.65%),
- tobacco smoking (45.95%),
- psychological stress (29.73%),
- diabetes mellitus type 1 (2.70%),
- diabetes mellitus type 2 (24.32%),
- ischemic heart disease (43.24%),
- cardiac arrhythmia (8.11%),
- heart valve damage (0%),
- previous stroke including TIA (21.62%),

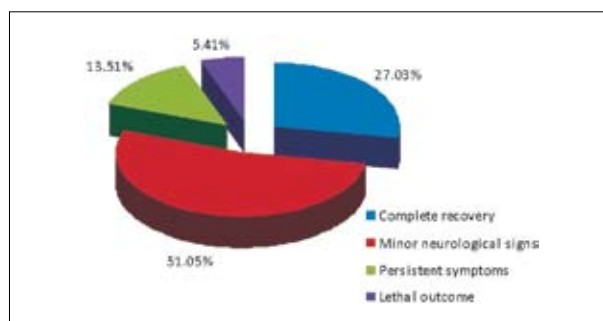


Fig. 3. Distribution of treatment outcomes

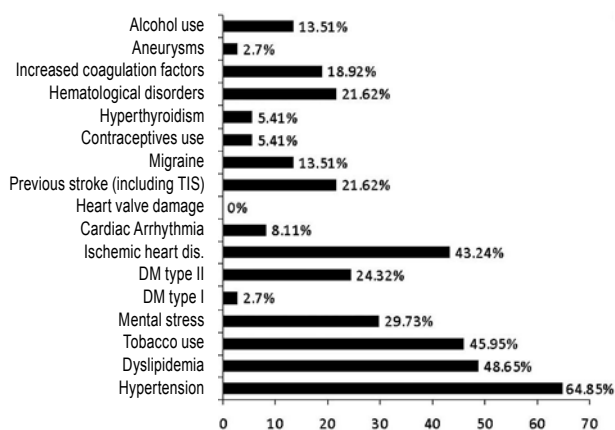


Fig. 4. Risk factors

- migraine (13.51%),
- use of contraceptives (5.41%),
- hyperthyroidism (5.41%),
- hematologic disorders (21.62%),
- increased coagulation factors (18.92%),
- aneurysms (2.70%),
- use of alcohol (13.51%).

Results are shown in Figures 1-4.

Discussion

During the one-year period, a total of 820 stroke patients were hospitalized, 132 (18.5%) of them belonging to the younger age group (aged 18-49). These data clearly indicate that a significant percentage of persons below 49 years of age suffered stroke.

Doctor Jennifer Ashton, medical correspondent for CBS News, presented data concerning the occurrence of stroke in younger age. Specifically, she based her report on various studies from different parts of the United States and concluded that in 1994 the percentage of younger patients in the total number of patients diagnosed with stroke was 4.5% (younger age defined as 20-45 years), whereas in 2005 this share was 7.3%¹⁷. These data appear to correlate with those obtained in the present study, however, taking into account different definition of younger age and different study years, i.e. 2007 and 1994, when this study was conducted.

It should be noted, however, that both sets of data point to a very important fact, namely, that the number of younger patients with stroke has been increasing in recent years. Dimitrijević *et al.* report on 10.80% of

stroke patients aged 15-50 in the total cohort of stroke patients treated at University Department of Neurology, Sarajevo University Clinical Hospital during the 1996-2000 period. In the total number of stroke patients, there were 51.35% of male and 48.65% of female patients, yielding a male to female (M:F) ratio of 1.055:1. In their comparative study in patients of younger age (18-49 years) from Malaysia and Australia, Kay Sin Tan *et al.* found a M:F=1.4:1 for Malaysia and M:F=1.54:1 for Australia¹⁹. So, the relationship of male and female subjects in this study indicated a slight male predominance in the occurrence of stroke, which is today a global observation.

Analysis of stroke prevalence in patients of younger age according to occupation showed that there was no particular occupation association with stroke. The majority of our patients had secondary education or were unemployed. Etiologic classification includes stroke division into ischemic and hemorrhagic stroke. Ischemic stroke was found in 94.59% and hemorrhagic stroke in only four (5.41%) younger stroke patients. All patients with ischemic stroke had a stroke of thrombosis type. Out of the four patients with hemorrhagic stroke, intracerebral hemorrhage was recorded in one patient and subarachnoid hemorrhage (SAH) in the remaining three patients. Data on the proportion of ischemic and hemorrhagic stroke reported by other authors differ to a varying degree from those recorded in the present study. During the 1982-1987 period, Bevan *et al.* conducted a study at Medical Center Hospital of Vermont, which included 113 patients aged 15-45: ischemic and hemorrhagic stroke was diagnosed in 42% and 58% of patients, respectively. In 2000, Marcoux investigated a sample of patients aged 30-45 from Lausanne, with the following results: ischemic stroke was present in as many as 88% and hemorrhagic stroke in only 12% of cases²⁰. In 2007, Ellis *et al.* from Medical University of South Carolina, included younger patients aged 18-45 in their study and report on ischemic stroke in 78% and hemorrhagic stroke in 22% of their patients.

Considering overall population of stroke patients (which is over 85% of the population older than 50), in the industrialized countries of Western Europe, ischemic stroke accounts for over 80% and hemorrhage for less than 20% of cases.

It is especially important to compare the information obtained during this study with the 1982-1987 period, when there were only 42% of ischemic stroke, compared with 94.59% of ischemic stroke recorded in this study. The other two listed studies showed a significant increase in the percentage of ischemic stroke in 2000 and 2007 in comparison to the 1982-1987 period, and this percentage is approximately equal to the percentage proportion of ischemic and hemorrhagic stroke in the general population.

Thus, the percentage of ischemic stroke at a younger age, as a characteristic of old age, has increased significantly during the last 25 years. The processes and pathologic changes that occur in cerebral blood vessels of young people are not different from those that take place in blood vessels of older patients, and in both cases they are mainly associated with atherosclerosis and subsequent thrombosis. These data are consistent with those reported by Jingle Liu and Jinpin Li from their study conducted at Guangxi Medical University, Department of Neurology, from September 2005 to June 2006. In the present study, younger patients with the diagnosis of stroke were hospitalized for a mean of 16.78 days, and the majority of patients ($n=125$) were hospitalized for 16 days (mode=16), standard deviation or average linear deviation from the mean 6.12 days. These results are consistent with those reported by Harsh Kumar *et al.*, Kalra from their study conducted in South India in 2009.

Concerning stroke outcome, we found that 94.59% of younger stroke patients survived and four (5.41%) patients died. Of 128 survivors, complete recovery was achieved in 27.03% of younger stroke patients; 54.05% of patients required rehabilitation or had mild signs of neurologic deficit; and 13.51% of patients had more severe signs requiring assistance of another person.

In their study, Marini *et al.* from the University of L'Aquila in Italy found the survival of younger persons (aged 15-45) with the diagnosis of stroke to be 86.5%. Generally, the survival of younger stroke patients can be considered good.

Hypertension as the most common risk factor for stroke was present in 64.85% of our younger stroke patients. A meta-analysis of 14 studies has shown that a reduction by only 5-6 mm Hg in diastolic blood pressure in patients with hypertension leads to a 42% decrease in the incidence of stroke. Similar data report

You *et al.* from their study conducted in Melbourne, which included patients aged 55 years and younger, where hypertension was found in 68.1% of patients.

The next most frequent risk factor is smoking, followed by dyslipidemia, which in our study was present in 48.65% of patients. There is a correlation between stroke and dyslipidemia, which also causes damage to blood vessels. A recent meta-analysis that included data from CARE and 4S study has confirmed the overall risk reduction of 31% using statins (pravastatin and simvastatin) for the development of all forms of stroke, except for those with fatal outcome. Similar information is presented by Kameshwar on patients from Finland (aged 15-49), with hyperlipidemia found in 43.3% of patients, whereas in South Asia it is a major risk factor recorded in 53.1% of patients (aged 15-49).

Response to stress enhances platelet aggregation, activates the renin-angiotensin system and production of angiotensin II, and leads to an increase in blood pressure. Stress is associated with a higher incidence of cardiovascular and cerebrovascular disease.

In the present study, a history of stress was reported by 29.73% of younger stroke patients.

Diabetes mellitus is a metabolic disorder characterized by abnormal glucose metabolism in terms of chronic hyperglycemia, and at the same time disturbed metabolism of lipids and proteins. This disorder accelerates atherosclerotic process and causes the formation of microangiopathy (changes in blood vessels, kidney, retina and nerves) and macroangiopathy (changes in blood vessels of the heart, brain and extremities).

In our study, diabetes type 1 was present in 2.70% and diabetes type 2 in 24.32% of patients, yielding 27.02% of patients with diabetes in total.

Nayak *et al.* report on the presence of diabetes in only 7% of patients aged 15-45 diagnosed with stroke, whereas You *et al.* found diabetes in 56.4% of stroke patients aged 15-55.

Atrial fibrillation and valvular heart disease increase the risk of cerebral ischemia because both can lead to cerebral embolism. In patients with chronic, stable atrial fibrillation, the risk of stroke is increased fivefold. When atrial fibrillation is a manifestation of rheumatic heart disease, the risk of brain embolism is increased up to 17 times. In the present study, cardiac arrhythmias were reported by 8.11% of patients.

Surviving stroke or TIA increases the possibility of a new stroke. In our study, 21.62% of patients had already had one or more strokes, including TIA. Vitanen *et al.* conclude that the probability of a new stroke is highest in the post acute period in first stroke survivors, the risk being higher by 5% each year, with a five-year cumulative risk of about 25%, although the stated value goes up to 42%.

Migraine is a risk factor for stroke, in particular the so-called migraine status, when migraine episode lasts for more than 72 hours, regardless of treatment. Headache is continuous or with interruptions for less than 4 hours. However, stroke may rarely occur during migraine episode of this type. In our study, migraine was present in 13.51% of younger patients diagnosed with stroke. In their study including patients aged 15-49 with ischemic stroke, Bašić-Kes *et al.* identified migraine in 16% of female patients and none of male patients, yielding 6.45% of patients diagnosed with migraine and stroke in total.

The risk of stroke, ischemic stroke in particular, is increased in people who take oral contraceptives. The incidence of stroke has moderately increased in Europe, whereas a threefold increase has been recorded in Africa, Asia and Latin America. A World Health Organization study conducted in developing countries revealed the risk of cerebral hemorrhage to have increased among the users of oral contraceptives. The risk was found to have increased with the dosage of oral contraceptives. In our study, the relationship between the use of oral contraceptives and stroke could be reflected by 11.11% of stroke patients using contraceptives.

Hematologic disorders or hypercoagulable states are responsible for 1% of all strokes, while at young age the figure increases to 2%-7%. The most common hematologic causes of ischemic stroke include anemia, factor V mutation, disruption of protein C and S, antiphospholipid syndrome, elevated LDL, elevated homocysteine, and factor XII deficiency. Numerous acquired or inherited prothrombotic states are associated with ischemic stroke. In the present study, hematologic disorders were present in 18.92% of younger patients with stroke.

Intracranial aneurysm is local expansion of the cerebral blood vessel lumen; the etiology of intracranial aneurysms has not yet been fully elucidated. Their most common clinical manifestation is subarachnoid

hemorrhage. In our study, aneurysm (basilar artery) was identified in one (2.70%) patient and caused SAH. Bevan *et al.* diagnosed aneurysms that caused SAH in 17% of cases during their 5-year study (1982-1987) in stroke patients aged 15-45.

Alcohol has been identified as a possible risk factor for stroke for nearly three centuries now, since as early as 1725, and in 1984 it was included in the group of "incompletely proven" risk factors for stroke. Regular alcohol abuse is often associated with an increased incidence of stroke; a possible explanation states that "heavy" drinkers have higher systolic and diastolic blood pressure than those who do not drink or drink only occasionally.

Smoking is undoubtedly an independent risk factor for stroke. One explanation is the acceleration of atherosclerosis. Quitting smoking does not change the immediate risk of stroke, but approaches or equalizes the risk of those who have never smoked only after 2-5 years of abstinence. In the present study, smoking as a risk factor was found in 57.76% of younger stroke patients. Similar data have been reported by Jovicevic *et al.* on 53.3% of patients aged 23-45 smoking cigarettes.

Conclusions

Stroke is a disease that does not spare younger population. In our study, 132 of 820 (18.5%) patients hospitalized for stroke during a one-year period were aged 18-49. Study results revealed men to prevail. Ischemic stroke predominated over hemorrhagic stroke (94.59% *vs.* 5.41%). The most common risk factor for stroke was hypertension (64.86%), followed by smoking (57.76%), dyslipidemia (48.65%), ischemic heart disease (43.32%), psychological stress (29.73%), diabetes mellitus type 2 (24.43%), previous stroke including TIA (21.62%), hematologic disorders (18.92%), migraine (13.51%), hyperthyroidism (13.51%), alcohol abuse (13.51%), cardiac arrhythmia (8.12%), use of contraceptives (5.41%), diabetes mellitus type 1 (2.70%), aneurysm (2.70%), and valve damage (0%). Concurrence of multiple risk factors increases the likelihood of stroke. Early recognition of stroke (ischemic, 3 hours) and use of currently most relevant therapy (thrombolytic therapy) enables recovery of neurologic deficit with a shorter hospital stay and lower degree of disability. The best way of prevention is healthy lifestyle and fight against risk factors.

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Sažetak

MOŽDANI UDAR U MLAĐOJ DOBI

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Moždani udar je iznenadno nastali poremećaj uzrokovan fokalnim poremećajem moždane cirkulacije, praćen neurološkim deficitom različitog intenziteta trajanja dužeg od 1 h; uglavnom se javlja u starijoj i srednjoj, a rjeđe u mlađoj životnoj dobi. Cilj rada bio je analizirati pojavu moždanog udara u mlađoj životnoj dobi (18-49 godina). Analizirani su svi oboljeli od moždanog udara u dobi 18-49 godina liječeni na Neurološkoj klinici u Sarajevu tijekom 2009. godine uz analizu čimbenika rizika. Od ukupno 820 bolesnika s moždanim udarom tijekom jednogodišnjeg razdoblja postotak bolesnika mlađe životne dobi bio je 18,5% (n=132). Muškaraca je bilo 51,35%, a žena 48,65%. Naveći broj moždanih udara bili su ishemijski (94,59%) moždani udari, dok je hemoragijskih moždanih udara bilo 5,41%. Kod oboljelih su potvrđeni slijedeći čimbenici rizika za moždani udar: hipertenzija (64,86%), pušenje (57,76%), dislipidemija (48,65%), ishemijska bolest srca (43,32%), psihički stres (29,73%), dijabetes melitus tip 2 (24,43%), prethodni moždani udar i drugo. Tijekom jednomjesečnog praćenja 27,03% bolesnika je postiglo potpun oporavak, 54,05% bolesnika zadržalo je blaže neurološke znakove, 13,51% znakove težeg deficita koji zahtijevaju tuđu pomoć, a 5,41% bolesnika je umrlo. U zaključku, moždani udar se javlja u znatnom postotku i u mlađoj životnoj dobi. Hipertenzija je uz pušenje, dijabetes i dislipidemiju te stres vodeći čimbenik rizika za nastanak moždanog udara i u mlađoj dobi. Pravodobno i primjereno liječenje doprinosi bržem oporavku, kraćem boravku u bolnici i ishodu s manje ukupnih posljedica. Najbolja prevencija je primarna, tj. borba protiv čimbenika rizika i zdrav način života.

Ključne riječi: *Moždani udar; Dobni čimbenici; Čimbenici rizika*

