STROKE PATIENTS TREATED AT DEPARTMENT OF NEUROLOGY, ŠIBENIK-KNIN COUNTY GENERAL HOSPITAL, 1996-2005

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SUMMARY – In this retrospective study, data on 3819 stroke patients, 1966 (51.5%) female and 1853 (48.5%) male, treated at Department of Neurology, Šibenik-Knin County General Hospital during the 1996-2005 period were analyzed. There were 3417 (89.5%) patients with ischemic stroke and 402 (10.5%) patients with hemorrhagic stroke. Analysis according to age decades revealed the 70-79 age group to account for the greatest number of both ischemic and hemorrhagic stroke patients *per* year. Stroke risk was found to rise significantly with each age decade irrespective of sex (χ^2=7764.19; *P*=0.0000001). Rural and urban population accounted for 56.9% and 43.1% of all stroke cases, respectively (*P*=0.0000001). During the study period, the number of stroke cases steadily increased from 313 in 1996 to 422 in 2005 *per* 112,891 county population, yielding a rise in stroke incidence over years (χ^2=24.63; *P*=0.003). The mean age of stroke patients increased from 72.5 years in 1996 to 74.6 years in 2005. The mean age of ischemic and hemorrhagic stroke patients was 73.2 and 66.7 years, respectively (*P*=0.0000). The stroke mortality rate increased from 75.2/100,000 in 1996 to 87.7/100,000 in 2000, and then decreased to 66.4/100,000 in 2005. The rate of hospital stroke mortality was reduced from 27.07% (95% CI, 21.62-33.47%) in 1996 to 17.44% (95% CI, 13.72-21.86%) in 2005 (*P*=0.005159), yielding a hospital mortality decrease by 9.63%. During the four-year study period, 808 patients died from stroke, showing a female predominance (F:M, 59.8% *vs.* 40.2%; *P*=0.000003092).

Key words: *Stroke – mortality; Stroke – prevention and control; Cerebral hemorrhage – mortality; Ishemic attack, transient; Croatia – epidemiology*

Introduction

According to the World Health Organization (WHO) data, 5,540,000 individuals die from stroke in the world *per* year. Stroke is the second leading cause of mortality in most countries worldwide, ranking third in some industrialized countries[1]. In Europe, stroke remains the second most common cause of mortality, with 1,280,000 deaths *per* year[2]. Statistical data show great differences between the Western and Eastern Europe countries, with a decreasing tendency in the incidence and mortality of stroke reported from the former *versus* an increase recorded in the latter[3,4]. In Western European countries, proper education of the population at large, along with appropriate prevention and switch to healthier lifestyle has led to a decline in the number of stroke patients and deaths.

In Croatia, stroke is the second leading cause of death. In 2007, a total of 52,367 people died, with cardiovascular disease accounting for 26,506 (50.62%) deaths. Ischemic heart disease ranked first, immediately followed by cerebrovascular disease accounting for 8323 (15.89%) deaths. Stroke mortality showed a female predominance (male to female ratio, 13.0%:18.82%)[5].

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Estimates for Europe suggest the population will decline from 728 million in 2000 to 705 million in 2050, while the incidence of stroke in the >65 age group will rise from 20% in 2000 to 35% in 2050[6]. According to the WHO and United Nations estimates, the rate of stroke patients will increase from 1.1 million *per* year in 2000 to 1.5 million *per* year in 2025[3].

Stroke is a major public health and socioeconomic problem due to long-term absenteeism from work and high percentage of disablement in stroke survivors[7].

The aim of the present study was to analyze the incidence of stroke and demographic characteristics of stroke patients in the Šibenik-Knin County during the 1996-2005 period.

Subjects and Methods

Data on all stroke patients treated at Department of Neurology, Šibenik-Knin County General Hospital during the 1996-2005 period were analyzed in this retrospective study. According to census data, the County had 112,891 inhabitants (there was no census in 1996, however, due to the war actions between 1991 and 1995 and consequential reduction in the number of inhabitants recorded in 2001 census, the 2001 census appeared to be logical choice as being more representative for 1996 than the 1991 census).

According to the International Classification of Diseases, 10th revision (ICD-X), stroke is classified into ischemic and hemorrhagic stroke. In our study, patients with first ever ischemic stroke and those with recurrent ischemic stroke were classified as ischemic stroke (ICD-X codes I63 and I64), whereas patients with intracerebral hematoma, subdural hematoma and subarachnoid hemorrhage were classified as hemorrhagic stroke (ICD-X codes I60, I61 and I62). Stroke incidence was analyzed according to years, patient age, overall patient mortality and in separate for ischemic and hemorrhagic stroke, patient sex and residence (urban *vs*. rural).

Statistical analysis was done by use of the Statistica version 6.0 (StatSoft, Inc., Tulsa, OK, USA) and MedCalc version 9.2.0.1 (MedCalc Software, Mariakerke, Belgium) statistical softwares. Descriptive statistics was employed to describe characteristics and measured variables, presented in tables. Arithmetic mean and standard deviation with 95% confidence interval (CI) were used to describe continuous variables. Category variables were presented as prevalence (%) and incidence rate *per* 1000 inhabitants with 95% CI. Analysis of variance was employed on comparison of continuous variables according to subgroups. On comparison of distribution of category variables according to groups, χ^2-test was used, and rate ratio (RR) and odds ratio (OR) were calculated, with 95% CI. The level of statistical significance was set at P=0.05.

Results

During the study period (1996-2005), 7389 patients were hospitalized at Department of Neurology (24 beds), Šibenik-Knin County General Hospital in Šibenik, 3819 (51.7%) of them for ischemic (n=3417; 89.5%) or hemorrhagic (n=402; 10.5%) stroke (Table 1). There were 1966 (51.5%) female and 1853 (48.5%) male patients. There was no statistically significant sex difference according to study years or stroke type, except for male predominance in the incidence of ischemic stroke in 2004; i.e. 241 male *versus* 204 female patients (RR 1.236; 95% CI 1.02-1.499; P=0.0306).

According to age decades, the highest rate of both ischemic and hemorrhagic stroke cases was recorded in the 70-79 age group in all study years. Stroke risk increased significantly with each age decade irrespective of sex (χ^2=7764.19; P=0.0000001), with age specific OR 1 in 19-49 age group (reference value), 9.83 in 50-59, 26.19 in 60-69, 68.467 in 70-79, 141.053 in 80-89 and 118.09 in 90-99 age group.

According to place of residence, 56.9% of stroke patients were from rural areas and 43.1% from urban setting, yielding a significantly higher morbidity rate in rural than urban population (3.96/1000, 95% CI 3.79-4.13 *vs*. 2.84/1000, 95% CI 2.71-2.98; P=0.0000001).

The number of stroke patients in the County increased with the years of observaion, from 313 patients *per* 112,891 inhabitants in 1996 through 389 patients in 2000 to 422 patients in 2005. The incidence of stroke was on an increase over years (χ^2=24.63; P=0.003), with a continuous significant increase in the incidence of ischemic stroke (χ^2=40.11; P=0.0000001). The incidence of hemorrhagic stroke showed an increase from 1996 to 2003 (χ^2=4.59; P=0.032), followed by a de-

Table 1. Stroke patients according to stroke type, place of residence, sex and number of deaths

	Stroke type	Rural		Urban	Sex	Deaths
	Ischemic	281	196	85	M 132	25
					F 149	47
1996	Hemorrhagic	32	16	16	M 20	9
					F 12	4
	Total	313	212	101	313	85 (75.2)*
	Ischemic	320	178	142	M 157	41
					F 163	44
1997	Hemorrhagic	39	22	17	M 22	6
					F 17	7
	Total	359	200	159	359	98 (86.8)*
	Ischemic	304	164	140	M 148	31
					F 156	38
1998	Hemorrhagic	40	21	19	M 22	8
					F 18	6
	Total	344	185	159	344	92 (81.5)*
	Ischemic	313	174	139	M 144	23
					F 169	45
1999	Hemorrhagic	43	20	23	M 22	11
					F 21	10
	Total	356	194	162	356	89 (78.8)*
	Ischemic	337	207	130	M 155	40
					F 182	47
2000	Hemorrhagic	52	34	18	M 26	7
					F 26	5
	Total	389	241	148	389	99 (87.7)*
	Ischemic	344	179	165	M 160	25
					F 184	37
2001	Hemorrhagic	49	26	23	M 26	10
					F 23	11
	Total	393	205	188	393	83 (73.5)*
	Ischemic	341	199	142	M 162	21
					F 179	44
2002	Hemorrhagic	50	28	22	M 23	6
					F 27	9
	Total	391	227	164	391	80 (70.9)*
	Ischemic	364	203	161	M 175	27
					F 189	43
2003	Hemorrhagic	43	23	20	M 22	4
					F 21	4
	Total	407	226	181	407	78 (69.1)*
	Ischemic	417	218	199	M 224	22
					F 193	37
2004	Hemorrhagic	28	12	16	M 17	3
					F 11	1
	Total	445	230	215	407	63 (55.8)*
	Ischemic	396	231	165	M 185	30
					F 211	43
2005	Hemorrhagic	26	12	14	M 11	1
					F 15	1
	Total	422	243	179	422	75 (66.4)*

*mortality rate *per* 100,000 inhabitants

Table 2. Increase in stroke incidence according to study years

Stroke type		1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
Ischemic	OR	1*	1.14	1.08	1.11	1.2	1.23	1.22	1.3	1.49	1.41
	P	<0.0000001									
Hemorrhagic	OR	1*	1.22	1.25	1.34	1.62	1.53	1.56	1.34	1.87	0.81
	P	0.032								0.00018	

*1 = reference value

crease in 2004 and 2005 (χ^2=13.97; *P*=0.00018) (Table 2, Fig. 1).

The cumulative mean age of stroke patients was 72.5 years in 1996 and increased to 74.6 years in 2005. The mean age of ischemic stroke patients was 73.2 years, significantly exceeding the mean age of hemorrhagic stroke patients of 66.7 years (ischemic stroke to hemorrhagic stroke: 73.2±9.8 years, 95% CI 72.8-73.5 *vs*. 66.7±12.0 years, 95% CI 65.6-67.9; F=148.20; *P*=0.0000) (Fig. 2).

The stroke lethality rate increased from 75.2/100,000 in 1996 to 87.7/100,000 in 2000, then showing a decline to 66.4/100,000 in 2005. The rate of hospital stroke lethality decreased from 27.07% (95% CI 21.62-33.47%) in 1996 to 17.44% (95% CI 13.72-21.86%) in 2005 (*P*=0.005159), yielding a 9.63% reduction during the period of observation. During the 10-year period, 808 stroke deaths were recorded. The stroke lethality rate was significantly higher in female than in male patients (82.95/100,000, 95% CI 75.72-90.69 *vs*. 59.45/100,000, 95% CI 53.16-66.28; *P*=0.000003092). According to stroke type, 425 (52.6%) female and 260 (32.2%) male patients died from ischemic stroke, whereas 58 (7.2%) female and

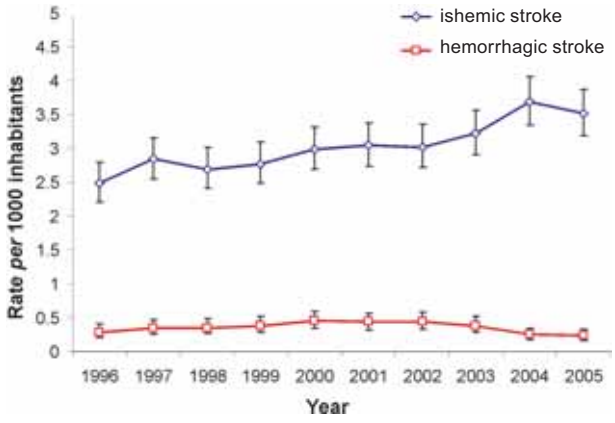

Fig. 1. Incidence of ischemic and hemorrhagic stroke per 1000 inhabitants of the Šibenik-Knin County according to study years.

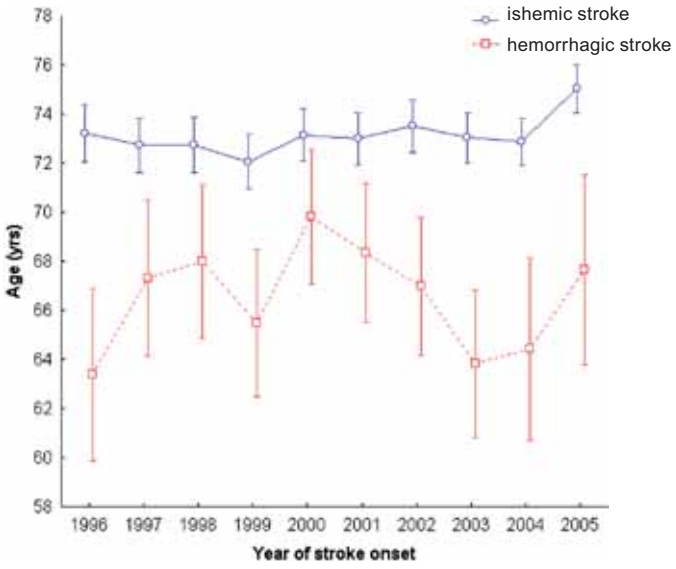

Fig. 2. Patient age at onset of ischemic and hemorrhagic stroke according to study years.

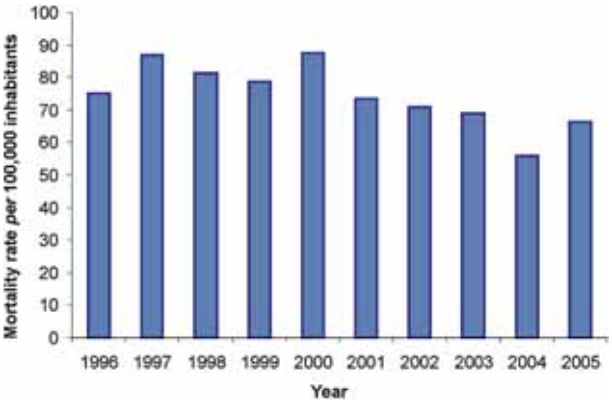

Fig. 3. Stroke mortality per 100,000 in Šibenik-Knin County according to study years.

65 (8%) male patients died from hemorrhagic stroke. The pattern of stroke mortality is illustrated in Fig. 3.

Discussion

During the 1996-2005 study period, the incidence of stroke among patients treated at Department of Neurology, Šibenik-Knin County General Hospital increased by 35%, with a continuous rise of ischemic stroke, whereas the incidence of hemorrhagic stroke showed an increase until 2003, followed by a decline thereafter. Our results are consistent with those reported by Lovrenčić-Huzjan *et al.* on the increase in the incidence of cerebrovascular disease in Zagreb by 57% from 1990 to 1999[8]. In the last decade of the 20th century, the incidence of stroke was observed to decline in some industrialized countries, however, major differences between Eastern and Western European countries persist (3,4). Medin *et al.* investigated stroke incidence in Sweden between 1989 and 2000, and also report it to rise[9]. Wolfe *et al.* explored the incidence of stroke in France (Dijon), England (London) and Germany (Erlangen) over a 3-year period and found it to be lowest in France, medium in England and highest in Germany[10]. Correia *et al.* report on Portugal to have the highest stroke incidence and mortality in Western Europe[11], whereas Rothwell *et al.* found the incidence of stroke to have declined from 1981-1984 to 2002-2004 period in Oxfordshire, Great Britain, attributing it to more efficient prevention and reduced presence of risk factors in the population[12].

The present study showed stroke to affect equally male and female patients. The only sex difference was recorded in 2004, with male predominance of ischemic stroke. These results differ from those reported by Seshadri *et al.*; assessing the presence of stroke risk factors in female subjects, they found women to be at greater exposure to stroke development[13]. Investigating sex differences in stroke epidemiology in the USA between 1999 and 2004, Reeves *et al.* found female sex to be associated with a higher prevalence of stroke and poorer recovery due to the higher prevalence of stroke in older age groups in women[14]. Lovrenčić-Huzjan *et al.* showed that the male to female ratio of stroke incidence did not change significantly between 1990 and 1999; the rate of recurrent stroke increased in male and decreased in female patients, whereas the rate of parenchymal hemorrhage increased in female patients[8].

In the Šibenik-Knin County, the mortality rate was higher in female than male stroke patients (59.8 *vs.* 40.2%), which is consistent with the higher mortality rate of female stroke patients in Croatia reported in 2007[5]. According to our results, ischemic stroke mortality showed a female predominance (female 52.6% *vs.* male 32.2%), whereas no sex predominance was observed in hemorrhagic stroke mortality (female 7.2% *vs.* male 8%). The overall mortality rate was on an increase until 2000, followed by a decline to 66.4/100,000 in 2005. The hospital lethality rate showed a decrease by 9.63%. Kadojić *et al.* investigated mortality rate in Croatia from 1958 to 1997 and demonstrated a 75% increase in the standardized mortality rate by 5-year intervals, i.e. from 118/100,000 in the first 5-year interval to 206/100,000 in the last 5-year interval. Specific mortality rates showed an increasing tendency in male and stagnation or reduction in female sex. Mortality rate was found to be higher in inland parts as compared with littoral areas[15]. In contrast, Lovrenčić-Huzjan *et al.* report on a decrease in the general mortality and male mortality, and an increase in female mortality in the Zagreb area[8].

Sans *et al.* analyzed mortality rates in 30 European countries and found the standardized mortality rate of cerebrovascular disease in the 45-74 age groups of both sexes in the 1990-1992 period to be lowest in Switzerland, France and Island, and highest in Bulgaria, Russian Federation and Ukraine[16]. In contrast to these data, great mortality differences have been reported from Mediterranean countries, e.g., between France and Portugal, the latter having the highest incidence and mortality rate among Western European countries[16]. Unlike the previously cited studies by Seshadri *et al.*[13] and Reeves *et al.*[14], Sans *et al.* found specific mortality rates to be lower for female than male sex[16]. A decrease in the mortality rate has been recorded in England and Sweden[9,12]. Sarti *et al.* observed the stroke mortality rate worldwide from 1968 to 1994 and found it to be comparable between Western Europe (Switzerland and France) and the USA, Canada and Australia[17].

The decrease in stroke mortality can be attributed to better therapy available in recent years, appropriate education of the population at large and improved

primary and secondary stroke prevention[18]. More favorable therapeutic outcome is achieved at institutions where treatment is administered at specialized stroke units[19].

Patients suffering from ischemic stroke are generally older than hemorrhagic stroke patients; both groups of stroke patients are most frequently affected at the age of 70-79. These data vary from those reported in 1998 on stroke patients treated at University Department of Neurology, Osijek University Hospital, where the mean age of both ischemic and hemorrhagic stroke patients was lower, the majority of patients being aged 61-70[20].

The risk of stroke increases with each age decade in both sexes. As women generally live longer than men, female sex is associated with a higher incidence of stroke in older age groups and poorer stroke outcome[14]. According to the American Heart Association Scientific Statement from 2001, the incidence of ischemic stroke doubles with each age decade after the age of 55[21].

In our study, patients from rural areas predominated over those from urban setting (56.9% *vs*. 43.1%; *P*=0.0000001); this finding could be explained by the lower level of education and thus inadequate knowledge and control of stroke risk factors in the former[22].

Conclusion

During the 10-year study period (1996-2005), an increase in the incidence of stroke among hospitalized patients was recorded in the Šibenik-Knin County. There were no sex differences in the incidence of stroke; however, the stroke mortality rate was higher in female patients. Generally, stroke mortality was found to be on a decrease, while the age of stroke patients increased and so did the risk of stroke with each decade of life. Also, patients from rural areas were found to predominate over those from urban setting.

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Sažetak

MOŽDANI UDAR KOD BOLESNIKA LIJEČENIH NA NEUROLOŠKOM ODJELU OPĆE BOLNICE ŠIBENSKO-KNINSKE ŽUPANIJE U RAZDOBLJU OD 1996. DO 2005. GODINE

A. Aleksić-Shihabi

Retrospektivnom analizom procijenio se ukupan broj bolesnika s moždanim udarom (MU) koji su liječeni na Odjelu neurologije Opće bolnice Šibensko-kninske županije u razdoblju od 1996. do 2005. godine. Analizom je obuhvaćeno 3819 oboljelih od MU. Bilo je 3417 (89,5%) bolesnika s ishemijskim MU i 402 (10,5%) bolesnika s hemoragijskim MU. Od ukupnog broja oboljelih bilo je 1966 (51,5%) žena i 1853 (48,5%) muškaraca. Analiza bolesnika s MU prema desetljećima života pokazala je kako je svake godine najveći broj oboljelih i za ishemijski i za hemoragijski MU bio u dobnoj skupini između 70. i 79. godine života. Utvrđen je značajan porast rizika za MU s porastom desetljeća starosti bez obzira na spol (χ^2=7764,19; *P*<0,0000001). Od ukupnog broja oboljelih stanovnici sela činili su 56,9%, a stanovnici grada 43,1%. Broj oboljelih neprekidno se povećavao, tako da je 1996. bilo 313 oboljelih na 112.891 stanovnika u županiji, 2000. godine ih je bilo 389, a 2005. je bilo 422 oboljelih od MU. S godinama je vidljiv porast incidencije oboljelih od MU (χ^2=24,63; *P*=0,003). Prosječna životna dob ukupno oboljelih od MU bila je 1996. 72,5 godine i povećavala se do 74,6 godina 2005. Za ishemijski MU prosječna životna dob bila je 73,2 godine, što je značajno više u odnosu na hemoragijski MU za koji je prosječna životna dob bila 66,7 godina (ishemijski prema hemoragijskom MU 73,2:66,7; *P*=0,0000). Broj umrlih je 1996. bio 75,2/100.000 i povećavao se do 2000. godine na 87,7/100.000, a nakon toga je u padu i 2005. iznosi 66,4/100.000. Stopa bolničke smrtnosti od MU za 1996. bila je 27,07% (95% CI, 21,62-33,47%) i smanjivala se do 17,44% (95% CI, 13,72-21,86%) u 2005. godini (*P*=0,005159). Pad postotka bolničke smrtnosti od 1996. do 2005. godine iznosi 9,63%. U desetogodišnjem razdoblju od MU je umrlo 808 osoba, i to više žena nego muškaraca (59,8%:40,2%).

Ključne riječi: *Moždani udar – smrtnost; Moždani udar – prevencija i kontrola; Moždano krvarenje – smrtnost; Ishemijski napadaj, prolazni; Hrvatska – epidemiologija*