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Professional paper

APPEARANCE, THERAPY AND OUTCOME OF ISCHEMIC CEREBRAL VASCULAR INCIDENT AT THE CLINICAL HOSPITAL TETOVO DURING JANUARY 2022 - JANUARY 2023

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Abstract

Background: Republic of North Macedonia faced with the demographic, economic and social transition for more than two decades. At the crossroads of this transition it is also the population of Tetovo with its surroundings. The neurology department in Clinical Hospital Tetovo faces challenges to provide adequate care to stroke patients.
Aim: To determine the number and distribution of stroke patients, to evaluate the treatment and outcomes and to determine with whom the patients in the period of January 2022 - January 2023 were relieved from this neurology department.
Methods: The present study was a descriptive as well as a comparative study. Target parameters were collected from medical documentation that was generated during patient treatment.
Results: For the specified period, a total of 286 patients, 152 males and 134 women were hospitalized. The most frequent neurological diseases were acute strokes (71.68%), TIA (3.49%) and other cerebrovascular diseases (4.89%), while 38 (18.54%) patients died, and 13 (6.34%) patients were taken home in serious health condition. Acute ischemic stroke (AIS) was the first most common cause of stroke, account for 81.95% of hospital admission for stroke, while acute hemorrhagic stroke (AHS) was the second most common cause of stroke, account for 18.05%. According to estimates, only two thrombolysis procedures were performed due to meeting the criteria for thrombolysis.
Conclusion: AIS in hospitalized patients is more likely to occur in elderly patients with cardiovascular comorbidities. Aging, comorbidities and acute stroke on admission along with impaired level of consciousness contribute to the fatal outcome.

Keywords: stroke, ischemic, hemorrhagic, treatment, outcomes

1. Introduction

Strokes are clinical syndromes that occur when the brain is not supplies with enough blood, either as a result of closing the arteries that supply the brain with blood or as a result of bleeding. Thus, strokes are divided into ischemic and hemorrhagic stroke and most of the stroke cases are ischemic (approx..85%) [European Stroke Organization (ESO, 2008)]. Over the last decades, stroke has mounted to be among the top causes of death globally [Roth, et al., 2018].

Estimated cost (direct and indirect) related to disorders of the brain in Europe was at 798 billion € in 2010 [Gustavsson, et al., 2011]; related to stroke was 38 billion € per year in the EU [Nichols, et al., 2013] and 33.9 billion USD per year in the USA [Benjamin, et al., 2017]. In the Republic of North Macedonia (NMK), significantly financially burdens both the republic and regional health insurance institutes [Kamberi, 2003].

Evidence from several studies has demonstrated that majority of patients remain with permanent invalids, and with a small amount of financial resources and persistent physical therapy, but only a small number of patients (one-third) recover [European Stroke Organization (ESO, 2008)]. In some earlier studies we demonstrated that stroke recovery profile and the stroke impact assessment in reported admission-based case hospitality rates in Clinical Hospital Tetovo (CHT) shown comparatively limited improvement [Kamberi, 2004; Камбери, 2004; Bajram, & Jera, 2006].

In past decades and today, stroke is still treated as a medical emergency ("the time is brain" concept). Acute and post – acute treatment, physical rehabilitation care in a specialize centers called stroke units has already

shown its effectiveness tried in acute stroke [European Stroke Organization (ESO, 2008)].

In neurology, diagnostic imaging as multi-layer computed tomography, magnetic resonance from the most sophisticated, enables very advanced treatments (modern treatment of cerebral ischemic disease – thrombolysis, thrombectomy). Also, these changed the situation of neurological services in many countries, including NMK.

Knowing that with the increase in hospital treatment of Covid-19 patients the number of hospitalized with stroke decreased in the neurology department of CHT [Бајрам, 2020] and the number of patients treated with standard reperfusion therapy with intravenous recombinant tissue plasminogen activator (IVRTPA) for acute ischemic stroke is lower compared to the years before the pandemic [Kamberi, 2022] the study aimed to determine the number and distribution of stroke patients, to evaluate treatment, outcomes and to determine in what condition patients in the period of January 2022 - January 2023 were discharged from the neurology department.

2. Materials and methods

2.1. Study designs: The present study performed with adult patients, in a government-funded public secondary hospital located in the count as mentioned in the previous studies [Kamberi, 2022; Kamberi, et al., 2016; Kamberi, & Vasilevska, 2005; Kamberi, Bajram and Farije, 2008]. In CHT, the department of neurology has 12 beds, with a monthly admission rate of approximately 22 patients. According issued guidelines from the ministry of health for the treatment of acute stroke in NMK, as an organized center in a specific location within the neurological department, with neurologists, nurses, and administrative professionals trained in the management of stroke also have algorithms for purpose of thrombolysis procedures, since the year 2014 when IVRTPA for acute ischemic stroke has started to be applied [Kamberi Bajram and Farije, 2019].

2.2. Study participants:

The initial sample

All consecutive patients older than 18 years admitted for a neurological disease were included in the initial study simple. For patients who were hospitalized initially for a suspected stroke, criterion was damage to neuronal tissue due to infarction or hemorrhage confirmed by cerebral imaging (usually computed tomography or magnetic resonance imaging). During 13-month period (January 2022 to January 2023), 286 patients (152 males and 134 women) were hospitalized; 205 of these were with a confirmed stroke diagnosis, representing more than 71% (71.68%) of total hospitalizations. For the present analysis, from the initial sample; were excluded eighty-one patients: patients with transient ischemic attacks (TIAs) (n =10), recurrent stroke (n = 6), cerebellar stroke (n = 8) and other frequent neurological diseases (n = 57).

Analyzed groups

Consequently, the study population consisted of 205 patients with acute stroke (from both types of stroke: ischemic or hemorrhagic), with a focal neurological impairment of sudden onset, lasting more than twenty - four hours, of presumed vascular origin. We defined stroke according to the WHO criteria [Hatano, 1976]. In total, 72.68% (n = 149) of the study population come to the hospital by ambulance. From them, 75.51% (n = 114) were from Tetovo, and 23.49% (n = 35) lived in rural areas around Tetovo. The rate of IVRTPA during the study period were 1.19% (n = 2). Further details about baseline characteristics of the stroke patients and stroke severity at admission are listed in Table 1.

We assessed stroke severity on the basis of the neurological deficits as previously reported by other authors [Heuschmann, et al., 2004]. The neurological deficits included in the score were: motor deficit, sensory deficit, presence of cortical signs such as aphasia, hemianopia, or neglect, dysarthria, ataxia, and involvement of cranial nerves. We selected this score because author is neurology specialist certified for urgent neurology, examination of extracranial carotid arteries with Doppler sound, treatment of acute stroke and thrombolysis procedures as well as a senior neurologist is familiar with the administration of the National Institutes of Health Stroke Scale (NIHSS) and thrombolytic therapy.

2.3. Eligibility criteria: Eligibility inclusion criteria were the patients older than 18 years; with a diagnosed acute stroke based on neurological examination and computed tomography findings without a history of previous stroke in a personal history.
Patients medical records with a non-conclusive diagnosis of ischemic stroke and hemorrhagic stroke and medical records without signed a written consent form were excluded.
During the inclusion period, due to hospital protocol all patients with the clinical signs of an acute stroke that are hospitalized for diagnosis and treatment undergo native computed tomography of the brain, electrocardiography and laboratory work-up with complete blood count, metabolic panel, markers of hemostasis in the first 12 hour of admission.
All stroke patients were contacted after admission directly, informed about the study protocol, and then signed a written consent form. The strokes patients who accepted participate were questioned about socio demographic and clinical data, such as age, gender, ethnicity and local of residence (city, village). Detailed clinical history also was investigated, including cardiovascular risk factors such as: arterial hypertension (HTA), diabetes mellitus (DM), chronic cardiomyopathy (CMP), atrial fibrillation (AF), hyperlipidemia (HLP), level of consciousness on admission (LOC), symptoms of neurological deficit (SND), outcome in discharge (OTD), length of stay (LOS)-hospitalized, defined as the days between discharge and hospitalization date and tomography report.
No personal information is presented in the analysis; therefore, we did not seek ethical approval by an institutional review board or ethic committee.

2.4. Methods:

Data collection

The present study was a descriptive as well as a comparative study. Target parameters were collected from medical documentation that was generated during patient treatment. Collected variables were entered into the participant`s electronic record in Microsoft Excel in a specially designed data table. Stroke patients with AIS and AHS were compared with regard to baseline demographic characteristics, stroke severity, lethality, and cardiovascular factors.

Statistical analysis

We described variables through mean or absolute/relative frequencies, according to the distribution and whether they were numerical or categorical. We carried out comparisons between variables using the following test: X^2 (Chi-square) test and T-test to analyzed the stroke types according to age, gender, ethnicity, LOC, SND, HTA, CMP, HLP, AF, DM, OTD and LOS date. Statistical analysis was performed using commercially available SPSS Statistics software (version 17.0). We computed medians and all tests were 2-tailed, and probability values of $P<0.05$ were considered significant.

3. Results

For the specified period, 286 patients were hospitalized in the neurology department of CHT, where 205 of them had a diagnosis of acute stroke, 104 (50.73%) males and 101 (49.27%) women. Acute ischemic stroke (AIS) was the first most common cause of stroke, account for 81.95% of hospital admission for stroke, while acute hemorrhagic stroke (AHS) was the second most common cause of stroke, account for 18.05%.
Target variables collected from a total of 205 hospitalized patients with AIS were analyzed and their demographic and clinical characteristics are summarized in Table 1.

Table 1. Target variables collected from study groups and their statistical analysis

	Patients with acute stroke		
	Patients with AIS (n = 168)	Patients with AHS (n = 37)	Statistical analysis*
Age	70.69 ± 10.101	68.97 ± 9.293	0.949
	Age groups, n (%)		
40-49 years	6 (3.57)	1 (2.70)	
50-59 years	23 (13.69)	5 (13.51)	
60-69 years	44 (26.19)	10 (27.03)	
70-79 years	60 (35.71)	17 (45.95)	
80-89 years	36 (21.43)	4 (10.81)	
	Gender, n (%)		
Men	77 (45.83)	27 (72.93)	
Women	91 (54.17)	10 (27.07)	0.0050
	Ethnic		
Albanian	117 (69.65)	26 (70.27)	0.9400
Macedonian	43 (25.59)	11 (29.73)	0.7560
Other	8 (4.76)	0	
	LOC, n (%)		
Alert	140 (83.33)	24 (64.87)	0.0206
Somnolent	0	0	
Soporous	1 (0.59)	0	
Coma	27 (16.07)	13 (35.13)	0.0155
	SND, n (%)		
Sensory-motor aphasia	22 (13.09)	2 (5.41)	0.3008
Sensory-motor dysphasia	37 (22.01)	1 (2.70)	0.0123
Right-sided hemiparesis	49 (29.17)	3 (0.08)	0.0140
Left-sided hemiparesis	31 (5.21)	4 (0.19)	0.3805
Right-sided hemiplegia	38 (0.23)	6 (0.16)	0.5237
Left-sided hemiplegia	40 (0.24)	19 (0.51)	0.0016
	Comorbidities, n (%)		
HTA	142 (84.52)	7 (72.93)	0.1518
CMP	66 (39.28)	15 (40.54)	0.8876
HLP	104 (61.90)	18 (48.65)	0.1929
AF	7 (4.17)	0	
DM	17 (10.12)	0	
	OTD, n (%)		
Alive	45 (86.31)	22 (59.46)	0.0004
Fatal	23 (13.69)	15 (40.54)	

To take from relatives	8 (4.76)	3 (8.11)	-
Transferred to another ward	2 (1.19)	0	
LOS, n (%)			
Total (alive and dead)	168 (5.37±2.596)	37 (4.78±3.599)	0.354
Alive	145 (5.72±2.538)	22 (5.77±3.791)	0.948

* X^2 (Chi-square) [https://www.graphpad.com/quickcalcs/contingency2/]

LOC - level of consciousness on admission, SND -symptoms of neurological deficit, HTA hypertension, CMP –chronic cardiomyopathy, HLP –hyperlipidemia, AF - atrial fibrillation and DM –diabetes mellitus, OTD - outcome in discharge, LOS - the length of stay.

As seen in Table 1., among patients with stroke, patients with AIS were older than those with AHS (70.69±10.101 versus 68.97±9.293 years, P=0.949). It is not surprising that the age group with the highest rates (37.56%) correspond to the most affected group, aged between 70 to 79 years.

In both sexes, ischemic and hemorrhagic strokes were presented with statistical frequency difference, P = 0.0050 (Chi squared equals 7,883).

The majority of the patients were Albanians 69.76%, Macedonians 26.34% and other 3.9%.

If comparing patients with and without changes in level of consciousness on admission (LOC) and further categorizing by whether they have a disease (ischemic stroke ore hemorrhagic stroke), these target variables were considered to be statistically significant (for alert level of consciousness on admission, Chi squared equals 5.361 with 1 degrees of freedom; the two-tailed P value equals 0.0206; respectively for comma Chi squared equals 5,855 with 1 degrees of freedom and the two-tailed P value equals 0.0155).

Overall, the association between two groups (ischemic or hemorrhagic) and symptoms of neurological deficit (SND), was considered to be statistically significant for patients with sensory-motor dysphasia (Chi squared equals 6,271 with 1 degrees of freedom; the two-tailed P value equals 0.0123), respectively for patients with right-sided hemiparesis (Chi squared equals 6,034 with 1 degrees of freedom; the two-tailed P value equals 0.0140), whereas for the patients with left-sided hemiplegia this association is considered to be very statistically significant (Chi squared equals 9,918 with 1 degrees of freedom; the two-tailed P value equals 0.0016).

Regarding comorbidities, the majority of the patients suffered from hypertension, cardiomyopathy, hyperlipidemia and diabetes. On the day of admission revealed previously undiagnosed atrial fibrillation in 7 patients (4.17%). Patients with AIS showed a higher probability of having comorbidities. If comparing patients with and without comorbidities in admission (hypertension, chronic cardiomyopathy, hyperlipidemia, atrial fibrillation and diabetes mellitus, and further categorizing by whether they have a disease (ischemic stroke ore hemorrhagic stroke), these target variables were with frequency difference but not with statistical significance (Table 1 show the two-tailed P>0.05).

According to estimates by the study results only two thrombolysis procedures were performed due to the fulfillment of the criteria for IVRTPA in patients with AIS, while one patient with AIS was hospitalized after thrombectomy intervention in another ward (these data are not shown in Table 1).

Hospital discharge rate measure the number of patients who leave neurological department after receiving care. Table 1 show selected. outcome in discharge (OTD) by stroke types. Among stroke survivors, 81.46% were discharged home with symptoms of neurological deficit (SND), differences were extremely statistically significant (Chi squared equals 12,753 with 1 degrees of freedom; the two-tailed P value equals 0.0004).

During the hospital stay, the patient`s condition deteriorated and despite all measures, 38 patients (23 with AIS, respectively 15 with AHS) died from cardiorespiratory failure. A 71-year-old male patient with AIS, positive for SARS-CoV-2, was transferred in the infectious ward, and an 86-year-old female patient, due to severe comorbidities was transferred in another hospital, and eight others patients were taken from the neurology department by family members in serious health condition.

In the group of patients with AIS, 23 (12.37%) patients died during their stay in the neurology department. While intrahospital lethality in hemorrhagic stroke was even higher, 40.54%. Number of patients with ischemic and hemorrhagic stroke as well as the lethality rate during the specified period is presented in figure 1.

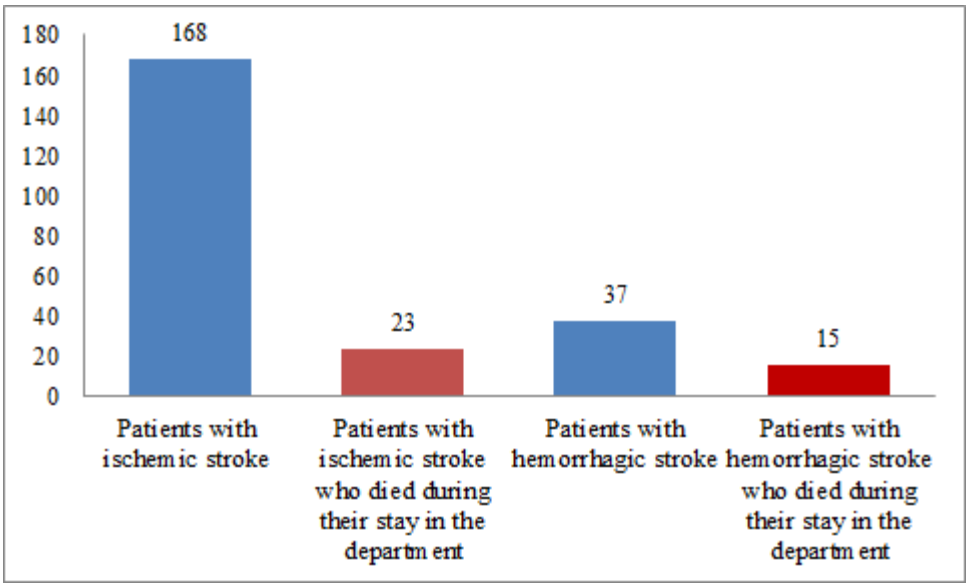

Figure 1. Number of patients with ischemic and hemorrhagic stroke as well as the lethality rate during the specified period

Among patients with stroke, the median length of stay in both stroke groups was similar, 5 days; also, mean length of stay in both stroke groups was similar; at 145 alive patients with AIS was 5.72±2.538 days (2 to 18 days), respectively at 22 alive patients with AHS was 5.77±3.791 days (1 to 14 days), P=0.948.

4. Discussion and conclusions

Republic of North Macedonia faced with the demographic, economic and social transition for more than two decades. At the crossroads of this transition it is also the population of Tetovo with its surroundings, for which population, the neurology department in CHT is the only one public health institution that offers it neurological services and faces challenges to provide adequate care to stroke patients.

In the past, the neurologist excelled as a clinician agile which comes up to the diagnosis based on anamnesis and somatic/neurological examination, with very limited therapeutic options [Kamberi, & Vasilevska, 2005]. Very quickly, and especially after the nineties, the situation changed substantially, imaging technology advanced enormously, multilayer computerized tomography, magnetic resonance from the most sophisticated, modern neurophysiological diagnostics with very advanced treatments (modern treatment of ischemic brain disease – thrombolysis, thrombectomy) changes the situation of neurological services in many countries [European Stroke Organization (ESO, 2008)], including NMK, and especially in the CHT, where according issued guidelines from the ministry of health for the treatment of acute stroke, in the absence of stroke network implementation it was organized an center in a specific location within the neurological department, with neurologists, nurses, and administrative professionals trained in the management of stroke, which also have algorithms for purpose of thrombolysis procedures, since the year 2014 when IVRTPA has started to be applied [Kamberi, Bajram and Farije, 2019].

Ischemic stroke, the predominant type of stroke, has a multifactorial etiology. Although a genetic predisposition to stroke is widely acknowledged [Bevan, et al., 2012; Go, et al., 2014] our understanding of genetic basis for ischemic stroke is limited [Kamberi, et al., 2016].

Same as before in the previous study [Bajram, & Kristina, 2005], the high proportion of acute strokes in Albanians reflect the demographic characteristics of Tetovo and its surroundings.
Two studies [Feiqin, et al., 2016; O`Donnel, et al., 2016] clearly show that 90% of the risk for stroke is due to treatable risk factors.
Hypertension or instable blood-pressure, diabetes, dehydration, inflammation, reduced renal function, reduced left ventricular ejection fraction, newly detected atrial fibrillation and previous myocardial infarction or stroke have been described as independent risk factors for cerebrovascular accidents [Nadav, et al., 2002; Dukkipati, et al., 2004].
This study carried out in a group of patients from the same geographical area demonstrated the role of hypertension, dyslipidemia, diabetes mellitus, atrial fibrillation and chronic cardiomyopathy as a risk factor for stroke development. These risk factors were more frequent, but if comparing patients with and without these risk factors and further categorizing by whether they have a disease (ischemic stroke and hemorrhagic stroke), separately these risk factors are considered to be not statistically significant. Significant risk factors for the development of stroke in this sample of participants was the simultaneous presence of more than two coexisting chronic diseases, something that is now known.
In our previous study [Stakle, & Bajram, 2004] in a group of 237 patients (62% women, 38% men) at the age of 31 year and above, all treated with insulin at the moment of examination, complications of diabetes were found in 72.6%, out of which 51.9% count for macroangiopathy. Among them with complications of diabetes, acute myocardial infarction had 6.3%, cerebral hemorrhage had 4.2% and gangrene had 2.63%. The high percentage of macroangiopathy as a complication of diabetes was due to the bad regulation as well as to use the inappropriate antidiabetic therapy for a longer period. Also, results of another a previous our study, show that diabetes is associated with cerebrovascular disease [Bajram, & Stakle, 2004]. However, in group of 124 patients with acute ischemic stroke and without previous diabetes mellitus [Bajram, 2004] post stroke hyperglycemia occurred in first 24 hours, in eight patients for 48 hours and in two after 72 hours.
In this study, our patients did not have family history of stroke and they were treated initially conservatively, expect in two cases that met the criteria for IVRTPA by the hospital protocol. This rate of IVRTPA during study period, do not correspond to the recommendations [European Stroke Organization (ESO, 2008)]. So, it is a cause for extensive health education, because reflects lack of awareness of the risk of consequences of stroke or the stigma created by the consequences of Covid-19 disease [Бајрам, 2020; Kamberi, 2022].
Similar to other studies, since the criteria for intravenous thrombolysis [Manawadu, et al., 2014] and success of reperfusion treatment is time-dependent [Ermine, et al., 2021; Menon, et al., 2014] whereas symptoms are often not recognized as an emergency [Alvaro, et al., 2008] while the arrival at the hospital was after several hours, these were the main reasons why there were a small number of patients treated with standard reperfusion therapy with IVRTPA. Also, there were not lack of possible most common contraindications, recent bleeding or terminal illness, reasons that another study points out [Dulli, et al., 2007]. The number of patients treated by intravenous thrombolytic therapy for acute ischemic stroke is variable in many regions of the world [Zhou, et al., 2019] including European countries [de Sousa, et al., 2018].
In terms of hospitalization, in our neurological department stroke care is not limited to intravenous thrombolytic therapy for acute ischemic stroke, but includes diagnostic and initiation of secondary prevention, physiotherapy, rehabilitation assessment and planning as well as counselling for patients and family member, as it happens in other countries [Lawrence, et al., 2015].
Length of hospitalization and in-hospital mortality are two well-known indicators of stroke care. In our study, we compared LOS of all stroke patients (alive and dead) with LOS of stroke patients discharged alive. Ischemic cases had longer LOS the hemorrhagic cases, but the median LOS of stroke cases was similar in both stroke types (ischemic and hemorrhagic) cases, similar to the one study in Argentina [Sposato, et al., 2008].

The case fatality rate reported in this hospitalization-based study for hemorrhagic stroke were higher (40.54%) and for ischemic stroke, respectively, was 12.37%. Hospital discharge rates from strokes in Europe shows very large variation between countries. Among Europe countries, Belgium has a leading place in terms of 30-day in-hospital fatalities for hemorrhagic stroke, whereas 30-day in-hospital fatalities for ischemic stroke varies between 2.8% in Denmark and 9.7% in Slovenia [Feigin, et al., 2009].
The main finding of this study was the worrying rate of comorbidities found in our sample. Stroke in hospitalized patients was more likely to occur in elderly patients with cardiovascular comorbidities.
Aging, comorbidities and acute stroke on admission along with impaired level of consciousness contribute to the fatal outcome.
Patients with AIS showed a high probability of having cardiovascular factors, while patients with AHS showed a high case fatality rate.
These findings highlight the need for measures to improve not only stroke awareness but also prehospital protocols in order to provide timely and propriate care for our stroke patients.

Declaration of conflicting interests

The author declared no potential conflict of interest with respect to the research, authorship, and/or publication of this article.

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