Culture Related Risk Factors In Stroke Development: A Paradigm From Greek Thrace

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Citation

Abstract

Objectives: Detection of any possible differences in types, relative frequency, incidence rates, age of onset, outcome and subsequent risk factors of stroke in the mixed Christian/Muslim population of Xanthi region, Thrace, Greece.

Subjects: 220 unselected patients, 157 Christians and 63 Muslims, who had been attacked by stroke.

Methods: Statistical analysis for all objectives were carried out between 4 population subgroups formed according to sex and religion.

Results: Muslims when compared with Christians (i) suffer from stroke at a younger age, (ii) tend to present haemorrhagic strokes more often, (iii) show a significantly lower incidence rate concerning ischemic strokes and (iv) present similar mortality.

Conclusions: Analysis of all known risk factors for stroke between the population subgroups revealed that Muslims, and especially women, are prone to hypertension, diabetes and hypercholesterolemia, which overwhelm their physical way of life. Appropriate preventive medicine programs, focusing mainly on the above risk factors, should be applied.

INTRODUCTION

The present literature concludes that stroke attacks women at an older age and at a lower rate mainly due to the prophylactic effect of estrogens on the cardiovascular system [1,2]. As far as the type of stroke is concerned, ischemic or haemorrhagic, there is no statistically proven difference between men and women. Apart from the use of contraceptives, no other known risk factor for stroke may seem to apply differently to women and men. Known risk factors for stroke are hypertension, diabetes, obesity, hypercholesterolemia, smoking, alcohol abuse, previous myocardial infarction, heart failure, chronic or paroxysmal atrial fibrillation, sick sinus syndrome, obstructive carotid angiopathy, peripheral vascular angiopathy, medical record of previous stroke and family history positive for stroke [3,4,5,6,7,8,9]. A number of other potent risk factors such as pulmonary embolism, endocarditis, myocarditis, use of contraceptives, secondary polycythaemia, medical record of migraine etc. are considered to play a role albeit unclear in the pathogenesis of stroke.

Minority population groups tend to present significant barriers concerning both acute stroke treatment and stroke prevention [10]. The former is explained in some minority groups by the existing linguistic deficiencies concerning mainly older people, which inhibits case history documentation, whereas the latter by the different application of risk factors [11].

The aim of this study is to detect any possible differences between population subgroups, based on sex and cultural habits, as reflected in religion, in the Perfecture of Xanthi, Thrace, Greece, concerning the types and the frequency of stroke, as well as the final outcome. These data would be useful for evaluation of the present health care status and for suggesting further action. Similar studies, analyzing stroke incidence and mortality, have been carried out in other population subgroups [12,13,14].

MATERIAL AND METHODS

This study was performed in the province of Thrace, Perfecture of Xanthi, an area with a mixture of Christian
(52.81%) and Muslim (47.19%) population of 99,607 in size (estimation of the mean true population for the period of the study) presenting a 49.54%/50.46% men/women ratio [15,16].

The study was based on 220 patients who had suffered from stroke and were still alive on arrival at the Emergency Unit of our Hospital between 9.2.1998 and 8.2.2000. Practically every single case of stroke reaches our hospital, which is the only one in the region, alive or deceased (for medical certification of the cause of death). All patients were hospitalized under the responsibility of the Internal Medicine Department under the close care of a neurologist.

All data concerning sex, age and religion were collated. Medical records were drawn up including:

- **Tobacco, alcohol and nutritional habits (presence or absence of Western-type diet)**
- **Hypertension, diabetes, hypercholesterolemia**
- **Chronic or paroxysmal atrial fibrillation, previous myocardial infarction, heart failure**
- **Previous stroke**
- **Obstructive carotid angiopathy, peripheral vascular angiopathy**
- **Sick sinus syndrome, endocarditis, myocarditis**
- **Pulmonary embolism, use of contraceptives and polycythaemia as part of history documentation.**

All patients underwent a thorough physical and neurological examination at least three times (on admission, 24 hours later and shortly before leaving our Department). Additionally, a routine blood and serum test including haematocrit, haemoglobin and plasma levels of glucose, urea, creatinine, main electrolytes and lipids as well as 12-lead ECG, chest radiography and CT scan were performed. A CT scan was requested to be performed immediately when patients were in a coma, or presented signs of meningeal stimulation, otherwise after a period of 24 hours. When the CT scan was negative but neurological signs persisted, a second CT followed 2 days later. A CT scan was omitted only in cases with well-documented medical history of ischemic attacks and minor current neurological pathology. Wherever a problem of differential diagnosis arose, a second CT scan or, preferably, a MRI or a MRI angiography was proposed. In cases where no risk factor was present an intense study for autoimmune angeitis including antinuclear antibodies (ANA), anti-dsDNA antibodies, anticytoplasmic antibodies (ANCA) and antiphospholipid antibodies as well as skin biopsy was added [17]. Homocysteine tests were omitted [18,19]. In the case of death, post-mortem findings were used only when it was impossible to document the underlying cause through medical record and physical examination.

The cerebral infarcts were categorized on the basis of CT scan findings as lacunar when CT scan showed small, deep infarcts measuring 3 to 15 mm, corresponding to the clinical syndrome (pure motor hemiparesis, pure sensory stroke, hemiparesis-ataxia, dysarthria-clumsy hand, hemichorea-ballismus), non-lacunar (atherothrombotic, cardioembolic, by other causes, of unknown etiology) when the CT scan showed infarcts >15mm and with negative CT scan. The haemorrhagic strokes were classified as intracranial haemorrhage (ICH), subarachnoid haemorrhage (SAH) and combined.

At the end of the hospitalization period, proposed treatment and the final outcome in terms of a modified Rankin Scale were written down. Fewer categories than those proposed by modified Rankin Scale were judged as inevitable, unless statistics are unreliable. Unfortunately, the requested one-year follow-up period has not been achieved in all cases, especially those concerning older Muslim population. Thus, under the danger of severe bias, the follow-up results were omitted.

A statistical analysis for all parameters named above was carried out between 4 population subgroups formed according to sex and religion (73 Christian men, 84 Christian women, 32 Muslim men and 31 Muslim women). Statistical tests included the Student’s unpaired t-test for quantitative parameters (e.g. age in years, Western-type diet in times per week etc.) and X2 for discrete parameters (e.g. presence or absence of hypertension or smoking). A modified ?2 test was used for the comparison of incidence rates based on the number of cases and the person-time units [20]. The level of statistical significance was set at P<0.05. All P values are given at two significant digits level. All probabilities refer to two-tailed tests [21,22]. Any possible difference between the mean age of invasion of stroke, the predominant type of stroke and its relative and/or absolute frequency and the final outcome would alert for the detection and reflection on one or more known or possible risk factors for stroke.
RESULTS

TYPES OF STROKE ACCORDING TO SEX AND RELIGION

During the study period, 220 cases of stroke were classified according to their type as ischemic (182 cases - 82.7%) and haemorrhagic (38 cases - 17.3%).

A total of 192 cases were documented by CT findings in combination with appropriate additional methods, as referred to the previous section. A total of 27 cases with well-documented medical histories of multiple ischemic strokes and minor transient or reversible neurological pathology were treated as new ischemic strokes and the CT scan was omitted [23]. A single case of haemorrhagic stroke was revealed by post-mortem study.

Ischemic strokes were classified according to CT findings as lacunar (48 out of 155 cases - 31.0%), non-lacunar (66 out of 155 cases - 42.5%) and having negative CT (41 out of 155 cases - 26.5%).

The distribution of lacunar ischemic strokes was:

- 17/115 in women and 31/105 in men (X2=6.990, f=1, P=0.0080)
- 34/157 in Christians and 14/63 in Muslims (X2=0.091, f=1, P=0.72)
- 8/84 in Christian women, 26/73 in Christian men, 9/31 in Muslim women and 5/32 in Muslim men. Comparing Christian women and men, X2=10.120, f=1, P=0.0060. That was not the case between Muslim women and men, where X2 0, f=1, P 1.0.

The haemorrhagic strokes were classified as intracranial (31 out of 38 cases - 81.6%), subarachnoid (5 out of 37 cases - 13.2%) and combined haemorrhage (2 out of 37 cases - 5.2%).

Two patients with subarachnoid haemorrhage stroke were dispatched intubated to neurosurgery units and survived with minor neurological damage.

The distribution of ischemic and haemorrhagic strokes is given in Table 1. When Christian women, Christian men, Muslim women and Muslim men are compared together, X2=7.031, f=3, P=0.072. When women are compared with men, X2=0.166, f=1, P=0.68 and when Christians are compared with Muslims, X2=5.831, f=1, P=0.016. The difference according to religion is attributed only to women (X2=5.566, f=1, P=0.019) and not to men (X2=1.096, f=1, P=0.30).

Figure 1

Table 1: Type and final outcome of the 220 hospitalized stroke patients of the present study (M=men, W=women, C=Christians, S=Muslims, I=ischemic stroke, H=haemorrhagic stroke).

<table>
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<td>4 &amp; 5</td>
<td>6</td>
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<tr>
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<td>5</td>
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<td>6</td>
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<td>0</td>
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INCIDENCE RATES OF STROKE ACCORDING TO SEX AND RELIGION

The incidence rates of ischemic stroke are 136/105203 cases/persons* years for Christians and 46/94011 cases/persons* years for Muslims (X2=35.078, f=1, P<0.001) and the relative risk is 2.642 with 95% confidence interval between 1.916 and 3.644.

The incidence rates of ischemic stroke in men are 63/52118 cases/persons*years for Christians and 25/46573 cases/persons*years for Muslims (X2=12.456, f=1, P<0.001) and the relative risk is 2.252 with 95% confidence interval between 1.424 and 3.530.

The incidence rates of ischemic stroke in women are 73/53085 cases/persons*years for Christians and 21/47438 cases/persons*years for Muslims (X2=23.294, f=1, P<0.001) and the relative risk is 3.106 with 95% confidence interval between 2.456 and 4.922.

Unlike the above results, all similar comparisons in cases of haemorrhagic stroke do not reveal statistically significant results.
SEASONAL DISTRIBUTION OF STROKE INCIDENCE

The distribution of the two-year period cases in the twelve months is 9 in January, 21 in February, 20 in March, 17 in April, 21 in May, 21 in June, 26 in July, 21 in August, 13 in September, 14 in October, 9 in November and 28 in December. Using the X2 for the goodness of fit for the season distribution we extract 10,014 (f=3) and for the monthly distribution 22,808 (f=11). P equals 0,018 and 0,00010, respectively.

HOSPITALIZATION PERIOD

Taking into consideration the mean duration of the hospitalization, the data taken from 204 cases showed 6,28 3,19 days for Christian women (n=76), 5,71 3,03 days for Christian men (n=66), 7,19 4,10 days for Muslim women and 5,10 3,48 days for Muslim men. There is no difference (P=0,93) between Christians and Muslims in general (t-value 0,155, f=202), nor between Christian and Muslim women (t-value 0,793, f=105, P=0,42), nor between Christian and Muslim men (t-value 0,846, f=95, P=0,40). On the opposite, quite a clear difference (P=0,027) is postulated to exist between women and men (t-value 2,192, f=202), which can be attributed mainly to the Muslim population (t-value 2,172, f=60, P=0,030) and not to Christians (t-value 1,081, f=140, P=0,28).

OUTCOME

The final outcome of the 220 patients is summarized again in Table 1. Comparison between Christian men, Christian women, Muslim men and Muslim women for the 5 categories of the modified Rankin Scale does not reveal any difference (X2=11,237, f=12, P=0,51).

There were 25/115 fatal cases in women and 23/105 cases in men (X2=0,001, f=1, P 1,0) and, taking religion into consideration, 30/157 cases in Christians and 18/63 cases in Muslims (X2=2,350, f=1, P=0,13). When ischemic strokes are compared with haemorrhagic ones, a prominent difference, well-documented in classic literature, is revealed as a total of 29 out of 182 patients with ischemic stroke and 19 out of 38 patients with haemorrhagic stroke who succumbed (X2=21,392, f=1, P=0,00010). There is no difference between men and women suffering from ischemic stroke (X2 0, f=1, P 1,0), nor between Christians and Muslims (X2=1,548, f=1, P=0,22). Similarly no difference is revealed between men and women suffering from haemorrhagic stroke (X2=0,106, f=1, P=0,75), nor between Christians and Muslims (X2=0,106, f=1, P=0,75).

From the total of 220 cases, 204 (92,7%) represented the first episode of stroke. The mean age of stroke incidence was found to be 70,60 11,55 years. All results concerning mean age of stroke invasion according to sex, religion and type are given in Table 2. There is also a schematic presentation, which helps visualization in Figure 1. The difference between Christians and Muslims is attributed practically only to women.

Figure 2

Table 2: Mean age of stroke invasion according to sex, religion and type (M=men, W=women, C=Christians, S=Muslims, I=ischemic stroke, H=haemorrhagic stroke).

<table>
<thead>
<tr>
<th>Group</th>
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<th>C</th>
<th>S</th>
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<td>65</td>
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<tr>
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</tbody>
</table>

Figure 3

Figure 1: Mean age of stroke invasion according to sex, religion and type of stroke (M=men, W=women, C=Christians, S=Muslims, I=ischemic stroke, H=haemorrhagic stroke). The red bars represent the total number of cases of group (left y-axis) and the black crosses above them the mean (horizontal line) and SD (vertical line) for each one (right y-axis).

ANALYSIS OF RISK FACTORS FOR STROKE ACCORDING TO SEX AND RELIGION

To explain potent differences concerning the type of stroke and the age of onset in Muslim women, all risk factors for stroke that may apply nonuniformly between Christians and Muslims and, especially, between i) Muslim women and Christian women and ii) Muslim men and women were analyzed. All data concerning hypertension, severe systolic hypertension, smoking, diabetes, hypercholesterolemia, atrial fibrillation and previous myocardial infarction were collated (Table 3 and Figure 2), analyzed and compared between these subgroups.
SUMMARY OF RESULTS

1. Muslims tend to present haemorrhagic strokes more often than Christians. The difference between Christians and Muslims in relative frequencies of ischemic and haemorrhagic strokes is again attributed only to women and is reflected in their elongated hospitalization.

2. Muslims, when compared to Christians, show a lower incidence rate concerning ischemic strokes, which is not repeated in haemorrhagic strokes. That difference may be well attributed to selective

Additional data regarding the prevalence of Smoking, Diabetes, Hypercholesterolemia, Atrial Fibrillation, and Myocardial Infarction are provided, along with statistical analysis using t-tests and chi-squared tests. The prevalence of Western-type diet was also estimated, showing a higher frequency in Christians compared to Muslims. The use of oral contraceptives by Muslim women in the present study has not been reported.
lack of risk factors that predispose for ischemic strokes in Muslims (e.g. atrial fibrillation) which are overwhelmed by severe systolic hypertension when haemorrhagic strokes are considered.

3. Muslims have a tendency to suffer from stroke at a younger age than Christians. The difference between Christian and Muslim subpopulation in mean age of stroke invasion is attributed practically only to women. The Muslim subpopulation is characterized by the reversal of the almost worldwide characteristic that women present a higher mean age of stroke invasion in comparison to men, mainly due to the prophylactic effect of estrogens [2].

4. There is no prominent statistical difference in the mortality between Christians and Muslims, although comparison with Athens registry provides evidence that support the opposite.

5. It is worth underlining the difference in lacunar ischemic strokes between Christian men and all other population subgroups. Christian men concentrate three major risk factors, hypercholesterolemia, smoking (women are favored) and diabetes (Muslim men are favored), but not hypertension, which is believed to be responsible mainly for non-lacunar infarcts. This finding is in keeping with present literature as far as etiology of lacunar infarcts is concerned [7].

DISCUSSION
Two risk factors have been found to apply differently between Christian and Muslim women: Western-type diet, which favors Muslim women, and severe systolic hypertension, which is against them. While it is well documented that haemorrhagic strokes are related very closely to elevated blood pressure [24], have a poorer outcome and are characterized by high mortality, we would expect to see these entire parameters decline in the Muslim women subgroup. This is true as far as severe systolic hypertension is concerned, which characterizes Muslim women in a considerably large proportion. Besides, population-level trends in systolic pressure showed a strong association with stroke event trends in women but not in men [25].

Another four factors have been detected to differ between Muslim men and women: smoking, which favors Muslim women, and hypertension, diabetes and hypercholesterolemia, which are against them.

A potent difference between Muslim women and all other subpopulations could be the surprisingly high incidence of depression [26]. In a series of 4963 patients hospitalized in our department during the time of the present study, the incidence rates of suicide attempts due to severe depression was 44 per 100,000 per year among Christian women and 83 per 100,000 per year among Muslim women (X2=11.976, P<0.001) [unpublished data]. This could be a mechanism that interacts with the effort to control hypertension, mainly due to neglectfulness of most people suffering from depression to strictly follow a certain treatment.

These differences in stroke prevalence and age of onset concerning Muslim women, which are attributed to the high incidence of severe hypertension in combination with high rates of diabetes and hypercholesterolemia among them, reflect:

- Their devotion to the traditional cuisine which is characterized by the use of animal fat instead of olive oil and the abundance of sweets,
- Their limited opportunities for physical exercise as they mostly deal with housekeeping and
- Their resistance to take advantage of preventative medical surveillance, which can be mainly attributed to the harsh landscape of many Pomak villages, a linguistical handicap as regards mainly older people, as well as strict religious ethics, affecting women to a greater extent. To interpret the latter, we emphasize on the fact that Muslims, and especially women, refuse to take their medication during Ramadan (which is an average period of one months yearly), strictly interpreting a religious call to refrain totally from any food or drink during the daylight, although a relevant paper claims that the Ramadan period is not negatively involved in differences concerning stroke incidence [29].

The Greek authorities have attempted to overcome the geographical problem by constructing a new national highway to Bulgarian frontiers through Pomak district and the linguistic problem by providing incentives to Muslim school graduates to follow academic careers and thus fulfill
the Muslims needs for affiliated doctors.

The mean time of the onset of the first episode of stroke in Muslim women is still about 4 years later than that referred to as the big Ege Stroke Registry concerning the Muslim population of Izmir in Western Turkey (62.3 ± 12.0 years, t=2.533, P=0.011) [30]. Nevertheless, the similarly low average age of stroke onset in two Muslim populations of different origins (Pomaks of Thrace and Turks of Izmir) [31] rules out the possibility that a common genetically determined factor could be responsible.

Comparing the present results with those of the Athens Registry [32] we deduce that there is no statistical difference in the average age of stroke onset (70.6 ± 11.9 years in 1042 stroke patients of Athens Registry, t=0.539, P=0.41) nor in the average mortality when Christians are taken into consideration (158 fatal cases out of 1042 stroke patients of Athens Registry, X2=1.624, P=0.20). The latter point is reversed when Muslims are added (X2=5.89, t=0.015), thus a higher mortality rate can be speculated. Additionally, a comparison concerning the average age of stroke onset with the data available from Arcadia Registry [33] shows that although men present a clear-cut difference (75 ± 11.9 years in 309 stroke patients of Arcadia Registry, t=3.280, P=0.0011), women are in about the same situation (76 ± 11.8 years in 246 stroke patients of Athens Registry, t=0.086, P=0.94).

The overall incidence of stroke in Muslims of Thrace (67 cases per 100,000 per year) is significantly lower than in other Muslim populations (137 cases per 100,000 per year in Isparta, Turkey) [26] and below the mean worldwide values [2]. This may well be attributed to the rigorous physical life that Muslims usually live in their mountain villages, and the low atrial fibrillation rate among them [9, 34, 35]. Nevertheless, when we look closely at haemorrhagic strokes, we deduce that the difference in incidence tends to reverse, as 17/35000x10-4 or 24.3 cases per 100,000 per year are attributed to Muslims and 21/35000x10-4 or 16.2 cases per 100,000 per year to Christians. In this case, the seemingly prophylactic effect of the good quality of life of Muslims and of the low atrial fibrillation rate is undermined by the high incidence of hypertension, diabetes and hypercholesterolemia among them. Therefore, the latter condition seems to be responsible for about 8 cases of haemorrhagic stroke per 100,000 per year and, taking the relevant mortality into consideration, for about 4 deaths amongst them. The average cost of antihypertensive, antidiabetic and hypocholesterolemic drugs [36] which have to be used in order to prevent these deaths (and, moreover, disabilities) in the target population is about 44,000 Euro per year (16 new cases of stroke in Muslim women/year* 11 years handicap in mean age of onset*250 Euro/year average cost of treatment), which may considered to be cost effective.

The present work has contributed to the enlightenment our knowledge on how culture and social habitants, as reflected in and influenced by two major religions may alternate the epidemiology of stroke. A few studies, which analyze stroke incidence and mortality, have been carried out in other population subgroups [12-14]. Despite that, the literature lacks of major works on that field and our experience is therefore limited.

Despite that the final results can not be stated before February 2004, the pilot phase has clarified that an intense effort should be made to enlighten the whole Muslim population about the fatal consequences of untreated or undertreated hypertension, diabetes and hypercholesterolemia, targeting both to non-pharmaceutical and pharmaceutical interventions [37, 38, 39, 40, 41, 42, 43, 44]. It has become common sense that effective preventative medicine should take into consideration the differences in risk factors among different ethnic groups, in order to be cost-effective [45-46].

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NOTES

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