Risk Factors in Stroke: A Clinical Study in Mexican Patients

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Abstract:

Mexicans hospitalized between July, 1967, and June, 1968, with clinically diagnosed stroke provided information on risk factors in a population from which little systematically collected information on stroke exists. The patients were beneficiaries of ISSSTE, a government-sponsored health care system. Postmortem examination in 20 patients indicated virtually 100% validity of diagnosis. Cerebral thrombosis, hemorrhage and embolus occurred in a ratio of 6:2:1. There was no sex difference in stroke frequency. Thrombosis and hemorrhage increased with age; embolus occurred more often in younger patients. Thrombosis tended to occur when at rest and in individuals with sedentary occupations; the opposite was found with hemorrhage and embolus. Obesity did not seem to predispose to stroke. Hypertension, heart disease and diabetes mellitus emerged as common antecedent conditions. There was a morning peak in onset of thrombosis and hemorrhage and an afternoon peak for embolus. No relation of onset to holidays or stress was noted. Thrombosis, hemorrhage and embolus all were associated with increased ambient temperature, and with low, slightly decreased and high humidity, respectively. An August-September (end of rainy season) peak in seasonal frequency occurred. The risk factors previously identified as being important mainly in northern populations seemed to be important in this Mexican population as well. Thus, ethnic and cultural variability exerted little effect on stroke frequency.

Additional Key Words: stroke frequency, occupation and activity prior to stroke, ethnic and cultural variability, meteorological factors, seasonal variability, obesity, diurnal variability, stress.

Methods

The Medical Center Hospital "20 de Noviembre" (CH20N) in Mexico City served as a source of stroke patients. This facility is a medical referral center for government workers and their dependents who are enrolled in the Government Workers Institution for Security and Social Services (ISSSTE). Medical care is provided at nominal cost to ISSSTE beneficiaries. Because of the high cost of private health facilities in the community and the recognized excellence of the ISSSTE medical facilities, ISSSTE beneficiaries prefer to use the ISSSTE medical facilities as previously shown. Moreover, the rate of utilization of the ISSSTE medical services is high with beneficiaries making an average of two visits a year to the hospital.

In 1968, the population eligible for medical care included about 600,000 individuals in the following proportions: government employees, 32%; spouses, 12%; children, 37%; and parents and grandparents, 19%. The age distribution of this population is shown in table 1. Women constituted 56% and men 44%. The average monthly income of ISSSTE beneficiaries was 1,500 pesos, which is somewhat above the mean for the community.

All patients with a clinical diagnosis of cerebral vascular accident (CVA) (thrombosis, hemorrhage or embolus) admitted to the CH20N between July 1, 1967, and June 30, 1968, were studied. The diagnosis of CVA was based on information from the patient and his family, a clinical examination, and cerebrospinal fluid
TABLE 1
ISSSTE Population in Mexico City by Age and Sex

<table>
<thead>
<tr>
<th>Age</th>
<th>Average 1963 through 1966 Male</th>
<th>Average 1963 through 1966 Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–24</td>
<td>132,044</td>
<td>139,571</td>
<td>271,615</td>
</tr>
<tr>
<td>25–49</td>
<td>86,880</td>
<td>131,966</td>
<td>218,846</td>
</tr>
<tr>
<td>&gt; 49</td>
<td>58,590</td>
<td>87,956</td>
<td>146,546</td>
</tr>
<tr>
<td>Total</td>
<td>277,514</td>
<td>359,493</td>
<td>637,007</td>
</tr>
<tr>
<td>Percent</td>
<td>44</td>
<td>56</td>
<td>100</td>
</tr>
</tbody>
</table>

findings. In some cases angiography was available and aided in diagnosis. Clinical evidence of cardiac disease, a cardiac murmur, a myocardial infarction within five years, or other embolic phenomena in lungs or kidneys influenced classification of the stroke as embolic. Blood or xanthochromia of the spinal fluid influenced classification of the stroke as hemorrhagic. Otherwise, cerebral thrombosis was diagnosed. Patients thought to have suffered primary subarachnoid hemorrhage or transient ischemic attacks with no neurological residual were excluded from the present study. The decision as to the type of stroke was made in conference by two of us (L. O. and E. C.), and did not always agree with the admitting diagnosis.

A questionnaire was developed and was systematically filled out by one of us (E. C.) for each stroke patient admitted to CH20N. The questionnaire included identifying information such as name, sex, age and marital status, and also questions on presumed risk factors in stroke. The questionnaire is outlined in table 2.

Results
A total of 206 patients was studied. The type of stroke was difficult to classify clinically in three patients (1%). In the remaining 203, 67% were diagnosed as having had a thrombotic stroke, 21% a hemorrhagic stroke, and 11% an embolic stroke. Twenty of the patients came to autopsy prior to the preparation of this report. The diagnosis of CVA was confirmed in each, and the clinical impression as to the type of stroke was confirmed in 90%, which suggests that the clinical classification had a high degree of validity.

All subjects included in the study were seen within one week of the onset of the stroke and most were seen within a few hours. The time between onset of stroke and admission to hospital was less than 24 hours in 64% and between 24 and 48 hours in 34%. In 2%, the time lapse (though under a week) could not be estimated more accurately. The time lapse between onset of the stroke and admission to the hospital was similar for all types of stroke.

The age distribution of this series of patients is shown in figure 1. The median age was 65 years. Thrombosis and hemorrhage increased in frequency with age in the ISSSTE population and both had a similar age distribution. Emboli, on the other hand, were more common among younger patients.

There were 119 women (57.8%) and 87 men (42.2%) in the stroke series. The ISSSTE population at risk also included an excess of women in almost exactly the same proportion. The sex
distribution of the various types of stroke is shown in table 3 (A). An excess of women was observed in each type of stroke but was most marked among patients with emboli.

The occupation of 70% of the patients in the series was rated as active, and in 25% it was sedentary. In 5%, the occupation was unknown or could not be classified. The occupation was classified as sedentary more often in those with thrombotic than in those with hemorrhagic stroke. Embolic strokes were associated with the lowest percent of patients in sedentary occupations. Although the frequency of patients with sedentary occupations among those with thrombosis was only slightly higher than in the group as a whole, it was twice as high as in those with hemorrhage and more than

| TABLE 3 |
| Risk Factors and Type of Stroke |
|---|---|---|---|---|
| | Thrombosis, % | Hemorrhage, % | Embolus, % | Total, % |
| A. Sex | Female | 54 | 61 | 68 | 57 |
| B. Occupation | Sedentary | 31 | 16 | 9 | 25 |
| C. Activity at onset | At repose | 66 | 18 | 41 | 53 |
| D. Build | Obese | 16 | 23 | 23 | 18 |
| E. Prior disease | Hypertension | 61 | 80 | 32 | 62 |
| | Cardiopathy | 34 | 14 | 95 | 36 |
| | Diabetes | 26 | 32 | 9 | 25 |
| F. Stress | Present | 12 | 16 | 9 | 12 |
| G. Tempo of onset | Sudden (within minutes) | 50 | 86 | 91 | 62 |
three times higher than in those with embolus (table 3[B]).

Only about one-fifth of the patients with hemorrhagic stroke were at repose immediately before onset, while two-thirds of those with thrombosis were at repose. Among those with embolic stroke, slightly more patients were active than at repose prior to onset (table 3[C]).

Eighteen percent of the patients were judged obese on admission and 23% were considered underweight. The body weight was not estimated in 6%. The remainder (53%) were thought to fall within rather broad limits of normal so far as weight was concerned. Thus, the distribution of patients by body weight did not suggest that obese or underweight individuals had a greater risk of stroke. The various types of strokes included similar percents of obese individuals, so that no obvious relationship between increased body weight and tendency toward a particular type of stroke was evident (table 3[D]).

The frequency of various illnesses prior to onset was examined. Hypertension was reported by 62%, cardiac disease by 36% and diabetes mellitus by 25%. Many other conditions were reported: among the more frequent were smoking (22 cases), alcoholism (19 cases), bronchitis (15 cases), previous stroke (19 cases), and atherosclerotic illnesses (17 cases).

The frequency of previous illnesses was tabulated in patients with different types of stroke. Hypertension was more common in patients with hemorrhagic stroke (80%) and, as might be anticipated from the diagnostic criteria, almost all patients with embolic stroke had evidence of cardiopathy (95%) (table 3[E]). Since a given patient could have more than one previous predisposing illness, the percentages of table 3(E) add up to more than 100%.

Whether a patient actually experienced more or less stress in relation to a particular event is obviously difficult to determine. Therefore, no attempt was made to ascertain the degree of stress of different events prior to onset of stroke. Emotional stress was simply judged subjectively by the examiner and was tabulated for each stroke type in table 3(F). It was judged to be present prior to onset of stroke in 12% of those with thrombosis, 16% of those with hemorrhage and 9% of those with embolism. These differences were not statistically significant.

Onset of symptoms and signs was sudden in 61% and more gradual (hours to a day or more) in 37%; in 2%, the rapidity of onset could not be specified. The rapidity of onset by type of stroke is shown in table 3(G). Equal proportions of patients with thrombosis presented with sudden and more gradual onset; the majority of patients with hemorrhage and almost all patients with embolus presented with sudden onset.

The time of day during which a stroke occurred was evaluated for each type, though small numbers made the result somewhat open to question (fig. 2). Both cerebral thrombosis and hemorrhage showed a bimodal diurnal distribution with preponderance of onset in the morning hours and a somewhat lower peak in the evening. The afternoon hours and early morning hours showed relatively fewer cases. Of course, some of those reporting onset during the morning hours may simply have recognized the evidence of stroke on attempting to get out of bed in the morning; the stroke may actually have occurred earlier. The paucity of cases in the afternoon hours is less easily explained. Embolus tended to differ in time of onset from both thrombosis and hemorrhage in that it was more frequent in the afternoon and evening hours.

Occurrence of various types of stroke could not be related to holidays. Fifteen percent of those with thrombosis, 18% of those with hemorrhage, and 5% of those with emboli occurred on a holiday. Since holidays (including Sunday) account for 15% of the days of the year, it is clear that there was neither increased nor decreased risk of a particular type of stroke on holidays.

Weather conditions were reviewed in relation to onset of stroke. In Mexico City, artificial heating is not generally used even in the colder months of the year, so that weather conditions in the patients' immediate environment were much closer to those measured at meteorological stations than is true in northern countries.

The mean temperature for the period of the study was 13.3°C, whereas the temperature for times when strokes were reported averaged slightly higher—14.9°C. The barometric pressure averaged 74.2 mm for the period of the study and 75.0 mm for the times when patients reported onset of stroke. Appreciable rainfall is limited to the summer months in Mexico City, although small amounts may fall throughout the year. The majority of strokes occurred on days when only about 1 mm of rain was recorded. There was no clustering of strokes on days of heavier rainfall and only 11 of the 206 strokes occurred when no rainfall could be measured. Humidity for the period of the study averaged 58.1% while for days on which strokes occurred, it was 62.2%. Average atmospheric conditions for each type of stroke are shown in table 4. Using the annual average as a standard, cerebral embolus was associated with a higher temperature and a higher humidity; cerebral hemorrhage with a slightly higher temperature and slightly decreased humidity; cerebral thrombosis with a higher temperature and lower
often prove disappointingly incomplete regarding the previous health of the patient, exact time of onset, activities of patients prior to onset of initial symptoms, and environmental conditions pertaining at the time of the stroke. Hence, inferences about predisposing factors cannot be drawn easily from retrospective accounts of strokes. The present study was designed to obtain information at the time of hospitalization about the occurrence of certain factors believed to operate as risk factors in stroke. Although still retrospective, this method assured that the records would be systematically collected and reasonably complete for at least some presumed risk factors.

Despite considerable differences in ethnic characteristics, climate and mode of life, the Mexican patients with stroke showed many similarities to stroke patients from hospital series in other populations. It would be worthwhile highlighting some of these similarities. Thrombosis, hemorrhage and embolus occurred in a ratio of 6:2:1 in the Mexican series, which is similar to that reported in several studies in northern United States, an area far removed geographically and climatologically from Mexico. The age distribution for each type of stroke and all types considered together was similar to age distributions of stroke patients in the upper Midwest. The risk of stroke among Mexican men and women was essentially equal as has been found in other populations.

Hypertension, cardiac disease and diabetes mellitus are commonly cited as predisposing illnesses in stroke patients in the United States and the same predisposing conditions emerged as common in the Mexican population. These same diseases also were common in a Puerto Rican and Jamaican stroke series. Smoking and alcoholism each were reported as antecedent conditions in approximately 10% of the stroke patients in Mexico; in a Minnesota series, smoking and alcoholism occurred in 25% and 20% of stroke patients, respectively. A 30% mortality in Mexico one year after the stroke approximated the mortality rate in other hospital series and in community studies. In other studies, the stroke mortality after one year was even higher than one-third. Body weight in the Mexican series appeared unimportant as a predisposing variable. On this point the literature is divided, with some investigators claiming that increased body weight poses an added risk of stroke, while other investigators found no association between body weight and stroke. Stroke among individuals with sedentary as opposed to active occupations has been studied, but no increased frequency has been observed in contrast to what has been reported for sedentary occupations and risk of coronary artery occlusions. Emotional stress is difficult to measure and, therefore, it is not surprising that the literature is conflicting with respect to the role of emotional stress as a predisposing factor in stroke.

Thus, in most of the above respects, the stroke patients in Mexico were quite similar to stroke patients in other hospital series from very different populations. The analysis implies that the factors predisposing to stroke are relatively insensitive to marked ethnic and cultural differences. This conclusion also was reached by Kurtzke on the basis of an analysis of mortality data on stroke and by Yablonski et al. on the basis of postmortem studies of cerebral vessels. The observation that genetically different population clusters do not necessarily have a different pattern of risk factors associated with
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Diurnal Variation in Onset of Stroke

<table>
<thead>
<tr>
<th>Time of Day</th>
<th>Thrombosis</th>
<th>Hemorrhage</th>
<th>Embolus</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 AM - 12 noon</td>
<td>50%</td>
<td>30%</td>
<td>20%</td>
<td>100%</td>
</tr>
<tr>
<td>12 noon - 6 PM</td>
<td>40%</td>
<td>35%</td>
<td>25%</td>
<td>100%</td>
</tr>
<tr>
<td>6 PM - 12 midnight</td>
<td>30%</td>
<td>30%</td>
<td>40%</td>
<td>100%</td>
</tr>
<tr>
<td>12 midnight - 6 AM</td>
<td>20%</td>
<td>25%</td>
<td>55%</td>
<td>100%</td>
</tr>
<tr>
<td>Unspecified</td>
<td>10%</td>
<td>15%</td>
<td>75%</td>
<td>100%</td>
</tr>
</tbody>
</table>

FIGURE 2

humidity. The mean rainfall on days when patients had embolus was higher than the annual average; the means when patients had thrombosis and hemorrhage were lower than the annual average.

The distribution of various types of stroke by month is shown in figure 3. There was a sharp peak for cerebral thrombosis in August and September, which corresponds to the end of the rainy season in Mexico. Cerebral hemorrhage also showed an August-September peak. Though emboli were relatively common in August and September, a peak was not so evident, and March and May also had more cases than the mean. The smaller total number of cases of emboli would tend, of course, to obscure all but the more striking peaks.

Discussion
Many studies of risk factors in CVA have been based on retrospective examinations of clinical records of stroke patients. These records, however,

TABLE 4
Type of Stroke Related to Atmospheric Conditions

<table>
<thead>
<tr>
<th>Mean atmospheric condition</th>
<th>Thrombosis</th>
<th>Hemorrhage</th>
<th>Embolus</th>
<th>Total strokes</th>
<th>Annual average</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temperature (°C)</td>
<td>15.0</td>
<td>14.2</td>
<td>16.8</td>
<td>14.9</td>
<td>13.3</td>
</tr>
<tr>
<td>Barometric pressure (mm)</td>
<td>74.1</td>
<td>74.6</td>
<td>73.6</td>
<td>75.0</td>
<td>74.2</td>
</tr>
<tr>
<td>Rainfall (cm)</td>
<td>3.6</td>
<td>3.8</td>
<td>6.4</td>
<td>—</td>
<td>4.4</td>
</tr>
<tr>
<td>Humidity (%)</td>
<td>40.7</td>
<td>57.0</td>
<td>64.3</td>
<td>62.2</td>
<td>58.1</td>
</tr>
</tbody>
</table>

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The conclusion that genetics do not contribute an independent risk of stroke. Alter and Kluznik have previously shown that genetics may contribute to increased risk perhaps through hypertension and other diseases but not independently. Marshall found similar results and also indicated that the role of the aging process is important.

The uniformity of characteristics of patients with stroke in different populations is in marked contrast to the differences among patients with coronary artery disease, which appears to differ widely in frequency in various populations. Therefore, cerebrovascular disease may be influenced to a lesser degree than coronary disease by ethnic and cultural differences.

Of additional interest in the Mexican study was the relationship of climatic factors to stroke frequency because such data are infrequently reported. Schuman et al. have shown an excess of stroke deaths following two successive heat waves in Michigan. In Mexico, the average temperature to which patients were exposed at the time the stroke allegedly occurred was higher than the average for the year in their area of residence. Hence, strokes apparently tended to occur on days with warmer average temperatures.

Climatic variables besides temperature have been studied in relation to stroke frequency. In Japan, in Mexico, cerebral hemorrhage tended to occur when temperatures were warm (above 25°C). However, cerebral hemorrhage also tended to occur in Japan when the humidity was below 40%, and the atmospheric pressure was increased which differed from what was observed in Mexico. In Japan, a falling temperature, pressure, and humidity also were associated with a higher frequency of cerebral hemorrhage. Chilaiditis et al. also noted an increased frequency of cerebral hemorrhage with abrupt rises in temperature and atmospheric pressure. Popkin noted an increased frequency of fatal strokes prior to storms, e.g., in periods of low barometric pressure. In the Mexican series, there was no apparent relationship between barometric pressure and strokes, as the mean pressure for type of stroke was almost identical with the mean pressure to which the general population was exposed.

There is disagreement in the literature regarding seasonal variation in stroke frequency. Allen et al. and Ochsner suggested that the highest incidence of stroke was in winter. On the other hand, Sharnoff et al. noted an increase in fatal thrombotic diseases in the spring. April and May were peak months. The lowest frequency occurred in November, which heralds colder weather in New York where Sharnoff et al. conducted their studies. Sharnoff et al. suggested that the mechanism accounting for the spring peak was that increased physical activity in that season released megakaryocytes from the lungs which, in turn, increased the tendency to thrombotic disease. In Mexico, the peak stroke frequency occurred in August and September, which is the beginning of colder but drier weather, instead of in the spring. The Mexican results, therefore, favored the findings of Allen et al. and Ochsner rather than those of Sharnoff et al. In Canada, Gordon observed increased stroke mortality both in winter and spring with low frequency in summer and fall. McDowell et al. noted significantly more admissions of patients with nonembolic strokes to Bellevue Hospital, New York, during the period of November to May. A Yugoslavian study showed a maximum incidence of stroke at the end of December and the beginning of January but the difference between incidence rates by month was not statistically significant. The Yugoslavian investigators also were unable to show significant effects of temperature, humidity or atmospheric pressure on stroke. In Japan, Ohno et al. observed peak frequency of cerebral infarction in February and cerebral hemorrhage occurred more frequently in January and February. Obviously, there is as yet no good consensus as to the seasonal variation of stroke frequency, but the evidence slightly favors increased rates of stroke in colder months.

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