Hypertension and Diabetes as Risk Factors in Stroke Patients

BY SYLVAN LAVY, M.D., ELDAD MELAMED, M.D., ESTHER CAHANE, M.D., AND AMIRAM CARMON, M.D.

Abstract:
Hypertension and Diabetes as Risk Factors in Stroke Patients

The occurrence of hypertension and diabetes in stroke patients was evaluated in a retrospective epidemiological study in the Jerusalem district. During the years 1960 through 1967, 1,522 new stroke cases (834 males and 688 females) were diagnosed and included in the study. Cerebral ischemia was diagnosed in 509 patients (33%), 181 patients (12%) had an intracerebral or subarachnoid hemorrhage and 832 patients (55%) had a stroke of undetermined type. For the total stroke series, 42% had hypertension. Almost the same percentage was found for males (41%) and females (43%). There was almost no sex predominance in the hypertensive stroke cases in the different age groups and for the various types of stroke. The frequency of hypertension among the stroke cases was low in the 40 to 49 age group, higher in the 50 to 59 age group, maximal in the 60 to 69 age group, and declining in the above 70 age group. The percentage of hypertensives was about the same for the ischemic and the undetermined types of stroke and for the total stroke series in the different age groups. It was found to be slightly higher in the hemorrhage type. The prevalence of hypertension among the male stroke cases was compared with the prevalence of hypertension in the general male population aged 40 and above (9.6%).

For the total stroke series, 20% had diabetes. The same percentage was found for males (19%) and females (20%). There was almost no sex predominance in the diabetic stroke cases in the different age groups and for the various types of stroke. There was no significant change in the distribution of diabetes in the various age groups and the different stroke types. The prevalence of diabetes among the male stroke cases was compared with its prevalence in the general male population aged 40 and above (5%).

Our study shows that hypertension and diabetes play an important role as risk factors in the development of cerebral ischemia and hemorrhage alike.

Additional Key Words
prevalence of diabetes mellitus
prevalence of arterial hypertension
cerebral ischemia
cerebral hemorrhage

Introduction

Arterial hypertension is recognized as a major contributory factor to the development of stroke and as such it is surpassed by no other risk factor. To a lesser degree, diabetes mellitus appears to be a predisposing factor in the morbidity of cerebrovascular events and is frequently found as a concomitant disease in stroke cases.

An epidemiological survey on cerebrovascular events that occurred in the period of 1960 through 1967 was performed in the Jerusalem district. This district is formed by the city of Jerusalem, the capital of Israel, the township of Beit Semesh and the villages surrounding them. The population (187,500 in 1960 and 230,000 in 1967) enjoys excellent medical services that are supplied by the General Workers Sick-Fund Benefit Society (85%), by social welfare aid from the municipality (10%) and by private practitioners (5%). Hospitalization services are supplied by the three local hospitals: the Hadassah University Hospital (which had the only neurological department in the district in that period), the Shaare-Zedek Hospital, and the Bikur-Holim Hospital. Almost every patient suffering a new stroke is referred by his physician to the emergency ward of one of the three local hospitals. The medical approach to those patients, generally shared by those hospitals, is to admit most of them either to the Neurological Department of the Hadassah University Hospital or to the Internal Medicine Departments of the other two hospitals, at least until the acute phase of the stroke is over. Most of the few stroke patients who were not admitted (usually the milder cases) were referred later on to...
the Neurological Outpatient Clinic of the Hadassah University Hospital, which supplied the only neurological consultation services in the district. We could then assume that the information regarding most of the new stroke cases was concentrated in the three local hospitals and the files of our Neurological Outpatient Clinic, enabling us to obtain a close estimation of the real occurrence of cerebrovascular events in the population of the district.

As a part of this retrospective study, data were collected concerning the occurrences of hypertension and diabetes among the stroke cases in our series. The material and data will be presented and discussed.

**Methods**

The new cases of cerebrovascular accidents that occurred in Jerusalem in the period of 1960 through 1967 were gathered from the registry sources of the three local hospitals: the Hadassah University Hospital, the Shaare-Zedek Hospital and the Bikur-Holim Hospital, and from the files of the Neurological Outpatient Clinic and other clinics of the Hadassah University Hospital. The new stroke cases were ascertained through detailed review of their medical records. The criteria we used for diagnosing and accepting a case as a new stroke were closely adherent to those outlined in the “Classification and Outline of Cerebrovascular Diseases” and were based on the history, clinical examination, and, when available, on diagnostic tests such as lumbar punctures, angiograms, operations and autopsies. In ischemic strokes we included diagnoses of cerebral thrombosis, cerebral embolism (as it was not always clinically possible to differentiate between them), and vertebrobasilar “completed” events. In hemorrhagic strokes we included diagnoses of intracerebral hemorrhage and intraventricular and subarachnoid hemorrhages. For the differentiation between the ischemic and hemorrhagic varieties, at least a lumbar puncture, angiogram, operation or autopsy was required. We classified the cases in whom no diagnostic procedures were performed as having a stroke “of undetermined type.” In this series only acute and completed cerebrovascular accidents were included. Cases diagnosed as having transient ischemic attacks and vertebrobasilar insufficiency were discarded. The stroke cases were considered as hypertensive if they fulfilled the following criteria: (a) a reliable history of diastolic hypertension of 100 mm Hg and above, and/or (b) at least two recordings of diastolic pressure of 100 mm Hg and above, taken ten days or more after the acute cerebrovascular event, on follow-up examinations. Patients with a history of hypertension were not considered to have hypertension if diastolic readings below 100 mm Hg were recorded on follow-up examinations. It served as a criterion only when no blood pressure recordings were available ten days or more after the acute cerebrovascular event (for example, death of a patient). Patients were considered to have diabetes mellitus if they fulfilled the following criteria: (a) a reliable history of diabetes, and/or (b) at least two fasting blood glucose levels exceeding 120 mg per 100 ml by all methods used in the different hospitals, performed ten days or more after the acute phase of the cerebrovascular event. Patients with a history of diabetes were not considered to have diabetes if blood glucose levels were below 120 mg per 100 ml on follow-up examinations. It served as a criterion only when no information about the glucose levels was available ten days or more after the acute stroke (for example, death of a patient). Only patients with overt diabetes were included in this study. The latent diabetics with positive glucose-tolerance tests were omitted.

The frequency rates of hypertension and diabetes among the male stroke cases were compared with those of the general male population aged 40 and above.

**Results**

In the period of 1960 through 1967, 1,522 new stroke cases (834 males and 688 females) fulfilling our criteria were identified in the district of Jerusalem and included in our study. The distribution of those cases according to the type of stroke was as follows: in 509 (33%) it was ischemic, in 181 (12%) it was hemorrhagic, including subarachnoid hemorrhage (31 cases), and 832 (55%) had a stroke of undetermined type.

According to our criteria, 42% of the total stroke series had hypertension (table 1). The same percentage was found for both sexes, 41% of the male patients and 43% of the female patients being hypertensive. There was almost no sex predominance (fig. 1) in the stroke patients having

**Table 1**

<table>
<thead>
<tr>
<th>Age</th>
<th>Ischemic stroke</th>
<th>Hemorrhagic stroke</th>
<th>Stroke of undetermined type</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male (%)</td>
<td>Female (%)</td>
<td>Total (%)</td>
</tr>
<tr>
<td>&lt;39</td>
<td>20</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>40–49</td>
<td>5</td>
<td>30</td>
<td>35</td>
</tr>
<tr>
<td>50–59</td>
<td>44</td>
<td>47</td>
<td>45</td>
</tr>
<tr>
<td>60–69</td>
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<td>70+</td>
<td>28</td>
<td>36</td>
<td>32</td>
</tr>
<tr>
<td>Total</td>
<td>41</td>
<td>43</td>
<td>42</td>
</tr>
</tbody>
</table>

**LAVY, MELAMED, CAHANE, CARMON**

*Stroke, Vol. 4, September-October 1973*
hypertension in the different age groups and for the various types of stroke, the figures being generally equal for males and females, except for a female preponderance for ischemia, hemorrhage and total stroke series in the 40 to 49 age group (table 1) (the figures for the under 40 age group were too low to be of any significance). The percentage of hypertensives was about the same, for the ischemic and undetermined types and for the total stroke series in the different age groups (figs. 2 and 3). The percentage of patients with hypertension was slightly but persistently higher in the hemorrhagic type for all the age groups. In the 40 to 49 age group this difference is significant (0.001 < P < 0.005). In the other age groups, however, there exists no significant difference (P < 0.10) between the hemorrhagic and ischemic types. Breakdown of hemorrhage patients was: intracerebral hemorrhage in 150 cases (83%) and primary subarachnoid hemorrhage in 31 cases (17%). Hypertension was present in 53% of the intracerebral hemorrhage patients and in 26% of the primary subarachnoid hemorrhage patients.

As regards the distribution of the hypertensive stroke cases according to age, it appears that the lower percentage is found in the 40 to 49 age group (except for females with hemorrhage). The frequency of hypertension among the stroke cases rises in the 50 to 59 age group; it is maximal in the 60 to 69 age group and declines again in the 70 plus age group. The highest percentage was demonstrated in the 60 to 69 age group in patients with hemorrhage, where 65% were found to have hypertension (figs. 2 and 3).

When compared with the prevalence of diastolic readings of 100 mm Hg and above in the general male population aged 40 and above, which was on the whole 9.6%, it is obvious that hypertension is associated with stroke in excess of four times more.

### THE SEX DISTRIBUTION OF DIABETES AND HYPERTENSION IN THE VARIOUS TYPES OF STROKE

**HYPERTENSION**

<table>
<thead>
<tr>
<th></th>
<th>Male (%)</th>
<th>Female (%)</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic</td>
<td>40</td>
<td>35</td>
<td>37.5</td>
</tr>
<tr>
<td>Hemorrhagic</td>
<td>50</td>
<td>45</td>
<td>47.5</td>
</tr>
<tr>
<td>Undetermined</td>
<td>30</td>
<td>25</td>
<td>27.5</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

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**DIABETES**

<table>
<thead>
<tr>
<th></th>
<th>Male (%)</th>
<th>Female (%)</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic</td>
<td>20</td>
<td>15</td>
<td>17.5</td>
</tr>
<tr>
<td>Hemorrhagic</td>
<td>10</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>Undetermined</td>
<td>30</td>
<td>25</td>
<td>27.5</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

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*Stroke, Vol. 4, September-October 1973*
than its appearance in the above-mentioned population, with some changes in the different age groups (fig. 4). In the 40 to 49 age group, there is no significant difference $(0.10 < P < 0.25)$ between the prevalence of male hypertensives in the stroke series and the general male population. In the other age groups there exists, however, a significant difference $(P < 0.001)$. The overall test, including the data from all the age groups, is significant $(P < 0.001)$.

According to our criteria, 20% of the total stroke series had diabetes mellitus (table 2). The same percentage was found for both sexes, 19% of the male cases and 20% of the female cases being diabetics. With some exceptions there was no sex predominance in the stroke patients having diabetes in the different age groups and for the various types of stroke, the figures being generally the same for males and females (fig. 1). There was a lower percentage of male diabetics with hemorrhage in the 50 to 59 and 60 to 69 age groups. No diabetics were found in the under 40 age group.

It appears that the percentage of diabetics in the various types of stroke is generally the same for the ischemic and undetermined types and for the total stroke series in the different age groups (figs. 2 and 3). The figures were slightly lower in the patients with hemorrhage. This difference between the number with hemorrhage and ischemia is not significant. There was no significant change in the distribution of diabetes among the stroke patients in the various age groups.

When compared with the prevalence of diabetes in the general male population aged 40 and above, which was on the whole 5%, it is obvious that diabetes is associated with stroke four times more than its appearance in the above-mentioned population. This ratio is approximately 6:1 in the 40 to 49 age group, 3:1 in the 50 to 59 group and 2:1 in the 60 plus age group (fig. 5). The difference between the prevalence of male diabetics in our stroke series and the general male population is significant in each age group $(P < 0.001)$. The overall test, including the data from all the age groups, is significant $(P < 0.001)$.

Hypertension and diabetes together were found in 8% of the total stroke series, the figures being almost the same for the various types of stroke. Hypertension was generally found to be two times...
more frequent than diabetes in our stroke cases. The difference is not significant for the 40 to 49 age group. It is significant in the other age groups (P < 0.001). The overall test, including data from all the age groups, is significant (P < 0.001) (McNemar test).

Discussion
At present, when the treatment of completed stroke is rather limited, it seems imperative that efforts should be directed toward its prevention. The stroke-prone person should be sought, identified, and treated in time, in order to try and diminish the proportions of the stroke problem. It is highly important to determine and recognize the characteristics which make these individuals susceptible to stroke.

It is commonly agreed upon and widely accepted that hypertension is significantly associated with cerebrovascular accidents, and is found in high

TABLE 2
The Age and Sex Distribution of Stroke Cases With Diabetes

<table>
<thead>
<tr>
<th>Age</th>
<th>Ischemic stroke Male (%)</th>
<th>Female (%)</th>
<th>Total (%)</th>
<th>Hemorrhagic stroke Male (%)</th>
<th>Female (%)</th>
<th>Total (%)</th>
<th>Stroke of undetermined type Male (%)</th>
<th>Female (%)</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;39</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<td>0</td>
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<tr>
<td>40–49</td>
<td>24</td>
<td>15</td>
<td>21</td>
<td>20</td>
<td>0</td>
<td>20</td>
<td>13</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>50–59</td>
<td>24</td>
<td>22</td>
<td>23</td>
<td>16</td>
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<td>60–69</td>
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<td>70+</td>
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<td>18</td>
<td>21</td>
<td>19</td>
<td>21</td>
<td>19</td>
<td>18</td>
</tr>
</tbody>
</table>

Total 20 20 20 11 17 14 21 21 21 19 20 20

Stroke, Vol. 4, September-October 1973 755
THE PREVALENCE OF MALE HYPERTENSIVES IN STROKE CASES AND IN GENERAL POPULATION

frequency among those patients. In our series, hypertension was arbitrarily diagnosed when diastolic readings of 100 mm Hg and above were recorded. As different criteria were used for the determination of hypertension in the various studies, it makes it rather difficult to compare the results. In our series hypertension was detected in 42% of the stroke cases. Gertler found almost the same percentage. It was present in 58% of nonembolic brain infarction cases in Louis' series. Meyer et al. demonstrated 31% hypertensives in his hospital series of nonhemorrhagic stroke patients. Seventy-five percent had hypertension in Baker and Katsumi's study, in which the same percentage was found in Minnesota and Japan. McDowell et al. reported 51% hypertensives in his series. According to Kurland, two-thirds of the stroke cases had hypertension. In the Framingham study only 15% of all the stroke patients were entirely normotensive. Had we employed the generally used criteria for the diagnosis of hypertension with systolic readings of 160 mm Hg and diastolic readings of 95 mm Hg and above, our figures would have been much higher. However, even though the figures we present are minimal figures, hypertension is found in high frequency in our series. It should be pointed out and stressed that in the Framingham study the risk of developing stroke was related not only to elevated diastolic pressure but to the mean arterial and systolic pressures as well. No critical level of blood pressure was found in that study and the risk of developing the cerebrovascular accident was simply proportional to the level from the lowest to the highest recorded.

It appears from the present study that hypertension is similarly associated with both male and female stroke cases in general. A female preponderance was found in the ischemic and hemorrhagic types for the 40 to 49 age group, in contrast with the Framingham study, where a slight male preponderance was found in the younger age groups and a slight female superiority in the older ones. It is possible that women do not tolerate hypertension better than men where stroke is concerned.

Stroke due to hemorrhage was associated with a slight but persistently higher (approximately by 10%) occurrence of hypertension however, which was found to have no statistical significance. The same association, 42% hypertensives in the ischemic type of stroke and 52% in the hemorrhagic type, was
RISK FACTORS IN STROKE

found by Gertler.\textsuperscript{5} In the Framingham study,\textsuperscript{11} the relative risk of hemorrhagic stroke appearing in hypertensive patients was no greater, surprisingly, than that noted for the ischemic ones.

The frequency of occurrence of hypertension in the stroke cases tended to rise with age until the 70 plus age group, where a decline was noted. Exact statistics on the prevalence of hypertension in males and females and in different age groups are not available, not only in Israel but in other countries as well, where surveys among selected groups suggest different rates for different age groups. We used a study performed in Israel consisting of 10,000 male civil servants and municipal workers aged 40 and above,\textsuperscript{2} in order to compare the prevalence of hypertension in our stroke series with its prevalence, if not in the general population, at least in a defined nonstroke one. Hypertension is associated more than four times as frequently with stroke cases than its prevalence in the above-mentioned population. We can conclude from our study that there exists a very close and definite association between hypertension and cerebrovascular events. We cannot, however, state an etiological relationship between the two as a result of our study, which was retrospective in nature, though it is our feeling that such a relationship does exist. It calls for a prospective epidemiological study to prove that hypertension is indeed a predisposing factor in the development of stroke. Such a relation was proved in the Framingham study.\textsuperscript{11} How does hypertension predispose to the development of stroke? This is still not completely understood. It can accelerate atherogenesis in the cerebral vessels, it can mechanically damage these vessels and it can indirectly, through the development of cardiac insufficiency, lead to reduced perfusion in previously narrowed cerebral vessels. It seems that hypertension is indeed one of the main characteristics of the stroke-prone individual. It should be detected early, treated, and controlled. There is evidence to suggest the success of such an approach.\textsuperscript{12, 13}

Diabetes mellitus frequently exists as a concomitant disease in cerebrovascular accidents and is considered, too, as a risk factor in the development of stroke, though less potent than hypertension. As with hypertension, it is rather difficult to compare the frequency of association of diabetes and stroke in the various studies, as different criteria are employed for its diagnosis. The occurrence of diabetes in stroke varies in the different series. Louis et al.\textsuperscript{6} found diabetes in 27% of their ischemic

THE PREVALENCE OF MALE DIABETICS IN STROKE CASES AND IN GENERAL POPULATION

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{prevalence_diabetics}
\caption{The prevalence of male diabetics in stroke cases and in general population.}
\end{figure}
nonembolic stroke cases. The rate of occurrence was 14% in Conant's series, 14 28% in Gertler's, 5 13% in Meyer's, 7 16% in McDowell's, 9 and 15% in Kurland's. 10 Baker and Katsuki 10 found the presence of diabetes in 30% of Japanese stroke cases and in only 10% of American ones. Najenson et al. 15 found evidence of diabetes in 30% of their stroke series. Adler 10 reported that 13% of his cases were diabetic. Lower figures are reported in other studies: Alex et al. 12—7%, Gurdjian 18—6%, and Baker 19—5%. When compared with this range of 5% to 30%, the frequency of diabetes in our stroke cases of 20% seems rather high. These are minimal figures, for we believe that some diabetics escaped detection in the present study (which was retrospective) and it is our feeling that the rate, therefore, should be even higher. This percentage would increase had we included the stroke cases with latent diabetes and positive glucose tolerance tests in this study.

Few studies have been done in Israel in order to establish the prevalence of diabetes in the population. According to Steinitz 20 it is in the order of 1.1%. Zaide 21 found it to be 0.81%. Cohen 22 reported the prevalence of diabetes as 2.5% among ashkenazi and 1% among sephardi Jews. According to Cohen, the prevalence of diabetes in the population aged 40 and above is 8.1% among ashkenazi and 4.5% among sephardi Jews. In Herman and Medalie's study 3 diabetes was identified in 5% of 10,000 male civil servants and municipal workers. Although the last figure of 5% is found in a rather defined male population, it can serve as a baseline. It appears that diabetes is associated with stroke four times as often as in the above-mentioned population (with different ratios in the various age groups).

The frequency of hypertension among all the male stroke cases in our series of 41% was twice that of diabetes (19%). Almost the same ratio is found between the prevalence of hypertension and diabetes among the male population aged 40 and above. 2,2 Therefore, one can speculate that diabetes is not less associated with the development of stroke than hypertension. The coefficient of association of diabetes with stroke is \( r = 0.64 \). The coefficient of association of hypertension with stroke is \( r = 0.73 \) (Yule's coefficient 23) and there is no significant difference \( (P < 0.5) \) between those two coefficients (Woolf's test). This speculation, of course, can be proved only by a prospective study.

Diabetes probably predisposes to the development of stroke by its contribution to the atherogenesis in the cerebral vessels by the multiple lipid disorders associated with it. There is no evidence at present that treatment and control of diabetics will indeed lower the occurrence of cerebrovascular accidents.

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LAVY, MELAMED, CAHANE, CARMON

758

Stroke, Vol. 4, September-October 1973
RISK FACTORS IN STROKE


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