Transient Cerebral Ischemic Attacks in the Young and Middle Aged
A Population Study

STURLA E. JOHNSON, M.D.,* AND HAVARD SKRE, M.D.†

SUMMARY During an investigation of coronary risk factors, a population 20 to 54 years old in Tromsø, Northern Norway was screened for transient ischemic cerebral attacks. Three simple screening questions were used. Sixteen thousand six hundred and twenty-one subjects participated in the study. Among the responders, a sample of 501 were evaluated neurologically and 10 men and 16 women identified as TIA cases. Mean age for men was 41.3 years, for women 33 years. Five women (mean age 24.4) had the events during pregnancy, pointing to pregnancy as a period of risk. Five-year incidence was found to be 2.5 per 1000. Clinical expressions and ratio carotid to vertebral-basilar TIA hardly differed from that found in materials of older patients. All 26 remained stroke-free during a mean observation period of 55 months. Known risk factors like hypertension, carotid stenosis and cardiac disease were found in only a few. Five women had low blood pressure. It is suggested that TIA in younger age groups may constitute a separate entity where, among other, haemodynamic factors and pregnancy play a role.

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diovascular and haematological disorders in particular. Blood pressure was measured with the patient recumbent for 2 minutes. All subjects met fasting. A venous blood sample was drawn from the cubital vein. A total of 275 samples, including all stroke and TIA cases, have been analysed for lipoproteins and lipoprotein markers. The results will appear elsewhere.

Identification of TIA in the present study was made after a close scrutiny of data collected during the interview. Whenever available, hospital records were checked. Our hospital is the only one in this area and records existed for 50% of those interviewed.

Vertigo alone as symptom was considered too unspecific to merit inclusion, as were syncope and drop attacks. Headache before or after the event or a history of recent migraine attacks also meant exclusion although headache can be a feature of TIA. There was one exception: A 35 year old women with classical migraine over 9 years whose attacks were stable and uniform and occurred 2-3 times a year. She was included on the basis of an episode with complete half-sided sensory loss of 10 minutes duration and without headache. Identification was in some cases difficult and required a second telephone interview in order to get more details. When in doubt, two or more identical episodes would mean inclusion. One episode was accepted when there could be little doubt about the ischmic nature like in transient hemiparesis or monocular blindness.

Results

Of the 21,329 persons summoned for the mass x-ray examination, 16,621 responded, delivering their answers to the 2 page primary questionnaire. Twenty-six replied affirmatively to the question referring to stroke. All of these were invited for a follow-up with the intention of verifying the diagnosis. Twenty-one were seen and examined. An overview of numbers is given in table 1. The results appear in table 2. Five of the 12 patients with thromboembolic stroke reported episodes of TIA in addition. Since these cases are not randomly selected, they were not included in the subsequent TIA group. Fourteen thousand six hundred and sixty-seven of the 16,621 persons participating in the mass x-ray examination returned the second questionnaire. One thousand, one hundred sixty-seven had given an affirmative answer to one or more of the TIA questions. Half of these, 588 persons, all born on even dates, were invited for further medical investigations, and 501 (85%) responded. Four hundred ninety-four subjects were seen personally by the authors while 7 could not attend for different reasons, but were interviewed by telephone. Of the 87 non-responders, one had died of coronary heart attack before the follow-up, 15 had moved and 11 declined.

As expected a large majority of those seen had no history indicating transient cerebral ischemia. Table 3 summarizes the diagnoses of this false positive group. The group includes 3 persons with previously unrecognized minor strokes. In the same group were a number of patients with specific non-cerebrovascular neurological conditions which had been diagnosed during earlier admissions to the hospital.

Twenty-six cases of TIA, 10 men and 16 women, were identified. Six of these already had the diagnosis from earlier admissions or visits to the outpatient clinic. For 25 subjects the events took place between 1969 and 1980. The exception was a woman whose event occurred during pregnancy 30 years earlier. Nine at the time of first TIA averaged 41.3 years for men (range 29-54) and 33 years for women (18-48). Five young women had TIA during the second half of pregnancy. If we leave out these who pathogenetically may belong to a different category, mean age rises to 36.8 years and equals that of men born after 1930 (37.2 years). Incidence of TIA over age is given in figure 1.

Only men and women born after 1st of January 1930 with first events 1975 through 1979 were considered for the estimation of incidence, in all five men and nine

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**Table 1** The Tromso Study. Sixteen Thousand Six Hundred and Twenty-One Men and Women 20 to 54 Years of Age.

<table>
<thead>
<tr>
<th>Classification</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attended first screening</td>
<td>16621</td>
</tr>
<tr>
<td>Self-reported stroke</td>
<td>26</td>
</tr>
<tr>
<td>Postal questionnaires</td>
<td>14667</td>
</tr>
<tr>
<td>Affirmative answers</td>
<td>1167</td>
</tr>
<tr>
<td>Selected for follow-up</td>
<td>588</td>
</tr>
<tr>
<td>Attended follow-up (85%)</td>
<td>501</td>
</tr>
<tr>
<td>TIA-cases found</td>
<td>26</td>
</tr>
</tbody>
</table>

**Table 2** Verification of 26 Self-reported Strokes in 17 Men (32-54 years) and 9 Women (28-30 years). Results of Follow-up and Review of Records.

<table>
<thead>
<tr>
<th>Classification</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thromboembolic infarction</td>
<td>12</td>
</tr>
<tr>
<td>Transient ischemic attack</td>
<td>1</td>
</tr>
<tr>
<td>Subarachnoid haemorrhage</td>
<td>7</td>
</tr>
<tr>
<td>Traumatic brain haemorrhage</td>
<td>1</td>
</tr>
<tr>
<td>Non-cerebrovascular conditions</td>
<td>4</td>
</tr>
<tr>
<td>Unknown</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>26</td>
</tr>
</tbody>
</table>

**Table 3** Classification of "False Positives" in Response to TIA Questions.

<table>
<thead>
<tr>
<th>Classification</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute or intermittent numbness/weakness due to cervical spondylosis, shoulder conditions, nerve entrapment, myositis</td>
<td>31.5</td>
</tr>
<tr>
<td>Sensory/motor symptoms due to lumbar disc lesions or orthopedic/rheumatic conditions</td>
<td>7.0</td>
</tr>
<tr>
<td>Migraine</td>
<td>8.9</td>
</tr>
<tr>
<td>Facial palsy (Bell's)</td>
<td>7.6</td>
</tr>
<tr>
<td>Psychoneurosis, hyperventilation syndrome</td>
<td>11.4</td>
</tr>
<tr>
<td>Eye disorders e.g. squint, refraction errors</td>
<td>9.5</td>
</tr>
<tr>
<td>Dizziness, near-syncope w/visual disturbances</td>
<td>5.5</td>
</tr>
<tr>
<td>Specific neurological disorders, e.g. stroke, epilepsy, traumatic and neoplastic brain lesions, MS, poliomyelitis, meningitis, polyneuropathy and myotonic dystrophy</td>
<td>7.0</td>
</tr>
<tr>
<td>Unrelated or non-classifiable disorders</td>
<td>11.6</td>
</tr>
<tr>
<td>Total</td>
<td>100.0</td>
</tr>
</tbody>
</table>

n = 473.
women. A 5-year overall incidence (first event) of TIA for men and women between 20 and 50 years was estimated to be about 2.5 per 1000.

In the TIA group, the majority were in good health at the time of the event. Four were being treated for hypertension and two of these had coronary heart attacks within five years of the cerebral event. In two of the others cardiac murmurs were heard on auscultation and one of these had rheumatic fever as a child. Six were markedly overweight, one of whom had undergone jejuno-ileal bypass surgery. The rest were generally healthy (table 4). None of the women were using contraceptive pills. Five young women (mean age 24.6) had TIA during pregnancy, four of them during the last trimester. One woman experienced similar TIA during 2 successive pregnancies. The examination revealed a bruit over the corresponding carotid artery. In two of the others were found possible bruits. None were under the influence of alcohol when the TIA occurred. Mostly, multiple attacks occurred within a few days, but 4 subjects reported recurrent episodes over more than four years. Figure 2 shows mean attack number over age. There were no overall sex differences. Ten subjects experienced only one attack whereas 4 subjects had more than five.

All the common manifestations of TIA were seen, like monocular blindness, hemiparesis, hemianesthesia and aphasia (table 5). Seventeen subjects experienced sensory symptoms either alone or in combination with other symptoms. In 20 subjects symptoms were thought to come from ischemia in the carotid artery territory. The vertebral-basilar territory was implicated in the remaining 6. Although the events might have taken place several years earlier, all remembered them well and could give detailed accounts. A similar experience of good patient memory is reported from the Evans County Study.12 In 17 out of 23 symptoms had caused sufficient alarm to make them consult a doctor. Eight were soon afterwards referred to our department where 6 underwent extra- and intracranial vessel angiography. Another 2 have since the study been admitted for angiography because of recurrent TIA. In all 8 angiographies were performed. Bilateral carotid aneurysms were demonstrated in one person with fibromuscular dysplasia. Another had extensive atheromatous lesions and stenosis in both internal carotids. Endarterectomy was carried out as an emergency. No abnormality was seen in the other 6.

At the time of neurological evaluation mean observation time was 55 months (range 12-132) without occurrence of stroke in 25 subjects. One person, a woman, has remained stroke-free for 30 years.

Over the last ten years an average of 60 patients

| TABLE 4 Follow-up Study of 26 TIA-cases 20-54 Years: Some Clinical Findings |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Systolic BP (mm Hg) mean | 131.3 (160–105) | 130.0 (110–150) | 131.3 (160–105) | 131.3 (160–105) | 131.3 (160–105) | 131.3 (160–105) | 131.3 (160–105) |
| Systolic BP ≥ 145. n = | 6 | 5 | 2 | 3 | 2 | 3 | 2 |
| Systolic BP ≤ 110. n = | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Diastolic BP, mean | 85.0 (110–70) | 85.0 (110–70) | 85.0 (110–70) | 85.0 (110–70) | 85.0 (110–70) | 85.0 (110–70) | 85.0 (110–70) |
| Diastolic BP ≥ 110. n = | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| Heart disease | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Overweight | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Carotid bruit, definite | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Carotid bruit, possible | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Carotid bruit, unpalpable pulse | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Total | 26 | 26 | 26 | 26 | 26 | 26 | 26 |
annually have been admitted to the neurological, medical and surgical departments under the diagnosis TIA (ICD no. 435.99). The hospital's databased diagnostic register has been checked to see if any TIA-cases admitted who were eligible for the follow-up study, had in fact been missed. None were found.

Discussion

Two methods are available if one wishes to study the occurrence of TIA in a population. Most studies so far have made use of data from medical records or, indirectly, from diagnostic registers. This means that only persons who seek medical attention for their symptoms are included. One would expect such estimates to be too low since a number of patients presumably never report their incidents. TIA symptoms, as the present study shows, are often sensory, very short-lived, appear only once and may not cause much alarm. One can safely assume that the younger the patient, the less regard he pays such symptoms. A population screening with the use of self-administered questionnaire is equally open to error. The form may have been incompletely filled in, misunderstood or lost or events may have been forgotten. It is impossible to say to what extent this affects results. From our experience the general public is motivated for health screenings once the object is made clear and people take care to answer the questions correctly. A great many said they welcomed the chance to get a medical check. This is also reflected in the good turn-out.

As for the 1954 subjects (11.8%) who did not respond to the second questionnaire, these do not differ in age from the rest. We suspect that a lower incidence of TIA would have been found in this group had it been followed up. Persons who experience symptoms are probably more alert to the need for a medical check than others and therefore likely to be found among the responders.

The questions used in the Tromsø Study may seem few and unspecific if compared with those used and recommended by other investigators. In a Danish study in some ways similar to the present, 5 simple questions were used. The nature of the Tromsø Study ruled out the use of additional questions. In our view too many and detailed questions can also cause errors and lead to higher non-response rate. It was decided instead to use few questions and to follow up with a personal evaluation of a large number of the respondents. This was done by qualified neurologists with access to hospital records. We therefore believe a high degree of case ascertainment was achieved.

As expected the Tromsø Study showed transient ischemic attacks to be rare in persons under 50–54. Earlier population studies differ from the present in method and age selection and directly comparable estimates of incidence are not available. The Danish Study linked to an investigation of heart disease in a Copenhagen suburb gives an estimate of 4/1000/year for the age 50–59 years. The Evans County survey covers subjects over 40 years and a sample of 15 to 39 year olds. Prevalence of TIA at the time of follow-up was 8/1000 under 54 years. There was a racial difference, whites having a higher rate than blacks. Japanese men in Hawaii over 45 years had an incidence of 0.7/1000 in the 45–49 year group. A recent Swedish survey based on data from hospital admissions, suggests an incidence as low as 4/100000/year under the age 55. The authors assume that nearly all TIA cases are referred for specialist evaluation, a view which is clearly open for debate. In comparison, The Rochester Study, also based on medical records, gives an incidence of 16/100000/year in the 45–54 year group. Allowing for the uncertainties connected with population screenings like the present and the small number of TIA cases found, our estimate of a 5-year incidence of 2.5/1000 seems reasonable. It must, however, be taken only as a pointer. The real incidence is likely to be higher for reasons stated earlier. Also, the figure does not include persons who suffered stroke or died after TIA. An interesting detail is the comparison between male/female ratios in the Swedish and Tromsø materials. There seems to be a trend towards a female dominance in the younger age strata and the reverse in the older age groups in both materials. Since our cases are so few, this must be taken with all due reservations.

A surprising number (17 out of 26) experienced sensory deficits, either alone or in combination with other symptoms. Karp reported 8 with sensory symptoms out of 26 but 18 of these were over 55 years old. This could imply that sensory TIA make up a larger proportion of cases in the young than in those of higher age. The number of cases with paresis of the limbs corresponds well in the two materials (9 in the Tromsø Study against 8 in the other). The attacks were mostly short, lasting less than 30 minutes in 20 subjects. In 11 the duration was less than 5 min.

The ratio of carotid to vertebral/basilar territory TIA was 4:1. This differs from the 2:1 ratio found in a middle and old age patient material in Rochester, and in a Dutch material of similar age but is equal to that found in a retirement community in Seal Beach.

In contrast to the attention given stroke, not much is found in the literature concerning transient ischemic attacks during pregnancy. Sporadic cases have been described but more often regarded as manifestations of migraine than TIA. None of our cases suffered from migraine during or after the pregnancy. In our experience TIA during the latter half of pregnancy is not uncommon. We have since the study encountered several additional cases, referred from the Department of Obstetrics. A report is about to be published. This very interesting phenomenon should, in our view, be further investigated with regard to pathogenesis and prognostic implications. All the five women in the study had uneventful deliveries.

There is a puzzling trend towards a higher TIA incidence in the age groups around 40 years, corresponding roughly with the highest mean recurrence rate. There is also a high incidence and TIA recurrence rate in age group 25–29, corresponding to the peak of TIA incidence in pregnancies. Since the number of cases is so small, such trends should not be overemphasized,
but they suggest two possibilities: Causes leading to TIA episodes in the actual age groups exert their maximum influence around the 40 years mark, or during the childbearing periods in the female. Further, these episodes are evidently of a more benign type than those occurring in older age, where approximately one third of TIA cases may experience a stroke later, half of them within the following month.18 Also other observations suggest that our "young" TIA cases constitute special etiological groups, since risk factors like hypertension, overweight, carotid stenosis, cardiac diseases, etc., were largely non-existent and hardly different from the population average.

This is in line with findings in another Norwegian study of cerebrovascular accidents, which comprised non-hypertensive males younger than 55 years of age admitted to hospital. TIA incidence peaked around 40 years, while stroke incidence prevailed later. In this study the antigen Ag(x), which is of a lipoprotein nature (Beta fraction), was abundant in TIA cases (59% positive, as against 35% in the population).20 Lack of this factor is regarded a risk factor in cardiac infarction, its role in TIA is obscure. Another possible risk factor in TIA may be low blood pressure in affected women. Of the 16 females in our series with TIA, 5 had systolic blood pressures ≤110 mm Hg, while such low figures were not found in 14 age-matched controls (women with Bell's palsy from the same study).

In a Dutch study from 1981,19 comprising 225 women (28% below 55 years), significant correlation was observed between low BP and TIA risk in all age groups.

On the basis of our own findings set in a context with other observations, it is reasonable to believe that early TIA may represent a rather benign condition, and perhaps constitute a separate entity(ies), where, among other, haemodynamic factors and pregnancy play a role.

References

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