Stroke is second among killers in persons above 40 years, which is significant challenge amid increasing longevity. Besides, the morbidity resulting from stroke imposes very heavy health care costs and ruin of quality of life in survivors. Risk factors of stroke are largely the same as for cardiovascular disease, needing similar prevention through appropriate measures. Most strokes are thrombo-embolic in origin but their pathogenic ground is laid gradually. Population segments need be examined to build local evidence base of risk factors for stroke. Interventions can thus be rationally planned. The gravity of oxidative stress and inflammatory mechanisms marked by the risk factor profile needs understanding and dictates prognosis and hence management. Present investigation relates to stroke patients hospitalized at paid tertiary care center in Nagpur central India toward generating local evidence.

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1. Introduction

Heavy mortality and morbidity attributable to stroke deserves intense consideration for sound preventive endeavours. Developing countries are much behind as stroke incidence continues to rise in contrast to declining incidence among developed countries (Feigin et al, 2009). Awareness and management of diverse risk factors is most likely explanation for the divergent trends (Wasay et al, 2011). There is little scope of generalized availability of the thrombolytic therapy to victims at large. Prevention is sole logical strategy therefore. Recognition and address of the risk factors linked to first incidence of stroke is crucial. Strategies need be designed also to check the very emergence of established risk factors, i.e. the primordial prevention approach. Interventions would have to focus on physical inactivity, smoking, wrong food habits etc. Averting recurrent stroke after surviving first episode also calls for intense risk factor control, i.e. secondary prevention (WHO,
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2. Subjects and Method

It was prospective, observational study of hospitalized stroke patients in Central India Institute of Medical Sciences Hospital Nagpur, over January 2003 to March 2004 period. Adult patients are included with range of age between 37 years to 76 years. Occurrence of sudden rapidly progressing neurological deterioration within past 24 hours and subsequent confirmation by brain CT scan (in most cases), formed the stroke eligibility and inclusion criterion. Attendant of the patient were explained study nature and objective and their informed written consent was obtained, assuring non disclosure of patient identity.

Socio-demographic information and details of clinical history were noted. Standard neurological exam performed and findings were recorded. Within 48 hours of hospitalization the regular investigation included, haemogram, sugar, lipid profile, urea, creatinine, electrolyte and ECG. Any other investigations were requisitioned as indicated.

Data collection on the cardiovascular risk factors in the stroke patients and their association to final outcome (discharge or death), was guided by following precepts/techniques:

1. Hypertensives were characterized as patients on antihypertensive drug therapy preceeding stroke episode and a persisting blood pressure above 140/90 mmHg on 7th day since the stroke event.

2. Diabetes was to be characterized as old diagnosis before stroke or evidence of fasting blood glucose level above 6.1 m mol/L, after the acute phase of stroke subsided (Alberti and Zimmett, 1998).

3. Hyper-cholesterolaemia was defined as treatment with lipid lowering drugs, prior to stroke or serum cholesterol level over 5.2m mol/L (Anonymous, 1987).

4. Waist circumferences were measured at end of expiration, by tape held horizontally at level of superior iliac crest without compression. Obesity was taken as values above 80 cm in females and 94 cm in males (vanderSande et al, 2001).

5. Current smoking status and alcohol intake history was elicited from attendants. Smoking instances of more than two cigarettes per day and alcohol intake at least once a week were the defining grounds.

6. ECG were performed in patients, to assess embolus supportive predisposition, if any

7. Physical activity status of the victims was enquired. Persons engaging in movable work over half the day (exclusive of rest and sitting); or engaged in some deliberate exercise daily, were categorized as physically active. Others with less than half day engagement in movable working were considered sedentary (vanderSande et al, 2001).

Ischemic or hemorrhagic pathology of stroke was elucidated with help of CT scan in most cases.

Statistics: Chi square test were used to compare
incidence and Students ‘t’ test in comparison of value data.

2.1. Observations

A total of 66 stroke patients, including 45 males and 21 females were covered by the study. Most of the patients were brought to the hospital within 24 hours of first symptoms. The distribution of stroke types in the two sexes under three age group categories was as under:

Table 1. Incidence of the stroke types

<table>
<thead>
<tr>
<th>Age Group</th>
<th>MALE(n=45)</th>
<th>FEMALE(n=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ischaemic</td>
<td>Haemorrhagic</td>
</tr>
<tr>
<td>37-44 yrs</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>45-59</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>60-76</td>
<td>29</td>
<td>8</td>
</tr>
</tbody>
</table>

Over all, there was gross predominance of ischaemic stroke in either sex and most strokes occurred in 60 years plus category. Younger age groups comprised less than fifth of all incidences of stroke, and in them, an even incidence of ischaemic and haemorrhagic strokes is apparent.

2.2. Traditional Vascular Risk Factors

Systemic hypertension was found in 55 (83.3 %), patients of stroke. Next in prevalence was physical inactivity in 47 (71.2 %) cases; obesity in 32 (48.4 %), and hypercholesterolaemia in 28 (42.4 %) cases. Prevalence of type 2 diabetes was in 18 (27.2 %) cases. Significantly greater percentage among females had obesity and hypercholesterolaemia. Smoking and alcohol consumption was exclusively found in males. Details are shown in table, under:

Table 2. Percentage frequency of risk factors of stroke in studied cases

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>N &amp; %age in MALES (45)</th>
<th>N &amp; %age in FEMALES (21)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall %age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>36(80%)</td>
<td>19(90%)</td>
<td>55(83.3%)</td>
</tr>
<tr>
<td>Physical Inactivity</td>
<td>31(68.8)</td>
<td>16(76%)</td>
<td>47(71.2%)</td>
</tr>
<tr>
<td>Obesity</td>
<td>14(31.1%)</td>
<td>18(85.7%) *</td>
<td>32(48.4%)</td>
</tr>
<tr>
<td>Hypercholesterolaemia</td>
<td>14(31.1%)</td>
<td>14(66.6%) *</td>
<td>28(42.4%)</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>14(31.1%)</td>
<td>4(19%)</td>
<td>18(27.2%)</td>
</tr>
<tr>
<td>Alcohol Consuming</td>
<td>13(28.8%)</td>
<td>0</td>
<td>13(19.6%)</td>
</tr>
<tr>
<td>Cigarette Smoking</td>
<td>11(24.4%)</td>
<td>0</td>
<td>11(16.6%)</td>
</tr>
</tbody>
</table>

Asterisk ‘*’ marks significant difference in compared incidence in two sexes. ECG evidence of left ventricular hypertrophy was found in only 28 cases(42.4%),16 males(35.5%) and 12 (57.1%).females.

3. Outcome of Hospitalized Stroke Patients

Median duration of hospitalization was 6 days (range 1-42 days, interquartile range 4-9 days). In all 15 (22.7%) of the 66 cases died.11 of these were of haemorrhagic stroke (mortality 52.3%) and rest 4 ischaemic stroke (mortality 8.8%). Median of the hospitalization mortality day was 5th (range 1-21, interquartile range 2-8 days) 7 (44.7%) of the mortality cases had developed aspiration pneumonia.

The dying patients at time of admission had significantly higher heart rate, diastolic blood pressure and blood sugar levels than the survivors. Surprizingly, HDL cholesterol levels of the dying patients were also higher compared to the survivors. Worse renal function indicators, urea and creatinine significantly associated bad outcome. Significantly high WBC counts also characterized the profile of the mortality cases.
**Table 3. Clinical and laboratory indices in cases as per outcome**

<table>
<thead>
<tr>
<th>Indices</th>
<th>MEAN+SD in mortality</th>
<th>MEAN+SD in discharges</th>
<th>p value Below</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Pressure</td>
<td>N=15</td>
<td>N=51</td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>179.9±52.6</td>
<td>172.8±41</td>
<td></td>
</tr>
<tr>
<td>Diastolic</td>
<td>107±27.6</td>
<td>101.2±22.3</td>
<td>0.05</td>
</tr>
<tr>
<td>Heart Rate</td>
<td>89.4±16.2</td>
<td>84.2±14.1</td>
<td>0.05</td>
</tr>
<tr>
<td>Blood Glucose m mol/L</td>
<td>10.6±4.3</td>
<td>9±5.3</td>
<td>0.05</td>
</tr>
<tr>
<td>Total Cholesterol m mol/L</td>
<td>5.4±2.02</td>
<td>5.1±1.88</td>
<td></td>
</tr>
<tr>
<td>HDL Choles. m mol/L</td>
<td>1.6±1</td>
<td>1.3±1</td>
<td>0.01</td>
</tr>
<tr>
<td>LDL Chole. m mol/L</td>
<td>4±2</td>
<td>3.4±1.6</td>
<td></td>
</tr>
<tr>
<td>Triglyceride m mol/L</td>
<td>1.5±0.95</td>
<td>1.4±0.82</td>
<td></td>
</tr>
<tr>
<td>Creatinine micro mol/L</td>
<td>176.2±252.2</td>
<td>109±142.8</td>
<td>0.05</td>
</tr>
<tr>
<td>Urea m mol/L</td>
<td>11.2±16.2</td>
<td>7.4±6.6</td>
<td>0.01</td>
</tr>
<tr>
<td>Hemoglobin g/dl</td>
<td>13.1±3.02</td>
<td>13.6±2.88</td>
<td></td>
</tr>
<tr>
<td>WBC Count x10 9</td>
<td>12.3±6.7</td>
<td>8.4±5.2</td>
<td>0.01</td>
</tr>
</tbody>
</table>

4. Discussion

Observed higher incidence of ischaemic stroke is in agreement with general pattern of some 80% strokes being thromboembolic in origin (Kidd, 2009). Age related increase in stroke incidence is also well known (Prasad and Singhal, 2010). In the younger patients higher incidence of haemorrhagic stroke is due to primacy of hypertensive etiology, precipitating habits and inadequate adaptation of blood vessels to hypertension with hypertrophy (Gunarathne et al, 2008).

Modifiable risk factors examined in this study are in agreement to earlier population based studies (Bhattacharya et al, 2005; Dalal et al, 2008). A study in Nepal found hypertension the commonest followed by smoking and alcohol consumption as stroke risk factors. Only small percentage of cases had diabetes or hypercholesterolaemia (Maskey et al, 2011). Observations of this study uphold hypertension as top risk factor. Observed incidences of left ventricular hypertrophy appear consequent to this and may increase thromboembolic risk. Differences in lifestyle, particularly physical activity (Golbidi and Laher, 2012), among hilly Nepali peasants and the urban central Indian lot may be expected to change risk factor hierarchy.

Established risk factors of cardiovascular disease eg. Hypertension, Smoking, drinking, physical inactivity, obesity etc contribute to excessive generation of reactive oxygen species (Halliwell and Gutteridge, 1989). Increased oxidative stress causes oxidation of LDL cholesterol promoting process of atherosclerotic plaque laying (Boullier et al, 2001). Patients with ischaemic heart disease, especially bearing hypertension, exhibit significant elevation of markers of oxidative stress (Risal et al, 2006). Decline in total plasma antioxidant activity is also demonstrated (Benzie and Strain, 1996). Smoking is severe oxidant insult compromising natural anti oxidant defence (Bruno et al, 2005). Observations in patients of present study strongly indite risk factors of oxidative stress.

Comparison of clinical and laboratory indices in the stroke cases with fatal outcome or recovery with live discharge, pointed to grave significance of heightened sympathetic activation at time of admission. Increased heart rate, blood sugar, diastolic blood pressure in dying patients apparently suggests this. Sympathetic cardiovascular activity is intricately linked with rennin angiotensin system. Activated angiotensin receptor mediates NADPH oxidase activatyon evolving severe oxidant stress with obvious pathogenic implication (Lopez- _Sendon et al, 2004; Molavi and Mehta, 2004). Besides menefestation of sympathoactivation, elevated glucose may have antedated stroke event and advance glycation end products which induce endoplasmic reticulum stress may be crucially compromising tissue vitality (Uchiki et al, 2012). It is difficult to explain the higher HDL cholesterol associating worse prognosis in this case series, as it
conflicts propositions drawn from large investigation (Gunarathe wt.al, 2008).

The ischaemia-reperfusion injury in stroke is essentially oxidant stress mediated phenomenon (Traystamn et al, 1991). A higher leukocyte count in subsequently fatal cases indicates heightened inflammatory state, possibly pre-existing stroke event which might have deteriorated further. Indeed, an elevated C reactive protein (CRP) profile, marking inflammatory state is seen to double incidence of ischaemic stroke (Sanchez-Moreno et al, 2004). CRP sets in motion multiple mechanisms of detriment in microcirculation, including up regulation of expression of angiotensin1 receptor (Colak et al, 2012). The preponderance of cardiovascular risk factors in present urban central Indian case series of stroke strongly supports causal role of free radical stress and inflammation, in populations in developing countries (Feigin, 2005).

Conventional cardiovascular and lipid lowering therapies with agents exhibiting pleotropic benefits against free radical stress and inflammation, eg angiotensin receptor blockers, newer beta blockers, statins etc need renewed consideration for strategic preventive management for stroke (Ceriello, 2003). Redemption from smoking, drinking, physical inactivity need to be strongly persued. Nutritional approaches designed for abeting free radical stress are being worked upon (Butterfield et al, 2002). Therapy of stroke also has rational scope for antioxidant intervention (Jureau, 2007). The wise pharmacokinetic/dynamic choice of antioxidant would be critical of course. Gingko biloba extract has shown promise in this regard (Saleem et al, 2008), that needs to be defined for prevention and management of stroke.

5. Acknowledgement

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References


