INTRODUCTION

Stroke is defined as the clinical syndrome of rapid onset of cerebral deficit (usually focal) lasting more than 24 hours or leading to death, with no apparent cause other than a vascular one. Stroke remains one of the leading causes of mortality and morbidity worldwide. Post-stroke disability and handicap have a significant physical and economic impact. The mortality of stroke is over 5.5 million per annum and two-thirds of these deaths occur in the developing world. Several risk factors have been implicated in influencing the extent of cerebral damage in acute stroke, such as high or low systolic blood pressure, elevated blood glucose and high temperature. The mortality was lower and outcome better in patients with mild hypothermia and both were worse in hyperthermic acute stroke patients.

Fever occurs in 15 - 40% of acute ischemic stroke patients. Pre-clinical studies have provided ample evidence for the harmful effects of elevated temperature on ischemic brain tissue. An increase in brain temperature, before and after the ischemic insult, has been shown to increase the total infarct volume. Temperature elevation may have an all-or-none response with a defined threshold, beyond which increased temperature aggravates ischemic injury. Hyperthermia leads to physiological and structural changes, including alteration of enzyme activity and damage to cytoskeletal proteins. Release of neurotoxic excitatory neurotransmitters (glutamate and glycine) and production of free radicals have also been proposed as mechanisms through which hyperthermia leads to tissue injury.

Hyperthermia (temperature > 37.5°C) was recorded in 15.9%, 11.0%, 17.2%, 19.1%, 17.9%, and 9.3% of the study patients at baseline, 8th hour, 24th hour, 48th hour, 72nd hour, and 7th day, respectively. Relationship between the intensity of hyperthermia and stroke outcome or infarct volume was stronger, when the fever developed earlier, and body temperature within the first 24 hours is the key determinant associated with greater cerebral damage; and when hyperthermia appears later, it is not an independent factor of poor outcome. In another study, hyperthermia was found in 18.3% patients on day one and in 25% patients on day two.

ORIGINAL ARTICLE

Frequency of Hyperthermia in Acute Ischemic Stroke Patients Visiting a Tertiary Care Hospital

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ABSTRACT

Objective: To determine the frequency of hyperthermia in acute ischemic stroke patients visiting a tertiary care hospital in a developing country.

Study Design: Cross-sectional, observational study.

Place and Duration of Study: Medical Wards of Civil Hospital, Karachi, from January to June 2013.

Methodology: Patients aged ≥ 18 years of either gender with acute ischemic stroke presenting within 24 hours of onset of symptoms were included. Written informed consent was obtained from all participants as well as approval of ethical review committee of the institute. Axillary temperature by mercury thermometer was monitored at the time of admission and after every 6 hours for 3 days. The data was analyzed using SPSS version 17.0 (SPSS Inc., IL, Chicago, USA).

Results: A total of 106 patients of ischemic stroke were included. The mean age of enrolled participants was 60.1 ±9.5 years. Among these, 61 (57.5%) were males and 45 (42.5%) females. Among all patients, 51.9% presented with loss of consciousness, 30.2% with slurred speech, 77.4% with limb weakness, and 9.4% with decrease vision. A total of 17 (16%) patients with ischemic stroke developed hyperthermia. When the prevalence of hyperthermia was stratified according to age, among patients of < 60 years of age, 26% developed hyperthermia compared to 7.1% in patients of ≥ 60 years of age (p=0.008). On gender stratification, among male patients, 14.8% developed hyperthermia compared to 17.8% in female patients (p=0.43).

Conclusion: It is concluded from this study that the frequency of hyperthermia in ischemic stroke was 16% and it should be looked for as it has significant impact on the outcome. The hyperthermia was significantly more common in younger adults as compared to older adults. However, gender had no influence on the prevalence rate of hyperthermia.

The objective of this study was to determine the prevalence and the magnitude of hyperthermia after acute ischemic stroke in our set-up. There are no data available in literature on this subject from Pakistan; this prompted us to collect data representing our population so as to give a better understanding on the subject. We believe that the results from this study will help in better planning by healthcare professionals in emphasizing means to treat hyperthermia, which may decrease the morbidity and mortality of acute ischemic stroke patients.

METHODOLOGY

This case series was collected from different medical wards of Civil Hospital, Karachi. All patients aged ≥ 18 years of either gender with acute ischemic stroke presenting within 24 hours of onset of symptoms diagnosed as defined below, and admitted in different medical wards of Civil Hospital, Karachi, were included. Patients with subarachnoid hemorrhage, intra-cerebral bleed, cerebellar bleed, tumor, trauma, central nervous system infection, systemic diseases like chronic renal failure, cardiac failure, chronic liver disease, sepsis, recent history of any brain surgery, and fever prior to onset of acute ischemic stroke, were excluded.

Acute ischemic stroke was defined as sudden onset of focal neurological deficit presenting within 24 hours, with at least one of these symptoms: sudden onset of weakness or numbness of body (usually one-sided), difficulty in speaking or understanding speech, sudden decrease in vision or in the level of consciousness, and computerized tomography (CT) scan brain showing hypodense area (which will appear as black) or no abnormality. Hyperthermia was labelled, if axillary temperature taken through mercury thermometer was > 37.5°C on admission or anytime every 6 hourly for 72 hours. The study sample was selected through non-probability, consecutive and purposive sampling method.

The study was conducted after taking approval from ethical review committee of the institute. All patients, admitted in medical units, Civil Hospital, Karachi with acute ischemic stroke, fulfilling the inclusion criteria, were included in the study. The purpose, risk, and benefit of the study were explained to the caretakers of the patients. Axillary temperature by mercury thermometer was monitored at the time of admission and after every 6 hours for 3 days. Data was recorded on a proforma for each patient by the researcher.

Sample size was calculated using WHO sample size calculator. Previous studies show the prevalence of hyperthermia in ischemic stroke patients as 16%. This is coupled with confidence level of 95%, and absolute precision of 7%. The sample required to meet the objective comes out to be n=106 patients of ischemic stroke. SPSS version 17.0 (SPSS Inc., IL, Chicago, USA) for windows was used for data analysis. Frequencies and percentages were calculated for gender, symptom, and hyperthermia. Mean ± Standard Deviation (SD) was calculated for age of the patients. Effect modifiers were controlled through stratification of age and gender. Chi-square test was applied after stratification to assess the statistical difference in the prevalence rates and the level of significance was taken as ≤ 0.05.

RESULTS

A total of 106 patients of ischemic stroke were enrolled in this study during the above mentioned study period. The mean age of enrolled participants was 60.1 ±9.5 years. Of 106 enrolled participants, 61 (57.5%) were males and 45 (42.5%) were females with male to female ratio of 1.3:1. Of 106 enrolled participants, 51.9% presented with loss of consciousness, 30.2% with slurred speech, 77.4% with limb weakness and 9.4% presented with decrease vision. Of 106 patients, 17 (16%) patients with ischemic stroke developed hyperthermia (Table I).

When the prevalence of hyperthermia was stratified according to age and gender of the enrolled participants, the results obtained are shown in Table II. Among patients of < 60 years of age, 26% developed hyperthermia compared to 7.1% in patients of ≥ 60 years of age and this was statistically significant (p=0.008). Among male and female patients, 23.5% and 24.2% developed hyperthermia respectively (p=0.78). The prevalence rate of hyperthermia in patients aged ≤ 60 years of ischemic stroke was 26%, while it was 7.1% in patients aged ≥ 60 years of age, which is statistically significant (p=0.008). The sex ratio of patients with hyperthermia was 1.3:1. The prevalence rates and the level of significance was taken as ≤ 0.05.

In Table II, it can be seen that 13 (26%) patients of < 60 years presented with hyperthermia, whereas 4 (7.1%) patients aged ≥ 60 years developed hyperthermia. Sex ratio of hyperthermia was 1.3:1. Among female patients, 24.2% developed hyperthermia, while 23.5% of male patients developed hyperthermia, which is statistically significant (p=0.78).
patients, 14.8% developed hyperthermia compared to 17.8% in female patients and this was statistically not significant (p=0.43).

**DISCUSSION**

Hyperthermia following ischemic stroke is a common but undesirable event and its pathophysiology and clinical importance are not fully recognized. Hyperthermia in ischemic stroke may result from the brain infarct itself. However, the progression of biochemical and inflammatory mechanisms, associated with cerebral ischemia, is also relevant. Consequently, the presence of hyperthermia accentuates ischemic mechanisms within the penumbra, an area of reversibly impaired neuronal function surrounding the infarct, contributing to conversion of the penumbra into an irreversible lesion. Therefore, hyperthermia following ischemic stroke seems to be an event that is both induced by and in turn, it gives rise to brain infarct progression. Both clinical and experimental studies show hyperthermia-dependent exacerbation of ischemic brain damage and stroke outcome. The detrimental effects of hyperthermia in human stroke are associated, in particular, with increased body temperature within the first 24 hours of the disease. The common occurrence of superimposed infections in stroke patients may be an important peripheral cause of poststroke hyperthermia. Pharmacological antipyretic medication is recommended in every case of hyperthermia following ischemic stroke, regardless of its cause, as any hyperthermia may worsen stroke outcome. There is currently no evidence from randomized trials to support the routine use of chemical or physical cooling therapy in acute ischemic stroke. Further understanding of the mechanisms, inducing hyperthermia and its contribution to an increase in the degree of injury during stroke, may lead to new and important therapeutic approaches.

To our knowledge, this is the first study from Pakistan on this subject. As such, its role is mainly that of an exploratory study and its findings will serve as baseline data for further research on this topic.

In this study, the mean age of enrolled participants was 60.1 ±9.5 years. Among these, 61 (57.5%) were male and 45 (42.5%) female with male to female ratio of 1:3.1. Similarly, Saini et al. reported male dominance with male to female ratio of 1.3:1.

In this study of 106 patients of ischemic stroke, 17 (16%) developed hyperthermia. Saini et al. reported that 15.9% of patients in their study had developed hyperthermia. These results are consistent with our study.

Clinical studies have reported hyperthermia in 15% to 61% of patients after ischemic stroke; only one study reported a low prevalence (5.3%) of hyperthermia. This wide variation may be partly dependent on the variability of time period after stroke when the temperature was checked and differences in definitions of hyperthermia. In this study, young adult patients of < 60 years of age developed hyperthermia significantly, more commonly (26%) compared to 7.1% in patients of ≥ 60 years of age (p=0.008). On the other hand, there was no significant difference in the prevalence of hyperthermia based on gender (p=0.43).

There are certain limitations in the study. This was a cross-sectional study carried out to determine the magnitude of the problem in our patient population. There is no follow-up information about the patients. The patients were recruited from different medical units of Civil Hospital, Karachi, and were observed for a period of 3 days from the onset of the stroke. We also did not analyze the severity of hyperthermia in the enrolled patients. However, the results from this study will serve as the baseline information for further studies on this topic and will help in planning better care of such patients.

**CONCLUSION**

The frequency of hyperthermia in acute ischemic stroke was 16%. The prevalence of hyperthermia was significantly more common in younger adults than in older adults. There was no significant difference in the prevalence of hyperthermia according to gender. Further studies are needed to determine the impact of hyperthermia on the outcome of patients.

**REFERENCES**

Frequency of hyperthermia in acute ischemic stroke patients visiting a tertiary care hospital


