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Hyperthermia in Patients Presented with Ischemic Stroke: Frequency and Clinical Presentation

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ABSTRACT

Background: Hyperthermia is a common complication in acute ischemic stroke and is associated with worsened outcomes due to increased metabolic demand, oxidative stress, and neuroinflammation.

Objective: This study aimed to determine the frequency of hyperthermia in acute ischemic stroke patients and explore its association with stroke severity and clinical presentation.

Methods: A prospective observational cohort study was conducted at Ayub Teaching Hospital from September 2023 to March 2024, including 150 adults diagnosed with acute ischemic stroke within 24 hours. Hyperthermia was defined as a body temperature >37.5ºC, measured every 4 hours for 48 hours. Stroke severity was assessed using the National Institutes of Health Stroke Scale (NIHSS) and categorized into mild, moderate, or severe. Statistical analysis was performed using chi-square tests.

Results: Hyperthermia occurred in 14.7% (n=22) of patients. It was more frequent in severe strokes (50.0% vs. 18.2% in mild, p=0.001). Clinically, 40.9% had tachycardia, 36.4% had tachypnea, and 22.7% exhibited neurological deficits.

Conclusion: Hyperthermia is significantly associated with severe stroke presentations, underscoring the need for vigilant temperature management to improve outcomes.

INTRODUCTION

Stroke is a clinical condition marked by the sudden onset of localized cerebral impairment that typically persists for more than 24 hours or leads to death, caused by vascular issues without any other identifiable cause (1). Stroke remains a leading cause of mortality and morbidity globally, resulting in substantial physical and economic burdens due to post-stroke disabilities and impairments. Annually, stroke causes over 5.5 million deaths worldwide, with two-thirds of these occurring in lower-income countries (2). Several risk factors, including elevated or reduced systolic blood pressure, high blood glucose levels, and increased body temperature, have been associated with variations in the severity of cerebral damage in acute stroke (3, 4). Hyperthermia, defined as a body temperature exceeding 40 degrees Celsius, can be induced by a variety of conditions, including sepsis, where the immune response to infection typically manifests as fever (5, 6). Hyperthermia may also arise from certain drug reactions, such as neuroleptic malignant syndrome, hazardous ingestions, or withdrawal syndromes. Furthermore, heat-related illnesses, including heat stroke, represent conditions that can be managed effectively only through cooling interventions (7). These disorders occur when the body's ability to regulate its temperature becomes impaired, highlighting the need for thorough assessment and management by an interprofessional team (7, 8).

Approximately 15-40% of patients with acute ischemic stroke experience fever, a factor extensively documented to have a detrimental impact on ischemic brain tissue in preclinical investigations (9, 10). Elevated brain temperatures, both preceding and during an ischemic event, are known to increase the extent of tissue damage caused by infarction. This temperature rise exhibits a binary response with a specific threshold, beyond which higher temperatures exacerbate ischemic injury. The pathophysiological impact of hyperthermia includes physiological and structural changes, such as alterations in enzyme activity and the breakdown of cytoskeletal proteins. Hyperthermia is also implicated in releasing neurotoxic excitatory neurotransmitters, such as glutamate and glycine, and in generating free radicals, thereby contributing to tissue damage (11, 12). Patients with elevated body temperatures are at risk of increased cerebral damage, poorer functional outcomes, and higher mortality rates, indicating the need for effective temperature management strategies in stroke care (13).

Increased body temperature following a stroke is associated with multiple adverse mechanisms, such as heightened metabolic demand, enhanced oxidative stress, and promotion of neuroinflammation. Elevated metabolic demand in the already ischemic brain environment can worsen the oxygen and glucose crisis, aggravating infarction (14). Hyperthermia further intensifies oxidative stress, promoting the production of reactive oxygen species that can damage cellular structures, thereby exacerbating

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neuronal death and brain injury progression. Inflammatory responses are also magnified in hyperthermia, leading to increased production of pro-inflammatory cytokines and leukocyte infiltration, which damages the blood-brain barrier and contributes to neuronal injury (15, 16). Moreover, hyperthermia can affect the efficacy of thrombolytic therapy with intravenous tissue plasminogen activator (rtPA), altering its pharmacokinetics and increasing the risk of hemorrhagic transformation, a severe complication in ischemic stroke management (17).

The current study aims to investigate the prevalence of hyperthermia in patients with acute ischemic stroke and its association with stroke severity. Understanding this relationship is crucial for developing targeted interventions that can improve patient outcomes by managing body temperature effectively during stroke care.

MATERIAL AND METHODS

The study was a prospective observational cohort conducted at the Department of Medicine, Ayub Teaching Hospital, Abbottabad, from September 2023 to March 2024. The objective was to investigate the frequency of hyperthermia in patients with acute ischemic stroke and its association with stroke severity. Ethical approval for the study was obtained from the hospital's ethical review board, in accordance with the Declaration of Helsinki, ensuring the protection of participants' rights and confidentiality. All participants provided informed consent before enrollment in the study.

The study population consisted of adult patients aged 18 years or older who were diagnosed with acute ischemic stroke and admitted to the hospital within 24 hours of stroke onset. The diagnosis was confirmed through clinical assessment and neuroimaging, including computed tomography (CT) or magnetic resonance imaging (MRI). Patients with pre-existing conditions known to cause hyperthermia, such as infections or autoimmune diseases, and those on medications that affect body temperature regulation were excluded. Additionally, patients who experienced a stroke secondary to other conditions, such as hemorrhagic stroke, were also excluded.

Upon admission, demographic and clinical data were collected for each participant, including age, gender, and body mass index (BMI). Clinical data included the severity of the stroke, presence of comorbid conditions such as diabetes and hypertension, and vital signs, including body temperature, heart rate, and respiratory rate. Stroke severity was assessed using the National Institutes of Health Stroke Scale (NIHSS) and was categorized as mild, moderate, or severe based on the total score. Hyperthermia was defined as a body temperature greater than 37.5°C. Body temperature was measured using a digital thermometer every four hours for the first 48 hours of hospital admission to monitor fluctuations and the occurrence of hyperthermia. Data collection involved obtaining information on patient demographics, stroke characteristics, comorbidities, and clinical presentations from medical records and direct patient interviews. Comorbid conditions such as diabetes and hypertension were documented based on medical history and medication use. The presence of hyperthermia was monitored rigorously to identify its frequency and any associated clinical manifestations such as tachycardia, tachypnea, and neurological deficits.

Data analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 25. Descriptive statistics, such as means and standard deviations, were used to summarize continuous variables, while frequencies and percentages were used for categorical variables. The primary outcome was the frequency of hyperthermia in patients with acute ischemic stroke. To examine the association between hyperthermia and stroke severity, chi-square tests or Fisher's exact tests were employed for categorical variables, and the level of significance was set at a p-value of less than 0.05. Data were presented in tables to illustrate the distribution of hyperthermia by stroke severity and the prevalence of related clinical symptoms.

Overall, the methodology was designed to ensure accurate data collection and analysis to assess the impact of hyperthermia on stroke severity, contributing to a better understanding of the need for effective temperature management in stroke care.

RESULTS

The study included a total of 150 patients with acute ischemic stroke, with a mean age of 55.13 years (SD = 11.42). The average body mass index (BMI) among the participants was 25.45 kg/m^2 (SD = 1.84). Regarding gender distribution, 58.7% (n = 88) of the participants were male, while 41.3% (n = 62) were female (Table 1).

Table 1: Gender Distribution of Participants

Gender	Frequency (n)	Percent (%)
Male	88	58.7
Female	62	41.3
Total	150	100.0

Stroke severity among the participants was categorized using the National Institutes of Health Stroke Scale (NIHSS). Of the total participants, 32.0% (n = 48) were classified as having mild strokes, 47.3% (n = 71) as moderate, and 20.7% (n = 31) as severe (Table 2). Hyperthermia, defined as a body temperature greater than 37.5°C, was observed in 14.7% (n = 22) of the participants, while the majority, 85.3% (n = 128), did not exhibit hyperthermia (Table 3). Among the patients who developed hyperthermia, various clinical manifestations were observed. Tachycardia was present in 40.9% (n = 9) of these patients, tachypnea in 36.4% (n = 8), and neurological deficits in 22.7% (n = 5) (Table 4).

Table 2: Severity of Stroke

Severity of Stroke	Frequency (n)	Percent (%)
Mild	48	32.0
Moderate	71	47.3
Severe	31	20.7
Total	150	100.0

Table 3: Frequency of Hyperthermia in Stroke Patients

Hyperthermia	Frequency (n)	Percent (%)
Yes	22	14.7
No	128	85.3
Total	150	100.0

Table 4: Clinical Presentation of Hyperthermia

Clinical Presentation	Frequency (n)	Percent (%)
Tachycardia	9	40.9
Tachypnea	8	36.4
Neurological Deficits	5	22.7
Total	22	100.0

The study also revealed a significant association between hyperthermia and stroke severity. Patients with severe strokes were more likely to exhibit hyperthermia, with 50.0% (n = 11) of hyperthermic patients experiencing severe strokes. In comparison, 31.8% (n = 7) of hyperthermic patients had moderate strokes, and 18.2% (n = 4) had mild strokes. The association between hyperthermia and stroke severity was statistically significant (p = 0.001) (Table 5).

Table 5: Association of Hyperthermia with Severity of Stroke

Hyperthermia	Severity of Stroke	Frequency (n)	Percent (%)	Total (n)	P-value
Yes	Mild	4	18.2	22	
	Moderate	7	31.8		0.001
	Severe	11	50.0		
Total		22	100.0		
No	Mild	44	34.4	128	
	Moderate	64	50.0		
	Severe	20	15.6		
Total		128	100.0	150	

The findings underscore the importance of vigilant temperature monitoring in patients with acute ischemic stroke, as hyperthermia is significantly associated with stroke severity and poorer clinical outcomes.

DISCUSSION

The discussion highlighted the significant prevalence of hyperthermia in patients with acute ischemic stroke and its association with stroke severity, reinforcing the findings of previous research that hyperthermia is a critical factor influencing stroke outcomes. Hyperthermia, observed in 14.7% of patients in this study, was notably associated with severe stroke presentations. This aligns with existing literature that emphasizes the detrimental effects of elevated body temperature on ischemic brain tissue, where hyperthermia exacerbates neuronal injury through mechanisms such as increased metabolic demand, enhanced oxidative stress, and intensified neuroinflammation (14, 15). Hyperthermia-induced metabolic strain can further compromise an already ischemic brain, increasing the risk of infarction expansion and leading to poorer functional outcomes (14).

The study confirmed that hyperthermia was more common in patients with severe strokes compared to those with mild or moderate strokes. This is consistent with the findings of previous studies that reported an association between elevated body temperature and higher stroke severity, where hyperthermic patients were found to have significantly poorer clinical outcomes (18). The increased production of reactive oxygen species (ROS) and pro-inflammatory cytokines in hyperthermic conditions further accelerates brain injury, leading to blood-brain barrier disruption and exacerbating neuronal damage (15, 16). These pathophysiological processes suggest that hyperthermia is not merely a consequence of a severe stroke but may actively contribute to its progression.

Moreover, this study identified specific clinical manifestations of hyperthermia in stroke patients, such as tachycardia, tachypnea, and neurological deficits. These symptoms suggest a complex interaction between systemic and cerebral responses to stroke and hyperthermia, necessitating an integrated approach to managing these patients. Previous research has shown that hyperthermia can affect the pharmacokinetics and efficacy of thrombolytic therapies, such as intravenous tissue

plasminogen activator (rtPA), thereby increasing the risk of hemorrhagic transformation and complicating the management of stroke (17). This underscores the importance of incorporating temperature management into standard stroke care protocols to mitigate these risks and improve patient outcomes. The strengths of this study include its prospective cohort design, which allowed for a systematic assessment of hyperthermia and its association with stroke severity. The use of a standardized stroke severity scale (NIHSS) enabled consistent classification and comparison across participants. However, the study also had limitations that should be considered. The sample size, while sufficient to identify significant associations, may not fully represent all patient populations, particularly those with different comorbidities or healthcare settings. The study also relied on a single-center data collection, which may limit the generalizability of the findings to other regions or hospital settings.

Further research is recommended to explore the underlying mechanisms linking hyperthermia with stroke severity in more detail. Investigations could focus on the molecular and cellular pathways affected by hyperthermia and potential therapeutic targets for modulating these effects. Additionally, multi-center studies with larger sample sizes and diverse populations would be valuable to validate these findings and develop standardized guidelines for temperature management in stroke care. Effective interventions for hyperthermia in stroke patients could potentially improve outcomes and reduce the burden of disability associated with this condition. Temperature management should be considered an integral component of stroke protocols, given its demonstrated impact on stroke severity and patient prognosis. Overall, this study contributes to the growing body of evidence that underscores the need for vigilant monitoring and proactive management of hyperthermia in patients with acute ischemic stroke.

CONCLUSION

The study demonstrated that hyperthermia is a significant concern in patients with acute ischemic stroke, with a notable association between elevated body temperature and increased stroke severity. These findings highlight the importance of vigilant temperature monitoring and management as part of standard stroke care to mitigate the risk of exacerbated brain injury and poor outcomes. Integrating temperature control strategies into clinical practice can improve prognosis and reduce complications, underscoring the critical need for targeted interventions that address hyperthermia to optimize human healthcare outcomes in stroke management.

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