International Journal of General Medicine Dovepress

Open Access Full Text Article ORIGINAL RESEARCH

Prevalence and Related Factors of Hypokalemia in Patients with Acute Ischemic Stroke

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Aim: This study aimed to investigate the prevalence and associated factors of hypokalemia in patients with acute ischemic stroke.

Methods: A cohort of 996 patients was assessed using a general data questionnaire, laboratory indicators, the NIH Stroke Scale (NIHSS), the Barthel Index (BI), the Frail scale, Nutritional Risk Screening (NRS-2002), and the Kubota drinking water test.

Results: Among the 996 patients, 205 (20.6%) were found to have hypokalemia. Logistic regression analysis identified several independent predictors of hypokalemia: age (OR 1.020, 95% CI 1.001–1.039, P=0.041), hypertension (OR 2.691, 95% CI 1.190–6.089, P=0.017), Frail score (OR 1.756, 95% CI 1.034–2.981, P=0.037), Kubota drinking water test grade 3 (OR 2.124, 95% CI 1.055–4.276, P=0.035), Kubota drinking water test grade 4 (OR 3.016, 95% CI 1.113–8.174, P=0.037), NIHSS score (OR 1.135, 95% CI 1.018–1.264, P=0.022), platelet count (OR 0.997, 95% CI 0.994–0.999, P=0.021), and urea nitrogen levels (OR 0.833, 95% CI 0.750–0.926, P=0.001).

Conclusion: The prevalence of hypokalemia is high in patients with acute ischemic stroke. Independent risk factors included age, hypertension, frailty, neurological function, swallowing function, platelet count and blood urea level.

Keywords: acute ischemic stroke, related factors, neurological function, function of deglutition, frail, laboratory indicators

Introduction

Stroke is a prevalent chronic non-communicable disease and ranks as the second leading cause of mortality globally.[1] Stroke has the characteristics of high prevalence, high recurrence rate, high disability rate, high mortality and high economic burden.[2] Data indicate that approximately 26 million individuals are diagnosed with stroke annually, with Acute Ischemic Stroke (AIS) accounting for 60%-80% of these cases.[3] AIS is a cerebrovascular event resulting from interrupted blood flow to the brain, caused by various etiologies.[4,5] This condition is characterized by hypoxic-ischemic necrosis of cerebral tissue,[6] leading to significant mortality and disability rates.[7] Additionally, patients may experience various complications, including cognitive impairment,[8] dysphagia,[9] and malnutrition.[10] Therefore, AIS needs extensive attention.

Potassium (K+) is a crucial electrolyte in the human body, essential for numerous physiological functions. Its primary roles encompass maintaining the potential difference between intracellular and extracellular compartments,[11] regulating muscle contraction,[12] modulating fluid[13] and acid-base balance,[14] facilitating nerve impulse conduction,[15] participating in energy metabolism[16] and enzymatic activities,[17] and regulating blood pressure.[18] Hypokalemia is a pathological condition defined by a peripheral blood potassium concentration below 3.5 mmol/L. Hypokalemia can be attributed to a range of etiological factors, broadly categorized into excessive potassium loss, aberrant potassium distribution, inadequate potassium intake, and miscellaneous causes. Excessive potassium loss is frequently associated with augmented renal excretion induced by specific pharmacological agents,[19] gastrointestinal disturbances such as vomiting and diarrhea,[20] and impaired renal reabsorption linked to particular nephropathies.[21] Abnormal potassium distribution may result from the administration of certain medications[22] or disturbances in

Received: 19 August 2024
Accepted: 25 November 2024
Published: 30 November 2024

acid-base homeostasis.[23] Inadequate potassium intake may result from prolonged dietary deficiencies or malabsorption disorders.[24] Additional contributing factors include hormonal influences[25] and genetic predispositions,[26] among others.

Hypokalemia is associated with an increased risk of atrial fibrillation, malignant arrhythmias, and mortality. Studies indicate that hypokalemia is a significant electrolyte disturbance commonly observed in stroke patients.[27] Potassium ions play a crucial role in maintaining the electrolyte balance of myocardial cells, and in hypokalemic patients, the risk of arrhythmias is heightened. Among stroke patients, these arrhythmias can worsen their condition and pose a serious threat to life.[28] Potassium deficiency may also lead to muscle weakness or paralysis. Stroke patients frequently experience hemiplegia or muscle weakness, and hypokalemia can exacerbate these impairments, complicating the rehabilitation process.[29] Additionally, potassium ions are essential for nerve conduction, so hypokalemia may aggravate central nervous system damage, impair nerve transmission, and further hinder cognitive and neurological recovery after a stroke. In severe cases, this can result in altered consciousness or even coma.[30] Given these risks, hypokalemia in stroke patients demands substantial clinical attention. However, research on factors related to hypokalemia in acute ischemic stroke remains limited. This study thus aims to investigate the prevalence and associated factors of hypokalemia in acute stroke patients. The findings are expected to aid in the early clinical identification of hypokalemia, support the development of targeted intervention strategies to improve patient outcomes, and suggest avenues for future research.

Materials and Methods

Study Design

A cross-sectional study was conducted to investigate the prevalence of hypokalemia in patients with acute ischemic stroke and to identify potential related factors. This study was conducted in accordance with the Declaration of Helsinki. Before participation, all subjects provided informed consent, and the study received approval from the Ethics Committee at the Affiliated Hospital of Jiangnan University.

Setting and Participants

The study utilized a convenience sampling method to select patients diagnosed with acute ischemic stroke who were hospitalized in the Department of Neurology at a Class III Grade A hospital in Wuxi between January 2021 and December 2022.

Participants met the following inclusion criteria: (1) diagnosis of acute ischemic stroke based on head CT or MRI findings and meeting established diagnostic criteria; (2) age 18 years or older; (3) within 7 days of stroke onset; (4) not eligible for thrombolysis or refusing thrombolysis; and (5) providing informed consent and volunteering for participation. Exclusion criteria included severe mental illness, cancer, severe chronic kidney disease, acute gastrointestinal disease, severe organ damage, hemodynamic instability, and diuretic use.

Sample Size

According to guidelines for sample size estimation in multivariate analysis, the sample size should be at least 10 to 15 times the number of independent variables.[31] Given that this study included 27 independent variables and accounting for a 10% attrition rate, a sample size of 300 to 450 cases was calculated. Ultimately, the final sample size for this study was 996 cases.

Measurements

The demographic data included variables such as gender, age, weight, height, body mass index (BMI), systolic and diastolic blood pressure, smoking and drinking history, and medical histories of heart disease, hypertension, diabetes, and antihypertensive medication usage. Laboratory tests measured white blood cell (WBC) count, red blood cell (RBC) count, hemoglobin (Hb) levels, platelet count, fasting plasma glucose (FPG) levels, total cholesterol (TC) levels, triglyceride (TG) levels, serum sodium (Na^+), serum potassium (K^+), blood urea nitrogen (BUN), and serum creatinine (sCre) levels. Other evaluations encompass neurological function assessment,[32] activities of daily living assessment,[33] frailty assessment,[34] nutritional risk assessment,[35] and function of deglutition assessment.[36]

Data Collection

General demographic data of the study subjects were obtained from the electronic medical record system. Serum potassium levels were measured within 24 hours of hospitalization by trained team members, using venous blood samples after a fasting period of at least 8 hours, in accordance with established clinical nursing protocols. Standard laboratory methods were employed to measure serum potassium levels in the hospital's laboratory department, with hypokalemia defined as serum potassium levels below 3.5 mmol/L. Investigators followed a standardized research protocol for one-on-one surveys, which included providing unified instructions, informing participants of the survey's purpose, explaining the methods and important considerations for completing the questionnaire, obtaining signed informed consent, and ensuring anonymity during the questionnaire process. The study implemented rigorous quality control measures, including on-the-spot checks, to ensure the integrity of the collected data. Out of the 1050 questionnaires distributed, 38 were refused, 16 were incomplete, and 996 were effectively collected, resulting in a recovery rate of 94.9%. See Figure 1 for details.

Statistical Analysis

The study employed descriptive statistics to present quantitative data. Data with a normal distribution were expressed as mean ± standard deviation, while skewed data were represented as median and interquartile range (M [P_{25}, P_{75}]). Patients were categorized into hypokalemia and non-hypokalemia groups. Comparisons of quantitative data between these groups were conducted using independent sample *t*-tests and χ^2 tests. Frequency and percentage were used for categorical data. Logistic regression analysis was performed to identify factors influencing hypokalemia in patients with acute ischemic stroke, with statistical significance set at $P<0.05$.

Results

A cohort of 996 patients diagnosed with acute ischemic stroke was included in the study, comprising 205 individuals (20.6%) with hypokalemia and 791 individuals (79.4%) without hypokalemia. The distribution of stroke severity among participants, assessed by the NIH Stroke Scale (NIHSS), was as follows: 67 patients (6.7%) had a score of 0–1, indicating normal or near-normal status; 498 patients (50.0%) had a mild stroke (NIHSS 1–4); 228 patients (22.9%) had a moderate

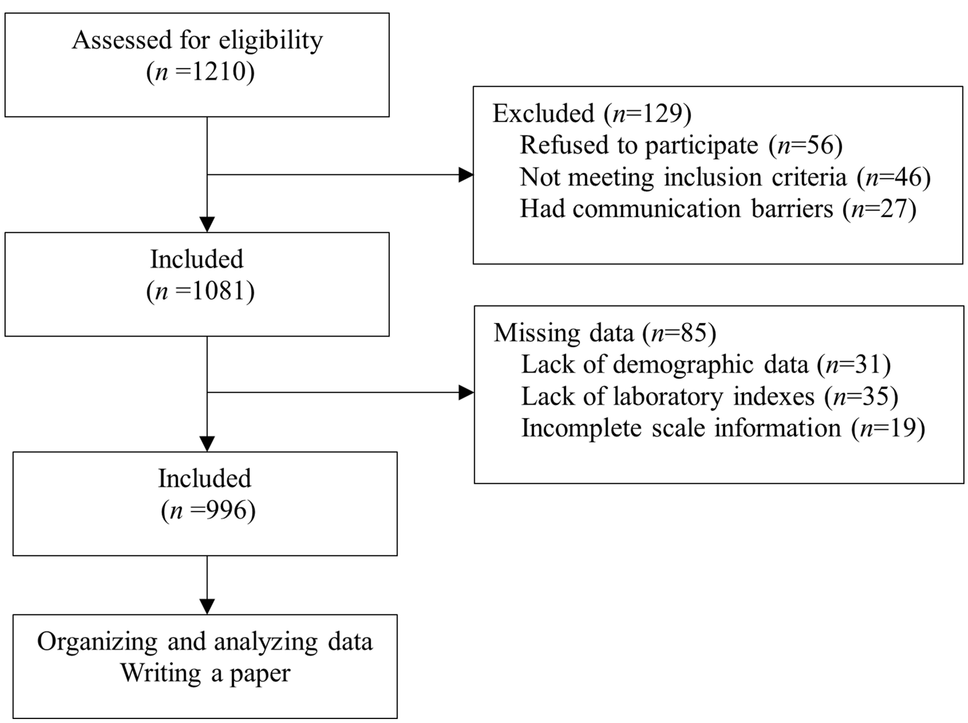

Figure 1 Enrollment and following flowcharts for the whole research project.

stroke (NIHSS 5–15); 132 patients (13.3%) had a moderate to severe stroke (NIHSS 15–20); and 71 patients (7.1%) had a severe stroke (NIHSS 21–42). A statistically significant difference (P < 0.05) was observed in the univariate analysis across various age groups, hypertension status, use of antihypertensive medication, self-care ability, Kubota drinking water test results, Frail score, NRS-2002 score, NIHSS score, platelet count, and urea nitrogen levels in patients with hypokalemia. Detailed findings are presented in Tables 1 and 2.

The occurrence of hypokalemia in patients with acute ischemic stroke was examined as the dependent variable in a logistic regression analysis. A statistically significant difference (P < 0.05) was observed across the independent

Table 1 Univariate Analysis of Categorical Information on Factors Influencing Hypokalemia in Patients with Acute Ischemic Stroke (n=996)

Variables	Low Potassium Group (n=205)	Non-Low Potassium Group (n=791)	χ^2	*P-value*
Gender(n,%)			2.361	0.124
Male	102(49.8)	441(55.8)		
Female	103(50.2)	350(44.2)		
Smoking(n,%)			0.015	0.903
No	203(99.0)	784(99.1)		
Yes	2(1.0)	7(0.9)		
Drinking(n,%)			0.048	0.827
No	204(99.5)	788(99.6)		
Yes	1(0.5)	3(0.4)		
Hypertension(n,%)			17.875	<0.001
No	35(17.1)	254(32.1)		
Yes	170(82.9)	537(67.9)		
Diabetes(n,%)			0.148	0.700
No	141(68.8)	555(70.2)		
Yes	64(31.2)	236(29.8)		
Heart disease(n,%)			1.176[b]	0.278
No	185(90.2)	732(92.5)		
Yes	20(9.8)	59(7.5)		
Taking blood pressure medication			12.932	<0.001
No	42(20.5)	265(33.5)		
Yes	163(79.5)	526(66.5)		
ADL			10.738	0.013
Full self-care	35(17.1)	212(26.8)		
Mild dysfunction	106(51.7)	397(50.2)		
Moderate dysfunction	32(15.6)	92(11.6)		
Severe dysfunction	32(15.6)	90(11.4)		
Kubota drinking test			30.200	<0.001
Level 1	103(50.2)	469(59.3)		
Level 2	65(31.7)	274(34.6)		
Level 3	22(10.7)	28(3.5)		
Level 4	11(5.4)	14(1.8)		
Level 5	4(2.0)	6(0.8)		
Frail score			17.933	<0.001
<3	72(35.1)	409(51.7)		
≥3	133(64.9)	382(48.3)		
NRS-2002 score			6.369	0.012
<3	77(37.6)	372(47.4)		
≥3	128(62.4)	416(52.6)		

Abbreviation: ADL, Activities of daily living.

Table 2 Hypokalemia in Patients with Acute Ischemic Stroke Affecting Factors of Logistic Regression Analysis (n=996)

Variables	Low Potassium Group (n=205)	Non-Low Potassium Group (n=791)	*t*	*P-value*
Age (years)	74.81±9.79	71.44±10.89	−4.289	<0.001
BMI (kg/m^2)	23.98±3.31	24.11±3.15	0.503	0.615
NIHSS score	4.03±2.84	3.19±1.97	−3.971	<0.001
Systolic blood pressure(mmHg)	146.70±21.80	144.30±20.40	−1.475	0.140
Diastolic blood pressure (mmHg)	80.23±13.12	78.32±12.23	−1.956	0.051
Leukocytes(10^9/L)	6.64±2.50	6.44±2.09	−1.057	0.291
Red blood cells(10^{12}/L)	4.18±0.54	4.23±0.53	1.072	0.284
Haemoglobin(g/L)	128.86±16.76	130.38±15.47	1.237	0.216
Platelets(10^9/L)	194.99±60.40	207.08±62.71	2.479	0.013
Fasting blood glucose(mmol/L)	6.14±2.31	5.93±2.33	−1.158	0.247
Total cholesterol(mmol/L)	3.83±1.02	4.19±4.82	1.053	0.293
Triglycerides(mmol/L)	1.49±1.17	1.49±0.95	0.012	0.991
Na$^+$(mmol/L)	139.57±5.09	139.65±2.83	0.207	0.836
Creatinine(umol/L)	74.39±26.32	77.29±26.75	1.387	0.166
Urea nitrogen(mmol/L)	4.91±1.70	5.36±2.10	2.836	0.005

Table 3 Hypokalemia in Patients with Acute Ischemic Stroke Affecting Factors of Logistic Regression Analysis (n = 996)

Variables	*B*	*SE*	*Wald* χ^2	*P-value*	*OR*(95% CI)
Constant	−2.468	0.861	8.213	0.004	
Age	0.019	0.010	4.190	0.041	1.020(1.001–1.039)
Hypertension					
Yes	0.990	0.417	5.649	0.017	2.691(1.190–6.089)
Frail score					
≥3	0.563	0.270	4.338	0.037	1.756(1.034–2.981)
Drinking water test					
Level 2	−0.047	0.187	0.062	0.803	0.954(0.662–1.377)
Level 3	0.753	0.357	4.456	0.035	2.124(1.055–4.276)
Level 4	1.104	0.509	4.707	0.030	3.016(1.113–8.174)
Level 5	0.649	0.822	0.623	0.430	1.914(0.382–9.586)
NIHSS score	0.126	0.055	11.476	0.022	1.135(1.018–1.264)
Platelets(10^9/L)	−0.003	0.001	5.340	0.021	0.997(0.994–0.999)
Urea nitrogen(mmol/L)	−0.182	0.054	11.4762	0.001	0.833(0.750–0.926)

variables. The results indicated that age, hypertension, Frail score, Kubota drinking water test, NIHSS score, platelet count, and urea nitrogen levels were independent related factors for hypokalemia in these patients, as shown in Table 3.

Discussion

To the best of our knowledge, there is a paucity of research on the factors associated with hypokalemia in patients with acute ischemic stroke. Hypokalemia has been linked to an increased risk of cardiac arrhythmias, including tachycardia, atrial fibrillation, and ventricular fibrillation, and in severe cases, it can result in cardiac arrest. Potassium is a crucial electrolyte for the conduction of neuromuscular impulses, and hypokalemia can manifest as muscle weakness, spasticity, and myalgia.[37] Severe hypokalemia can induce rhabdomyolysis and compromise respiratory muscle function, potentially leading to dyspnea or respiratory failure.[38] This study identifies age, hypertension, frailty, swallowing function, neurological status, platelet levels, and blood urea as factors influencing hypokalemia in patients with acute ischemic stroke. Recognizing these factors enables medical professionals to prioritize high-risk individuals in diagnosis and treatment, enhance the comprehensive care of stroke patients, anticipate the likelihood of hypokalemia, and implement timely intervention strategies.

Prior research has demonstrated a positive correlation between advanced age in patients with ischemic stroke and an increased likelihood of hypokalemia, a finding further substantiated by the current study.[39,40] The etiology of this phenomenon may be attributed to age-related declines in renal function and reduced glomerular filtration rate (GFR),[41] which impair the kidney's ability to regulate electrolytes effectively.[39] Consequently, older individuals are more susceptible to hypokalemia due to unstable potassium excretion. Additionally, the digestive and absorptive capabilities of older adults diminish over time, leading to inadequate dietary potassium intake and further increasing susceptibility to hypokalemia. Ischemic stroke represents a significant physiological stressor that activates both the sympathetic nervous system and the hypothalamic-pituitary-adrenal (HPA) axis.[42] Older adults exhibit a diminished capacity to regulate stress responses, potentially exacerbating electrolyte imbalances. Therefore, it is imperative to prioritize monitoring serum potassium levels in elderly patients and to enhance health education efforts targeted at this population. Encouraging the consumption of potassium-rich foods, such as potatoes, is recommended to help maintain water and electrolyte balance.

Current research indicates a potential correlation between hypokalemia, hypertension, and frailty in stroke patients. Diuretics, such as thiazides or loop diuretics, are commonly used to manage hypertension by enhancing sodium and water excretion, which increases urine output and potassium excretion, ultimately resulting in hypokalemia.[43] Additionally, patients with hypertension may experience activation of the renin-angiotensin-aldosterone system (RAAS), leading to heightened aldosterone levels. Aldosterone plays a crucial role in regulating sodium and water balance through potassium excretion. Consequently, RAAS activation can increase potassium excretion, elevating the risk of hypokalemia.[44,45] In line with the research conducted by Fujisawa et al, individuals with frailty are more susceptible to developing hypokalemia.[46] This frailty may be attributed to the malnutrition commonly observed in frail patients, leading to inadequate intake of essential electrolytes, such as potassium. Frailty can also impair intestinal function, resulting in inadequate absorption of dietary potassium and an increased risk of hypokalemia.[47] Furthermore, the presence of multiple complications in stroke patients may impact the pharmacokinetics and pharmacodynamics of medications, potentially leading to electrolyte imbalances.[48]

This study posits a potential association between hypokalemia and neurological and swallowing function in patients with ischemic stroke. The findings indicate that patients with a higher NIHSS score for ischemic stroke are more likely to experience hypokalemia, consistent with previous research by Hossain.[49] The onset of acute stroke may lead to dysfunction in the neuroendocrine system, resulting in water and electrolyte imbalances.[50] Furthermore, the correlation between cerebral apoplexy, pulmonary infection, and fever may lead to fluid loss and gastrointestinal dysfunction, subsequently causing electrolyte imbalances and hypokalemia.[51] Additionally, this research revealed a higher prevalence of hypokalemia in patients with acute ischemic stroke, particularly those scoring grade 3 or 4 on the Kubota water swallowing test. This phenomenon could be attributed to inadequate dietary intake resulting from more pronounced dysphagia, ultimately leading to hypokalemia. However, patients classified as grade 5 did not exhibit a notably elevated prevalence, likely due to the limited number of individuals with severe dysphagia reaching grade 5 in the clinical setting. Future research should aim to increase the sample size to further investigate the relationship between grade 5 patients and the incidence of hypokalemia.

This study has identified a correlation between higher urea nitrogen levels and a decreased incidence of hypokalemia in patients with ischemic stroke. This relationship may be attributed to factors such as renal metabolism and the activation of relevant neurohormones. During the acute phase of ischemic stroke, patients experience heightened stress levels, resulting in increased sympathetic activity and decreased vagal nerve excitability. This neuromodulation alteration is expected to expedite renal catabolism and enhance blood urea production.[52] However, renal ischemia and hypoxia induced by stress hinder the kidneys' ability to efficiently excrete metabolites, leading to decreased potassium excretion and subsequently lowering the occurrence of hypokalemia. The research also discovered a negative correlation between platelet count and hypokalemia in patients with ischemic stroke. This relationship may be attributed to the common use of antiplatelet medications, such as aspirin or clopidogrel, among individuals with ischemic cerebral apoplexy. These drugs are known to enhance blood coagulation function and reduce platelet activation, potentially resulting in electrolyte imbalances and disruptions in potassium homeostasis.[53] Moreover, the inflammatory response plays a crucial role in the pathogenesis of ischemic stroke. Inflammatory mediators such as cytokines may affect electrolyte balance. Elevated platelet counts may indicate a more robust inflammatory reaction, while inflammatory mediators can modulate renal potassium handling to decrease potassium excretion, potentially mitigating the development of hypokalemia.[54]

This study is subject to several limitations. Firstly, its cross-sectional design and dependence on a singular serum potassium measurement to represent potassium levels restrict the findings to indicating associations between specific factors and hypokalemia, rather than establishing causation. Secondly, constraints in data collection limited the study to using serum potassium concentration as a sole indicator, without capturing or conducting a detailed analysis of the potential impacts of variables such as fluid intake and urine output on serum potassium levels. Despite these limitations, the study provides preliminary insights into potential correlates of hypokalemia. Future research should utilize multiple measurements and longitudinal designs to more thoroughly evaluate changes in potassium levels, integrating variables such as fluid intake, potassium supplementation, and medication use to enhance the accuracy and reliability of the results.

Conclusion

This study highlights the significant prevalence of hypokalemia among patients with acute ischemic stroke, identifying age, hypertension, frailty, neurological function, swallowing ability, platelet count, and blood urea levels as factors associated with its occurrence. These findings emphasize the need for targeted, proactive management strategies to address hypokalemia in this patient population. Healthcare providers should incorporate routine potassium monitoring alongside assessments of neurological and swallowing functions, while also carefully managing hypertension and medication use. By tailoring interventions to individual risk profiles, clinicians can better prevent the onset of hypokalemia and its complications, ultimately supporting more effective recovery and enhancing quality of life. The insights from this study provide a basis for refining clinical protocols and prioritizing resource allocation in stroke care, with the potential for long-term improvements in patient outcomes.

Acknowledgments

The authors thank all participants in this study for their support. The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation. This research was funded by the Science and Technology Achievements and Appropriate Technology Promotion Project of Wuxi Municipal Commission of Health and Family Planning (grant no. T201748), Jiangsu Province Health Vocational and Technical Education Research Project (WJ202311) and "Qinglan Project" of the Young and Middle-aged Academic Leader of Jiangsu College.

Disclosure

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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