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Risk Factors Analysis of Hospital-Acquired Anemia in Cerebral Stroke Patients

Xinmin Liu[1], Fengming Ni[2] and Lan Gao[1]*

[1]*Department of Neurology, The First Hospital of Jilin University, 130000, China*
[2]*Department of Gastrointestinal Medicine, The First Hospital of Jilin University, 130000, China*

ABSTRACT

We aimed to investigate the incidence and risk factors of hospital-acquired anemia (HAA) in stroke patients. We used retrospective analysis method, research on the incidence of HAA in 560 patients with cerebral apoplexy, the patients had incomed in the department of neurology of our hospital from January 1, 2017 to December 31, 2018, the patients also had incomed in the N-ICU. We used the single factor and multiple factors regression analysis in patients with HAA on age, gender, diagnosis, and the correlation of hospitalization days. The incidence of HAA in stroke patients was 32.7% (183/560). Logistic regression analysis showed that, age (OR=1.048) and length of stay (OR=1.043) were independent risk factors for HAA, while gender and diagnosis had no statistical significance (P > 0.05). The area under the ROC curve of age and length of stay were 0.663 and 0.571, respectively. The optimal cutoff values were age over 65 and length of stay over 26 days. Diagnosis was of significance in univariate analysis, but of no significance in multivariate analysis. This is because the age had potential influence, and diagnosis was not the real influencing factor of HAA. To conclude the incidence of HAA is higher in patients with stroke who have been hospitalized in ICU. Age and length of stay are independent risk factors. Patients with cerebral stroke that age> 65 years old and length of stay> 26 days were more likely to develop HAA. Early warning mechanism and corresponding preventive measures of HAA in stroke patients should be established in clinical practice. Meanwhile, nutrition management of stroke patients should be strengthened, hemoglobin should be monitored regularly, HAA should be detected in time and anemia should be corrected by active measures. Future multicenter studies should be conducted to observe the incidence of HAA in patients receiving enteral nutrition or parenteral nutrition versus those not receiving these treatments. At the same time, stroke patients receiving rehabilitation treatment can be included in the study, and rehabilitation treatment and nutrition program can be determined according to the correlation between daily energy expenditure and HAA after rehabilitation treatment.

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XL and LG conducted the experiments in this study. FN and LG contributed to the design and interpretation of the current study and wrote the article. All authors read, revised, and approved the final manuscript.

Key words
Cerebral stroke, Hospital-acquired anemia, Incidence, Risk factors

INTRODUCTION

Stroke is a common neurological disease with a high incidence in the elderly population (Feng and Pei, 2021). Due to the different locations of the lesions, patients may have disturbance of consciousness or dysphagia, affecting their eating and nutritional status. Hospital-acquired anemia (HAA) refers to a condition in which hospitalized patients with normal hemoglobin (Hgb) at admission show Hgb below normal level (Ahmed, 2014; Vander Bom and Cannegieter, 2015). Although HAA usually involves multiple factors, for critically ill patients, loss from phlebotomy is a potentially avoidable major cause. Several domestic and foreign studies have shown that HAA still remains problem decades after 1973 (Eyster and Bernene, 1973; Greenwood, 2000; Woodhouse, 2001; Eckardt, 2001; Thavendiranathan *et al*., 2005; Chant *et al*., 2006; Pabla *et al*., 2009; Salisbury *et al*., 2011; Tosiri *et al*., 2010; Branco *et al*., 2012; Lyon *et al*., 2013; Coene *et al*., 2015; Levi, 2015). When studying specific patient populations, the incidence of HAA ranges from 20% to 70% in renal insufficiency patients admitted in the intensive care unit (ICU) or hospitalized for invasive treatment. The most important sequelae of anemia are lower oxygen-carrying capacity of the blood, resulting in increased cardiac output, a change in the oxyhemoglobin dissociation curve, and increased oxygen extraction, thus possibly reducing oxygen delivery at the tissue level. Studies have demonstrated

* Corresponding author: gaolan@jlu.edu.cn
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that the presence of HAA in various surgeries and medical patients worsens in-hospital and post-hospital outcomes (Ahmed, 2014). At present, there is no clinical study on the incidence and risk factors of hospital-acquired anemia in cerebral stroke patients. This study reviewed the data of cerebral stroke patients admitted to N-ICU of neurology department in our hospital from January 1, 2017 to December 31, 2018, and studied the incidence and risk factors of HAA in these patients.

MATERIALS AND METHODS

In this study, data were collected from 881 cerebral stroke patients admitted to neurology ICU of our hospital from January 1, 2017 to December 31, 2018. A total of 560 patients met the inclusion criteria. Table I lists the study sample exclusion reasons and the number of exclusion. Inclusion criteria: (1) Conform to the diagnosis of cerebral stroke (CNS, 1997) and confirmed by head CT scan or MRI; (2) Age≥18 years old; (3) Hospital stay≥7 days; (4) ICU hospital stay≥24 h; (5) EN≥ 3 days during the period (energy intake is calculated at 25-30kcal/kg/d); (6) Normal Hgb value at admission; (7) Each hospitalization requires at least 2 Hgb measurement values, one at the time of admission, one at the time of discharge after treatment. Exclusion criteria: (i) Patients who terminates treatment due to various reasons during the study period (such as giving up treatment, death, etc.). (ii) Those who receives red blood cell suspension transfusion 48 hours before admission. (iii) With anemia at admission. (iv) Hemoglobin above the normal range at admission; Acute hemorrhage at the time of admission.

The age, gender, discharge diagnosis, hospital stay, Hgb value at admission, and Hgb value before discharge were collected from electronic medical records. The incidence of HAA was analyzed for ICU hospitalized stroke patients. Univariate and multivariate regression analysis was performed on the age, gender, hospital stay, and diagnosis of the enrolled patients to study the risk factors for HAA in cerebral stroke patients.

According to the World Health Organization (WHO) criteria, anemia is defined as Hgb <13 g/dL in men and <12 g/dL in women (WHO, 1968). Anemia is further classified as mild when Hgb is >11 g/dL (but below normal value for each gender), moderate when Hgb is >9 g/dL and <11 g/dL, and severe when Hgb is <9 g/dL (Ahmed, 2014).

All data were recorded in the form of double entry after verification by two people. The incidence of HAA is expressed as a percentage. Univariate analysis was performed on age, sex, diagnosis, and hospital stay. Measurement data were expressed as mean ± standard deviation. Comparison between groups was performed using t test, and counting data was tested using $\chi 2$ test. In the univariate analysis, each significant variable ($P<0.05$) was included in the multivariate regression analysis,

Table I. Reasons and numbers for inclusion and exclusion of study samples.

	Item	Number (person)
Included sample	Meet inclusion criteria	560
Excluded sample	Abnormal hemoglobin at admission (above or below normal range)	183
	No routine blood collection during hospitalization	27
	One blood routine collection during hospitalization	98
	No clear diagnosis of ischemic and hemorrhagic stroke	13

Table II. Univariate analysis of HAA in cerebral stroke patients.

Variable	HAA group (n=183)	Non-HAA group (n=377)	t/X2	P value
Gender [case (%)]			0.456	0.499
Male	124(67.8)	266(70.6)		
Female	59(32.2)	111(29.4)		
Diagnosis [case (%)]			5.142	0.023
Ischemic stroke	143(78.1)	260(69.0)		
Hemorrhagic stroke	40(21.9)	117(31.0)		
Age (years, x±s)	66.9±12.4	60.4±12	6.167	<0.001
Hospital stay (day, x±s)	20.7±12.5	16.7±7.9	3.971	<0.001

and the area under the curve and optimal cut-off value of each risk factor were calculated based on the ROC curve. All statistical analyses of the experimental data were performed in Microsoft Excel and SPSS 19.0 statistical software, and P<0.05 indicates statistically significant difference.

RESULTS

Of the 560 patients enrolled, 183 patients developed hospital-acquired anemia (HAA), with an incidence rate of 32.7% (183/560). According to the two hemoglobin values, the patients were divided into HAA group and non-HAA group. Univariate analysis showed that HAA group was older than non-HAA group, with longer hospital stay than the non-HAA group. The number of HAA cases was greater in ischemic stroke patients than in hemorrhagic stroke patients, and the difference was statistically significant (P<0.05). There was no statistically significant gender difference between the two groups (P>0.05).

According to the univariate results, the inclusion criterion was <0.05, and the exclusion criterion was >0.1. Logistic regression analysis was performed on age, diagnosis, and hospital stay using the stepwise forwards method (the model was meaningful as a whole, and the overall prediction rate was 70.7%). Age and hospital stay had a statistically significant effect on the incidence of HAA (P<0.05), while the effect of diagnosis was not statistically significant (Table III).

Diagnoses with no statistically significant effect on the incidence of HAA were excluded, and a second Logistic regression analysis was performed (the model was meaningful as a whole, and the overall prediction rate was 71.1). The results revealed that age and hospital stay were independent risk factors for HAA in cerebral stroke patients (Table III). Diagnosis was meaningful in univariate analysis, but not in multivariate analysis, which is due to the potential effect of age. Nonetheless, diagnosis was not a real factor in the incidence of HAA.

The ROC curve was used for model fit analysis (Fig. 1), the area under the curve was 0.681 and close to 70% (P<0.05), with maximum Youden index 0.272, sensitivity 0.601, and specificity 0.671.

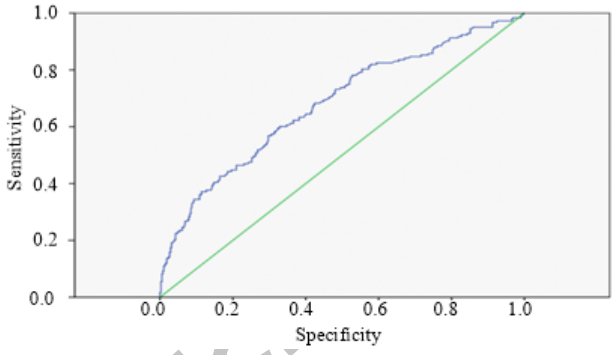

Fig. 1. ROC curve.

The ROC curve was plotted for age, with AUC 0.663, optimal cut-off value 64.5 years, Youden index 0.253, sensitivity 0.623, and specificity 0.63. The Roc curve was plotted for hospital stay, with AUC 0.571, optimal cut-off value 25.5 days, Youden index 0.197, sensitivity 0.290, and specificity 0.907. The optimal cut-off values for HAA after cerebral stroke were age > 65 years and hospital stay > 26 days (rounded).

DISCUSSION

The data of 881 stroke patients with ICU hospitalization history were collected, and 560 eligible patients were finally enrolled. The incidence of HAA was 32.7% in cerebral stroke patients with hospitalization history. The risk factors of HAA in stroke patients were analyzed by univariate and multivariate analysis, so as to provide a basis for clinical practice. Cerebral stroke patients are prone to malnutrition after the onset

Table III. Multivariate regression analysis of HAA in cerebral stroke patients 1 and 2.

	Regression coefficient	Standard error	Wald X2	P value	Relative risk degree	95%CI
Patient 1						
Age	0.045	0.008	29.062	0	1.046	1.029~1.063
Diagnosis	0.306	0.225	1.851	0.174	1.358	0.874~2.110
Hospital stay	0.043	0.01	19.315	0	1.044	1.024~1.064
Patient 2						
Age	0.047	0.008	33.544	0	1.048	1.031~1.065
Hospital stay	0.042	0.01	18.665	0	1.043	1.023~1.063
Constant	-4.483	0.575	60.833	0	0.011	-

due to disturbance of consciousness and swallowing dysfunction. In the intensive care unit, approximately 90% patients have a decreased hemoglobin level on the third day of ICU treatment, and the incidence of HAA is significant in ICU (Raghavan and Marik, 2005). For cerebral stroke patients who have been hospitalized in the ICU, nutritional management should be strengthened. For instance, nutritional support in different ways can be provided according to the swallowing function assessment results; daily energy and protein requirements can be calculated according to the disease severity and body weight.

This study shows that age and hospital stay are independent risk factors for HAA in cerebral stroke patients, and the influence of diagnosis and gender on the incidence of HAA is not statistically significant. This study reveals that the age of patients with HAA is greater than 65 years old. Although no clear consensus has been reached on the risk factors of HAA, most researchers agree that age above 65 years old is associated with malnutrition (Greenwood, 2000). Therefore, for cerebral stroke patients over 65 years old, nutrition should be strengthened and hemoglobin should be checked regularly.

This study suggests that the incidence of HAA is related to the hospital stay of cerebral stroke patients, and hospital stay longer than 26 days is the optimal cut-off value. Therefore, with the increase of hospital stay, especially for patients hospitalized for more than 26 days, the nutritional status evaluation should still be included in regular evaluation process to grasp changes in albumin and hemoglobin. Hospital stay should be shortened as much as possible to reduce the incidence of HAA. At present, the hospital stay of stroke patients is shortened, and most patients choose to be transferred to other medical institutions for rehabilitation treatment after discharge, rather than home care. Therefore, it is still necessary to pay attention to the prevention of HAA in stroke patients even though the hospitalization days of stroke patients are significantly shortened. In the future, stroke patients receiving rehabilitation therapy can be included in the study, and rehabilitation therapy and nutrition program can be determined according to the correlation between daily energy expenditure and HAA after rehabilitation therapy.

The early warning and prevention mechanism of HAA should be established in clinical practice. At present, there is still insufficient clinical understanding of HAA in cerebral stroke patients. Among the 881 patients in this study, 98 patients received only one blood routine examination during their hospitalization, and 27 patients received none. Although unnecessary laboratory tests should be reduced (Greenwood, 2000), regular blood routine examination is still necessary for malnourished cerebral stroke patients at a high risk of the disease. Doctors should seek measures to prevent HAA while reducing unnecessary blood collection (Vander Bom and Cannegieter, 2015), and multidisciplinary collaboration is important.

Due to the limitations of retrospective and observational design, this study lacked data on gastrointestinal bleeding events caused by stress ulcers, intravenous blood transfusion and intravenous fluids, and hemoglobin after discharge for stroke patients. Therefore, it was not possible to evaluate the recovery of anemia in HAA patients after discharge.

In this tudy, laboratory blood volume was not collected during hospital stay. According to the research of Van der Bom and Cannegieter (2015), blood collection for laboratory diagnosis is not the main cause of HAA. Healthy people need to replace 1% of their blood volume per day, that is, about 50 ml of total blood volume (TBV), but this ability is impaired in hospitalized patients, lowering their threshold for tolerable blood loss (Woodhouse, 2001). Therefore, the necessity for some laboratory tests in hospitalized stroke patients remains to be discussed. In future studies, blood loss due to in-hospital laboratory tests can be included as a variable in the analysis.

CONCLUSION

Cerebral stroke patients with ICU hospitalization experience have a higher incidence of HAA. Age and hospital stay are independent risk factors. The optimal cut-off value of HAA in cerebral stroke is age > 65 years and hospital stay > 26 days. Clinically, an early warning mechanism and corresponding preventive measures should be established for HAA in cerebral stroke patients, and multidisciplinary cooperation should be valued. It is necessary to strengthen the nutritional management of cerebral stroke patients, regularly monitor hemoglobin, detect HAA in time, and actively take measures to correct anemia.

Ethical approval

The study was carried out in compliance with guidelines issued by Ethical Review Board Committee of the First Hospital of Jilin University, China.

IRB approval

This study was approved by the Advanced Studies Research Board of the First Hospital of Jilin University, 130000, China.

Statement of conflict of interest

The authors have declared no conflict of interest.

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