Scholars Journal of Applied Medical Sciences
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Neurology

Association of Admission Anaemia with the Severity of Acute Ischemic Stroke: A Study in a Tertiary Care Hospital

Ranjit Kumar Ghosh[1*], Abu Nasir Rizvi[2], Priyanka Paul[3], Mominul Islam[4], Munadi Al Islam[5], Anisul Hasan[6]

[1]Medical Officer, Department of Neurology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh
[2]Professor and Chairman, Department of Neurology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh
[3]Assistant Professor, Department of Statistics, Comilla University, Cumilla, Bangladesh
[4]Resident, Phase-B, Neurology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh
[5]FCPS Trainee, Neurology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh
[6]Resident Phase-B, Neurology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh

DOI: 10.36347/sjams.2023.v11i07.005 | **Received:** 16.05.2023 | **Accepted:** 23.06.2023 | **Published:** 09.07.2023

***Corresponding author:** Ranjit Kumar Ghosh
Medical Officer, Department of Neurology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh

Abstract **Original Research Article**

***Background*:** Acute ischemic stroke imposes substantial disability, economic, and social burdens. Prevention plays a vital role in reducing morbidity and mortality. Reduced hemoglobin concentration in ischemic stroke patients hampers oxygen delivery to neuronal tissue, leading to adverse effects on the ischemic penumbra and increasing the risk of infarct expansion. By addressing anemia and identifying other associated risk factors, we can effectively enhance stroke prevention strategies and mitigate its overall impact on individuals and society. Understanding the multifaceted nature of ischemic stroke and implementing comprehensive prevention measures is key to minimizing its devastating consequences. ***Objectives*:** The purpose of this study is to show the association of admission anaemia with the Severity of Acute Ischemic Stroke. ***Method and Materials*:** This cross-sectional study was carried out in the Department of Neurology, Dhaka Medical College and Hospital (DMCH), Dhaka for a period of two years. Two hundred and seventy- nine patients with acute ischemic stroke were selected consecutively through screening with a set of inclusion and exclusion criteria. Each patient underwent a CT of the head and/or MRI of the brain and blood tests, including hemoglobin (Hb) concentration on the first day of hospitalization. Demographic and risk factors from all subjects were collected with a structured questionnaire. The neurological state of the patients was assessed on the first day of hospitalization by the National Institute of Health Stroke Scale (NIHSS). After data collection analysis was done by SPSS for Windows version 26. A p-value ≤ 0.05 was considered statistically significant. ***Results*:** The frequency of anemia in acute ischemic stroke patients was 39.1%, in males it was 35.8%, and in females 44.7%. Frequency Anemia was observed more among the older patients than younger patients but there was no significant difference. Anemia was found highest in the age group 51 – 60 years and lowest in the age group ≤40 years. Diabetes mellitus and CKD were significantly higher in anemic patients than in non-anemic patients. Admission anemia was found significantly higher among the patients with severe stroke (46.8%) [p=0.027]. 100% severe anemic patients had a severe stroke, 57.7% moderate anemic patients had a severe stroke, 29.6% mild anemic patients had a severe stroke and 23.5% normal patients had a severe stroke. On the other hand, 34.1% of normal patients had a moderate stroke, 32.1% of mild anemic patients had a moderate stroke, 3.8% of moderate anemic patients had a moderate stroke and no severe anemic patients had a moderate stroke. This indicates that the severity of stroke increases with the severity of anemia which is statistically significant. ***Conclusion*:** Anaemia is incredibly prevalent among patients diagnosed with acute ischemic stroke and has been consistently linked to several adverse outcomes. Studies have shown a strong association between admission anaemia and the severity of the stroke. Furthermore, the severity of stroke also increases with the severity of anaemia.

Keywords: Admission Anemia, Acute Ischemic Stroke, severity of stroke, Grading of anaemia.

INTRODUCTION

Stroke is a prevalent medical emergency that occurs when there is a sudden disruption of blood supply to the brain or the rupture of intracerebral vessels, leading to either ischemic or hemorrhagic damage and resulting in focal neurological deficits. Ischemic strokes constitute the majority (85%) of all strokes, while hemorrhagic strokes make up the

remaining 15% [1]. In terms of global impact, stroke ranks as the second leading cause of mortality and is a major contributor to long-term disabilities worldwide [19]. The Global Burden of Disease (GBD) study conducted in 2013 reported that stroke was responsible for approximately 6.5 million deaths, and an estimated 10.3 million individuals experienced a stroke during that year. Notably, the majority of these deaths occurred in low and middle-income countries. Without effective and timely interventions, the projected global death toll from stroke is expected to rise to 7.8 million by 2030 [2, 3]. In the context of Bangladesh, the World Health Organization (WHO) has ranked stroke mortality as 84th in the world in 2011. However, there has been a significant shift in ranking, with Bangladesh now placed at 34th in the world as of 2017, highlighting the growing impact of stroke in the country [World Health Rankings, 2011 and 2017]. These statistics underscore the urgent need for effective strategies in stroke prevention, management, and rehabilitation to address the rising burden of stroke-related morbidity and mortality globally, with particular attention to the specific challenges faced by countries like Bangladesh.

Stroke is a prevalent medical emergency that can occur due to a sudden reduction in blood supply to the brain or the rupture of intracerebral vessels, leading to hemorrhage and resulting in focal neurological deficits. The vast majority of strokes (over 99%) have an arterial origin, with approximately 85% being ischemic strokes and the remaining 15% being hemorrhagic strokes [1]. Globally, stroke is the second leading cause of mortality and one of the major contributors to long-term disability [19]. According to the Global Burden of Disease (GBD) study conducted in 2013, stroke was responsible for approximately 6.5 million deaths, and an estimated 10.3 million individuals experienced a stroke in the same year. It is important to note that the majority of these deaths occurred in low and middle-income countries. Without adequate and timely interventions, the projected global death toll from stroke is expected to rise to 7.8 million by 2030 [2, 3]. In Bangladesh, the World Health Organization (WHO) ranked stroke mortality as the 84th leading cause of death in the world in 2011. However, this ranking shifted significantly by 2017, with Bangladesh now placed at the 34th position, indicating an increased impact of stroke in the country [World Health Rankings, 2011 and 2017].

The WHO also reported that the number of disability-adjusted life years (DALY) lost per 1000 individuals due to stroke was 485, with an age-standardized DALY rate of 864 per 100,000 people in 2011 [WHO, 2011]. A study conducted by neurologists at Dhaka Medical College Hospital in Bangladesh in 2011 revealed a stroke prevalence of 3 per thousand populations, highlighting the potential future economic burden of stroke in the country [4].

While stroke is commonly associated with hypertension and atherosclerosis, there are various other less common causes that can contribute to stroke, including cardioembolism, hematologic disorders, substance abuse, trauma, dissections, oral contraceptive use, connective tissue disorders, pregnancy, post-partum stage, and migraine. However, the underlying cause of stroke in young patients remains undetermined in approximately 30% of cases [5]. Anemia is known to be associated with increased mortality, decreased physical performance, and disability, regardless of the underlying cause [6]. Low hemoglobin levels can result in reduced oxygen-carrying capacity, inflammatory responses, alterations in blood viscosity, and impairment of cerebral autoregulation [7].

The role of anemia in the outcomes of acute ischemic strokes has been a topic of interest. It has been suggested that anemia could contribute to poor recovery even after successful therapeutic reperfusion. On one hand, anemia has been associated with increased stroke severity as it hampers the delivery of oxygen to neurons in the ischemic penumbra, potentially leading to unfavorable functional outcomes. On the other hand, anemia itself may directly impact functional disability [8]. Retrospective analyses have provided recent evidence indicating that anemia can serve as a predictor of mortality following a stroke [9, 17]. However, some prospective studies have yielded mixed results regarding the relationship between anemia and stroke outcomes when adjusting for factors like smoking and blood pressure [10]. Moreover, previous studies have primarily focused on the association between anemia and stroke-related mortality. Studying the relationship between anemia and stroke outcomes at an early stage is crucial, as long-term functional outcomes are strongly influenced by the level of disability during the early phases of the disease. This has important implications for stroke management, as the presence of anemia in an individual patient may impact their prognosis after the stroke. However, there is currently a lack of sufficient research published in this region addressing this specific issue.

OBJECTIVE

The aim of the study was to evaluate the association of admission anemia with the severity of acute ischemic stroke in Dhaka Medical College Hospital (DMCH), Dhaka.

METHOD AND MATERIALS

This cross-sectional study was conducted at the Department of Neurology, Dhaka Medical College and Hospital (DMCH) in Dhaka, spanning from July 2020 to June 2022. Prior to commencing the study, ethical clearance was obtained from the Ethical Review Committee of DMCH to ensure adherence to ethical guidelines. The study enrolled patients with acute

ischemic stroke who were admitted within 72 hours of symptom onset and were at least 18 years of age. The patients were selected through purposive sampling and were specifically recruited from the Neurology and Medicine wards of DMCH.

Certain exclusion criteria were applied during the participant selection process. Patients with recurrent stroke, hemorrhagic stroke, transient ischemic attack, venous stroke, sickle cell disease, hemoglobinopathies, polycythemia, hematological malignancies, or other malignancies were excluded from the study to maintain a specific focus on acute ischemic stroke cases. Prior to participation, patients or their legal guardians were provided with comprehensive information regarding the objectives and procedures of the study. Informed written consent was obtained from the participants.

The study involved collecting clinical histories and conducting relevant examinations for each participant. Demographic details such as age and sex were recorded. Acute ischemic stroke was diagnosed based on the World Health Organization (WHO) criteria and confirmed using radiological imaging, including computed tomography (CT) and/or magnetic resonance imaging (MRI) of the brain, as per the 1989 WHO guidelines for stroke diagnosis. All CT scans and MRIs were evaluated by a consultant radiologist, ensuring accuracy and consistency in the diagnosis of acute ischemic stroke.

The severity of stroke on the first day of hospitalization was assessed using the National Institutes of Health Stroke Scale (NIHSS) score. The NIHSS score serves as a standardized tool for evaluating stroke severity and was employed by the investigator in this study to quantify the severity of acute ischemic stroke among the participants.

Laboratory Procedure

Prior to conducting the laboratory procedures, the necessary permission was obtained from the Department of Hematology at Dhaka Medical College and Hospital (DMCH). The laboratory tests included a complete blood count (CBC) and peripheral blood film (PBF) analysis. To perform the CBC, a venous blood sample of 3ml was collected using an EDTA tube, which was specifically designed as a vacuum tube. The collected blood sample was gently mixed by shaking it at least 5 times. A unique barcode was assigned to each tube to ensure proper identification and tracking throughout the process. The EDTA tube was then placed in a fully automated Hematology analyzer (Sysmex XE-5000, Japan) for analysis. Hemoglobin (Hb) levels were estimated using the Spectrophotometric method, while the total and differential counts were determined using the fluorescent flow cytometric method. Red blood cell (RBC) and platelet counts were obtained using the electrical impedance method. The results of these analyses were generated within one minute when the samples were processed in the fully automated hematology analyzer (Sysmex XE- 5000). In addition to the CBC, a peripheral blood film (PBF) analysis was also performed. The PBF was conducted in conjunction with the CBC and was carried out at the Department of Hematology, DMCH.

Data Analysis

Data were entered, cleaned, and analyzed using Statistical Package for Social Sciences (SPSS-26) software. For background variables and socio-demographic variables, descriptive statistics and relative frequency were generated. Continuous variables were statistically described in terms of mean and standard deviations (Mean± SD). Statistical significance was defined as $p<0.05$ and the confidence interval was set at 95% level.

RESULTS

This study initially included a total of 308 patients with acute ischemic stroke who met the specified inclusion and exclusion criteria and were admitted to DMCH. Following their discharge from the hospital, a group of 29 patients were lost to follow-up. Therefore, the final analysis included data from 279 patients who successfully completed the follow-up period. The analysis of the results utilized appropriate statistical tests and the findings are presented in the relevant table and figure.

Table I: The frequency of anemia among the study population.

	Population	Anemia	Percentage (%)
Total	**279**	**109**	**39.1**
Male	176	63	35.8
Female	103	46	44.7

Table I shows the frequency of anemia among the study subjects. The frequency of anemia in acute ischemic stroke patients was 39.1%, in males it was 35.8%, and in females 44.7%.

Table II: Baseline characteristics of the study subjects with and without anemia (n=279)

	All patients(N=279)	Anemic(N=109)	Non-anemic(N=170)	p-value
Age (years)				
≤40	27 (9.7)	7 (6.4)	20 (11.8)	[a]0.226
41 - 50	42 (15.1)	14 (12.8)	28 (16.5)	
51 - 60	82 (29.4)	34 (31.2)	48 (28.2)	
61 - 70	74 (26.5)	27 (24.8)	47 (27.6)	
>70	54 (19.4)	27 (24.8)	27 (15.9)	
Mean ± SD	60.40 ± 14.35	62.77 ± 14.17	58.89 ± 14.30	[b]0.102
Hypertension	180 (64.5)	66 (66.0)	114 (63.7)	[a]0.699
Diabetes mellitus	78 (28.0)	38 (34.9)	40 (23.5)	[a]0.040
Dyslipidemia	98 (35.1)	43 (39.4)	55 (32.4)	[a]0.226
History of IHD	40 (14.3)	11 (11.0)	29 (16.2)	[a]0.235
Smoking history				
Non-smoker	143 (51.3)	56 (56.0)	87 (48.6)	[a]0.289
Smoker (Current+Ex)	136 (48.7)	44 (44.0)	92 (51.4)	
Alcohol consumption	12 (4.3)	4 (3.7)	8 (4.7)	[c]0.667
Family history of stroke	75 (26.9)	29 (26.6)	46 (27.1)	[a]0.934
AF	12 (4.3)	7 (6.4)	5 (2.9)	0.162
CKD	19 (6.8)	13 (11.9)	6 (3.5)	0.007
Side of infarct				
Right	101 (36.2)	38 (34.9)	63 (37.1)	[a]0.710
Left	178 (63.8)	71 (65.1)	107 (62.9)	

[a]Chi-Square, [b]Unpaired t and [c]Fisher's Exact test was done

Table II shows the baseline characteristics of acute ischemic stroke patients with and without anemia. Anemia was observed more among the older patients than younger patients but there was no significant difference. Anemia was found highest in the age group 51–60 years and lowest in the age group ≤40 years. Diabetes mellitus and CKD were significantly higher in anemic patients than in nonanemic patients.

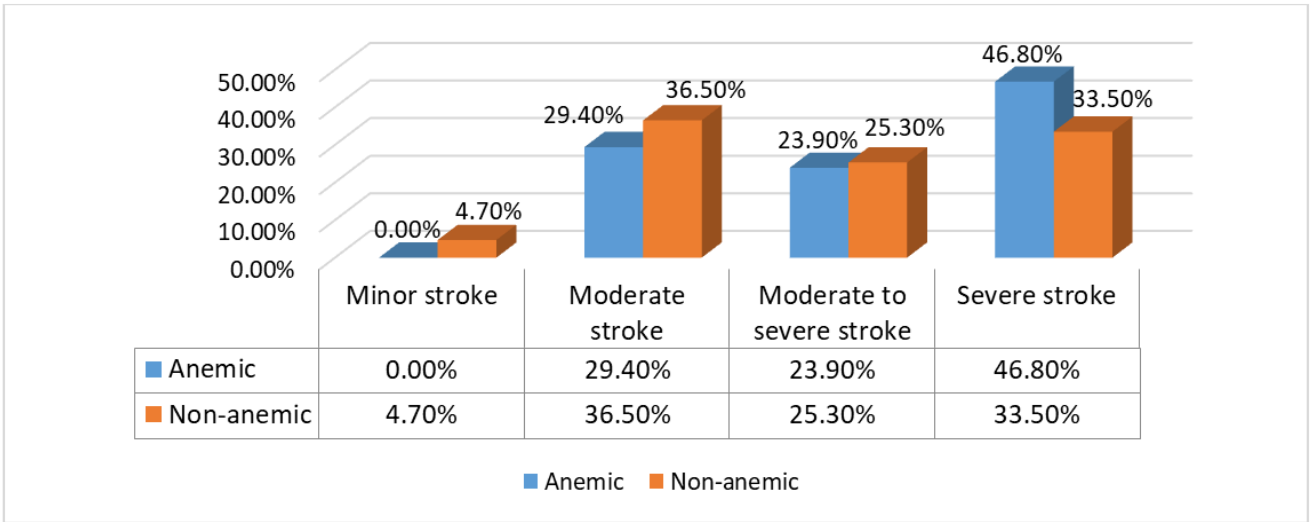

Fig. 1: Association of admission anemia with severity (NIHSS) of stroke (n=279)

Fig. 1 indicates the association of admission anemia with the severity of stroke. Anemia was found significantly higher among the patients with severe stroke (46.8%) [p=0.027, where p-value derived from Chi-Square test].

Table III: Association of grading of anemia with the severity of stroke (n=279)

Severity of Anemia	Total (N=279)	NIHSS				P-value
		Minor stroke	Moderate stroke	Moderate to severe stroke	Severe stroke	
Severe anemia	2	0(0.0%)	0(0.0%)	0(0.0%)	2(100.0%)	0.001
Moderate anemia	26	0(0.0%)	1(3.8%)	10(38.5%)	15(57.7%)	
Mild anemia	81	3(3.7%)	26(32.1%)	28(34.6%)	24(29.6%)	
Normal	170	30(17.6%)	58(34.1%)	42(24.7%)	40(23.5%)	
Total	**279**	**33(11.8%)**	**85(30.5%)**	**80(28.7%)**	**81(29.0%)**	

Table III shows the association of the grading of anemia with the severity of stroke. 100% of severely anemic patients had a severe stroke, 57.7% of moderate anemic patients had a severe stroke, 29.6% of mild anemic patients had a severe stroke and 23.5% of normal patients had a severe stroke. On the other hand, 34.1% of normal patients had a moderate stroke, 32.1% of mild anemic patients had a moderate stroke, 3.8% of moderate anemic patients had a moderate stroke and no severe anemic patients had a moderate stroke. This indicates that the severity of stroke increases with the severity of anemia which is statistically significant (p-value, P=0.001).

DISCUSSION

This study aimed to investigate the association between admission anemia and the severity of acute ischemic stroke, focusing on the context of middle-income countries like Bangladesh. Initially, a total of 308 patients with acute ischemic stroke were included in the study. However, 29 individuals were subsequently excluded, resulting in the analysis of data from 279 patients. The prevalence of anemia among acute ischemic stroke patients in this study was found to be 39.1%, with 35.8% being male and 44.7% being female. Similar studies, referenced as [11] and [12], reported anemia prevalence rates of 39.6% and approximately 30%, respectively, among acute stroke patients.

The prevalence of anemia in acute stroke patients has been estimated to range from 17% to 29% according to references [13] and [14]. Various studies, including [8, 15-17], have reported anemia rates ranging from 6% to 44% in acute ischemic stroke patients. Although this study observed a higher occurrence of anemia among older patients, the difference was not statistically significant. However, another study referenced as [9] found a significant association between anemia and older age in stroke patients, as well as a higher prevalence of anemia among smokers compared to non-smokers. Regarding comorbidities, this study found a significant association between anemia and diabetes mellitus in acute ischemic stroke patients. However, there were no significant differences observed in terms of hypertension, dyslipidemia, history of ischemic heart disease (IHD), or atrial fibrillation between anemic and non-anemic patients. This finding aligns with the study referenced as [8].

One of the key contributions of this study lies in its exploration of anemia prevalence among individuals suffering from acute ischemic stroke. The documented prevalence rate of anemia in this population was found to be considerable, emphasizing the significance of addressing this condition in stroke management. Understanding the high prevalence of anemia within this specific group of patients allows healthcare providers to recognize it as a common comorbidity, guiding them towards adopting appropriate screening and treatment strategies. Anemia was significantly more prevalent among patients with severe stroke, and the frequency of severe stroke increased with stroke severity. Similar findings were reported in reference [11], where anemia was significantly more prevalent among severe stroke patients. The findings of this study hold significant value in expanding our understanding of the relationship between admission anemia and the severity of acute ischemic stroke, particularly within the context of middle-income countries such as Bangladesh. By shedding light on various aspects, this study provides valuable insights into the prevalence of anemia among patients with acute ischemic stroke, its association with age and smoking, as well as its impact on stroke severity. Overall, this study significantly contributes to our understanding of admission anemia in the context of acute ischemic stroke, particularly within middle-income countries like Bangladesh. By elucidating the prevalence of anemia, its relationship with age and smoking, and its impact on stroke severity, this research provides crucial insights that can inform clinical practice, enhance patient care, and guide future research efforts in the field of stroke management.

Limitations of the Study

It is important to acknowledge the limitations inherent in our study. Firstly, it is worth noting that our research was conducted solely at a single center, which may introduce biases and limit the generalizability of our findings to a broader population. Secondly, our study involved a small sample size which may not broadly provide a comprehensive understanding of the long-term implications or effects of the phenomenon under investigation. Lastly, we did not gather any

information regarding the underlying causes or duration of anemia prior to the occurrence of the stroke, which restricts our ability to fully explore the relationship between anemia and stroke severity.

CONCLUSION

Anemia frequently occurs among patients with acute ischemic stroke, and its presence upon admission has been linked to the severity of the stroke. Moreover, the frequency of severity of acute ischemic stroke tends to increase as severity of anaemia worsens. Recognizing the potential implications, treating anemia in individuals with acute ischemic stroke becomes crucial as it can enhance oxygen delivery to the brain. Therefore, healthcare providers should prioritize early identification and meticulous treatment of anemia in these patients, aiming to promote better brain oxygenation, reduce stroke severity and optimize outcomes.

Conflict of Interest: None.

RECOMMENDATION

Anaemia holds significance as a contributing factor for severity of acute ischemic stroke. Given its potential impact, it may be necessary to conduct more studies regarding this issue. While the evidence supporting the treatment of anaemia in acute ischemic stroke is currently lacking, it is advisable to prioritize screening and addressing anaemia in the general population. By doing so, we can aim to minimize the severity of acute ischemic and detrimental effects of it on the occurrence and progression of acute ischemic stroke until more conclusive evidence regarding specific interventions on management of anaemia in acute ischemic patients becomes available.

REFERENCES

1. Langhorne, P. (2018). Stroke medicine. In: Ralston, S.H., Penman, I.D., Strachan, M.W.J., Hobson, R.P. (eds) Davidson's principles and practice of Medicine. 23rd ed., Elsevier, pp.1149-1153.
2. Strong, K., Mathers, C., & Bonita, R. (2007). Preventing stroke: saving lives around the world. *The Lancet Neurology*, *6*(2), 182-187.
3. Zhou, R., Wang, M., Huang, H., Li, W., Hu, Y., & Wu, T. (2018). Lower vitamin D status is associated with an increased risk of ischemic stroke: a systematic review and meta-analysis. *Nutrients*, *10*(3), 277.
4. Mohammad, Q. D., Habib, M., Hoque, A., Alam, B., Haque, B., Hossain, S., Rahman, K. M., & Khan, S. U. (2011). Prevalence of stroke above forty years. *Mymensingh medical journal: MMJ*, *20*(4), 640-644.
5. Akins, P. T., Glenn, S., Nemeth, P. M., & Derdeyn, C. P. (1996). Carotid artery thrombus associated with severe iron-deficiency anemia and thrombocytosis. *Stroke*, *27*(5), 1002-1005.
6. Penninx, B. W., Pahor, M., Cesari, M., Corsi, A. M., Woodman, R. C., Bandinelli, S., ... & Ferrucci, L. (2004). Anemia is associated with disability and decreased physical performance and muscle strength in the elderly. *Journal of the American Geriatrics Society*, *52*(5), 719-724.
7. Vila, N., Castillo, J., Dávalos, A., & Chamorro, A. (2000). Proinflammatory cytokines and early neurological worsening in ischemic stroke. *Stroke*, *31*(10), 2325-2329.
8. Akpinar, C. K., Gurkas, E., & Aytac, E. (2018). Moderate to severe anemia is associated with poor functional outcome in acute stroke patients treated with mechanical thrombectomy. *Interventional Neurology*, *7*(1-2), 12-18.
9. Milionis, H., Papavasileiou, V., Eskandari, A., D'Ambrogio-Remillard, S., Ntaios, G., & Michel, P. (2015). Anemia on admission predicts short-and long-term outcomes in patients with acute ischemic stroke. *International Journal of Stroke*, *10*(2), 224-230.
10. Kannel, W. B., Gordon, T., Wolf, P. A., & McNamara, P. (1972). Hemolobin and the risk of cerebral infarction: The Framingham study. *Stroke*, *3*(4), 409-420.
11. Khan, M. F., Shamael, I., Zaman, Q., Mahmood, A., & Siddiqui, M. (2018). Association of anemia with stroke severity in acute ischemic stroke patients. *Cureus*, *10*(6), 1-7.
12. Lasek-Bal, A., Holecki, M., Stęposz, A., & Duława, J. (2015). The impact of anemia on the course and short-term prognosis in patients with first ever ischemic stroke. *Neurologiai Neurochirurgia Polska*, *49*(2), 107-112.
13. Del Fabbro, P., Luthi, J. C., Carrera, E., Michel, P., Burnier, M., & Burnand, B. (2010). Anemia and chronic kidney disease are potential risk factors for mortality in stroke patients: a historic cohort study. *BMC nephrology*, *11*(1), 1-10.
14. Huang, W. Y., Chen, I. C., Meng, L., Weng, W. C., & Peng, T. I. (2009). The influence of anemia on clinical presentation and outcome of patients with first-ever atherosclerosis-related ischemic stroke. *Journal of Clinical Neuroscience*, 16(5), 645-649.
15. Tanne, D., Molshatzki, N., Merzeliak, O., Tsabari, R., Toashi, M., & Schwammenthal, Y. (2010). Anemia status, hemoglobin concentration and outcome after acute stroke: a cohort study. *BMC neurology*, *10*(1), 1-7.
16. Corona, L. P., Duarte, Y. A. D. O., & Lebrão, M. L. (2014). Prevalence of anemia and associated factors in older adults: evidence from the SABE Study. *Revista de SaúdePública*, *48*(5), 723-431.
17. Li, Z., Zhou, T., Li, Y., Chen, P., & Chen, L. (2016). Anemia increases the mortality risk in patients with stroke: A meta-analysis of cohort studies. *Scientific reports*, *6*(1), 1-8.

18. Fabjan, T. H., Penko, M., & Hojs, R. (2019). Anemia on admission and long-term mortality risk in patients with acute ischemic stroke. *Advances in Clinical and Experimental Medicine*, *28*(10), 1419-1424.

19. Katan, M., & Luft, A. (2018). Global burden of stroke. In Seminars in neurology. *Thieme Medical Publishers*, *38*(02), 208-211.