Post CVA Iron Deficiency Anaemia Among Patients Admitted to Samarra General Hospitals

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Abstract

One of the most common causes of death and disability in the elderly is stroke. The Elderly are susceptible to iron deficiency anaemia (IDA). Evidence suggests that IDA usually affect the outcome of cases even after proper treatment. In the present study, we sought to investigate the association between cerebrovascular stroke and iron deficiency anaemia via measurement of serum iron level, iron binding capacities and serum level of ferritin and transferrin alongside brain magnetic resonance, venography, and angiography. we studied a group of (100) cerebrovascular patients in Samarra General Hospital suffering from iron deficiency anaemia and investigated clinically to be confirmed by magnetic resonance imaging (MRI), serum ferritin levels and studied the correlation between IDA and stroke and the effect of it on the outcome of cases by follow up for 2 months. The outcome has revealed that the percentage of IDA is higher in CVA patients compared to the control group. Conclusion: The outcome concluded that anaemia could coexist with CVA and henceforth further complicate the situation so treatment of anaemia is of paramount importance. These findings shed light on the prevalence of IDA in post-stroke patients and underscore the crucial need for early detection and treatment.

Keywords

Cerebrovascular Accident, Anemia, Iron, Ferritin

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Anaemia is generally defined as a decrease in haemoglobin (Hb) level, a decrease in hematocrit (HCT) value or a decrease in RBC count. Anaemia may be macrocytic, microcytic, or normocytic. Anemic patients usually present with variable symptoms, some of which include tiredness, weakness, and decreased exercise tolerance. In some severe cases, patients may come with syncope¹. Iron level in the body is important in haemoglobin production and most of the essential functions of the body, so its low level leads to a decrease in iron stores and, subsequently, iron deficiency anaemia. Many factors may lead to IDA as chronic bleeding, such as piles, peptic ulcers, and dysfunctional uterine bleeding. It may occur due to dietary insufficiency of iron or malabsorption. Normal HB value range in adult males from 13.5-18 g/dl and in females from 12-15 g/dl^{2, 3}. The relationship between cerebrovascular stroke and anaemia is not clear now, but theoretically, there is a connection between anaemia and the nervous system, which is affected by low oxygen levels, which are carried by haemoglobin⁴. Anemic patients usually suffer from hyperdynamic circulation, which has a role in affecting the endothelial integrity of the blood

vessels and increasing the risk of thrombus formation that generally leads to emboli, which cause stroke ². Anaemia (by different types) is usually present in about 17% to 28% of stroke patients and also affect strongly the mortality rate and outcome of cases ⁴. This study aims to screen the prevalence of post-stroke iron deficiency anaemia and the management of these cases among patients admitted to Samara General Hospital; after a CVA, patients often experience various health issues that can contribute to developing IDA. These include decreased appetite, dysphagia, reduced gastrointestinal motility and altered nutritional intake due to physical disabilities. In addition, the use of antiplatelet and anticoagulant medications may increase the risk of gastrointestinal bleeding, further exacerbating anaemia in those patients³. IDA significantly affects the recovery and quality of life of stroke survivors. Anaemia is associated with fatigue, weakness, dizziness, and delayed functional recovery. In addition, IDA can impair cognitive function and post-stroke cognitive deficits. Identification and management of IDA among post-CVA patients are essential to improve their recovery outcomes ⁵. This study is done on

cerebrovascular accident patients who were admitted to the emergency unit of Samarra General Hospital and complicated by iron deficiency anaemia as a sequela of stroke from January 2023 to January 2024. As our patients in this study were admitted to the hospital for stroke, we obtained previous consent for being in this study and also for follow-up from the closest relative according to the ethics in our community. Continuous anaemia may affect large blood vessels leading to arterial hypertrophy and arterial remodeling, hence, understanding the causes and underlying pathology contributes to enhancing our knowledge of vascular diseases.

MATERIALS AND METHODS

Sample size: In this study, we take a sample of one hundred stroke patients (age 55-70 years, 1:1 male/female ratio), 35 males are smokers and 10 are females, up to 92% of the patients sample have hyperlipidemia, and 56 of patients are type 2 diabetes (24 are males and 32 are females) and 80 of patients are hypertensive (42 are males and 38 females), all cases are prone to MRI and diagnosed to have stoke ^{1, 6}.All patients were primarily admitted

Table 1: Patient Demography and Compiling Diseases.

to the intensive care unit and neurological wards. The diagnosis of iron deficiency anaemia was first estimated at the first follow-up visits in the second month after discharge from the hospital. Follow-up visits include CBC and transferrin level tests to monitor iron and transferrin levels' elevation, stability, or decrease in some cases. We considered that the cases are IDA when serum ferritin level is lower than 12 ug/L. Cases are admitted to ICU within 6-8 hours after the occurrence of stroke with a mean time of $6.6 \pm 1.5h^{7,8}$.

RESULTS

The age groups of participants ranged from 50-70 years, higher numbers were those with an age range of 61-70 years (30% and 34%) and the lowest were within the range of 50-60 years (12 and 13%) control and CVA patients, respectively. The age of the control group was nearly matched with the CVA patient group, nonetheless, the control group were healthy and the patient group was associated with compiling diseases, including 56% diabetics, 80% hypertensive, and 45% smokers (Table 1).

Variable	Categories	Control	CVA Patients
Age Category	50-60 years	12	13
	51-60 years	30	29
	61-70 years	30	34
	>70 years	28	24
Diabetes Mellitus		0	56
Hypertension		0	80
Smoking Status		0	45

The incidence of IDA in the CVA group (56.3%) is significantly higher than the control group (25.2%) (Table 2). Those who have shown IDA mostly were female (54%) in the CVA group versus mostly male (60%) in the control group.

Low serum ferritin (82%) has been reported in CVA compared to 5% in the control group (p=0.00001). Moreover, most patients diagnosed with ischemic (90%) type of stroke and only 10% diagnosed as hemorrhagic (Table 2)

Table 2: Incidence of Iron Deficiency Anaemia.

	Control % 25.2		CVA Patients % 56.3		Chi-Square	P Value
lda						
Sex	Female	Male	Female	Male		
	40	60	54	46	3.9	0.047
Serum Ferritin	Normal	Low	Normal	Low		
	95*	5	18	82*	120.6	0.00001
Type of Stroke			Ischaemic	Haemorrhagic		
			90	10		

Data expressed as a percentage, *indicate significantly higher at p<0.05 using Chi-square

DISCUSSION

In our study, we find that iron deficiency anaemia is a common problem in CVA patients after hospital admission, leading to a significant decrease in hemoglobin level. Eventually, there is an increase in the volume of infarction due to a decrease in oxygen supply to the brain, hence the increase in the final infarction volume. One of the most common causes is hemodilution which is done after hospital admission. It depends on many factors such as the severity of the stroke, whether the patient is conscious or not, the age of the patient as it is significantly increased in the elderly, whether oral feeding is present or depends totally on parenteral feeding and perfusion time ^{4, 9-15}. Oxygen delivery to the brain can be measured using the formula Hb×Q× SaO₂ multiplied by 1.39 as Q is blood flow and SaO₂ is oxygen saturations in arteries so any decrease in Hb level will affect oxygen supply to the brain and increase in infarction growth entering the patient in a vicious circle as we need to increase blood flow to the brain and more decrease in Hb level and worsen of anaemia which strongly affect the outcome of cases ¹⁶⁻²². Although there is a shortage of studies that analyze the relationship between stroke and iron deficiency anaemia. Alexander et. al. found that instances of aphasia and hemiparesis are associated with IDA and after that deteriorate to cerebral infarction and stroke ²³. Iron is one of the most important minerals responsible for the development and integrity of the central nervous system. Hence, iron deficiency anaemia as a medical condition has very importance in CNS defects such as (cranial nerve palsies, stroke and pseudo tumour cerebri)⁹. Regarding pathogenesis that occurs with iron deficiency anaemia thrombocytosis is usually prominent in these cases and occurs due to an increase in platelet production which arises due to the rise in the level of erythropoietin that occurs in anaemic patients secondary to an increase in megakaryocytes and hence thrombus formation¹⁰. hyperdynamic circulation leads to defects in the blood vessels' endothelium leading to its breakage. This defect may lead to the formation of a thrombus; in some occasions, separation of thrombus will occur, leading to embolism and stroke ²¹⁻²⁴. Maguire et. al. conducted a study between stroke and IDA in young ages and found that more than 53% of cases are associated with IDA ²⁴. The same pathology in the endothelium of the brain's blood vessels leads to inflammation, damage to its tissues, and then hypoxia ⁹. In our study, males represented 46 % and females 54% of stroke cases. Although we find different percentages of males and females in our sample some studies show increasing stroke levels in males more than females the mechanism is unknown, but it may have a relation to testosterone levels ¹¹. In our study, we have 56 cases of anaemic patients associated with stroke with a percentage of 25% to the control group. In our research, we found that 56% of stroke patients have anaemia as the ratio between the cases group and control group was 1:2. Hence, we find that cases came to Sammara General hospital in stroke 56% of them suffering from IDA . So we can consider that IDA is a vital risk factor for stroke and has significant importance. Hence, supplementation and follow-up for cases is essential to decrease risk of recurrence ¹².

Regarding types of strokes, there is an increase in the incidence of Cerebral venous thrombosis more than acute ischemic stroke in our cases of iron deficiency anaemia. Pathogenesis can be explained by thrombus formation due to increased viscosity of microcytic cells and endothelial damage, which are vital predisposing factors for thrombus formation and increased platelet count ^{4, 13-17}. Although one of the most common causes of death in stroke patients is thrombocytosis which may easily lead to different CNS infarctions thrombocytopenia that occurs in association with IDA is primary and benign not act as a cause of death as in reactive one ^{18, 19}. Consultation with a haematologist is required if elevation of platelet count persists, is unexplained, or is symptomatic. Our data indicates that thrombocytosis, IDA, and MCV in multivariate analysis were independent predictive risk factors for stroke (P< 0.05). Changes in platelet count (PLT) and platelet parameters have been reported in IDA. However, the relationship between iron metabolism and thrombopoiesis is not fully known ¹⁷. Some investigators

speculated that the elevated erythropoietin levels in patients with irondeficiency anaemia might modestly increase platelet production by crossreacting with the thrombopoietin receptor ¹⁸. Dealing with risk factors of cerebrovascular stroke has great importance in minimizing the incidence and the outcome of cases and hence decreases the risk and the rate of stroke in individual cases or specific communities so we can deal with single risk factor or with groups of them ¹⁹ for example we can use some prophylaxis in certain conditions as using antiplatelets treatment to decrease the risk of stroke, or we can treat the risk factor itself by treating iron deficiency anaemia.

A general method of preventing risk factors is screening a wide sample of healthy people for specific risk factors that may lead to stroke and dealing with them to minimize the incidence. This method is called primordial prevention⁸. The second level is to deal with a sample of people who already have risk factors such as iron deficiency anaemia but no history of cerebrovascular accidents to prevent or decrease their incidence ⁶. The most advanced level of prevention is to deal with the cases which suffer from stroke actually to prevent their recurrence .so we try in all cases to correct serum iron levels, dealing with any cause of bleeding, follow a healthy lifestyle life by weight control (healthy diet and programmed activity) also stop smoking, controlling blood glucose level, hypertension and hyperlipidemia⁵. The management of post-stroke IDA involves a multimodal approach to treating both the underlying cause and anaemia itself. This includes administering oral and intravenous iron supplementation, optimising nutrition and dietary intake, and dealing with any secondary causes of bleeding-additionally, close monitoring of haematological parameters ¹⁸. Moreover, long-term pharmacological therapy and blood transfusion should be initiated for moderate to severe anaemia cases, respectively 18-26.

CONCLUSION

Post-CVA IDA is a common complication that can significantly impact the recovery and well-being of stroke survivors—understanding the prevalence and effective management strategies by implementing timely detection, appropriate interventions, and collaborative outcomes and quality of life for patients experiencing post-CVA IDA. In our developing countries, it is essential to detect iron deficiency anaemia as early as possible so that we can treat it before a life-threatening complication like stroke develops. To avoid subsequent complications, the study provided insights into treating older age groups and severe anaemia cases as a priority when coexisting with CVA. This ultimately opens the horizon for further studies highlighting the linkage between anaemia and CVA at molecular or subcellular levels.

REFERENCES

 P. J. Mehta, S. Chapman, A. Jayam-Trouth, and M. Kurukumbi, "Acute ischemic stroke secondary to iron deficiency anemia: a case report," *Case Reports in Neurological Medicine*, vol. 2012, no. 1, p. 487080, 2012. M. Panpalli Ates, "Iron-deficiency anemia leading to transient ischemic attacks due to intraluminal carotid artery thrombus," *Case Reports in Neurological Medicine*, vol. 2013, no. 1, p. 813415, 2013.

3. M. Almohri, S. Al Salehi, A. Al Ghawi, E. Husain, and M. Al

Fardan, "Prevalence of Anemia, and Associated Risk Factors among Pregnant Women Attending Primary Healthcare Centers in the Kingdom of Bahrain," *Bahrain Medical Bulletin*, vol. 45, no. 3, 2023.

^{2.} H. Batur Caglayan, B. Nazliel, C. Irkec, A. Dumlu, A. Filiz, and

^{4.} A. G. Munts, P. J. van Genderen, D. Dippel, F. van Kooten, and

P. J. Koudstaal, "Coagulation disorders in young adults with acute cerebral ischaemia," *Journal of neurology*, vol. 245, pp. 21-25, 1997.

- S. E. Vermeer, W. T. Longstreth, and P. J. Koudstaal, "Silent brain infarcts: a systematic review," *The Lancet Neurology*, vol. 6, no. 7, pp. 611-619, 2007.
- W. S. Weintraub *et al.*, "Value of primordial and primary prevention for cardiovascular disease: a policy statement from the American Heart Association," *Circulation*, vol. 124, no. 8, pp. 967-990, 2011.
- E. McLean, M. Cogswell, I. Egli, D. Wojdyla, and B. De Benoist, "Worldwide prevalence of anaemia, WHO vitamin and mineral nutrition information system, 1993–2005," *Public health nutrition*, vol. 12, no. 4, pp. 444-454, 2009.
- H. Y. Ismail and S. A. Salam Hamid Al-Sultan, "ASSOCIATION OF CORONARY ATHEROSCLEROSIS WITH STUTZERIMONAS STUTZERI STRAINS (HASA 1, 2, 3, ANd 4) OF BIOFILMFORMING BACTERIA," *Medical Journal/Medicinski Časopis*, vol. 57, no. 2, 2023.
- Y.-K. Keung and J. Owen, "Iron deficiency and thrombosis: literature review," *Clinical and Applied Thrombosis/Hemostasis*, vol. 10, no. 4, pp. 387-391, 2004.
- B. Lozoff, N. K. Klein, E. C. Nelson, D. K. McClish, M. Manuel, and M. E. Chacon, "Behavior of infants with iron-deficiency anemia," *Child development*, vol. 69, no. 1, pp. 24-36, 1998.
- A. Zhu, M. Kaneshiro, and J. D. Kaunitz, "Evaluation and treatment of iron deficiency anemia: a gastroenterological perspective," *Digestive diseases and sciences*, vol. 55, no. 3, pp. 548-559, 2010.

- 12. M. B. Zimmermann and R. F. Hurrell, "Nutritional iron deficiency," *The lancet*, vol. 370, no. 9586, pp. 511-520, 2007.
- M.-J. Park *et al.*, "The relationship between iron parameters and platelet parameters in women with iron deficiency anemia and thrombocytosis," *Platelets*, vol. 24, no. 5, pp. 348-351, 2013.
- T. Nagai, N. Komatsu, Y. Sakata, Y. Miura, and K. Ozawa, "Iron deficiency anemia with marked thrombocytosis complicated by central retinal vein occlusion," *Internal Medicine*, vol. 44, no. 10, pp. 1090-1092, 2005.
- G. Kaiafa *et al.*, "Anemia and stroke: Where do we stand?," *Acta Neurologica Scandinavica*, vol. 135, no. 6, pp. 596-602, 2017.
- X. Douay, C. Lucas, C. Caron, J. Goudemand, and D. Leys, "Antithrombin, protein C and protein S levels in 127 consecutive young adults with ischemic stroke," *Acta Neurologica Scandinavica*, vol. 98, no. 2, pp. 124-127, 1998.
- P. Munot, C. De Vile, C. Hemingway, R. Gunny, and V. Ganesan, "Severe iron deficiency anaemia and ischaemic stroke in children," *Archives of disease in childhood*, vol. 96, no. 3, pp. 276-279, 2011.
- J. L. Carson, "Morbidity risk assessment in the surgically anemic patient," *The American journal of surgery*, vol. 170, no. 6, pp. S32-S36, 1995.
- K. M. Musallam *et al.*, "Preoperative Hematocrit Concentration and the Risk of Stroke in Patients Undergoing Isolated Coronary-Artery Bypass Grafting," *Anemia*, vol. 2013, no. 1, p. 206829, 2013.
- 20. M. Kuriyan and J. L. Carson, "Anemia and clinical outcomes,"

Anesthesiology Clinics of North America, vol. 23, no. 2, pp. 315-325, 2005.

- S. Chaker *et al.*, "Thrombocytopenia associated with iron deficiency: a rare differential diagnosis of auto-immune thrombocytopenic purpura," *La Revue de Medecine Interne*, vol. 31, no. 9, pp. 631-636, 2010.
- D. K. Reasoner, K. H. Ryu, B. J. Hindman, J. Cutkomp, and T. Smith, "Marked hemodilution increases neurologic injury after focal cerebral ischemia in rabbits," *Anesthesia & Analgesia*, vol. 82, no. 1, pp. 61-67, 1996.
- M. B. Alexander, "Iron deficiency anemia, thrombocytosis, and cerebrovascular accident," *Southern Medical Journal*, vol. 76, no. 5, pp. 662-663, 1983.
- J. L. Maguire, G. deveber, and P. C. Parkin, "Association between iron-deficiency anemia and stroke in young children," *Pediatrics*, vol. 120, no. 5, pp. 1053-1057, 2007.
- H.-F. Chen, T.-F. Ho, Y.-H. Kuo, and J.-H. Chien, "Association between Anemia Severity and Ischemic Stroke Incidence: A Retrospective Cohort Study," *International Journal of Environmental Research and Public Health*, vol. 20, no. 5, p. 3849, 2023.
- W. Yaakoubi, K. Taamallah, A. Haggui, N. Hajlaoui, and W. Fehri, "Prognostic contribution of two-dimensional left atrial strain in patients with asymptomatic mitral stenosis in the Tunisian population," *Med Cas*, vol. 56, pp. 95-100, 2022.