Annals of Medicine and Surgery 78 (2022) 103815

Contents lists available at ScienceDirect

Annals of Medicine and Surgery

journal homepage: www.elsevier.com/locate/amsu

Cross-sectional Study

Moyamoya syndrome and stroke among pediatric sickle cell disease patients in Sudan: A cross-sectional study

Muhab Elmahdi [a], Tarig Fadalla [b,*], Mazin Suliman [b], Mohamedzain Elsayed [b], Ahmed Mohmmed Awad Elhaj [a], Haytham Hussein [b]

[a] Department of Surgery, University of Khartoum, Khartoum, Sudan
[b] Ribat Neurospine Center, Ribat University Hospital, The National Ribat University, Khartoum, Sudan

ARTICLE INFO

Keywords:
Sickle cell disease
Stroke
Moyamoya syndrome
Sudan

ABSTRACT

Background: Sickle cell disease (SCD) is autosomal recessive hemolytic anemia due to hemoglobinopathy commonly in Sub-Saharan Africa, and particularly in Sudan. The disease induces a pro-inflammatory cascade in the intimal layer that leads to hyperplasia and progressive stenosis in the major vessel of the circle of Willis. This is associated with the development of Moyamoya collaterals. The aim of this study is to highlight the frequency of Moyamoya syndrome in Sudanese pediatric patients with sickle cell disease presenting with stroke.

Materials and methods: A descriptive cross-sectional hospital-based study was conducted in the Department of Hematology at Gaafar Ibnauf Pediatric Tertiary Hospital in Khartoum state in Sudan, in the period between March 2021 and August 2021. Secondary data has been collected from the medical record after ethical approval and informed consent.

Results: A total of 104 patients were included in the study. The males were the majority, about 60 (57.7) compared to 44 (42.3%) females. More than half of our study population was in the school-age 54 compared to 42 adolescents and only 8 patients of preschool age. Only 50 out of 104 patients had diagnostic MRA which revealed features of Moyamoya syndrome in 48 (96%) patients. Motor weakness (100%), aphasia (52.9%), and facial palsy (35%) were the major stroke presentations. The left anterior circulation territory was the most common site of moyamoya features involvement in 31 patients out of 48.

Conclusion: Stroke is a common problem in Sudanese pediatric patients with sickle cell disease, with a very high frequency of Moyamoya vasculopathy among patients with stroke presentation. The burden of Moyamoya syndrome in Sudanese pediatric patients with sickle cell disease is underestimated due to the cost of the available screening and diagnostic tools.

1. Introduction

Sickle cell disease is considered one of the significant causes of anemia in Sudan, especially in the western part of the country. it is an autosomal recessive blood disorder that leads to the production of red blood cells that appear abnormal. The disease occurs due to a mutation in the gene that encodes the hemoglobin. Substitution of valine to glutamic acid in position number 6 in the β-globin chain, will cause deoxygenated sickle hemoglobin to form polymers that ultimately destroy red blood cells [1,2]. Neurologic complications in sickle cell disease include silent cerebral ischemia, ischemic/hemorrhagic stroke, posterior reversible encephalopathy syndrome, cerebral fat embolism, cerebral venous sinus thrombosis, and Moyamoya syndrome [3].

Moyamoya disease is a cerebrovascular disease that predisposes affected patients to stroke and is accompanied by progressive stenosis of the intracranial internal carotid artery and its proximal branches. The decrease in blood flow of the main blood vessels of the anterior cerebral circulation leads to the compensatory development of small blood vessels near the apex of the carotid artery, the cortical surface, the pia mater, and the branches of the external carotid artery supplying the dura mater, and the base of the skull. In rare cases, the process also involves the posterior circulation, including the basilar artery and posterior cerebral artery [4].

The disease was initially named "bilateral internal carotid artery hypoplasia" in 1957, then due to the characteristic hazy appearance of the abnormally dilated collateral blood vessel network during

* Corresponding author.
E-mail address: tarigfadalla@gmail.com (T. Fadalla).

https://doi.org/10.1016/j.amsu.2022.103815
Received 5 April 2022; Received in revised form 12 May 2022; Accepted 14 May 2022
Available online 21 May 2022

angiography, the name changed into Moyamoya (Japanese word means puff of smoke). Although "spontaneous circle of Willis occlusion" has recently been suggested as an alternative to the more evocative name "Moyamoya disease", the International Classification of Diseases recognizes "Moyamoya disease" as the specific name for this disease [5–7].

Clinical features of Moyamoya can be attributed to changes in the hemodynamics caused by internal carotid artery stenosis, there are two main types of symptoms: symptoms caused by cerebral ischemia (i.e. TIA, Ischemic stroke) and symptoms caused by the harmful consequences of the compensatory Moyamoya vessel formation (i.e., hemorrhage, headache, seizure). Children have a higher rate of complete stroke; due to their immature oral and reporting skills, this renders them unable to clearly communicate symptoms of TIA, thereby delaying diagnosis and increasing the likelihood of a complete stroke [4].

Patients with characteristic Moyamoya vascular disease and recognized related conditions like sickle cell disease are classified as Moyamoya syndrome, while patients without known related risk factors are referred to as Moyamoya disease [4]. Other related conditions are radiation therapy, Down syndrome, and Neurofibromatosis type 1 [8].

Due to its major socioeconomic and health care sequelae of moyamoya syndrome among patients with sickle cell disease patients and constitutes a serious health problem. In Fact, Sickle cell anemia is an endemic disease in Sudan. However, there is scanty data to reflect the overlaps of cerebrovascular presentations of sickle cell anemia with moyamoya syndrome in Sudan in particular and Africa in general. The aim of this study is to highlight the frequency of Moyamoya syndrome in Sudanese pediatric patients with sickle cell disease presenting with stroke to encourage the implementation of early detective and preventive measures that will consequently have a great social and financial outcome, especially taking into account the considerable prevalence of sickle cell anemia among Sudanese population.

2. Methods

We conducted a descriptive cross-sectional study in the department of Hematology at Gaafar Ibnauf Pediatric Tertiary Hospital which is the largest pediatric hospital in Khartoum State with 498 beds the hospital is one of the largest pediatric hospitals in Africa [9]. This study was a total coverage collecting all the records of the Sudanese sickle cell disease patients who presented with Stroke at Gaafar Ibnauf Pediatric Tertiary Hospital during the period from March 2021 until August 2021. Exclusion criteria included any patients with a history of diagnosis with Down Syndrome or neurofibromatosis.

The study variables included sociodemographic variables such as the Age of the patient, the Gender of the patient, the ethnicity of the parents, and the residency of the patient. Clinical features variables such as the age of the patient when diagnosed with sickle cell disease, the age of the patient when diagnosed with the 1st stroke, the age of the patient when diagnosed with Moyamoya syndrome, the frequency of stroke, and the presenting symptoms. The radiological and angiographic variables included the diagnostic imaging modalities used, the radiological distribution of stroke involvement, and the angiographic distribution of Moyamoya involvement. Moyamoya syndrome is diagnosed in sickle cell disease when MRA revealed stenosis or occlusion in the terminal portion of ICA and the proximal portions of ACA and MCA with an abnormal vascular network in basal ganglia whether unilateral or bilateral [10].

Statistical analysis was performed using (IBM) SPSS statistic 26. The descriptive analysis was carried out by computing frequencies and percentages for categorical variables. Ethical approval was obtained from the Sudan Medical Specialization Board and permission was obtained from the administration of Gaafar Ibnauf Pediatric Tertiary Hospital. The study is compliant with STORCSS criteria [11] and the registration number of the study was researchregistry7771.

3. Results

In total, 104 patients were included in the study. Males outnumbered females by a margin of about 60 (57.7%) to 44 (42.3%). In addition, patients were divided into four age groups: Infant (<1 year) Toddler and preschool (1–5 years), school-age (6–11 years), and Adolescent (12–18 years) in order to assess the impact of the stroke in child development. More than half of our study population was in the school-age 54 compared to 42 adolescents and only 8 patients of preschool age. (Table 1).

In terms of ethnic and geographical distribution, the fathers were 43 (42%) from Afro-Asian tribes, 40 (38%) from Nilo-Saharan tribes, and 21 (20%) from Niger-Congo tribes. While the mothers were 47(45%) from Afro-Asian tribes, 41(40%) were Nilo-Saharan, and 16 (15%) were Niger-Congo (Table 2). As well as half (52 patient/50%) of the patients live in the Western states, 24 (23.1%) in the Central states, 18 (17.3%) in the Eastern states, 7 (6.7%) in the Southern states, and only 3(2.9%) in the Northern states. (Table 1).

Regarding the age of patients when they are diagnosed with sickle cell anemia, age of the first stroke, and the frequency of stroke, there were 58 (55.8%) patients diagnosed with sickle cell disease before their first year of life, with a mean age of 6 months, followed by 29 (27.9) patients diagnosed between (1–5 years), and 16 patients diagnosed between (1–5 years) (6–11 years). In the study, only one patient was diagnosed after the age of 12 years (Fig. 1). Besides, The majority of the patients, 55 (52.9%), had a stroke between the first and fifth years of their lives, followed by 43 patients who had a stroke during their school-age (6–12 years) and only 5 who had a stroke during adolescence (13–18 years), also 56 (53.8%) patients had a stroke at least once. While 48 (46.2%) of patients had multiple strokes (Table 1).

In terms of clinical manifestations, the entire study population suffered from weakness. Aphasia was the second most common symptom in 55 patients, accounting for more than half of our study population. This is followed by facial weakness in 37 patients and seizures in 22 patients. Patients with a decreased level of consciousness and pseudobulbar palsy numbered 15 and 11, respectively. along with 72 (69.2%) of patients reported weakness on the right side, while 23 (22.1%) reported weakness on the left side. In 9 (8.7%) of the patients, the weakness involved both sides of the body (Table 3).

Moyamoya angiographic features were found in 48 of the 50 patients who had a Brain MRA, while the remaining 54 patients did not have a Brain MRA. 36 (34.6%) patients were diagnosed with moyamoya between the ages of 6 and 12, followed by 13 (12.5%) patients diagnosed between the ages of 1 and 5, and only 6 (5.8%) patients diagnosed after the age of 12 (Fig. 1).

Regarding diagnostic methods in stroke presentation, brain CT scan

Table 1
Shows Demographic data of the patients).

Characteristic	Category	Frequency (N)	Percentage (%)
Gender	**Male**	**60**	**57.7**
	Female	**44**	**42.3**
Age	**Infants (<1 year)**	**0**	**0**
	Toddlers and preschool (1–5 years)	**8**	**7.7**
	School age (6–11 years)	**54**	**52**
	Adolescent (12–18 years)	**42**	**40.3**
Geographical distribution	**Western states**	**52**	**50**
	Central states	**24**	**23.1**
	Eastern states	**18**	**17.3**
	Southern states	**7**	**6.7**
	Northern states	**3**	**2.9**
Frequency of stroke	**Once**	**56**	**53.8**
	Multiple	**48**	**46.2**

Table 2
Shows the ethnic distribution of parents).

Characteristics	Category	Frequency (N)	Percentage (%)
Fathers	**Afro-Asian tribes**	**43**	**42%**
	Nilo-Saharan tribes	**40**	**38%**
	Niger-Congo tribes	**21**	**20%**
Mothers	**Afro-Asian tribes**	**47**	**45%**
	Nilo-Saharan tribes	**41**	**40%**
	Niger-Congo tribes	**16**	**15%**

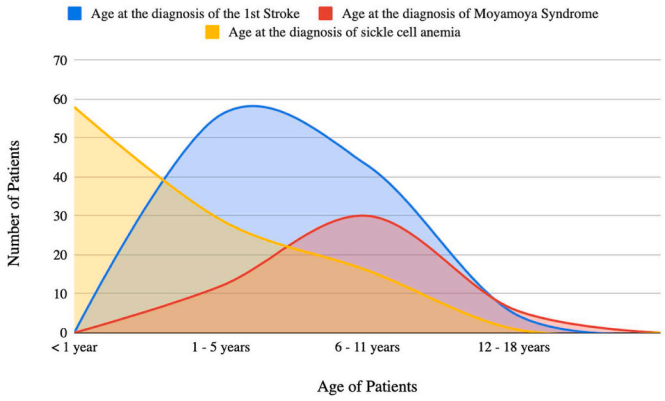

Fig. 1. Shows the relationship between the age of the diagnosis of moyamoya syndrome, sickle cell anemia and the 1st stroke.

Table 3
Shows the clinical presentation of the patients).

Characteristics	Frequency	Percentage
Right side weakness	**65**	**62.5%**
Left side weakness	**30**	**28.8%**
Bilateral weakness	**9**	**8.7%**
Aphasia	**55**	**52.9%**
Facial palsy	**37**	**35.6%**
Convulsions	**22**	**21.2%**
Decrease level of consciousness	**15**	**14.4%**
Pseudobulbar palsy	**11**	**10.6%**

and brain MRI were the most commonly used modalities in 99 and 80 patients, respectively. MRA was performed on 50 patients, and transcranial Doppler was used in only three of them. Notably, none of the study participants underwent digital subtraction angiography (DSA) as a mode of diagnosis. Apart from that, in the territory involved in brain CT or MRI, 68 patients had strokes in the left anterior territory, while 29 patients had strokes in the right anterior territory. While 12 patients experienced a stroke in the posterior circulation, only seven experienced a stroke in the bilateral anterior circulation territory (Table 4).

This trend is also reflected in the involvement of Moyamoya syndrome in Brain MRA, with 31 patients suffering from Moyamoya in the left anterior circulation territory and 15 patients suffering from Moyamoya in the right anterior circulation territory. Moyamoya, on the other hand, affects bilateral anterior circulation in 9 patients and posterior circulation in 7 patients (Table 5).

Table 4
Shows the location of stroke).

Location of Stroke	Frequency (N)	Percentage (%)
Right anterior circulation territory	**29**	**27.9%**
Left anterior circulation territory	**68**	**65.4%**
Bilateral circulation territory	**7**	**6.7%**
Posterior circulation territory	**12**	**11.5%**

Table 5
Shows the location of Moyamoya Syndrome).

Location of Moyamoya	Frequency (N)	Percentage (%)
Right anterior circulation territory	**15**	**28.8%**
Left anterior circulation territory	**31**	**59.60%**
Bilateral circulation territory	**9**	**17.30%**
Posterior circulation territory	**7**	**13.50%**

4. Discussion

Moyamoya has been considered a rare disease located mostly in Japan and Eastern Asia territory. However, with recent development in neuroimaging modalities, particularly Magnetic Resonant Angiography (MRA), the burden of this condition increased considerably to be discovered in other continents [12].in sub-Saharan Africa including Sudan Sickle cell disease (SCD) is considered one of the known predisposing conditions for moyamoya syndrome [4].

Our study comprised 104 pediatric patients with sickle cell disease presenting with stroke. Only 50 out of 104 patients had diagnostic MRA which revealed features of Moyamoya syndrome in 48 (96%) patients., this study seems to include the highest number of Moyamoya patients reported in the African continent in literature. Hammond et al. reported only 17 patients of Moyamoya disease with acquired HIV infection in South Africa which is more than two folds lower than our study population [13]. A systematic review and meta-analysis conducted by Noubiaq et al. explained the lack of data as a consequence of the unaffordability of specific diagnostic tools for Moyamoya disease [14]. This is applied in our case in Sudan where insufficient health resources, lack of healthcare personnel training, scanty information, and studies, with lack of public awareness, have led to alarming early mortality and morbidity [14,15].

The distribution of sickle cell anemia in Sudan is varied due to ethnic and demographic factors, our study reflects a high frequency of the disease in Afro-Asiatic tribes around (father 42%, mother 45%) followed by Nilo-Saharan (father 38%, mother 40%) and Niger-Congo (father 20%, mother 15%).similarly, this finding is supported by the results of the work of Sabahalzain et al. [16]. Additionally, most of the patients live in western states with 56 (54%) patients, followed by central states with 26 (25%) patients. This may be due to gradual migrations of countryside inhabitants to the central part of Sudan, particularly the capital Khartoum.

The first stroke presentation was more common to occur in toddler and preschool age children (55 patients), followed by school-aged children (43 patients) which seems to have a significant correlation and substantial detrimental impact on their academic performance as well as developmental growth, particularly in cognitive and processing speed. Furthermore, multiple stroke presentations were reported in almost half of our study population (48 patients) which is in line with the findings of Scott R et al., who reported that the risk of multiple strokes increased by two folds in patients with Moyamoya disease [17].

Another obvious finding to emerge from the analysis is that motor weakness was found in all of our study population. These results correlate with the findings of Yan Ma et al. in which unilateral limb weakness is the most common symptom of stroke in pediatric patients [18] The commonest side of weakness was the right side in 65 patients. Additionally, the second prominent symptom was aphasia which was reported in 55 patients, more than half of the study population. Followed by facial weakness in 37 patients. Other clinical findings include convulsions and altered level of consciousness and pseudobulbar palsy in 22,15 and 11 patients respectively.

The commonest imaging modality used in our study to diagnose stroke was CT, which was done in 99 patients. MRI was conducted in 80 patients, while MRA was used in 50 patients only. This variation can be clarified by the limited financial means of patients. Although transcranial Doppler ultrasound is non-invasive and non-prohibitive

diagnostic for early detection of the risk of stroke in patients with sickle cell disease, only 3 patients in our study population conducted transcranial Doppler ultrasound. This observation could be explained due to the paucity of trained and qualified personnel to perform transcranial Doppler.

In terms of stroke involvement, 68 patients suffered from a stroke in the left anterior circulation territory, this finding supports that the majority of our patients reported right-side weakness. The right anterior circulation stroke was found in 29 patients. While bilateral and posterior circulation strokes are rare, 7 and 12 patients were reported respectively. This might be explained by the fact that the left common carotid artery is a direct branch from the aortic arch. Similarly, Brain MRA revealed that the most frequent site of Moyamoya involvement in our population was left anterior circulation territory in 31 patients which was twofold more than 15 patients with Moyamoya vasculopathy in the right anterior circulation. Contrarily, 9 patients were diagnosed with Moyamoya in bilateral anterior circulation more than 7 reported Moyamoya in the posterior circulation.

Our study is the first study in Sudan to address Stoke and Moyamoya syndrome in pediatric sickle cell disease patients. Moreover, after performing a narrative review, our study included the largest number of patients with Moyamoya syndrome associated with stroke in pediatric patients with sickle cell disease in Africa. Conversely, the study size was limited by the cost of the available diagnostic imaging (i.e. TCD, MRA, and DSA). in addition to the unequal distribution of dedicated healthcare services, especially in the remote area, and the Lack of awareness and trained healthcare personnel.

5. Conclusion

Stroke is a common problem in Sudanese pediatric patients with sickle cell disease, with a very high frequency of stroke presentation among patients with Moyamoya syndrome. The burden of Moyamoya syndrome in Sudanese pediatric patients with sickle cell disease is underestimated due to the cost of the available screening and diagnostic tools. Our study reported 104 patients with stroke and sickle cell anemia. Only 50 patients had MRA which revealed Moyamoya syndrome in 48 patients. However, a larger study is needed with regional and international collaboration to address the prevalence of Moyamoya syndrome among patients with sickle cell disease. Moreover, early detection protocol for Moyamoya vasculopathy in pediatric sickle cell disease patients is of paramount value for early preventive and therapeutic measures to decrease the risk of Stroke and subsequently its long-term morbidity and mortality.

Ethical approval

The ethical approval was obtained from Sudan Medical Specialization Board.

Source of funding

None.

Author contribution

Muhab Elmahdi: Involved in study design, data acquisition, drafting the article, revising it critically and finally approved the manuscript. Tarig Fadalla: Involved in study design, data acquisition, drafting the article, revising it critically and finally approved the manuscript. Mazin Suliman:Involved in study design, data acquisition, drafting the article, revising it critically and finally approved the manuscript. Mohamedzain Elsayed: Involved in study design, data acquisition, drafting the article, revising it critically and finally approved the manuscript. Ahmed Mohmmed Awad Elhaj: Involved in the design of the study, drafting the article, revising it critically and finally approved the manuscript Haytham Hussein: involved in the study revision only.

Trial registry number

1 Name of the registry: Research Registry
2 Unique Identifying number or registration ID: researchregistry7771
3 Hyperlink to your specific registration: https://www.researchregistry.com/browse-the-registry#home/registrationdetails/6246a23c77cd46001e0deae5/

Guarantor

Muhab Elmahdi.

Declaration of competing interest

The authors declare no conflict of interest of any kind.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2022.103815.

References

[1] A. Eldin, M. Mustafa, O. Abdlgadir, N. Mohamed, H. Elsheikh, A clinical and hematological study on the sickle cell anemia among children in El Obeid hospitals, Sudan (2018) 66–71.
[2] M.A. Adam, N.K. Adam, B.A. Mohamed, Prevalence of sickle cell disease and sickle cell trait among children admitted to Al Fashir Teaching Hospital North Darfur State, Sudan, BMC Res. Notes 12 (1) (2019 Oct 16) 659, https://doi.org/10.1186/s13104-019-4682-5. PMID: 31619285; PMCID: PMC6796395.
[3] S. Farooq, F.D. Testai, Neurologic complications of sickle cell disease, Curr. Neurol. Neurosci. Rep. 19 (4) (2019 Feb 28) 17, https://doi.org/10.1007/s11910-019-0932-0.PMID:30820687.
[4] R.M. Scott, E.R. Smith, Moyamoya disease and moyamoya syndrome, N. Engl. J. Med. 360 (12) (2009 Mar 19) 1226–1237, https://doi.org/10.1056/NEJMra0804622.PMID:19297575.
[5] K.S.K. Takeuchi, Hypoplasia of the bilateral internal carotid arteries, Brain Nerve (9) (1957) 37–43.
[6] J. Suzuki, A. Takaku, Cerebrovascular "moyamoya" disease. Disease showing abnormal net-like vessels in base of brain, Arch. Neurol. 20 (3) (1969 Mar) 288–299, https://doi.org/10.1001/archneur.1969.00480090076012.PMID:5775283.
[7] Research committee on the pathology and treatment of spontaneous occlusion of the circle of Willis; health labour sciences research grant for research on measures for infractable diseases. Guidelines for diagnosis and treatment of moyamoya disease (spontaneous occlusion of the circle of Willis), Neurol. Med.-Chir. 52 (5) (2012) 245–266, https://doi.org/10.2176/nmc.52.245.PMID:22870528.
[8] J.R. Gatti, A.G. Torriente, L.R. Sun, Clinical presentation and stroke incidence differ by moyamoya Etiology, J. Child Neurol. 36 (4) (2021 Mar) 272–280, https://doi.org/10.1177/0883073820967160.Epub.2020.Nov.6. PMID: 33155871.
[9] M.O. Swar, Building Gaafar Ibnauf children's hospital: unprecedented story, Sudan J Paediatr 15 (2) (2015) 100–108.
[10] Research Committee on the Pathology and Treatment of Spontaneous Occlusion of the Circle of Willis; Health Labour Sciences Research Grant for Research on Measures for Infractable Diseases, Guidelines for diagnosis and treatment of moyamoya disease (spontaneous occlusion of the circle of Willis), Neurol. Med.-Chir. 52 (5) (2012) 245–266, https://doi.org/10.2176/nmc.52.245.PMID:22870528.
[11] G. Mathew, R. Agha, For the STROCSS Group, Strocss 2021: strengthening the Reporting of cohort, cross-sectional and case-control studies in Surgery, Int. J. Surg. 96 (2021), 106165.
[12] O.Y. Bang, J.W. Chung, D.H. Kim, H.H. Won, J.Y. Yeon, C.S. Ki, H.J. Shin, J.S. Kim, S.C. Hong, D.K. Kim, A. Koizumi, Moyamoya disease and spectrums of RNF213 vasculopathy, Transl Stroke Res 11 (4) (2020 Aug) 580–589, https://doi.org/10.1007/s12975-019-00743-6. Epub 2019 Oct 24. PMID: 31650369.
[13] C.K. Hammond, A. Shapson-Coe, R. Govender, R. Van Toorn, A. Ndondo, N. Wieselthaler, et al., Moyamoya syndrome in South African children with HIV-1 infection, J. Child Neurol. 31 (8) (2016) 1010–1017.
[14] J.J. Noubiap, M.K. Mengnjo, N. Nicastro, J. Kamtchum-Tatuene, Neurologic complications of sickle cell disease in Africa: a systematic review and meta-analysis, Neurology 89 (14) (2017 Oct 3) 1516–1524, https://doi.org/10.1212/WNL.0000000000004537. Epub 2017 Sep 1. PMID: 28864674; PMCID: PMC5631172.
[15] M.R. DeBaun, F.J. Kirkham, Central nervous system complications and management in sickle cell disease, Blood 127 (7) (2016 Feb 18) 829–838, https://doi.org/10.1182/blood-2015-09-618579. Epub 2016 Jan 12. PMID: 26758917.

[16] M.M. Sabahelzain, H. Hamamy, The ethnic distribution of sickle cell disease in Sudan, Pan Afr Med J 18 (2014) 13, https://doi.org/10.11604/pamj.2014.18.13.3280. (Accessed 3 May 2014).
[17] S.R. Dobson, K.R. Holden, P.J. Nietert, J.K. Cure, J.H. Laver, D. Disco, M. R. Abboud, Moyamoya syndrome in childhood sickle cell disease: a predictive factor for recurrent cerebrovascular events, Blood 99 (9) (2002 May 1) 3144–3150, https://doi.org/10.1182/blood.v99.9.3144.PMID:11964276.
[18] Yan Ma, Qiaoyun Guo, Yali Yan, Ye Zhang, Zhijie Lin, Jianying Zhang, Kaijuan Wang, Chunhua Song, Moyamoya disease: a retrospective study of 198 cases, Med. Clínica 153 (Issue 12) (2019) 441–445, https://doi.org/10.1016/j.medcli.2019.02.024, 0025–7753.