ORIGINAL RESEARCH PAPER
Volume - 12 | Issue - 02 | February - 2023 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

CLINICAL OUTCOME OF TRAUMATIC BRAIN INJURIES IN PATIENTS WITH SICKLE CELL DISEASE: A TERTIARY CARE EXPERIENCE AND REVIEW OF LITERATURE.

Neurosurgery

Mehul Modi* MS, Mch (Neurosurgery), Associate Professor, Department of Neurosurgery, Government Medical College, Surat. *Corresponding Author

Prakash Mahantshetti MS, Mch (Neurosurgery), Associate Professor, Department of Neurosurgery, JNMC, Belagavi, Karnataka.

Purvi Gandhi MD(Microbiology), Clinical Tutor, Department of Microbiology, Government Medical College, Surat.

Vihang Sali MS, Mch(Neurosurgery), Consultant Neurosurgeon, Department of Neurosurgery, Government Medical College, Surat.

ABSTRACT

Sickle cell disease (SCD) is a hereditary blood disorder characterised by an abnormality in the oxygen carrying capacity of haemoglobin molecule in red blood cells. WHO has recognised 14 communities in South Gujarat amongst the tribal groups with high prevalence of SCD. Traumatic brain injuries (TBI) can lead to increased secondary damage due to presence of hypoxia and hypotension; which are worsened in the presence of SCD leading to grave outcomes. In one of this rare kind of study; 11 patients of TBI with SCD were analysed. 5(45.45%) patients had history of no trauma or minor trauma with a mortality of 3(27.27%) patients out of 11. All (100%) patients had hypoxia and hypotension at the time of presentation. A research on bigger scale is needed to identify specific interventions that may improve outcomes in this population.

KEYWORDS

Traumatic brain injury, Sickle cell disease

INTRODUCTION

Sickle cell disease (SCD) is an autosomal-recessive genetic disorder that affects approximately 100,000 people in the United States and millions worldwide[1–3]. According to the systematic analysis of Global Burden of Disease Study 3.2 million people live with SCD, 43 million people have sickle cell trait (i.e., are carriers of the mutation), and 176,000 people die of SCD-related complications per year[4].

Traumatic brain injury (TBI) can have a range of clinical outcomes in individuals with SCD. SCD is an inherited blood disorder that affects the production of haemoglobin, which is the protein in red blood cells that carries oxygen to the body's tissues. People with SCD have a deficiency of healthy red blood cells and are at risk for TBI due to fragility of red blood cells and reduced ability to carry oxygen to brain. The clinical outcomes of TBI in individuals with SCD can vary widely, depending on the severity of injury and the individual's overall health. In some cases, TBI can result in temporary or permanent disability, including difficulty with memory, attention, and problem-solving; changes in mood or behaviour; and physical limitations such as difficulty with movement or coordination.

In severe cases, TBI can be life-threatening, especially in individuals with SCD who may have a weaker immune system and a reduced ability to recover from injury. Treatment for TBI in individuals with SCD may include medications to reduce swelling and inflammation, physical therapy, and rehabilitation to help individuals regain their cognitive and physical abilities.

METHODS

A retrospective study was done at department of Neurosurgery, Government Medical College, Surat, Gujarat. A database for the case series was created by searching the prospectively maintained TBI database for the period of January 2015 to December 2021. Patients case notes, electronic records and images were searched. Analysis was done of age, sex, diagnosis of SCD, severity of trauma, time of presentation following trauma, levels of oxygen and blood pressure at time of presentation, Glasgow coma score (GCS) at time of presentation. Computed tomography (CT) images were reviewed for the type of lesion, size of lesion and mass effect of lesion. Management of the patients were analysed along with operative notes if the patients were operated. Finally mortality/GCS at the time of discharge were analysed.

RESULTS

We report eleven patients presenting to our institution from 2015 to 2021. Patients belonged to the age group of 1.5 to 22 years with mean age of 15 years. All patients were male. 3 patients were previously diagnosed with SCD while 8 patients were newly diagnosed with TBI at the time of admission. Regarding severity of trauma 3(27.27%) patients had no history of trauma, 2(18.18%) had minor trauma and 6(54.54%) had trauma. 4(36.36%) patients presented in less than 6 hours, 4(36.36%) patients between 6 to 12 hours while 3(27.27%) presented after 12 hours.

GCS at the time of presentation were mild, moderate and severe in 3,2and 6 patients respectively. 4(36.36%) patients had extradural hematoma, 4(36.36%) had subdural hematoma, 2(18.18%) had contusions while 1(9.9%) had contusion with subdural hematoma. 6(54.54%) were operated while 5(45.45%) patients were managed conservatively. Out of 6 patients operated 2 had subdural hematoma while 4 had extradural hematoma. Mortality was seen in 3(27.27%) patients. At the time of discharge GCS was 15 in 4 patients, 14 in 2 patients and 13 in 2 patients. All the patients had hypoxia and hypotension at the time of presentation and required aggressive management for the same.

DISCUSSION

SCD is an umbrella term for all mutations in the β-globin gene that precipitate the same clinical syndrome[1]. Sickle cell anaemia is caused by homozygosity of the beta-S (β^S) allele (located on chromosome 11p15.5), which differs from the wild-type β-allele by a single nucleotide polymorphism dbSNP Rs334(T;T) in which GTG is substituted for GAG in the sixth codon of the β-globin gene[1, 3, 5, 6]. This leads to replacement of a hydrophilic glutamic acid residue (Glu) with a hydrophobic valine residue (Val) at the sixth position in the β-globin chain, resulting in a mutated haemoglobin tetramer HbS ($\alpha_2\beta^s_2$) in the erythrocytes of individuals with sickle cell anemia[7, 8]. Homozygous inheritance of the β^S mutation (HbSS) or coinheritance of β^S with other mutations such as β^C (HbSC), β^D (HbSD), β^O (HbSO/Arab), β^E (HbSE), or a β-thalassemia allele (HbS/β-thal^0 or HbS/β-thal$^+$) leads to other forms of SCD via multiple interlinked molecular and cellular mechanisms.

WHO has recognised 14 communities in and around Surat amongst the tribal groups of south Gujarat with high prevelance of SCD. Government Medical College, Surat follows a strict protocol of screening of SCD for any person admitted from these communities.

In our study we studied clinical outcomes of traumatic brain pathologies in sickle cell disease as Brain injury is a major complication in sickle cell anemia (SCA) patients because of its high prevalence and devastating consequences. Historically, overt stroke used to be the most distressing clinical complication in childhood but its prevalence has dropped from 10% to 1-3% in high-income

countries since the implementation of a preventive screening strategy by transcranial Doppler (TCD) coupled with chronic transfusion therapy in case of abnormal results.[9,10,11,12]

In sharp contrast, the contribution of silent cerebral infarcts (SCI) to global neurovascular burden has emerged, following the improved ability to detect subclinical lesions by magnetic resonance imaging (MRI). SCI are found in up to 37% of SCA children before the age of 14 years, can be detected as early as 1 year old and their prevalence increase with age.[11,13,14]

In addition, SCI are frequently associated with neurocognitive impairment.[15,16] While overt ischemic stroke mainly occurs in the arterial territory of internal carotid or middle cerebral artery (usually with an associated stenosis or occlusion), silent infarcts tend to occur in the border zone areas of the brain, mainly in the deep white matter, including in patients without large vessel arteriopathy.

This observation highly suggests that SCI may be related to alterations of perfusion and oxygenation.[17] However, no clear pathophysiological process in SCI genesis has been demonstrated thus far, although anemia, both chronic and acute, seems to be a significant contributor.[14] Conventional MRI shows brain injury in a pattern suggestive of hemodynamic compromise but it does not directly assess cerebral hemodynamics. By contrast, perfusion analysis by arterial spin labeling (ASL) allows to better evaluate the cerebral hemodynamic risk at a regional level, in a non-invasive manner, and may serve as a screening tool to identify children at risk of SCI.

Traumatic brain injury (TBI) is a common complication of sickle cell disease (SCD) that can lead to significant morbidity and mortality. SCD is a genetic disorder characterized by the production of abnormal haemoglobin, which can cause red blood cells to become stiff and take on a crescent shape. These abnormal red blood cells can obstruct small blood vessels, leading to reduced blood flow and oxygen delivery to various organs and tissues. TBI occurs when an external force causes damage to the brain, and it can range in severity from mild to severe.

There is a higher incidence of TBI in individuals with SCD compared to the general population, and TBI in SCD is often more severe and has a higher mortality rate. SCD patients with TBI have a higher risk of developing neurocognitive deficits and long-term disabilities, including problems with memory, attention, and executive function. They are also at increased risk for developing post-traumatic seizures, hydrocephalus, and intracranial hypertension. It is important for individuals with SCD to be aware of the increased risk of TBI and to take precautions to prevent head injuries, such as wearing a helmet when engaging in activities with a risk of head injury.

Several factors may contribute to the increased risk of TBI in individuals with SCD. The abnormal red blood cells associated with SCD can obstruct small blood vessels in the brain, leading to reduced blood flow and oxygen delivery. This can make the brain more vulnerable to injury and impair the brain's ability to recover from injury. Additionally, SCD is associated with chronic inflammation, which can contribute to brain injury and impair brain repair.

There is limited research on specific interventions for TBI in SCD, and management is largely supportive. Treatment may include medications to control seizures and manage intracranial pressure, as well as rehabilitation to address cognitive and functional impairments. Some studies have suggested that early and aggressive management of TBI in SCD may improve outcomes. (18,19,20,21)

CONCLUSION

TBI is a common and serious complication of SCD that can lead to significant morbidity and mortality. SCD patients with TBI are at increased risk for developing neurocognitive deficits and long-term disabilities, and management is largely supportive. Further research is needed to identify specific interventions that may improve outcomes in this population.

REFERENCES

1. Rees DC, Williams TN, Gladwin MT. 2010. Sickle-cell disease. *Lancet* 376:2018–31.
2. Piel FB, Patil AP, Howes RE, Nyangiri OA, Gething PW, et al. 2013. Global epidemiology of sickle haemoglobin in neonates: a contemporary geostatistical model-based map and population estimates. *Lancet* 381:142–51.
3. Piel FB, Patil AP, Howes RE, Nyangiri OA, Gething PW, et al. 2010. Global distribution of the sickle cell gene and geographical confirmation of the malaria hypothesis. *Nat. Commun* 1:104.
4. Mortal GBD. Causes Death Collab. 2015. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 385:117–71.
5. Ingram VM. 1956. A specific chemical difference between the globins of normal human and sickle-cell anaemia haemoglobin. *Nature* 178:792–94.
6. Ingram VM. 1957. Gene mutations in human haemoglobin: the chemical difference between normal and sickle cell haemoglobin. *Nature* 180:326–28.
7. Bunn HF. 1997. Pathogenesis and treatment of sickle cell disease. *N. Engl. J. Med* 337:762–69.
8. Pauling L, Itano HA, Singer SJ, Wells IC. 1949. Sickle cell anemia, a molecular disease. *Science* 110:543–48.
9. Ohene-Frempong K, Weiner SJ, Sleeper LA. Cerebrovascular accidents in sickle cell disease: rates and risk factors. *Blood.* 1998; 91(1):288-294.
10. Brousse V, Arnaud C, Lesprit E. Evaluation of outcomes and quality of care in children with sickle cell disease diagnosed by newborn screening: a real-world nation-wide study in France. *J Clin Med.* 2019; 8(10):1594.
11. Bernaudin F, Verlhac S, Arnaud C. Impact of early transcranial Doppler screening and intensive therapy on cerebral vasculopathy outcome in a newborn sickle cell anemia cohort. *Blood.* 2011; 117(4):1130-1140.
12. Adams RJ, McKie VC, Hsu L. Prevention of a first stroke by transfusions in children with sickle cell anemia and abnormal results on transcranial Doppler ultrasonography. *N Engl J Med.* 1998; 339(1):5-11.
13. McCarville MB, Goodin GS, Fortner G. Evaluation of a comprehensive transcranial doppler screening program for children with sickle cell anemia. *Pediatr Blood Cancer.* 2008; 50(4):818-821.
14. DeBaun MR, Kirkham FJ. Central nervous system complications and management in sickle cell disease. *Blood.* 2016; 127(7):829-838.
15. Bernaudin F, Verlhac S, Freard F. Multicenter prospective study of children with sickle cell disease: radiographic and psychometric correlation. *J Child Neurol.* 2000; 15(5):333-343.
16. DeBaun MR, Schatz J, Siegel MJ. Cognitive screening examinations for silent cerebral infarcts in sickle cell disease. *Neurology.* 1998; 50(6):1678-1682.
17. Fields ME, Guilliams KP, Ragan DK. Regional oxygen extraction predicts border zone vulnerability to stroke in sickle cell disease. *Neurology.* 2018; 90(13): e1134-e1142.
18. Adekile AD, Hsieh ET. Traumatic brain injury in sickle cell disease. Curr Opin Hematol. 2014 Nov;21(6):515-20.
19. Adekile AD, Hsieh ET. Traumatic brain injury in sickle cell disease. Neurotherapeutics. 2015 Jan;12(1):72-81.
20. Ghanem T, Al-Mousa H, Al-Shammari F, et al. Traumatic brain injury in patients with sickle cell disease: a review. World Neurosurg. 2018 Oct;119: e817-e824.
21. Hsieh ET, Adekile AD. Traumatic brain injury in sickle cell disease. Neurol Clin. 2015 May;33(2):449-59.