Research Article

Silent Cerebral Infarcts and Retinal changes in patients with Sickle cell Disease

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Abstract

Background: CNS Complications of SCD include headache, seizures, cerebral venous thrombosis, and strokes. 11% and 20% of children with sickle cell anaemia will have overt and silent strokes respectively before their 18th birthday. 14-20% of SCD patients will develop Sickle cell Retinopathy. **Aim of study:** To look for SCI and Retinal changes in SCD children. **Design-** Prospective Cross sectional study. **Participants-** Below 16 yrs in a tertiary care hospital MYH/CNBC Indore, MP. **Method:** 40 children with SCD < 16 years admitted to Department of Paediatrics, MYH / CNBC Hospital, Indore, from December 2014 to October 2015 were selected and underwent MRI evaluation of brain and fundus examination. **Result:** Only 6 (15%) had presence of AV tortuosity with dialatation and 4 (10%) had presence of SCI ($p>0.05$) out of 40. All patients with SCI had presence of AV tortuosity ($p=0.001$). **Statistical Analysis:** Kruskal wallis test was applied. **Conclusion:** 40 children with SCD below the age of 16 years were included, 4(10%) had SCI and 6 (15%) had AV tortuosity and dilatation of retinal vessels. Asymptomatic children of SCD with unanticipated silent infarcts are highly predictive of subsequent clinical stroke and progressive silent infarction. So, these patients should receive frequent blood transfusion to decrease the level of HbS and Hydroxyurea to increase the HbF levels to prevent further subsequent clinical stroke. Also these children should undergo regular ophthalmic checkup for retinal changes and evaluation by MRI Brain for early detection of cerebral infarcts to prevent future occurrence of stroke.

Keywords: Arteriovenous tortuosity, Sickle Cell Disease, Silent Cerebral Infarcts.

Introduction

Sickle cell disease is having multi-systemic complications, starting with a single base pair of DNA, at the 6th codon of the beta globin chain, which involves almost every system of human body [1]. In India, (Lehman and Kutbush, 1952) sickle cell anemia was first detected in tribes of Nilgiri hills, in Southern India after 42 years of its discovery by James Herrick. Later subsequent studies conducted by various workers confirmed high distribution of HbS gene in Central, Southern and North Eastern India. In certain states such as Madhya Pradesh, Chattisgarh, Maharashtra, Orissa, Jharkand and Gujarat it forms major public health problem. The signs and symptoms of sickle cell vary markedly both with time in the same individual and between different individuals. Some people have mild symptoms while others have severe symptoms and are to be hospitalized for treatment. Pain is the most common complaint in children. It can be severe, acute or chronic, usually in the legs and lower back. Other symptoms include irritability, jaundice, aplastic crisis, acute chest syndrome, splenic and hepatic sequestration [2. In adolescence or adulthood, symptoms of childhood continue along with new symptoms like delayed puberty, severe joint pain, stroke, retinopathy, pulmonary hypertension, nephropathy. The patho-physiologic processes that lead to sickle cell disease related complications result from combination of haemolysis and vasoocclusion. The management of many complications of sickle cell disease continues to improve especially where neurologic complications remain a significant problem. CNS Complications include headache, seizures, cerebral venous thrombosis, and strokes. 11% and 20% of children with sickle cell

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anaemia will have overt and silent strokes respectively before their 18th birthday. Cognitive functions and fine motor skills are known to be affected in these patients [1]. 14-20% of Sickle cell disease patients will develop Sickle cell Retinopathy. Retinopathy is classified as either proliferative or nonproliferative. Retinopathy in sickle cell disease occurs due to arteriolar occlusion and ischemia of the peripheral retinal vasculature. Permanent vision loss is rare [3].

Materials and Method

Type of study – Prospective Cross Sectional Study
Place of study– The present study was conducted in diagnosed Sickle Cell Disease patients admitted to Department Of Pediatrics, MYH/CNBC Hospital, Indore, below the age of 16 years. This study was carried over for one year in Department Of Pediatrics, MYH/CNBC Hospital, Indore.
Sample size – 40 cases
Source of data – The study includes children with sickle cell disease with age group < 16 years in Department of Paediatrics MYH/CNBC Hospital, Indore.
Method– Children with sickle cell disease were evaluated by conducting MRI imaging of Brain (1.5 Tesla) and Fundus examination was conducted by Senior Consultant of Department of Ophthalmology to look for presence of Silent cerebral Infarcts and Retinal changes respectively. Results were interpretated using Kruskal Wallis test by using computerized SPSS system.

Inclusion Criteria

- All patients with sickle cell disease belonging to age of < 16 years with no evidence of clinical stroke

Exclusion Criteria

- All Patients of sickle cell disease with evidence of clinical stroke.
- Those who were not giving consent.

Result

Maximum number of patients 12 (37.5%) belonged to the age group between 8-12 years, 15(30%) belonged to age group of less than 8 years, 13(32.5%) belonged to age group 12-16 years. Maximum number of patients were male children 28(70%). Profile of sickle cell disease in our study maximum patients belonged to Sickle cell anemia that is 18(45%), Minimum constituted by Sickle with persistence of fetal Hb 6(15%).Patients constituted by Sickle β+thalassemia , Sickle β0 thalassemia were 9(22.5%) and 7 (17.5%) respectively. All 40 patients were evaluated for retinal changes, only 6 (15%) had presence of arteriovenous tortuosity with dialatation. 4 (10%) had incidental findings of out of which 2 had pale disc, 1 patient had myopic fundus with atrophy and 1 had presence of bilateral papilledema. Fundus examination of rest of the 30 (75%) patients was Normal. Out of 6 patients who had arteriovenous tortuosity 4 belonged to 12-16 years age group and 2 in 8- 12 years age group and none in the age group less than 8 years. Out of 40 patients 4 had presence of silent cerebral infarcts that is 10% of the total. 36 patients (90%) had no silent cerebral infarcts. Out of 36 patients who had no cerebral infarcts in MRI Brain, 4 had incidental findings that constituted 10% of the total. Small bifrontal haemorrhages in anterior paramedian frontal regions, arachnoid cyst , benign intracranial hypertension, Pachymeningitis with focal cerebritis in frontal region were observed in 1 patient each. Out of the 4 patients who had presence of silent cerebral infarcts 3 belonged to the age group 12-16 years and 1 belonged to the age group 8-12 years. Out of 6 patients who had arteriovenous tortuosity, all 4(100%) patients who developed silent cerebral infarcts were present in this group. Out of the 4 patients who developed silent cerebral infarcts, maximum that patients belonged to sickle cell anemia, and 1 that is belonged to sickle β0 thalassemia. By application of Kruskal wallis test, Silent cerebral infarcts and retinal changes in patients with sickle cell disease was not found to be statistically significant. But relation between presence of silent cerebral infarcts in those patients with presence of arteriovenous tortuosity was found to be statistically significant (p value of 0.001)

Table No. 1: Age wise distribution of cases

Age (years)	No. of Cases (n=40)	Percentage
< 8 years	12	30%
8-12 years	15	37.5%
>12 years	13	32.5%

Table No. 2: Sex wise distribution of cases

Sex	No. of cases (n = 40)	Percentage
Male	28	70%
Female	12	30%

Table No. 3: Profile of sickle cell disease in our study

Diagnosis	Number of patients (n = 40)	Percentage
Homozygous Sickle cell anemia	18	45%
Sickle β+ thalassemia	9	22.5%
Sickle β0 thalassemia	7	17.5%
Sickle with persistent fetal haemoglobin	6	15%

Table No. 4: Retinal changes

Fundal changes	Total number of cases (n=40)	Percentage
AV Tortuosity	6	15%
Others	4	10%
Normal	30	75%

Table No. 5: Age wise distribution of fundus changes

Total number of patients (n=40)		Presence of AV Tortuosity (n=6)	Percentage
< 8 years	(n=12)	0	0%
8-12 years	(n= 15)	2	33.33%
12-16 years	(n=13)	4	66.66%

Table No. 6: Presence of silent cerebral infarcts in present study

MRI Brain Findings	Total (n=40)	Percentage
Silent cerebral infarcts	4	10%
No Infarcts	36	90%

Table No. 7: Distribution of silent cerebral infarcts in each age group

Age Groups wise distribution of Cases (total=40)	Silent Cerebral Infarcts in MRI (n=4)	Percentage in each group
< 8 years	0	0%
8- 12 years	1	25%
12-16 years	3	75%

Table No. 8: Silent cerebral infarcts and AV tortuosity

MRI Brain (n=40)	Fundus Findings (n=40)		
	AV Tortuosity (n=6)	Normal (n=30)	Others (n=4)
Silent Cerebral Infarcts (n=4)	4	0	0
No Infarcts (n=36)	2	30	4
% SCI in each group	66.66%	0%	0%

Discussion

The present study was conducted in a tertiary care teaching hospital, Mahatma Gandhi Memorial Medical College associated Maharaja Yeshwant Rao and Chacha Nehru Bal Chikitsalaya Hospitals. Indore, surrounded by the sickle cell belt of Madhya Pradesh. The signs and symptoms of other common diseases overlap with the symptoms of SCD. Recurrent attacks of musculoskeletal pain, anemia, frequent respiratory infections, jaundice and splenomegaly are the typical features which should arouse suspicion of sickle cell disease. The present study is conducted to highlight the less frequently discussed Central Nervous System and Retinal complications in sickle cell disease patients. To look for the presence of silent cerebral infarcts and identify retinal changes in sickle cell disease patients.

A total of 40 children under 16 years of age were included during the study period. Among these children 28 (70%) were males and 12 (30%) were females. 45% had homozygous sickle cell disease, 22.5% had coexisting thalassemia β+, 17.5% had coexisting thalassemia β0,15% had coexisting hereditary persistence of fetal haemoglobin. In our study out of 40 patients that were evaluated for retinal changes only 6 (15%) had presence of arteriovenous tortuosity with dialatation. 4 (10%) had incidental findings of out of which 2 had pale disc, 1 patient had myopic fundus with atrophy and 1 had presence of bilateral papilledema. Fundus examination of rest of the 30 (75%) patients was Normal. Out of 6 patients who had arteriovenous tortuosity 4 (66%) belonged to 12-16 years age group and 2(33%) in 8-12 years age group and none in less than 8 years age group.

Only Arteriovenous tourtuosity was present in 15% of patients and no other features of sickle cell retinopathy was observed. AV tortuosity was found maximum in age group 12-16 years. No retinal changes were appreciated in patients less than 8 years. U.V Eruchalu et al found No child (aged 3 to 13 years) had ocular symptoms [5]. Retinal pathology was found only in patients over 8 years. Retinal lesions were found in 12 (32.4%) of the children. The most common lesion was retinal infarcts (14.9%), and choroidal infarct in 1 patient (2.7%). Neovasclularization was observed in 2 patients (5.4%). As per J. F. TALBOT et al in their study on Sickle cell retinopathy, Ophthalmological examinations were performed on 74 children, aged 5-7 retinal vessel abnormality, occurring in 30/59 (51%) SS children and in 11/37 (30%) SC children. Peripheral arteriolar closure was observed in 14 (24%) SS children and in 6 (16%) SC children. Arteriovenous anastomoses were seen in 3 children, but proliferative retinopathy was not identified. The prevalence of peripheral vascular closure and retinal patches showed a significant upward trend with age.

Out of the 4 patients who had presence of silent cerebral infarcts 3 belonged to age group 12-16 years (75%), 1(25%) to the age group of 8-12 years, and none among less than 8 years age group. In our study we did not find any silent cerebral infarcts below age of 8 years, maximum infarcts were present in age group more than 12 years but it was not found to be statistically significant.

As per Charles T. Quinn et al Acute silent cerebral ischemic events were detected on 1.3% of MRIs (10 of 771) in 652 children (mean age, 10.0 years), with an incidence of 47.3 events per 100 patient-years (95% CI, 22.7–87.2) [7]. As per R Grant Steen et al at mean age of 10 years, overall prevalence of infarction, ischemia, or atrophy in patients with SCD was 44% (82 of 185), and prevalence of vasculopathy was 55% (102 of 185), in their study without evidence of a significant referral bias [8].

As per Thomas R. Kinney et al in their study among 42 patients (18.3%) patient had silent cerebral infarcts [9].
In our study out of 6 patients who had arteriovenous tortuosity, all 4(100%) patients who developed silent cerebral infarcts were present in this group. And none in group with normal fundus or other fundus findings. The relation between silent cerebral infarcts and presence of AV tortuosity was found to be stastiscally significant with p value of 0.001. Maximum 3 patients with silent cerebral infarcts belonged to sickle cell anemia, and 1 belonged to sickle β0 thalassemia and none in Sickle with persistence of fetal haemoglobin or Sickle β+ thalassemia group. Risk of development of silent cerebral infarcts was higher in patients with sickle cell anemia than in other sickle cell diseases but it was not found to be statistically insignificant.

Limitations: Due to small sample size data obtained was not found to be statistically significant.

Conclusion

The main objective of the study was to identify the Silent cerebral infarcts and retinal changes in children with sickle cell disease. Risk of development of silent

cerebral infarcts is higher in Sickle cell anemia than in other sickle cell diseases.

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