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EVALUATING SPLENIC DYSFUNCTION IN SICKLE CELL DISEASE-AFFECTED CHILDREN

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ABSTRACT

Background: Sickle cell disease, or SCD, is a chronic form of hemolytic anemia that causes increasing damage to key organs through sporadic acute complications. The assessment of the prevalence of splenic dysfunction in children with sickle cell disease in Indian subjects is not well documented in the literature.

Aim: The purpose of this study was to evaluate the prevalence and determinants of splenic dysfunction in children with sickle cell disease from India.

Methods: 132 children with sickle cell disease, ages 1 to 15, were evaluated for splenic dysfunction in this study. Ultrasonography and clinical examination were used to measure the size of each subject's spleen.

Using autologous red blood cells labeled with Technetium-99m (99mTc) and Howell Jolly bodies in peripheral smears, spleen dysfunction was evaluated. Clinical and laboratory factors of splenic dysfunction were evaluated using multiple logistic regression.

Results: 4.6% (n=6) and 19.7% (n=26) of the study participants had absent or impaired splenic function as determined by 9mTc scintigraphy, respectively. 7.5% (n=10) of the kid subjects had Howell Jolly bodies in their peripheral smear; all 10 had splenomegaly, and three had aberrant scintigraphy uptake.

HbS > 70%, reticulocyte count > 4%, children not receiving hydroxyurea, > 5 blood transfusions, > 3 hospitalization occurrences in the past, > 4 episodes of vaso-occlusive crisis (VOC), and age >5 years were independent predictors of splenic dysfunction observed in the study.

The current study shows that antibiotic prophylaxis can be tailored for children from India who have a high prevalence of splenic dysfunction. HbS > 70%, reticulocyte count > 4%, children not getting hydroxyurea, > 5 blood transfusions, > 3 hospitalization events in the past, > 4 occurrences of vaso-occlusive crisis (VOC), and age >5 years are all indicators of splenic dysfunction in Indian children.

Keywords: sickle cell disease, splenectomy, splenic dysfunction, Howell Jolly bodies

Overview

Sickle cell disease, also known as sickle cell disease, is a chronic form of hemolytic anemia that progressively damages essential organs due to sporadic acute problems. One of the most frequently targeted organs in individuals with sickle cell disease (SCD) is the spleen, which is impacted early in life. There is extensive literature on the impact of SCD, including hyposplenism in babies. Sickle cell disease in young children typically manifests as a sequestration crisis due to splenomegaly and elevated splenic red pulp activity, which may coexist with functional loss. However, splenic atrophy and auto-splenectomy by mid-childhood are caused by recurrent bouts of numerous splenic infarcts and vaso-

occlusion. One

Loss of splenic function raises the risk of infection from high-mortality encapsulated pathogens. According to data from Western nations, sickle cell disease patients experience early splenic dysfunction. However, it has been demonstrated that individuals from Asia, the Middle East, and Africa eventually suffer splenic dysfunction. Alpha thalassemia coexistence, long-term red blood cell transfusions, and the usage of HU (hydroxyurea) have all been shown to have positive impacts on the preservation of splenic function.Two

It is crucial to reduce the threshold for suspicion and treatment of infections in individuals with splenic dysfunction by identifying the risk factors. Additionally, it may aid in determining whether penicillin preventative prophylaxis is necessary. The frequency of splenic dysfunction in children with sickle cell disease in the Indian context is not well documented in the literature.3 Therefore, the current study sought to evaluate the clinical characteristics, laboratory data, prevalence, and predictors of splenic dysfunction in Indian children with sickle cell disease.

MATERIALS AND METHODS

The current study sought to evaluate the clinical characteristics, laboratory results, prevalence, and predictors of splenic dysfunction in Indian children with sickle cell disease.

The Institute's Department of Pediatrics provided the study participants. Prior to their involvement in the study, all participants provided written and verbal informed consent.

Using homozygous HbSS and HbS >50% on high-performance liquid chromatography, the study evaluated 132 kid patients of both genders, ages 1 to 15, who had sickle cell disease. Malignancy, celiac disease, chronic liver disease, diabetes mellitus, nephrotic syndrome, tuberculosis, immunological deficiencies, congenital malformations, diseases that could affect spleen function, splenectomized subjects, and subjects whose parents did not give their consent to participate in the study were among the exclusion criteria.

Following the study subjects' final inclusion, each patient underwent a thorough clinical evaluation after a thorough history was obtained. A pre-made organized proforma was used to collect data on a variety of problems, including hydroxyurea intake, mean hemoglobin, the number of blood transfusions received, infections requiring hospitalization, and VOC (vaso-occlusive crisis). Subjects who experienced any disease-related complications, needed a blood transfusion for congestive heart failure, or had hemoglobin levels below 5 g/dL were advised to be hospitalized. Ultrasonography and clinical evaluation were used to measure the size of the spleen.Four measurements were taken by two radiologists.

Paired blood cultures, HJB (Howell Jolly bodies) on peripheral blood smear examination, RBC (red blood cell) indices, and CBC (complete blood counts) were among the laboratory data evaluated. Howell Jolly bodies were found in few cells per 1000 red blood cells in a peripheral smear of the participants; a count of more than 665/106 RBCs was considered indicative of asplenia.5

Splenic function was also evaluated by scintigraphy using autologous red blood cells tagged with Technetium-99m (99mTc). After administering intravenous stannous pyrophosphate for ten to twenty minutes, five to eight milliliters of blood were drawn into a syringe covered with 99m Tc. After being heated to 49.5°C in a water bath for 20 minutes, tagged red blood cells were injected into the infant.Six

Within an hour of injection, planar pictures were obtained utilizing the SPECT CT anterior detector. Based on uptake that was patchy or not visible, uptake that was less than the liver, and uptake that was equivalent to the liver, the splenic function was categorized as missing, reduced, and normal. Hospital records and the individuals' medical histories were used to collect clinical events such the requirement for hospitalization, blood transfusions, sequestration crises, painful crises, and serious infections.

The collected data was statistically evaluated using the Chi-square test, multiple logistic regression, and descriptive measures using SPSS (Statistical Package for the Social Sciences) software version 24.0 (IBM Corp., Armonk, NY, USA).

The mean, standard deviation, frequency, and percentages were used to express the results. A p-value of less than 0.05 was deemed statistically significant.

RESULTS

The current study sought to evaluate the clinical characteristics, laboratory results, prevalence, and predictors of splenic dysfunction in Indian children with sickle cell disease. In this study, 132 children with sickle cell disease, ages 1 to 15, were

evaluated and screened for splenic dysfunction. In the study, there were 51.5% (n=68) females and 48.4% (n=64) males. 36.3% (n=48) of the participants were between the ages of 1 and 5, and 67.6% (n=84) were females between the ages of 6 and 15.

74.25% (n=98), 21.21% (n=28), 92.43% (n=122), and 83.3% (n=110) of the research participants had a history of blood transfusion, severe infections, vaso-occlusive crises, and hospitalization, respectively. In 6.06% (n = 4), 13.64% (n = 18), 9.09% (n = 12), 4.55% (n = 6), 36.3% (n = 48), 22.7% (n = 30), 34.8% (n = 46), 62.1% (n = 82), and 63.6% (n = 84). 100% (n=132) of the study participants received vaccinations in accordance with the national immunization schedule, and 3% (n=4) received penicillin prophylaxis. Meningococcal, H. influenza B, and pneumococcal vaccines were given to 7.6% (n=10), 12.1% (n=17), and 34.9% (n=46) of the patients in the optional vaccination history, respectively.

Hepatitis B, abscess, meningitis, enteric fever, septic arthritis, osteomyelitis, and pneumonia were the infection types found in 1.5% (n=2), 1.5% (n=2), 1.5% (n=2), 3% (n=4), 6% (n=8), and 7.5% (n=10) of the study participants, respectively. 7.5% (n=10) of the participants had Howell Jolly bodies. For 62.5% (n=30), 78.6% (n=44), and 71.4% (n=20), the duration of hydroxyurea splenomegaly was 0–5, 6–10, and 11–15 years. According to scintigraphy, 4.6% (n=6), 19.7% (n=26), and 75.7% (n=100) of the individuals had missing splenic function, impaired splenic function, and good splenic function, respectively (Table 2).

Splenic dysfunction and no dysfunction were observed in 4.1% (n=2) and 58% (n=28) of study subjects aged 0-5 years who had palpable spleens, and in 4.1% (n=2) and 33.3% (n=16) of study subjects who had non-palpable spleens, respectively. Splenic dysfunction and no dysfunction were observed in 25% (n=14) and 53.5% (n=30) of the 6–10-year-old patients with palpable spleens, respectively, and in 10.7% (n=6) of the non-palpable participants.

Splenic dysfunction and no dysfunction were observed in 14.2% (n=4) and 57.1% (n=16) of the 11–15-year-old individuals with palpable spleens, respectively, and in 14.28% (n=4) of the subjects with non-palpable spleens, respectively (Table 3). According to the study's findings, reticulocyte counts more than 4% were observed in 22 and 40 individuals with splenic dysfunction and those without, respectively, with p=0.03. Reticulocyte count >4%, Hb <6 g/dl, HbS levels >70%, not on hydroxyurea, history of >5 blood transfusions, history of >3 hospitalizations, history of >4 VOC, severe infection, and age >5 years were all associated with significant splenic dysfunction (p=0.03, 0.002, 0.01, 0.02, 0.01, 0.001, 0.001, and 0.01 (Table 4).

Reticulocyte count >4%, HbS levels >70%, not on hydroxyurea, history of >5 blood transfusions, history of >3 hospitalizations, history of >4 VOC, severe infection, and age >5 years were significant predictors of splenic dysfunction in sickle cell disease study participants (p=0.03, 0.01, 0.01, 0.02, 0.001, and 0.03, respectively).

DISCUSSION

In this study, 132 children with sickle cell disease, ages 1 to 15, were evaluated and screened for splenic dysfunction. In the study, there were 51.5% (n=68) females and 48.4% (n=64) males. 36.3% (n=48) of the participants were between the ages of 1 and 5, and 67.6% (n=84) were females between the ages of 6 and 15.

74.25% (n=98), 21.21% (n=28), 92.43% (n=122), and 83.3% (n=110) of the research participants had a history of blood transfusion, severe infections, vaso-occlusive crises, and hospitalization, respectively. In 6.06% (n=4), 13.64% (n=18), 9.09% (n=12), 4.55% (n=6), 36.3% (n=48), 22.7% (n=30), 34.8% (n=46), 62.1% (n=82), and 63.6% (n=84) of the individuals, respectively. These findings were similar to those of earlier research by Lammers AJ et al. (2012) and George A et al. whose authors evaluated participants with similar demographic information.

Regarding the disease statistics among study participants, 3% (n=4) had penicillin prophylaxis, and 100% (n=132) had received vaccinations in accordance with the national immunization schedule. Meningococcal, H. influenza B, and pneumococcal vaccines were given to 7.6% (n=10), 12.1% (n=17), and 34.9% (n=46) of the patients in the optional vaccination history, respectively. Hepatitis B, abscess, meningitis, enteric fever, septic arthritis, osteomyelitis, and pneumonia were the infection types found in 1.5% (n=2), 1.5% (n=2), 1.5% (n=2), 3% (n=4), 6% (n=8), and 7.5% (n=10) of the study participants, respectively. 7.5% (n=10) of the participants had Howell Jolly bodies. For 62.5% (n=30), 78.6% (n=44), and 71.4% (n=20), the duration of hydroxyurea splenomegaly was 0–5, 6–10, and 11–15 years.

Scintigraphy revealed that 4.6% (n=6), 19.7% (n=26), and 75.7% (n=100) patients had nonexistent splenic function, impaired splenic function, and good splenic function, respectively. These illness characteristics were comparable to those found in

studies by Wang WC et al. (2011) and Abd El-Ghany SM et al, where the authors reported disease data similar to the current study.

According to the study's findings, splenic dysfunction and no dysfunction were observed in 4.1% (n=2) and 58% (n=28) of subjects aged 0–5 who had palpable spleens, and in 4.1% (n=2) and 33.3% (n=16) of subjects with non-palpable spleens, respectively.

Splenic dysfunction and no dysfunction were observed in 25% (n=14) and 53.5% (n=30) of the 6–10-year-old patients with palpable spleens, respectively, and in 10.7% (n=6) of the non-palpable participants. Splenic dysfunction and no dysfunction were observed in 14.2% (n=4) and 57.1% (n=16) of the 11–15-year-old participants with palpable spleens, respectively, and in 14.28% (n=4) of the non-palpable subjects. These findings were in line with research by Morrissey BJ et al. (2015) and Tewari S et al. (2015), where the authors' reports of splenic dysfunction associated with splenomegaly were similar to the current study.

Reticulocyte counts >4% were seen in 22 and 40 research participants with splenic dysfunction and those without, respectively, with p=0.03. Reticulocyte count >4%, Hb <6 g/dl, HbS levels >70%, not on hydroxyurea, history of >5 blood transfusions, history of >3 hospitalizations, history of >4 VOC, severe infection, and age >5 years were all associated with significant splenic dysfunction (p=0.03, 0.002, 0.01, 0.02, 0.01, 0.001, 0.001, and 0.01).

These results were consistent with those of Dave K et al. and Colombatti R et al, who found that factors affecting splenic function in subjects with SCD included reticulocyte count >4%, Hb <6 g/dl, HbS levels >70%, not on hydroxyurea, history of >5 blood transfusions, history of >3 hospitalizations, history of >4 VOC, severe infection, and age >5 years.

Reticulocyte count >4%, HbS levels >70%, not on hydroxyurea, history of >5 blood transfusions, history of >3 hospitalizations, history of >4 VOC, severe infection, and age >5 years were significant predictors of splenic dysfunction in sickle cell disease study participants (p=0.03, 0.01, 0.01, 0.02, 0.001, and 0.03, respectively).These findings were consistent with research by Jain D et al. and Ladu AI et al, which found that in subjects with SKD similar to the current study, reticulocyte count >4%, HbS levels >70%, not on hydroxyurea, history of >5 blood transfusions, history of >3 hospitalizations, history of >4 VOC, severe infection, and age >5 years were independent predictors of splenic dysfunction.

CONCLUSIONS

Considering its limitations, the present study concludes that the prevalence of splenic dysfunction in child subjects from India is high and antibiotic prophylaxis can be individualized in these children. The independent of splenic dysfunction in Indian children is HbS > 70%, reticulocyte count > 4%, children not receiving hydroxyurea, > 5 blood transfusions, > 3 hospitalization events in the past, > 4 episodes of vaso-occlusive crisis (VOC), and age >5 years.

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S. No	Characteristics	Number (n)	Percentage (%)
1.	**Gender**		
a)	Males	64	48.4
b)	Females	68	51.5
2.	**Age group (years)**		
a)	1-5	48	36.3
b)	6-15	84	67.6
3.	**History**		
a)	Blood transfusion	98	74.25
b)	Severe infections	28	21.21
c)	Vaso-occlusive crisis	122	92.43
d)	Hospitalization	110	83.3
4.	**Presenting symptoms**		
a)	Stroke	4	6.06
b)	Breathlessness	18	13.64
c)	Chest pain	12	9.09
d)	Hematuria	6	4.55
e)	Anemia	48	36.3
f)	Jaundice	30	22.7
g)	Abdominal pain	46	34.8
h)	Fever	82	62.1
i)	Acute painful crisis	84	63.6

Table 1: Demographic data on study participants

S. No	Disease characteristics	Number (n)	Percentage (%)
1.	**Vaccinated as national immunization schedule**	132	100
2.	**Prophylaxis with penicillin**	4	3
3.	**Optional vaccination history**		
a)	Meningococcal	10	7.6
b)	H. influenza B	17	12.1
c)	Pneumococcal vaccine	46	34.9
4.	**Infection type**		

a)	Hepatitis B	2	1.5
b)	Abscess	2	1.5
c)	Meningitis	2	1.5
d)	Enteric fever	4	3
e)	Septic arthritis	4	3
f)	Osteomyelitis	8	6
g)	Pneumonia	10	7.5
5.	**Howell Jolly bodies present**	10	7.5
6.	**Hydroxyurea splenomegaly duration (years)**		
a)	0-5 (n=48)	30	62.5
b)	6-10 (n=56)	44	78.6
c)	11-15 (n=28)	20	71.4
7.	**Scintigraphy**		
a)	Absent splenic function	6	4.6
b)	Impaired splenic function	26	19.7
c)	Good splenic function	100	75.7

Table 2: Disease data in study subjects

S. No	Age years (n)	Spleen palpable				Spleen non-palpable			
		Dysfunction		No dysfunction		Dysfunction		No dysfunction	
		n	%	n	%	n	%	n	%
1.	**0-5 (48)**	2	4.1	28	58	2	4.1	16	33.3
2.	**6-10 (56)**	14	25	30	53.5	6	10.7	6	10.7
3.	**11-15 (28)**	4	14.2	16	57.1	4	14.28	4	14.28
4.	**Total (132)**	20		74		12		26	

Table 3: Splenic dysfunction related to splenomegaly in study subjects from different age groups

S. No	Variables	Splenic dysfunction	No splenic dysfunction	p-value
1.	**Reticulocyte count >4%**	22	40	**0.03**
2.	**Hb <6 g/dl**	24	30	**0.002**
3.	**HbS levels >70%**	20	26	**0.01**
4.	**Not on hydroxyurea**	24	40	**0.02**
5.	**History of >5 blood transfusions**	12	10	**0.01**
6.	**Splenomegaly**	20	74	0.26
7.	**History of >3 hospitalization**	18	26	**0.01**
8.	**History of >4 VOC**	24	28	**0.001**
9.	**Severe infection**	14	14	**0.001**
10.	**Age >5 years**	28	56	**0.01**

Table 4: factors affecting splenic dysfunction in study subjects

S. No	Parameters	Number (n)	Percentage (%)	Adjusted OR (95% CI)	p-value
1.	**Reticulocyte count >4%**	22	68.73	3.376 (1.036, 10.992)	**0.03**
2.	**Hb <6 g/dl**	24	75	1.843 (0.524, 6.463)	0.31
3.	**HbS levels >70%**	20	55.55	4.485 (1.383, 14.575)	**0.01**
4.	**Not on hydroxyurea**	24	75	4.11 (1.22, 14.15)	**0.01**
5.	**History of >5 blood transfusions**	12	37.5	4.131 (1.203, 14.174)	**0.01**
6.	**Splenomegaly**	20	55.55	0.584 (0.176, 1.897)	0.38
7.	**History of >3 hospitalization**	18	56.25	3.517 (1.103, 11.237)	**0.02**
8.	**History of >4 VOC**	24	75	6.990 (1.990, 24.547)	**0.001**
9.	**Age >5 years**	28	87.5	4.577 (1.041, 20.095)	**0.03**

Table 5: Prediction of splenic dysfunction in study subjects with sickle cell disease