ORIGINAL ARTICLE

Splenic Dysfunction in Children With Sickle Cell Disease: A Single Centre Experience From Central India

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ABSTRACT

Objective: To assess the incidence and predictors of splenic dysfunction in children with sickle cell disease (SCD).

Methods: A cross-sectional study was conducted between June 2019 and December 2020 where children aged 1 to 15 years of age with SCD were screened for splenic dysfunction. Children who were splenectomised, those with other diseases known to affect splenic function like congenital malformations, immunodeficiencies, and chronic diseases like tuberculosis, nephrotic syndrome, diabetes mellitus, chronic liver disease, celiac disease or malignancy were excluded. Splenic size was assessed by clinical examination and ultrasonography. Splenic dysfunction was assessed using splenic scintigraphy using Technetium-99m (^{99m}Tc) labeled autologous RBCs and by the presence of Howell Jolly bodies in the peripheral smear. Laboratory and clinical predictors of splenic dysfunction were assessed by multiple logistic regression.

Results: We evaluated 66 children with SCD with a mean (SD) age of 7.41 (3.3) years. Impaired and absent splenic function as assessed by ^{99m}Tc scintigraphy was found in 13 (19.7%), and 3 (4.6%) children, respectively. Howell Jolly bodies in peripheral smear were found in 5 (7.5%) children; 3 of them had abnormal uptake on scintigraphy; all five had splenomegaly. Age > 5 years, > 4 episodes of vaso-occlusive crisis (VOC), > 3 hospitalization events in the past, > 5 blood transfusions, children not receiving hydroxyurea, reticulocyte count > 4%, and HbS > 70% were independent predictors of splenic dysfunction.

Conclusion: The prevalence of splenic dysfunction in children with SCD in Central India is lower than that reported from the West. The decision to start antibiotic prophylaxis can be individualized in these children.

Keywords: Howell Jolly bodies, Pneumococcus, Spleen, Splenectomy, Sickle cell disease

INTRODUCTION

Sickle cell disease (SCD) is a chronic hemolytic anemia associated with episodic acute complications resulting in progressive damage to vital organs. The spleen is one of the target organs affected early, with evidence of hyposplenism reported even in infants [1]. Young children with SCD often present with sequestration crisis with increased activity of the splenic red pulp and splenomegaly, which may coexist with loss of function. However, repeated episodes of vaso-occlusion and multiple splenic infarcts lead to splenic atrophy and auto splenectomy by mid-childhood [1].

Loss of splenic function leads to an increased risk of infections from encapsulated organisms with a high mortality. While data from the West suggests an early onset of splenic dysfunction in SCD [2,3], patients from Asia, Middle East and Africa have been reported to develop splenic dysfunction much later [4,5]. Some factors like the coexistence of alpha thalassemia, the use of hydroxyurea (HU), and chronic red cell transfusions have shown beneficial effects on the preservation of splenic function [4-6]. Identification of risk factors for splenic dysfunction will necessitate lowering the threshold for suspecting and treating infections in these patients. Additionally, it will help determine the need for institution of preventive prophylaxis with

penicillin. Studies on the prevalence of splenic dysfunction in children with SCD from India are scant [5,7]. Hence, this study was planned to assess the prevalence and the clinical and laboratory determinants of splenic function in Indian children with SCD.

METHODS

This cross-sectional observational study was conducted in a tertiary care center in central India from June 2019 to December 2020, after obtaining approval from the institutional ethics committee. Children aged 1 to 15 years with SCD (homozygous HbSS with high-performance liquid chromatography showing HbS >50%) were assessed for enrolment in the study after obtaining informed written consent from parents and assent from older children, as applicable. Children who were splenectomised, or were suffering from other diseases known to affect splenic function like congenital malformations, immune deficiencies, chronic diseases like tuberculosis, nephrotic syndrome, diabetes mellitus, chronic liver disease, celiac disease or malignancy were excluded.

As there was no published literature from India related to the prevalence of splenic dysfunction in children with SCD, the sample size was calculated as 60, assuming the prevalence of splenic dysfunction in children with SCD as 10% with an allowable error of 8% at 5% significance level.

A detailed history including clinical presentation, complications like episodes of painful crises or vaso-occlusive crisis (VOC), infections requiring hospitalization, the number of blood transfusions received, mean hemoglobin, and consumption of hydroxyurea were noted in a case record form at enrolment. Hospitalization was indicated in case of development of any disease-related complication or a need for blood transfusion (Hb < 5 g/dL or presence of congestive cardiac failure). The size of the spleen was assessed by clinical examination as well as by ultrasonography [8]. Measurements were taken by two radiologists in sagittal (longitudinal) and transverse planes (width) with the maximum dimension taken into account. Complete blood count (CBC), red blood cell (RBC) indices, and peripheral blood smear examination for Howell Jolly bodies (HJB), and paired blood cultures were sent as per protocol. The presence of Howell Jolly bodies in patient's peripheral smear was reported as the number of cells per 1000 RBCs with a count of more than $665/10^6$ RBCs being diagnostic of asplenia [1]

Splenic function was also assessed by scintigraphy using Technetium-99m (^{99m}Tc) labeled autologous RBCs. Stannous pyrophosphate was administered intravenously and after 10-20 minutes, 5 to 8 ml of blood was withdrawn into a syringe shielded with ^{99m}Tc. The labeled RBCs were then heated in a water bath at 49.5°C for 20 minutes and subsequently, the child was injected with labeled RBCs [9]. Planar images were taken with an anterior detector after one hour of injection by gamma camera/ SPECT CT machine (NM670DR, GE Healthcare). The splenic function was classified as normal (uptake equal to that of liver), decreased (uptake lesser than liver) and absent (uptake was patchy or not visualized spleen) (**Fig. 1**). Clinical events like any severe infections, painful crises, sequestration crises, requirement of blood transfusions, and need for hospitalization were obtained by history and from hospital records.

Statistical analysis: Data were analyzed using SPSS software version 21.0. Descriptive statistics were used for quantitative variables. Continuous variables were presented as mean (SD) and median (IQR). Parametric and non-parametric tests were used for normally distributed and skewed data, respectively. *Chi*-square test and

univariate and multivariable regression models were used to examine the association between different variables and splenic dysfunction. $P < 0.05$ was considered statistically significant.

A model was planned to predict splenic dysfunction taking below mentioned parameters which were found statistically significant on univariate analysis using the predicted splenic dysfunction = $1 / (1 + \exp^{(-a)})$, Where a = (- 4.1451 + 1.3097 x Age – 1 + 0.98889 x History of major infection – 1 + 1.486 x VOC – 1-0.82896 x Number of admissions – 1 + 0.3915 x BT number – 1 + 1.353 x Treatment history of hydroxyurea – 1 + 1.479 x HbS concentration in HPLC – 1 + 0.154 x Reticulocyte count – 1). A predicted value ≥ 0.5 was considered as splenic dysfunction.

RESULTS

Out of 80 eligible participants with SCD, we enrolled 66 children (34 boys). The mean (SD) age of the study group was 7.41 (3.3) years, and the mean (SD) age at diagnosis was 4.21 (3.06) years. Most of the patients were residents of Raipur (39%) and the most common caste was Sahu (39.3%) followed by Ganda (13.6%) and Kurmi (7%).

The most common presenting complaint was found to be acute painful crisis (63.6%) followed by fever (62.1%) and anemia (36.4%). The most common indication of admissions was VOC followed by anemia and fever. The mean (SD) hemoglobin was 7.62 (1.9) g/dL. At enrolment, 51.1% patients ($n = 34$) were receiving hydroxyurea therapy and 3% ($n = 2$) were receiving penicillin prophylaxis. Coverage with pneumococcal, H. influenzae B and meningococcal vaccines was found in 34.9%, 12.1% and 7.6%, respectively (**Table I**).

Infections were found in 21.2% of children (**Table I**). The most common infections encountered were pneumonia ($n = 5$; 35.5%) followed by osteomyelitis ($n = 4$; 28.6 %). Pneumococcal sepsis was not seen in any patient. Only one child had blood culture-positive sepsis (*Salmonella paratyphi A*).

Splenomegaly was detected on examination in 47 (71.2%) children, confirmed on ultrasonography in all. Splenomegaly detected by examination in various age groups is shown in **Table II**. Another 3 patients revealed splenic enlargement on ultrasonography, which could not be detected on manual palpation. Ultrasonogram also revealed the absence of spleen in one patient. We did not find any association between splenomegaly and splenic dysfunction ($P = 0.376$). Splenic function as assessed by scintigraphy showed dysfunction in 16 (24.2%), of which impaired function was seen in 13 (19.7%), and absent function in 3 (4.6%). Only 2 out of 24 (8.3%) children below 5 years had splenic dysfunction, as compared to 14 out of 42 (33.3%) children aged 5-15 years ($P = 0.022$). The presence of HJBs in peripheral smear was found in 5 (7.5%) cases only; 3 of them had abnormal uptake on scintigraphy.

On univariate analysis, it was found that significant splenic dysfunction was associated with factors like age > 5 years, history of infection, > 4 vaso-occlusive crisis (VOC) episodes, > 3 hospitalizations, > 5 red blood cell transfusions, Hb < 6 g/dL, not receiving hydroxyurea, reticulocyte count > 4% and HbS concentration > 70% (**Table III)**. Multivariate regression analysis revealed that age > 5 years, > 4 vaso-occlusive crisis (VOC) episodes, > 3 hospitalizations, not receiving hydroxyurea, received > 5 blood transfusions, reticulocyte count > 4% and HbS > 70% were independent risk factor for splenic dysfunction (**Table IV)**. A model was found to predict splenic dysfunction with the above parameters which were found to be statistically significant with a coefficient of determination of 74.1%. A predicted value ≥ 0.5 was considered as splenic dysfunction.

DISCUSSION

Out of 66 children with SCD, 24.24% had impaired or absent splenic function detected on scintigraphy. The prevalence of splenic dysfunction in under-five children was one-fourth (8.3%) compared to that seen in children aged 5-15 years (33.33%). Unlike data from the West, majority of children aged 6-15 years in our study (66.6%) had a good splenic function, which is similar to that reported from Middle East [10,11]. The Indian form of SCD belongs to the Asian haplotype also known as Arab-Indian haplotype which has a milder course. Some of the reasons accounted for this milder phenotype in Asians compared to the West are due to coinheritance of alpha thalassemia trait, and higher values of fetal hemoglobin [5].

Splenic dysfunction was seen in two children aged below 5 years in our study. This underscores the importance of screening programs including newborn screening which help in the early diagnosis leading to the early institution of adequate care, counselling and therapy [12,13]. Acute painful crisis was the most common presenting symptom [14,15]. Geography and other precipitating factors such as dehydration due to tropical climate make pain crisis the most common manifestation of SCD in our setting [16].

Since splenic scintigraphy is not readily available at all centres, we developed a model for predicting splenic dysfunction using the risk factors found to be significant on multivariable analysis which may be useful to take decisions on subsequent management and prophylaxis therapy. The most common infection seen in our study was pneumonia (7.8%) followed by osteomyelitis (6%). Only one case was positive for blood cultures (*Salmonella paratyphi A*). This is similar to observations by Morrissey et al where bacteremia was seen in 3.4% with salmonella being the most common isolate [17]. Serious infections were found in 21% (n = 14) of children across all ages (up to 15 years). Hence, taking into account the relatively lower rate of infections and adequate splenic function in most children with SCD, antibiotic prophylaxis may be initiated based on the splenic scintigraphy screening results and individualized based on the presence of risk factors. We are reporting VOC episodes followed by anemia and fever as the commonest indications for hospitalization, which are similar to the findings by Abd El-Ghany et al and Akar et al [18,19].

We did not find any association between splenomegaly and splenic dysfunction, indicating no correlation of spleen volume with splenic function [1]. The concept of functional asplenia in the presence of palpable spleen, can be explained by hemodynamic diversion leading to shunting of blood away from filtration beds and limitation of erythrophagocytosis overwhelmed by sickled RBCs [20]. Higher HbS (>70%) was associated with splenic dysfunction which is explained by the fact that increased HbS predisposes to sickling and VOC causing end-organ damage. We found that 75% of patients with splenic dysfunction were not receiving hydroxyurea at enrolment while among patients with preserved splenic function, 60% were on hydroxyurea. While a large multicentric trial [21] showed the beneficial effects of hydroxyurea therapy in SCD concerning splenic function, another study from Texas [22] reported that hydroxyurea therapy may increase the risk of splenic dysfunction in SCD, particularly when initiated before two years of age. The type of genetic makeup and haplotype should be explored as factors for such diverse outcomes. Splenic dysfunction assessed by HJB, was present in 5 children, but, only 3 of them had splenic dysfunction when assessed by scintigraphy, indicating the presence of HJ bodies may not be specific of splenic dysfunction [23].

The strengths of our study include the use of splenic scintigraphy using ^{99m}Tc labelled autologous RBCs, a reliable test, to assess splenic dysfunction. All tests were performed by the same clinician. A robust sample size enabled us to draw valid conclusions. Our limitations include that we did not screen all children for alpha thalassemia. Since that our study only included patients from Central India, the results may not be representative of the entire subcontinent.

We conclude that the prevalence of splenic dysfunction in children with SCD in Central India is lower than that reported from the West. The decision to start antibiotic prophylaxis can be individualized in these children. We advise conducting more studies from other regions of the SCD belt in India.

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Contributors: AG: Executed the idea, supervision of the study, substantial contribution to drafting the manuscript and final approval; JJ: Data collection and analysis: SJ: Addressed and resolved any questions related to the accuracy or integrity of the work;. DV: Conceived the idea, devised the protocol; MR: Interpreted the data. SSy: Approved the manuscript after revising for important intellectual content; SShah: Refined the idea, approved the protocol. All authors approved the manuscript submitted for publication.

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WHAT THIS STUDY ADDS?

- Indian children with sickle cell disease have a lower rate of splenic dysfunction.
- Accurate assessment of splenic dysfunction using splenic scintigraphy can be used to provide a tailored treatment approach to children with SCD with underlying risk factors like age >5 years, history of > 4 episodes of vaso-occlusive crisis, > 3 hospitalization events in the past, > 5 blood transfusions, children not receiving hydroxyurea, reticulocyte count > 4% and HbS > 70%.

REFERENCES

1. Brousse V, Buffet P, Rees D. The spleen and sickle cell disease: the sickled spleen. Br J Haematol. 2014;166:165-76.
2. El Hoss S, Cochet S, Marin Met al. Insights into determinants of spleen injury in sickle cell anemia. Blood Adv. 2019;3:2328–36.
3. Rogers ZR, Wang WC, Luo Zet al.. Biomarkers of splenic function in infants with sickle cell anemia: baseline data from the BABY HUG Trial. Blood. 2011;117:2614–7.
4. Wali YA, Al-Lamki Z, Hussein SSet al. Splenic function in Omani children with sickle cell disease: correlation with severity index, hemoglobin phenotype, iron status, and alpha-thalassemia trait. Pediatr Hematol Oncol. 2002;19:491–500.

5. Serjeant B, Hambleton I, Serjeant G. Retained Splenic Function in an Indian Population with Homozygous Sickle Cell Disease May Have Important Clinical Significance. Indian J Community Med. 2021;46:715-8.
6. Ladu AI, Satumari NA, Abba AM, Abulfathi FA, Jeffery C, Adekile A, Bates I. Clinical and laboratory factors associated with splenic dysfunction among patients with sickle cell disease in a malaria endemic region. Trans R Soc Trop Med Hyg. 2023;117:859-66.
7. Jain D, Tokalwar R, Upadhye D, Colah R, Serjeant GR. Homozygous sickle cell disease in Central India & Jamaica: A comparison of newborn cohorts. Indian J Med Res. 2020;151:326-32.
8. Dhingra B, Sharma S, Mishra D, Kumari R, Pandey RM, Aggarwal S. Normal values of liver and spleen size by ultrasonography in Indian children. Indian Pediatr. 2010;47:487-92.
9. Ziessman HA, O'Malley JP, Thrall JH, Fahey FH. Nuclear Medicine, Fourth Edition. Elsevier Inc; 2013. p.464.
10. Al-Awamy B, Wilson WA, Pearson HA. Splenic function in sickle cell disease in the Eastern Province of Saudi Arabia. J Pediatr. 1984;104:714-7.
11. Wali YA, Al-Lamki Z, Hussein SS, et al. Splenic function in Omani children with sickle cell disease: correlation with severity index, hemoglobin phenotype, iron status, and alpha-thalassemia trait. Pediatr Hematol Oncol. 2002;19:491-500.
12. Colombatti R, Martella M, Cattaneo L, et al. Results of a multicenter universal newborn screening program for sickle cell disease in Italy: a call to action. Pediatr Blood Cancer. 2019;66:e27657.
13. Dave K, Desai S, Italia Y, Mukherjee MB, Mehta P, Desai G. Newborn screening and clinical profile of children with sickle cell disease in a tribal area of Gujarat. Indian Pediatr. 2022;59:230-3.
14. Kamble M, Chatruvedi P. Epidemiology of sickle cell disease in a rural hospital of central India. Indian Pediatr. 2000;37:391-6.
15. Shah V, Muley P, Choraria C, Rana P, Kanaria D, Markana A. Clinical and hematological profile of sickle cell disease affected children in rural tertiary level hospital. J Pediatr Res. 2017;4:204-8.
16. Tewari S, Brousse V, Piel FB, Menzel S, Rees DC. Environmental determinants of severity in sickle cell disease. Haematologica. 2015;100:1108-16.
17. Morrissey BJ, Bycroft TP, Almossawi O, Wilkey OB, Daniels JG. Incidence and predictors of bacterial infection in febrile children with sickle cell disease. Hemoglobin. 2015;39:316-9.
18. Abd El-Ghany SM, Tabbakh AT, Nur KI, Abdelrahman RY, Etarji SM, Almuzaini BY. Analysis of causes of hospitalization among children with sickle cell disease in a group of private hospitals in Jeddah, Saudi Arabia. J Blood Med. 2021;12:733-40.
19. Akar NA, Adekile A. Ten-year review of hospital admissions among children with sickle cell disease in Kuwait. Med PrincPract. 2008;17:404-8.
20. Pearson HA, Spencer RP, Cornelius EA. Functional asplenia in sickle-cell anemia. N Engl J Med. 1969;281:923-6.
21. Wang WC, Ware RE, Miller ST, et al. Hydroxycarbamide in very young children with sickle-cell anemia: a multicentre, randomised, controlled trial (BABY HUG). Lancet. 2011;377:1663-72.

22. George A, Conneely SE, Mangum R, Lupo PJ, Scheurer ME. Splenic complications in sickle cell disease: a retrospective cohort review. Blood. 2021;138 Supplement 1:766.
23. Lammers AJ, de Porto AP, Bennink RJ, et al. Hyposplenism: comparison of different methods for determining splenic function. Am J Hematol. 2012;87:484-9.

Table I Baseline Characteristics of the Study Population (*n* = 66)

Parameters		Total (*n*=66) n (%)
Age group	1 – 5 years	24 (36.36)
	6 – 15 years	42 (67.64
Gender	Male	32 (48.48%)
	Female	34 (51.52%)
Presenting Symptoms	Fever	41 (62.12)
	Pain in abdomen	23 (34.85)
	Jaundice	15 (22.73)
	Anemia	24 (36.36)
	Hematuria	3 (4.55)
	Chest pain	6 (9.09)
	Breathlessness	9 (13.64)
	Stroke	2 (6.06)
Past history	Hospitalization	55 (83.3)
	Vaso-occlusive crisis	61 (92.43)
	Severe infections	14 (21.21)
	Blood transfusion	49 (74.25)
Prophylaxis	Penicillin	2 (3.0)
Vaccinations	National immunization schedule	66 (100)
History of optional Vaccines	Pneumococcal vaccine	23 (34.9)
	H. influenzae B	8 (12.1)
	Meningococcal	5 (7.6)
Type of infections	Pneumonia	5 (7.57)
	Osteomyelitis	4 (6)
	Septic arthritis	2 (3)
	Enteric fever	2 (3)
	Meningitis	1 (1.5)
	Abscess	1 (1.5)
	Hepatitis B	1 (1.5)
On hydroxyurea		34 (51.15)
Splenomegaly[a]	0-5 years (*n* = 24)	15 (62.5)
	6-10 years (*n* = 28)	22 (78.6)
	11-15 years (*n* = 14)	10 (71.4)
Howell Jolly bodies	Present	5 (7.5)
Scintigraphy	Good splenic function	50 (75.7)
	Impaired splenic function	13 (19.7)
	Absent splenic function	3 (4.6)

Values expressed as n (%)
[a]*assessed on clinical examination*

Table II Splenic Dysfunction in Relation to Splenomegaly in Different Age-groups

Age-group (n)	*Palpable spleen n (%)*		*Non-palpable spleen n (%)*	
	Splenic dysfunction present	*Splenic dysfunction absent*	*Splenic dysfunction present*	*Splenic dysfunction absent*
0-5 years (*n* = 24)	1 (4.1%)	14 (58%)	1 (4.1%)	8 (33.3%)
6-10 years (*n* = 28)	7 (25%)	15 (53.5%)	3 (10.7%)	3 (10.7%)
11-15 years (*n* = 14)	2 (14.2%)	8 (57.1%)	2 (14.28)	2 (14.28%)
Total (*n* = 66)	10	37	6	13

Table III Factors Affecting Splenic Dysfunction

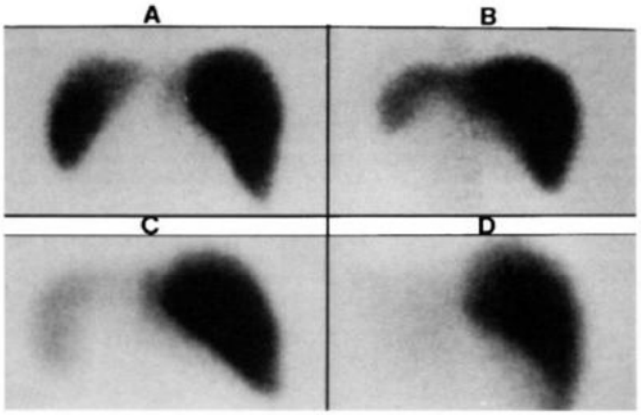
Parameter	*Splenic dysfunction*		*Odds Ratio (95% CI)*	*P Value*
	Present	*Absent*		
Age > 5 y	14	28	5.5	0.022
Severe infection	7	7	4.8	0.001
History of recurrent (>4) VOC	12	14	7.7	0.002
History of repeated (>3) hospitalisation	9	13	3.6	0.025
Splenomegaly[a]	10	37	0.6	0.280
History of recurrent (>5) blood transfusions	6	5	5.4	0.010
Not receiving hydroxyurea	12	20	4.5	0.031
HbS levels > 70%	10	13	1.7	0.028
Hb < 6 g/dL	12	15	7.0	0.003
Reticulocyte count > 4%	11	20	2.2	0.044

Hb Hemoglobin, VOC Vaso-occlusive crisis
[a]assessed on clinical examination

Table IV. Predictors of Splenic Dysfunction in Sickle Cell Anemia

Parameter	***n (%)***	***Beta-coefficient***	***Adjusted Odds Ratio (95%CI)***	***P value***
Age > 5 years	14 (87.5)	1.521	4.579 (1.043, 20.097)	0.044
VOC >4 episodes	12 (75)	1.945	6.992 (1.992, 24.549)	0.002
Number of hospital admissions >3	9 (56.25)	1.258	3.519 (1.101, 11.239)	0.034
Not receiving hydroxyurea	12 (75)	1.42	4.13 (1.20, 14.17)	0.024
Received >5 blood transfusions	6 (37.5)	1.629	4.133 (1.205, 14.172)	0.019
HbS >70% on HPLC	10 (55.55)	1.501	4.487 (1.381, 14.577)	0.013
Splenomegaly [a]	10 (55.55)	-0.542	0.582 (0.178, 1.899)	0.369
Hb <6 g/dL	12 (75)	0.612	1.845 (0.526, 6.465)	0.339
Reticulocyte count > 4%	11 (68.75)	1.217	3.378 (1.038, 10.990)	0.043

Hb Hemoglobin, VOC Vaso-occlusive crisis
[a]assessed on clinical examination
Predicted Splenic dysfunction = 1 / (1 + exp$^{(-a)}$), where a = (-4.1451+1.3097 x Age – 1+0.98889 x History of major infection – 1 +1.486 x VOC – 1-0.82896 x Number of admissions – 1+0.3915 x BT number – 1 +1.353 x Treatment history of hydroxyurea – 1 +1.479 x Hb S in HPLC – 1 +0.154 x reticulocyte count – 1).
If the predicted splenic dysfunction value comes below 0.5 then there will be no splenic dysfunction and if value comes ≥ 0.5, then splenic dysfunction will be present. The coefficient of determination is 74.1% for this model.



Web Fig. 1 Splenic scintigraphy (A) Normal function, (B) Decreased function, (C) Absent function: Patchy uptake, (D) Absent function: Absent uptake