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Case Study

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Sickle Cell Anaemia: Case Presentations from the Indian Tribal Population and Discussion on the Clinicopathologic Aspects

Ruchi Kumari[1] and Manisha Shukla[2*]

[1]School of Biotechnology, Kalinga Institute of Industrial Technology University, Bhubaneswar, Odisha, India
[2]Department of Biotechnology, Pandit S.N. Shukla University, Shahdol, Madhya Pradesh, India

**Corresponding author*

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A B S T R A C T

Sickle cell anaemia (SCA) is one of the gravest inherited disorders which cannot be cured and greatly impacts a person's quality of life. It is a red blood cell-related disorder which happens due to a mutation in haemoglobin gene. This paper details the pathophysiology and clinical presentation of three homozygous sickle cell anaemia patients from three different age groups from the tribal population of Shahdol, Madhya Pradesh and throws light on their complaints, prognosis, hospital visits, tests, recommendations, and the likely course of medical and surgical management. The degree of severity varies from person to person based on access to early screening and diagnosis and knowledge of the clinical interventions available. The paper discusses all the 3 cases comprehensively and connects the dots between the common complaints. Hepatopathy and splenopathy in the afflicted patients are a common observation in SCA patients and a threshold point where the physical ailment becomes inevitable. A high neutrophil to lymphocyte ratio (NLR) is another observation and it can be investigated more in depth to aid in SCA identification. The paper also emphasises on newborn screening in the highly affected tribal populations to save them from the later complications and on educating them about SCA.

Introduction

Sickle cell disease (SCD) is an autosomal recessive molecular disease resulting from a point mutation in haemoglobin beta gene on chromosome 11p15. The mutation is a consequence of the amino acid valine replacing glutamic acid in the B chains of haemoglobin A (HbA) molecule resulting in the formation of the faulty Haemoglobin S (HbS). Individuals with homozygous mutation for HbS, also known as HbSS, suffer from the condition sickle cell anaemia (SCA) in which the normal biconcave red blood cells (RBCs) become sickle shaped, rigid and sticky causing obstruction in blood flow, shortage of RBCs and reduced oxygen supply. This leads to fatal symptoms and eventually shorter

life expectancy in the affected people. The heterozygous individuals carry one sickle cell gene and one normal adult Hb gene resulting in only sickle-cell trait (HbAS) (Figure 1). These individuals are carriers and can pass on the trait to their children.

The global prevalence of homozygous SCD is ~112/100,000 live births with a10x higher prevalence in Africa with 1125/100,000. It affects populations worldwide with higher occurrence in Africa, South America, the Caribbean, Central America, India, Saudi Arabia and Mediterranean nations. India accounts for the highest number of cases in South Asia with approximately 20 million of people with SCD. It extensively exists in tribal populations with nearly 1 in 86 births having SCD. SCD infant screening programmes conducted on both village and state levels through the primary Hb solubility and electrophoresis tests have found higher frequencies in the states of Madhya Pradesh, Gujarat, Maharashtra, Odisha, Rajasthan, Chhattisgarh, Andhra Pradesh, and Karnataka. Among these states, Madhya Pradesh reports an average of 6500 cases of SCA annually comprising of tribal populations spread across the districts. The State Haemoglobinopathy Mission found higher prevalence of sickle cell trait in tribal people of Shahdol district, 28.6% in Panika and 5.1% in Scheduled caste (Choudhary) in a total of 405 blood samples screened. Homozygous SCA was reported in 3.3% of the tribal population (Singh *et al.,* 2009; Singh *et al.,* 2016)**.**

The clinical presentation of SCD varies from person to person based on the underlying genetics, access to early screening and diagnosis and knowledge of the clinical interventions available. It is generally characterized by haemolyticanaemia, acute and chronic ischemic damage to tissues due to vaso-occlusion, splenic infarction and atrophy, renal dysfunction, dactylitis, acute chest syndrome and recurring a plastic episodes due to bacterial and parvoviral and pneumococcal infections. Individuals with HbSS reportedly have a mild to low average blood Hb concentration ~6-11.0 g/dl, normal MCV ~87-92fl, high TWBCs ~17-20 × 103/µL and a higher platelet count as compared to patients with SCT. As end-organ dysfunction is a chronic fatality presented by SCA patients, neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) are often calculated to predict SCA pathophysiology. A progressive increase in NLR and PLR ratios are found in patients with SCA exhibiting renal dysfunction in vaso-occlusive crisis stage as compared to patients in steady state against HbAA controls (Alagbe and Olaniyi, 2019).

Initial screening happens based on the Hb solubility test. If found positive, the pathophysiology is detected through diagnostic tests like haemoglobin electrophoresis and chromatography (HPLC) tests to measure the percentage of HbF, HbA and HbS followed by HPLC of parents and sibling samples to construct the genetic history.

Blood transfusions and medications to treat the symptoms are the usual therapeutic interventions recommended. Blood transfusion aims to infuse blood with increased oxygen-carrying capacity and reduce the HbS%. But chronic transfusion leads to increased iron load with the need for iron chelation therapy post 1-2 years of transfusion based on the ferritin levels. Deferoxamine, deferiprone and deferasirox are commonly used for iron chelation.

Hydroxyurea, a ribonuclease reductase inhibitor, which works by increasing the levels of HbF and helps keep the RBCs bigger and rounder preventing sickling, is the most promising medication available. Other than that, drugs like L-glutamine (Endari) and Crizanlizumab are prescribed for reducing the episodes of pain crises in patients above 16 years. Voxelotor is given to patients older than 12 to improve blood flow and alleviate the risk of anaemia. Some pain-relieving medications are also prescribed. Penicillin prophylaxis in infants nearly 2 months old to up to the age of 5 years helps keep infections in check and vaccinations against pneumonia, hepatitis B, flu, meningitis, etc are essential preventative therapies for children. Patients suffering from splenic complications might

eventually need splenectomy due to splenic abscess, increased RBC sequestration or hypersplenism (splenomegaly). However, all these therapies are palliative and do not cure SCA completely. Stem cell or bone marrow transplant is the only way to completely cure SCA by replacing the unhealthy sickle-shape blood forming cells (stem cells) with healthy cells. Allogeneic transplant is done taking cells from a family member, relative, unrelated donor or from umbilical cord blood. Based on HLA-typing, a matching donor is found. However, not all patients are eligible for hematopoietic stem cell transplantation (HSCT) depending upon the complications involved. Another curative option being explored for SCA is gene therapy that involves gene editing or modification using genetic tools like viral vectors to alter the mutation to suppress HbS production or to enhance HbF and HbA synthesis.

Case Series

Case Presentation 1

A 17-year-old boy presented to the National Institute of Research in Tribal Health (ICMR-NIRTH), Jabalpur with a history of blood transfusions from the age of 2 years, occurrence of jaundice in 2009 and 2013 and episodes of pain in different body parts. In March 2023, he was diagnosed with HbSS condition by HPLC testing. The patient had a height of 155 cm and weight 48 kgs (BMR=1298 kcal/day) during presentation with B-positive blood group.

The blood pathology report showed reduced levels of RBC and haemoglobin (Table 1). The percentage volume of red blood cells in blood (haematocrit) was also found to be very less than the normal. The GRA, PCT and P-LCC returned higher values than normal. However, the sickling test came out to be negative from the study of red blood cell morphology. Hence, due to other indications, HPLC was recommended for a confirmatory diagnosis. The Division of Genetic Disorders, ICMR-NIRTH, confirmed Hb-SS condition through the electrophoresis pattern.

The SGOT/AST values present in the blood biochemistry report indicated liver damage with increased bilirubin values. An AST of 73 U/L was reported (Table 2). The report showed elevated levels of total serum bilirubin suggestive of increased blood haemolysis and of possible damage to the liver because of vaso-occlusion.

Patient's serology report came out negative for Hepatitis B surface antigen (HBsAg) rapid test and Hepatitis C virus (HCV) rapid test. The biochemistry evaluation report for the blood sample turned out normal with the random blood sugar value, blood urea, serum creatinine and serum electrolyte (K^+& Na^+) values lying within the normal range.

The diagnosis for ultrasound imaging (USG) for upper abdomen was done on March 6. The scan reports showed a liver size of 15.5 cm and normal diameter for portal vein (PV), no dilation in common bile duct (CBD) and intra hepatic biliary radicals (IHBR). A sonolucent gall bladder, small spleen size (4.4 cm) and heterogeneous hypoechoic lesions were noted. Borderline hepatomegaly and aortocaval pre-aortic, para-aortic, and mesenteric lymph nodes were interpreted.

The USG for upper abdomen done on March 10 resulted in hepatomegaly (16 cm liver) with slightly raised echotexture, further reduced spleen size of 3.5 cm and multiple mesenteric pre- and para-aortic lymph nodes found with the largest measuring 14 x 6 mm.

Parents' blood electrophoresis tests could not be conducted due to unavailability of samples and hence pedigree analysis could not be done. The patient had received blood transfusion only once at the age of 2 years and had a normal life until jaundice surfaced at the age of 4 years. Post the entire diagnosis and confirmation, the condition was found not to be severe and manageable with regular administration of 5 mg folic acid supplement as a haematinic to reduce sickling of RBCs and restore normal Hb.

Case Presentation 2

A 30-year-old female presented with symptoms of body ache and pain in hands, feet, and stomach. She had a surgery for splenectomy at the age of 14 years, and she has been on regular blood transfusion since then. Her father was a sickle cell anaemia patient (HbSS) who had splenectomy but died at the age of 38 years.

However, her mother is heterozygous (HbAS) with no symptoms and a normal life. Among siblings, she has two brothers, both homozygous for sickle cell anaemia with spleen removed and one heterozygous sister. She is married to a normal person with no mutation for sickle cell anaemia (HbAA) and has a 10-year-old heterozygous son with sickle cell trait but no symptoms as confirmed through blood electrophoresis pattern (Figure 2).

The patient had received blood transfusion after splenectomy. Drugs prescribed at that time were Moxikind CV 375, Polybion injection, Maxicef O 300 mg and folic acid tablets to function as nutritional supplements to restore oxygen supply and fight bacterial infections.

The patient was diagnosed with HbSS at the age of 21 years through the blood electrophoresis report. The foetal haemoglobin (HbF) percentage was 16.67%. The ultrasonography report for upper abdomen came out to be normal. At 24 years of age, the patient complained of pain in the bilateral groin off and on for the past 4 years and aggravated since few days with difficulty in walking. On orthopaedic examination, tenderness was observed over the groin and the left axis was found at a higher level with shortening present.

The patient was diagnosed with bilateral hip arthritis. The medicine prescribed included Tramadol 2-amp injection, Hydroxyurea 500 mg, Udiliv 150 mg, Polybion syrup, Etova tablets, Pan 40 tablets, and Calcimax for a month. Physiotherapy comprising of hip abduction and hip flexion exercises was also advised along with plentiful of oral fluids. The patient again complained of persisting pain in both sides of the hip at the age of 27 years. X-ray for both the hips was observed for the anteroposterior oblique position. Avascular necrosis of bilateral hip was noted, and total hip replacement was advised. The case was referred to a higher centre for medical opinion on the management of the painful crisis condition. Again at 30 years of age, for the same complain, doctor prescribed Ultracet tablets in case of pain, hydroxyurea 500 mg and folic acid 5 mg along with Vit D3. The doctor also referred the case to orthopaedics for total hip replacement.

Patient's investigation profile revealed reduced Hb 8.3 g/dl, reduced packed cell volume of 35% (Table 3). The mean corpuscular volume was noted to be normal, but the average Hb concentration in each RBC was less than normal. The neutrophil-to-lymphocyte ratio was calculated as 2.

The blood biochemistry report revealed erythrocyte sedimentation rate (ESR) as 27.9%. The serum bilirubin levels were also reported to be significantly higher than normal (Table 4). The chest X-ray and ECG reports were normal.

The patient had been admitted with a poor general condition with complain of fever, abdominal pain, and pain in multiple joints. On treatment with medications such as hydroxyurea, analgesics like paracetamol and tramadol, the patient improved symptomatically and clinically on examination.

Case Presentation 3

A 11-year-old girl (weight 22.2 kg) presented with symptoms like swelling in hand and face, stomach pain, chest pain, swelling in liver and enlarged spleen. She had been diagnosed with homozygous sickle cell anaemia at the age of 4 years through haemoglobin electrophoresis (Figure 3). The capillary zone electrophoresis reported an HbS level of 64.9 % suggestive of sickle cell disease and parental studies were recommended (Table 5).The electrophoresis test performed again at the age of 10

years yielded a value of HbS 48%.The patient's mother tested positive for sickling while her father has not been tested yet. The patient has 2 siblings: a 10-year-old sister with sickle cell trait (HbAS) and a 7-year-old brother (HbAA). Around 40% sickling was observed in the patient's red blood cells. The patient has O-positive blood group.

The patient receives blood transfusion 2 to 3 times every month. Owing to this, she tested positive for iron overloading in serum ferritin tests reporting a significantly high value of 1172.3 ng/ml at the age of 10 years and 991.64 ng/ml at 12 years. As such, she was given iron chelation therapy.

Patient's complete blood count profile revealed low values of Hb 6.9 g/dl, HCT 19% and total erythrocyte count 2 million/µl, higher value of red blood cell distribution width (RDW-CV) 22.5%, a considerably higher than normal NLR ratio of 3.5 and a very high platelet count131 x 10^3/µl at the age of 11 years (Table 6).

The physical and microscopic urine examination yielded normal results. Trace levels of albumin was found in chemical investigation of urine. The Widal test was found to be positive for O (surface) antigens and H (flagellar) antigens indicating bacterial infection in the blood and enteric fever. The SGPT or alanine aminotransferase test value was found to be 61.77 iu/l, higher than the normal range of 5-35 iu/l, indicating liver disorder of injury (Table 7).

Ultrasonography of the whole abdomen revealed mildly enlarged liver, distended gall bladder, normal-sized pancreas, and mild hepatosplenomegaly with a spleen size of 10 cm at the age of 6 years. The scan was negative for any intrahepatic radicles. No signs of pleural effusion, ascitesor lymphadenopathy were observed. The urinary bladder did not show the presence of any mass or calculi and both kidneys were of normal size.

The child was administered Hb1 vaccine when 4 years old and Hep A1 at 5 years to protect against hepatitis virus. Naproxen 250 mg, Trixon plus kid, Flexon (ibuprofen 400 mg + paracetamol 325 mg, hydroxyurea 500 mg, folic acid 5 mg and Zincovit were medicines prescribed for palliative treatment.

As the patient is of a very young age, the possibility for bone marrow transplant was also inquired. HLA (human leukocyte antigen) typing was done to find if her younger sister could be a match. Fortunately, her sister turned out to be a 12/12 match to the patient making her the best potential donor for bone marrow transplant. The transplant is scheduled to happen in September 2023.

Results and Discussion

Case 1

The blood pathology report values (Table1) indicated high granulocyte count, higher platelet volume in blood and platelet-large cell count showing higher% of larger platelets in circulation. All these might imply thrombosis and vaso-occlusive crisis (VOC) as platelets are activated in the steady state in SCD patients which enhances during VOC (Villagra *et al.*, 2007). However, sickling of RBCs was confirmed as negative based on the observed Hb morphology.

The blood electrophoresis showed positive results for HbSS confirming that the patient has homozygous sickle cell anaemia. For further consolidation of test result, the doctor asserted that parents' blood samples are required for complete investigation to issue a final confirmatory report.

AST or aspartate aminotransferase levels detected in blood biochemistry tests measures the amount of liver enzyme in the blood to detect liver health. A higher AST of 73 U/L was found which could be due to liver ischaemia or vaso-occlusive crisis, liver enlargement in the patient, or the accumulation of sickled-shape RBCs in the lobular parenchyma of liver. The elevated level of total serum bilirubin was indicative of increased haemolysis of the sickled-cell RBCs and hence free Hb in blood causing pale

eyes and skin that explains the occurrence of jaundice in the patient. In this scenario, blood transfusion to replace the damaged red blood cells and drugs like Voxelotor that aid in reducing cell sickling can help treat the jaundice. The higher bilirubin levels can also be indicative of liver dysfunction due to blocked blood supply to the liver.

The negative blood serology report ruled out the risk of viral hepatitis B and C which is a common consequence of frequent blood transfusion in SCA patients (Banerjee and DeBaun, 2023).

Hepatomegaly was confirmed through the ultrasound imaging of the upper abdomen. It is a result of sickled cells causing obstruction of the sinusoids resulting in pain and a declining haematocrit with increased liver size. This happens as the sickle cells die faster than the liver can filter them out leading to increased serum bilirubin and meanwhile the obstructed blood flow causes reduced oxygen supply and hepatic dysfunction.

Because of hepatomegaly, the patient suffered from jaundice in two consecutive years. However, it was manageable in the patient with a healthy diet, increased water consumption to help excrete the bilirubin, avoiding exhaustive physical activities and regular administration of 5 mg folic acid (folate or Vitamin B9) supplement to help make new red blood cells. Also, no further blood transfusion was required.

Case 2

The patient had complained of generalized body pain, more concentrated to quadrants of the abdomen. The persisting joint pain, splenomegaly resulting in splenectomy, complete blood count report with reduced haemoglobin and high NLR ratio as compared to the normal and higher serum bilirubin levels were all consistent with sickle cell pain crisis.

The splenectomy done at the age of 14 years is well-explained by the fact that spleen is one of the early organs to be affected in SCA. Splenomegaly followed by splenectomy in the patient must have been performed due to progressive atrophy in the organ due to repeated occurrence of vaso-occlusion and infarction caused by sickling. The considerably high foetal haemoglobin level reported in the patient is an important etiologic factor for splenomegaly subjecting the patient to acute splenic sequestration crisis and hence, splenectomy becomes the evident step for patient management.

The NLR ratio found is higher than what is generally reported in normal females(1-1.2) (Table 3). NLR is a potential biomarker for SCD which has been reported to be higher in sickle cell patients in vaso-occlusive crisis then steady state patients or healthy controls. Hence, the high NLR noted can imply bacterial infection, fever, inflammation, and pain.

The high serum bilirubin level aligns with RBC sickling and degradation. This can result in ischaemia, sequestration and cholestasis and depending upon the severity might causeliver dysfunction due to hyperbilirubinemia.

The clinical management of the patient was more focused on treating the symptoms for physiological improvement. Medicines like Moxikind CV 375 and Maxicef O were given to treat bacterial infections following splenectomy and polybion injection and folic acid tablets were prescribed as vitamin B-complex supplements to aid in red blood cell production to treat the anaemia.

For treating the bilateral hip arthritis, the patient was prescribed drugs like Tramadol to relieve severe pain in the joints, Udiliv for protecting the liver, Etova as a non-steroidal anti-inflammatory drug to treat the pain and inflammation in the hip arthritis and Calcimax to maintain the calcium levels for arthritis. Hydroxyurea was also given to reduce sickling ensuring improved blood flow and oxygen delivery to the organs. The bilateral hip arthritis gradually worsened and by the age of 27 years, avascular necrosis of bilateral hip was noted. As

such, for the pain and crisis management, total hip replacement was advised. This has been referred to the higher medical centre for final decision, however, hip replacement has not been finalized yet. Meanwhile, the patient is being treated with Ultracet tablets to reduce pain, hydroxyurea 500 mg and folic acid 5 mg along with Vit D3 to regulate calcium level and maintain bone health.

With the above diagnosis and case history, the patient is not expected to have a good life span. The condition might worsen post total hip replacement as the patient would be impacted with very limited physical activity and the chances of bacterial infection might increase due to the prosthetics due to the existing blood condition. However, it might be a necessary step to improve the immediate quality of life and relieve the chronic pain.

Case 3

The patient had known complain of sickle cell anaemia with an enlarged spleen and liver. She had pain in different body parts which is a common SCD symptom due to sickle cell crisis. The sickle cells obstruct the blood flow to the chest, joints and abdomen.

The swelling in hand and face is because of the inflammatory response generated by the body to oxygen-deprived tissues because of vaso-occlusion. Based on the intensity of crisis, the pain can be acute or chronic (Okpala *et al.*, 2002).

A larger variation in size of RBCs beyond the normal range was confirmed by the high red blood cell distribution width reported in CBC test. This is an indicator of cell sickling and hence, the low haemoglobin value due to shorter lifespan of sickled red blood cells. As a result, the patient required frequent blood transfusion leading to iron overload. Excess iron build up could be a cause of more painful episodes. To prevent any organ damage, iron chelation therapy was given to the patient to bind to the extra iron and remove it from the body through faeces and urine. The chelation therapy was given based on frequency and type of transfusion, the amount of iron sequestered and the degree of damage in patient's liver and heart. Drugs like Deferoxamine (IV/IM/SC administration) and Deferiprone and Deferasirox (oral administration) are commonly used as iron chelating agents. The drug used for this patient is not known (Walter and Patrick, 2009).

The NLR ratio calculated for the patient is quite higher than the normal suggestive of patient's immune response to inflammation with increasing neutrophil count due to stress and reducing lymphocytes due to apoptosis.

The high NLR ratio can be indicative of progression of SCA in the patient and tissue or organ damage due to oxidative stress and necrosis resulting in action from the innate and adaptive immune systems and inflammatory insults (Emokpae and Mathias Abiodun, 2016). Naproxen 250 was given to provide relief from muscle, joint and stomach pain and to treat the inflammation.

The patient was found positive for the Widal test confirming bacterial infection. Trixon plus kid tablet was prescribed to fight against the bacterial infection and prevent growth and spread. Flexon tablet, a mixture of ibuprofen and paracetamol, was given as an analgesic to alleviate the pain, infection-related enteric fever, and inflammation.

The patient's ultrasonography (USG) reports showed enlarged spleen which is a very common observation in sickle cell anaemia patients as the sickle-shaped RBCs are pointy and sticky. They clog the spleen's blood vessels and obstruct blood flow.

As the sequestration builds up, spleen gets bigger in size. Persisting splenic sequestration results develops pallor, weakness, and increased heart rate. It also explains the abdominal pain in the patient. That is why the patient required frequent blood transfusion to offset the impact of sickle cell accumulation and splenomegaly (Kane *et al.*, 2023).

Table.1 Blood pathology findings at the time of admission

Complete Blood Count	Result	Normal Range
White blood cells	15,500/mm^3	4000-15,000/mm^3
Red blood cells	3.02 million/mm3	4.2-6.9 million/mm^3
Haemoglobin	9.4 g/dl	Male: 13-17 g/dl
Polymorphs	69%	40-75%
Lymphocytes	24%	20-40%
Monocytes	4%	2-10%
Eosinophils	3%	1-7%
Basophils	0%	0-1%
Total Platelet Count	2.95 lakhs/mm3	1.5-4.5 lakhs/mm^3
Haematocrit	27%	41-50%
MCV	90 fl	80-100 fl
MCH	31 pg	27-34 pg
MCHC	34 g/dl	30-35 g/dl
RDW-CV	14.7%	11-14.5%
GRA	10,340/ mm^3	2000-7000/mm^3
PCT	0.306%	0.108-0.282%
P-LCC	121 X 10^9/l	30-90 X 10^9/l
Differential count:		
Lymphocytes	3180/mm^3	800-4000/mm^3
Sickling Test	Negative	
Interpretation	HPLC for confirmation	

Fig.1 Pictorial representation of Sickle Cell Disease.

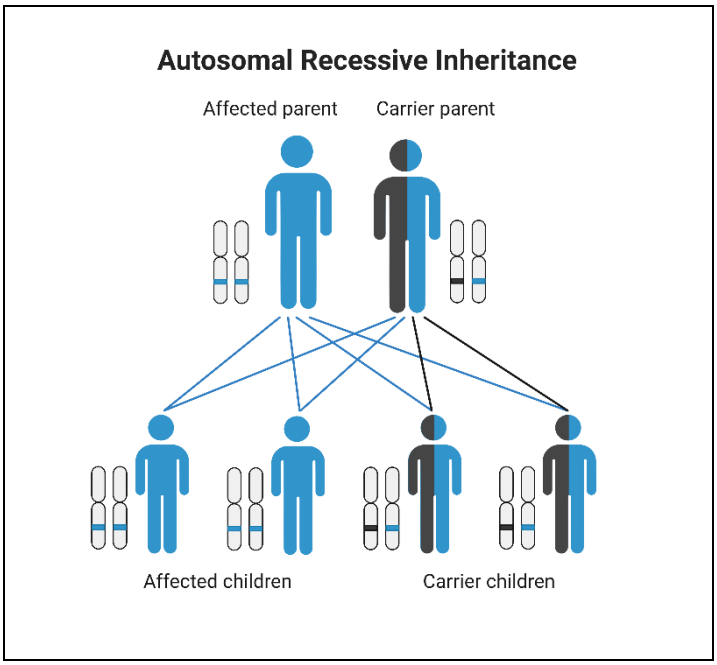


Table.2 Blood biochemistry investigation report

Test	Patient's Value	Normal Value
SGOT (AST)	73 U/L	0-37 U/L
Total Serum Bilirubin	2.92 mg/dl	0.2-1.2 mg/dl
Direct Bilirubin	0.69 mg/dl	0.0-0.4 mg/dl
Indirect Bilirubin	2.23 mg/dl	0.4-0.8 mg/dl

Table.3 Complete Blood Count Report

Complete Blood Count:	Result	Normal Range
Haemoglobin (Hb)	8.3 g/dl	Female 11-16 g/dl
PCV	35%	40-52%
MCV	91.3 fl	76-96 fl
MCH	23.4 pg	27-34 pg
MCHC	30.6 mg/dl	31-36 mg/dl
RBC	4.6 million/mm^3	4.2-5.5 million/mm^3
Platelet	1.7 lac/mm^3	1.4-4.4 lac/mm^3
Total Leukocyte Count (TLC)	8700/mm^3	4000-11000/mm^3
Differential Leukocyte Count (DLC):		
Neutrophils	60%	40-70%
Lymphocytes	30%	20-40%
Eosinophils	7%	0-6%
Monocytes	3%	2-8%
Basophils	0%	0-1%

Table.4 Blood Biochemistry Report

Test	Patient's Value	Normal Value
Total Serum Bilirubin	3.53 mg/dl	0.2-1.2 mg/dl
Direct Bilirubin	0.67 mg/dl	0.0-0.4 mg/dl
Indirect Bilirubin	2.86 mg/dl	0.4-0.8 mg/dl

Table.5 Haemoglobin Electrophoresis Report

Type of Haemoglobin	Percentage (%) [4 years]	Percentage (%) [10 years]
HbA	1.4	7.9
HbF	32.4	43.1
HbS	64.9	48.0
HbA2	1.3	1.0

Table.6 Complete Blood Count Report

Complete Blood Count:	Result [9 years old]	Result [11 years old]	Normal Range
Haemoglobin (Hb)	12 g/dl	6.9 g/dl	Female:13.6-19.6 g/dl
HCT	36%	19%	40-54%
Total Erythrocyte Count	4.76 x 10^6/µl	2.01 x 10^6/µl	4-6 x 10^6/µl
MCV	75.6 fl	94.7 fl	76-96 fl
MCH	25.2 pg	34.3 pg	27-32 pg
MCHC	33.3 g/dl	36.3 g/dl	32-37 g/dl
RDW-CV	15.2%	22.5%	11.5-14.5%
Total Leukocyte Count	8.02 x 10^3/µl	5.1 x 10^3/µl	4-11 x 10^3/µl
Neutrophils	54.7%	73%	50-65%
Lymphocytes	31.7%	21%	20-45%
Eosinophils	7.4%	5%	1-6%
Monocytes	6%	1%	2-8%
Basophils	0.2%	0%	<1%
Platelet Count	364 x 10^3/µl	131 x 10^8/µl	150-450 x 10^3/µl
PDW	9.6 fl	17 fl	15-17 fl
MPV	9.2 fl	7.8 fl	7.4-10.4 fl
PCT	0.33%	1.02%	0.15-0.62%

Table.7 Widal test

Blood Widal	1:40	1:80	1:160	1:320
H	+	+	-	-
O		+	+	-
AH		-	-	-
BH	-	-	-	-
Interpretation	Positive for Widal			

Fig.2 Case Presentation 2, Pedigree Analysis

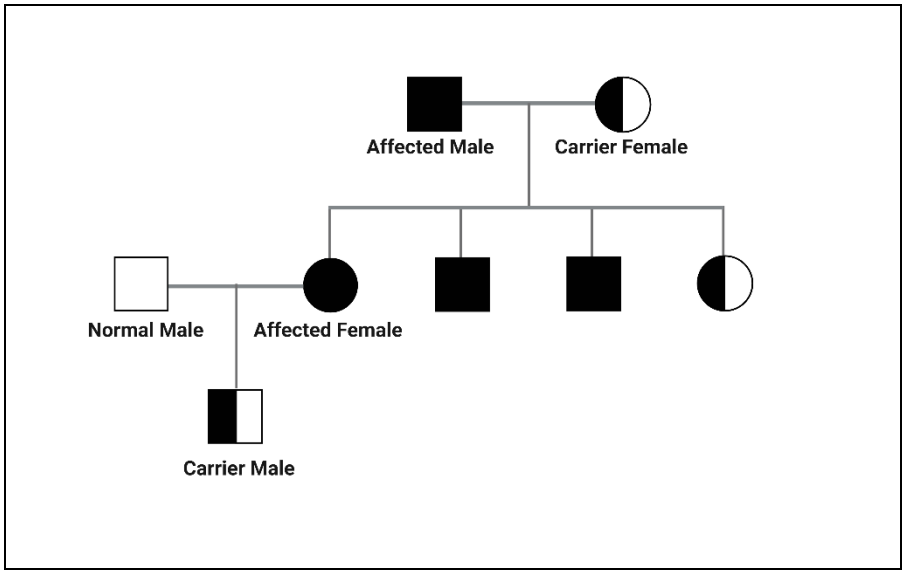
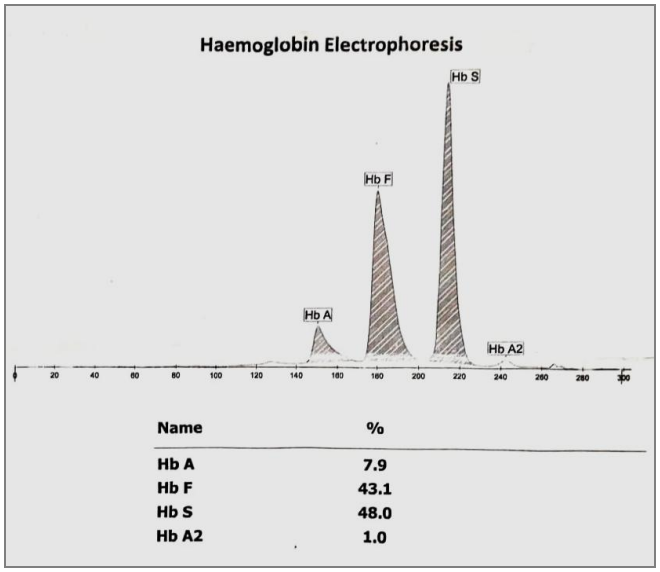


Fig.3 Case Presentation 3, Electrophoresis Result



The enlarged liver revealed in patient's USG report can be a consequence of vaso-occlusion due to cell sickling or multiple transfusions causing iron overload in the patient as seen in her ferritin test reports or due to the chances of viral hepatitis due to frequent blood intake (Banerjee and DeBaun, 2023).

The chronic haemolysis due to sickled cells can also be the reason behind developing gallstones which can travel to the common bile duct, blocking it and causing distended gallbladder in the patient (Martins *et al.*, 2017).

The elevated enzyme levels for the serum aminotransferase (SGPT/ALT) found in the blood biochemistry test is also reflective of the hepatic dysfunction (Kamble *et al.*, 2022).

The patient's haemoglobin electrophoresis reports revealed the presence of high amount of foetal haemoglobin or HbF which is associated with reduced symptoms and sickle cell complications as

HbF inhibits the intracellular HbS polymerization and hence reduces sickling (Antwi-Boasiako *et al.*, 2015).

Hydroxyurea was prescribed to the patient to reduce sickling and folic acid tablets to treat anaemia. Zincovit syrup was also advised as a nutritional supplement to help generate RBCs and manage anaemia.

Besides these palliative treatment regimens, the patient has found her younger sibling as a matching donor and is scheduled to have bone marrow transplant in a couple of months. The haematopoietic stem cell transplant is a safe option for this patient as a 100% match is found with the donor with null chances of graft vs host disease (Hoppe and Walters, 2001).

The 3 case studies presented bring into light the lives of sickle cell patients in three different age groups, the first one is a teenager, second is an adult woman, while the third is a child. The common complaint was that of pain in stomach, joints, and muscles and all of these patients were prescribed analgesics to treat the pain.

The varying level of pain in these patients is reflective of the vaso-occlusive crisis caused by sickle cells and the amount of damage caused in the organs. Most commonly affected organs are liver and spleen which get enlarged at first and either continue to remain so or become subjected to progressive atrophy later. To prevent the repercussions, one patient had undergone splenectomy. Hepatic dysfunction with enlarged liver or symptoms like jaundice due to increased serum bilirubin are also commonly observed in sickle cell patients. It is treated with hydroxyurea, zinc, folic acid and other supplements depending upon the patient's condition. Other than medicinal treatment, the only curative option available is bone marrow transplant but it involves another level of complexity from finding a matching donor to toxic immunosuppressive medications and the critical procedure.

Also, a higher-than-normal NLR ratio was observed in sickle cell patients. This is consistent with other findings and hence can be instrumental in mapping the progress of the sickle cell disease in these patients. This NLR ratio can help to determine the severity of disease in patients diagnosed with SCA and hence determine the immediate care they need.

Looking at the inherent nature and genetic predisposition involved in sickle cell disease, healthcare professionals and medical units can also engage in educating the tribal people. This would encourage newborn screening to identify the sickle cell patients before they present with complications and thus provide them with comprehensive care. It would also enhance prenatal diagnosis in couples once they are aware of the complications of SCA on genetic counselling.

Abbreviations

SCA, Sickle Cell Anaemia; SCD, Sickle Cell Disease; Hb, Haemoglobin; NLR, neutrophil lymphocyte ratio; HbF, foetal haemoglobin; MCV, Mean Corpuscular Volume; AST, Aspartate Transaminase; PCV, Packed Cell Volume.

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Conflict of Interest

None

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