Sickle cell Anemia Control Mission

A Project designed by

Jan Swasthya Shayog

for

the comprehensive management of sickle cell disease

in 6 districts of eastern Madhya Pradesh

Implementation Agencies

1. Jan Swasthya Shayog, Ganiyari
2. District Health Society, Anuppur, Madhya Pradesh
3. District Health Society, Dindori, Madhya Pradesh
4. District Health Society, Mandla, Madhya Pradesh
5. District Health Society, Shahdol, Madhya Pradesh
6. District Health Society, Umaria, Madhya Pradesh
7. District Health Society, Sidhi, Madhya Pradesh

Funded by

1. National Health Mission, Bhopal, Madhya Pradesh
2. District Mineral Fund, Anuppur, Madhya Pradesh

Initial support by -

SRIJAN (Self-Reliant Initiative through Joint Action)

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Introduction -

Sickle cell disease, a hemoglobinopathy, is one of the most common genetic disorders globally[2]. It is rampant in rural, central India, especially among tribal communities living in forested, hilly areas[5]. Introduction of the Sickle gene in the population was a part of the natural selection process for the tribal people from forested regions which were malaria-endemic. Sickle cell trait (AS) confers relative resistance to Severe falciparum malaria; thus, it results in low parasite count by disabling the parasite from concentrating in the RBCs; thereby, decreasing the risk of severe falciparum malaria[8]. With consanguinity and the tendency of the population of getting married within the clan, this population was maximally affected by SCD.

Since early childhood, patients with this illness suffer acute painful complications such as acute chest syndrome, dactylitis, bone pain, bone infection, stroke, and splenic sequestration crisis. Splenic dysfunction early on leads to increased chances of premature death due to overwhelming infections. Those who are fortunate to survive into adulthood often have crippling avascular necrosis of the femoral head and sometimes the head of the humerus. Chronic pain, anaemia, renal complications, stroke sequelae, retinopathy, and pulmonary hypertension are the hallmarks of untreated patients who often suffer and die in silence and ignominy[2]. These patients can also lead a respectable and normal life if the disease is detected early and if comprehensive care is provided to them. There have been many successful models for the provision of comprehensive care to SCD patients in different parts of India as well as in the world.

Intervention Area (Basic information about the area)

6 Tribal predominant districts of Eastern MP.

Table 1: Demographic details of the intervention area

District	Total population	ST Population	% of ST population
Anuppur	7,49,521	3,59,020	47.9
Dindori	7,04,524	4,55,789	66.7
Mandla	9,24,716	5,90,435	63.8
Umaria	6,44,758	300,687	46.6
Shahdol	10,66,063	4,47,402	52.8
Sidhi	11,27,033	3,13,304	27.8

(Ref: Census 2011, Table 14, No. & % of SC and ST population(rural)in CD blocks)

Out of the above-mentioned intervention areas, **screening, diagnosis and management of SCD patients by the project team** was done in Anuppur district. Anuppur district comprises 4 blocks, 282 Gram Panchayats, and 585 villages. It has a sex ratio of 975 females for 1000 males. Besides one District Hospital, there are 8 Community Health Centers, 17 Primary Health Centers, and 186 Sub-Health Centers functional in the District. The other crucial part of the model was **strengthening the Public Health System (DH to PHCs) for diagnosis and management of SCD by training and mentoring.** This component was implemented in 6 districts. One district hospital

and one FRU in each District Anuppur, Dindori, Mandla, Sidhi, Shahdol and Umaria and 6 additional CHCs of Anuppur (A total of 18 facilities) covered for capacity building work.

The rationale of the intervention

There is no affordable cure for Sickle cell Disease, though early recognition and long term medical management can reduce the incidence of life-threatening complications and improve the quality of life and the patient's lifespan. Early diagnosis and appropriate management are the cornerstones of any program to address this problem. And this can only be done by first generating awareness and counselling among the health care providers and community. It is observed that this disorder is prevalent among backward communities in MP especially Baiga, Kewat, Yadav, Sindhi, Kol, Panika, Patel, Bandhey/Khandey, Mehra, Gond, Mahar, Rathore, Chaudhari, and Kushwaha, to name a few.

The secondary data reveals that the sickle cell trait frequency is up to 35% in central India. According to ICMR Jabalpur's research, the prevalence of the Sickle Cell gene in the Madhya Pradesh state is 10% - 33% in 22 tribal districts. [8]. The tribal-dominated districts of Orissa, Madhya Pradesh and Maharashtra state have the highest occurrence. Madhya Pradesh has the highest burden of Sickle Cell Disease in India with an estimated 9,61,492 citizens of tribal ethnicity having sickle cell trait and 67,861 suffering from sickle cell disease (SS). The recent process of maternal death reviews, conducted by Jan Swasthya Sahyog (JSS) in the selected districts of eastern Madhya Pradesh brought about the realisation that possibly many unexplained maternal deaths could be due to sickle cell disease and its complications. Based on the MDRs conducted in the region, a specific CME module on the management of sickle cell disease as a part of Maternal complications was developed and implemented in collaboration with the National Health Mission, Madhya Pradesh. It was observed that the disease burden in the district of Anuppur is also very high.

This was concluded from a sample of observations done from private labs in Anuppur, though the Public Health System does not have a significant number of cases registered with them. We found 108 patients of the Anuppur district from various sources, and out of them only 18 cases were registered in government records (of these only 4 were registered in DH of Anuppur). The care provided for these patients in these public health facilities was very little, erratic and of poor quality. Also, there has been no program running exclusively for SCA or hemoglobinopathies. A pilot of screening, diagnosis & management in 70 villages across two blocks, was conducted for 6 months (March'18 - August'18) with one Project Executive, one staff nurse for collection of samples, counselling (pre-and post-screening), & with a lab technician for Hb estimation, solubility, and electrophoresis testing. It was done by JSS & SRIJAN NGOs. Jan Swsthya Sahyog is a voluntary non-profit organisation working to improve the health of rural communities in central India for the last two decades. As part of the pilot, family members of already diagnosed patients (from Nagpur, Raipur, and Jabalpur), and pregnant women who visited CHC Kotma were screened. JSS then proposed the following Sickle Cell Anemia Control MIssion, which was approved by the National Health Mission.

Sickle cell Anemia Control Mission

Model description -

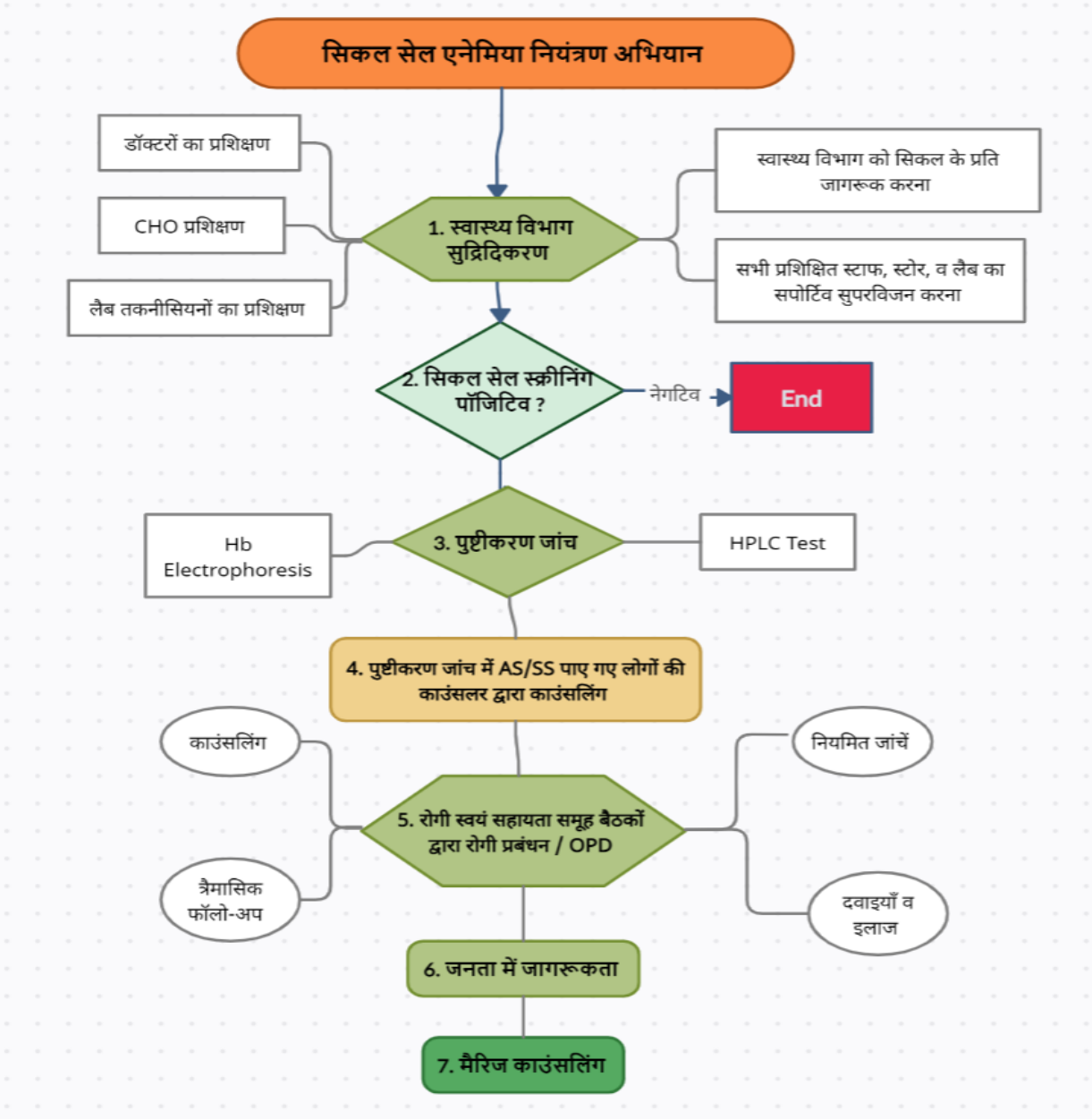


Figure - Stepwise interventions needed for the proper management of SCD

The proposed model has two parts:

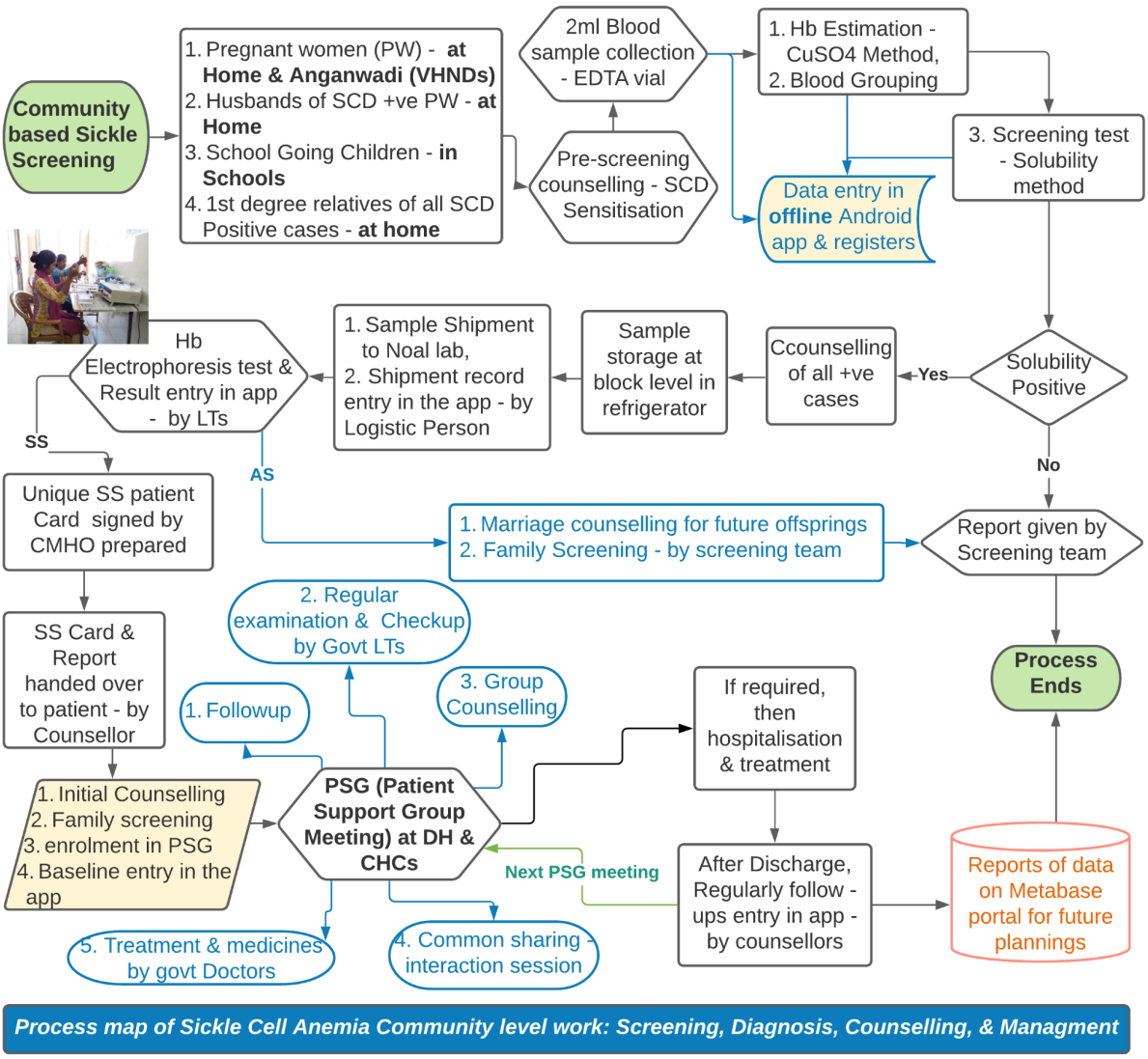
1. **Screening, diagnosis and management of SCD patients by PMU (Project management Unit) of JSS/CSO** - Comprises 5 screening teams (3 members in each), 2 counsellors, 2 logistic managers, 2 nodal lab technicians, 1 Data entry operator, 1 district coordinator, 1 Project Coordinator, 1 Lab Mentor.
2. **Strengthening Public Health System (DH to PHCs) for diagnosis and management of SCD by training and mentoring** - Lab Mentor, District Coordinator, Project Coordinator from the PMU was used for this part also. Trainers were hired from the Jan Swasthya Sahyog's Hospital.

Both components have to go hand in hand. The total Proposed duration is almost 5 years (June 2018 to March 2023). The aim of the program is to attain self-sufficiency in the Public Health facilities to diagnose and manage SCD. It will be key to either recruit counsellors at the block level and a part-time program officer at the district level at the end of this project. Refresher training and mentoring will still be required at a lesser intensive pace. Technical CSO partners or the State training division can take this responsibility.

The intervention began in August 2018 with the **training** of lab technicians, nursing staff, Medical officers, as well as specialists in internal medicine, paediatrics, obstetrics, and anaesthesia. The purpose of this was to ensure they were aware of the high prevalence of the gene in these areas, the potential complications and risks it may present during pregnancy and the postpartum period, as well as the need for screening and diagnosis, and the appropriate management of those with SCD (including handling complications and comprehensive care). In addition to Hb estimations, staff in the laboratory were trained to perform solubility tests including antenatal patients and to perform Hb electrophoresis as a confirmatory test. With support from the district and State Health Department, the availability of drugs for management were ensured at the District Hospital and First Referral Unit. Post-training, supportive supervision and mentoring were provided to the facility staff by the project team.

1. **Screening, diagnosis and management of SCD patients by Project Team (JSS) (Intensive work) -**

Sickle cell Anemia Control Mission



Picture 2: Detailed Process mapping of the activities of intensive work of sickle cell program

a. Screening: Intensive work to manage the disease was done in the District of Anuppur. We used a contact tracing screening strategy instead of mass screening because sickle cell disease is genetic. It saves time, money, & other resources & we can reach persons with a higher likelihood in a shorter time. In an initial ground survey, we found 100 SCD patients already diagnosed (From private labs in the district). We screened four targeted groups -

i. Pregnant women with SCD are at high risk of death and other pregnancy-related complications. Hence we started with the door-to-door screening of all pregnant women. To target maximum pregnant women in less time, we also screened pregnant women in Anganwadi on VHNDs (Village health & Nutrition days).

ii. Our next focus of screening were the husbands of sickle positive pregnant women. The presence of the Sickle gene in them decides the chances of SCD

in their future child. If the pregnancy can result in a homozygous child, then MTP was suggested to the couple by the counsellor.

iii. Screening of all the 1st blood relatives of each screened-positive case was also done parallelly from the beginning.

iv. In the one year program, we found that most of the patients (SS) are coming from the age group of 0 - 18 years group so next, we started screening school-going children in the schools.

In the field, a Solubility test was done for screening of sickle gene with Hemoglobin estimation using the Copper Sulphate method. Positive samples were sent to the nodal lab in the district for confirmatory testing, using Gel-based Hb electrophoresis. Few cases were equivocal due to heterozygosity when the sample was sent to the HPLC lab for confirmation.

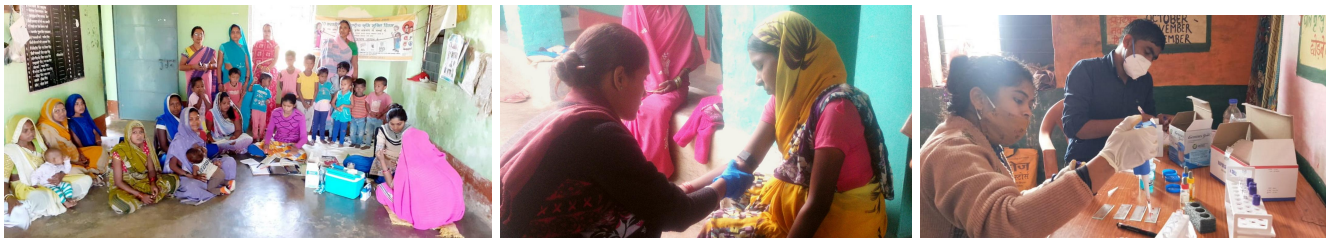


Figure - 1. Sickle cell screening of PW & Children in Aanganwadi, 2. Sample drawing, 3. Solubility test performing LT

There are a total of 5 screening teams, each consisting of 1 resource person and one ANM. Each team added an additional lab technician later on. After taking informed consent in writing from each screened person, their personal details were recorded in an android based app (Avni). Then a 2ml blood sample was drawn and Hb estimation for anaemia was done in the field using the copper sulphate method. For those with Hb less than 7 gm/dl the required quantity of the whole blood in a 2ml working solubility buffer is double i.e. 40 ul. Otherwise, if Hb is greater than 7gm/dl then we mix 20 ul whole blood in the 2ml of working solubility buffer. The solubility test was performed using commercially available kits. Later the rate contract was done by the State for the solubility kits which were used after 1 year. The test was considered positive if the solution in the test tube (Working solubility buffer + whole blood) becomes turbid.

The team stores the positive samples in the refrigerator of the field offices. During screening the teams keep the samples in ice packs for the safety of samples. Data is being recorded by the resource person in an android app called "Avni", which works in offline mode and the collected data can be synced with the server when the user is in network range. The screening teams are capable of collecting 100+ samples in a day, but due to many circumstances & factors the team collects on an average 60 samples/day.

b. Diagnosis: Sample is shipped by the logistic managers of the project team and Hb electrophoresis test for confirmation of the type of gene is conducted at the nodal Lab. A low cost (I**NR 14,000 per machine & INR 25 per sample**) agarose based Hb electrophoresis machine developed by JSS was used to confirm the genotype of the positive solubility cases. The per-test cost is around Rupees 25. The machine provides the results after an hour in the form of AS, SS, or Others (see picture 2). A control sample is used each time to ensure quality. The laboratory technician at the nodal lab sends the sample to the outsourced HPLC labs if the result is not confirmed (other) in the Hb

Electrophoresis machine. Nearly 5% - 10% of all positive cases are caused by Sickle Beta-thalassemia or any other haemoglobin variant associated with Sickle Hemoglobin that needs an HPLC test. The HPLC lab provides results within 2-3 days.

Picture 3: JSS Made Hb Electrophoresis machine (Agarosegel-based)

c. Management:

i. **Counselling of SS and AS cases–** The management of sickle cell anaemia is ensured by the counselling process for each of the SS and AS cases. If an individual is diagnosed with SCD (SS) counsellor visits their home with the diagnosis report & a laminated patient ID card to hand over them with advice to carry on them. After the handover counsellor does the initial counselling of the patient and fills the baseline form. Furthermore, the implications for the future progeny of the presence of this gene and how that risk may be mitigated were also discussed. During this visit, the counsellor registers them to a PSG group (explained in the next section). By visiting the patients of SCD or by telephone (directly or through the local ASHA), counsellors remain in touch with them. SS patients are then enrolled in their nearby PSG meetings. Patients whose condition is more severe were kept in the follow-up with counsellors.

For AS cases: They are being provided diagnosis reports with proper counselling by the screening team's ANM & Lab technician that they are not patient and do not need any kind of treatment for sickle cell disease. The team also suggests that if they want to avoid children with SCD then they should avoid marrying a sickle gene person. Or if they are already married then they have explained the risk of having sickle cell babies and the scope of MTP (Medical Termination of pregnancy) if they can get their neonatal test done from anywhere. The same information in Hindi is also provided to them in the backside of the reports and each case (AS or SS) has been provided with one booklet of the disease in Hindi.

In case of need, a helpline number was provided and they were assured of 24x7 services.

ii. **Using Patient Support Group Meetings**- Patients were initially treated at the district hospital or community health centres where they were seen. These patients were grouped into groups (often forty to fifty patients), which began meeting regularly on a monthly basis at these facilities. The meetings were structured so

that patients could share experiences and speak openly about their problems with others in their situation. Patient Support Group meetings allowed doctors and members of the project team to examine patients as a part of their regular OPD and follow-up process, perform laboratory tests, and provide them with medicine for one month. Patients had group counselling sessions and need-based individual counselling by doctors and counsellors. The team of the Sickle project provided support and gentle help throughout this process.

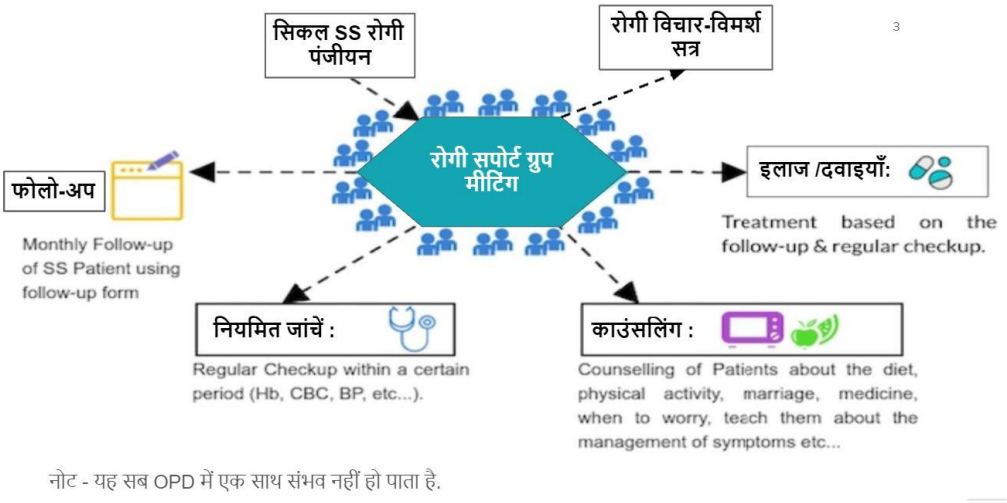


Figure - Model of Sickle Cell Patient Support Group Meetings


Figure - PSG Meetings in Anuppur

iii. **Patient care coordination for hospitalised cases in the District Hospital –** During the follow-up of sickle cell disease cases at the time of their hospitalisation in the facility, the process of treatment is reviewed by the sickle team in the facilities. Doctors and staff nurses have been provided training on the treatment protocols. Any concerns of the hospitalized patients are conveyed to the medical officer/specialist. The medical officer/specialists are provided with the standard treatment guideline to manage SCD whosoever has not received it earlier.

iv. **By arranging emergency blood donors for patients -** Blood is made available to SCD patients on a non-replacement, non-reimbursed basis through the helpline number. The district administration supported more frequent blood donation camps so that the District Blood Bank's stock increased. Also, a list of more than 400+ voluntary blood donors of different blood groups was prepared and shared with the blood bank and with local youth leaders.

d. IEC activities

i. Multiple meetings were done with doctors, Nurses, Lab Technicians

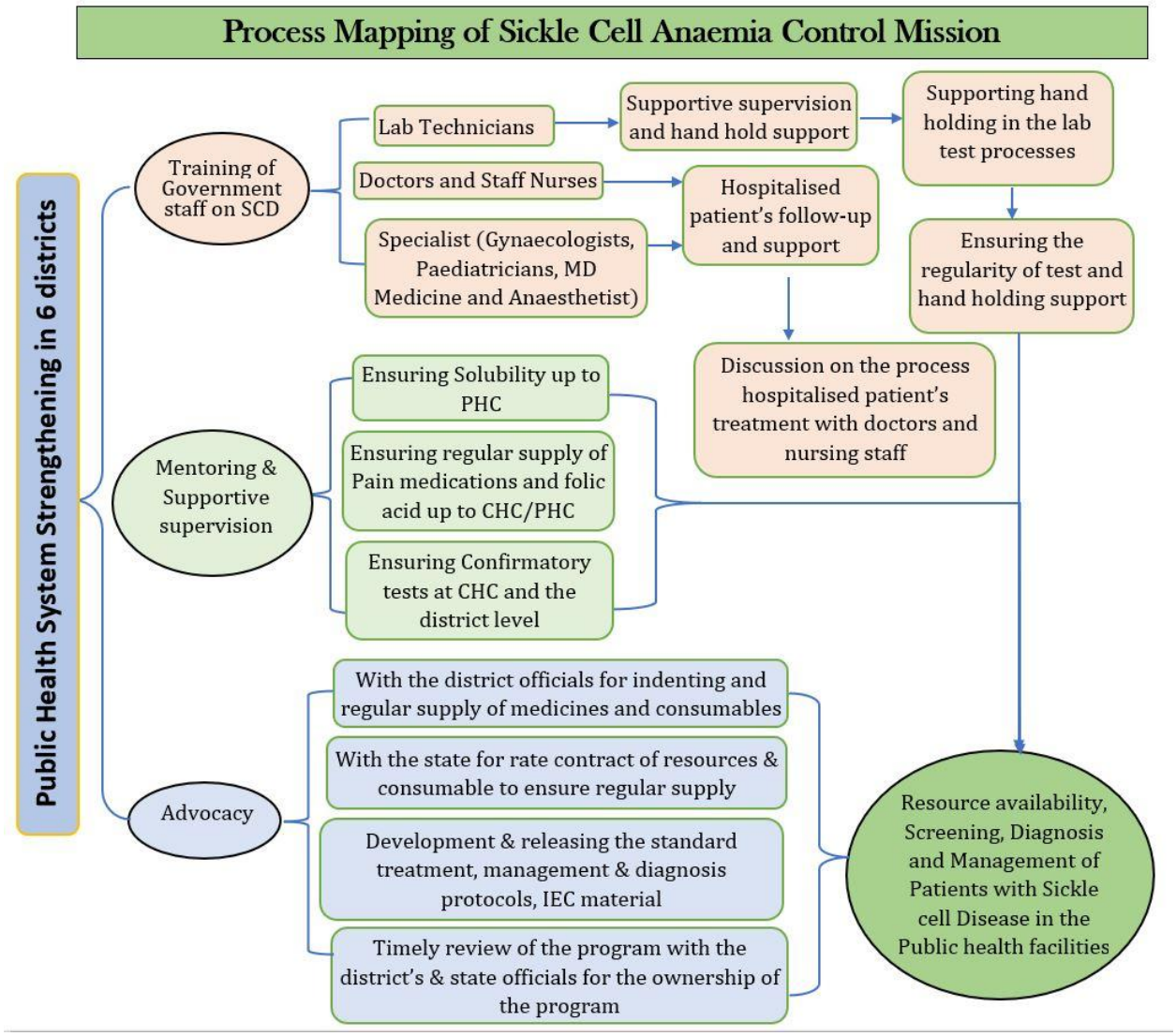
ii. Awareness meetings were done with the government school teachers
iii. ASHAs, Anganwadi Workers, & ANMs were sensitized one to one before the sickle cell screening individually by screenign team members. Screening team meeting 4 times at least in a year to these health workers.
iv. Some big gatherings were also conducted on various occasions for the awareness in public.
v. District collector involved and discussed about the SCD in their weekly TL Meetings.
vi. Flexes were pasted in all government health facilities up to Sub centre level.
vii. Marathon for blood donation awareness

Figure - IEC Materials developed by JSS for Doctors, Lab Technicians, & patients / public

e. Data collection of sickle cases through AVNI app

Avni is an Android app developed in the program that collects data from the field, called the Avni field app. One of the best things about the app is that it can work offline. Due to the fact that most of the field areas are not connected to the internet. Therefore, the data get synced with the server whenever s/he enters the network range. Following sync, all other users will be able to access it as well. Data of all the persons screened was filled by a resource person in the screening teams, then the logistic persons does the shipment of samples and enters the shipment records in the app, then lab results of confirmatory tests were filled by lab technicians of the nodal lab. After the confirmation test, the baseline & follow-up data was filled in by counsellors. Reports of the data are accessible by the coordinators, district & state level stakeholders from a separate web-based portal.

2. Strengthening Public Health System (DH to PHCs) for diagnosis and management of SCD by training and mentoring :



Picture 5: Process flow of Health System strengthening activity of the program

a. Diagnostics services -

I. Availability of solubility kits up to PHC level

II. Establishing a nodal lab for the confirmatory test of sickle at the district level as well as ensuring the availability of a low-cost electrophoresis machine (for the confirmatory test) up to CHC level.

III. training of lab technicians on the screening and diagnosis of sickle cell cases along with the confirmatory tests.

IV. supportive supervision of the diagnostics services by lab mentors at DH and CHC for hands-on training and support.

Interaction with DPM, Mandla during Day Care Centre visit in District Hospital, Mandla

Lab Mentor of JSS doing handson training on solubility test in front of Facilities Lab Technicians.

b. Out-Patient care (OPD)-

i. Ensuring the availability of medicines (Hydroxyurea, Folic acid) upto PHC level.

ii. Ensuring diagnostic facility at DH and CHC level.

iii. A dedicated day organised through peer support group meetings in the DH and CHCs, monthly/by monthly/ quarterly, for the patients with sickle cell disease. The counsellors also support the sickle patients through counselling, providing help in arranging blood as well as the treatment at the district level. The counsellors also help the district's hospital blood cell in organising regular blood donation camps to ensure the availability of blood without replacement to the sickle patients.

c. In-Patient care -

i. Training of Lab Technicians of DH & CHCs for the diagnosis & screening.

ii. Training of doctors of DH & CHCs on the management of Sickle Cell Disease.

iii. Training of Staff nurses for patient care

iv. Installing Hb Electrophoresis Machine in 2 CHCs & 1 DH, also ensuring continuous supply of reagents & Consumables required for the confirmatory test.

v. Pushing the government to put the Solubility test kits in the state rate contract. Till the time rate contract not done, JSS will supply the solubility test kits.

vi. Ensuring continuous supply of drugs (Hydroxyurea 500 mg, Folic acid 5mg, Tramadol 50mg) from the system.

vii. Supportive Supervision of trained staff.

d. Material Development -

i. Doctors' manual for the management of sickle cell disease.

ii. Lab technician's manual for the screening, diagnosis of sickle cell disease.

iii. Patients counselling book (Hindi) and pamphlet for sickle patients. This book is also being used as the awareness booklet

iv. Sickle cell Kundali,

v. Pain management flowchart of an SCD patient in emergency

Supportive supervision visit CHC Pali (BMO & LT)

Orientation of Staff nurses of DH Umaria

CHC LT learning the right practice for sickle testing with support of JSS team.

Govt Doctor's training on SCD management by JSS

e. Advocacy -

1. Advocacy to bring solubility under rate contract
2. Advocacy at the district and state level for the availability of pain control drugs.
3. Advocacy For low cost & reliable Agarose based Hb Electrophoresis machine for confirmatory testing of screened positive cases, developed by JSS developed with the state. JSS also made it available in each of the 6 districts at the District Hospital and the FRU. JSS also ensured a continuous supply of reagents & consumables because these were not in-state rate contracts yet.
4. The review of the sickle program every six months from the state NHM - The maternal health department of NHM MP conducted regular reviews of sickle cell anaemia program to get the progress of the program from the district's officials, in order to ensure the ownership of the program. The review process also helped in the smooth functioning, coordination, management, training and implementation of the program.

References:

1. Banerjee S, Dave K, Desai G, Babaria P, Gupta R. Initial outcomes of a comprehensive care model for patients with sickle cell disease in a tribal population in rural Western India. Annals of Global Health [Internet]. 2016 Aug 1 [cited 2021 Nov 10];82(3). Available from: https://annalsofglobalhealth.org/articles/1278
2. Sedrak A, Kondamudi NP. Sickle Cell Disease. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 [cited 2021 Nov 11]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK482384/
3. Nimgaonkar V, Krishnamurti L, Prabhakar H, Menon N. Comprehensive integrated care for patients with sickle cell disease in a remote aboriginal tribal population in southern India. Pediatric Blood & Cancer. 2014;61(4):702–5.
4. Sheshadri V, Shabeer P, Santhirapala V, Jayaram A, Krishnamurti L, Menon N. Mortality in sickle cell disease: A population-based study in an aboriginal community in the Gudalur Valley, Nilgiris, Tamil Nadu, India. Pediatr Blood Cancer. 2021 Mar;68(3):e28875.
5. Samal J, Meshram FA. A Cross Sectional Study on Sickle Cell Disease among Backward Communities of Gadchiroli, Maharashtra, India. Indian Journal of Public Health Research & Development. 5(2):117.
6. Marcheco-Teruel B. Sickle Cell Anemia in Cuba: Prevention and Management, 1982-2018. MEDICC review. 2019 Oct 1;21:34.
7. Patra PK, Chauhan VS, Khodiar PK, Dalla AR, Serjeant GR. Screening for the sickle cell gene in Chhattisgarh state, India: an approach to a major public health problem. Journal of Community Genetics. 2011 Sep;2(3):147.
8. Gupta: Sickle cell disease load in Madhya Pradesh - Google Scholar [Internet]. [cited 2021 Nov 10]. Available from: https://scholar.google.com/scholar_lookup?journal=Newslett+Regional+Med+Res+Centre+Tribals+Jabalpur&title=Sickle+cell+disease+load+in+Madhya+Pradesh.+RMRCT+Update&author=RB+Gupta&volume=3&publication_year=2006&pages=1-6&
9. Colah R, Mukherjee M, Ghosh K. Sickle cell disease in India. Curr Opin Hematol. 2014;21(3):215-23.
10. Colah RB, Mukherjee MB, Martin S, Ghosh K. Sickle cell disease in tribal populations in India. Indian J Med Res. 2015;141(5):509-15.
11. Ghosh K, Colah R, Manglani M, Choudhry VP, Verma I, Madan N, et al. Guidelines for screening, diagnosis and management of hemoglobinopathies. Indian J Hum Genet. 2014;20(2):101-19
12. Italia K, Kangne H, Shanmukaiah C, Nadkarni AH, Ghosh K, Colah RB. Variable phenotypes of sickle cell disease in India with the Arab-Indian haplotype. Br J Haematol. 2015;168(1):156-9.
13. Patra PK, Chauhan VS, Khodiar PK, et al. Screening for the sickle cell gene in Chhattisgarh state, India: An approach to a major public health problem. J Commun Genet 2011;2:147–151.
14. Nikhar HS, Meshram SU, Shinde GB. A comprehensive review of diverse issues related to sickle cell disease. East Afr J Public Health 2011;8:164–169.
15. Mohanty D, Das K. Genetic counselling in tribals in India. Indian J Med Res 2011;134:561–571.
16. Chandrashekar V, Soni M. Hemoglobin disorders in South India. ISRN Hematol 2011;2011:748939.
17. Singh H, Dulhani N, Kumar BN, et al. Effective control of sickle cell disease with HU therapy. Indian J Pharmacol 2010;42:32–35.
18. Dangi CB, Sajid M, Sawke GK, et al. Sickle cell hemoglobinopathies in district Bhopal. Indian J Hum Genet 2010;16:100–102.

19. Balgir RS. Genetic diversity of hemoglobinopathies, G6PD deficiency, and ABO and Rhesus blood groups in two isolates of a primitive Kharia Tribe in Sundargarh District of Northwestern Orissa, India. J Commun Genet 2010;1:117–123.
20. Italia K, Jain D, Gattani S, et al. HU in sickle cell disease—A study of clinico-pharmacological efficacy in the Indian haplotype. Blood Cells Mol Dis 2009;42:25–31.
21. Balgir RS. Infant mortality and reproductive wastage associated with different genotypes of haemoglobinopathies in Orissa, India. Ann Hum Biol 2007;34:16–25.
22. Patel AB, Athavale AM. Sickle cell disease in central India. Indian J Pediatr 2004;71:789–793. 16. Chhotray GP, Dash BP, Ranjit M. Spectrum of hemoglobinopathies in Orissa, India. Haemoglobin 2004;28:117–122.
23. Babu BV, Leela BL, Kusuma YS. Sickle cell disease among tribes of Andhra Pradesh and Orissa, India. Anthropol Anz 2002;60:169–174.
24. Menon A, Salim KA. Sickle cell disease in south India. J Assoc Physicians India 1993;41:617.