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SICKLE CELL ANEMIA PREVENTION AND CONTROL IN CHHATTISGARH

A POLICY BRIEF FOR DEPARTMENT OF HEALTH & FAIMILY WELFARE, GOVERNMENT OF CHHATTISGARH

The purpose of this report is to inform the deliberations among policymakers and stakeholders. It summarizes the available evidence related to control of sickle cell anemia in Chhattisgarh. It was prepared as a background document to be discussed at meetings of those engaged in developing sickle cell anemia prevention and control policy. It also contains recommendations for developing a comprehensive policy. It aims to provide various policy options that can be used during deliberations to reduce the burden of sickle cell anemia in Chhattisgarh .

Table of Contents:

Addressing Sickle Cell Anemia in Chhattisgarh

Policy Brief (Executive Summary)

The Need for a policy

- State government has started with various initiatives for control of sickle cell anemia. These initiatives are triggered by awareness in sections of the public and in the political leadership of the extent of this problem. The plans are based largely on perceptions of well meaning clinicians and public personalities on what would be the most effective form of control and address some dimensions of the problem. There is a need to examine the sickle cell problem from a public health lens and draw up a structured plan, linked to measurable outcomes and budgets and to a vision of a sustained reduction of the incidence and suffering due to this disease.

- The main strategy deployed has been mass screening, especially of adolescents, with the expectation that knowledge about having the sickle cell trait would induce young men and women from entering into marriage with others having the same trait- and that this would over time lead to an elimination of what is perceived as an "incurable disease." There are however concerns about the effectiveness of this strategy. Screening coverage is limited, and only a modest proportion of those suspected submit for confirmation. Even when confirmed, anticipated actions with regard to subsequent choices of partners in marriage does not take place. There is a need to identify alternative approaches of prevention which would be cost effective and socially acceptable.

- There is an unmet need for treating tens of thousands of individuals who are diagnosed with Sickle Cell Disease (SCD)- either because they were symptomatic or because the disease was identified during various screening camps. There is no clear understanding of what is the state government commitment in this regard.

- Based on sporadic surveys and screening camps, we now have reasonable estimates of how many persons have the trait and how many have the disease . However there is no plan for sustained collection of information on disease incidence and prevalence or ensuring that the existing estimates are validated.

- There is a need to define what facilities must be identified for delivery of preventive, promotive and curative services with regard to this disease- and the standards with regard to equipment, consumables, skills and protocols of care needed to ensure this. In the absence of a clear policy articulation many persons with SCD are unable to access the treatment they need in the health care facilities.

- In addition to suffering due to the disease, families of persons affected with SCD face great financial hardship. There is a need for policy clarity on financial requirement to provide these services and of strategies to ensure financial protection for the victims of this disease so that they do not face financial hardship or impoverishment as a consequence of seeking care.

- There is also policy clarity required on how to combine more active uncovering of the disease and at the same time prevent the stigmatization that accompanies the disease. Stigmatization is a barrier to treatment and at efforts at inter-generational reduction of disease prevalence. On one hand the political pressure emanates from specific communities – by caste and geography. And on the other hand these communities would not even like to be named for fear of stigmatization

Contexts of the problem

The Epidemiological Context:

- A programme designed to detect the sickle cell trait and sickle cell disease has screened 359,823 subjects among 2,087 (99.7%) of the villages in Raipur District, Chhattisgarh State, India between October 2007 and June 2010. The sickle cell trait occurred in 33,467 (9.30%) and an SS phenotype in 747 (0.21%).(Pradeep K. Patra 2011)A study conducted in Rajnandgaon district, also documented that 9.75% of the examined population carries a sickle cell gene. (Paunipagar PV 2006)

- Extrapolating from these figures we estimate that there would be about 25 lakh persons carrying the gene and there are about 60,000 persons with the disease. Caution needs to be exercised in using these estimates, since tribal populations especially in the southern and northern ends of the state have not been so screened. There are reasons to believe (based on specific field areas) that the disease prevalence could be much higher is the disease is looked for actively in patients with a number of leading symptoms like persistent anaemia, frequent respiratory infections etc. We know that with treatment 95% of newborns with SCD will reach adulthood of detected and treated appropriately. But it would be less than 50% if undetected.

- Screening at adolescence which is the main source of information would completely miss this population. Given Chhattisgarh high and unexplained under 5 mortality in a number of districts, the known fact that the largest proportion of these deaths are due to respiratory infections and that respiratory infections are the most common clinical manifestation in young children- the health system needs to get alerted to the possibility of a much higher SCD morbidity rate than existing projections.

- Data provided by Sickle Cell Institute, Raipur is suggestive of the fact that sickle cell anaemia is unevenly distributed. It has higher prevalence amongst specific communities. Prevalence rates by community are non-existent.

The Health Systems Context:

- A Chhattisgarh Sickle Cell Screening Project was launched in 2010. The main strategy was to screen persons of all age groups for the disease and the strain using solubility test. By subsequent counselling of unmarried adolescents and young people with the trait from marrying another person with the same trait, it was hoped to reduce the prevalence in the next generation. However there is no evidence that this approach succeeded- and a number of anecdotal reports that it did not. A sample of young women identified with the trait and given a card who were interviewed as part of this study, reported that this would not be a factor in choosing a spouse if otherwise it was found suitable and were unsure whether prior knowledge of the trait was of any help.

- Government of Chhattisgarh has started a mobile clinic for sickle cell anaemia in 2010, which according to verbal reports mainly visits schools for screening of cases. There is little data available on outcomes of this effort- and little to support either efficacy or effectiveness of this approach. Even as a visible token of government intention, it may have a limited contribution to make.

- Measures at health sector strengthening in the last decade have touched upon making diagnosis and care for sickle cell disease available at the primary health centre level. The reality is however that testing for sickle cell disease is not a part of routine newborn screening even after the introduction of Rashtriya Bal Swashtya Karyakram. The required high index of suspicion for symptoms indicative of the disease and testing for SCD is limited and patchy. Availability of drugs for those with the disease could be even more limited and a number of those on treatment said that drugs like hydroxyurea could be available for free only in tertiary care centers and that too prescribed only for a limited number of days. Even in pharmacies on a payment basis the access is limited.

- The government has set up sickle cell institute at Raipur to work towards providing assistance to patients suffering from sickle cell anaemia and also carry out research on the subject. This provides one sort of resource and institutional capacity to address this disease..T

- There is a political will across the State and at the highest levels of governance to support sickle cell anaemia prevention and control activities. Driven by this political will and priority that this programme enjoys, there is since 2010, a well funded state scheme as well as funds sanctioned under NHM. However given the lack of policy clarity and a clear and comprehensive approach these funds return unutilized as part of a technically sound public health approach- rather than being limited to immediate clinical perceptions. There is also a concern that these funds are utilized as part of a technically sound public health approach- rather than being limited to immediate clinical perceptions.

- There have been very good models of SCD management and control undertaken by field NGOs and resource groups like Jan Swashtya Sahyog that can be learnt from and scaled up. There are also other Indian examples like from Bissam Cuttack as well as many international examples that can be learnt from to construct a public health policy that addressed sickle cell disease.

The Social Context:

- There are three social contexts – that are important, to consider in the making of policy. First is the health-seeking behaviour with respect to the disease especially in the context of newborns. Second – and closely related is access to health care. The third is the social context of the institution of marriage in these communities. .

- Health-seeking from modern qualified medical health care facilities is much poorer in Chhattisgarh as compared to other states and regions. One index of this is the high levels of home delivery that characterise this state. Traditional healers, local RMPs and Ayush Physicians close the gaps in access- but these providers have little to offer in terms of either detection or response to this disease. The primary health centre and sub-centers also are designed to deliver a limited range of RCH services, and do not see themselves as responding to a disease that is neither a RCH priority, nor a communicable disease priority, nor even listed within the usual portrayals of non-communicable diseases. It is this social and political context that can best explain the poor performance of health systems in detecting or responding to SCD.

- The social context of adolescent marriage is defined by the institutions of marriages. Marriages in these communities are arranged, usually by patriarchs of the community, on multiple social considerations, with varied and often limited degrees of consultation and participation of the young couple. To votaries of adolescent screening, adding one more layer/dimension of considerations into making the match seems logical and acceptable, even supportive of the voice of the elders in match making. There is little conversation about gender and ethical dimensions of such choice. However because of a shortage of girls in some of these communities (not so much amongst tribal-but certainly amongst the middle level agrarian castes) , and because of the very many barriers to making a match, young persons are unlikely to accept another barrier that further disempowers them from making their choice. And even to elders it is not lack of awareness of the relationship between traits and disease, but the desirability of adding another layer that may undermine the effectiveness of such a genetic stock improvement approach.

Recommendations

We recommend a policy statement that reads as follows:
"The Government of Chhattisgarh has recognized sickle cell anemia as a major public health concern and commits to a policy to address sickle cell anemia in the state based on two principles (1) Every patient with the disease would be detected early and provided with adequate diagnostic and treatment facilities so that there is no loss of life and there is a major reduction in suffering due to this condition (2) There is increasing awareness and empowerment so that families and individuals make choices that lead to a decreased prevalence of the disease across generations."

The scientific basis of this understanding lies in the knowledge that the disease should no longer be considered "incurable" . Though it does not admit of cure in the usual sense, modern medical science and health systems knows how to ensure a near normal longevity and quality of life in the affected individual, without any financial hardship. There are other nations that have achieved this, and we can too. Even for reduction of the context where individuals and families are able to make more appropriate choices about marriage and childbirth. Vertical programme focused narrowly and exclusively on identifying and isolating the gene are not likely to be successful.

To implement such a policy the main strategies shall be:

Secondary Prevention:

- Identification of newborns with sickle cell disease. The most effective and pragmatic approach to achieving such identification in the context of Chhattisgarh state would be screening in all pregnant women, and if positive testing husbands and if both test positive for either trait or disease then mandatory testing of newborn with the appropriate blood test. In addition testing of all individuals with symptoms indicative of the disease, all siblings of the children with disease and all children of adults with disease would be screened.
- Screening of pregnant women is to be done at the site of ANC or institutional delivery preferably at the earliest contact. If she is screened positive, husband will called to VHND or sub-centre to screen through solubility test. If either are screened positive, samples will be taken by ANM for electrophoresis. If both are confirmed found SCD/trait positive – treatment and counseling will be provided for them and later newborn sample will be taken (at institutional delivery or BCG site) and sent to higher centres (Medical Colleges) for HPLC.
- For other suspected cases and their siblings, the screening would be conducted at CHCs or district hospital. The above screening recommendation is based on an understanding that without treatment only half the children would reach adulthood and with treatment over 95% can be expected to do so. This would also contribute significantly to reduction of under 5 mortality due to respiratory infections (currently the most common cause of under 5 mortality).

- Pneumococcal vaccination would be provided to all the children who have been diagnosed with sickle cell anemia. PCV 13 vaccines would be provided to all the children who have been diagnosed with sickle cell anemia. For Infants (6 weeks to 6 months of age) 0.5 ml injection is administered at 2, 4, 6, and 12 to 15 months of age for 4 total doses. (on the same timings as DPT vaccines)
- Babies diagnosed with sickle cell would be given daily antibiotics, starting at 2 months of age and continuing through 5 years of age. Penicillin (125 mg twice daily) could be the drug of choice, unless a child is allergic to it.
- Daily folic acid supplementation will be provided to all the patients with sickle cell disease. For the children below 3 years of age, we can provide the same in syrup form.

Access to Treatment:

- Access to health care in designated health care facilities for all patients irrespective of their ability to pay for it. This will be achieved by free care at primary level and back up referral services at CHC or district level. In practice due to limited capacity at PHC level, the PHC may be equipped with diagnostics for screening and provide for continued access to medical and routine follow up care. The CHC or district hospitals which are earmarked as designated referral facilities, would provide confirmation of the disease and make the treatment plan, respond to complications and exercise oversight over the PHCs with respect to continuity of care and health outcomes.
- In-Patient care and free blood transfusion facilities would be provided to those suffering from sickle cell crisis. This could be achieved through a series of designated referral facilities.

  To start with designated referral facilities are likely to be the same facilities which are functional as FRUs.- which currently are present in all District hospitals and a small percentage of CHCs.
- Hydroxyurea would be provided for those who had suffered from three or more episodes of sickle cell crisis or other serious symptoms in last 1 year.

  All the above mentioned health services would be provided at state expense.
- Free transport and referral facilities would be provided in case of emergency. This could be achieved through integration with the existing 102 and 108 ambulance services.
- Every designated referral facility (mostly district hospitals and designated CHC and select private hospitals) would have at least a team of 3 to 5 persons including 2 doctors and 3 nurses for providing key inputs for diagnostics, counseling, prescribing a treatment plan, early identification of complications and management of sickle cell crisis. Designated referral facilities would have the capacity to conduct confirmatory electrophoresis test, and develop and guide a treatment plan that can be followed by frontline workers for continued access to medication and regular check-ups.

Sickle Cell Data Base

- A sickle cell registry would be started that would maintain a data bank of those affected, treatment strategies and outcomes. This would inform both policy and implementation.

Primary Prevention: Inter-generational Reduction in incidence:

Potentially the prevalence of SCDs could be reduced if those with sickle cell trait do not intermarry. Learning from experience, and on ethical grounds, the state shall achieve this by offering free screening for adolescents and pregnant women who ask for it on a voluntary basis.

It is expected as awareness of the disease increases, more and more young men and women would make informed choices of whether they want to have the test, and whether they choose to risk the child etc.

In a situation where survival of children with disease could increase considerably, there is an even greater need to emphasize choice. Reasons of cost -effectiveness also support such an approach.

Community Mobilization and Participation:

- Prevent stigma: The rise in the level of awareness regarding the transmission and effective management of the disease could help to prevent the stigma faced by the patients. Active supplemental measures of Behaviour Change Communication would also be used to reduce and eliminate stigma.
- Encourage adherence to treatment: Better compliance to the treatment regimen would be ensured by providing effective counseling services to the patients. This would also be achieved by *formation of sickle cell support groups* for the patient.
- Empower young to make a choice: Developing the ability of young patients to make an informed choice for getting screened would increase the community participation.
- The rationale and justification and budgetary implications of these policy recommendations are given in the main text.

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Comprehensive Report
Towards a Policy to Address Sickle Cell Disease in Chhattisgarh State:

An Analysis of the Context and Policy Options:

I. Introduction

Chhattisgarh should be considered as a 'nucleus' of the sickle cell disorder in India though it is prevalent in its neighboring states - Maharashtra, Orissa, Jharkhand, Madhya Pradesh and parts of Andhra Pradesh. The number of sickle cell anemia patients is drastically rising in the state, mainly in certain communities, and despite the state government's best efforts the situation is alarming.

II. The Need for a policy

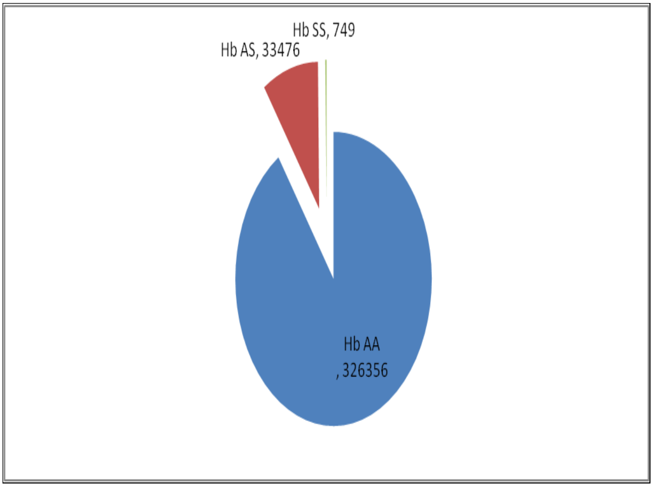
- State government has started with various initiatives for control of sickle cell anaemia. These initiatives are triggered by awareness in sections of the public and in the political leadership of the extent of this problem. Certain communities had recognised that there was a very high prevalence of sickle cell disease in their caste groups living in Chhattisgarh and were seeking government action to address this problem. A number of clinicians perceived this a disease which admits of no cure- since it is a genetic disease. They also recognised its close link with intra-caste marriage with a geographically small area. But it was potentially possible to arrange for marriages such that the chances of the disease in the offspring could be minimised. It was almost logical to deploy a strategy that addressed this dimension. But in the lack of public awareness of other options and other experiences of control the resulting government policy was lopsided with a neglect of all other dimensions of this issue.
- The main strategy deployed was thus mass screening, especially of adolescents, with the expectation that knowledge about having the sickle cell trait would induce young men and women from entering into marriage with others having the same trait- and that this would over time lead to an elimination of what is are however concerns about the effectiveness of this strategy. Screening coverage is limited, and only a modest proportion of those suspected submit for confirmation. Even when confirmed, anticipated actions with regard to subsequent choices of partners in marriage does not take place. There is a need to identify alternative approaches of prevention which would be cost effective and socially acceptable.
- There is an unmet need for treating tens of thousands of individuals who are diagnosed with Sickle Cell Disease (SCD)- either because they were symptomatic or because the disease was identified during various screening camps. There is no clear understanding of what is the state government commitment in this regard.
- There are now reasonable estimates of how many have the trait and how many have the disease based on sporadic surveys and screening camps- but there is no plan for sustained collection of information on disease incidence or ensuring that the estimates are validated. On one hand the political pressure emanates from specific communities, and on the other hand these communities would not even liked to be named for fear of stigmatization.
- There is a need for part structured plan and vision on the sustained reduction of the incidence and suffering due to this disease. There is also a need for policy clarity on financial requirement to provide these services and to ensure financial protection for the victims of this disease so that they do not face financial hardship or impoverishment to as a consequence of seeking care.

Context of the problem

The burden and distribution of disease:

- A programme designed to detect the sickle cell trait a sickle cell disease has screened 359,823 subjects among 2,087 (99.7%) of the villages in Raipur District, Chhattisgarh State, India between October 2007 and June 2010. The sickle cell trait occurred in 33,467 (9.30%) and an SS phenotype in 747 (0.21%). (Pradeep K. Patra 2011)Another study conducted in Rajnandgaon district, also documented that 9.75% of the examined population carries a sickle cell gene. (Paunipagar PV 2006)

RESULT OF SCREENING PROGRAM IN 2087 VILLAGES OF UNDIVIDED RAIPUR



- Extrapolating from these figures we estimate that there would be about 25 lakh persons carrying the gene and about 60,000 persons with the disease. Caution needs to be exercised in using these estimates, since tribal populations especially in the southern and northern ends of the state have not been so screened. There are reasons to believe (based on specific field areas) that the disease prevalence could be much higher is the disease is looked for actively in suspect patients.

- In Chhattisgarh State the sickle hemoglobin is common in Central and Southern parts i.e. barring few districts like Raigarh, Jashpur, Surguja, and Koriya. The tribes of Chhattisgarh which have shown high prevalence rates of sickle hemoglobin are: Halba of Rajnandgaon and Durg districts, Muria and Hillmaria of Bastar districts. The studies also suggest that the Scheduled Castes and some of the OBC groups like Sahu, Chandrakar, Kurmi and Yadav of Southern and Central Western Chhattisgarh also have sickle haemoglobin which is almost in the same proportion as that of tribals of the area. There are 12 districts in Chhattisgarh which fall in main sickle cell belt of the state. These districts are: Dantewada, Bastar, Kanker, Korba, Mahasumund, Rajnandgaon, Dhamtari, Kawardha, Bilaspur, Durg, Raipur and Jangjir- Champa.

2. Efforts of the government

- **Sickle Cell Institute:** The government has set up Sickle Cell Institute at Raipur to work towards providing assistance to patients suffering from sickle cell anaemia and also carry out research on the subject. This provides one sort of resource and institutional capacity to address this disease. The data provided by Sickle Cell Institute, Raipur is also suggestive of the fact that sickle cell anaemia is unevenly distributed. It has higher prevalence amongst specific communities.

- **A Chhattisgarh Sickle Cell Screening Project:** It was launched in 2010 with a main strategy to screen persons of all age groups for the disease and the strain using solubility test. By subsequent counselling of unmarried adolescents and young people with the trait from marrying another person with the same trait, it was hoped to reduce the prevalence in the next generation. However there is no evidence that this approach succeeded- and some anecdotal reports that it did not. Young women who had been identified with the trait and given a card, reported that this would not be a factor in choosing a spouse if otherwise it was found suitable and were unsure whether it was of any help. Moreover some of them reported that they have to face a discrimination based on their declared status of diseased and trait.

- **Mobile Clinic for sickle cell anemia:** Government of Chhattisgarh has started a mobile clinic for sickle cell anaemia in 2010, which according to verbal reports mainly visits schools for screening of cases. There is little data available that can be used for assessing efficacy and effectiveness of this approach.

- **The much needed political will:** There is a political will across the State and at the highest levels of governance to support sickle cell anemia prevention and control activities. Driven by this political will and priority that this programme enjoys, there is since 2010, a well funded state scheme as well as funds sanctioned under NHM. However given the lack of policy clarity and a clear and comprehensive approach these funds return unutilized year after year.There is also a concern that these funds are utilized as part of a technically sound public health approach- rather than being limited to immediate clinical perceptions.

3. The success stories

There have been very good models of SCD management and control undertaken by field NGOs and resource groups like Jan Swashtya Sahyog that can be learnt from and scaled up. There are also other Indian examples like from Bissam Cuttack as well as many international examples that can be learnt from to construct a public health policy that addressed sickle cell disease.

IV. Principles of a Policy to address Sickle Cell Disease :

- Though Sickle Cell Disease is not curable in a literal understanding of the word - It is possible to keep the patient symptom free and with a normal life span if there are assured diagnostic , therapeutic and support services that are available. The focus of policy would thus be on early identification and secondary prevention.

- Though Sickle Cell Disease has no technical option for prevention in the short term its prevalence rate can be reduced by increased awareness and more informed choice by young people with respect to marriage and childbirth.

- Policy must be aware of the concerns related to the introduction of new technological options that impact on gender relations in the context of a society which is still patriarchal and women's choice and decision making is still limited. Issues of privacy, confidentiality and autonomy need to be retained. The decision on Mandatory Universal screening must be informed by evidence of effectiveness and considerations of cost effectiveness, the risk of discrimination, equity, and autonomy.

- Since most of the affected are in poor communities- financial protection against the costs of care- and the challenge of ensuring universal access to care – not only for detection and financial protection but for management of complications such as sickle cell crisis- must inform the making of policy.

- The prevention and management of sickle cell disease will not constitute a separate vertical programme. It would be integrated with the health care system. However a technically qualified resource team would be required to build capacity for and guide the programme.

Examining the Technical Choices & Policy Options

The Policy Brief suggests some major new initiatives, each of which is a choice of technology or a policy choice or both. Given below is the evidential basis and considerations on which these choices are made- and the alternative options that we decided against. It includes the resolutions agreed in the workshop Organised by SHRC in collaboration with Department of Health and Family Welfare Chhattisgarh on 4th December 2015 at Raipur. The workshop included experts from Sickle Cell Institute, Chhattisgarh, NGOs an Government specialists working on sickle cell problem in Chhattisgarh and in high burden areas like Maharashtra and MP, experienced doctors from Government, Private and Charitable sectors, diagnostics experts from CMC Vellore and AIIMS Raipur, SCD patients, community organizations and representatives from Directorate of Health Services CG.

Some of the key resource persons and participants in the workshop were Dr. P K Patra, Director General, Sickle Cell Institute, Medical College, Raipur, Dr. Deepti Jain- Professor GMC, Nagpur, Dr. Raja Subramaniam- NIRTH Jabalpur, Dr. Eunice Sindhuvi E.- Professor, CMC Vellore, Dr. Manisha Ruikar- Professor AIIMS, Raipur, Dr. Rajib Dasgupta- Professor & Chairperson, Centre of Social Medicine & Community Health JNU, Dr. K R Antony-Ex Director SHRC, Dr. Yogesh Jain- JSS, Ganiyari, Dr. Nighat Hussain, Pathologist, AIIMS Raipur, Dr. Naveen Tirkey- Professor, Medical College Raipur, Dr. Atul Jindal, Assit. Professor AIIMS Raipur, Dr. Saibal Jana-Saheed Hospital, Dallirajahara, Dr. S Pambhoi Joint Director Surguja, Dr. Alka Gupta- Deputy Director- Maternal Health, DHS Raipur, Representative of RSBY CG, Shri Sampat Ramteke- President Sickle Cell Society of India, Nagpur and many other Clinicians, Academics, Health workers and Activists.

For each of the policy option recommended in the initial brief, the response of the workshop is recorded. The final recommendations are based on the consensus arrived in the workshop.

Q 1. Why is screening of all newborns for sickle cell disease recommended:

1. *Because identification of SCD allows for prevention of morbidity and mortality from the disease- through active secondary prevention measures:*Long back in 1986, the demonstration that prophylactic penicillin markedly reduces the incidence of pneumococcal sepsis(Gaston MH, 1986) provided a powerful incentive for the widespread implementation of neonatal screening for sickle cell disease (Panel, 1987). Subsequent experience demonstrated that neonatal screening, when linked to timely diagnostic testing, parental education, and comprehensive care, markedly reduces morbidity and mortality from sickle cell disease in infancy and early childhood (Harris MS, 1989)

2. *Because it could lead to a signficant decrease in infant and under- 5 mortality*. Preference for newborn screening is based on an understanding that without treatment only half the children would reach adulthood and with treatment over 95% can be expected to do so. As most of the deaths due to SCD occur in first three years of life, this would also contribute significantly to reduction of under 5 mortality due to respiratory infections. (Currently the most common cause of under 5 mortality).

3. *Because there is precedence—best practices- that provides evidence to support the effectiveness of this measure* : Many countries including Jamaica, Ghana, USA, Canada have relied upon newborn screening as an effective measure in management of SCD.

Newborn screening (NBS) for sickle cell disease (SCD) has occurred in Jamaica since 1973 in two periods, the most recent being since 1995. As a result significant improvements in morbidity and mortality of children affected with the disease have occurred in these because of the implementation of simple interventions. (King L1, April, 2014)

4. *Because there is a favourable health systems context due to RBSK*. A new scheme funded by NHM calls for screening of newborns. The screening for SCDs is not currently emphasized in this scheme- but given the fact that we do actively screen for many other conditions with a lessor degree of prevalence the economic justification for this is strengthened.

5. *Because it will contribute to primary prevention-* for the act of screening can be act of alerting the family to the probability of having subsequent children with SCD. Also any child with sickle cell trait gets identified for future reference.

6. *Cautions and Limitations* : The capacity to undertake this screening is the primary caution. This requires, as a start, adequate diagnostic capability in every site of institutional delivery and a preparedness (skills, diagnostics) to do the testing and to provide the necessary treatment where a child is detected with SCD. On the other hand, the benefits are significant not only to the family but to the community as well. One major positive consideration why the effort is worth it is political – a desire to see that the fruits of genomic science should not remaina luxury available only to the developed nations and affluent sections of our society.

Response from workshop: The workshop agreed that early identification of the disease in newborns is very much needed. The consensus was that HPLC is the preferred option for newborn screening. However considering the limited availability of HPLC in Chhattisgarh (at the moment available only in Medical College hospitals), it was decided to identify newborns with SCD by first screening all pregnant women with the universally available low-cost solubility test and if positive also testing the husband- and if both are positive then only such newborn tested for SCD.

Q 2. Should all newborns be screened?

1. *Why this question?:* Newborn screening is now integrated into routine neonatal practice in many parts of the world, and the overall ethical acceptability of newborn screening programmes is well recognized. One option that we considered and did not recommend is to limit newborn screening only to high risk communities/caste groups. One important reason for considering this option was costs and capacity.

It would appear much easier to implement and to finance if this test need not be extended to all newborns- but only those at higher risk.

2. *The public health criteria for choosing universal screening* :Neonatal screening programmes can be offered universally or selectively. Universal screening is by definition making the test for SCD, a routine public health intervention offered to the entire newborn population. Perhaps the most cited source of universal screening criteria are the 1968 Wilson and Jungner principles of early disease detection. (see box:) Sickle cell disease is prevalent in Chhattisgarh. Though there is no cure in the formal sense there is now treatment available that provides for a normal life expectancy and freedom from symptoms and suffering. The technologies for diagnosis and treatment are available, and it is potentially possible to ensure universal access to these. Therefore literature on the subject concludes that universal newborn screening could be recommended. (Zeuner 1999)

Precedence and international evidence: Universal screening of newborns for sickle cell disease is part of the NHS (National Health Services) protocols for the United Kingdom, where thanks to its national institute of clinical excellence there is specific expertise in making technology assessments. (ref. NHS SCD & Thalassemia screening programme, July 2004). Such newborn screening is also implemented in most of the United States. And these nations have a lesser prevalence than is being reported for Chhattisgarh. Selective or targeted screening concentrates on subpopulations with the aim of identifying high-risk infants and, indirectly, of identifying high-risk parents to offer them the opportunity of screening in future pregnancies. The decision whether to adopt a universal or selective strategy involves complex arguments about the risk of discrimination, equity, and cost-effectiveness. There is some evidence from other nations (give reference from Georgia in US) that programmes that screen in only specific high-risk segments of a population tend to miss individuals who are inaccurately registered. Although the disease is prevalent in certain groups, it is not possible to define accurately an individual's heritage using physical appearance or surname. Leaving the selection based on certain criteria to the discretion of individual physicians or health care.

Response from workshop: The workshop examined the ethical issues and agreed that the logic for universal newborn screening is valid however, considering the limited availability of HPLC testing in state at the moment, the route should be through maternal screening. The logic for universal newborn screening can be extended to maternal screening but it should be based on informed consent.

facilities is also not considered justified when the benefits are so high and when there are dangers of iniquitous access to tests based on physician discretion.

4. *Social considerations: Selective Screening and Stigma*: A high risk approach to newborn screening in Chhattisgarh would require that babies born of certain caste groups are screened more often and even within that families at risk are identified. While political pressure for action on SCD emanates from such politically important community groupings- these same forces would resent an equation between caste and disease. Within communities identification of high risk families would also put pressures on the institutions of the family and marriage, often with adverse impacts being borne by women. Given our findings on the high levels of stigmatization selective screening would neither be feasible nor desirable.

5. Epidemiological Considerations: There is just not enough epidemiological data available to rule out significant levels of prevalence in tribal populations. Anecdotally there are a high number of cases detected in all social groups in a given geography, when appropriate services are available. The problems noted in international experience would then be more acute in Chhattisgarh's circumstances.

NHS Sickle Cell and Thalassemia Screening Programme, Policy for Newborn Screening, London, July 2004, http://www-phm.umds.ac.uk/ haemscreening/Documents/ NewbornScreeningPolicy.pdf (accessed on 04/08/04)

Does Newborn Screening for SCD fulfill the criteria for universal screening?

According to Wilson and Jungner principles of early disease detection, conditions that are screened for should:

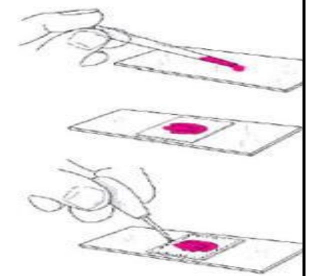
- Present an important health problem (i.e. be relatively prevalent);
- An acceptable treatment be available to treat the screened condition
- Facilities for diagnosis and treatment be widely available:
- The cost (including diagnosing and treating patients) be economically balanced in relation to possible expenditure on medical care as a whole:
- The diagnosed patients benefit from timely follow-up

Q.3 Which diagnostic test should be preferred for NBS?

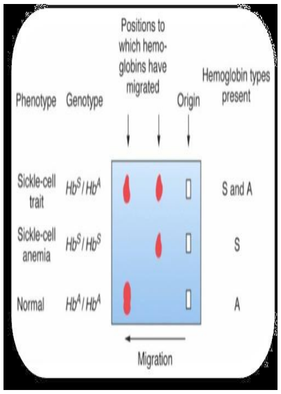
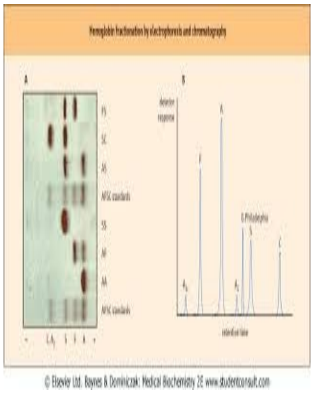
A. There are several recommended testing methods for diagnosis of sickling disorders and other hemoglobinopathies. The usual screening tests- especially solubility test are not be reliable for infants until they are at least 6 months old because of the presence of haemoglobin F as the predominant haemoglobin at birth. Infants with sickle cell disease or trait will not produce significant amounts of haemoglobin S until several months after birth; therefore, this test may give a false-negative result if performed too early (if haemoglobin S is <10%). The choices therefore are (1)For confirmatory tests: Haemoglobin Electrophoresis including both cellulose acetate and citrate agars (one is not sufficient), Isoelectric focusing (IEF) and High Performance Liquid Chromatography (**HPLC)** are considered proven, reliable and accurate methods for defining an infant's haemoglobin phenotype. Though HPLC is more accurate and requires less technical skills, IEF has been preferred because of its cost effectiveness and greater capacity to make it universally access. This is based on international studies (average cost per baby tested by IEF and HPLC was pound 3.51 and pound 3.83 respectively in an UK study.(E K Cronin, 1998)) and it is also based on opinion of interviewed experts.

- The costs per IEF test as practiced today are approximately Rs 200-250 whereas per HPLC it could be as high as 300-350. HPLC is available currently only at the medical college hospital whereas IEF is available wider and can be made available at all district hospitals.

Screening test for those above the age of 6 months:

Slide test √	**Solubility test**
	
Requires technical skills to handle microscope, prepare slides, etc. More reliable Takes more time to yield results. **Overall cost per test is higher.**	Easy to learn and perform Gives immediate results Needs less preparations **Overall cost is lesser (approx. Rs. 29 per test)**

Confirmatory test for those above the age of 6 months:

Electrophoresis	**HPLC**
	 © Elsevier Ltd. Baynes & Dominiczak: Medical Biochemistry 2E www.studentconsult.com
Labour intensive Time consuming method Less efficient when quantifying low concentrations of HbA2 and HbF or detecting HbH or HbBart's. **Overall cost per test is lower (Rs 80-100 approx)**	Sensitive and precise method Simple Superior resolution Rapid assay time Accurate quantification of Hb fractions **Overall cost per test is higher (Rs 350 approx)**

References:
http://www.chromatographyonline.com/essence-modern-hplc-advantages-limitations-fundamentals-and-opportunities.
(1)https://labtestsonline.org/understanding/analyses/sickle/tab/test/
http://www.idph.state.il.us/HealthWellness/fs/sickle.htm

Cautionary Note : We note however that these technical statements can be taken as preliminary and exploratory. Good technology assessment that comments on costs, ease of organization at every site of institutional delivery, and sensitivity and specificity of the tests needs to be studied – before we conclude on the best choice.

Response from workshop: The workshop consensus was that HPLC should be the preferred test for identifying the disease in newborns. There is inadequate experience in the country with IEF and it can even prove difficult to arrange maintenance of IEF equipment.

Question 4: Should *all people* with SCD get Pneumococcal Vaccine or should it be restricted to children below 5 or only to newborns?

A. We have concluded that all newborns screened should get pneumococcal vaccines. The evidence for this was that before early screening for sickle cell disease and the use of preventive antibiotics in children, 35% of infants with sickle cell died from infections. (1) The common causes of death include bacterial infection (the most common cause), stroke or bleeding into the brain, and kidney, heart, or liver failure. Infection is the major cause of death in children younger than age 5 or children with dysfunctional spleen (2).

The question was raised as to whether pneumococcal vaccine should be offered to all children when detected for SCD and further whether even in adults- detected as SCD in adult screening programmes or during treatment for any illness- this same vaccine should be offered. The risk of bacterial infections does diminish after three years of age. Nevertheless, bacterial infections are the most common cause of death at any age. (3)

We also note that pneumococcal vaccine is one of the candidate vaccines for universal immunization programme and is widely offered to infants in the private sector. In such a context its access and cost effectiveness are assured for any age group. Hence we have recommended offering the vaccine as part of the treatment protocol to all persons detected with SCD.

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2. http://www.medicinenet.com/sickle_cell/page4.htm

3.https://www.urmc.rochester.edu/encyclopedia/content.aspx?ContentTypeID=90&ContentID=P02327

Response from workshop: All children under five with SCD need to be included. Currently we will not be offering it to children with SCD above 5 years of age- but it could be provided on individual request.

Question 5: Should all adolescents be screened?

1. *Why this question?*

Because this is the most important and widespread action currently ongoing in the state. There has been considerable debate over the value of screening for Sickle Cell Anaemia in persons of reproductive age and we set out the points for and against below:

2. *Main reasons for screening:* The disease is seen as incurable. However primary prevention can be assured if those adolescents with sickle cell trait are detected and encouraged from inter-marrying. In essence it is a process of improving the genetic pool in communities with high degree of consanguinity. The argument seems persuasive in a community where arranged marriages within the community is the norm.

3. *Main reasons against screening adolescents* : Experts critical of this approach cite evidence that sickle cell screening programs in the past have failed to adequately educate patients and the public about the significant differences between sickle cell trait and sickle cell disease. This has resulted in unnecessary anxiety for carriers and inappropriate labelling by insurers and employers. In addition, there is no evidence that counselling, however comprehensive, will be remembered throughout the individual's reproductive life, influence partner selection, alter use of prenatal testing, or ultimately reduce the rate of births of affected children.

4. *Public health criteria for screening* : Screening adolescents does not fit the accepted public health criteria for screening. The focus is on detecting asymptomatic normal persons- and not on detecting disease at all. Most with the disease would have died before adolescence. Those with the trait face no health threat- though there is a risk for their children. What is offered on detection is not treatment- but a social and family action.

5.*Counter arguments in favour of screening:* Proponents argue that the intended objective is genetic counselling to facilitate informed decision making by prospective parents. In this regard, clinicians are responsible for making the individual aware of the diagnosis, the risk to future offspring, and the recommended methods to reduce that risk, regardless of the strength of the evidence that such counselling reduces the number of affected offspring. (cgmh.org).

6. *Counter arguments against screening* : Critics of the above argument point to a high investment in counselling that must necessarily accompany all adolescent screening. If provided, testing should be accompanied by counselling, which should include a description of the significance of the disease, how it is inherited, the availability of a screening test, and the implications to individuals and their offspring of a positive result. Privacy and confidentiality must be maintained. All of these can be assured in a context of voluntary screening in select centers- but not in a massive campaign strategy where whole populations are screened all at once.

7. *In conclusion*: There are arguments for and against. The policy brief makes a choice-it takes the position that this would have the lowest priority as an avenue for public health investment- and the reasons for screening are adequately addressed by an information campaign with voluntary testing- and therefore recommends against population level screening of all adolescents. Cost effectiveness studies are recommended.

Response from workshop: This was one of the most debated issues in workshop. The workshop agreed that the adolescent screening should be voluntary and for this awareness can be created gradually. Provision of curative services can help in creating demand for prevention too. Making adolescent universal or compulsory can have severe ethical and even legal problems.

Question 6: Should Hydroxyurea be given to all or on selective basis?

1.Why this question? The benefits of hydroxyurea (HU) are not in question. Clearly this is the only approved disease modifying drugs to be given to anyone above 24 months of age. HU is of clear benefit to patients with moderate to severe sickle cell disease. Indications for HU therapy include recurrent VOC (3 or more severe episodes requiring admission in the last 12 months), recurrent ACS (2 or more episodes in a lifetime), severe symptomatic anemia, and recurrent priapism, alternative to transfusion to prevent new or recurrent stroke especially where transfusion is not feasible (Ware, 2010). The protocols do not recommend giving it to all persons with SCD irrespective of symptom status.

2. Experience from the field: However a programme against SCDs being undertaken in JSS has been giving it for all patients with SCD who were ever symptomatic and report a good response. This they point is justified on clinical grounds- since almost all of them are symptomatic and regular HU therapy reduces symptoms and suffering considerably clinical grounds- since almost all of them are symptomatic and regular HU therapy reduces symptoms and suffering considerably. Also that sickle cell crisis can be devastating as a disease and financial catastrophe- and in a context where management of SCD crisis is so poor- HU therapy for all SCD is a valid measure of secondary prevention.

3. The reasons for restricting access. We find the argument for public provision of HU as secondary prevention in all cases of SCD with HU persuasive. We note that currently there is considerable financial and even availability barriers to access on a prescription and out of pocket route- and therefore continuity of care and access requires public procurement and access through public health care facilities. However costs of doing so would be high- and can be reduced substantially if only those with more than 3 episodes of complications are given continued medication with HU. Meanwhile a well designed study in the state context would help estimate effectiveness and cost effectiveness of a continued 365 day medication with HU for all those with SCD. It would also take time for the health system to develop the capacity to ensure such a 365 day supply to all with the disease, and it is therefore better they start up with a smaller case load. Hence the choice of an option where continued medication with HU is provided only to those who have 3 or more episodes of crisis or other serious symptoms within the last 12 months.

Response from workshop: The workshop agreed that hydroxy-urea needs to be given to SCD patients. There was consensus on the criteria as well that HU is provided to those who have 3 or more episodes of crisis or other serious symptoms within the last 12 months.

Q. 7. Should antibiotic prophylaxis be given to all babies with SCD?

1. Why this question? It is being recommended that antibiotic prophylaxis be given to all babies with SCD until 5 years of age to avoid the risk of pneumococcal infection. But we note that it would be the introduction of a new practice.

2. Proven efficacy: The efficacy of oral penicillin as primary prophylaxis in SCD was clearly demonstrated in pivotal trials published nearly 25 years ago. In a study by Gaston et al, children who were randomized to the daily oral penicillin prophylaxis arm of the study had an 85% reduction in the probability of infection compared with those given placebo. This study provided much-needed impetus for states in the

United States to adopt universal newborn testing to ensure that all children with SCD were identified, with a strong recommendation for prompt penicillin initiation. The clear benefit of newborn screening combined with penicillin prophylaxis is demonstrated by decreases in SCD-related mortality among black children under the age of 4 years by 68% from 1983-1986 to 1999-2002, with the largest decrease occurring after 2000, when the 7-valent pneumococcal vaccine was added to the schedule of recommended immunizations for all children. In the sub-group of age five and above, episodes of pneumococcal infections occurred at lower rates than anticipated in both arms of this randomized, double-blind, placebo controlled study and no significant difference could be detected. The conclusion was that penicillin prophylaxis could be safely discontinued at age 5 years, although some paediatric haematologists continue to recommend indefinite prophylaxis given concerns about infection susceptibility.(Thompson, 2011)

3. There are no Indian studies, but death due to pneumococcal respiratory infection is common, and hence penicillin prophylaxis recommended for all children below 5 with SCD. We have not examined how essential penicillin prophylaxis is in babies who are fully immunized for pneumococcal vaccine- but since the latter will take some time to introduce, the penicillin prophylaxis is recommended for immediate start up.

Response from workshop: The workshop consensus was that daily oral penicillin should be given to all babies with SCD from 2 months onwards (125 mg twice daily) till five years of age. It should also be given to children fully-immunized with pneumococcal vaccine as the prophylaxis can be useful for many other infections which are common for children with SCD. Currently we will not be offering it to children with SCD above 5 years of age- but it could be provided on individual request.

Q.8. At what level should we provide for continued access to hydoxyurea medication in proven SCD's recommended this treatment- PHC, CHC or DH ?

1. Currently patients with SCD access HU only at the medical college level- and this gives only one or two weeks of drugs. Because of inability to come again and again- even those who urgently need it- cannot access these drugs on a regular basis. It costs about Rs. 6000 per month/ per year to access on a regular basis- and much more if the access is from the private sector.
2. Making it available as close to patient as feasible is essential for medication compliance. There is a need to structure the access similar to that for anti-HIV or anti-TB drugs. The patients monthly quota of medicines should be provided at the nearest convenient facility in a pre-packaged form which is labeled by name and sent there from the district warehouse. This nearest facility could be PHC, CHC or DH. The district warehouse would have the list of facilities and the number of patients registered with each. Since this is only a dispensation point- even sub-centers and dispensaries can be included.

Response from workshop: The continued access to Hydroxy Urea should be from CHC and above. In high patient load areas, PHC should also provide it. Training of providers needs to be carried out from district hospitals, CHCs and PHCs (with high burden).

Q.9. Should we recommend mobile medical clinics for SCD?

1. The background : Government of Chhattisgarh has started a mobile clinic for sickle cell anemia in 2010, which according to verbal reports mainly visits schools for screening of cases. Its role is seen as screening is done, and those tested positive would be provided with confirmatory test, counseling and treatment as well.

2. *The problems:* There is little data available that can be used for assessing efficacy and effectiveness of this approach. If confirmatory test is available there is some value addition as compared to usual camp based screening- but the problems of follow up on positive cases and even on those detected with traits remain.

3. *The choice of options*: Much of the concerns of adolescent screening for sickle cell trait apply to these mobile medical clinics as adolescents are the main focus of its screening activity. Costs would however be more. A cost effectiveness analysis is suggested- but prima facie based on prioritization- this is a low priority intervention and not recommended.

Response from workshop: Mobile clinics were not recommended by the workshop.

Q. 10. Should we encourage and offer voluntary testing for adolescents and pregnant?

1. Though mass screening or universal screening of adolescents has been discouraged, one option considered was to make screening for disease and trait available on demand and free of user fees in PHCs and CHCs and other higher health care facilities. This would be accompanied by - health communication that educates the public on SCD and promotes adolescents and pregnant women to consider voluntary testing.

One advantage of this would be that those who are at risk or who want to make an informed choice on marriage, pregnancy, child birth etc could do so. Because it is voluntary some of the earlier fears are not there- and it is available for those who are unmarried, married and even those who are pregnant. It is expected as awareness of the disease increases, more and more young men and women would make informed choices of whether they want to have the test, and whether they choose to risk the child etc. In a situation where survival of children with disease could increase considerably, there is an even greater need to emphasize choice. Reasons of cost-effectiveness also support such an approach as compared to mandatory universal adolescent screening.

Response from workshop: The testing for adolescent should be voluntary. For pregnant women, it must be made available pro-actively during ANC check-ups but testing should be preceded by informed consent.

Recommendations:

Based on the discussion of the policy options we arrive at a list of recommendations that are presented as part of the policy brief and not repeated here for sake of brevity.

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ANNEXURE -1
THE EMOTIONAL AND SOCIAL IMPACT

In assessing the seriousness of this disease, no one should underestimate its emotional and social impact. For the family, nothing is more heartbreaking than watching their child endure extreme pain and life-threatening medical conditions. The patient endures not only the pain itself but also the emotional strain from unpredictable bouts of pain, fear of death, and lost time and social isolation at school and work. Academic grades among patients average less than C, even in children with a low frequency of hospitalization (averaging 17 days a year).

These problems continue over the years, and both children and adults with sickle cell disease often suffer from depression. The financial costs of medical treatments combined with lost work can be very burdensome.

Any chronic illness places stress on the patient and family, but sickle cell patients and caregivers often face great obstacles in finding psychological support for the disease. Communities in which many sickle cell patients live generally lack services that can meet their needs, and professionals who work in their medical facilities are often overworked. In a study comparing patients with different kinds of long-term illnesses, those with sickle cell disease gave the lowest scores to their doctors and other professional caregivers for compassion, and were least satisfied with their medical care.

It is very important for patients and their caregivers to find emotional and psychological support. No one should or can endure this life-long disease alone. Unfortunately, studies indicate that most patients do not receive even basic supportive care that could help reduce the anxiety and intensity of pain that occurs when a sickle cell crisis erupts.

The case study given below illustrates some of these problems:

Story of a survivor

(Author-Narayan Tripathi, SHRC Raipur)

A few years back, 35 years old Savitha Sahu (name changed) used to work as a daily wage worker. But now she is unable to perform her routine activities. She was diagnosed with sickle cell anemia when she reported severe anemic complications during her second pregnancy. After her first baby, the next two children died within one year of their birth. Both had low birth weight babies with childhood complications. She told that both had sickle cell disease.

Her fourth child also suffers from sickle cell disease. He is five years old and is lucky enough to survive till his fifth birthday. Child was very weak since birth. Two years back pain episodes exaggerated and complications worsened. Then parents took the child to a private hospital where they admitted the child. The hospital demanded rupees twenty thousands from them for any injection course. The hospital staff also claimed that this will be a kind of complete cure. Going beyond their affordability limitation, parents gathered rupees fourteen thousands, after which they stopped the treatment. But the treatment did not appear to be curative at all.

Reportedly, the pain episodes and complications became graver and child condition was more deteriorating. This led to the requirement of blood transfusion. Since then, the child receives blood transfused after every six months. Savitha prefers to take her child to private health facilities rather than government facilities because the latter often has unavailability of medicine or blood or treatment for the disease.

Parents reported that during the severe pain episodes, this five year old child cries and begs his own parents to cut his legs so that he will not have to tolerate more pain. The expressions on the face of the parents were a mirror to depict the agony of the children who do not have enough vocabulary to express

They enrolled the child in the school this year but he hardly goes for once or twice in a week. He is having very irritable nature of mood and poor in learning. From the last two months child is on hydoxyurea and folic acid medication. Reportedly he has got some relief from the pain and sufferings. But this treatment continues to prove catastrophic for them as they have already spent all their savings in the treatment of child.

Savita herself is a patient with sickle cell disease and experiences frequent severe painful episodes and anemic complications. But she is not undergoing treatment because it is unaffordable. "The family is unable to save a single penny after undergoing child's treatment expenses and other household expenditure." she told.

Annexure – 2

India failing adivasi tribes with sickle cell

(source: http://infochangeindia.org/public-health/features/india-failing-adivasi-tribes-with-sickle-cell.html, accessed Nov 15, 2015)

With the spotlight on lifestyle diseases like diabetes and hypertension, traditional illnesses like sickle cell disease, which affects tribals all across India, are not receiving the attention they deserve. Among India's tribals, prevalence varies widely. The *Genetic Atlas of Indian Tribes*, published in the 1970s, states that some adivasi communities lack the sickle cell gene entirely, while in others more than 40% of individuals tested carried the sickle cell trait; however many of these figures are not definitive as the sample sizes involved were quite small.

Devjibhai Rathwa and his family have sickle cell anaemia but do not know the exact nature of the ailment

Devjibhai's younger children with identification cards that help doctors and health workers make a quick diagnosis

Devji's family comprised daughter Kokila, barely five, who kept complaining of abdominal pain instead of playing with her older brother, Dinesh. Their young mother, Sancharben, was at her wits' end because the youngest child, Arjun, wouldn't stop crying. The three-year-old had a painful left ear. Sancharben herself was anaemic and suffered from frequent joint pains. The eldest child, Surekha, a shy eight-year-old, was somehow managing the kitchen and the daily chores. Devjibhai, who was in his early-30s, appeared stunned by the bizarre health problems. He did not know the exact nature of the ailment.. "Kokila has sickle cell disease, inherited from Sancharben who carries a sickle cell trait," explained Rajendra Varia, a health worker with Bhasha, who accompanied me. "The other family members need to undergo blood tests. Arjun may have inherited the red blood cell disorder. It is typical to adivasis. It is painful and could kill."

Tribals, even their children, do not (normally) cry. The sickle cell pain alone makes them cry," observed Ganesh Devy, the Baroda-based writer-activist who founded Bhasha to work among tribals. "The pain can be relieved. But what about the right to have a complete blood cell like every other human being? It should be a cause for alarm if social conditions start making them incomplete or fragmented."

ANNEXURE- 3

MORE ABOUT THE DISEASE- THE CLINICAL DETAILS

Sickle-cell disease (SCD) is the most common single-gene blood disorder in the world and represents a significant public health problem in India. (Arjunan 2013). India has the highest number of sickle gene carriers in the world. It is a genetic condition in which the red blood cells (RBCs) contain hemoglobin S (HbS), an abnormal form of the oxygen-carrying protein. These RBCs under the influence of faulty gene become hard and sticky and resemble a C shaped farm tool called sickle.

The symptoms and/or complications of the disease are:

Pain due to sickle cell crises. The most common symptoms of sickle cell disease are episodes of pain that can last for extended periods of time. The pain can occur throughout the body and often involves the bones, joints, lungs, and stomach.

Anemia. Sickle cell disease is a hemolytic anemia, meaning that the abnormal, sickled RBCs break down (hemolyze) more quickly than normal red blood cells and cannot be replaced by the body as quickly as needed, thus leading to a decreased number of RBCs and reduced ability of the RBCs to transport oxygen throughout the body.

Increased number and frequency of infections, especially pneumonia, which is the leading cause of death in children with sickle cell disease.

Coughing, chest pain, and fever suspected to be caused by a serious complication of sickle cell disease called acute chest syndrome.

Other symptoms may include retina damage and vision loss, growth problems in children, leg ulcers in the lower part of the leg, gallstones, and painful extended erections of the penis called priapism. Because sickled RBCs do not easily flow throughout the body due to their characteristic sickle shape, they can become trapped in various areas and cause serious complications. These can include splenic sequestration (a rapid enlargement of the spleen), damage to organs, tissues, or bones due to a lack of blood flow (such as to the kidneys) or stroke, which occurs in 10% of children affected by sickle cell disease.

Sickle Cell Crisis: The hallmark of sickle cell disease is a group of devastating symptoms known collectively as a *sickle cell crisis* (also sometimes known as a *vaso-occlusive crisis*). Sickle cell crises are episodes of pain that occur with varying frequency and severity in different patients and are usually followed by periods of remission. Severe sickle cell pain has been described as being equivalent to cancer pain and more severe than postsurgical pain. It most commonly occurs in the lower back, leg, abdomen, and chest, usually in two or more locations. Episodes usually recur in the same areas. Acute chest syndrome is a particularly serious complication of sickle cell crisis. It occurs in the lungs and can be extremely serious and even life threatening.

Prognosis

Children with sickle cell disease are very susceptible to infections, usually because their damaged spleens are unable to protect the body from bacteria. Signs of impaired lung function may occur even in very early years. As children with sickle cell disease live longer, older patients are now facing medical problems related to the long-term adverse effects of the disease process. The most serious dangers are acute chest syndrome, long-term damage to major organs, stroke, and complications during pregnancy such as high blood pressure in the mother and low birth weight in the infant.

Treatment

Treatment goals for sickle cell disease aim to relieve pain, prevent infections, and manage complications. Patients should seek care from a doctor who specializes in blood disorders (hematologist) or a clinic that is experienced in treating sickle cell disease.
Bone marrow transplantation is the only potential cure, but it is used in only a small number of cases as few patients are able to find donors who are suitable genetic matches. Blood transfusions are given to prevent worsening anemia and prevent stroke.

Drug treatments for sickle cell disease include:

- Antibiotics, usually penicillin, are commonly given to infants and young children, as well as adults, to help prevent infections.
- Pain relief medication ranging from nonprescription nonsteroidal anti-inflammatory drugs (NSAIDs) to opiods are given to control pain.
- Hydroxyurea is prescribed for patients with moderate-to-severe sickle cell disease to help reduce the frequency of pain episodes and acute chest syndrome. It is approved

TREATMENT OF SICKLE CELL DISEASE DURING PREGNANCY

Women with sickle cell disease can successfully carry pregnancy to term or near term. If a patient reports that she is interested in, or already trying to conceive, hydroxyurea should be immediately discontinued. A patients pregnancy should be co-managed by high risk obstetrics and the primary and mid-level sickle cell providers. Painful episodes during a pregnancy should be managed as they would for non-pregnant patients with adequate hydration, oxygenation and analgesia. Opioid analgesics should not be withheld from a patient just because she is pregnant since fetal or newborn addiction is rarely an issue. More importantly, the patient herself should remain as healthy and comfortable as possible throughout the pregnancy.
Prophylactic transfusions during pregnancy are not indicated unless there are complications which would ordinarily be treated with transfusions, such as acute chest syndrome. Studies have shown that there is no overall decrease in crisis frequency, premature labor or premature deliveries for women who are prophylactically transfused throughout their pregnancy (Koshy, 1988)

Immunization Schedule for Pneumococcal Vaccination

Infants (6 weeks to 6 months)	0.5 ml intramuscular injection administered at 2, 4, 6, and 12 to 15 months of age for 4 total doses; The first dose may be given as young as 6 weeks of age, but is typically given at 8 weeks (2 months of age) The 3 remaining doses are usually given at 4, 6, and 12 to 15 months of age. The recommended dosing interval is 4 to 8 weeks. The minimum interval between doses in children less than year of age is 4 weeks. The minimum interval between the third and fourth dose is 8 weeks.
Infants (7 to 11 months)	0.5 ml for 3 total doses; 2 doses at least 4 weeks apart, followed by a third dose at 12 to 15 months, separated from second dose by at least 8 weeks.
Children (12 to 23 months)	0.5 ml for 2 total doses, at least 8 weeks apart.
Children (24 to 59 months)	Healthy children: 0.5 ml as a single dose.
Children (24 to 71 months with underlying medical conditions)	ACIP recommendations: 0.5 ml for a total of 2 doses, separated by 8 weeks.