

Excerpt of symposium on Sickle cell disease*

Sickle cell disease (SCD) is a public health burden in India, as exemplified by the fact that nearly 20 million people suffer from it in the country, generating a huge psychological burden to society and an economic burden to the nation¹. In India, SCD is mainly prevalent among unprivileged communities. There is an unmet need to control SCD in the country. For the prevention of SCD in India, screening at the community level has been conducted at various times; however, they were conducted at small scales and limited to one-time screening. Due to a lack of follow-up by carriers for counselling, these small screening programmes could not fulfil the objective of preventing SCD in India.

Recently, under the leadership of the Prime Minister of India, a mission to eliminate SCD by 2047 has been announced. It will focus on awareness creation, universal screening of approximately seven crore people in the 0–40 age group, and counselling through collaborative efforts of central ministries and state governments.

To formulate the strategies for this mission, ICMR-National Institute of Research in Tribal Health (ICMR-NIRTH), Jabalpur, Madhya Pradesh (MP), where international and national experts shared their knowledge in order to formulate a roadmap for prevention and management of SCD in India. In this symposium, 16 eminent speakers shared their expertise on the status of SCD in India, including its genesis, epidemiology, therapies and efforts taken by the Government. Three interconnected perspectives were discussed, i.e. to understand the evolution and current status of SCD, address the issues surrounding this disease, and pave a pathway to achieve the goal of the nation, i.e. mission for the elimination of SCD by 2047.

Throughout the symposium, interaction between talented young students, patients, experts and Government dignitaries was proactively encouraged.

The symposium commenced with an introductory speech from the organizers Rajnarayan Tiwari (Director, ICMR-NIREH, Bhopal) and Aparup Das (Director, ICMR-NIRTH). The efforts taken by ICMR since 1986 in the field of tribal health and well-

ness were highlighted. This was followed by inaugural talks by all the dignitaries present. Vinita Srivastava (Ministry of Tribal Affairs (MoTA), Government of India (GoI)) highlighted the efforts that are being taken in the form of a strategic roadmap for the prevention, control and management of SCD. The strategic pillars of the roadmap included affordable, accessible and quality care for all SCD patients. Srivastava underlined that to achieve this landmark, mass screening activities would be carried out in two phases: phase I for individuals below 18 years of age and phase II for those below 40 years of age. Appropriate strategies will be formulated for managing SCD patients at the primary, secondary and tertiary care facilities and followed up.

R. Jaya (MoTA, GoI) mentioned that during the SCD elimination mission, a total of seven crore tribal people will be screened for haemoglobinopathies. Further, she emphasized the need for regular counselling to be given to family members, especially mothers and the affected children, for the day-to-day management of SCD. She suggested data management and analytics for a better understanding of the incidence and penetration of the disease. Additionally, the need for training was highlighted along with increased provision for budget, which could be made available as a 'grant-in-aid' from GoI via Article 275 of the Indian Constitution.

Mohammed Suleman (Government of MP) mentioned the steps taken by the Government of MP in line with the SCD elimination mission, reflecting a positive approach towards cooperative federalism. He elaborated on the pilot project launched in two districts of MP – Jhabua and Alirajpur – for mass screening, the success of which was shown by the fact that in six months, over 50% of the 8.26 lakh population had been screened for SCD.

Prabhuram Choudhary (Minister of Public Health and Family Welfare, Government of MP) emphasized the 'household screening model' which was being followed, under which even if one individual had tested positive, screening of the entire family is recommended, enhancing the coverage of disease detection. He focused on the need for separate counselling for sickle cell trait (SCT) and SCD.

Arjun Munda (Union Minister of Tribal Affairs, GoI) mentioned the two main deficits present in the current system: infra-

structural deficit and awareness deficit, which could be bridged using a multi-stakeholder approach, i.e. through community mobilization, involvement of self-help groups, etc. He also emphasized pre- and post-counselling of the community to do away with any stigma related to the disease.

Mangubhai C. Patel (Governor of MP) gave three basic guidelines to act as the backbone for managing and eliminating SCD. These are timely genetic counselling with a valid card, improving the life of the diseased carriers and community awareness. The need for a proper action plan was emphasized with components of public awareness, screening, counselling and data management. Awareness should be given not only to diseased persons but also to the public. He also encouraged the Government to take steps for integration with AYUSH on new innovative therapies for the disease for a better lifestyle for SCD patients.

Following the inauguration speeches, various experts in SCD shared their experiences with diagnosing and managing this disease.

On the first day of the symposium, the special lectures commenced with a keynote address by Graham Serjeant (Sickle Cell Trust, Jamaica), a well-renowned global authority in SCD. He started his talk with the natural history of the disease and its high prevalence among people of sub-Saharan Africa, South Asia, the Middle East and the Mediterranean countries. Further, he illustrated the clinical difference between Asian and Benin haplotype patients. Serjeant showed that patients with the Asian haplotype have higher haemoglobin levels, lower reticulocyte count and much higher foetal haemoglobin (HbF), demonstrating persisting splenic functions and an 'anti-sickling' effect in the haplotype. The session concluded with the message that much more research needs to be done on the Asian haplotype of the Indian population to define and develop optimal modes of therapy.

S. Rajasubramaniam (ICMR-NIRTH) provided an epidemiological understanding of the disease. He mentioned that in India, approximately 3–5% of the people are carriers; however, carrier frequency increases to 35% among certain tribal groups (the primary affected group). Furthermore, some Schedule Caste and other Backward Classes also have a high prevalence of SCD. He raised concern about the fact that the real burden of the nation remains unknown

*A report on the symposium on Sickle cell disease in India held on 22 and 23 February 2023 at ICMR-National Institute for Research in Environmental Health (ICMR-NIREH), Bhopal.

due to gender bias, exclusion of non-tribals, lack of indigenized studies, etc. Therefore, a prevention strategy should be formulated by screening high-prevalence non-tribal areas in a programmatic mode, which will further help in designing corrective health policies.

These screening activities require advanced diagnosis, which was addressed by Reena Das (PGIMER, Chandigarh). She elaborated on the recently validated point-of-care tests like SickScan (BioMedomics, USA), Hemotype SC (Silverlake, USA) and Gazelle (HemeDx, India), etc., to be used for early detection of SCD. Emphasis was given to the 'ASSURED' criterion for SCD testing, i.e. Affordable, Sensitive, Specific, User-friendly, Rapid, Equipment-free and Delivered to those who need it. All these tests are easy to use and, therefore, can be made available at Health and Wellness Centres/Primary Health Centre and Community Health Centre.

The next talk on ante-natal care and newborn screening was delivered by Anita Nadkarni (ICMR-National Institute of Immunohaematology, Mumbai). She mentioned that early diagnosis in newborns and early therapeutic intervention leads to decreased morbidity and mortality. Nadkarni described the methods and components of newborn screening. For the prevention of disease, she discussed the importance of prenatal diagnosis. The take-home message was that neonatal screening for comprehensive care and prenatal diagnosis for community control of SCD must go hand-in-hand for a successful programme.

In pursuance of the above, Dipty Jain (Mahan Trust, Nandurbar, Maharashtra) provided a deeper understanding of the morbidities, often known as 'presentation', in SCD patients. She emphasized that the disease presents itself in three severe forms: painful events, bacterial infections and anaemia, which eventually lead to a high mortality rate and reduction in life expectancy (20–25 years lower than the non-SCD population). Therefore, a comprehensive health management guideline should be drafted according to the phenotype of Indian SCD patients, which should be available in different healthcare settings.

Though these mortalities cannot be prevented completely, they can be minimized by imparting quality critical care for SCD patients in the ICU. This aspect was well addressed by Jyotish Patel (Sickle Cell Super-Specialty Hospital, Bardoli), who showed that an SCD critical case needs more care and 30 min prioritized approach is the need of the hour. He emphasized the

need for additional facilities in the ICU, such as bedside HPLC for monitoring of HbS during exchange transfusion, CT scan, multi-parameter monitor, etc. of SCD in ICU. Patel also talked about the severity of the SCD crisis along with factors that enhance these crises, like stress, environmental factors, etc.

Nonetheless, these critical stages of the SCD crisis can be avoided by the day-to-day care of patients. Pradeep Sihare (Children's Hospital, Bilaspur) took up this aspect in his talk. He used the US model to explain how interventions like hydroxyurea and infection control have improved life expectancy in India as well. Further, he pointed out that increased life expectancy has changed the fatal pediatric disease into an adult chronic disease, thus requiring a life cycle-care approach. Therefore, a comprehensive care plan was highlighted, including pain and fever management at home, telemedicine service through WhatsApp consultation, routine examinations like X-rays and MRI, along with treatment of psycho-social issues.

The day concluded with emphasis on emerging technologies and new therapies that can prove to be a transformational step in the lives of SCD patients. This was elaborated upon by Tulika Seth (AIIMS, New Delhi), who spotlighted the partial and curative treatment therapies present today. While FDA-approved drugs like L-glutamate, crizanlizumab and voxelotor act as partial treatment therapies, CRISPR technology for gene therapy and gene editing is being explored for curative therapy. Further, she emphasized the need to analyse the SCD severity level in India and draft guidelines regarding the eligibility criterion for hematopoietic stem cell transplantation accordingly.

The second day of the symposium began with a special lecture by Bhavna Dhingra (AIIMS, Bhopal), who talked about the role of blood transfusion in treating SCD. It should be noted that blood transfusion should be given only when a patient's haemoglobin falls significantly below the baseline haemoglobin levels. Therefore, regular monitoring of haemoglobin levels should be done. Further precautions that need to be taken include cross-matching blood components, avoiding cases of over-transfusion, early management of post-transfusion complications, delivery of iron chelation therapy according to the recommended protocol, etc. She elaborated on the goals and rationale of blood transfusion, including dilution of HbS, suppression of

erythropoietin and increased Hb oxygen because of chain reaction. A recommended blood transfusion strategy for SCD was thus presented.

Eli Mohapatra (AIIMS, Raipur) highlighted that the need for blood transfusion can be reduced to 50% using the therapeutic drug hydroxyurea. An antimetabolite, hydroxyurea, also reduces the frequency of painful episodes, increases the level of HbF and decreases the rate of acute chest syndrome (ACS) episodes. She showed the efficacy of hydroxyurea by giving examples of previously conducted studies across the globe. In India, the treatment of infants begins from nine months (earlier two years) with a starting dose of 10–15 mg/kg/day, while the US guidelines prescribe 20 mg/kg/day. After a detailed discussion among all experts, it was concluded that hydroxyurea should be started at lower doses, i.e. 10–15 mg/kg/day.

The next lecture focused on managing pregnancy in SCD, an aspect highlighted by Jyotish Patel. Even though genetic counselling and prenatal diagnosis prescribe SCD patients to avoid having babies, the 'Right to Birth' forms a vital part of our fundamental right under Article 21 of the Indian Constitution. Patel informed about the precautions one must take during pregnancy to avoid risks such as preeclampsia, eclampsia and postpartum haemorrhage.

Subsequent to this, a lecture on the only known cure for SCD was delivered by Rahul Bhargava (BMT, Fortis). He began by mentioning the limitations of hydroxyurea. He stressed the poor accessibility of the drug in tribal areas and emphasized the negative impact of hydroxyurea in youth, like a decrease in sperm count in males. Therefore, bone marrow transplant (BMT) should be promoted, emphasising that not every SCD patient deserves a BMT. He discussed the selection criteria for a patient based on severity score, the different approaches of BMT and the recommended strategies. To date, only about 1000–1500 individuals have undergone HCT worldwide since it is difficult to find HLA-matched donors. Therefore, strategies like haploidentical BMT are being performed. Further, the need for new transplant centres in SCD-endemic areas was highlighted due to India's limited number of transplant centres.

However, these strategies and therapies can only remain effective when the patients are treated and diagnosed in a timely manner. Such efforts are being taken by a non-profit-based organization under the

leadership of Yazdi Italia. The organization diagnosed its first patient in 1978, and subsequently, the journey has transformed from misdiagnosis and mistreatment to making Gujarat the first state in India to incorporate the Sickle Cell Anemia Control Programme in 2006. Italia emphasized how this PPP (public-private partnership)-based Gujarat model has become the best-case practice of the nation, which includes colour-coded cards for marriage counselling, free delivery of hydroxyurea, Swa Suraksha programme (a people's movement) to focus on the rural population, etc. This model must be replicated in the entire country.

In pursuance of this model, the Government of MP has initiated the State Hemoglobinopathy Mission in 2021 with a comprehensive plan of action for the elimination of SCD. This aspect was taken up by Ruby Khan (National Health Mission, Bhopal), who elaborated upon the action plan that included provisions in the state budget for screening and management of

sickle-cell patients, strengthening of health facilities (laboratory diagnostics, treatment facility, etc.) and develop a Sickle Cell Portal for digital health record maintenance.

The last lecture of the day was given by Seema Jain (Central Council for Research in Ayurvedic Sciences, Ministry of AYUSH, GoI), who showed the relevance of Ayurveda in controlling and managing SCD. Though SCD is not described per se in Ayurvedic texts, there is a reference to 'Pandu disease', having the same characteristics as SCD in terms of pathogenesis and cardinal symptoms. The treatment is based on preventing hereditary disease and using natural drugs like aloe vera as an anti-inflammatory drug, Guduchi (*Tinospora cordifolia*) as a painkiller, Bhringraj, citrus fruits for vitamin C, etc.

The two-day symposium concluded with a panel discussion with Ravindra Kumar (ICMR-NIRTH) as the moderator. Through this session, various doubts and questions were resolved to bring more clarity to the

participants about the issues related to SCD. The vote of thanks was given by Rajasubramaniam.

1. Brousse, V. and Rees, D. C., *Indian J. Med. Res.*, 2021, **154**, 4-7.

ACKNOWLEDGEMENTS. We thank the Director, ICMR-NIRTH, Jabalpur for encouragement and providing the necessary facilities. We also thank Dr Suyesh Srivastava and Deepika Patel (ICMR-NIRTH, Jabalpur) for their valuable suggestions.

Ayushi Narayan, CSIR-Institute of Genomics and Integrative Biology, New Delhi 110 007, India; **Vinita Shrivastava**, Ministry of Tribal Affairs, Government of India, New Delhi 110 001, India; **Ravindra Kumar***, ICMR-National Institute of Research in Tribal Health, Jabalpur 482 003, India.

*e-mail: ravindra.kum@icmr.gov.in

MEETING REPORT

Weed management*

An international conference was organized to tackle the enormous losses caused by weeds in different agroecosystems and to discuss the future weed management strategies. More than 500 delegates, including eminent scientists, academicians, students, personnel from the pesticide industry and progressive farmers, participated in it. The conference aimed to share knowledge and ideas on available technologies for managing weeds in different agroecosystems and gain input on addressing emerging challenges.

The inaugural address by Himanshu Pathak (ICAR, New Delhi) highlighted the importance of weeds in a sustainable food system and the impact of climate change on weed dynamics. S. K. Chaudhari (ICAR, New Delhi) mentioned the weeds cause an economic loss of around US\$ 11 billion annually in ten major crops in India. Herbicide resistance, pesticide residues, weed flora shift and weed management in con-

servation agriculture are some of the major concerns in modern agriculture. Developing herbicide-tolerant crops, genome editing, bioherbicide and nanoherbicide development, and precision weed management are new areas in weed science. In the keynote address by Trilochan Mohapatra (ICAR, New Delhi), weed population dynamics in a changing climate, nutrient and weed interactions, weed competitiveness and invasiveness, breeding crops for competitiveness to biotic stresses, and the mechanism of herbicide tolerance in weeds were discussed. There is a need to understand gene sequences in weeds. Genetic manipulation, such as RNAi technology, must be introduced to develop herbicide resistance in crops.

The first plenary lecture by Yoshiharu Fujii (Tokyo University of Agriculture and Technology, Japan) on 'Allelopathy utilization for weed control: challenges and perspectives' highlighted the importance of the allelopathy concept in weed management. Nearly 4000 plants and cover crops having allelopathic potential were selected for further utilization. Two traditional cover plants, namely *Mucuna pruriens* and *Vicia villosa* showed allelopathic activity, which are useful for weed management in organic farming. In the next presentation by Prasanta C. Bhowmik (University of

Massachusetts, USA) on 'Bioavailability of allelochemicals in soil environment under climate change: challenges and perspectives', stress was given on the importance of adding crop residues, which will help suppress the allelochemicals through the exudate of allelochemicals. *Brassica nigra*, *Avena fatua*, *Fagopyrum esculentum*, *Secale cereale*, *Sorghum bicolor* and *Triticum aestivum* release allelochemicals such as DIBOA, DIBOA-glycoside, dhurrin, isoflavonoids, isothiocyanate, juglone, momilactone, scopoletin and sorgoleone. The process of new herbicide molecule development was discussed in the next presentation by Shoumo Mitra (Corteva Agriscience, Singapore) on 'Current herbicide development scenario: need to launch reduced risk herbicides'. The pesticide industry emphasises green solutions through reduced-risk compounds and green-chemistry innovations for meeting the farmers' needs and consumers' preferences while protecting the environment and natural resources.

The next presentation by Bhagirath Singh Chauhan (University of Queensland, Australia) was on 'Weed biology: an important science to develop effective weed input on addressing strategies'. To develop an innovative, economical and sustainable integrated weed management (IWM) system, good

*A report on the international conference on 'Weed Problems and Management Challenges: Future Perspectives' held at the Anand Agricultural University (AAU), Anand from 20 to 23 December 2022 and organized by the Indian Society of Weed Science (ISWS), Indian Council of Agricultural Research-Directorate of Weed Research (ICAR-DWR) and AAU.