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POLICY INTERVENTION FOR SICKLE CELL ANEMIA MITIGATION WITH SPECIAL REFERENCE TO NUTRITION AND TECHNOLOGY DIFFUSION

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ABSTRACT: The aetiology of sickle cell disease (SCD), a neglected blood-related illness with growing global health significance, is the transversion of the amino acid glutamine to the amino acid valine at the sixth position of the globin protein. India is thought to have the second-highest prevalence worldwide, notably among the socioeconomically deprived tribal populations. The case load is known to rise among the tribal population due to a lack of macro and micronutrient availability. In order to combat malnutrition in developing countries, the SCD populations have been recommended dietary allowance (RDA) for these nutrients is egregiously inadequate. This review highlights various studies conducted between year 1985 to 2022 on nutritional behaviour among SCD patients and policy intervention for SCD mitigation, with a focus on opportunities and problems as well as a strategic framework for diversification to work in this context.Further the review highlights the importance of macronutrients (proteins, vitamin D, glutamate, etc.) and micronutrients (zinc, magnesium, vitamin E, etc.) as dietary supplements, herbal management of sickle cell anemia (SCA), vegetable food products, food processing intervention, and safe drinking water management offered from Council of Scientific and Research Central Food Technological Research Institute (CSIR-CFTRI) technologies. According to this article, nutrition is crucial for the management of SCD, and new technologies introduction to tribal areas can assist manage SCD patients with very nutrient-dense dietary supplements.

Keywords: Sickle cell disease (SCD), sickle cell anemia (SCA), macronutrient, micronutrient, CSIR-CFTRI, TRIFED.

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1. INTRODUCTION

Sickle cell disease (SCD) is one of the most prevalent monogenic blood illnesses with an autosomal recessive inheritance in nature [1]. The pathophysiology of SCD is caused by a single nucleotide change from Glu to Val at position 6 of the β-globin gene, arises from the polymerization of the ensuing sickle hemoglobin variation (HbS), which sets off a series of modifications to erythrocytes [2] making it a life threatening disorder with lower life expectancy. It is anticipated that there will be an increase in the number of births with sickle cell anemia (SCA) from 300,000 to more than 400,000 between 2010 to 2050 [3]. Sub-Saharan Africa is the first in terms of number of SCD birth and India has been classified as the second worst impacted country in the world including the fact that some of the highest βS allele frequencies have been documented in Indian population [4].The scheduled tribal (ST) and scheduled caste (SC) communities of India make up the majority of the SCD population. According to the Census of India 2011 [5], the tribal population of India is 8.6 per cent of the total population which is about 67.8 million people. The states of Madhya Pradesh, Maharashtra, Odisha, Gujarat, Rajasthan, Jharkhand, Chhattisgarh, Andhra Pradesh, West Bengal and Karnataka account for around 83 per cent of the total scheduled tribe population in the country and majority of these tribal groups live in rural areas. These are the demographic segments that are the most socioeconomically deprived in the nation [6].The highest prevalence of SCD is seen in Madhya Pradesh (Central India) with number of 9, 61,492 sickle heterozygotes and 67,861 sickle homozygotes which contributed 10 to 33 per cent of HbS prevalence in 27 of the 48 districts [7], Maharashtra 20 to 30% (north region of Maharashtra) [8], Kerala 18.2 to 34.1% (Wayanad district) [9], Gujarat 13 to 31% where sickle cell carriers was 11.37 % HbS (6.3 to 22.7%) [10] as well as β-thalassaemia trait (6.3 to 13.6 %) [11], 2% in Orissa (Eastern India), 0.7-2% in Assam (North East India), 0.4-1% in Andhra Pradesh (Southern India) [12]. SCD leads to painful crisis majorly in patients, during 1980's there was first consideration to patient through oral nutritional treatment required for clinical care [13]. Then, during another decade (1990's) it is classified that under-nutrition has been identified as a critical feature of SCD [14]. With increasing years' nutritional interventions applied to adolescents as well as adult SCD to understand role of nutrients for reduction of manifestations among SCD patients [15]. Although there are hundreds of publications every year on role of nutrients, there are no known nutritional policies at state or country level. A person's primary need is nutrition for growth, mentally as well as physically especially in SCD mitigation patients. Nutrients play crucial role in cellular level because each mechanism requires

energy. Numerous minerals, including iron, cobalt, magnesium, and micronutrients, including vitamin A, folate, B6, B12, and other B vitamins are directly required for the formation of RBC, Hb synthesis, and iron absorption, as well as antioxidant defense and cellular energetic [16]. Generally, in SCD red blood cells (RBC) transformed into sickled shape from disc shape under deoxygenated condition so that mineral deficiency in SCD (e.g. thalassaemia) mass affect to RBC production and its life expectancy. Nutrient deficiencies, even mild to moderate ones, are thought to have an influence on the development of a country because they affect physical and cognitive development, physical growth, and labor capability [17]. The methods implemented till now to lessen the impact of inadequacies is limited to using additional sources or fortified meals. Past successes with regard to supplementation or fortification strategies may have contributed to the decrease of specific clinical forms of micronutrient deficiency that are prevalent in the population, such as Pellagra (niacin), beriberi (vitamin B1), rickets (vitamin D), goitre (iodine), and neural tube defects (folic acid). Nutritional blindness has been eradicated, and Bitot's spot (vitamin A deficiency) has decreased in clinical prevalence [18]. It is challenging to address mild to moderate deficits of a variety of micronutrients that are indicated by biomarkers, and they may not be responsive to a single short term intervention. According to a 2003 report by the National Nutrition Monitoring Bureau (NNMB), dietary iron consumption is extremely inadequate and insufficient in most states, i.e., meeting less than 50% of RDA [19]. Their research also uncovered a counterintuitive link between iron consumption and iron deficient anemia (IDA) [19]. For the results to last, it might be necessary to take a more all encompassing strategy with a package of interventions that includes the ideal combination of whole meals, diets, and micronutrients. These should be combined such that the shift from single or multiple micronutrient therapies to dietary diversification, which is the best sustainable approach, is seamless. In order to tackle micronutrient deficiencies in poor countries, the article will concentrate on policy intervention for SCD mitigation, with an emphasis on obstacles and possibilities as well as a strategic framework for diversification to operate in the setting [18]. The goal of this review is to highlight the material that has been published between year 1985 and 2022 on management of SCD mitigation policies and the role of nutrition and technology dissemination. A nation's development is impacted by hidden hunger, which is defined as mild to severe deficits of macro or micronutrients that affect physical and cognitive development, physical growth, and labor capability. Socioeconomic affected peoples (mostly tribal) are totally depends on the labor activity and agriculture. They do hard work in early age for getting food but due to overburden and cost of market associated available foods, didn’t get a perfect diet which result in malnutrition so that their health development remains limited.

Why we need to address availability of nutrition among SCDs

Sickle cell disease patients have macro- or micronutrient deficiencies, however early research on dietary habits reveals that sickle cell patients' food and nutrient intake is at or above

recommendations and is not substantially different from that of healthy controls. This suggests that higher rates of nutrients deficiency may be due to increased needs of many nutrients in sickle cell patients [19]. Because it is now known how important nutrients are for managing disease, their usage in the world's health care delivery system has risen to the forefront. Since SCD is among the disease plaguing a sizeable population of the developing world and the cost implication of its management is very high and is characterized by anemia and immunological disturbances, including the generation of free radicals; a balance between minerals and anti-oxidants is imperative in maintaining red cell membrane integrity and function [17]. It is well recognised that the case burden is increased by the tribal population's lack of accessto macro- and micronutrients [19]. The population with SCD consumes far less of these nutrients than the recommended dietary allowance (RDA) [19, 20]. The current approach includes symptomatic and topical treatments. Although the hinterlands are where many of those grains are grown, in India have succeeded in distributing rice and wheat through public distribution system (PDS) but not nutri-grains or food goods. Farming has been disrupted by migration [21]. The household income of these SCD populations has considerably decreased due to environmental effects associated with climate change and a lack of possibilities for employment [22].

Effect of macronutrients on sickle cell disease

Sickle cell patients frequently complain loss of appetite, which may be related to the ongoing inflammatory condition and inadequate knowledge of nutritional needs, which leads to a number of nutritional inadequacies and subpar clinical consequences. These nutrient deficiencies are associated with immunologic, growth, and maturation abnormalities [23]. Numerous explanations for the low levels of energy and nutrients seen in SCD patients have been put forth, despite the fact that the nutritional deficits, these patients experience are poorly understood. These include; reduced intake potentially from the anorexic effects of co-morbidities such as pain [24], decreased absorption of nutrients, increased degradation and losses of nutrients, increased requirements as a result of elevated basal metabolic rate [25], and alterations in metabolic pathways. A balance between minerals and antioxidants is important in maintaining red cell membrane integrity and function [26]. Minerals such as copper, zinc, iron, chromium, magnesium, selenium, and antioxidant vitamins like vitamin C and E as well as vitamin A may be needed to perform these protective roles [27]. Additionally, due to their roles in hemoglobin synthesis and production of red blood cells [28], adequate status of vitamin B6 and folate will aid the process of compensating for the rapid loss of red blood cells that occurs in SCD patients. The evidence indicating a role of macronutrient during 1980’s deficits was mostly indirect and sparse at the time of the initial evaluation of dietary issues in sickle cell disease in 1987 [29], and this condition has persisted into the decade [30, 31]. Heyman and colleagues in 1985, reported the first and most concrete evidence of inadequate macronutrient intake [32] through a small diet supplementation trial in 5 pre-adolescents which helped to many

researchers to create framework during next decades (1990's and 2000's). His findings showed that malnutrition plays a role as one of the complications of HbSS and that regular food supplements may be beneficial [32]. In order to support children's growth and the production of hemoglobin, protein is a crucial macronutrient. To maintain a healthy metabolism and physiological functions, children with SCD may need more food than is advised [33]. This is because higher protein turnover has been reported among SCD patients; there is consistent evidence of poor growth among SCD children compared to non-SCD [33, 34]. This increased requirement is poorly understood but it has been suggested that hyper-metabolism due to shortened life-span of erythrocytes places an increased demand on protein stores, accelerates whole body protein turnover and consequently increases energy expenditure [35]. There is some information suggesting that increased dietary requirements as much as needed in pregnancy and growth is necessary to improve clinical outcomes [21], although currently, there are no special dietary recommendations for protein and/or energy for patients with SCD. A study report stated that nutrient feeding to sickle mice with HbSS genotype, high protein and L-arginine supplements [36, 37] n-3 fatty acids have shown significant reductions in inflammation, oxidative stress, red cell density, and pain episodes, as well as improved micro vascular function, even though the Heyman's study was constrained by the small sample size and nature of the design. While L-glutamine supplements [38] decreased the resting energy expenditure in HbSS children, other earlier supplementing studies for amino acids employing different end objectives, such as oral L-arginine treatment for pulmonary hypertension in HbSS adults, were beneficial. The first direct physiological assessments of enhanced protein turnover and energy expenditure in HbSS adults were published in 1989 by Badaloo and co-workers (39). This suggested increased protein and energy needs [39]. By using direct measures of resting energy expenditure (REE), enhanced protein turnover [41, 42], and protein catabolism, several following publications have validated children's and teens' greater than average energy needs [43]. Fatty acids are crucial parts of cell membranes and may help SCD patients' general health as well as their clinical results by preserving and enhancing them. In particular, omega-3 and omega-6 necessary polyunsaturated fatty acids (PUFA) are required for the synthesis and repair of cell membranes, as well as for children's growth, which is crucial for brain development and the maturation of sensory systems [43]. Vaso-occlusive crises (VOC) in sickle cell disease are heavily influenced by aggregation of blood cells, their adhesion to vascular endothelium, and inflammation. Omega-3 (n−3) fatty acids (DHA and EPA) have been shown to have anti aggregatory, anti-adhesive, anti-inflammatory, and vasodilatory properties [44]. Therefore, it has been hypothesized that fatty acids may help sickle cell patients have better clinical results, especially in terms of a decrease in painful episodes [45]. According to these results; there will be a larger need for macronutrient metabolism to keep up with the greatly accelerated erythopoietic rate toward faster red cell replacement in HbSS patients. For additional knowledge about the macronutrient and their properties please see **Table 1**.

Table 1. Macronutrients and their properties

Macronutrient	Properties	References
Proteins	Improved Weight gain & decrease in level of inflammation	[34]
Arginine	decreased oxidative stress, improved muscle strength and endurance	[35, 36]
Glutamate, Omega-3 fatty acids	Decreased resting energy expenditure, Decrease in number of pain episodes and thrombotic activities	[37, 44]
Vitamine D	It is vital for calcium homeostasis and essential for bone mineralization	[36, 38]

Effect of micronutrients on SCD

Micronutrients are essential vitamins and minerals required for good health. Some micronutrient deficiencies have been associated with sickle cell disease. These include iron, zinc, copper, folic acid, pyridoxine and vitamin E [21]. Reduced intake, impaired intestinal absorption, and accelerated degradation of certain elements are potential processes by which micronutrient insufficiency may occur in sickle cell disease. Properties of micronutrients are mentioned in **Table 2.**

Table 2. Micronutrients and their properties;

Micronutrient	Properties	References
Zinc (Zn)	- Enhanced thymulin activity, decreased bacterial infection and hospitalization due to excruciating crises, enhanced sexual development, and enhanced reproductive ability. - Improvement in linear growth. - Improved sexual maturation.	[46, 47]
Magnesium (Mg)	Decrease in number of painful days. Decreased length of hospital stay.	[47, 48, 50]
Vitamin E (Vit. E)	- Decreased lipid peroxidation and improved erythrocyte membrane stability. - Improved weight gain and decreased frequency of hospital admission. - Increased hematocrit and decrease in number of painful crisis.	[44, 46]
Copper (Cu)	- Functioning of different metalloenzymes.	[45, 47, 49]

Numerous studies have been done on the function of these deficits, including how they affect development and immunity [46, 47]. In this circumstance, it has been discovered that certain vitamins and minerals are helpful in controlling anemia. These include folate, copper (Cu), zinc (Zn), and iron (Fe) [44]. Hemoglobin production depends heavily on iron, and the metabolism of iron is significantly influenced by the minerals copper and zinc [48]. It is generally recognized that iron is important for mammals biologically. Therefore, given its function in oxygen transport and several metalloenzymes involved in oxidative phosphorylation, its significance in this condition of hemoglobin depletion cannot be overstated. It is well recognized that copper is necessary for the efficient operation of several metalloenzymes, including ceruloplasmin, which is involved in iron metabolism. Anemia is known to be brought on by copper deficiency. Unknown is the mechanism through which copper deficiency causes anemia [49]. Magnesium (Mg) is the second most abundant

intracellular cation in the body. Magnesium homeostasis is governed by intestinal absorption and renal excretion; aside its role in stabilizing the structure of ATP in ATP dependent enzyme catalyzed reactions, *In-vitro* experiments showed that magnesium could decrease sickle cell hemoglobin polymerization by 48% [50]. Available studies on the level of magnesium in SCD patients have reported conflicting results, in a study to determine the effect of magnesium on length of stay for pediatric sickle cell pain crisis, those who received intravenous magnesium showed a decrease in the length of hospital stay for approximately five days to an average of three days ($p< 0.01$) [51]. However, the Magnesium for Children in Crises (MAGiC) study conducted among 4-21 year olds with SCD or Sβ0_Thallasemia [52] showed that intravenous magnesium did not shorten length of hospital stay, nor did it improve the quality of life for the patients. In addition, Goldman and colleagues found that although children with SCD took intravenous magnesium well, there was no difference in the average length of stay among Canadian kids [52]. The authors suggested the available evidence intravenous interventions do not support the inclusion of magnesium in the management of SCD [53]. Zinc is involved in all major aspects of cellular functions including metabolism, detoxification, antioxidant defenses, signal transduction, and gene regulation [54]. Manifestations of zinc deficiency include anorexia, skin lesions, growth retardation, neurosensory defects, and immune dysfunction in humans [55]. More research has been done on zinc than any other mineral when it comes to SCD and nutrition. The deficiency of zinc has been reported more among people with 'HbSS' genotype, the most severe form of SCD [56]. A cochrane review on this subject indicated that zinc supplemented SCD patients showed reduction in both frequencies of crises and infections [57]. Therefore, the existing research implies that SCD patients who take zinc supplements may benefit in various ways. However, the majority of the studies that were evaluated only included adults, thus multi-center trials involving kids will be required before this can be incorporated into the treatment of SCD. Folic acid is a crucial vitamin for the treatment of SCD as it is required for the development of brain neurotransmitters and red blood cells (RBC). It has been recommended that diet for sickle cell patients should be high in folate as needed in much as pregnancy (400 to 600 mcg daily) because of the increased production of erythrocytes needed to replace the cells being continuously destroyed and to prevent megaloblastic erythropoiesis [58]. The limited literature indicates that although folic acid supplementation may increase serum folate level, its effect on anemia and other symptoms of SCD among children remains unclear [59]. The most significant lipid-soluble antioxidant in a cell is vitamin E. The vitamin is essential for defending the body from the harmful effects of ROS, which are produced metabolically or found in the environment. Sickle cell patients are known to be oxidatively stressed and deficient in antioxidant micronutrients [60]. Sickle erythrocytes and their membranes are susceptible to endogenous free-radical-mediated oxidative damage due tochronic redox imbalance in red cells that often results in continuous generation of reactive oxygen species (ROS) with clinical manifestations of mild to

severe hemolysis [50]. Numerous patho-physiological circumstances, including hypoxia, inflammation, infection, dehydration, and a vitamin or mineral shortage that inhibits antioxidant enzymes, can cause a significant increase in the generation of ROS. There have been reports of low circulating levels of vitamins C and E in SCD patients [61, 62], Amer and co-workers [63], reported 20-50% lower levels of reduced glutathione (GSH), the major intracellular scavenger of ROS and 10-30 fold higher production of ROS in sickle cell patients compared to HbAA controls ($p<0.005$) [63]. However, a randomized controlled trial that evaluated the effect of vitamins C and E supplementation in adults with sickle cell anemia reported no improvement, but rather an increase in hemolytic markers [64]. A possible reason for the lack of improvement is the observation that the reduced vitamin E anti-oxidant capacities of SCD was related to transfusion status, but not sickle crises [65].

Traditional herbal management

The only treatment for SCA is a bone marrow transplant, which needs a donor who is a member of your family who is incredibly compatible. At best, there is an 85% disease free survival rate, with a 7% death rate from transplant related causes and a 9% graft failure rate [66]. This technique is so advance and costly. Other hand, since ancient era (Ayurveda), maximum health issues are managing through herbal treatments, currently some studies has been done through the herbal management such as, Fagara (*Fagara zanthoxyloides*) - 25 drops of the extract three times daily changed the frequency of the unpleasant day from three to one per year (in particular study the patient recovered fully) [67] The anti-sickling effect of *Tinospora cardifolia* (Guduchi) was first discovered [68]. On the other hand, three isomeric divanilloylquinic acids, known as burkinabin A, B, and C, were identified as possible anti-sickling elements of *F. zanthoxyloides* (root). However, other researchers have suggested para-hydroxybenzoic acid, para-flurobenzoic acid, vanillic acid, and coumarins [69]. *Carica papaya* unripe fruit or leaves were fermented for five days at a concentration of 2.5 mg per mL of water and showed anti-sickling effects of 87% inhibitory and 74% reversal activities. While chloroform extract was inert, methanol extract exhibited 64% inhibitory and 55% reversal actions. It was believed that phenylalanine, tyrosine, and glycine were to blame [70]. Unknown as to the origin of garlic (bulb), allicin in garlic is a powerful stimulator of the transient receptor potential cation vanilloid type 1 (TRPV1) channel that lowers blood pressure and cholesterol. Additionally, garlic is utilized to treat a variety of infectious diseases, including respiratory infections in SCA [71]. Phenylalanine, regarded to be the main active ingredient in *Cajanus cajan* seed and a component of the anti-sickness herbal remedy Ciklavit, was created by two academics in Nigeria, Ekeke and Shode [72]. Although *Sorghum bicolor* and *Pterocarpus osun* are abundant in vivid red/orange flavonoids, it is unknown what causes them to function as they do. In particular, if they include folic acid or its analogues, they probably operate as hematonics. Given their blood red color, ancient Yoruba sages may have included them under the influence of the "Doctrine of Signatures," which has been noted

elsewhere [73]. It had been assumed that *Piper guineense* and clove are primarily where Niprisan's active ingredients that lessen the severity of or lessen the frequency of SCA crises reside [74].

Agricultural intervention for managing nutritional requirements

Introduce across the tribal hamlets

Moringa (*Moringa oleifera*) (fig. A), known as the miracle herb, and curry leaf (fig. E) plantations [75] cultivation of mushrooms (fig. B) (such as shitake) and Spirulina (fig. C) (known to lower ROS in SCD patients) [76]. Since many of the traditional water sources have vanished or become contaminated as a result of mining operations, artificial ponds for aquaculture (fish farming) (fig. D) are necessary [18]. We can bring back traditional cultivars, particularly millets hamlets in tribes (known to keep these types alive) also the involvement of Krishi Vigyan Kendra (KVKs) is required [73].

Figures 1

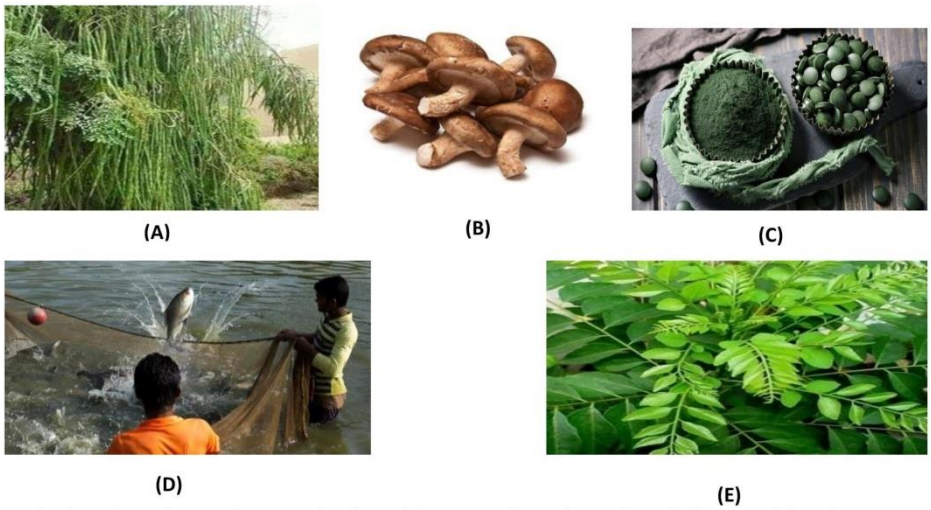

Figure 1 showing the various agricultural interventions introduced for nutritional management across tribal hamlets (fig. (A) Moringa, (B) Mushroom, (C) Spirulina, (D) Fish farming and (E) Curry leaf).

Moringa, banana, spirulina, sprouts, green peas-based food products need to be introduced as part of mid-day-meal/SCD patient supplements in the SCD regions to mitigate the recurrence of SCD by 2030 according to Sustainable Development Goals (SGD) (UN, Department of Economic and Social Affairs) [78]. An increasing body of research shows that among certain smallholder farmers, production diversification and food diversity are positively correlated. However, there are impediments that can be grouped into a vicious cycle of unsustainable intensification of agricultural practices that result in land degradation, decreased productivity, diminished purchasing power, and decreasing output of food crops. Public sector assistance for important cereal crops and associated market signals are significant deterrents to production diversification for poor farmers caught in this cycle. Local veggies and other indigenous commodities are supplanted by "substitute" goods whose demand is greater and whose production is made easier (e.g. maize). The end result is a decrease in

the availability of/access to a variety of foods and an increase in the consumption of bland, low-nutrient diets [81]. The Decade of Action Resolution and the 2030 Agenda have significant connections across their different (economic, social, and environmental) components, highlighting the significance of achieving interconnected goals like eradicating hunger and improving nutrition [78].

Food processing intervention for addressing nutritional deficiencies among SCDs

Wheat flour, rice, and bakery items are examples of widely eaten food commodities that have been fortified. The national mission on supply of nutritionally fortified food supplements to tribal population is an urgent necessity [18]. Introducing technologies for processing agricultural and forest produce from tribal communities: leaf cup makers, solar tomato dryers, pedal-operated kodo processors, curry leaf processors, etc. are just a few of the free technologies that CSIR laboratories such as Council of Scientific and Industrial Research - Central Food Technological Research Institute (CSIR-CFTRI) have made available. These technologies can significantly raise the per-capita income of the SCD population. Tripartite agreements between Tribal Community Groups-Research Institutes (TRIFED) are required in order to teach SCD population on food processing technologies and to increase their resource creation. The chances of getting better nutrition will increase as a result of these actions. Especially in SCD regions, create cold-chains or tribal food technology parks (Ministry of Tribal Affairs, Govt. of India) [79].

Safe drinking water for safe food

The community with SCD still has serious concerns about safe drinking water. Patients with SCD have a significant burden due to heavy metal poisoning. Nationwide, integrated water treatment facilities must be built utilising corporate social responsibility (CSR) money and the assistance of other partners. It is necessary to distribute portable water purifiers like the TERAFIL (Terracotta) Water Filter, which costs 40 rupees and has a three-year lifespan and was created by the CSIR's Institute of Minerals and Materials Technology in Bhubaneshwar [77].

Logistics for delivering Nutrition

The provision of high quality nourishment and medical treatment is significantly hampered by a lack of transportation infrastructure. Both the provision of healthcare and the distribution of nutrition to the target groups depend greatly on last-mile connection. The implementation of local transportation services is necessary. Banks offer subsidised auto loans; they should be made more widely known and used [78].

Accessibility to quality electricity

Equipment used in food processing needs a reliable power source. The development of solar power plants supported by CSR money has to pick up speed. Due to climate change in remote areas power supply through power cable are generally interrupted.

2. CONCLUSION

This paper provides perspectives and examples of potential research opportunities to advance knowledge about the role of nutrition in SCD and conditions and suggests the promise of an integrated and transformative nutritional interventional research approach that addresses fundamental discoveries and implementation science at national and worldwide level. Investigations spanning the spectrum of basic, epidemiologic, clinical trial, and implementation science research but addressing limited studies about nutrition policies and technologies diffusion approaches which could be beneficial to public health. This review evaluating the impact of macro and micronutrient supplementation on SCD morbidity and technology diffusion, it has shown that oral nutrition supplementation significantly improved growth as well as decreased viral episodes [35]. While another study observed that nasogastric routed supplement may accelerate growth and reduce the incidence and severity of complications in growth-retarded children with SCD [36]. In several literatures, the diagnosis of mild zinc deficiency was based on the assay of zinc in lymphocytes, granulocytes, and platelets which help to provide a possible mechanism for the role of zinc on T cell functions to understand molecular mechanism of immune response in SCD patient by providing Zn supplement [47]. Mg, Cu and Vit. E, (micro nutrients) help to protect red cell membranes from free radical mediated oxidative stress which is crucial to their management [48, 49] and macro nutrients such as proteins, arginine supplement treatment was given to mice were decreased hemolysis was observed [38], Omega-3 fatty acids and Vit. D [34, 36] was discovered to be beneficial for lowering bacterial infection, VOC, and enhancing weight growth. In previous research, researcher utilizing *F. zanthoxyloides* extract shown the effectiveness of herbal treatments for SCD in reducing discomfort [67]. Leave extract of *T. cardifolia,* show potential activity of reverse shape change of HbSS [69] and *C. cajan* [68]*,* and *C. papaya* extract help in reduction of painful episodes [70]. According to reviews of a variety of publications, most of the studies have been done with small sample size with limited variables so further there is a need for more additional longitudinal research in this field with larger sample sizes and longer follow-up times. Before making any suggestions, specific interventions, such as those in food processing, must be thoroughly studied. Technologies including pedal-operated kodo processing machines, solar tomato dryers, leaf cup makers, and curry leaf processors are provided by the national mission [18]. Additional technologies that are accessible for free and that the SCD area needs to apply include those from the Tribal Community Groups-Research Institutes (TRIFED) and CSIR-CFTRI. However, among those with SCD, access to safe drinking water continues to be a key challenge. Patients with SCD have a significant burden due to heavy metal poisoning. Using CSR money, integrated water treatment facilities must be built in the nation's tribal areas. Delivering nutrition efficiently is essential for managing SCD patients who reside in mobile areas. Community-based transportation services must be put in place to address this issue.There are signs that, as compared to those who don't have SCD, SCD patients often exhibit sub-optimal levels of the majority of nutrients. There is also a lack of information, particularly from

Africa, where the illness is quite common. Small-scale studies have revealed possible advantages for zinc, folate, vitamin D, and polyunsaturated fatty acids. However, there aren't enough large-scale studies to back up claims that taking supplements containing different nutrients taken into account in this analysis will be beneficial [80]. Despite these drawbacks, nutritional supplements should be taken into account as a crucial part of SCD therapy. In order to meet nutritional needs and adequacy, it is advised to eat a variety of foods, which may also be advantageous for SCD patients. Thus, this dietary component should be taken into account in further investigations on the function of nutrition in the maintenance of sickle cell disease. In conclusion, it is evident that little study has been done on the potential link between SCD morbidity and nutritional insufficiency. However, particular therapies need to be thoroughly studied before any suggestions can be given. Nutritional therapy may be a significant factor in increasing survival in SCD patients. According to the currently available research, both macro and micronutrition can improve health, and agricultural interventions like organic food farming [59], aquaculture [18], and introducing traditional cultivation to SCD-containing areas through KVK [73] or other bodies may help SCD patients meet their nutritional needs and prevent malnutrition.

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HUMAN AND ANIMAL RIGHTS

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CONSENT FOR PUBLICATION

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