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Review Article

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Food consumption and nutritional status of children with sickle cell disease: a systematic review

Consumo alimentar e estado nutricional de crianças com doença falciforme: uma revisão sistemática

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Abstract
OBJECTIVE: To describe the food consumption and nutritional status of children with Sickle Cell Disease (SCD). METHODS: The study was carried out through the systematic review using the PICO strategy. Articles were collected from electronic databases: Virtual Health Library (VHL), PubMed and SciELO (Scientific Electronic Library Online), based on publications in the last 10 years, in Portuguese and English, with a population of children diagnosed with SCD. and age up to 12 years old. For identification and selection of articles, the PRISMA flow diagram was used. RESULTS: After selection, 07 articles were included in the review, all of which were cross-sectional, with geographic distribution covering Brazil, Nigeria and Ghana. Which consists of 12,120 female and male children who participated in the research, with the exception of the control group. The studies used some criteria for assessing nutritional status, food consumption and socioeconomic profile. FINAL CONSIDERATIONS: The low socioeconomic status, added to the unbalanced food intake, still cause important changes in the growth and development process of children who inherit Sickle Cell Disease. General and dietary interventions, adapted to the reality of these individuals, allow a positive impact on the quality of life of this public.
Keywords: Child**,** Sickle cell anemia, Food intake.

Resumo
OBJETIVO: Descrever sobre o consumo alimentar e o estado nutricional de crianças com Doença Falciforme (DF). MÉTODOS: O estudo foi realizado por meio da revisão sistemática utilizando a estratégia PICO. Os artigos foram coletados nas bases de dados eletrônicas: Biblioteca Virtual de Saúde (BVS), PubMed e SciELO (Scientific Electronic Library Online), a partir de publicações nos últimos 10 anos, nos idiomas português e inglês, com população de crianças diagnosticadas com DF e idade até 12 anos incompletos. Para identificação e seleção dos artigos utilizou-se o diagrama de fluxo PRISMA. RESULTADOS: Após seleção, 07 artigos foram incluídos na revisão, todos eram do tipo transversal, com distribuição geográfica abrangendo Brasil, Nigéria e Gana. O qual se constitui com 12.120 crianças do sexo feminino e masculino que participaram das pesquisas, com exceção do grupo controle. Os estudos utilizaram alguns critérios de avaliação do estado nutricional, consumo alimentar e perfil socioeconômico. CONSIDERAÇÕES FINAIS: O baixo nível socioeconômico somado a ingestão pouco balanceada de alimentos, ainda provocam modificações importantes no processo de crescimento e desenvolvimento de crianças que herdam a Doença Falciforme. Intervenções gerais e alimentares, adequadas à realidade desses indivíduos possibilitam um impacto positivo na qualidade de vida deste público.
Palavras-chave: Criança**,** Anemia Falciforme, Ingestão de alimentos.

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Introduction

Childhood is a fundamental period for the growth and development of human beings, mainly in the processes that involve the body's biological maturation, and a balanced diet can contribute positively to this mechanism. Understanding the eating behavior in this age group is essential and deserves full attention, since inadequate or insufficient consumption of nutrients can trigger deficiencies or excesses, and consequently significantly compromise the nutritional status[1].

A health condition present in our society capable of modifying this dynamic of infant feeding is Sickle Cell Disease (SCD)[2,3], which is considered a relevant public health problem, characterized as one of the most common genetic and hereditary diseases worldwide in the childhood[4]. SCD originated on the African continent, and there is evidence that individuals have inherited it in different regions of the planet[5]. In Brazil, its dissemination occurred due to the African diaspora, during the colonial period, for the purposes of the slave trade[1].

According to data from the World Health Organization (WHO)[6] around 5% of the world's population lives with characteristic genes for hemoglobin disorders, mainly SCD and thalassemia. According to the *Programa Nacional de Triagem Neonatal* (PNTN), for every thousand children born alive in Brazil, one is diagnosed with the disease. Thus, the country has an annual birth estimate of 3,500 children with the disease and 180,000 with sickle cell trait (SCT). However, the distribution of this clinical condition is not homogeneous, as the North and Northeast regions have higher rates of incidence and prevalence of this clinical condition, due to the high prevalence of the Afro-descendant population[5].

It is worth emphasizing that SCD encompasses several hemoglobinopathies present on the planet[2], it is chronic and incurable[5]. It is a mutation in the gene that produces hemoglobin (Hb). This alteration occurs in the structure of hemoglobin A (HbA), originating another, mutant, called hemoglobin S (HbS), of recessive inheritance[4].

Clinical manifestations and secondary complications, as well as less favored socioeconomic and cultural characteristics can lead to a reduction in the expectation and quality of life of this public, therefore, care related to food and nutrition is important in the care of individuals with SCD, since that there is a significant increase in dietary needs, due to the high demand for energy and micronutrients, and children with this condition tend to have a more limited physical profile compared to others considered healthy[7,8].

It is important to point out that the inheritance produced by the 350 years of slavery produced immense social inequality in Brazil[9,10], which strongly affected the black population who still live in the worst circumstances of life, in situations of unhealthy conditions, low education, insufficient remuneration, inadequate health conditions and difficulties in meeting their basic needs, as well as eating enough to maintain their vital activities[11], which is a potentiating element in the inadequate prognosis of this health condition[8].

Given the above, this research aims to analyze the pattern of food consumption and the nutritional status of children with Sickle Cell Disease, in addition to trying to understand the impacts of the limitations of the socioeconomic profile on the health of this population.

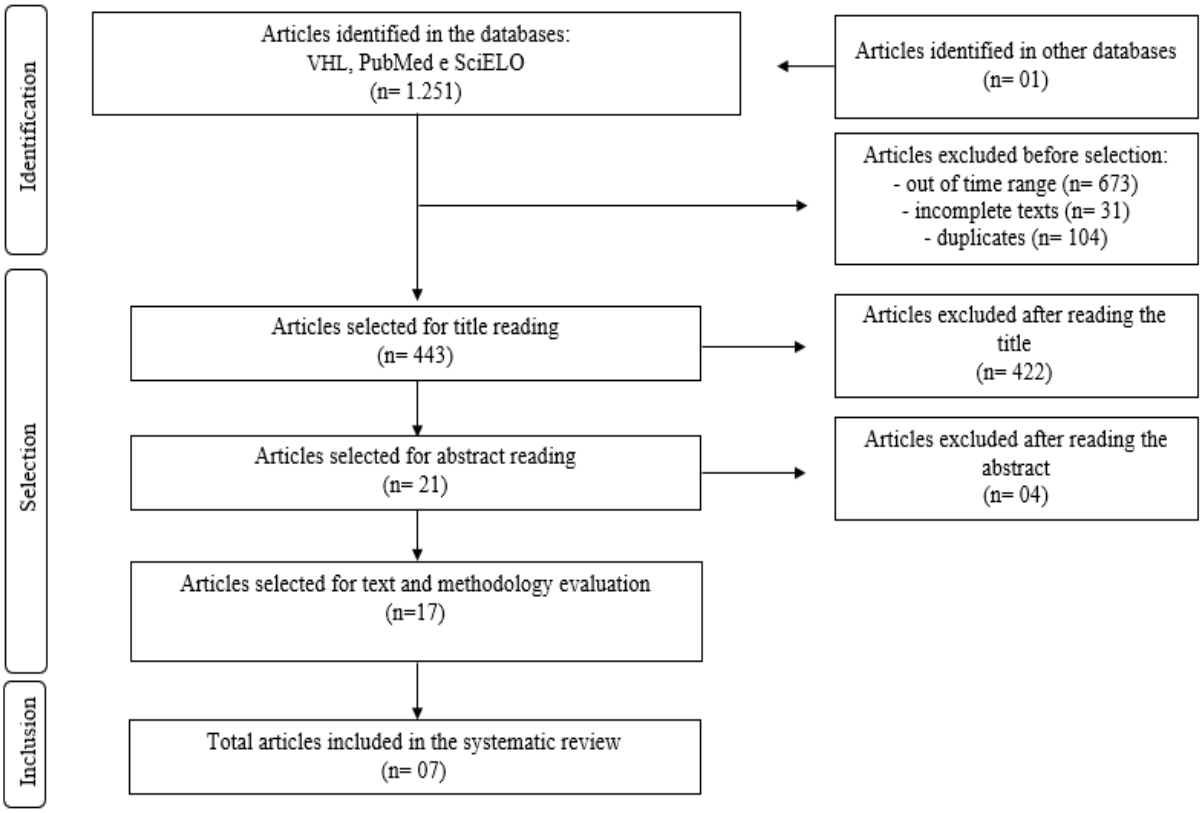
Materials and Methods

This study is a systematic review of the literature, with a collection period carried out between February and October 2021. The research covers articles that used as design, cross-sectional studies, published in the last 10 years, in Portuguese and English, with no need for financial investment to prepare this work. The study was structured using the PICO strategy[12], an acronym for Population (children diagnosed with SCD aged up to 12 years old), Intervention (food consumption and nutritional status), Context (not applicable) and Outcomes /Outcome (impact of disease on factors related to food and nutrition).

Searches for articles were carried out in electronic databases: Virtual Health Library (VHL), PubMed and SciELO (Scientific Electronic Library Online). The keywords used were: Nutrition, Food Consumption, Nutrition Status, Sickle Cell Disease and their respective translations into Portuguese (in addition to the Boolean operators "AND" and "OR"), chosen after consulting the Health Sciences Descriptors (DeCS). The tracking was carried out through the words found in the titles, subjects and abstracts of the articles.

Some filters available in the databases were added to limit the search - *textos completos*; text availability: full text; *intervalo de ano de publicação: últimos 10 anos*; publications dates: 10 years. The articles collected were selected by screening titles (first step), abstracts (second step) and full reading (third step). Subsequently, an exploratory reading of the selected studies was carried out, followed by a selective and analytical reading. The PRISMA[13] flowchart (**Figure 1**) was used for identification and selection of articles.

Figure 1 - Flow diagram for article identification and selection.



Source: elaborated by the authors, based on the PRISMA flow diagram[13].

The information extracted from the selected articles was systematized in **Table 1**, containing the following data: author(s), year, country(ies), study design, study objective, population, age, evaluation and instruments, results; in order to order the data relevant to the research.

To assess the quality of the articles, the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies[14] was used, consisting of 14 criteria, as shown in **Chart 1**. The articles were classified as good, regular or poor quality, which were evaluated by two independent evaluators.

Chart 1 - Keywords used in the electronic search in Portuguese and English.

PORTUGUESE	ENGLISH
Nutrição	*Nutrition; Nutrition Science; Nutrition Sciences; Nutrition, Public Health; Nutritional Science; Science, Nutrition; Science, Nutritional; Sciences, Nutrition; Sciences, Nutritional.*
Consumo alimentar	*Food Consumption.*
Estado nutricional	*Nutrition Status; Status, Nutrition; Status, Nutritional.*
Doença Falciforme	*Anemias, Sickle Cell; Cell Disease, Sickle; Cell Diseases, Sickle;Cell Disorder, Sickle; Cell Disorders, Sickle; Disease, Hemoglobin S; HbS Disease; Hemoglobin S Disease; Hemoglobin S Diseases; Sickle Cell Anemia;* *Sickle Cell Anemias; Sickle Cell Disease; Sickle Cell Diseases; Sickle Cell Disorder; Sickle Cell Disorders; Sickling Disorder Due to Hemoglobin S.*

Source: prepared by the authors, 2021.

The process of selection and data extraction from the articles, as well as the identification of methodological aspects, was carried out by two independent reviewers. When there was any disagreement between them, the reviewers read the entire article again for reassessment. If the divergence persisted, a third reviewer could decide which studies should be selected, however, there was no need.

Results

The database search initially resulted in 1,252 articles. Of these, 808 were excluded before the selection process, as they were outside the proposed time interval (n= 673), with incomplete texts (n= 31) and in duplicates (n= 104), resulting in 443 articles for title reading. After screening the titles, 422 articles were excluded, as they did not contemplate the objective of the work, and 21 articles were selected. Of these, 17 were selected by reading the abstract, as they seemed to fit the selection criteria. However, after evaluating the text and methodology, it was found that 10 of them did not meet all the inclusion criteria, resulting in the final selection of 07 articles, as shown in **Figure 1**. All articles were read analytically and selectively, being organized in a table with relevant research information, as shown in **Table 1**.

Table 1 - Clinical, nutritional and socioeconomic/demographic characteristics of children diagnosed with SCD, based on studies published between 2011 and 2021.

Author(s)	Country(ies)	Study design	Results
Islam et al., 2021	Nigeria	Transversal.	It was found that there is an association between SCD, dwarfism and low weight in children under five years of age in an environment burdened with child malnutrition and a high mortality rate.
Santos et al., 2020	Brazil	Sectional (transverse).	It was found that children with SCD are still clinically vulnerable, because they have serious clinical complications. The percentage of overweight was significant. The lack of social equity experienced by this group amplifies the complications resulting from the disease.
Botelho et al., 2019	Brazil	Descriptive transversal.	There was a perception that micronutrient intake was not low and no association was found between nutritional status and micronutrient intake. In contrast, a high percentage of children had low dietary diversity.
Boadu; Ohemeng; Renner, 2018	Ghana	Transversal.	It was noticed that, in general, children with SCD had low energy intake and, consequently, insufficient or totally deficient consumption of micronutrients, mainly calcium, vitamins E, B12, A and C, zinc, folate and magnesium. The percentage of malnourished children, low stature and low weight was associated with the clinical condition.
Adegoke et al., 2017	Brazil and Nigeria	Descriptive transversal.	Higher occurrences of low weight and short stature among Nigerian children with SCD, while the occurrence of overweight or obesity was higher in Brazil.
Pinho et al., 2012	Brazil	Transversal and quantitative in nature.	It was identified that the anthropometric indicators were within the limits of eutrophy (appropriate height and weight for age), however dietary intake was inadequate (little variation in the daily menu, with low intake of fruits and vegetables, milk and derivatives), impacting directly on the consumption of micronutrients, which was insufficient, mainly calcium, iron, folic acid, vitamin B12 and vitamin D.
Animasahun et al., 2011.	Nigeria.	Prospective, transversal and analytical.	It was found that low socioeconomic status has an adverse effect on the nutritional status and hemoglobin of patients with SCD.

Source: prepared by the authors, 2021.

With regard to the general characteristics of the articles (**Table 1**), all studies are cross-sectional (100%), with publications between 2011 and 2021. The surveys were carried out with the following geographic distribution: Brazil (n= 03); Nigeria (n= 02); Ghana (n= 01); Brazil and Nigeria (n= 01). The studies used populations with 12 to 11,420 children diagnosed with SCD, a total of 12,120 female and male participants, with the exception of the control group. Only 01 article did not inform the sex of the sample. The children's age range ranged from 06 months to 12 years.

The studies, for the most part, used the following evaluation criteria for data collection: diagnostic methods (n= 05); assessment of nutritional status (n= 07); analysis of food consumption (n= 04) and determination of the amount of macro and micronutrients (n= 03); classification of socioeconomic status (n= 05) and/or sociodemographic (n= 03).

To confirm the disease in the analyzed children, the most used diagnostic methods were clinical data

obtained from medical records and/or hematological parameters: sickle cell *status;* hemoglobin level; test on a hemoglobinometer; assessment of hemoglobin concentration.

The characterization of the socioeconomic and sociodemographic situation was approached according to the following points: material goods of the families; level of education of those responsible; information about basic sanitation and housing conditions; income and family size; parents' level of education and occupation. To obtain the data, some used questionnaires (semi-structured or pre-tested).

Regarding the use of parameters to assess nutritional status, all studies used at least two of the following anthropometric measurements: weight, height, BMI, weight for age, height for age, weight for height, BMI for age, Triceps Skinfold (TSF), Arm Circumference (AC), Arm Fat Area (AFA) and Arm Muscular Area (AMA).

The assessment of food consumption was based on the use of at least one of these tools: 24-hour dietary recall; food frequency questionnaire; programs and software for calculating the amounts of macro and micronutrients consumed; estimation of nutrient intake, comparing with the recommendations for the age group, according to the RDAs (Recommended Dietary Allowances); analysis of consumption of ultra-processed foods.

As for the results related to the evaluation of the quality of the articles selected for review, described in **Table 2**, all were compliant with criteria 1, 6, 7, 8, 9, 11, 12 and 14; one of the articles did not specify and did not define the study population, as portrayed in criterion 2; five of the analyzed articles did not report whether the participation rate of eligible people was at least 50%, as stated in criterion 3; one of the studies did not report whether the participants were selected from the same populations, and also did not justify the sample size, as informed in criteria 4 and 5; five of them did not report whether exposures were assessed more than once over time, as predicted in criterion 10; one survey did not inform about the loss of follow-up, as mentioned in criterion 13. After applying the tool, the articles presented the following classifications: good quality (n= 04) and fair quality (n= 03). Articles classified as poor quality were not used for the study.

Table 2 - Quality assessment of articles selected for review (n= 07).

Studies / **Criteria**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**Quality**
Islam et al., 2021	Y	Y	Y	Y	Y	N	N	Y	Y	NR	Y	NA	Y	Y	Good
Santos et al., 2020	Y	N	NR	NR	N	N	N	Y	Y	NR	Y	NA	NR	Y	Regular
Botelho et al., 2019	Y	Y	NR	Y	Y	N	N	Y	Y	Y	Y	NA	Y	Y	Good
Boadu; Ohemeng; Renner, 2018	Y	Y	NR	Y	Y	N	N	Y	Y	NR	Y	NA	Y	Y	Regular
Adegoke et al., 2017	Y	Y	NR	Y	Y	N	N	Y	Y	NR	Y	NA	Y	Y	Good
Pinho et al., 2012	Y	Y	Y	Y	Y	N	N	Y	Y	Y	Y	NA	Y	Y	Good

Animasahun et al., 2011.	Y	Y	NR	Y	Y	N	N	Y	Y	NR	Y	NA	Y	Y	Regular

Source: elaborated by the authors, based on the *Study Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies,* 2021[14].

(1) Was the research question or objective in this article clearly stated? (2) Was the study population clearly specified and defined? (3) Was the participation rate of eligible persons at least 50%? (4) Were all subjects selected or recruited from the same or similar populations (including the same time period)? Were the inclusion and exclusion criteria for participating in the study pre-specified and uniformly applied to all participants? (5) Has a sample size rationale, description of power, or variance and effect estimates been provided? (6) For the analyzes in this article, were the exposures of interest measured before the outcome(s) to be measured? (7) Was the timeframe long enough to reasonably expect an association between exposure and outcome, if any? (8) For exposures that may vary in amount or level, did the study examine different exposure levels as related to outcome (eg, exposure categories or exposure measured as a continuous variable)? (9) Were exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants? (10) Have exposures been assessed more than once over time? (11) Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants? (12) Were outcome assessors blinded to participants' exposure status? (13) Was the loss to follow-up after baseline 20% or less? (14) Were the main confounding variables measured and statistically adjusted for their impact on the relationship between exposure(s) and outcome(s)?
Y, yes; N, no; CD, unable to determine; NR, not reported; NA, not applicable.

Discussion

Among the characteristics observed in the analyzed articles, the results presented by Islam et al[15] , Boadu; Ohemeng; Renner[16] , Adegoke et al[17] and Animasahun et al[18] revealed that there is a greater association between SCD and the percentage of malnourished children with low weight and short stature, therefore, the disease still affects the nutritional status of these individuals during childhood. Corroborating these findings, the authors of a systematic review study observed that body measurements (weight and height) and anthropometric indicators (height/age; weight/age; weight/height) of children with the disease were lower when compared to those reference values for this age group[19].

In contrast, a study by Ukoha et al[20] in a city in southeastern Nigeria, on the nutritional status of children and adolescents with SCD found that there is not only evidence of the coexistence of malnutrition among this population, but also an increase in the number of cases of overnutrition. This situation may be directly linked to the nutritional transition that has been progressively occurring in recent years, through changes in living standards, involving economic, technological and cultural advances, income distribution and urbanization[21]. Reinforcing this fact, Adegoke et al[17], Santos et al[22] and Botelho et al[23] found a higher frequency of overweight in Brazilian children with SCD, when compared to other studies of people with this clinical condition, linking the changes in the nutritional profile to the mentioned factors previously.

It is pertinent to point out that the two extremes of nutritional classifications are harmful and worrying in individuals with the disease, since malnutrition is related to the reduction of plasmatic concentrations of hemoglobin, greater risks of infection and mortality, while excess weight increases the risk of blood perfusion and organ overload, as well as increasing the chances of this group developing Systemic Arterial Hypertension, asthma and sleep apnea[22,23].

In view of these facts, it is noteworthy that, due to the transitory process that permeates the nutritional aspects, there is a finding that there have been improvements in the development of this population, and Pinho et al[24] identified in their study that more than 90% of the children had adequate height and weight

for age, and the nutritional status of eutrophy prevailed over the others. Linked to this perspective, the importance of early diagnosis and access to health care is widely relevant, since these factors can significantly minimize growth decline, as well as improve the characteristic signs and symptoms of FD and reduce the high rates of infant mortality[15,16,22].

Thus, to improve understanding of the severity of this clinical condition, laboratory analyzes are performed as a control method. In this sense, among the laboratory factors associated with a higher risk of death, the low level of Hb[25] stands out. Some participants had a significantly lower mean Hb concentration when compared to reference values. They associated the reduction with one of the main complications of the disease, which is premature hemolysis, which triggers severe cases of anemia. Hb levels below the recommended level can also lead to other consequences, such as cerebrovascular accident (CVA) and other more complex cases[15,16,18]. Adding to these findings, in another study, the values of Mean Hematocrit, Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Hemoglobin Concentration (MCHC) and percentage of Fetal Hemoglobin (HbF%) were notably lower in Nigerian children[17].

In addition to these points, the data show that chronic hemolysis leads to loss of integrity of the red blood cell membrane, and these elements correlate with deficiencies in antioxidant nutrients (act as potent inhibitors of polymerization of sickle cell hemoglobin), folate (necessary for the production of red blood cells) and iron[16]. That is, nutritional micro deficiencies represent a relevant problem among children with SCD, due to the impacts of implications and complications on this clinical condition in children[24].

On perspectives involving nutrient intake, Boadu; Ohemeng; Renner[16] noticed in their research that there was adequate protein intake, on the other hand, low intake of folate, magnesium, calcium, vitamin A and vitamins C and E (antioxidant properties). In another study, calcium and iron intake was inadequate; of folic acid, vitamin B12 and vitamin D was below the recommended level; of vitamin A and C did not stand out significantly within any level[24]. However, in the research carried out by Botelho et al[23], the authors observed that only folic acid intake was below the recommended level. They attributed this information to the low consumption of dark green vegetables. Consumption of zinc and iron was quite high in the study population. There is a concern that must be taken into account, as iron overload may be associated with frequent blood transfusions common in these individuals.

Regarding the food diversity of the children analyzed in the studies, Pinho et al[24] found that there was no variation in the menu (food monotony). In addition, they noticed that the participants consumed at least three meals a day (breakfast, lunch and dinner), but snacks (morning and afternoon) and supper were not always eaten. Still, they were able to analyze that the quantity and quality of meals were not adequate for the age group and physiological state of the participants. Botelho et al[23], in turn, found that a high percentage of participants had low dietary diversity, especially in the consumption of fruits and vegetables.

Regarding the degree of influence of the socioeconomic situation on the health of these individuals, Islam et al[15] and Animasahun et al[18] noticed that anthropometric measurements progressively decreased according to the reduction of the social class to which the children belonged. Such data were more present in studies carried out among countries on the African continent.

In research carried out in Brazil, there was divergence in findings, since Pinho et al[24] considered that despite the children's families having low education and living in poverty, they had access to

basic urban infrastructure services, so they believe that this it may have contributed to their having a nutritional status of eutrophy; and Santos et al[22] realized that the socioeconomic situation directly interferes with health care and consequently with the prognosis of diseases, especially with regard to social inequalities and complications in people's lives

It should be taken into account that the problems that permeate the health of the black population could be minimized based on the effectiveness of programs and policies established in some countries, however it is possible to visualize a very opposite context. Despite the implementation of these resources, negligence is still very noticeable[26]. The structural racism that still brutally affects the daily lives of this population, in which the perversity established by the inequality experienced, tries to be camouflaged by the achism of the non-existence of such acts, leaving them on the sidelines of the necessary care to maintain or improve the quality of life[27]. In addition, the difficulty of acquiring the necessary supplies for daily food consumption, in addition to disjointed care practices with a biological focus, which disregards integral actions that permeate the nutritionist's attention, are still determining factors for the reduced development of children with the disease[28.29].

Conclusion

Nutrition is intertwined with different situations during all life cycles of human beings. In the initial phase of life, the body undergoes necessary physiological transformations, both quantitatively and qualitatively. In this period, a careful look is able to minimize future implications related to food. However, it is perceived that some intrinsic and extrinsic elements are capable of modifying this process considerably, so it is essential to analyze the aspects that run through this theme.

The findings of this study prove that SCD still manages to interfere considerably in the development of individuals who inherit this disease, especially in children. The alterations that surround the pathophysiology of the disease reach different body regions, triggering complications that hinder the general well-being of these people. In addition, the low socioeconomic level, which is very common in this population, makes it difficult to acquire basic food components for the body to function, and this factor is linked to the structural racism that is so present and cruel in our society.

A compilation of actions could reduce the complexities that intertwine this disease, with actions aimed at tangible and effective public policies, as well as encouraging family counseling that involves points that strengthen the nutritional education of this public.

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