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REVIEW ARTICLE

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Nutrition, Metabolism, and Prevention of NCDs

Pica in sickle cell disease: nutritional management and implications

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ABSTRACT

Background: Individuals with sickle cell disease (SCD) frequently experience nutritional disturbances, including deficiencies in essential micronutrients. Iron and zinc deficiency anemia has been specifically associated with pica, an atypical eating behavior. **Aims**: This systematic review aimed to characterize pica among individuals with SCD, focusing on potential nutritional causes. **Methods:** A comprehensive literature search was conducted across the MEDLINE (PubMed), Latin American and Caribbean Center on Health Sciences Information (Bireme), and Google Scholar databases from July 2017 to January 2024. Eligible articles included original observational studies, interventions, and case reports involving individuals with SCD across all age groups. Literature reviews, doctoral or master's theses, unrelated studies, and duplicate publications were excluded. **Results**: Ten studies were selected that described the occurrence of pica episodes in the SCD population and explored potential associated nutritional causes. The most prevalent genotype was Hb SS, with ages ranging from 2 to 23 years. Males were more predominant than females in the included studies. Approximately 51.05% of the studied population exhibited pica behavior. Some studies observed that children with pica behavior had low weight and/or height and abnormal laboratory test results. The most commonly consumed objects were paper, foam, fabric, dust, soil, clay, and rubber, although the quantity and frequency of object consumption were not reported in most studies. The most reported symptoms associated with pica behavior included abdominal pain, vomiting, constipation, vaso-occlusive events, dizziness, and fatigue. Clinical interventions in the studies were pain medication, intestinal cleansing, intestinal resection, intravenous hydration, antibiotic therapy, gastric "bezoar" removal, and cognitive-behavioral therapy. The majority of the studied population was monitored by health centers, with frequent return visits. In all studies, physicians were responsible for clinical care. **Conclusion**: A significant association between SCD and pica was evident in the reviewed studies. Iron and zinc deficiencies emerged as potential contributing factors to this atypical eating behavior.

Keywords: Pica, sickle cell disease, iron, zinc, eating disorders.

ARTICLE INFORMATION

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1 Introduction

Sickle cell disease (SCD) is a genetic hematologic disorder characterized by the presence of hemoglobin S (HbS) (Kato et al., 2018; Williams & Thein, 2018) Globally, approximately 5.7 million live births are affected by HbS, with about 300,000 born each year with the HbSS genotype predominantly in Sub-Saharan Africa (Kato et al., 2018; Piel et al., 2013). In Brazil, estimates indicate approximately one case of SCD per 1,000 live births (Cançado & Jesus, 2007) with the highest incidences in the states of Bahia, Rio de Janeiro, and Minas Gerais (Januario, 2002; Kato et al., 2018).

The most severe form of SCD is the HbSS homozygote (referred to as sickle cell anemia), and individuals with this genotype tend to experience higher morbidity and mortality related to the disease. Additionally, individuals with this genotype manifest chronic anemia, often accompanied by recurrent vaso-occlusive events, pain, and multi-organ failure (Cordovil et al., 2023; Kassim et al., 2013; Williams & Thein, 2018).

Individuals with SCD can also experience nutritional disorders, such as changes in nutritional status and

deficiencies in macro and micronutrients (Gonçalves et al., 2021; Souza et al., 2016). Among these deficiencies, the literature has shown specific ones, such as iron and zinc deficiency anemia, that may be associated with a feeding disorder called pica (Hackworth & Williams, 2003; Thompson & Habie, 2016).

Pica, also known as picamalacia, is considered an eating disorder characterized by the persistent ingestion of non-nutritive and non-food substances for at least one month in the last six months (American Psychiatric Association, 2003; Rodrigues, 2019). Scientific studies have shown a high prevalence of pica among young individuals with SCD, with approximately 34 – 66% of pediatric patients with SCD exhibiting symptoms related to pica (Hackworth & Williams, 2003; Lemanek et al., 2002).

Given the need to understand aspects related to pica in SCD, this study aims to conduct a narrative review of the main characteristics of pica occurrence in the SCD population, emphasizing possible nutrition-related causes. This study also intends to propose guidelines and recommendations for healthcare professionals on how to manage the presence of pica in patients with SCD in their clinical practice.

2 Methods

A comprehensive literature search was conducted across the MEDLINE (PubMed), Latin American and Caribbean Center on Health Sciences Information (Bireme), and Google Scholar databases from July 2017 to January 2024. T Search terms included “sickle cell disease”, “sickle cell anemia”, “pica”, and “picamalacia”. Boolean operators "OR" and "AND" were employed to refine the search. Given the specific nature of the topic, no limitations were imposed on publication year, language, or geographic location. Eligible articles were selected from original observational studies, interventions, and case reports, involving individuals with SCD across all age groups. Exclusion criteria comprised literature reviews, doctoral or master's theses, unrelated studies, and duplicate publications. An initial screening of titles and abstracts was conducted to identify potentially relevant articles. Subsequently, full-text assessments were performed to confirm eligibility based on the predetermined criteria. Of the 1,487 articles identified, 10 observational studies (eight descriptive and two analytical) met the inclusion criteria (Figure 1).

Data extraction focused on study methodology, participant characteristics (age, gender, genotype, nutritional status, geographic location), follow-up duration, dietary patterns, laboratory findings, pica behaviors, associated symptoms, and reported interventions. These data were synthesized to identify thematic patterns and similarities among studies.

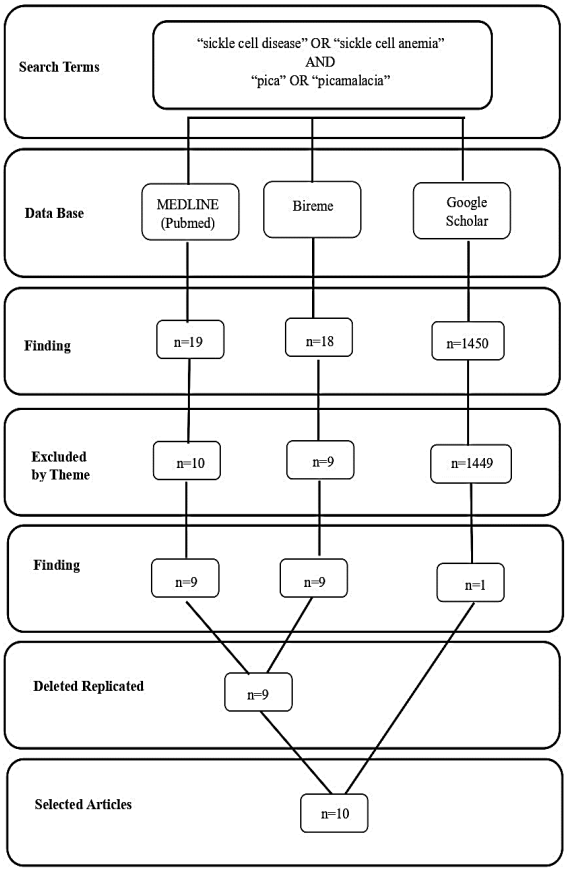

Figure 1. Flow diagram for the process of study selection

3 Results

3.1 Characteristics of scientific studies

Ten studies were included investigating the relationship between the occurrence of pica episodes in the population with Sickle Cell Disease (SCD), as well as the possible associated nutritional causes. The majority of the studies included patients with the HbSS genotype, followed by Hb SC and HbSβ+. The age range of participants spanned from 2 to 23 years, indicating a predominantly young population. A single study focused on a pregnant woman. Males were predominant among the 10 studies (n = 283), compared to females (n = 256). Considering the total population of the ten studies (n = 809), 51.05% (n = 413) of SCD patients exhibited pica behavior (Table 1). Only three case report studies and 1 case series study addressed the number of women of childbearing age (O’Callaghan & Gold, 2012; Al Achkar et al., 2012; Kolthof et al., 2008; Altepeter et al., 2011).

Table 1. General characteristics of the included studies (n=10) about pica and sickle cell disease

Study/Reference	Location	Design	Population			Age (y)	Genotype
			F	M	*n*		
Hackworth et al. 2003	USA	Case-report	0	3	3	11,15 y	Hb SO Hb SS Hb SC
Lemanek et. al. 2002	USA	Longitudinal	71	75	146	2-16y	Hb SS Hb SC Hb Sβ
Ahmed *et. al.*, 2015	Republic of Sudan	Case-control, hospital-based	64 (SG) 23 (CG)	90 (SG) 27 (CG)	154(SG) 50 (CG)	2-18y	Hb SS
Ivascu et al. 2001	USA	Cross-sectional	62	63	125	03-19y	Hb SS Hb SC Hb Sβ$^+$
O'Callaghan & Gold, 2012	USA	Cases series	1	1	2	7, 10y	Hb SS
Aloni *et. al.*, 2015	Belgium	Cross-sectional	31	24	55	>3y	NI
Al Achkar et al. 2012	USA	Case-report	1	0	1	23y	NI
Issaivanan et al. 2009	USA	Case-report	1	0	1	3y 6m	Hb SS
Kolthof et al. 2008	Netherlands	Case-report	1	0	1	17y	NI
Altepeter et al. 2011	USA	Case-report	1	0	1	17y	Hb Sβ$^+$

F: female; M: male; Y: years; U: uninformed; NI: not identified in the study; SG: study group; CG: control group; CG: Cases group

3.2 Nutritional status

Three studies reported lower weight and/or height among children exhibiting pica compared to age-appropriate norms (Hackworth & Williams, 2003; Ahmed, 2015; Ivascu et al., 2001). Conversely, O'Callaghan & Gold, 2012 found no deviations in weight and height and Aloni et al., (2015) reported no significant difference in Body Mass Index (BMI) between pica and non-pica groups.

3.3 Laboratory assessment

Seven studies, including one case-control study, identified altered laboratory parameters in the study population. These abnormalities included hemoglobin, leukocytes, hematocrit, mean corpuscular volume (MCV) levels, as well as decreased platelet counts and elevated reticulocyte counts (Ahmed, 2015; Hackworth & Williams, 2003; Issaivanan et al. 2009). The study by Al Achkar et al., (2012) also observed alterations in other parameters, such as low levels of albumin and high levels of liver transaminases and bilirubin, while Issaivanan et al., (2009) also observed alterations in other parameters, such as low levels of albumin and high levels of liver transaminases and bilirubin.

3.4 Food consumption

Dietary intake was assessed through questionnaires in only two studies by Lemanek et al. (2002) and O'Callaghan & Gold, 2012. While one study specified food items such as French fries, donuts, and popcorn, the overall dietary patterns remained largely unexplored.

The most frequently consumed non-food items included paper, sofa foam, pillow foam, fabric, powder (baby anti-rash powder, for example), soil, hair, clay, and rubber. However, most studies provided limited data on consumption quantities and frequencies. Two studies by Kolthof et al., (2008) and Al Achkar et al., (2012) reported more specific details: one case involved repeated ingestion of sofa foam from 12 to 17 years old. In the second study, there was a report of consuming 1 cup or more of soil in one episode, and this consumption increased in frequency and quantity when the patient became pregnant (Al Achkar, 2012).

In one case from the study by Hackworth & Williams, 2003, one participant expressed a mistaken belief that rubber foam possessed caloric value justifying its consumption.

3.5 Other findings

The most frequently reported symptoms associated with pica included abdominal pain, vomiting, constipation, vaso-occlusive crises (acute pain in the legs, abdomen, back, and chest), dizziness, fatigue, hypertrophy of the tonsils and adenoids, and depressive symptoms (Hackworth & Williams, 2003; Lemanek et al., 2002; Altepeter et al., 2011). In a severe case, a patient experienced pericardial effusion secondary to a bacterial infection, as reported by Hackworth & Williams, 2003.

Among the interventions performed, four studies reported treatment with pain medications (acetaminophen with codeine, toradol, and morphine sulfate) (Issaivanan et al. 2009), intestinal cleansing, laparotomy, and intestinal resection (Altepeter et al., 2011), intravenous fluid hydration and

antibiotic therapy (Al Achkar, 2012) and removal of gastric bezoar (non-digestible substances wholly or partially) (O'Callaghan & Gold, 2012). One study reported the successful cessation of pica following cognitive-behavioral therapy (Kolthof et al., 2008).

The majority of patients (six out of the ten studies) were under ongoing care at healthcare centers (Aloni et al., 2015; Kolthof et al., 2008; Lemanek et al., 2002). In a minority of cases (three studies), patients were attended through hospital emergency care (Al Achkar, 2012; Altepeter et al., 2011; Issaivanan et al. 2009) and one study did not mention the type of consultation (Hackworth & Williams, 2003). Medical doctors were the sole healthcare providers involved in patient management, with no reported involvement of other specialists, such as nutritionists or dieticians.

4 Discussion

The reviewed literature consistently linked pica to 1) irregular eating patterns; 2) affecting children with sickle cell disease (SCD); and 3) micronutrient deficiencies, particularly iron and zinc, that emerged as potential etiological factors (Figure 2).

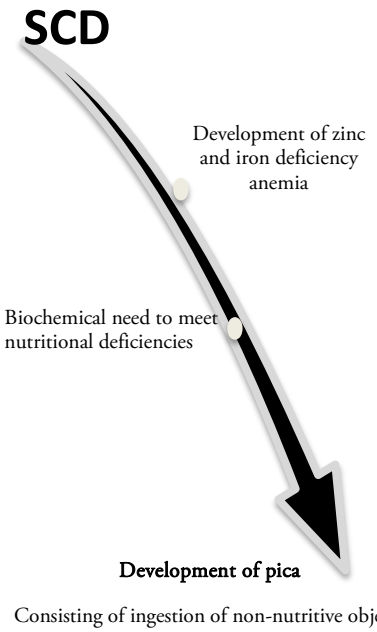

Figure 2. Possible trigger factors for pica in sickle cell disease

Ivascu et al., (2001) and Ahmed, (2015) studies indicated that possible nutritional causes associated with pica in SCD seem to be linked to micronutrient deficiencies, contributing to abnormal food cravings. The body's need for these nutrients can exacerbate cravings for source substances, even if they are nutrient-poor (Rodrigues, 2019; Rodrigues et al., 2021). The association between iron deficiency and pica remains controversial, as some authors found no differences in iron levels between patients with and without pica (Ahmed, 2015; Aloni et al., 2015). According to Ivascu et al., (2001) there is still not enough evidence to identify the relationship between micronutrient deficiency and pica, although this theory has been explored over the years and possibly gained strength in more recent studies, advocating iron and zinc deficiencies as causes of pica.

Blood cell transfusion therapy, a common management strategy for SCD, can paradoxically lead to iron overload (Patel et al., 2023). According to Ivascu et al., (2001), iron deficiency is less prevalent among elderly patients with SCD, potentially due to transfusion-related iron supplementation. Hormonal factors, such as delayed puberty in females, may also contribute to reduced iron requirements in this population (Ivascu et al., 2001).

On the other hand, Issaivanan et al. (2009) claim that iron deficiency anemia has been implicated as a potential etiology of pica in SCD and is frequently associated with malnutrition. Aloni et al., (2015) stated that there is still no consensus to postulate whether pica causes anemia or if severe anemia leads to pica behavior. The impact of dietary factors, such as excessive consumption of anti-nutritional substances, on iron absorption and its potential role in pica development warrants further investigation.

The relationship between pica and zinc is better elucidated. Studies suggest that zinc deficiency is present in most SCD patients, possibly caused by chronic renal injury and tubular dysfunction (Ahmed, 2015; Ivascu et al., 2001; Orozco-González, 2019). Supplementation with both iron and zinc has been reported to ameliorate pica symptoms in some cases (Rodrigues et al., 2011; Ivascu et al., 2001). However, iron supplementation should be discontinued after the first blood transfusion to avoid iron overload in these patients (Rodrigues et al., 2011).

The predominant SCD genotype among study participants was HbSS, followed by HbSC and HbSβ+. The HbSS genotype can be differentiated from other genotypes by its morphology. In this diagnosis, sickle-shaped, target cells, and erythroblasts are frequent, causing blood flow obstruction and frequent pain, justifying the greater clinical severity of the disease. Some researchers proposed an association between pain associated with these crises and the development of pica (Lemanek et al., 2002; Issaivanan et al. 2009; O'Callaghan & Gold, 2012; Rodrigues, 2019).

Table 2. Main procedures in the investigation of pica in patients with sickle cell disease

Situation	Conduct
Related to the time in which the question should be asked	
First Time Consultation (Outpatients)	Always ask patients or responsible family members.
Subsequent consultations (Outpatients)	Frequent questioning in the presence of f pica. Frequent questioning in the presence of signs presented by patients. Inquire if there are reports of incidence or recurrence in nutritional follow-up, either by the patient, family members, or healthcare professionals.
Infirmary (Inpatients)	Always inquire upon hospital admission to the patient or caregivers. Frequent questioning in the presence or suspicion of signs/symptoms presented by patients. Inquire if there are reports or suspicion of incidence or recurrence during hospitalization, either by the patient, family members, or healthcare professionals. Patients with pica admitted should be followed up in outpatient care upon discharge.
Related to the period of consumption of non-nutritive and non-food substances	
Current period	Question, investigate and record whether the patient currently ingests non-edible substances, such as: bricks, toothpaste, soap, chalk, refrigerator ice (gas), paper, rubber, earth, etc. Record type, quantity and frequency of substances ingested.
Past period	Question, investigate and record whether the patient has ingested inedible substances in the past, even if there is no current consumption. Record age range, period (years, months or days) or related event (e.g. pregnancy, school, psychological changes or family problems). Record type, quantity and frequency of substances ingested Note: be careful with recall or memory bias.

The ten studies included individuals aged 2 to 23 years, indicating a prevalence among younger individuals. One theory presented to justify pica behavior in younger children is their ability to report their eating patterns. Older children may feel uncomfortable about reporting non-food substance consumption (Ivascu et al., 2001; Lemanek et al., 2002).

Nutritional status analysis (including three studies) revealed that children with pica often exhibited growth parameters below expected norms. This was attributed to increased caloric requirements associated with the hypermetabolic state of SCD (Ahmed, 2015; Ivascu et al., 2001; Kolthof et al., 2008). This hypermetabolic state makes it difficult to reach caloric needs, thus preventing patients from achieving ideal weight and height. However, according to Ivascu et al., (2001) it is unknown whether pica is the cause or effect of lower body weight. Another reason may be zinc deficiency, indicated by Issaivanan et al. (2009) as a potential contributing factor of decreased linear growth and sexual maturation, with zinc supplementation eliminating pica behavior.

While the majority of studies focused on pediatric populations, one study examined pica among pregnant women with SCD22. Emotional factors, chronic anemia, and underlying medical conditions were proposed as potential etiologies. In other studies, evaluating the relationship between pregnancy and pica, it was observed that this condition may be associated with anemia, constipation, intestinal obstruction, dental problems, parasitic infections, toxoplasmosis, hypertensive syndromes in pregnancy, interference with nutrient absorption, lead poisoning, and hyperkalemia (Corbett et al., 2003; Saunders et al., 2009). Other factors related to the increased prevalence of pica in pregnancy include low education levels and being African American (Fawcett et al., 2011). Roy et al., (2018) observed that pica was prevalent and strongly associated with iron deficiency and food insecurity among Hispanic women living in the United States.

The ingestion of non-nutritive substances poses significant health risks. Reportedly consumed items included paper, fabric, soil, rubber, mattress foam, and powder (baby rash ointment, for example), among other substances. Potential consequences encompass dental damage, infections, gastrointestinal complications, and impaired nutrient absorption Severe outcomes such as lead poisoning and neurological impairment have also been documented (Aloni et al., 2015; Altepeter et al., 2011; Issaivanan et al. 2009). According to Issaivanan et al. (2009) lead neuropathy is frequent in children with SCD.

Laboratory findings consistently revealed abnormalities in patients with pica. Ahmed, (2015) observed that in the pica group, hemoglobin levels were significantly lower compared to controls (79.3 ± 18.3 g/ L vs. 90.2 ± 28.0 g/L, p = 0.02). Aloni et al., (2015) and Kolthof et al., (2008) observed a higher hemolytic rate in patients with pica, justifying lower hemoglobin and hematocrit values in children with pica and SCD compared

to those without pica. Reticulocytes (immature red blood cells) increase when hemoglobin is prematurely destroyed, which is common in SCD (Carden et al., 2020).

Dos Santos et al., 2023; Rodrigues et al., 2021; Santos et al., 2023). Given the potential severity of pica-related complications, therapeutic interventions should prioritize behavior modification

Table 3. Main recommendations in the nutritional management of pica in patients with sickle cell disease

Relationship with Reference Hematologist and Interdisciplinary Team	Practice matrix support. As a matrix nutritionist (inpatients or outpatients), you could inform and discuss cases with the reference hematologist and the interdisciplinary team through consultations or clinical sessions (round). Get support, if necessary, from psychologists, especially regarding harm reduction. Get support, if necessary, from social workers, especially in financial difficulties and purchasing food. Always set up a specific social support network.
Pica Monitoring	Use instruments such as usual food consumption (1st-time consultation), food record, or 24-hour recall monitoring the times, frequency, quantity, and type of substances and materials consumed. Monitor for changes in clinical or laboratory tests that may be related to pica.
Promotion of Healthy Eating	Encourage the consumption of healthy foods. Encourage the consumption of fruits, vegetables, and greens daily. Discourage the consumption of ultra-processed foods. Creating educational materials and homemade recipes could help reduce the consumption of non-nutritive or food substances.
Harm Reduction	Wean the consumption of non-food substances or materials gradually until the intake of these substances is eliminated. Work with reducing the frequency of substances through consultation-by-consultation agreements. Work and agree on the exchange of consumption derived from foods/preparations of interest (what they like or have an affective aspect) at the time the patient thinks or remembers wanting to ingest the substances.

Source: Cordovil, 2019; Hemorio, 2018; Meirelles et al., 2021 and Gonçalves et al. 2023

The observed correlation between pica and altered laboratory parameters suggests a potential link to the severity of hemolytic processes in SCD. However, the precise nature of this relationship remains unclear. It is uncertain whether pica exacerbates hemolysis or vice versa. However, it is known that these laboratory data are markers of more severe SCD symptoms. The precise relationship between anemia and pica remains inconclusive. While some studies suggest a causal link between iron deficiency anemia and pica, others propose that pica may contribute to anemia through impaired nutrient absorption. Further research is necessary to elucidate the complex interplay between these factors.

4.1 Nutritional management in pica

Comprehensive management of pica in individuals with sickle cell disease (SCD) requires a multidisciplinary approach involving hematologists, nutritionists, psychologists, and social workers.

The diagnosis of pica requires persistent consumption of non-nutritive substances for at least one month, excluding culturally sanctioned practices or symptoms of other mental disorders (American Psychiatric Association, 2013; da Silva Goncalves

until complete elimination of occurrences (American Psychiatric Association, 2013; Carden et al., 2020; State Institute of Hematology Arthur Siqueira Cavalcante (Hemorio), 2018; Rodrigues et al., 2021). A systematic inquiry into pica behavior, as outlined in Table 2, is essential for effective management.

Effective management of pica requires a collaborative approach involving hematologists and other healthcare professionals. An interdisciplinary team can comprehensively assess various factors contributing to pica, including environmental and socioeconomic determinants. This will help to identify possible social inequalities that could promote decreased access to good quality food and lead to food insecurity. Nutritional monitoring, as shown in Table 3, is essential for identifying and addressing dietary imbalances associated with pica with regard to the ingestion of non-nutritive or food substances (Table 3). Given that pica can affect individuals across different life stages, it is important for the nutritionist and the multidisciplinary team accompanying the patient to be attentive to the specificities of each group.

Particular attention should be directed towards the unique circumstances of pregnant women. Various factors, including physiological, environmental, nutritional, psychological, socioeconomic, and cultural factors, have been implicated in the etiology of pica during pregnancy (Ayeta et al., 2015; Dunker et al., 2010). Among the emotional factors, anxiety stands out, which can accompany women throughout gestation, potentially leading to maladaptive or non-functional behaviors, such as pica (Ayeta et al., 2015). Some studies have noted that pica occurs in pregnant women as a way to cope with anxiety and stress during pregnancy (Ayeta et al., 2015; Young, 2010). Therefore, the team needs to assess the presence of emotional triggers (such as anxiety and stress) to propose preventive interventions and coping strategies in contexts of vulnerability, especially when considering pica associated with undesirable outcomes in pregnancy (Ayeta et al., 2015).

4.2 Potentials, challenges, and implications of the study

To the best of our knowledge, this review study distinguishes itself as the most recent publication on the topic, providing the most current data available. A notable aspect of this study is its comprehensive examination of pica across various age groups, rather than focusing solely on children or pregnant women, as observed in studies by López et al. (2004), Fawcett et al. (2016), Gonçalves et al. (2023), and Rodrigues et al. (2019).

Pica during pregnancy has been associated with a range of adverse maternal and fetal outcomes. Conditions such as hypertensive disorders, anemia, nutrient absorption interferences, lead poisoning, and gestational diabetes, have been associated with pica (Ayeta *et* al., 2015; Ezzeddin *et* al., 2015; Saunders *et* al., 2009; Thihalolipavan *et* al., 2013), while pica itself has been suggested as a risk factor for cesarean delivery (Ezzeddin *et* al., 2015). Fetal complications including preterm birth, low birth weight, and decreased fetal growth have also been reported (Kachani, & Cordás, 2009). Therefore, Early identification and management of pica are crucial for optimizing maternal and child health (Ayeta *et* al., 2015). Additionally, it is crucial to promote awareness of the importance of early pica diagnosis to implement preventive practices for maternal and child health (Ayeta *et* al., 2015). Optimal maternal nutritional status is imperative for fetal health and development. Given the high prevalence (about 30%) of anemia among pregnant women, proactive screening and intervention are crucial in the Unified Health System (SUS) network (Saunders *et* al., 2009). Women with inadequate nutrient intake are exposed to potential adverse effects during pregnancy. The coexistence of pica with other eating disorders, such as anorexia or bulimia, significantly exacerbates nutritional risks for pregnant women. Comprehensive dietary counseling is imperative to address these challenges and mitigate the potential for helminth infections and micronutrient deficiencies (Saunders *et* al., 2009).

Pica remains underdiagnosed and underreported during pregnancy due to associated stigma and embarrassment (Ayeta *et* al., 2015; Ezzeddin *et* al., 2015). Healthcare providers must establish trusting relationships to facilitate open communication and encourage disclosure of pica behaviors.

In pediatric populations, the etiology of pica is complex, involving a combination of biological and psychosocial factors (Rodrigues *et* al., 2021). Nutritional deficiencies (e.g., iron and zinc), disease severity (hemoglobin levels, hematocrit, and reticulocyte count), and growth parameters have been implicated as biological contributors. Concurrently, individual and family stress, disordered eating behaviors, socioeconomic challenges, food insecurity, emotional impulsivity, and a family history of pica represent potential psychosocial risk factors (Rodrigues *et* al., 2021).

Various intervention strategies have been proposed for addressing pediatric pica in SCD. This includes providing verbal praise, affection, or a tangible reward when the child engages in pica-related behaviors (e.g., chewing gum, eating real food) (Burke L. & Smith, 1999; Rodrigues *et* al., 2021; Piazza *et* al., 1998) offering acceptable substitutes that mimic the characteristics of the preferred pica item, such as texture, taste, or appearance (Myles & Hirsch,1996; Piazza *et* al., 1998; Rodrigues *et* al., 2021); reducing or removing access to desired pica items and offering alternative resources, such as toys, engaging activities, and parental interactions (Burke L. & Smith, 1999; Madden *et* al., 1981; Rodrigues *et* al., 2021); and utilizing psychotherapy and cognitive-behavioral therapy (Kalfus *et* al., 1988; Rodrigues *et* al., 2021). It is advisable for health professionals to incorporate these proposed interventions into their clinical practice, especially when managing children exhibiting pica behavior.

According to Chalker, (2017), interviews may not be the most effective method for investigating pica in children and adolescents. It is crucial to employ diagnostic methods that can identify the consumption of non-food substances, such as stool examination, blood biochemical tests, and oral evaluation for potential dental wear. Furthermore, health professionals or caregivers should consider using a "safe bait", an object deliberately placed to trigger pica behavior as a means of identifying the disorder (Chalker, 2017). The assessment of the elderly individuals should also be comprehensive, as pica in this demographic may result from prolonged inadequate or insufficient nutrient intake. Additionally, neurological disorders in the elderly can exacerbate poor eating habits. Therefore, regular medical examinations, evaluations of the living

environment, and interviews with caregivers are recommended (Chalker, 2017).

The lack of validated instruments for assessing pica complicates the investigation of this condition and likely leads to an underestimation of its prevalence. This underscores the need for further research (Ayeta *et* al., 2015; Santos *et* al., 2016; Saunders *et* al., 2009). Furthermore, there should be a focus on improving the screening of other eating disorders with obstetric consequences associated with pica and integrating these assessments into the routine of health professionals (Santos *et* al., 2016).

Despite the insights provided, significant gaps remain in our understanding of pica behavior in individuals with SCD. Contributing factors may include stress, psychological, social, cultural, and nutritional elements, with the latter being the most substantiated. However, it is currently unclear whether pica is a cause or effect of micronutrient deficiencies, particularly in iron and zinc. This ambiguity underscores the need for further longitudinal studies to elucidate these relationships. Although some of the studies referenced in this review involve large sample sizes, several were based on data from only one or two individuals, thereby limiting the generalizability of the findings. Therefore, future research should prioritize studies that focus on the most affected groups, namely children and adolescents, using representative samples to enhance the robustness and applicability of the results.

5 Conclusion

The majority of the identified studies established a positive association between sickle cell anemia and pica, with deficiencies in the micronutrients zinc and iron being identified as the primary contributors to irregular eating habits. The consumption of non-food substances may occur as an attempt to fulfill biochemical needs caused by nutritional deficiencies. Psychological or emotional disturbances were mentioned as reasons for the occurrence of this eating disorder, highlighting the need for interdisciplinary healthcare team involvement. The correlation between pica and low body weight in children/adolescents requires nutritional intervention. Further longitudinal studies are needed to elucidate the real association between the deficiency of certain micronutrients and pica in SCD.

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Authors 04: Conceptualization, Methodology, Project Administration, Resources and Supervision.

Authors 05: Conceptualization, Investigation, Methodology, Visualization, Writing, Review & Editing, Project Administration, Resources, Supervision and Validation.

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