Birth and Growth Medical Journal
2025;34(4):200-205. doi:10.25753/BirthGrowthMJ.v34.i4.36976

# CLINICAL CASE REPORTS

## Psychopathology in children and adolescents with sickle cell disease followed up in a pediatric hematology unit of a tertiary hospital in Portugal

Francisca Bastos Maia[1], Emília Costa[2], Inês Cardoso[3]

### ABSTRACT

**Introduction:** Sickle cell disease (SCD) is a chronic disease characterized by abnormal hemoglobin. The existing literature highlights a heightened prevalence of emotional problems among children and adolescents with SCD, with depressive and anxiety disorders reported more frequently. This study aimed to quantify the proportion of patients with SCD with the SS phenotype at a tertiary hospital in Portugal who were referred to the hospital's Child and Adolescent Psychiatry (CAP)/ Psychology services, and to identify any diagnosed psychopathology.

**Methods:** This was a descriptive, retrospective observational study conducted to analyze the prevalence of psychopathology in children and adolescents with SCD. We reviewed the records of 30 patients followed up in the Pediatric Hematology Unit of Hospital Santo António during 2023. A descriptive statistical analysis was performed.

**Results:** Of the 23 patients with SCD who met the inclusion criteria and were included in the study, five (22%) were referred to CAP/Psychology services. Among these, two (40%) were diagnosed with attention-deficit/hyperactivity disorder (ADHD). One of these patients with ADHD had comorbid major depressive disorder, insomnia, specific learning disorder, and primary nocturnal enuresis, while the other presented comorbid trichotillomania and oppositional defiant disorder.

**Conclusion:** Over a fifth of the children and adolescents with SCD followed up in our hospital's pediatric hematology unit were referred for mental health consultation. Based on these results, a multidisciplinary approach to SCD care that includes CAP services is recommended to screen for and treat mental health problems.

**Keywords:** ADHD; anxiety; depression; psychological problems; psychopathology; sickle cell disease

1. Department of Child and Adolescent Psychiatry, Centro Materno-Infantil do Norte, Unidade Local de Saúde de Santo António, 4050-651 Porto, Portugal. franciscabbmaia@gmail.com; u21080@chporto.min-saude.pt
2. Department of Pediatrics, Centro Materno-Infantil do Norte, Unidade Local de Saúde de Santo António, 4050-651 Porto, Portugal. u08020@chporto.min-saude.pt

## INTRODUCTION

Sickle cell disease (SCD) is a chronic, recessively transmitted disease characterized by abnormal hemoglobin that affects 400,000 newborns a year, with higher prevalence in sub-Saharan African countries. In addition to chronic hemolytic anemia, SCD can lead to serious medical complications, including cerebrovascular disease, severe infections, and recurrent acute pain of vaso-occlusive origin.[1]

Several studies indicate a higher prevalence of emotional problems among children and adolescents with SCD compared to healthy control individuals: 36%-46% for depressive disorders and 9%-19% for anxiety disorders.[2,3] The most frequently reported neuropsychiatric problems in this population are depression, anxiety, learning problems, and attention-deficit/hyperactivity disorder (ADHD).[4] Notably, these children often experience neurocognitive impairments and learning problems, difficulties with interpersonal relationships, low self-esteem, and maladaptive coping strategies.[5] Nocturnal enuresis is also more prevalent and persistent in patients with SCD compared to the general population.[6]

The prevalence of emotional disorders in children and adolescents with SCD is not significantly different from that found in children and adolescents with other chronic diseases like type 1 diabetes mellitus (T1D). For example, a study conducted in Nigeria showed that approximately 38% of patients with SCD, and 42% of patients with T1D, met at least half of the criteria for symptoms of anxiety or depressive disorders, according to the Diagnostic and Statistical Manual of Mental Disorders IV (DSM-IV).[7]

The pain episodes experienced by children and adolescents with SCD can lead to frequent and/or prolonged hospitalizations, resulting in social withdrawal, which may have a negative impact on normal emotional, socio-behavioral, and cognitive development, ultimately affecting quality of life.[8]

Given the high prevalence of chronic pain in SCD, which ranges from 23% to 65%, it is likely to have a profound impact on sleep quality.[1,9] In fact, 21%-41% of children and adolescents with SCD report some form of insomnia.[10] Furthermore, findings from polysomnography studies reveal that approximately 36% of children with SCD experience sleep disordered breathing, while 23% exhibit periodic limb movement disorder.[11] Poor sleep patterns in patients with SCD have been correlated with higher pain levels, increased risk of stroke, greater healthcare utilization, and heightened negative mood.[12]

The aim of this study was to determine how many patients with SCD (with the SS phenotype) followed up in a pediatric hematology unit of a tertiary hospital in Portugal have received Child and Adolescent Psychiatry (CAP)/Psychology services, as well as to identify the psychiatric disorders diagnosed in these individuals.

## METHODS

### Study Design

This was a descriptive and retrospective observational study conducted to analyze the prevalence of psychopathology in children and adolescents with SCD with the SS phenotype.

### Study Population

Among 30 patients followed up in the Pediatric Hematology Unit of Hospital Santo António during 2023, 23 met the inclusion criteria (i.e., were diagnosed with the SCD SS phenotype). Patients with other SCD phenotypes, such as SC and SBeta, were excluded from the analysis.

### Study Variables

The variables analyzed in this study were:

- Number of patients referred to CAP/Psychology services;
- Age at referral;
- Established psychiatric diagnoses;
- Associated psychiatric comorbidities;
- Therapeutic interventions implemented (e.g., psychotherapy, medication, discharge);
- Average number of hospitalizations among referred vs. non-referred patients.

### Data Sources

The data were extracted from the electronic medical records of the Pediatric Hematology Unit of Hospital Santo António in Porto, Portugal.

### Data Analysis

A descriptive statistical analysis was conducted to determine the prevalence of referrals, type of diagnosed psychopathology, and the therapeutic interventions performed.

## RESULTS

Among the 23 patients diagnosed with SCD and the SS phenotype in our hospital, five (22%) were referred to CAP/Psychology services. Referral to mental health professionals occurred at school age (6–12 years) in two cases (40%) and during adolescence (13–18 years) in three cases (60%). Of the referred cases, only two (40%) patients presented psychopathology, both diagnosed with ADHD, according to the revised 5$^{th}$ edition of the DSM (DSM-5-TR). In one instance, there was co-occurrence of major depressive disorder, insomnia disorder, primary nocturnal enuresis, and specific learning disorder with impairment in written expression. In the other case, there was comorbid trichotillomania and oppositional defiant disorder (ODD).[13] Additionally, another patient exhibited subclinical anxiety and maladaptive coping

mechanisms, such as eating raw rice.

Regarding the management of the referred cases, one patient (20%) was discharged, two (40%) were directed to Psychology services, and two (40%) were prescribed medication. The two patients who met the criteria for mental disorders and kept being followed up for CAP care are described below.

Patients with SCD who were referred to CAP/Psychology services exhibited an average of 15.2 hospitalizations in one year, contrasting with an average of 2.6 hospitalizations per patient among those without such referral

| **Table 1 - Demographic and clinical characteristics of patients with SCD referred to CAP/Psychiatry Services (n=5) Characteristic** | | **No. of patients (%)** |
|---|---|---|
| Sex | Female | 2 (40%) |
| | Male | 3 (60%) |
| Age range at the time of the referral to CAP/Psychology | 6-12 years | 2 (40%) |
| | 13-18 years | 3 (60%) |
| Age at diagnosis of SCD | <3 years | 3 (60%) |
| | ≥3 years | 2 (40%) |
| Country of origin | Angola | 5 (100%) |
| Main symptoms of SCD | Anemia | 3 (60%) |
| | Pain crises | 2 (40%) |
| Reasons for referral to CAP/Psychology | Difficulties in adapting to the disease and its complications | 4 (80%) |
| | Anxiety about academic issues and the future | 1 (20%) |
| Psychopathology? | Yes | 3 (60%) |
| | No | 2 (40%) |
| Orientation | Discharge | 1 (20%) |
| | Referral to Psychology | 2 (40%) |
| | Medication | 2 (40%) |

**Case 1**

A teenage girl who is currently 13 years old was referred to the CAP consultation at the age of six owing to almost daily episodes of nighttime awakenings, accompanied by intense and inconsolable crying, along with emotional instability. In addition to SCD, she had primary nocturnal enuresis, which was being treated with oxybutynin. During the first CAP consultation, it was determined that the child experienced nighttime awakenings that required the presence of an adult, along with reports of fears and nightmares. Given this context, psychotherapeutic follow-up was recommended.

At the age of 10, this child was referred to the Sleep Pathology consultation for disrupted sleep patterns following pain episodes. Melatonin and oxitriptan were prescribed, along with behavioral recommendations, such as a reward system for encouraging independent sleep and minimizing nighttime awakenings. Polysomnography revealed a sleep efficiency of 94%, with absence of obstructive sleep apnea syndrome and periodic limb movements of sleep, and two episodes of nocturnal enuresis. She exhibited fragmented sleep, with a predominance of nighttime awakenings. Additionally, the child exhibited symptoms suggestive of restless legs syndrome, prompting the initiation of treatment with gabapentin, which led to symptom improvement.

As the child progressed in school, learning difficulties were detected at the age of 11, prompting a referral to the

Developmental Pediatrics consultation. A cognitive assessment was conducted using the Wechsler Intelligence Scale for Children: 3rd edition, revealing an intelligence quotient within the average range for the child's age group. Additionally, the D2 Test of Attention indicated low percentiles for selective attention, sustained attention, concentration, and attentional control. Based on these findings, the pediatrician suggested a diagnosis of ADHD and a potential specific learning disorder with impairment in written expression. Consequently, she was prescribed extended-release methylphenidate and referred to a speech therapist.

At the age of 12, she resumed CAP care in a private setting, where she continues to be followed up, and was prescribed sertraline for depressive symptoms.

**Case 2**

A 13-year-old male adolescent was referred to the CAP consultation because of challenges in coping with the broad impact of his illness and its ramifications, such as daily medication, frequent hospitalizations, and restrictions on sports activities. Additionally, his parents expressed concerns about managing impulsive and aggressive behaviors, as well as episodes of trichotillomania. Aside from SCD, the relevant personal history included prior suspicion of ADHD and prescription of modified-release methylphenidate, reported during the Developmental Pediatrics consultations. However, he discontinued follow-up due to lack of engagement.

In the first CAP consultation, the adolescent's mother expressed noticing increased irritability and decreased frustration tolerance in her son since she began focusing more on his younger sister. Furthermore, she disclosed that over the previous two years, the adolescent had been engaging in hair-pulling behaviors during periods of emotional dysregulation and frustration. Reports from his previous school indicated issues with attention and low persistence in tasks. The mother mentioned that her son never took the prescribed modified-release methylphenidate. Currently in the 7th grade, he maintains a satisfactory academic performance. Notably, he had repeated two school years, once upon relocating from his home country to Portugal, and the other time due to multiple hospitalizations.

Given his background, the CAP specialist diagnosed him with trichotillomania as a coping mechanism for emotional regulation, primarily triggered by family conflicts. Additionally, he displayed symptoms of ADHD and ODD. Consequently, he was prescribed extended-release methylphenidate and continued to receive ongoing CAP care.

## DISCUSSION

As reported in the existing literature on other chronic diseases, patients with SCD have more internalizing disorders, including somatic complaints, anxiety, and depressive symptoms.[14] These symptoms may be attributed to diverse factors, such as the lifelong nature of the illness, the unpredictable nature of pain crises, the feelings of frustration or injustice and the cognitive dysfunction experienced during childhood.[15] Additionally, research studies indicate a higher prevalence of depression and anxiety among children with SCD compared to control groups.[16] In our patient population, only one female patient met criteria for major depressive disorder, requiring antidepressant medication. However, it is worth noting that at least one adolescent in our study population exhibited subclinical anxiety symptoms, although not meeting the criteria for anxiety disorder.

On the other hand, issues related to self-esteem, dissatisfaction with body image, and social isolation have been observed in children with SCD.[17] In our study cohort, two adolescents were under the care of pediatric endocrinologists owing to growth delay, a factor that could contribute to their dissatisfaction with body image. Additionally, one adolescent referred to the CAP consultation, who was residing in an institution in Portugal for better management of his SCD while his family stayed in Angola, exhibited social isolation from peers, both at school and the institution, possibly as a coping mechanism. In fact, all the patients in our study population were from Angola, where this disease is more prevalent. Furthermore, emigration to another country can bring additional distress and contribute to the emergence of emotional and behavioral symptoms in these patients.

A 2014 study showed that children with SCD exhibited a higher frequency of somatic complaints compared to the control group.[16] Notably, these individuals may experience chronic pain directly linked to SCD or exhibit additional somatic psychiatric symptoms. Such complaints could potentially serve as underlying indicators of undiagnosed depression or anxiety. Therefore, it is advisable to consider referral to CAP services for patients with SCD who present with persistent somatic complaints.[14]

In our study, both individuals presenting with psychopathology were diagnosed with ADHD. Current evidence suggests that children with SCD are at an elevated risk of developing concentration issues, particularly sustained attention problems. This may be attributed to frontal lobe abnormalities, particularly anterior infarcts, which play a significant role in attention deficits.[4] However, no risk of stroke was identified in any of these patients by a series of transcranial Dopplers. Furthermore, some neurocognitive features are shared between ADHD and SCD, namely impaired attention, executive functions, and working memory.[4]

Brain damage resulting from SCD complications may begin early in life, leading to a spectrum of neurologic syndromes, including cognitive difficulties and diminished language abilities.[18] Indeed, at least one patient referred to the CAP consultation had a history of receiving speech therapy.

A 2014 study revealed that children with SCD exhibited heightened emotional reactivity and more aggressive behavior than the control group.[16] In fact, the male adolescent followed

up in the CAP consultation displayed heteroaggressive behaviors in situations of frustration intolerance.

In addition, a 2013 study reported a prevalence of nocturnal enuresis of 26% in children with SCD vs. 4% in the control group.[6] In our cohort, one out of the five patients referred to CAP services had a diagnosis of primary nocturnal enuresis. Daniel et al. noted that children with SCD are more prone to experiencing enuresis, night awakenings, and respiratory distress during sleep.[19]

In a study of sleep problems among adolescents with SCD, those with the condition reported significantly poorer overall sleep quality compared to their healthy counterparts. They struggled in particular with falling asleep, maintaining sleep, and reinitiating sleep after waking up in the middle of the night.[12] The most significant difference observed between adolescents with SCD and their healthy peers was in the ability to maintain sleep. This discrepancy could be attributed to nighttime pain leading to awakenings.[12] Interestingly, one patient referred to the CAP consultation for sleep problems, who was later followed up in the Sleep Pathology consultation, experienced nighttime awakenings possibly associated with painful crises.

Recent research indicates that children and adolescents with SCD experience significant reduction in quality of life across emotional, physical, social, and academic domains compared to their healthy peers. Additionally, hospitalizations for disease management, particularly for pain, can impact participation in recreational activities and school attendance and be associated with psychiatric and psychosocial challenges.[1]

This study has several limitations that should be acknowledged. First, the small sample size (n=23) limits the generalizability of the findings to broader populations of children and adolescents with SCD. Second, the retrospective design relies on the accuracy and completeness of electronic medical records, which may have led to missing or underreported data. Additionally, since the study was conducted within a single tertiary hospital, the findings may not be applicable to patients followed up in other healthcare settings, particularly in regions with different health system structures, resources, and cultural perceptions of mental health.

Another limitation is the absence of a control group of children without SCD, or with other chronic illnesses such as T1D, to compare the prevalence of psychiatric disorders. Lastly, potential confounding factors, such as socioeconomic status, family dynamics, and migration-related stressors, were not systematically evaluated. These variables could significantly impact mental health outcomes and may explain some of the emotional and behavioral symptoms observed in the study population.

## CONCLUSION

In summary, in our hospital's hematology unit, patients with SCD were referred for mental health consultations at a moderate rate. In this context, it seems reasonable to consider creating a multidisciplinary SCD consultation that includes CAP specialists, in order to screen for mental health problems, as well as to train and educate pediatricians about mental health problems in this patient population.

## AUTHORSHIP

Francisca Bastos Maia – Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Writing – original draft

Emília Costa – Conceptualization; Data curation; Methodology; Supervision; Writing – review & editing

Inês Cardoso – Supervision; Writing – review & editing

## REFERENCES

1. Gunes S, Aldemir R, Gunes A, Ekinci O. Parent-reported sleep problems in children and adolescents with sickle cell disease: relationship to health-related quality of life. Arch Med Sci. 2021 Jan 26;18(3):659-665. doi: https://doi.org/10.5114/aoms/124154. PMID: 35591824; PMCID: PMC9103506.
2. Jerrell JM, Tripathi A, McIntyre RS. Prevalence and treatment of depression in children and adolescents with sickle cell disease: a retrospective cohort study. Prim Care Companion CNS Disord. 2011;13(2):PCC.10m01063. doi: https://doi.org/10.4088/PCC.10m01063. PMID: 21977359; PMCID: PMC3184596.
3. Al Zahrani OS, Mukhtar O, Al Subaie M, Al Howiti WE. Systematic psychiatric assessment of patients with sickle cell disease. Saudi Med J. 2019 Jan;40(1):59-65. doi: https://doi.org/10.15537/smj.2019.1.22919. PMID: 30617382; PMCID: PMC6452608.
4. Berkelhammer LD, Williamson AL, Sanford SD, Dirksen CL, Sharp WG, Margulies AS, *et al*. Neurocognitive sequelae of pediatric sickle cell disease: a review of the literature. Child Neuropsychol. 2007 Mar;13(2):120-31. doi: https://doi.org/10.1080/09297040600800956. PMID: 17364569.
5. Hijmans CT, Grootenhuis MA, Oosterlaan J, Last BF, Heijboer H, Peters M, *et al*. Behavioral and emotional problems in children with sickle cell disease and healthy siblings: Multiple informants, multiple measures. Pediatr Blood Cancer. 2009 Dec 15;53(7):1277-83. doi: https://doi.org/10.1002/pbc.22257. PMID: 19731327.
6. Ekinci O, Celik T, Ünal Ş, Oktay G, Toros F, Ozer C. Nocturnal enuresis in sickle cell disease and thalassemia major: associated factors in a clinical sample. Int J Hematol. 2013 Oct;98(4):430-6. doi: https://doi.org/10.1007/s12185-

013-1422-9. Epub 2013 Sep 8. PMID: 24014263.
7. Bakare MO, Omigbodun OO, Kuteyi OB, Meremikwu MM, Agomoh AO. Psychological complications of childhood chronic physical illness in Nigerian children and their mothers: the implication for developing pediatric liaison services. Child Adolesc Psychiatry Ment Health. 2008 Nov 19;2(1):34. doi: https://doi.org/10.1186/1753-2000-2-34. PMID: 19019212; PMCID: PMC259608.
8. Edwards CL, Scales MT, Loughlin C, Bennett GG, Harris-Peterson S, De Castro LM, *et al*. A brief review of the pathophysiology, associated pain, and psychosocial issues in sickle cell disease. Int J Behav Med. 2005;12(3):171-9. doi: https://doi.org/10.1207/s15327558ijbm1203_6. PMID: 16083320.
9. Vroom DC, Rodgers-Melnick SN, Brown T, Owusu-Ansah A, Dusek JA. Pain screening in youth with sickle cell disease: A quality improvement study. Pediatr Blood Cancer. 2024 May;71(5):e30912. doi: https://doi.org/10.1002/pbc.30912. Epub 2024 Feb 13. PMID: 38348535.
10. Hankins JS, Verevkina NI, Smeltzer MP, Wu S, Aygun B, Clarke DF. Assessment of sleep-related disorders in children with sickle cell disease. Hemoglobin. 2014;38(4):244-51. doi: https://doi.org/10.3109/03630269.2014.919941. Epub 2014 Jun 18. PMID: 24941261.
11. Rogers VE, Marcus CL, Jawad AF, Smith-Whitley K, Ohene-Frempong K, Bowdre C, *et al*. Periodic limb movements and disrupted sleep in children with sickle cell disease. Sleep. 2011 Jul 1;34(7):899-908. doi: https://doi.org/10.5665/SLEEP.1124. Erratum in: Sleep. 2012 Jun;35(6):725. PMID: 21731140; PMCID: PMC3119832.
12. Valrie CR, Trout KL, Bond KE, Ladd RJ, Huber NL, Alston KJ, *et al*. Sleep Problem Risk for Adolescents With Sickle Cell Disease: Sociodemographic, Physical, and Disease-related Correlates. J Pediatr Hematol Oncol. 2018 Mar;40(2):116-121. doi: https://doi.org/10.1097/MPH.0000000000001067. PMID: 29324574; PMCID: PMC5820179.
13. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-5-TR). American Psychiatric Association Publishing 2022. https://doi.org/10.1176/appi.books.9780890425787.
14. Ekinci O, Celik T, Unal S, Ozer C. Psychiatric problems in children and adolescents with sickle cell disease, based on parent and teacher reports. Turk J Haematol. 2012 Sep;29(3):259-64. doi: https://doi.org/10.5505/tjh.2012.15986. Epub 2012 Oct 5. PMID: 24744670; PMCID: PMC3986751.
15. Levenson JL. Psychiatric issues in adults with sickle cell. Prime Psychiatry. 2008; 15(5):45-49.
16. Bakri MH, Ismail EA, Elsedfy GO, Amr MA, Ibrahim A. Behavioral impact of sickle cell disease in young children with repeated hospitalization. Saudi J Anaesth. 2014 Oct;8(4):504-9. doi: https://doi.org/10.4103/1658-354X.140867. PMID: 25422609; PMCID: PMC4236938.
17. Hurtig AL, Park KB. Adjustment and coping in adolescents with sickle cell disease. Ann N Y Acad Sci. 1989;565:172-82. doi: https://doi.org/10.1111/j.1749-6632.1989.tb24164.x. PMID: 2774423.
18. Hariman LM, Griffith ER, Hurtig AL, Keehn MT. Functional outcomes of children with sickle-cell disease affected by stroke. Arch Phys Med Rehabil. 1991 Jun;72(7):498-502. PMID: 2059123.
19. Daniel LC, Grant M, Kothare SV, Dampier C, Barakat LP. Sleep patterns in pediatric sickle cell disease. Pediatr Blood Cancer. 2010 Sep;55(3):501-7. doi: https://doi.org/10.1002/pbc.22564. PMID: 20658622.

**CORRESPONDENCE TO**

Francisca Bastos Maia
Department of Child and Adolescent Psychiatry
Centro Materno-Infantil do Norte
Unidade de Local de Saúde de Santo António
Largo da Maternidade de Júlio Dinis, 45
4050-651 Porto
Email: franciscabbmaia@gmail.com

Received for publication: 14.08.2024
Accepted in revised form: 25.06.2025