Prevalence of sickle cell disease in adults with delayed diagnosis

Prevalência da doença falciforme em adultos com diagnóstico tardio

Prevalencia de la anemia falciforme en adultos con diagnóstico tardío

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Descritores
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Descriptores
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Abstract
Objective: To estimate the prevalence of sickle cell disease in adults with delayed diagnosis, receiving treatment at hematology outpatient clinics in the health network of the state of Mato Grosso do Sul, between 2013 and 2017; to describe sociodemographic characteristics; to verify associations between genotypes in relation to current age, the genotypes, and age at diagnosis.
Methods: A retrospective, cross-sectional study with data collected at two teaching hospitals. The variables investigated were: year of treatment, genotype, sex, date of birth, age at diagnosis, and city in which they lived. Prevalence was estimated per point, using a 95% confidence interval.
Results: The prevalence was 3.9% in 103 adults with sickle cell disease: 60 female and 43 male. The HbSS genotype was predominant, followed by HbSC. The median age was 35 for HbSS, and 31 for HbSC. Median age at diagnosis was five years for HbSS, and 21 for HbSC. No association was found between age (years) of patients and genotype (chi-square test p=0.601), or between genotype and age group (chi-square test p= 0,318).
Conclusion: The most frequent genotype was HbSS, followed by HbSC. The diagnosis of patients with hemoglobin SC occurred later in life than those with the hemoglobin SS genotype. Sociodemographic variables and delayed diagnosis warns for the need to strengthen actions in the health network, which interfere significantly in the morbidity and mortality of adults with sickle cell disease.

Resumo
Objetivo: Estimar a prevalência da doença falciforme em adultos com diagnóstico tardio, em tratamento nos ambulatórios de hematologia na rede de saúde do Estado do Mato Grosso do Sul de 2013 a 2017; descrever as características sociodemográficas; verificar associações entre os genótipos em relação a idade atual, os genótipos e a idade ao diagnóstico.
Métodos: Estudo transversal, retrospectivo, com dados coletados em dois hospitais de ensino. As variáveis investigadas foram: ano do atendimento, genótipo, sexo, data de nascimento, idade ao diagnóstico, naturalidade e procedência. A prevalência foi estimada por ponto (%) e intervalo de confiança de 95%.
Resultados: A prevalência foi 3,9%, com 103 adultos com doença falciforme, sendo 60 do sexo feminino e 43 do masculino. Predominou o genótipo HbSS, seguido pelo HbSC. A mediana de idade foi de 35 para os HbSS e 31 para os HbSC. A mediana de idade ao diagnóstico foi cinco anos para os HbSS e 21 para HbSC. Não houve associação entre idade (anos) dos pacientes e genótipo (teste Qui-quadrado p=0,601) e nem entre genótipo e faixa etária (teste Qui-quadrado p= 0,318).
Conclusão: O genótipo mais frequente foi o HbSS, seguido pelo HbSC. O diagnóstico dos pacientes com SC foi mais tardio do que naqueles com genótipo SS. As variáveis sociodemográficas e o diagnóstico tardio alertam para a necessidade de fortalecimento de ações na rede de saúde, que interferem sensivelmente na morbimortalidade de adultos com Doença Falciforme.

Resumen
Objetivo: Estimar la prevalencia de la anemia falciforme en adultos con diagnóstico tardío, en tratamiento ambulatorio de hematología de la red de salud del estado de Mato Grosso do Sul de 2013 a 2017; describir las características sociodemográficas; verificar asociaciones entre los genotipos con relación a la edad actual, los genotipos y la edad de diagnóstico.
Métodos: Estudio transversal, retrospectivo, con datos recopilados en dos hospitales universitarios. Las variables investigadas fueron: año de atención, genotipo, sexo, fecha de nacimiento, edad de diagnóstico, naturalidad y procedencia. La prevalencia fue estimada por punto (%) e intervalo de confianza de 95%.
Resultados: La prevalencia fue 3,9%, con 103 adultos con anemia falciforme, 60 de sexo femenino y 43 masculino. Predominó el genotipo HbSS, seguido de HbSC. La mediana de edad fue 35 años en los HbSS y 31 en los HbSC. La mediana de edad de diagnóstico fue 5 años en los HbSS y 21 en los HbSC. No hubo relación entre edad (años) de los pacientes y genotipo (prueba ^{2} de Pearson p=0,601) y tampoco entre genotipo y grupo de edad (prueba ^{2} de Pearson p=0,318).
Conclusión: El genotipo más frecuente fue el HbSS, seguido del HbSC. El diagnóstico de los pacientes con SC fue más tardío que el de los de genotipo SS: Las variables sociodemográficas y el diagnóstico tardío advierten sobre la necesidad de fortalecer acciones en la red de salud, que interfieren sensiblemente en la morbimortalidad de adultos con anemia falciforme.

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Introduction

Mutations in the hemoglobin (Hb) gene are often encountered, and migrations of populations have contributed to their presence in most countries. According to the Globin Gene Server, 1,327 hemoglobin variants were described, distributed across several racial and/or ethnic groups, most without any clinical repercussions. However, when associated, these variants can exhibit relevant pathophysiology.[1] About 1.1% of couples worldwide possess the risk of having children with some type of hemoglobin disorder, and 2.7 of every 1000 conceptions are affected.[2]

Sickle cell disease (SCD) consists of the most common genetic disorder in the population; it leads to a multisystemic disorder caused by a single genetic mutation, and is characterized by the presence of hemoglobin S (HbS). When the oxygen tension is decreased, HbS undergoes the polymerization process, changing the morphology of the erythrocyte, which assumes a sickle shape. This phenomenon results in important events in the pathophysiology of the disease, such as vessel occlusion and hemolysis. Sickle cell disease can present as a homozygous form, with severe manifestation of the disease (HbSS - sickle cell anemia), in association with other hemoglobin: HbSC, HbSD, HbSE and Sβ-thalassemia ($S\beta^+$ and $S\beta^0$); it can also present in the heterozygous form (HbAS - sickle cell trait), where there is no clinical manifestation.[3,4]

International, non-voluntary migration derived from the slave trade introduced the HbS gene into the Americas between the 16th and 18th centuries, and promoted the distribution of SCD far beyond its origins in Africa.[4] The prevalence of HbAS in Brazil is higher in the north and northeast, between 6% and 10%, while in the south and southeast, it represents 2% and 3% of the population, respectively.[4,5]

The overall number of people with SCD will increase as a consequence of improved survival in low- and middle- income countries, as well as population migration to higher income countries.[2] The diversity and heterogeneous distribution of Hb has become a challenge to the health network, which needs to develop strategies based on the local characteristics. Thus, genetic epidemiological data can be interpreted as indicators for organization of the care network, which includes screening, adequate care, and genetic counseling.[6].

Early diagnosis of SCD should occur during neonatal screening, which includes a tracking methodology in the 0-28 day old population, and is responsible for timely selection of children for appropriate therapy, in order to avoid sequelae and death.[7].

The mortality in sickle-cell anemia has significant decreased in children in the last decades, while the mortality rate for adults has gradually increased.[8,9] According to a study performed in the National Center for Health Statistics, between 1979 and 2005, there were 16,654 deaths related to SCD. The mortality rate in individuals over 19 years of age increased by 1% ($p < 0.001$) each year, with a mean age at death of 33.4 years for men, and 36.9 years for women.[8] Even in the hydroxyurea era, early adult mortality remains high.[10] This phenomenon, still unexplained, has been widely researched worldwide.

The Mato Grosso do Sul (MS) state health network has been involved in the development of the HbS care program since the inclusion of hemoglobinopathies in the National Neonatal Screening Program (PNTN), in 2001. After reformulation of the program in 2012, the access was expanded and diagnosis extended to all 79 municipalities in the state, consolidating neonatal screening as a public policy in the southern portions of the central western region of Brazil.[11]

A cohort study conducted in MS, with 63 patients (5 to 63 years) monitored for 30 years (from 1980 to 2010) showed that they did not obtain neonatal screening.[12] Thus, the existence of adults with delayed SCD diagnosis, who received care from the health network, and who were born before the implementation of the PNTN, or from cities with low coverage in the initial years of that program, has been questioned. These are patients who were not treated early and did not receive genetic counseling; receive preventive efforts for infectious complications, appropriate immunizations, or safe transfusions.

This research is based on the need of having a specialized multidisciplinary referral service for adults with SCD in the health care network in Mato Grosso do Sul; and also, the lack of data on prevalence of SCD in adults; absence of sociodemographic, clinical, and laboratory data in available institutional databases; the increase in the life expectancy of this population; the lack of patient monitoring in the transition from pediatric care to the adult general hematology outpatient clinic; and increased population migration.

The objective of this study is to estimate the prevalence of sickle cell disease in adults with delayed diagnosis, in treatment at hematology outpatient clinics in the health network of the state of Mato Grosso do Sul, between 2013 and 2017; to describe the sociodemographic characteristics of this population; to verify associations between genotypes in relation to current age, the genotypes, and the age at diagnosis.

Methods

This was a cross-sectional, retrospective study conducted in the databases of the Medical and Statistical Archive Service (SAME) of the Maria Aparecida Pedrossian (HUMAP) teaching hospitals of the Federal University of Mato Grosso do Sul (UFMS), and the Regional Hospital of Mato Grosso do Sul (HRMS). The research was conducted between December of 2017 and July of 2018, after approval from the Ethics and Research Committee with Human Beings of UFMS, under opinion 2,407,766 / 2017.

The research was performed with data collected from the clinical records of the adult patients in treatment in the General Hematology Outpatient Clinics of HUMAP and the HRMS, between the years of 2013 and 2017. The sample included the clinical records of adults (age >18 years), diagnosed with SCD according to the International Code of Disease (ICD 10): D57.0 - Sickle-cell anemia with crisis; D57.1 Sickle cell anemia without crisis; and D57.2 - Double heterozygous sickling disorders, confirmed by Hb electrophoresis documented in the clinical records.

Data collection occurred with two researchers reviewing the registries independently, to ensure accuracy. The patient tracking process was completed using the SAME database in both hospitals, with identification of adults receiving care from the hematology outpatient clinics of each institution, during the period of 2013 - 2017, regardless of the number of visits performed in the period. The data were organized according to the main ICD code provided for the registered hematological monitoring. Listings of the two institutions were cross-checked to identify duplications, with each patient included only once each year. The electronic database search identified 147 clinical records matching the inclusion criteria.

In the second step, physical analysis of each medical record was performed, excluding data from the clinical records for the following reasons: patients with other hemolytic hemoglobinopathies who, during the investigation, received a temporary SCD diagnosis (n=25); those diagnosed with other thalassemias, but who were registered in some assessment as SCD (n=10); those with sickle cell trait (n=3); and those with incomplete data records (n=6).

The variables collected from the medical records were: year of care, genotype, sex, date of birth, age at data collection, age at diagnosis, and city in which they lived (origin).

In order to minimize exclusions due to lack of data in the clinical records, the incomplete sociodemographic variables, such as age at the diagnosis time and origin, were recovered from the SAME database of the Santa Casa de Campo Grande Hospital (SCCG), as this institution provides care for patients in emergency situations, and has a blood transfusion agency. The Hb electrophoresis tests not located in the SAME database of the hospitals were obtained from the databases of the state department of pharmaceutical assistance (CEAF) of the Department of Health of Mato Grosso do Sul (MS), in the Hemorrede (hematology network) of MS state (HEMOSUL), or the Institute of Research, Education and Diagnosis of the Association of Parents and Friends of the Exceptional (IPED/APAE). All the institutions involved are accredited

by the Unified Health System (SUS) and are part of the MS health care network.

The data were collected and organized in a spreadsheet by institution, year of service, and ICD code. For statistical analysis, prevalence was estimated per point, and a confidence interval (CI) of 95% was adopted, using the adjusted Wald method, with the Z distribution.[13] In order to calculate prevalence, all adults receiving care in the HUMAP and HRMS services between 2013 - 2017 were included.

As the samples did not pass the Shapiro-Wilk test, the comparison between the genotypes in relation to the patients' current age and the age at diagnosis was performed using the non-parametric Mann-Whitney test. The evaluation of the association between the genotype of the disease and the age groups and diagnosis was performed using the chi-square test. The statistical analysis was performed in the SigmaPlot program, version 12.5, considering a level of significance of 5%.

Results

The estimated prevalence per point, and 95% confidence interval (CI), of adults with SCD treated at hematology outpatient clinics in the city of Campo Grande, MS, was 3.9 (3.1808-4.6495), in the period of 2013 - 2017 (Table 1). Among the total accumulated 2,676 adults seen in these five years, 103 had the hemoglobinopathy S diagnosis confirmed.

Table 1. Prevalence of sickle cell disease, estimated per point, and 95% confidence interval in adults from the hematology outpatient clinics (n = 103)

Year	No. Adults Receiving Care	No. Adults with SCD	Prevalence *	CI**
2013	586	19	3.5469	2.0542-5.0395
2014	755	32	4.4701	2.9998-5.9404
2015	1.113	52	4.8280	3.5708-6.0852
2016	1.036	41	4.1276	2.9185-5.3367
2017	1.228	50	4.2149	3.0928-5.3370
Total	2.676***	103***	3.9152	3.1808-4.6495

* Estimative of prevalence per point; ** Estimate of prevalence by SCD - 95% confidence interval; *** Total number of adults accumulated in the period

Among the adults with SCD, 69.9% (72) had SS; 27.2% (28) had SC; and 2.9% (3) had Sβ Thalassemia; 60 were female and 43 were male; 85.4% (88) were in the age range of 18-49, and 14.6% (15) were 50 years or older (Table 2).

Table 2. Adults with sickle cell disease receiving care from the hematology outpatient clinic (n = 103)

Variables	n(%)
Genotype	
SS	72(69.9)
SC	28(27.2)
Sβ Thalassemia	3(2.9)
Sex	
Female	60(58.3)
Male	43(41.7)
Age group	
18 – 49	88(85.4)
50 or older	15(14.6)
Age at diagnosis	
< 1 year	15(14.6)
≥ 1 - 5 years	40(38.8)
≥ 6 - 10 years	15(14.6)
≥ 11 years	33(32.0)
Place of birth	
Campo Grande (capital)	45(43.7)
Interior	37(35.9)
Other states	21(20.4)
Origin	
Campo Grande (capital)	67(65.1)
Interior	34(33.0)
Other states	2(1.9)

The median age was 35 (18 to 70) years for the HbSS genotype (72); 31(18-82) years for HbSC (28); and 25 (18 - 30) years for Sβ Thalassemia. The median age at diagnosis was five (0-38) years in the HbSS patients; 21 (1 - 82) years in the HbSC; and four (0 - 14) years in S Beta Thalassemia. There was no association between patient's age (years) and genotype (chi-square test p=0.601). The age group of 18 - 49 years was selected in the present study based on a previous survey, conducted with 32 patients with SCD, monitored between the years of 1980 – 2010, in the state of Mato Grosso do Sul, with a mean age of 25.65 ± 11.92 years.

As for the place of birth of the participants, 43.7% (45) were born in Campo Grande; 35.9% (37) were from the interior of the state; and 20.4% (21) came to MS as children from other states in Brazil. Regarding the city in which they lived (origin), patients from 18 MS municipalities were identified, with Campo Grande, the state capital, represented by 65% (67) of these people; 33% (34) were from interior of the state; and two patients were from other states (Table 2).

Patients with Sβ Thalassemia ($S\beta^+$ and $S\beta^0$) could not be differentiated, and were ignored for the analysis of the associations between the genotypes.

No association between genotype and age group (chi-square test p=0.318) was identified. In the binomial test, however, the percentage of patients in the age group, 18 - 49 years, (Table 3) is significantly higher than the one related to the group age >50 years, both in the SS genotype (binomial test p<0.001) and in the SC genotype (p<0.004).

Table 3. Relationship between genotype, age, and age range of adults with sickle cell disease treated at a hematology outpatient clinic (n = 100)

Age (years)	Genotype		p-value
	SS (n=72)	SC (n=28)	
	35 (18 - 70)	31 (18 - 82)	0.601
Age group			
18 - 49	87.5 (63)	78.6 (22)	0.417
>50	12.5 (9)	21.4 (6)	

The results are presented using medians (minimum to maximum) or relative frequencies (absolute frequency) for age group; p-value from the Mann-Whitney test (age), or from the chi-square test (age groups)

The age at diagnosis of patients with the SC genotype was significantly higher than among patients with the SS genotype (Mann-Whitney test, p<0.001). An association was found between age group at diagnosis and disease genotype (Chi-square test, p<0.001), and the percentage of patients diagnosed in less than one year was higher in SS patients than in SC patients. The percentage of patients who were diagnosed when they were older than 11 years of age was higher in SC than in SS. In the post-test between the age groups, the chi-square test with the Bonferroni correction was used (Table 4).

Table 4. Relationship between genotype, age, and age group with the diagnosis of adults with sickle cell disease treated at a hematology outpatient clinic (n = 100)

Age group at diagnosis	Genotype		p-value
	SS (n=72)	SC (n=28)	
	5 (0 - 38)b	21 (1 - 82)a	<0.001
< 1 year	19.4 (14)a	0 (0)b	
≥ 1 - 5 years	40.3 (29)a	35.7(10)a	<0.001
≥ 6 - 10 years	19.4 (14)a	3.6 (1)a	
≥ 11 years	20.8 (15)b	60.7 (17)a	

The results are presented using medians (minimum to maximum) or in relative frequencies (absolute frequency) for age group; p-value using the Mann-Whitney (age) or chi-square (age groups) test. Different letters in the lines indicate significant difference between genotypes (Mann-Whitney test or Chi-square test, p<0.05)

No significant association was found between the genotype and the place of birth of the patients (Q-square test p=0.183), nor with origin.

Discussion

Population-based surveillance data can be used to describe the patterns of use of health services by these patients.[11,14] In MS, the estimated prevalence of adults with delayed diagnosis of SCD treated at outpatient hematology clinics in the health care network was 3.9% between 2013 - 2017. Because it is unpublished data, this prevalence will be the starting point for monitoring of adults with SCD in the coming years, and will accompany the transition from pediatric care to the adult outpatient clinic, considering that children screened in the early years of the PNTN in MS will turn 18 in 2019.

Observational studies developed by the research group, "Nucleus of Interdisciplinary Study of Sickle Cell Disease - NEIDF" verified the prevalence of hemoglobin S, and the PNTN coverage index in MS, beginning in 2000.[11,12,15,16] In the study that evaluated the implementation of PNTN in MS (2001-2015), 543,690 samples were screened of 612,909 live births in the state. The most frequent genotype was HbSS, with 67 cases (69.9%), with a prevalence of 0.0127%; this was followed by 23 cases of HbSC, with a prevalence of 0.0046%. Heterozygotes (HbAS) totaled 9,200 children, with a prevalence of 1.6925.[14]

The most frequent genotype in this study was HbSS, verified in 72 cases (69.9%), followed by HbSC in 28 (27.2%), and 3 (2.95%) of Sβ Thalassemia. These results corroborate the numbers of adults with sickle cell disease receiving follow-up care at referral services; considering the population density and distribution of the genotypes, and are in agreement with the worldwide occurrence of the S gene. In a sample of 542 patients receiving care in North Carolina, USA, 427 (78.8%) had HbSS; 70 (12.9%), HbSC; 23 (4.2%), $S\beta^+$; and 22 (4.1%), $S\beta^0$. [17-20] In Chicago, USA, HbSS corresponded to 102 (77%) patients, followed by 15 cases (11.45%) HbSC, and 15 (11.45) with other variants.[15] At King's College Hospital, London, UK, 712 patients were observed for 10 years (2004-2013); there were 444 (62%) with HbSS; 229 (32%) with HbSC; 33 (5%) with $HbS\beta^+$; and 6 (1%) with $HbS\beta^0$.[19]

In an investigation to characterize the haplotypes of the betaglobin S gene in MS, it was identified that 26 (55.3%) of the blood samples represented females, and 21 (44.7%) were from males.[20] One study with 78 participants, in southern Saudi Arabia, identified a larger proportion of women (64.1%) with SCD.[21] In another observational study conducted in the state of Wisconsin, the number of women receiving care in the outpatient clinic was 64 (65%).[22] Also in the United States, in another study conducted by the University of Illinois, 86 (65%) were women.[18] The reason why adult women with sickle-cell anemia live longer than men is unknown.[12] Relatively lower blood viscosity in women, due to low levels of Hb and hematocrit, may be one of the possible causes.[9]

The median age of participants in the present study was 35 (18-70) for those with HbSS, and 31 (18-82) for HbSC patients; there was no association between age and genotype. These results are similar to those found in a study of 132 African-American individuals, whose participants ranged in age from 15 - 70 years, with a mean age of 34.2 years.[18] In another study, in the USA, with 542 adults (18 - 84 years), the mean age was 32 years.[17] In the United Kingdom, a higher average was observed; 32 years in cases of HbSS; and 39 years for HbSC. [19] Other studies, however, present a lower average age. A study of 200 participants with HbSS (1 - 49 years old) attending the hematology clinics of Lagos University Hospital, Nigeria, revealed that the mean age was 18.8 ± 14.39 years; in another, developed in southern Saudi Arabia, with a group of 78 receiving care at a referral hospital, the mean was 26.4 ± 9.2 years.[21]

The advent of neonatal screening, antibiotic prophylaxis, better vaccines, safer blood transfusion, iron chelation, and hydroxyurea therapy have improved the survival of patients with SCD.[17,23-27] The life expectancy of children has increased, and SCD changed from a childhood disease to become a chronic disease. [14,16,24,26] However, for adult patients, mortality remains high.

The concentration of adults, in the age range between 18 - 49 years, in this study is significantly higher than that referring to those of an age > 50 years. However, even with more optimistic data, as observed in the retrospective cohort study conducted in Rio de Janeiro (n = 1676), between January of 1998 and December of 2012, with HbSS and $S\beta^0$ patients, the median survival age for men was 53.3 years and, for women, 56.5 years; and the remaining life expectancy of patients with sickle cell anemia was lower than that of Brazilians in general. [20] This phenomenon was also demonstrated in the cohort study (n = 161), including SS genotypes; SC; $S\beta^0$; $S\beta^+$ and SD, performed at the University of North Carolina, between August of 2004 and December of 2014, where the median age of survival was 50.2 years.[10]

Regarding the age at diagnosis of SCD of the patients treated in this study, the median of 5 (0-38) years in cases of HbSS, and 21 (1-82) in cases of HbSC was identified. This median characterizes a delayed diagnosis for these patients due to the pathophysiology of the disease, which involves a complex combination of vasoocclusion, hemolysis, endothelial dysfunction, and inflammation.[23] Thus, it is necessary to reflect upon what represents the early SCD diagnosis for the patient, regarding coping with the complications and the suffering that could have been mitigated or avoided.

Early diagnosis in SCD contributes to the initiation of care in the first weeks of life, through immunization, prophylaxis with penicillin, and guidelines for the early recognition of splenic sequestration by mothers and caregivers. Up to the fifth year of life, the period of the highest rates of serious complications and death, "prophylactic treatment is basically the essence of therapy". [7, 24]

However, regular treatment, adherence to treatment, family support, and lifestyle are important for reducing morbidity and mortality.[9] In the state of MS, human and technological resources are concentrated in the municipalities of Campo Grande and Dourados, revealing a low resolution for the treatment of hemoglobinopathies in health microregions. The access to the hematologist in the public network depends on the agreement of the municipality of origin of the patient with the capital, ordered by a state central of regulation, which can generate a repressed demand for consultation. In addition, the territorial dimension

of MS (357,125 km²) is a difficulty factor, since there are municipalities that are 420 km from the hematology outpatient clinic. The distance to the centers of reference constitutes a barrier to the implementation of a comprehensive program of care for patients with SCD.[28,29] People in rural areas, who travel relatively long distances in search of health care, and those who travel for a longer period of time had less access to consultations and treatment, which demonstrates the difficulty faced by rural dwellers and those living in poverty.[28,29] These aspects should be considered relevant when considering the historical aspects, and the economic and social distribution of the S gene in the Brazilian population.[4]

The limitations of this study are related to the unavailability of complete data in ambulatory care services. A comprehensive manual search was required at various points in the health care network, compiling and cross-checking data to minimize bias. Even so, these data are extremely relevant as a source of information, with a view to improving health care services for people with SCD.

Conclusion

The estimated prevalence of adults with SCD treated at hematology outpatient clinics in the state of Mato Grosso do Sul was 3.9% from 2013 to 2017. Of the 103 adults with SCD, 60 were female and 43 were male. Median age was 35 years for those with HbSS and 31 for those with HbSC. The most frequent genotype was HbSS, followed by HbSC. The median age at diagnosis of the adults receiving care for HbSS was five years, and for HbSC, 21 years. The diagnosis of patients with SC was later than those of the SS genotype. These sociodemographic variables, and the delayed diagnosis of SCD, identified in this study, point to the need to strengthen the actions of the health network that significantly interfere in the morbidity, early mortality, and quality of life of people with SCD. The results of this study are expected to be a starting point for the creation of an up-to-date database in Mato Grosso do Sul, which serves as a guideline for managers in establishing mechanisms to regulate access to the health network, especially in the transition of pediatric/adolescent outpatient care to that of the adult. This also contributes to the creation of a specialized multidisciplinary reference service for adults with SCD in the health care network in this state. Future longitudinal, epidemiological studies with adolescents and children screened by the PNTN may reveal another SCD scenario in MS in the coming years.

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Collaborations

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