Biol Blood Marrow Transplant 25 (2019) 2103–2109

Biology of Blood and Marrow Transplantation

journal homepage: www.bbmt.org

Identification and Characterization of Hematopoietic Stem Cell Transplant Candidates in a Sickle Cell Disease Cohort

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Article history:
Received 17 March 2019
Accepted 14 June 2019

Key Words:
Sickle cell disease
Hematopoietic stem cell transplantation
Bone marrow transplantation
Candidates for HSCT

A B S T R A C T

Sickle cell disease (SCD) is associated with significant morbidity, and allogeneic hematopoietic stem cell transplantation (HSCT) remains the primary curative treatment. Recently, the Brazilian Ministry of Health released a regulation that required the publically funded healthcare system to pay for HSCT for SCD patients with defined indications. We used an existing 2794-member SCD cohort established during 2013 to 2015 to characterize candidates for HSCT and estimate the number of possible donors. Of 2064 patients with SC anemia (SCA), 152 of 974 children (16%) and 279 of 1090 adults (26%) had at least 1 HSCT indication. The most common indication for transplant was stroke (n = 239) followed by avascular necrosis (n = 96), priapism (n = 82), cerebrovascular disease (n = 55), >2 vaso-occlusive episodes (n = 38), alloantibodies and chronic transfusion therapy (n = 18), and >2 acute chest syndrome episodes (n = 11). Increasing age, number of transfusions, abnormal transcranial Doppler, retinopathy, dactylitis, and use of hydroxyurea were more frequent in the 152 children with an indication for HSCT compared with 822 without ($P < .001$). Of 152 children and 279 adults meeting the eligibility definition, 77 (50%) and 204 (73%), respectively, had at least 1 non-SCD full sibling who could potentially serve as a donor. In conclusion, in a large cohort of SCA patients, 16% of children and 26% of adults had at least 1 indication for HSCT; these indications were associated with the severity of the disease. This study provides clinical data necessary for estimating the costs and infrastructure that would be required to implement HSCT in a public healthcare system.

INTRODUCTION

Sickle cell disease (SCD) has a high prevalence in many developing countries, representing a public health problem. In Brazil it is estimated that 3500 affected children are born annually, and there are 35,000 to 50,000 people living with SCD [1]. Many advances have been made in recent decades to decrease mortality and improve quality of life in SCD, including improvements in medical care and SCD education,

Financial disclosure: See Acknowledgments on page 2109.

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https://doi.org/10.1016/j.bbmt.2019.06.013
1083-8791/

vaccines, antibiotic prophylaxis, hydroxyurea, and transfusions. However, hematopoietic stem cell transplantation (HSCT) remains the primary curative treatment.

More than 1200 transplants for SCD have been performed worldwide, primarily in the United States and Europe, with favorable results overall [2]. Limitations to HSCT include availability of an HLA-matched sibling donor, identification of the ideal conditioning regimen, prevention of chronic graft-versus-host disease, reduction of transplant-related mortality, and selection of appropriate candidates for HSCT. Despite encouraging results, most countries where the prevalence of SCD is high may not consider HSCT as a viable treatment because of cost and lack of infrastructure to conduct this complex clinical procedure. In Brazil few centers have performed transplants for SCD and the treating institutions supported all costs, making widespread adoption infeasible [3].

In December 2015 the Brazilian Ministry of Health (MoH) published a regulation that promulgates HSCT for SCD through the public healthcare system (Sistema Único de Saúde) and established that the public health care system will cover the

Table 1
Sociodemographic Characteristics of Patients in the REDS III SCD Cohort in Brazil

	Children <16 yr	Adults ≥ 16 yr	Total
	(n = 1370)	(n = 1424)	(n = 2794)
Hemocenter			
HBH	361 (26.4)	421 (29.6)	782
JFO	138 (10.1)	136 (9.5)	274
MOC	187 (13.7)	176 (12.4)	363
HEMORIO	365(26.4)	355 (24.9)	720
HEMOPE	233 (17)	317 (22.3)	550
HCFMUSP	86 (6.3)	19 (1.3)	105
SCD type			
SCA (SS/SB0/SD/SQuebec-Chori)	974*	1090	2064
SS	933* (68.2)	1041 (73.1)	1976
SB0	40 (2.9)	43 (3)	83
Other	1 (.1)	6 (.5)	7
SB+/SC/SHPFH/SKWoolwich	394	334	728
SB+	40 (2.9)	40 (2.9)	80
SC	351 (25.6)	293 (20.6)	644
Other	3 (.3)	1 (.1)	4
Average age, yr (range)	9 (0-15)	27 (16-77)	2795
Gender			
Male	701 (51.2)	613 (43)	1314
Female	669 (48.8)	811 (57)	1480
Race			
White	185 (13.5)	114 (8)	299
Black	277 (20.2)	471 (33.1)	748
Mixed	855 (62.4)	782 (55)	1637
Other	53 (3.9)	57 (4)	110
Monthly income			
<700 Reais† (USD <300)	277 (20)	219 (15)	496
701-1400 Reais (USD 301-602)	32 (2)	85 (6)	117
1401-3000 Reais (USD 603-1290)	215 (15)	314 (22)	529
≥3000 Reais (USD >1290)	822 (60)	738 (52)	1560
Education (≥6 years old)			
Never attended	11 (1.1)	10 (0.7)	21
Elementary school complete	998 (95.1)	535 (37.7)	1533
High school complete	41 (3.9)	651 (45.8)	692
Adult education Technical course	0	84 (5.9)	84
College/postgraduate	0	141 (9.9)	141
Marital status (≥18 years old)			
Single	N/A	698 (56)	698
Living together	N/A	171 (14)	171
Married	N/A	294 (24)	294
Separated/divorced	N/A	52 (4)	52
Widower	N/A	14 (1)	14

Values are n (%) unless otherwise defined. HBH indicates Hemocenter of Belo Horizonte; JFO, Hemocenter of Juiz de Fora; MOC, Hemocenter of Montes Claros; HEMORIO, Hemocenter of Rio de Janeiro; HEMOPE, Hemocenter of Pernambuco; HCFMUSP, Hospital das Clínicas- Faculdade de Medicina da USP, Instituto da Criança; N/A, not applicable.

* Two SS patients transplanted before enrollment were excluded from this analysis.

** Exchange conversion in 2014 related to BRL and USD: 1 BRL (Reais) = .43 USD.

cost of HSCT for SCD children with defined indications [4]. In February 2018 the MoH updated the regulation, expanding those covered to people over age 16 years [5]. Various American and European groups have also established guidelines for allotransplants in SCD that differ slightly from each other [6–11] and from the Brazilian regulation. The number of patients who would be eligible as candidates for HSCT according to the MoH recommendation and therefore the infrastructure required to implement this procedure are unknown.

The Recipient Epidemiology and Donor Evaluation Study-III (REDS-III) Brazil SCD cohort is a large multicenter cohort established to characterize health outcomes in the Brazilian SCD population [12,13]. We aimed to identify the number of patients within the REDS-III SCD cohort eligible for HSCT according to MoH recommendations, estimate the proportion of candidates who have a full sibling to potentially serve as an HSCT donor, and compare the demographic, clinical, and laboratory characteristics of patients with and without an HSCT indication.

METHODS

The REDS-III SCD cohort was established to investigate outcomes in a sample of SCD patients in Brazil. The baseline clinical and demographic profile of the cohort has been described elsewhere [13]. Briefly, patients were randomly selected as eligible from lists of active patients (clinical encounter in the last 3 years) at hematology centers that include sickle cell treatment (called hemocenters) in 6 cities in Brazil (Belo Horizonte, Juiz de Fora, Montes Claros, Sao Paulo, Rio de Janeiro, and Recife). The cohort was enrolled from 2013 to 2015.

We defined patients < 16 years old as children and those ≥ 16 years old as adults for this analysis. This age threshold was chosen because the original MoH guidelines restricted HSCT eligibility to ages 16 or less because previous studies have used this age limit to define eligibility for HSCT [14] because of the superior results of HSCT in younger patients [5].

A cross-sectional analysis of enrollment data was conducted to identify the number of HSCT candidates according to the MoH criteria [5]. These criteria specify only patients with sickle cell anemia (SCA; defined as homozygous SS or Sβ0 by the MoH) with an HLA-matched sibling are eligible. We included 6 patients with SD and 1 patient with SQuebec-CHORI in the SCA group in this analysis considering the similarly severe clinical phenotype of these genotypes [15–19]. The clinical indications for HSCT defined by the MoH include presence of at least 1 of the following: stroke, cerebrovascular disease, >2 antibodies while on chronic transfusion therapy (CTT), or ≥1 of the following despite treatment with hydroxyurea: >2 vaso-occlusive episodes (VOE) or acute chest syndrome (ACS) episodes in the last year, more than 1 episode of priapism, and avascular necrosis (AVN) of more than 1 joint. We included all patients with a history of priapism or AVN as potentially eligible for HSCT to estimate the maximum number of patients who might qualify. In a sensitivity analysis we estimated the possible range of eligible patients if none or all patients with a history of multiple episodes of priapism or more than 1 joint affected were considered eligible for HSCT. The demographic, clinical, and laboratory profile of patients with at least 1 indication for HSCT were compared with patients with no indication for HSCT.

On enrollment into the cohort, the number of siblings, full siblings, and siblings with SCD was recorded for each participant. For this analysis, siblings with a diagnosis of SCD were excluded from the number of full siblings to define the potential number of HSCT donors for candidates.

Characteristics between patients with or without an indication for HSCT were compared using the chi-square test for categorical variables and the *t*-test or Wilcoxon rank sum test, as appropriate, for continuous variables. A $P \leq .05$ was considered significant. The REDS-III SCD cohort study was approved by national and local Brazilian ethics committees and the institutional review boards at the University of California San Francisco and Research Triangle Institute, International (which is the data coordinating center for REDS-III).

RESULTS

There were 2794 patients enrolled into the REDS-III SCD cohort (demographic profile of the cohort is summarized in Table 1). Of 2064 patients with SCA, 974 were children (<16 years) and 1090 were adults (≥ 16 years).

The number of children eligible for HSCT was 152, 16% of the total of SCA children (Table 2). The most common indication for transplant in these children was stroke. Of 152 potential candidates aged < 16 years, 111 had only 1 indication and 41 had 2 or more indications (Table 3). The number of adults with an indication making them eligible for HSCT was 279 (26% of 1090 SCA adults) (Table 2). The most common indication for transplant in adults was also stroke. Of 279 candidates aged ≥ 16 years, 222 of had only 1 indication and 57 had 2 or more indications (Table 3). Many indications of the MoH are criteria only if occurred despite hydroxyurea treatment, and 39% of our SCA patients were treated with hydroxyurea.

We compared the characteristics of children having at least 1 indication with those with no indication (results summarized in Table 4). The chance of being a candidate for a transplant increases with increasing age. HSCT candidates were more likely to have multiple clinical complications of SCD, such as abnormal transcranial Doppler (TCD; defined by a time-averaged mean blood flow velocity in the middle cerebral artery or in the internal carotid artery ≥ 200 cm/s) [20], dactylitis, retinopathy, microalbuminuria, and a higher number of lifetime VOE and ACS. Splenic sequestration was not significantly different between those with and without an indication.

Considering current treatments, pediatric candidates for HSCT were more likely to be on chronic transfusion therapy and hydroxyurea (Table 4). As expected, the higher the number of transfusions received, a marker of SCD severity, the

Table 2
REDS-III SCA Children and Adults with Indications for HSCT according to Brazilian Ministry of Health

	Children < 16 yr	Adults ≥ 16 yr	Total
	(n = 974)	(n = 1090)	(n = 2064)
Stroke	97 (10)	142 (13)	239 (11.6)
Cerebrovascular disease*	33 (3)	22 (2)	55 (2.7)
>2 VOE/yr and HU	18 (2)	20 (2)	85 (4.1)
>2 ACS /yr and HU	8 (1)	3 (<1)	26 (1.3)
Priapism and HU, male only	20 (2)	62 (6)	82 (4)
>2 alloantibodies and chronic transfusion	7 (1)	11 (1)	38 (1.8)
AVN and HU	12 (1)	84 (8)	96 (4.7)
Total no. of patients with any indications for HSCT†	152 (16)	279 (26)	431 (21)

Values are n (%).
HU indicates hydroxyurea/hydroxycarbamide.
* Prevalence of cerebrovascular disease in the entire cohort. However, imaging to screen for cerebrovascular disease was not performed in 752 children and 839 adults; therefore, cerebrovascular disease status was unknown in 77% of cohort participants. For all other criteria, data regarding clinical outcome was missing in <2% of cohort participants.
† Patients can have more than 1 indication.

Table 3
Number of REDS-III SCA Children and Adults with 0, 1, 2, or ≥ 3 Indications according to MoH

No. of Indications for HSCT	Children < 16 yr (n = 974)	Adults ≥ 16 yr (n = 1090)
0	822 (84)	811 (74)
≥1	152 (16)	279 (26)
1	111 (11)	222 (20)
2	39 (4)	50 (5)
≥3	2 (<1)	7 (<1)

Values are n (%).

more likely the patient had an indication for transplant (Table 4). There were no significant differences between the 2 groups of children regarding vital signs and laboratory tests (hemoglobin, leucocytes, platelets, lactate dehydrogenase, creatinine), except for fetal hemoglobin, which was higher in the group without an indication for transplant ($P < .001$).

We also compared the characteristics of adults having at least 1 indication with those with no indication for transplant. Adult candidates were more likely to be male and to have complications such as retinopathy and to have higher numbers of lifetime VOE and ACS (Table 5). Similar to children, adults eligible for HSCT were more likely to have higher lifetime transfusion exposure and to be treated with chronic transfusions and hydroxyurea compared with adults who were not eligible (Table 5).

Seventy-two children who were candidates for HSCT (47% of 152) did not have full siblings. Fifty percent had 1 or more full siblings without SCD who could potentially be donors for the transplant. Only 11% had more than 2 full siblings. Three patients were excluded from this analysis because the number of siblings was unknown.

Seventy-four adults who were candidates for HSCT (26% of 296) did not have full siblings, and 204 (73% of 279) had 1 or more full siblings without SCD who could potentially be donors for the transplant. Also, 27% had more than 2 full siblings. Only 1 patient was excluded from this analysis because the number of siblings was unknown. In total, the number of children and adults with at least 1 sibling without SCD was 281, which represents 13.6% of the total SCA patients (2064) and 65% of the 431 patients with an HSCT indication. A summary of participants in the REDS-III Brazil SCD cohort and proportion of children and adults with an indication and a full sibling are illustrated in Figure 1.

DISCUSSION

The REDS-III cohort is a large and multicenter cohort of SCD patients in Brazil. We identified the proportion of patients in this cohort who would be eligible for HSCT to estimate the number of Brazilian SCD patients who might be eligible for

Table 4
Comparison of Demographic, Clinical, and Treatment Data between REDS III SCA Patients < 16 yr with 0 and ≥ 1 Indications for HSCT according to MoH

	0 HSCT Indication (n = 822)	≥ 1 HSCT Indication (n = 152)	*P*
	n (%) or Median (Range)	n(%) or Median (Range)	
Demographic Data			
Age, yr	9 (0-15)	11 (3-15)	<.001
0 < 4	103 (12)	3 (2)	<.001
4 < 8	228 (28)	30 (20)	
8 < 12	255 (31)	50 (33)	
≥12	236 (29)	69 (45)	
Gender			
Male	406 (49)	64 (42)	.1
Female	416 (50)	88 /58)	
Clinical Complications			
Abnormal TCD	197 (24)	66 (43)	<.001
Dactylitis	183 (22)	53 (35)	<.001
Retinopathy	8 (1)	2 (1)	<.001
Microalbuminuria*	16 (2)	11 (7)	<.001
Lifetime VOE	653 (2) (0-34)	129 (3) (0-30)	<.001
Lifetime ACS	566 (2) (0-20)	123 (3) (0-15)	.03
Treatment data			
Ever transfused	692 (84)	152 (100)	<.001
No. of transfusions			
0- 5	450 (55)	23 (15)	<.001
6- 10	145 (18)	16 (11)	
11- 20	100 (12)	22 (15)	
21- 40	53 (6)	20 (13)	
>40	35 (4)	69 (45)	
Unknown	39 (5)	2 (1)	
Patients under CTT	52 (6)	88 (58)	<.001
Treatment with HU	278 (34)	92 (61)	<.001

CTT indicates chronic transfusion therapy.

* Prevalence of known microalbuminuria in the entire cohort. However, only laboratory results documented in the medical record in the year before enrollment were abstracted. Urine analysis was only documented in 148 of SCA children. The prevalence of microalbuminuria restricted to SCA children with a urine analysis was 30% and 14% ($P = .03$) for children with and without an HSCT indication, respectively.

Table 5
Comparison of Demographic, Clinical, and Treatment Data between REDS III SCA Patients ≥ 16 yr with 0 and ≥ 1 Indications for HSCT according to MoH

	0 HSCT Indication (n = 811)	≥1 HSCT Indication (n = 279)	*P*
	n (%) or Median (Range)	n (%) or Median (Range)	
Demographic data			
Age, yr	27 (16-74)	25 (16-71)	.23
16-19	176 (22)	63 (23)	.24
20-29	284 (35)	112 (40)	
30-39	205 (25)	62 (22)	
40-49	100 (12)	25 (9)	
50-59	38 (5)	11 (4)	
≥60	8 (1)	6 (2)	
Gender			
Male	322 (40)	146 (52)	<.001
Female	489 (60)	133 (48)	
Clinical complications			
Dactylitis	67 (8)	28 (10)	.4
Retinopathy	53 (7)	19 (7)	<.001
Microalbuminuria*	52 (6)	20 (7)	.8
Lifetime VOE	617 (5) (0-300)	224 (6) (0-500)	.03
Lifetime ACS	466 (3) (0- 30)	176 (3) (0- 30)	<.001
Treatment data			
Ever transfused	770 (95)	277 (99)	.001
No. of transfusions			
0-5	268 (33)	29 (10)	<.001
6-10	159 (20)	28 (10)	
11-20	125 (15)	40 (14)	
21-40	92 (11)	43 (16)	
>40	85 (11)	120 (43)	
Unknown	82 (10)	19 (7)	
Patients under CTT	36 (4)	104 (37)	<.001
Treatment with HU	236 (29)	200 (72)	<.001

* Prevalence of known microalbuminuria in the entire cohort. However, only laboratory results documented in the medical record in the year before enrollment were abstracted. Urine analysis was only documented in 234 of SCA adults. The prevalence of microalbuminuria restricted to SCA adults with a urine analysis was 55% and 46% ($P = .9$) for adults with and without an HSCT indication, respectively.

HSCT transplant according to newly established regulations by the Brazilian MoH, which are similar to other international recommendations for allogeneic HSCT.

We identified 152 SCA children < 16 years old and 279 adults ≥ 16 years old who met the MoH criteria in a cohort of 2794 SCD patients (15.4% of the entire cohort and 20.8% of the SCA patients). We described the profile and compared clinical characteristics and baseline laboratory measures between the children and adults with and without an HSCT indication.

We found that SCD phenotypes such as abnormal TCD, dactylitis, retinopathy, and lifetime VOE were significantly more common in HSCT candidates < 16 years old. As age increases in the pediatric SCA population, the chance of being a candidate for transplant also increases, because some complications will appear over time. Abnormal TCD was significantly more common in the group of children with an indication. The Brazilian regulation does not consider patients with abnormal TCD eligible for HSCT. Other guidelines and experts in the field would consider this an appropriate indication [7–10], because abnormal TCD will demand a lifelong treatment with chronic transfusions, which is associated with potential adverse events such as alloimmunization, iron overload, and also high costs [20].

This analysis of the REDS-III SCD cohort reinforces inclusion of adults as potential candidates for HSCT. Twenty-six percent of the SCA adult patients (279 patients) had 1 or more indication for HSCT. The large number of patients ≥ 16 years old who received a high number of transfusions and treatment with hydroxyurea indicates that the severity of the disease in adulthood justifies aggressive treatment. Efforts to develop reliable and suitable scores for adult patients to match the disease severity to the need for HSCT should be undertaken.

The best time to perform an HSCT in a patient's life is a matter of debate, but it is generally accepted that early referral for transplant should be considered when an indication is identified to allow timely screening for an HLA-identical sibling [11,21]. Many young adults would be expected to achieve the same benefit of cure, but the current ability to predict disease progression is very limited.

Our analysis reports the number of REDS-III participants potentially eligible for HSCT; however, the exact number of candidates is confirmed by having an indication and HLA matched sibling according to the Brazilian MoH regulation. Each full sibling has a 25% chance of being an HLA-identical match. Previous publications have used birth data and statistical modeling to describe the probability of identifying an HLA matched sibling among US population cohorts divided by age and race/ethnicity assuming average family size. A range of probabilities has been reported based on data sources used and assumption of models. Mentzer et al. [14] reported the probability of finding a fully HLA matched donors among SCD patients of 18%. A more recent study in Brazil tested 1230 siblings for HLA compatibility and identified 296 compatible

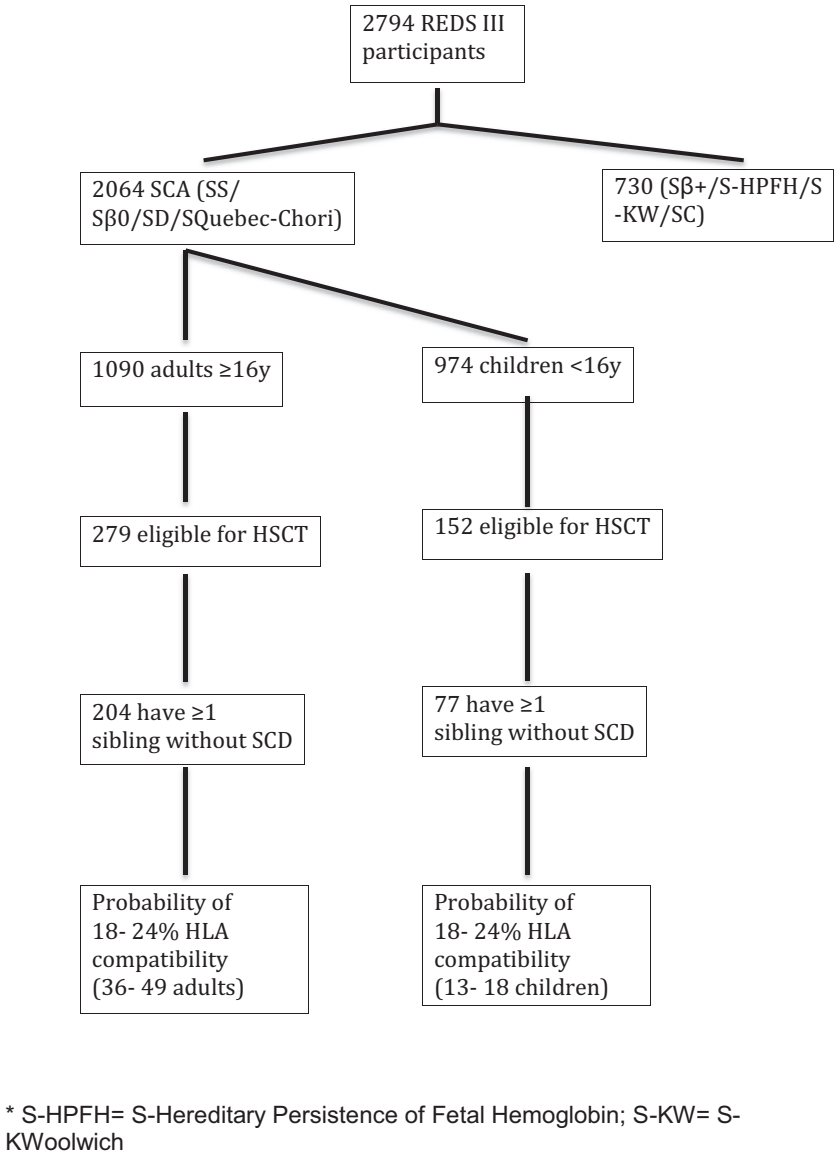

Figure 1. Flow diagram of participants in the REDS-III Brazil SCD cohort and candidates eligible for HSCT. S-HPFH indicates S-hereditary persistence of fetal hemoglobin; S-KW, S-KWoolwich.

siblings (24.1%) [22]. If a range of 18% to 24% HLA compatible siblings among HSCT eligible REDS-III patients were assumed, 49 to 67 of the 431 identified candidates would be estimated to have a suitable donor for transplant. To confirm the exact number of transplants to be performed, siblings should be tested for HLA compatibility. Unfortunately, data on HLA typing of siblings were not available for this analysis, but it is recommended that treating physicians perform HLA tests for those patients with an indication for transplant. With the recent encouraging results of haploidentical transplants [23], siblings and parents are potential donors, thus considerably increasing the possible number of transplants for SCD patients. However, haploidentical HSCT for SCD patients is still experimental, and further studies need to confirm this approach.

This study has limitations. The REDS-III Brazil SCD cohort study did not collect clinical data exactly as defined in the MoH regulation. For example, at cohort enrollment only history of any priapism or AVN was recorded in the REDS-III database without specification of number of episodes or joints with AVN affected. We considered all patients with history of AVN and priapism as eligible for HSCT for the purposes of this analysis. If none of these patients had multiple episodes/affected joints, the number of eligible HSCT candidates would decrease by 139 from 431 to 292. Many of these patients likely will have or have already had multiple episodes, and comparisons of outcomes between patients with and without an indication were not significantly different whether all of this subset of patients were included or excluded from the analysis.

Because most SCA participants (77%) did not have a screening magnetic resonance imaging or angiography to define the presence of cerebral vascular disease and only 14.8% of screened children and 8.7% of screened adults were known to have cardiovascular disease, our analysis could have underestimated the total number of HSCT candidates based on this criteria. However, at this time the infrastructure to routinely and frequently perform magnetic resonance imaging or angiography is not established at most public institutions where SCD patients are typically treated in Brazil.

One could argue that other indications for HSCT such as AVN and priapism included in our study because they are defined by the Brazilian MoH are not included in other guidelines or prospective trials for HSCT in SCD and may have overestimated the proportion of HSCT candidates according to other guidelines. Therefore, the proportion of eligible patients may change based on criteria used and number of patients who have required screening tests to define all criteria. Finally, most current eligibility criteria are based on a person having severe complications of SCD. It is likely indications may evolve over time as HSCT outcome becomes safer [6,11].

The estimated number of patients eligible for HSCT presented in this analysis is based on presence of a defined indication but does not account for the fact that some patients may not be fit for transplant because comorbidities may limit the ability of the patient to tolerate a myeloablative or reduced-intensity conditioning regimen. The MoH regulation does not define contraindications for HSCT, but we believe accurate evaluation of comorbidity scores before transplant is mandatory, particularly in adults [24,25]. Cardiopulmonary, hepatic, and renal complications should be carefully evaluated to define the benefit and risks of transplantation. Treating physicians must define these risks. Currently, some prospective trials are designed to mitigate the development of HSCT complications by using varied transplant approaches including different type of donors, conditioning regimens, and GVHD prophylaxis regimens [23].

Some patients with indications may have been missed if screening tests were not performed (eg, magnetic resonance imaging to diagnose cerebral vascular disease) or patients were not treated with hydroxyurea. Incomplete clinical assessment or treatment can delay referral to the transplant center, unfortunately allowing time for other complications to appear before the referral and potentially contraindicating the HSCT.

Another potential limitation is the degree to which the REDS-III Brazil SCD cohort is representative of the entire population of SCD patients in Brazil. We have not directly compared the distribution of sickle cell genotypes in REDS-III with the distribution reported in different states in Brazil. Even so, the effort to generate a representative sample from hemocenters in 6 different cities and the inclusion of specific clinical indication data make these numbers more representative for Brazil than any other currently available data source.

In conclusion, this study provides important, real-world data regarding how indications for HSCT regulations in Brazil might impact SCD patients. We have estimated that 16% of SCA children and 26% of SCA adults are potential candidates for HSCT. These percentages can be used to plan for the number of patients in Brazil who could qualify for HSCT, and this analysis provides critical data that can be used to estimate financial cost and infrastructure that would be required to implement HSCT as a curative treatment option. In addition, our estimates could be applied in other countries with a high prevalence of SCD who lack access to similar cohort data. Despite publication of the first MoH regulation nearly 3 years ago, systematic screening for eligibility criteria and HLA testing of siblings is not routinely performed in all centers. Our data suggest almost one-fourth of the SCA population has clinical indications for HSCT; therefore, Brazil should expand the capacity to make a cure of the disease possible for those with suitable donors.

ACKNOWLEDGMENTS

The authors thank the National Heart, Lung, and Blood Institute, Vitalant Research Institute, Research Triangle Institute, and Brazilian and American REDS-III research staff.

Financial disclosure: The authors have nothing to disclose.

Conflict of interest statement: There are no conflicts of interest to report.

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