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ORIGINAL ARTICLE

Patient care in cystic fibrosis centers: a real-world analysis in Brazil

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ABSTRACT

Objective: To analyze the characteristics of cystic fibrosis (CF) care centers (CFCCs) in Brazil. **Methods:** A questionnaire was sent to the coordinators of all 51 registered CFCCs between May and September of 2021. **Results:** The response rate was 100%. Southeastern Brazil is the region where most of the CFCCs in the country are located (21 centers; 41%), followed by the southern and northeastern regions (11 centers each; 21.5%), the central-western region (6; 12%), and the northern region (2; 4%). A total of 4,371 patients with CF were cared for in Brazil during the study period, ranging from 7 to 240 patients per center (mean, 86 patients/center; median, 75 patients/center); 2,197 patients (50%) were cared for in centers in the southeastern region of the country, particularly in the state of São Paulo (33%), the remaining patients being treated in southern Brazil (1,014 patients, 23%), northeastern Brazil (665 patients, 15%), central-western Brazil (354 patients, 8%), and northern Brazil (141 patients, 4%). Overall, 47 centers (92%) reported having an incomplete multidisciplinary team; 4 (8%) lacked essential team members; 6 (12%) lacked a physical therapist; 5 (10%) lacked a dietitian; 17 (33%) lacked outpatient nursing care; 13 (25%) lacked outpatient social work services; 14 (27%) lacked a psychologist; and 32 (63%) lacked a clinical pharmacist. Seven CFCCs (14%) in the northern and northeastern regions of Brazil reported that the quality of newborn screening for CF was poor. All centers reported having difficulties in accessing CF medications. **Conclusions:** Brazilian CFCCs experience multiple problems, including inadequate staffing, infrastructure, testing, and medication supply. There is an urgent need to regulate the implementation of CF referral centers and an appropriate network structure for the diagnosis and follow-up of CF patients using optimal treatment recommendations.

Keywords: Cystic fibrosis; Neonatal screening; Quality of life; Genetic diseases, inborn; Lung diseases.

INTRODUCTION

Cystic fibrosis (CF) is a multisystem genetic disorder with a chronic and progressive course that mainly affects the respiratory and digestive systems, respiratory failure secondary to lung disease being the main cause of short life expectancy of patients.[1] The increasingly early diagnosis, currently made primarily through neonatal screening, and the improved effectiveness of treatment performed in specialist CF centers are associated with improved quality of life and increased survival in patients with CF.[2] New medications aimed at correcting the dysfunction of the CF transmembrane conductance regulator (CFTR), a protein affected in CF, are known as CFTR modulators and promise even better results.[1-7] Given the complexity of CF, several medical specialties are involved in patient care.

Better quality of life, better nutritional status, and longer survival in patients with CF are associated with routine specialist care provided in CF care centers (CFCCs). In accordance with international models, CF patients treated at CFCCs are routinely cared for by a multidisciplinary team, and this allows for more comprehensive and effective treatments.[1-7] The multidisciplinary team should be sufficiently trained and composed of health care professionals who take care of the various clinical aspects of CF in children, adolescents, and adults. In addition, such teams should provide guidance on proper bronchial hygiene therapy and pulmonary performance, as well as on the most adequate nutrition for each patient and on the care required for the use of all medications, catheters, and devices. Teams should also take care of the emotional and social aspects of CF in a standardized manner.[2,7] In addition to the multidisciplinary team, CFCCs should have an appropriate infrastructure of care and trained staff to meet the needs related to the diagnosis, follow-up, and treatment of CF.[7]

In Brazil, the 2001 National Neonatal Screening Program included screening for CF in all newborns from phase III implementation onwards. The Program stipulates that patients diagnosed with CF should be treated in the *Sistema Único de Saúde* (SUS, Brazilian Unified Health Care System), which is the national public health care system funded by federal taxes and

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operated by state and municipal governments, in a specialist CF multidisciplinary outpatient clinic or in a CFCC that can provide appropriate patient counseling, monitoring, and treatment and also rely on a network of ancillary services.[8] A support hospital network with pediatric and adult ICUs, emergency departments, and inpatient units should be available. Patient care flow should follow current *Protocolos Clínicos e Diretrizes Terapêuticas* (PCDTs, Clinical Protocols and Therapeutic Guidelines) for the treatment of CF.[8] However, the Brazilian Ministry of Health provides neither a clear-cut, well-established, up-to-date definition of the composition and qualifications of CFCCs nor any standardization for delivery of care. In fact, state governments are responsible for the SUS accreditation of CFCCs, whereas CFCCs themselves are responsible for the organization of services and teams.

There are several CFCCs in Brazil. However, we are unaware of their characteristics and limitations in terms of personnel, infrastructure, and access to tests and medications. In the present analysis, we sought to understand and describe the status of Brazilian CFCCs critically in order to propose actions to adapt and standardize these centers so that a standardized delivery of care is achieved throughout the country.

METHODS

Data were provided by the coordinators of all CFCCs registered with both the *Grupo Brasileiro de Estudos de Fibrose Cística* (GBEFC, Brazilian CF Study Group) and CF patient associations. GBEFC is a nonprofit, non-governmental association consisting of various health care professionals specializing in the diagnosis and treatment of CF. GBEFC aims to disseminate knowledge on CF in Brazil, assisting health care professionals in the diagnosis of the disease; stimulate greater interest in CF on the part of health care professionals, hospitals, and public and private agencies in order to produce greater scientific knowledge through attendance at conferences and involvement in research; and discuss, develop, and update PCDT for CF in Brazil.

A questionnaire was sent via e-mail or mobile instant messaging to all coordinators of the CFCCs, including questions regarding the following: 1) total number of patients with CF at the CFCC; 2) CFCC address; 3) medical specialty of the coordinator and age of the patients receiving care; 4) whether or not the center infrastructure is appropriate (if no, give reasons); 5) whether or not the following medical specialties are part of the medical team or not: pediatric pulmonologist, pediatric gastroenterologist, adult pulmonologist, and adult gastroenterologist; 6) whether or not the following specialists are involved in multidisciplinary care: physical therapist, dietitian, nurse, social worker, psychologist, clinical pharmacist, and physical educator; 7) whether or not the CFCC is linked to a CF neonatal screening program; 8) whether the quality of CF neonatal screening at the CFCC is considered to be very good, good, or bad (if bad, give reasons); 9) whether or not genetic testing for CF is available at the CFCC, 10) whether or not the sweat test is available for CF diagnosis; 11) which technique is used for the sweat test (conductivity, Gibson-Cooke, or coulometric titration); 12) whether or not there are any complaints about the sweat test (if yes, explain), 13) whether or not the CFCC has access to the following medications: pancrelipase, dornase alfa, and inhaled tobramycin; and 14) whether or not there are any complaints about CF medications (if yes, explain). The questionnaire was sent between May and September of 2021. All data were entered into a Microsoft Excel spreadsheet to be processed and analyzed.

As most of the data are qualitative, we performed a descriptive analysis using absolute and relative frequencies. Quantitative data were expressed as means and/or medians.

RESULTS

A total of 51 CFCCs that met the inclusion criteria in Brazil, and all of the coordinators of these centers completed the questionnaire. Among the coordinators, 48 (94%) are pediatric or adult pulmonologists and 3 (6%) are pediatric gastroenterologists. Five states (Acre, Amapá, Roraima, Rondônia, and Tocantins), all of which are located in the northern region of Brazil, have no CFCCs. In the remaining Brazilian states, there is at least 1 CFCC per state. Southeastern Brazil is the region where most of the CFCCs are located (21 centers, 41%), followed by southern Brazil (11 centers, 21.5%), northeastern Brazil (11 centers, 21.5%), central-western Brazil (6 centers, 12%), and northern Brazil (2 centers, 4%). Of the 51 CFCCs, 40 (78%) are located in state capitals, whereas 11 (22%) are located in major inland cities; almost all CFCCs are affiliated with university hospitals. Thirty-four CFCCs (67%) care for more than 50 patients, whereas 17 centers (33%) care for less than 50 patients (Table 1).

Twenty-one CFCCs (41%) exclusively provide pediatric care however, the definition of pediatric age varies across centers: 0-12 years of age, 0-14 years of age, or 0-18 years of age. Nineteen CFCCs (37%) care for both children and adults, whereas 11 centers (22%) care for adults only. Adult CFCCs are located in the states of Ceará, Espírito Santo, Minas Gerais, Rio de Janeiro, São Paulo, Paraná, Rio Grande do Sul, and Santa Catarina, as well as in the Federal District of Brasília.

A total of 4,371 patients were being cared for in the 51 CFCCs during the study period. The number of patients cared for at each center varied widely, ranging from 7 to 240 patients (mean, 86 patients/center; median, 75 patients/center). Half of the patients (2,197 patients) were cared for in centers located in the southeastern region of Brazil, particularly in the state of São Paulo, where 33% (1,213) of all Brazilian patients with CF were treated, the remaining being

Table 1. Characteristics of cystic fibrosis care centers in Brazil (N = 51) between May and September of 2021.[a,b]

Type of cystic fibrosis care center			
	Pediatric center	21 (41)	
	Pediatric/adult center	19 (37)	
	Adult center	11 (22)	
Region	**Center/patient**	**Center per state/patient per state**	
North	2 (4)/141 (4)	Acre	-/-
		Amapá	-/-
		Amazonas	1/9
		Tocantins	-/-
		Roraima	-/-
		Rondônia	-/-
		Pará	1/132
Northeast	11 (21.5)/665 (15)	Alagoas	1/38
		Bahia	2/220
		Ceará	2/121
		Maranhão	1/25
		Paraíba	1/20
		Pernambuco	1/120
		Piauí	1/30
		Rio Grande do Norte	1/37
		Sergipe	1/54
Central-West	6 (12)/354 (8)	Federal District	2/138
		Goiás	2/116
		Mato Grosso	1/51
		Mato Grosso do Sul	1/49
Southeast	21 (41)/2,197 (50)	Espírito Santo	2/135
		Minas Gerais	6/560
		Rio de Janeiro	3/289
		São Paulo	10/1,213
South	11 (21.5)/1,014 (23)	Paraná	3/372
		Rio Grande do Sul	4/416
		Santa Catarina	4/226

[a]Values expressed as n (%) or n/n. [b]Total number of patients = 4,371.

treated in southern Brazil (1,014 patients, 23%), northeastern Brazil (665 patients, 15%), central-western Brazil (354 patients, 8%), and northern Brazil (141 patients, 4%). Based on population density estimates from the Brazilian Institute of Geography and Statistics in July of 2020,[9] the distribution of CF patients is proportional to the number of individuals in the southeastern, central-western, and northern regions of Brazil. However, in southern Brazil, there is a higher density of CF patients (23% of all Brazilian CF patients) and a lower population density (14% of the Brazilian population), whereas, in northeastern Brazil, there is a lower density of CF patients (15% of all Brazilian CF patients) and a higher population density (27% of the Brazilian population).

In addition, 3 CFCCs provide outpatient care only and are highly dependent on the local characteristics of the SUS to hospitalize patients if necessary.

All CFCCs have experienced difficulties. There were many complaints about the infrastructure of the centers, including (in order of frequency) lack of rooms for proper care, lack of places for patient segregation, lack of hospital beds for inpatient admission, inadequate care for adult patients (provided by pediatric teams in pediatric outpatient clinics), lack of a pediatric-to-adult transition program, delay in performing tests, and lack of basic tests, such as fecal elastase-1 to determine pancreatic insufficiency and pulmonary function tests (spirometry), among others (Chart 1).

In all CFCCs, the medical team providing care in a shared outpatient setting had at least one pediatric and/or adult pulmonologist, but only 29 centers (57%) had a gastroenterologist for simultaneous outpatient care. Three centers reported that the number of physicians was insufficient to meet patient demand. A common complaint was limited access to other medical specialties (e.g., endocrinology, psychiatry, and rheumatology), which were restricted to referral and back-referral processes between institutions or between services within the same institution.

Forty-seven CFCCs (92%) reported that they had a multidisciplinary team, but the team was usually incomplete; 4 CFCCs (8%) lacked essential

Chart 1. Major problems reported in cystic fibrosis care centers in Brazil, 2021.

- lack of rooms for proper care
- lack of places for patient segregation
- lack of hospital beds for inpatient admission
- inadequate care for adult patients (provided by pediatric teams in pediatric outpatient clinics)
- lack of a pediatric-to-adult transition program
- delay in performing tests
- lack of basic tests, such as fecal elastase-1 to determine pancreatic insufficiency and of pulmonary function tests (spirometry) to assess lung disease progression
- insufficient number of physicians to meet patient demand
- limited access to other medical specialties
- incomplete multidisciplinary team
- multidisciplinary team members shared with other services
- multidisciplinary team members replaced or assigned other duties
- irregular neonatal screening in some states
- sweat test not covered by the Brazilian public health care system for patients over two years of age
- high cost of supplies for the collection and analysis of sweat chloride
- lack of trained personnel to perform sweat tests
- irregular supply of medications, with frequent shortages and inefficient distribution

multidisciplinary team members. Six CFCCs (12%) lacked a physical therapist, 5 (10%) lacked a dietitian, 17 (33%) lacked outpatient nursing care, 13 (25%) lacked outpatient social work services, 14 (27%) lacked a psychologist, and 32 (63%) lacked a clinical pharmacist. Only 1 CFCC had a physical educator in the outpatient clinic. In addition to an incomplete team, all coordinators reported that the multidisciplinary team members were shared with other services or frequently replaced and assigned other duties. Throughout the COVID-19 pandemic, the diversion of health care professionals, especially adult pulmonologists and physical therapists, to care for COVID-19 patients was an aggravating factor that had a great impact on the care of adult CF patients.

All pediatric CFCCs reported being linked to CF neonatal screening centers. However, we have no information on neonatal screening in the northern states that do not have a CFCC. Seven CFCCs (14%) in the northern and the northeastern regions of Brazil reported that the quality of newborn screening for CF was poor, with a significant delay in collecting the second sample for immunoreactive trypsinogen testing and in communicating screening test results, as well as irregularities in the performance/quality of the screening-related sweat test. In the southern, southeastern, and central-western regions of Brazil, the quality of neonatal screening for CF was reported to be good or very good, with occasional problems related to the lack of materials and/or personnel. Genetic testing, which should complement the diagnosis, was not readily available in all regions through health services provided by the SUS.

At least one laboratory is accredited to perform the sweat test in each state, being often linked to the neonatal screening referral center, but not necessarily linked to the CFCC. However, the SUS subsidizes the sweat test only for patients up to 2 years of age. The technique utilized to collect and measure sweat chloride varied from center to center: 2 centers used conductivity measurements, 5 centers used manual titration (the Gibson-Cooke method), and the remaining centers were affiliated with laboratories that used coulometric titration. Major complaints about the sweat test included lack of coverage by the SUS for patients over 2 years of age, high cost of supplies for the collection and measurement of sweat chloride, lack of supplies, and lack of trained personnel.

All CFCCs reported having access to the medications listed in the 2017 CF PCDT,[10] namely pancrelipase, dornase alfa, and inhaled tobramycin. However, all centers complained about the irregular supply of medications, with frequent shortages and inefficient distribution. Several coordinators reported that the lack of patient adherence to treatment might be related to the irregular provision of medications.

DISCUSSION

This brief analysis of the status of Brazilian CFCCs reveals the different realities faced by patients with CF across the country and the presence of difficulties in 100% of the CFCCs. Standardization of delivery of care in CFCCs can be challenging in a country of continental dimensions such as Brazil, with a culturally and socially diverse population, limited financial resources, and considerable variability in public health policies among the different states and municipalities. Without proper resources, CFCCs are at risk of providing fragmented, non-comprehensive, non-standardized, ineffective care, thus increasing the financial burden on our health care system. We should therefore establish priorities and suggest improvements.

All of the 51 Brazilian CFCCs registered with the GBEFC and spread across the country strive to follow the recommendations for the provision of standardized multidisciplinary care to patients with CF. However, there are chronic problems in all centers: there are few physicians for many patients; centers lack specialists and medical specialties, thus making multidisciplinary teams incomplete; team members are shared with other services and are often assigned other duties; and

qualifications and training of health care professionals vary considerably. In addition, only a few centers are qualified to provide care to adult patients; most centers are located in state capitals, and patients need to travel long distances; the infrastructure of CFCCs is seriously inadequate; centers lack rooms for proper care; neonatal screening is not regularly performed; sweat testing is often discontinued, and patients have their diagnosis delayed; and centers lack tests to assess disease progression and hospital beds for inpatient admission. In short, health care professionals strive to provide proper care, and Brazilian patients with CF struggle to have access to effective treatment.

Patients are heterogeneously distributed across Brazilian CFCCs, with a large number of patients in the southeastern and southern regions of the country (68% of cases) and only a few in the northern region (4%). This distribution supports the variable incidence of CF previously reported in Brazil,[11] known to be related to regional ethnic characteristics and miscegenation as a result of the colonization/immigration process in the country. This great variability poses a challenge to physicians and managers of specialist CFCCs, as the health departments of each state are responsible for the planning and distribution of such centers, which should be in accordance with the rates of live births and the incidence of CF in the state in order to ensure an adequate operational flow to facilitate user access and care coverage while reducing unnecessary costs and/or inadequate use of existing resources. However, despite the publication of some of our data and of those from the *Registro Brasileiro de Fibrose Cística* (REBRAFC, Brazilian CF Registry), the results of neonatal screening are poorly disseminated at the national/state levels, whether regarding screening for CF or other diseases.

Brazilian CFCCs present a wide spectrum of issues, ranging from large centers with many patients but insufficient staff to meet the demand to small centers with few patients and many difficulties in implementing multidisciplinary care. Better planning of the distribution of patients across CFCCs might lead to better patient care and better organization of teams, obviating the need for patients to travel long distances. Currently, 78% of the CFCCs are located in state capitals, whereas the remaining centers are located in major inland cities, often affiliated with medical schools. According to data from the 2018 REBRAFC annual report, 43 registered patients were born in the northern states that do not have a CFCC.[12] These patients are probably being cared for in other states or have moved to another city to receive treatment.

Brazilian CF care teams are often incomplete, and team members are frequently replaced, negatively affecting the quality of care. These health care professionals do not have a specific contract to provide CF care and often need to assume multiple roles. Institutions have no financial incentives to support the implementation of CFCCs, which reveals little interest in maintaining large skilled teams to provide exclusive care to patients with CF. Moreover, the lack of specific resources hinders the availability not only of more expensive ancillary tests, especially the sweat test, but also of simple pulmonary function tests and fecal elastase-1 measurements to determine pancreatic insufficiency.

Despite the difficulties, Brazil as a whole shows an increasing number of patients with CF reaching adulthood (about 25% of patients are over 18 years of age), and the increasingly early diagnosis has been associated with neonatal screening. According to data from the 2018 REBRAFC annual report, 1,406 cases had been diagnosed through neonatal screening since 2009, accounting for almost 60% of all new diagnoses.[12] However, the quality of the process of neonatal screening and diagnostic confirmation unfortunately remains inadequate and highly variable. There are delays in communicating screening test results and, consequently, in confirming the diagnosis in some states, which is inconsistent with all the investment in early diagnosis. It is therefore essential to identify the difficulties and better organize the services. Improving the interaction between CF screening services and CFCCs may facilitate this process.

Performing the sweat test is another critical point. Because it is a high-cost test with a complex technique, it is poorly available and associated with quality problems. Reformulating the sweat test funding policies is of paramount importance.

All CFCCs reported an irregular supply of medications, with frequent shortages and inefficient distribution, even when considering the medications included in the 2017 CF PCDT. Access to other medications, vitamins, supplements, devices, oxygen, and other resources needed by patients with CF is even more problematic, substantially affecting patient adherence to treatment. The recent publication of a new CF PCDT,[13] more comprehensive and complete, includes ivacaftor, which is one of the novel CFTR modulators that may be helpful. However, it is still necessary to improve the administrative and organizational processes in the states and their respective public pharmacies.

Each CFCC should be committed to provide high-quality, humanized, comprehensive, well-coordinated care, aiming to grasp the full complexity of CF. The implementation of qualified, well-equipped, integrated centers can result in considerable savings to the SUS, especially when compared with the provision of fragmented, non-comprehensive care. Few Brazilian states have consolidated public policies on CF. In most states, we have enormous difficulties in regularizing CF-related services with health managers and secretaries due to the lack of documents that properly describe the necessary conditions for the implementation of these services. Therefore, there is a great need to regulate the implementation of CF referral centers in Brazil and to establish a network of appropriately trained and qualified centers to confirm

Chart 2. Required features of cystic fibrosis referral centers according to the Brazilian Cystic Fibrosis Study Group.

1. A multidisciplinary team of CF specialist health care professionals:
   a. Pediatric and/or adult pulmonologist and pediatric and/or adult gastroenterologist
   b. Physical therapist
   c. Dietitian
   d. Nurse
   e. Psychologist
   f. Clinical pharmacist
   g. Social worker
      i. The team should be trained and qualified to care for patients with CF
      ii. The ratio of 1 attending physician/50 patients is recommended
      iii. The recommended workload for each health care professional should be as follows: coordinating physician—96 h/week; pulmonologist—120 h/week; gastroenterologist—48 h/week; physical therapist—240 h/week; dietitian—96 h/week; nurse—240 h/week; psychologist—96 h/week; pharmacist—72 h/week; and social worker—96 h/week
      iv. An adult health care team should be available when the number of patients > 18 years of age in the center exceeds 20
      v. Appointments should be provided for patients every 2-3 months
      vi. The multidisciplinary team should be supported with training and continuing professional development
2. Access to other medical specialties, such as genetics, endocrinology, psychiatry, rheumatology, pediatric surgery, thoracic surgery, nephrology, otolaryngology, specialist pain management, and palliative care
3. Facilities should be appropriate due to the possibility of contamination/cross-infection between patients and have a sufficient number of rooms to allow adequate patient segregation
4. Own/affiliated laboratories for ancillary diagnostic tests:
   1. Quantitative sweat chloride measurement in accordance with international reference documents[14]
   2. *CF transmembrane conductance regulator* (*CFTR*) gene sequencing
5. Emergency care available 24 h/day
6. Availability of support hospital beds for inpatient admissions
7. Access to:
   1. Pulmonary function testing
   2. A microbiology laboratory with experience and resources to identify typical CF-associated pathogens
   3. Chest radiography, CT, pulmonary angiography, abdominal ultrasound, and bone densitometry
   4. Fecal pancreatic elastase-1 testing
   5. Clinical pathology laboratory capable of performing routine tests
8. Respiratory (flexible bronchoscopy) and digestive endoscopy

CF: cystic fibrosis.

the diagnosis of CF and follow-up of CF patients using established treatment recommendations. Therefore, GBEFC recommends that Brazilian CF referral centers be constituted in accordance with the features described in Chart 2.

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AUTHOR CONTRIBUTIONS

EFAP was responsible for data collection. All of the authors equally contributed to study conception and design; data analysis and interpretation; statistical analysis; drafting and critical revision of the manuscript; and approval of the final version of the manuscript.

CONFLICTS OF INTEREST

None declared.

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