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Drug and others products shortage in Brazilian health services in the scenario imposed by COVID-19

Escassez de medicamentos e outros produtos nos serviços de saúde brasileiros no cenário imposto pela COVID-19

Escasez de medicamentos y otros productos en los servicios de salud brasileños en el escenario impuesto por la COVID-19

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Abstract
Objective: We aimed at investigating and describing the drug and material resources in health shortage in the Brazilian services during the COVID-19 pandemic. Methods: We conducted a cross-sectional study in the format of an online survey with closed questions. Information was sought about the institutional and care profile, pharmaceutical service organization, non-compliance in the stock, or lack of drugs and other health products between April and October 2020. We performed descriptive, univariate, and multivariate statistical analyses, such as Fisher's t-test, chi-square test, and the Multiple Correspondence and Hierarchical Cluster analyses. A p-value below 0.05 and a 95% significance level were considered. Results: 228 Brazilian institutions, most located in the capital cities, with specific beds for COVID-19 and public administration, were included in the study. Grouping by similarity separated the study sample into five heterogeneous clusters. Eighty-four percent of the services indicated a drugs shortage, especially neuromuscular blocking agents (64.9%), hypnotics and sedatives (52.9%), vasoactive drugs (37.3%), and antiinfective agents (30%). Conclusion: In all the clusters, there were reports of a shortage of items considered essential in the management of critically-ill patients, corroborating the perception that this was a significant challenge for pharmaceutical assistance in various Brazilian services during the COVID-19 pandemic.
Keywords: COVID-19; Health services; Pharmaceutical services; Surveys and questionnaires.

Resumo
Objetivo: Objetivou-se investigar e descrever os recursos medicamentosos e materiais em falta de saúde nos serviços brasileiros durante a pandemia de COVID-19. Métodos: Foi realizado um estudo transversal no formato de questionário online com perguntas fechadas. Foram buscadas informações sobre o perfil institucional e assistencial, organização do serviço farmacêutico, não conformidade no estoque ou falta de medicamentos e outros produtos de saúde entre abril e outubro de 2020. Realizamos análises estatísticas descritivas, univariadas e multivariadas, como t de Fisher -teste, teste do qui-quadrado e análise de múltipla correspondência e agrupamento hierárquico. Considerou-se valor de p abaixo de 0,05 e nível de significância de 95%. Resultados: 228 instituições brasileiras, a maioria localizadas nas capitais, com leitos específicos para COVID-19 e administração pública, foram incluídas no estudo. O agrupamento por similaridade separou a amostra do estudo em cinco conglomerados heterogêneos. Oitenta e quatro

por cento dos serviços indicaram falta de medicamentos, principalmente bloqueadores neuromusculares (64,9%), hipnóticos e sedativos (52,9%), drogas vasoativas (37,3%) e anti-infecciosos (30%). Conclusão: Em todos os clusters, houve relatos de escassez de itens considerados essenciais no manejo de pacientes críticos, corroborando a percepção de que esse foi um desafio significativo para a assistência farmacêutica em diversos serviços brasileiros durante a pandemia de COVID-19.
Palavras-chave: COVID-19; Serviços de saúde; Serviços farmacêuticos; Pesquisas e questionários.

Resumen
Objetivo: Nuestro objetivo fue investigar y describir los medicamentos y recursos materiales en escasez de salud en los servicios brasileños durante la pandemia de COVID-19. Métodos: Realizamos un estudio transversal en formato de encuesta online con preguntas cerradas. Se buscó información sobre el perfil institucional y asistencial, organización del servicio farmacéutico, incumplimiento en el stock o falta de medicamentos y otros productos sanitarios entre abril y octubre de 2020. Se realizaron análisis estadísticos descriptivos, univariados y multivariados, como la t de Fisher. -test, chi-square test, y los análisis de Correspondencia Múltiple y Cluster Jerárquico. Se consideró un valor de p por debajo de 0,05 y un nivel de significancia del 95%. Resultados: 228 instituciones brasileñas, la mayoría ubicadas en las capitales, con camas específicas para COVID-19 y administración pública, fueron incluidas en el estudio. La agrupación por similitud separó la muestra del estudio en cinco grupos heterogéneos. El 84% de los servicios indicó desabastecimiento de medicamentos, en especial bloqueadores neuromusculares (64,9%), hipnóticos y sedantes (52,9%), fármacos vasoactivos (37,3%) y antiinfecciosos (30%). Conclusión: En todos los conglomerados, hubo relatos de escasez de artículos considerados esenciales en el manejo de pacientes críticos, lo que corrobora la percepción de que ese fue un desafío importante para la asistencia farmacéutica en varios servicios brasileños durante la pandemia de COVID-19.
Palabras clave: COVID-19; Servicios de salud; Servicios farmacéuticos; Encuestas y cuestionarios.

1. Introduction

Eventually, shortage of health products is associated with negative clinical outcomes and increased hospital costs related to health care (African COVID-19 Critical Care Outcomes Study (ACCCOS) Investigators, 2021; Fox et al., 2009). Such a shortage is influenced by logistics, political issues, actions of regulatory agencies on tax and customs barriers, and environmental factors such as floods and natural tragedies (Reis & Perini, 2008). Although the shortage of health products has been previously reported (Pauwels et al., 2015; Rosa et al., 2016; Videau et al., 2019), the demand for the treatment of severe cases and complications related to the COVID-19 was unpredictable. Therefore, the pharmaceutical service scheduling was significantly impacted (Wallis et al., 2020). Several countries reported shortages during the COVID-19 pandemic (Commissioner, 2020; Martinez et al., 2020; Pauwels et al., 2015; Shukar et al., 2021; Sociedade Brasileira de Farmácia Hospitalar, 2021). However, varied data suggest that the scarcity of pharmaceutical products affected different countries in a peculiar manner[11], showing worse in low and middle-income countries (African COVID-19 Critical Care Outcomes Study (ACCCOS) Investigators, 2021; Don Eliseo Lucero-Prisno et al., 2020; Shukar et al., 2021), mainly when they depend on technologies coming from the international market (Pauwels et al., 2015; Reis & Perini, 2008).

In 2020, the National Health Surveillance Agency (*Agência Nacional de Vigilância Sanitária*, ANVISA) launched monitoring actions. It generated indicators using the manufacturers' data about the stock of the entire logistics chain of drugs used in managing patients affected by COVID-19 (Agência Nacional de Vigilância Sanitária, 2021). However, there are gaps in the systematization of information and tools to foresee risk factors for the shortage of health products (Miljković et al., 2020).

Studies were released demonstrating the crucial role of the pharmacist in inventory management during the pandemic caused by COVID-19 (Passos et al., 2021; Silva & Araújo, 2020, 2020). Additionally, the consolidation of this data can represent an alternative to face the problem in advance, contributing to its organization and updating (Vogler & Fischer, 2020). Thus, this study aimed at investigating and describing the shortage of health products and associated factors during the first year of the pandemic caused by COVID-19 in the Brazilian health services.

2. Methodology

Study design and inclusion and exclusion criteria

We conducted a cross-sectional study with a convenience sample at the national level. We included public and private health services (emergency care units and hospitals), with and without COVID-19 wards. Services with duplicate data (identified by the name of the institution and city) were excluded. Despite the limited generalization of non-probabilistic convenience samples, they remain the standard within developmental science. Adoption of probability samples is rarely feasible in some study designs, as in the case of a survey, like the one conducted in this study (Jager et al., 2017).

Data collection and organization

We invited pharmacists working in health services to participate in the research, publicizing it through email for Brazilian Society Hospital Pharmacy and Health Services members and messages on social networks. A link was shared on these platforms with guidelines, the Informed Consent Form (ICF), and the research survey (self-applied online questionnaire). A similar methodology was used by Omer et al to investigate the shortage of medicines in tertiary hospitals (Omer et al., 2021).

Data collection took place between September 5th and October 25th, 2020, with the aid of the Google Forms® platform. The data obtained were exported to a Microsoft Excel® spreadsheet, stratified, and described according to the institutional and care profile. We classified drugs according to the third level of the Anatomical Therapeutic Chemical (ATC) classification system (AlRuthia et al., 2017).

First, we developed the questionnaire based on published studies on the same topic(*Cadastro Nacional de Estabelecimentos de Saúde*, 2021; Don Eliseo Lucero-Prisno et al., 2020; Hoss & Caten, 2010; Miljković et al., 2020). Then, we applied a pilot group composed of four pharmacists' specialists in hospital pharmacy. They suggested minor modifications before initiating data collection for the survey (content validity). We excluded the pilot group answers in the study. The final questionnaire version had 29 closed questions, with possible answer options or a "not applicable" option, depending on the type of question.

The information collected was related to the following factors or dimensions:

(i) Institutional profile: location (city or state), legal nature (public, private or philanthropic), and management model (municipal, state, or federal, when applicable) of the institution.

(ii) Care profile: (service offering general or specialty care), size (small/up to 50 beds, medium/from 51 to 149 beds and large/more than 150 beds) and availability or not of Intensive Care Unit (ICU) beds and for patients undergoing treatment due to COVID-19;

(iii) The action plan existence for the Pharmacy Service activities and description of the activities related to the management of inputs (selection, planning, acquisition, storage, distribution, and use of drugs) during the pandemic;

(iv) Shortage: confirmation of stockout or lack of drugs and other health products in the period between April and October 2020 in the service researched;

(v) Respondent characterization: the pharmacist's age, experience time, qualification, and performance areas.

We also included three open questions to specify or detail the drugs with a shortage record, recent incorporation in the institution, or increased consumption (Everitt & Dunn, 2001).

Analysis

For comparison purposes, we collected the information about the population and the number of beds available in each

state from the records of the Brazilian Institute of Geography and Statistics (Instituto Brasileiro de Geografia e Estatística, IBGE)(IBGE | Biblioteca | Detalhes | L'Analyse des donnees / rediges et publies sous la direction du Professeur J. P. Benzecri. -, 2021), of the SUS IT Department of SUS (DATASUS)(Cadastro Nacional de Estabelecimentos de Saúde, 2021) and the National Register of Health Institutions (Cadastro Nacional de Estabelecimentos de Saúde, CNES)(*Cadastro Nacional de Estabelecimentos de Saúde*, 2021).

The similarity between the participating institutions was assessed with descriptive and univariate statistical analyses (Fisher's t or chi-square). In addition, we also performed multivariate analyses: Multiple Correspondence Analysis (MCA) and Hierarchical Cluster Analysis (also called Clustering Analysis - CA). A p-value below 0.05 and a 95% significance level were considered(Everitt & Dunn, 2001).

MCA separated the health units by the factorial axes formed(AlRuthia et al., 2017; Hoss & Ten Caten, 2010; Ying et al., 2020). Categorical variables were included in this analysis, where the starting point was a matrix with points from a vectorial space. Similarities in the answers grouped the data correlated with each other. The eigenvalues in the vector-matrix determined the information present in each factorial axis of the graph. The data represented by percentages were reassessed, and each variable' coding over-estimation was deducted (Abdi & Valentin, 2007; Carvalho & Struchiner, 1992; Greenacre & Hastie, 1987; Pauwels et al., 2014)

The Research Ethics Committee approved this study of the Clinical Hospital of the Federal University of Goiás under CAAE: 36030320.9.0000.5078. The participants were informed about the research risks and benefits. After agreeing to participate voluntarily, they signed the Free and Informed Consent Form (FICF) and applied online before answering the questionnaire. The participants' identity was preserved.

3. Results

We received 257 answers. Although, we excluded 29 for duplicates. Then, we analyzed data of 228 participating institutions from all the Brazilian states and *Distrito Federal*. Most informed institutions were located in the capital cities, had public administration (49%) and exclusive beds for the treatment of patients with COVID-19 (88.6%), and treated patients served by the Unified Health System (*Sistema Único de Saúde*, SUS) (Table 1).

Table 1. Characterization of the health services participating in the study, Brazil, 2020 (N=228). (Continue)

	Total of participating institutions	**Institutions with shortage N=193**
Variable	**N (%)**	**N (%)**
Number of beds		
More than 500	13 (5.1)	13 (6.7)
From 151 to 500	81 (35.7)	69 (35.8)
From 51 to 150	77 (33.8)	66 (34.2)
Up to 50	57 (25.0)	45 (23.3)
Legal nature		
Public administration	111 (48.7)	97 (50.3)
Private administration	61 (26.8)	45 (23.3)
Philanthropic institutions	42 (18.4)	38 (19.7)
Legal nature		
Charity institutions	8 (3.5)	7 (3.6)
Others	6 (2.6)	6 (3.1)
Serving the SUS		
Yes	184 (80.7)	153 (79.3)
No	44 (19.3)	40 (20.7)
Type of service		
Emergency Care Unit (ECU)	15 (6.6)	14 (7.3)
Field hospital	19 (8.3)	17 (8.8)
General hospital	90 (39.5)	89 (46.1)
Specialized hospital	104 (45.6)	102 (52.8)
Distribution of the institutions by regions		
Southeast	76 (33.3)	58 (30.1)
Northeast	62 (27.2)	55 (28.5)
South	30 (13.2)	26 (13.5)
North	33 (14.5)	29 (15.0)
Midwest	27 (11.8)	25 (13.0)
Distribution of the institutions located outside the states' capital cities		
Southeast	22 (9.6)	18 (9.3)
Northeast	19 (8.3)	18 (9.3)
South	14 (6.1)	11 (5.7)
Midwest	13 (5.7)	11 (5.7)
Total	228 (100.0)	193 (84.6)

Source: Authors.

Almost all (93.9%) stated that contingency plans were prepared to cope with the pandemic. In 84.6% of these institutions, the Pharmacy service devised the plans. Altogether, the participating institutions totaled 40,532 hospital beds, 6,882 in ICUs (Table 2).

Table 2. Distribution of the health services participating in the study by Brazilian regions, 2020 (N=228). (Continue)

State	Institutions by type		ECU	Participating institutions	Institutions that reported shortage	Hospital/ICU beds in institutions that reported shortage	
	General Hospital	Specialized Hospital		N (%)	N (%)	Ward	ICU
North Region							
Acre	15	5	5	4 (16.0)	4 (100.0)	175	60
Amapá	12	2	3	4 (23.5)	4 (100.0)	225	48
Amazonas	79	22	15	2 (1.7)	2 (100.0)	88	22
Pará	219	28	34	14 (5.0)	13 (92.9)	2,533	414
Rondônia	78	7	1	3 (3.5)	2 (66.7)	188	45
Roraima	12	2	1	1 (6.7)	1 (100.0)	140	20
Tocantins	64	7	17	5 (5.7)	3 (60.0)	300	29
Northeast Region							
Alagoas	54	28	21	2 (1.9)	2 (100.0)	126	42
Bahia	479	73	99	9 (1.4)	9 (100.0)	844	161
Ceará	227	55	52	6 (1.8)	6 (100.0)	772	114
Maranhão	237	30	20	3 (1.0)	3 (100.0)	236	117
Paraíba	99	35	24	4 (2.5)	3 (75.0)	371	56
Pernambuco	252	48	41	26 (7.6)	22 (91.7)	5,536	795
Piauí	95	16	5	5 (4.3)	4 (80.0)	683	102
Rio G. do N.	82	24	19	5 (4.0)	4 (80.0)	525	62
Sergipe	30	11	10	2 (3.9)	2 (100.0)	121	10
Midwest Region							
Goiás	340	83	37	10 (2.2)	9 (90.0)	504	216
Distrito Federal	43	21	13	4 (5.2)	4 (100.0)	831	141
Mato Grosso	153	10	38	7 (3.5)	6 (86.0)	298	135
Mato Gr. do S.	99	9	18	6 (4.8)	6 (100.0)	839	205
Southeast Region							
Espírito Santo	89	15	32	5 (3.7)	5 (100.0)	1,057	166
Minas Gerais	577	51	114	13 (1.8)	10 (76.9)	1,380	211
Rio de Janeiro	332	132	118	26 (4.5)	18 (69.2)	2,780	610
São Paulo	801	152	335	32 (2.5)	25 (78.1)	4,086	1,163
South Region							
Paraná	388	47	101	14 (2.6)	12 (85.7)	1,158	307
Santa Catarina	199	24	57	4 (1.4)	3 (75.0)	338	50
Rio G. do S.	332	132	118	12 (2.1)	11 (91.7)	4,442	635
TOTAL	5,387	1,069	1,348	228 (100.0)	193 (100.0)	30,576	5,936

Key: ICU = Intensive Care Unit; G. do N. = Grande do Norte; G. do S. = Grande do Sul; Gr. do S. = Grosso do Sul; ECA = emergency care unit. Source: Authors.

Shortage of health products was reported by 84.6% of the institutions and all the Brazilian states. However, when exclusive beds stratified the participating institutions to care for patients affected by COVID-19, the shortage percentage reported was 90.5%.

The main difficulties pointed out by the respondents concerning the purchase of drugs during the pandemic were as follows: increased prices when compared to previous periods (89.9%), non-compliance with delivery deadlines (82.0%), and request to cancel commitments, purchases, or contracts (42.6%).

The acquisition scheduling process was also influenced, especially by the lack of reliable epidemiological information regarding the reality of the impact exerted by the pandemic on the market (Table 3). The answers verified that the public institutions had a statistically significant tendency to show insufficient scheduling in view of the considerable seasonal variation, a contributing factor to the risk of stockouts.

Table 3. Frequency indicated by the respondents regarding the potential interfering factors in stock scheduling during the COVID-19 pandemic, Brazil, 2020.

Institutions that reported shortage	Public	Private	Charity/ Philanthropic	
	N (%)	N (%)	N (%)	p-value
	97 (87.4)	45 (73.8)	45 (90.0)	0.0285
Identification of the factors				
	N=97	N=45	N=45	
Caution in the managers due to the high financial impact on the institution	33 (34.0)	17 (37.8)	21 (46.7)	0.3644
Budget/Financial limitation	7 (7.2)	4 (8.9)	5 (11.1)	0.6959
Communication difficulty between management and care unit	24 (24.7)	6 (13.3)	7 (15.6)	0.2525
Scarce epidemiological data for an effective forecast of essential inputs	46 (47.4)	20 (44.4)	21 (46.7)	0.9464
Insufficient scheduling in the face of significant seasonal variation	46 (47.4)	6 (13.3)	4 (8.9)	<0.0001
Inappropriate use/lack of knowledge about available products (example: use of appropriate PPE in different hospital sectors)	22 (22.7)	3 (6.7)	12 (26.7)	0.0345
Lack of information about the real acquisition needs	0 (0.0)	2 (4.4)	1 (2.2)	0.1095
None of the answers apply	3 (3.1)	1 (2.2)	4 (8.9)	0.3815

Source: Authors.

The participating services reported problems regarding stocking disruption, mostly for muscle relaxants (M03A; 64.9%), hypnotics and sedatives (N05C; 52.9%), and cardiac stimulants (C01C; 37.3%). In addition, nearly one-third of the institutions (30.3%) reported a shortage of antimicrobials for systemic use (J01). Considering the therapeutic/pharmacological subgroup of the drugs, according to the third level of ATC, other classes of drugs, such as B01A, H02A, A02B, B05X, A10A (antithrombotic agents, corticosteroids for systemic use, drugs for peptic ulcer and gastroesophageal reflux disease, intravenous additive solutions, insulins, and analogs, respectively) were reported by 0.4% to 3% of the 228 institutions.

There was an expansion of the drugs selected in most (75.0%) of the participating services during the first months of the COVID-19 pandemic. Almost all of the classes above had new drug options incorporated, namely: muscle relaxants (29.3%), hypnotics/sedatives (26.8%), corticosteroids (13.6%), antithrombotic agents (13.2%), cardiac stimulants (7.9%), drugs for obstructive airway diseases (4.4%), vitamins (2.6%) and mineral supplements (2.2%). In 127 services, this process was mediated by a multidisciplinary pharmacy and therapeutic (or similar) team or commission. The main drugs related to the classes above are exemplified in Table 4.

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Table 4. Drugs that were incorporated for use or had an evident increase in consumption in health care institutions during the COVID-19 pandemic, Brazil, 2020 (N=228).

ATC Group	Classification	drug	N (%)
J	J01FA10	Azithromycin	150 (65.8)
P	P01BA01/P01BA02	Chloroquine/Hydroxychloroquine	136 (59.6)
P	P02CF01	Ivermectin	136 (59.6)
J	J05AH02	Oseltamivir	117 (51.3)
M	H02AB02	Dexamethasone	28 (12.3)
P	P01AX11	Nitazoxanide	24 (10.5)
J	J01DD04	Ceftriaxone	23 (10.1)
M	M03AC11	Cisatracurium	18 (7.9)
M	M03AC04	Atracurium	9 (3.9)
L	L04AC07	Tocilizumab	4 (1.8)
A	A03FA04	Bromopride	1 (0.4)
A	A02BC01	Omeprazole	2 (0.9)

Source: Authors.

In MCA, 46.4% of the information was obtained in the first three factorial axes. According to the similarity profile in the answers to each of the proposed variables, the hospital units were grouped into five clusters. The variables related to the

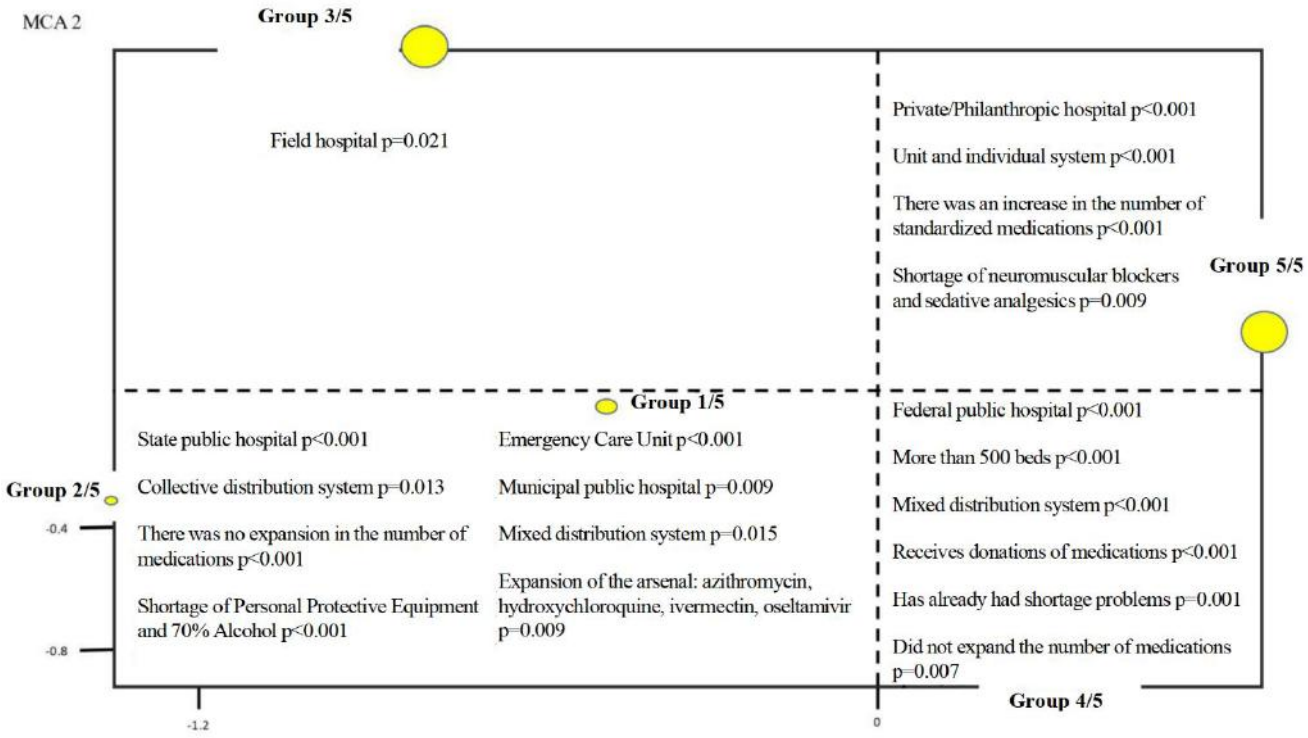
characterization of the institutions (size, legal nature), type of drug distribution, or shortage of health products that presented *p*-values below 0.05 in the clustering are shown in Figure 1.

A separation was verified in clusters 1 to 3 and clusters 4 and 5. In the first factorial axis (clusters 1, 2, and 3), the health units with less complexity (mainly ECUs), mostly public (state and municipal), and with up to 50 beds were segregated. Field hospitals were also observed in this axis (Cluster 2). Most of the institutions grouped in these three clusters (85%) reported the need to expand the number of drugs selected. In addition, all the institutions in these clusters indicated a shortage of inputs, such as 70% alcohol, Personal Protective Equipment (PPE), and several types of drugs.

In the other axis, in the MCA, a similarity was noticed in clusters 4 and 5, mainly consisting of federal and private public health units, of greater complexity, which specified lack of sedative analgesics and muscle blockers (Figure 1).

However, the shortage variable was not statistically significant in MCA or in CA. This was due to the predominance of the "yes" answer for the shortage by most participants, without forming a pattern that differentiated clusters 1, 2 and 3 from clusters 4 and 5 in the MCA. A total of 105 respondents (54%) confirmed that they would have initiated all the possible actions to prevent a shortage.

Figure 1: Distribution of the Clustering Analysis clusters in the factor axis graph of the Multiple Correspondence Analysis (Brazil, 2020).



Source: Authors.

4. Discussion

This is the first Brazilian study to investigate the shortage of inputs intended for health care experienced in the country during the COVID-19 pandemic. The results described a shortage of health products experienced during the first months of the COVID-19 pandemic in a convenience sample of 228 health services from all the Brazilian states, totaling 40,500 hospital beds. There was greater participation of respondents from health units (hospitals) with up to 150 beds (Figure 1), which was

expected, given the predominance of small-sized health institutions in Brazil (Botega et al., 2020; Nascimento et al., 2013). Brazil is a country of continental dimensions with drastic variability of socioeconomic conditions across its states (Melo et al., 2017). Although minimum standards are established for hospital pharmacies and health services (Sociedade Brasileira de Farmácia Hospitalar, 2021), there is heterogeneity in the Brazilian hospital pharmacy services (Nascimento et al., 2013). Despite this, most participating services suffered a shortage, regardless of their characteristics. Slightly more than half of the institutions with shortage alleged that they implemented all the possible mitigating measures, although unsuccessfully. The predominance of shortage was not observed in Brazilian regions with more inhabitants, such as the Southeast region.

During the study period, Brazil was one of the countries in the world with the highest number of confirmed cases and deaths due to complications caused by the new coronavirus infection (World Health Organization, 2021). The spatial distribution of the number of cases and deaths, however, was heterogeneous across the Brazilian states, as transmissibility of the coronavirus is affected by social factors, such as each region's ability to maintain the isolation measures, population density, hospital beds and other resources available for the management of these patients (Castro et al., 2021).

The lack of indispensable drugs for treating patients with COVID-19 can be related to the mortality rate (Sen-Crowe et al., 2021). Therefore, it is fundamental that accurate information involving the need for these hospital supplies, especially those with difficult access, is monitored with the perspective of prioritizing effective prevention and intervention actions. Shortage exerts an influence on the clinical practices and on the care process and is directly related to the outcome. A global study concluded that multiple factors can influence the mortality rates of patients with COVID-19, and that availability of supplies is probably one of them (Sen-Crowe et al., 2021).

Pointed out by nearly 85% of the respondents, shortage has been a constant problem for health care for several decades. However, the global concern about lack of drugs was exacerbated in the fight against the pandemic, forcing the health authorities to explore and implement strategies to prevent and mitigate the problem (Bohand et al., 2021; Rosa et al., 2016). In general, it may be due to several reasons, including production delays and interruptions (Ayati et al., 2020; Ventola, 2011). At the beginning of the COVID-19 pandemic, several countries closed their external and internal borders and, as a result, reduced transportation, directly affecting the production and flow of drugs and health products and restricting their global supply chain. In addition to that, there was an increase in emergency stocks in several countries, in an attempt to avoid or postpone interruption of the pharmaceutical assistance cycle (Ayati et al., 2020).

As expected, there was shortage in public and private services, with and without specific beds for COVID-19, as the main suppliers are, for the most part, the same in the country. Problems related to shortage of health products can be more prevalent in countries with no autonomy in the production of pharmaceutical supplies, such as Brazil(Chaves et al., 2021; Clews, 2021). Although the Brazilian pharmaceutical industry started to be developed in 2000, this follow-up is still quite dependent on imported inputs. A conjectured long-term effect on the pharmaceutical industry is the tendency for many countries to seek autonomy in the production of pharmaceutical inputs (Ayati et al., 2020).

The critical scenario imposed by the pandemic, with increased demand and unavailability of pharmaceutical inputs, caused an exchange rate impact, increasing the prices of foreign products(Fernandes et al., 2021). The practice of increasing prices in the sale of drugs was mentioned by 89.9% of the services and published in the Brazilian press (FenaSaúde, 2021). Expenditure in drugs for intubation, such as midazolam, was increased more than 500%(*Shortages catalogue | European Medicines Agency*, 2021). Despite the price control regulations, the increase in the prices of drugs in a context of limited supply or reduced competition has already been discussed in the literature(FenaSaúde, 2021; Wallis et al., 2020).

The absence of epidemiological data at the time of the research and their wide variation were the main factors pointed out by most of the respondents, which seemed to interfere in the scheduling regarding the acquisition of drugs, especially in

public institutions that face more restrictions in the management of financial resources, according to the respondents. Even with the proposal of mathematical models, this unpredictability in demand for care was an aspect pointed out in the Brazilian and international contexts(Martinez et al., 2020; Wallis et al., 2020).

Brazil structured a unified health system for access(Castro et al., 2019). The responding institutions, linked to the Unified Health System (SUS), pointed out poor scheduling because of the significant seasonal variation, contributing to stockout risk. In Brazil, the difficulties in the processes for the scheduling and acquisition of drugs precede the pandemic. Bureaucratization has been indicated as the main responsible for problems related to the scheduling of stocks (Ministério da Saúde, 2018; Secretaria de Governo, 2021). It is fundamental to have consistent budget planning, with well-defined management priorities and expenditure planning, so the public system can play its due role (Secretaria de Governo, 2021). The pandemic was not predicted in 2019 for the 2020 fiscal year planning, as this variable and its magnitude were unknown at the time. Nevertheless, even in the face of these issues, shortage was not more prevalent in the public institutions.

Most institutions related the neuromuscular blocking agents and sedative-hypnotic drug unavailability. The vasoactive drugs and antimicrobials also stood out as the classes with the most significant shortage indices. These drugs are usually indispensable in the management of patients under intensive care. Nearly 70% of the patients affected by COVID-19, on mechanical ventilation, need neuromuscular blockers (Ferrando et al., 2020).

In Saudi Arabia, a study conducted in the online survey format also assessed the availability of essential drugs and personal protective items during the COVID-19 pandemic. The authors described the shortage of health products, especially cisatracurium, enoxaparin, dexamethasone, methylprednisolone and hydroxychloroquine (Aljadeed et al., 2021).

The Food and Drug Administration (FDA) health agency identified 115 pharmaceutical inputs with insufficient availability to meet the demand during the pandemic in the USA. Neuromuscular blockers (cisatracurium), sedatives (dexmedetomidine, midazolam, fentanyl, and etomidate), beta-lactam antibiotics (cefazolin, cephalothin, ceftazidime/avibactam, ceftozolone/tazobactam, imipenem/cilastatin) were the main unavailable drugs(Food and Drug Administration, 2021). The European Medicines Agency (EMA) also reported supply problems for midazolam, ceftozolone/tazobactam, fondaparinux and tigecycline, among others(European Medicines Agency, 2018).

Some scientific societies also conducted surveys to monitor the problem (Fox et al., 2009; Sociedade Brasileira de Farmácia Hospitalar, 2021). For example, in the USA, the American Society of Health-System Pharmacists (ASHP) conducted a survey during July 2020 with 131 correspondents(Ministério da Saúde, 2018). It indicated that drugs used in intensive care units were being replenished, except for neuromuscular blockers. In Brazil, most (65.4%) of the 731 participating hospital and clinical pharmacists indicated, in June 2020, that the health units in which they worked were not supplied and structured for the care needs in the following three months, according to a survey carried out by the Brazilian Society of Hospital Pharmacy(Sociedade Brasileira de Farmácia Hospitalar, 2021). Despite shortage of health products in several countries, their intensity varies. For example, one study indicated that the drug shortage increased by 300% in Australia while, in the USA, it only increased by 37% in 2020(Cameron & Bushell, 2021). Unfortunately, shortage monitoring in Brazil was initiated due to the pandemic; therefore, we were unable to measure the extent to which the pandemic affected the shortage of health supplies in the country (Agência Nacional de Vigilância Sanitária, 2021).

The unavailable drugs were mainly those in which there was a considerable change in consumption or incorporated during the first year of the pandemic (Table 4). In Brazil, many patients receive azithromycin, chloroquine/hydroxychloroquine, ivermectin, and nitazoxanide Brazil for COVID-19 treatment (Paumgartten & Oliveira, 2020). In the analysis of the institution clusters, we noticed that services with more beds and a drug distribution system that allows for their greater control (such as individual or unit doses) also suffered from a lack of drugs. We conjectured that large-

sized tertiary-level hospitals received more patients with a worse severity profile of COVID-19. Accordingly, they consumed more supplies and, even with higher safety stocks and strict control of the arsenal through the distribution system, they could not prevent a shortage.

Expansion of the therapeutic arsenal was a measure to mitigate shortage widely reported among the respondents. This action had not been reported in the previous studies (Badreldin & Atallah, 2021; Bohand et al., 2021; Shukar et al., 2021). Another measure was the adoption of an action plan. The importance of devising an action plan for shortage cases, listing care priorities, management strategies and possible therapeutic alternatives, is already indicated in the literature. Among the coping strategies, we emphasize the need to seek and increase the volume of (i) information about the problem and (ii) pharmaceutical care management strategies, aiming at scheduling and seeking other specific alternatives (exchange of drugs, maintenance of safety stock, etc.) in certain health contexts(Chaves et al., 2021; Palomar-Fernández & Álvarez-Díaz, 2020).

Studies related to the discussion of the causes for the shortage and the organization of the pharmaceutical sector are still substantial gaps in the field[17]. In addition, the lack of published reports about the responses by the health system to the COVID-19 pandemic has emphasized the need to systematically capture internally-generated data as a strategy for consolidating information that might support decision-making in the health services (Cundell et al., 2020).

Ying and colleagues (Ying et al., 2020) indicated that active pharmaceutical care management methodologies helped mitigate shortages in a Chinese hospital during the COVID-19 pandemic, such as management of donated drugs, implementation, expansion of the drug stock, and conduction of pharmacoeconomic studies. Multiple brainstorming sessions to identify potential threats to providing quality care to patients with COVID-19, creating reports to determine drug supply and daily consumption rates also contributed to minimizing shortage during the first COVID-19 wave (Pulk et al., 2020). Pharmacists in the United Kingdom have been working in the strategic management of COVID-19, acting as leaders in the national chain of drugs, prioritizing sedatives and antibiotics. In Qatar, a pharmaceutical supply group was responsible for monitoring the shortage of health products (Merchan et al., 2020).

Some actions can mitigate the possible consequences of scenarios with the shortage of pharmaceutical inputs (Fox et al., 2009). Changes and adaptations in hospital units to alleviate the lack of drugs are crucial, mainly given the possibility of new waves. Measures such as implementing a situational diagnosis team and reviewing the essential drugs required successfully created the necessary storage space for new items and anticipating information about any interruptions in the supply chain (Merchan et al., 2020). High-income countries have developed countless strategies to manage the shortage of health products (World Health Organization, 2016). However, the measures may not be effective for developing countries considering different scenarios. For example, the American Society of Health-System Pharmacists (ASHP) attributes the shortage of health products to the following causes: 57% to unknown causes, 2% to regulatory issues, 14% to bureaucratic issues, 12% to demand greater than supply, 8% to manufacturing problems and 7% to lack of raw material (American Society of Health-System Pharmacists, 2021), while the factors most mentioned in our study as related to shortage were “Scarce epidemiological data for effective forecasting of essential inputs” and “Insufficient scheduling carried out in view of the significant seasonal variation”.

However, it is noteworthy that, even if there is internal planning that tries to mitigate a potential shortage of drugs and/or health products, when shortage does occur, whether in the national or international market, there is very little that can be done by the local manager, as seen in the current scenario of the COVID-19 pandemic (Merchan et al., 2020).

The causes for the shortage of health products are complex and varied. Before the COVID-19 pandemic, high-income countries conducted research studies on the topic (Acosta et al., 2019). However, low- and middle-income countries live an

opposing reality (Schweitzer, 2013). The situation of drug shortage also varied across the different countries. In high-income countries, almost all classes of drugs are affected, and their stock is reduced in different periods.

Some limitations of this study are also noted. As this is an online survey with no funding, we decided to analyze a convenience sample, precluding generalization of the findings to other health services in the country. Given the number of Brazilian health units, it was impossible to obtain a significant sample *n*, estimated at 800 participating services (Oliveira, Ely Francina Tannuri; Grácio, Maria Claudia Cabrini, 2022). The diverse information obtained portrays a punctual scenario within a specific period, considered the "first COVID-19 wave", and it is not possible to assess the evolution of the stock situation in the participating health units.

The need for monitoring by the managing units is evident and, above all, the urgency of implementing actions to minimize shortage. Furthermore, the scenario imposed by the COVID-19 pandemic requires harmonization of the national records so that it is possible to develop joint solutions sustainably and as soon as possible (Vogler & Fischer, 2020)

5. Conclusion

Most participating services reported shortages during the COVID-19 pandemic, especially for essential drugs to maintain life in the ICU, such as neuromuscular blockers. Expansion of the therapeutic arsenal to search for drugs that meet the hospitalized patients' demand seems to have been a mitigation measure adopted by the participating institutions.

Cluster analysis allowed assessing shortage in the most diverse health services, pointing to an endemic problem during the COVID-19 pandemic. We did not notice any correlation between characteristics inherent to the health services and shortage of inputs. Most of the respondents implemented all the measures they deemed feasible to mitigate the shortage of drugs. Despite the country's diversity, the report frequency regarding shortage was uniform across the Brazilian states. For this reason, the results found suggest that external factors may have driven the reality experienced by the Brazilian health services. Future research and a national program for the supply of pharmaceutical ingredients are essential to improve knowledge about this problem and to avoid drugs stockouts.

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