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Challenges to the consolidation of pharmacovigilance practices in Brazil: limitations of the hospital pharmacist

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Abstract

Aims: The aim of this study was to present the needs of hospital pharmacists in pharmacovigilance practices.

Methods: This study has a cross-sectional design and was carried out with hospital pharmacists in Brazil. The sample was obtained by voluntary recruitment. Pharmacists who worked at Brazilian hospitals and were registered in their respective regulatory councils were invited to participate in the present study. A personalized questionnaire was developed by the authors and was electronically filled out by the respondents on the platform 'Google forms'. The questionnaire was nationally available on the digital platform of the Pharmacy Federal Council, the Brazilian Society of Hospital Pharmacy and Health Services, four Pharmacy regional councils and the social network farmacêuticoclínico®. Quantitative variables were analyzed by mean and standard deviation. The qualitative variables were analyzed by means of absolute and relative frequency. Difficulties related to pharmacovigilance activities are presented in an Ishikawa diagram in the Supplemental Material online.

Results: Of the 27 federative units of Brazil, we obtained answers from pharmacists located in 85.2% ($n = 23$) of them. Among the pharmacovigilance practices developed by Brazilian pharmacists, the adverse drug reaction investigation (55.4%) and notification activities (47.0%) were worthy of note. Numerous difficulties were reported by the pharmacists, highlighting the difficulty in monitoring the medication and imputation of causality (27.7%). After categorizing the difficulties reported, it was observed that the category 'people involved' (45.1%) stood out from the others.

Conclusion: This study pointed out numerous challenges to pharmacovigilance practices involving pharmacists in Brazil. It is believed that the correction of certain difficulties may impact on the better consolidation of pharmacovigilance activities in the country. However, regulatory agencies at all hierarchical levels of pharmacovigilance must work together to make it possible.

Keywords: hospitals, pharmacists, pharmacovigilance

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Plain language Summary

Challenges to the consolidation of pharmacovigilance

This is a study that seeks to present the needs of Brazilian hospital pharmacists in relation to pharmacovigilance activities. Through online interviews, pharmacists answered a questionnaire, presented the pharmacovigilance activities they develop and expressed

their anxieties and difficulties for the development of these activities. With this study, it was concluded that numerous activities of active search, investigation and notification of adverse drug reaction are developed by Brazilian pharmacists. However, each pharmacist performs a different method of pharmacovigilance. In addition, it was observed that among the interviewees there was a perception of insufficient professional training and a shortage of professionals to assist in pharmacovigilance activities. These were the main difficulties reported. Therefore, the search for models or agile solutions to solve problems involving adverse drug reactions seems necessary for a better consolidation of pharmacovigilance services in Brazil.

Introduction

Pharmacovigilance is defined by the World Health Organization (WHO) as 'the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem'.[1] After 50 years of the WHO Program for International Drug Monitoring, which has set up the modern pharmacovigilance, ways to manage elementary situations are still being refined, and pharmacovigilance remains affected by old challenges.[2–4]

Although the recent improvements in science and technology have changed the nature of such challenges, some questions still impose barriers to the effectiveness of this strategy. Willingness to engage the public, collaboration and partnerships, incorporate informatics, adopt a global approach and assess the impact of efforts appear to be ongoing challenges in drug safety surveillance.[4–6] Fragile knowledge about the use of medicines in pediatrics is also a challenge to ensure this safety.

In Brazil, the challenges have no differences. The underreporting of adverse drug reactions (ADRs), whose main causes are the ignorance, insecurity or indifference of health professionals,[7] the culture of disregard for rules of the State legislation, the low equity in the allocation of pharmacovigilance resources in the Brazilian territory, the incompatibility between the national and global database, and the ineffective monitoring and enforcement of regulatory agencies seem to reinforce the global challenges.[3,8,9]

In this context, hospitals seem to be the driving force of pharmacovigilance in Brazil, representing the main centers for reporting ADRs.[10] In particular, sentinel hospitals set up an ADR reporting network that strengthens the pharmacovigilance. Furthermore, safety programs in the use of medicines ascribe responsibility to the pharmacist towards drug safety indicators.[10,11]

Regarding this healthcare professional, studies point out the substantial role of the pharmacist in reporting ADRs, both in number and in the quality of reports.[12,13] However, many issues are still raised. Is the pharmacist prepared to meet legal requirements assigned by the regulatory agencies? What are the difficulties faced by this professional that may hinder your best performance in pharmacovigilance? Are the regulatory agencies offering support to a better performance of the pharmacist in this program?

On one hand, it is believed that the pharmacist needs more training and support to optimize his role in pharmacovigilance.[14,15] On the other hand, it is believed that during the drafting and execution of legal guidelines, regulatory agencies should understand the needs of professionals who will execute them. Therefore, this study aimed to present evidence on the activities, difficulties and knowledge of hospital pharmacists, and the access to information on the use of information tools and e-accessibility while performing pharmacovigilance activities in Brazil.

Methods

The present study was written based on the Strengthening the Reporting of Observational studies in Epidemiology statement and was approved by the ethics committee of the Federal University of Sergipe Foundation, in registration through CAAE: 90850318.4.0000.5546.

Study design and population

This study had a cross-sectional design carried out with hospital pharmacists in Brazil. Brazil is a

country with 27 federative units that currently has a density of 9.1 pharmacists per 10,000 inhabitants.[16] In 2018, the country had 6.934 hospital pharmacists registered on the federal regulatory council, corresponding to 3.1% (6934/221,258) of the total number of registered pharmacists.[17]

The period of data collection occurred between 1 March and 31 May 2018. The sample was obtained by voluntary recruitment. Pharmacists who worked at Brazilian hospitals and were registered in their respective regulatory councils were invited to participate in the present study. We excluded pharmacists who, by mistake, answered the questionnaire and declared that they did not have any professional experience in hospital environments.

Questionnaire and variables

A personalized questionnaire was constructed by the authors. The questionnaire included: (i) closed questions about professional characteristics (training time, hospital working time, experience in working with a pediatric population, previous enrollment in graduate programs); (ii) open-ended questions about demographic characteristics (age and place of professional performance) and pharmacovigilance activities (techniques used in the work environment, more challenging techniques, reason that the respondent attributes the difficulty to); (iii) closed questions (five-point Likert-type scale) on: research activities of ADRs, collection of information on the incidence of ADRs, importance of interviewing the patient and making information regarding ADRs readily available to healthcare professionals; and (iv) mixed questions about the use of information tools and e-accessibility.

Data collection

Data collection was performed with no regard to time management nor under the supervision of an evaluator. The questionnaire was electronically filled out by the respondents on the platform 'Google forms' and prior consent was obtained. The online questionnaire provided the volunteers with the option whether or not to consent to their participation in the research, after presenting the informed consent form.

The questionnaire was made nationally available on the digital platform of the Pharmacy Federal Council and the Brazilian Society of Hospital Pharmacy and Health Services. At the federation level, the questionnaire was only available on the digital platform of the pharmacy regional councils of Amapá, Minas Gerais, Mato Grosso and Mato Grosso do Sul, although all Brazilian regional councils were triggered for the dissemination of the questionnaire.

The questionnaire was also made available *via* personal emails and digital platforms unique to pharmacists, namely, the group of hospital clinical pharmacists of the social network farmacêuticoclínico®.

Data analysis

Quantitative variables were analyzed by mean and standard deviation. The qualitative variables were analyzed by means of absolute and relative frequency by a pharmacist with specialization in hospital pharmacoepidemiology (PHSA) and were presented as follows: (i) demographic and professional characteristics were subdivided by regions of Brazil; (ii) the pharmacovigilance activities reported by the respondents were grouped into three categories: active search, investigation and notification of ADRs; (iii) difficulties related to pharmacovigilance activities were presented in an Ishikawa diagram (Supplemental Material online) grouped into categories corresponding to the main characteristics described; in addition to this diagram, a radar chart was used to group the difficulties into categories, namely: people involved, used methods, work environment, obtaining information, pharmacovigilance measures; and (iv) the variables obtained by Likert scale were presented in a stacked divergent bars chart.

Results

Demographic and occupational characteristics of pharmacists

A total of 84 pharmacists answered the questionnaire. Of the respondents, 83 met the eligibility criteria and were included in the present study. The demographic and occupational characteristics of the included population can be observed in Table 1. The mean age of this population was 34.2 years ($\sigma = 7.1$ years). Of the 27 federative units, we obtained answers from pharmacists located in 23 (85.2%). We did not get answers

Table 1. Demographic and occupational characteristics by Brazilian region.

	Midwest	Northeast	North	South	Southeast	Total
Age (mean ± σ)	33.6 (±7.5)	31.7 (±5.9)	39.9 (±8.5)	36.3 (±10.1)	35.8 (±5.6)	34.2 (±7.1)
Training time	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)
<1 year	1 (1.2)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.4)
1–2 years	1 (1.2)	5 (6.0)	0 (0.0)	1 (1.2)	1 (1.2)	8 (9.6)
2–3 years	0 (0.0)	3 (3.6)	0 (0.0)	0 (0.0)	0 (0.0)	3 (3.6)
3–4 years	0 (0.0)	3 (3.6)	0 (0.0)	0 (0.0)	3 (3.6)	6 (7.2)
4–5 years	0 (0.0)	5 (6.0)	0 (0.0)	0 (0.0)	1 (1.2)	6 (7.2)
>5 years	3 (3.6)	24 (28.9)	10 (12.0)	6 (7.2)	15 (18.1)	58 (69.9)
Total	5 (6.0)	41 (49.4)	10 (12.0)	7 (8.4)	20 (24.1)	83 (100.0)
Previous enrollment in graduate programs						
Specialist	2 (2.4)	23 (27.7)	6 (7.2)	4 (4.8)	12 (14.4)	47 (56.6)
Master	1 (1.2)	9 (10.8)	3 (3.6)	1 (1.2)	3 (3.6)	17 (20.5)
PhD	0 (0.0)	3 (3.6)	1 (1.2)	1 (1.2)	1 (1.2)	6 (7.2)
Post doc	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)
None of the previous options	2 (2.4)	5 (6.0)	0 (0.0)	1 (1.2)	4 (4.8)	12 (14.4)
Total	5 (6.0)	41 (49.4)	10 (12.0)	7 (8.4)	20 (24.1)	83 (100.0)
Hospital working time						
<1 year	2 (2.4)	5 (6.0)	0 (0.0)	1 (1.2)	0 (0.0)	8 (9.6)
1–2 years	0 (0.0)	10 (12.0)	1 (1.2)	2 (2.4)	1 (1.2)	14 (16.8)
2–3 years	0 (0.0)	8 (9.6)	0 (0.0)	1 (1.2)	1 (1.2)	10 (12.0)
3–4 years	1 (1.2)	5 (6.0)	0 (0.0)	0 (0.0)	1 (1.2)	7 (8.4)
4–5 years	0 (0.0)	1 (1.2)	2 (2.4)	0 (0.0)	2 (2.4)	5 (6.0)
>5 years	2 (2.4)	12 (14.4)	7 (8.4)	3 (3.6)	15 (18.1)	39 (47.0)
Total	5 (6.0)	41 (49.4)	10 (12.0)	7 (8.4)	20 (24.1)	83 (100.0)
Experience in working with pediatric population	2 (2.4)	28 (33.7)	9 (10.8)	5 (6.0)	17 (20.5)	61 (73.5)

σ, standard deviation; *n*, number of respondents

from pharmacists registered in the regional councils of Alagoas, Amapá, Piauí and Roraima. Some respondents declared a time of professional training inferior to the time worked in hospital environments. The respondent probably worked in hospitals before completing graduation.

Pharmacovigilance practices developed and associated difficulties

Among the pharmacovigilance practices developed by Brazilian pharmacists, the ADR investigation (55.4%) stood out on active search (41.0%) and notification activities (47.0%) (Table 2). It is noteworthy that respondents did not always report the approach taken in the active search for ADRs.

Difficulties involved in pharmacovigilance practices

Many obstacles were reported by the pharmacists, highlighting the difficulty in monitoring the medication and imputation of causality (27.7%) (Figure 1; Supplemental Figure 1). After categorizing the difficulties reported, it was observed that the category 'people involved' (45.1%) stood out among the others, followed by 'work environment' (25.5%) (Supplemental Figure 1).

Knowledge about the research process and active search for ADRs

Although many problems were raised, most pharmacists claimed to have no difficulties to: (i) identify suspected medicines among the prescribed ones (66.2%); (ii) differentiate the clinical picture and the adverse drug event (48.2%); (iii) find information on the incidence of adverse drug events (71.1%); and (iv) be able to identify patients at risk for ADRs in the hospital beds (65.1%) (Figure 2).

Access to information

Regarding the collection and access to information, 83 (100%) pharmacists considered it important to collect information about the history of ADRs and the availability of information about drugs and drug interactions. In order to contribute to the access of information, the majority (42; 50.6%) reported not having a free wireless network in the hospital where they work. Eighty-two respondents (98.8%) would take a computer, tablet or cell phone to work.

To obtain information about medicines, 67 (80.7%) of the pharmacists used applications or software. The most used were MICROMEDEX (39.0%), Medscape (24.4%), UptoDate (20.7%), Drugs.com (14.6%) and Epocrates (7.3%).

Discussion

Since the 1960s, with the 'thalidomide epidemic', there has been a global effort towards the advent of pharmacovigilance. In Brazil, after almost 20 years, the first regional pharmacovigilance centers were created. However, it was not until the late 1990s that the pharmacovigilance field was strengthened with the creation of the Brazilian Health Surveillance Agency (ANVISA).[8,10]

From this period to date, pharmacovigilance in Brazil has focused on notification;[10] however, it has not been proved to have a direct impact on patient care yet.[18] Although there is a surveillance network for medicine and a small production and dissemination of information to healthcare professionals about the health risk for some medicines, there is no effective monitoring of the notified events at national level or any responses that may directly impact the patient involved.[10]

In addition to these findings from the literature, the reporting rates in Brazil are still lower than the rates foreseen by the global regulatory agencies.[10] There have been several attempts to improve notification, but they do not appear to be reflecting concrete results.[19] Under this perspective and based on our results, the support to healthcare professionals involved in this practice does not seem adequate in the country.

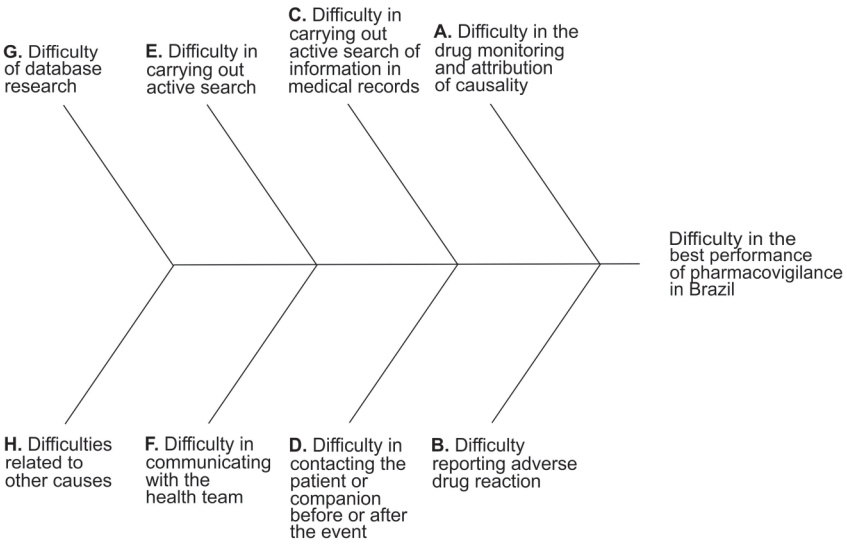
When observing the reports found in the present study regarding absence or difficulty of access to information, lack of knowledge, clinical inexperience, uncertainty in confirming an ADR, insufficient technical background, poor understanding of the diseases in question, poor patient safety culture, concern of administrative process, unavailability of an exclusive professional, we believe that, in fact, financial support is not being directed to human resources. Endorsing such, the main reported category related to the difficulties related to pharmacovigilance practices was 'people involved'.

Having an exclusive hospital pharmacovigilance service, according to the reports observed in this study, seems to have an impact on better results for patient safety. Statements on insufficient technical framework, absence of unique professionals and fear endorsed this conclusion.

Table 2. Pharmacovigilance practices developed by Brazilian pharmacists.

Pharmacovigilance practices developed	*n* (%)
Active search	34 (41.0)
Trigger tool†	11 (13.2)
Interview with patient, family member and/or companion‡	7 (8.4)
Monitoring of medical records	6 (7.2)
Signs of ADR by the multidisciplinary team *in loco*	4 (4.8)
Monitoring of prescription drug interactions	1 (1.2)
Investigation	46 (55.4)
Collection of information with the patient, family member and/or companion	28 (33.7)
Pharmaceutical anamnesis including, or not, patient interview§	18 (21.7)
Collection of family or individual ADR history	9 (10.8)
Pharmacotherapy follow-up or monitoring of signs and symptoms	3 (3.6)
Photographic register	1 (1.2)
Causality and tracing of suspected drugs (e.g. Naranjo, Lasagna, WHO) or by analysis of temporality or rechallenge	19 (22.9)
Review of pharmacotherapy with or without checking drug interactions or of prescription errors	16 (19.3)
Review of records in medical records	13 (15.6)
Search for information in the literature	12 (14.4)
Collection of information with the multiprofessional team	11 (13.2)
Analysis and detailing of the product¶	6 (7.2)
Evaluation or request for laboratory tests	5 (6.0)
Assessment of preparation and administration technique	5 (6.0)
Gravity analysis	3 (3.6)
Contact with the notifier	2 (2.4)
Patient care	1 (1.2)
Identification of those involved in the event	1 (1.2)
Notification	39 (47.0)
Notification to pharmacovigilance services of own hospital	37 (44.6)
Notification to the competent surveillance authority	5 (6.0)
Notification to the manufacturer of the medicinal product	2 (2.4)
Does not develop activities	10 (12.0)
Responsibility of the core of health surveillance	3 (3.6)

†Involves evaluation of laboratory tests, prescription of drug triggers (antidotes, antihistamine, corticoid) and abrupt suspension of medication.
‡Involves pharmacotherapy follow-up and evaluation of signs and symptoms at the bedside.
§Intended to better understand the suspected event (e.g. sequence of events, nature of the injury or ADR, date, time, location, symptoms or injury description).
Refers to excipients; storage conditions; lot; manufacturer's regularity, request for sample analysis of the product to the supplier.
ADR, adverse drug reaction; *n*, number of respondents; WHO, World Health Organization.



	A	B	C	D	E	F	G	H
n	23	17	17	16	12	9	7	15
%	27.7	20.5	20.5	19.3	14.5	10.8	8.4	18.1

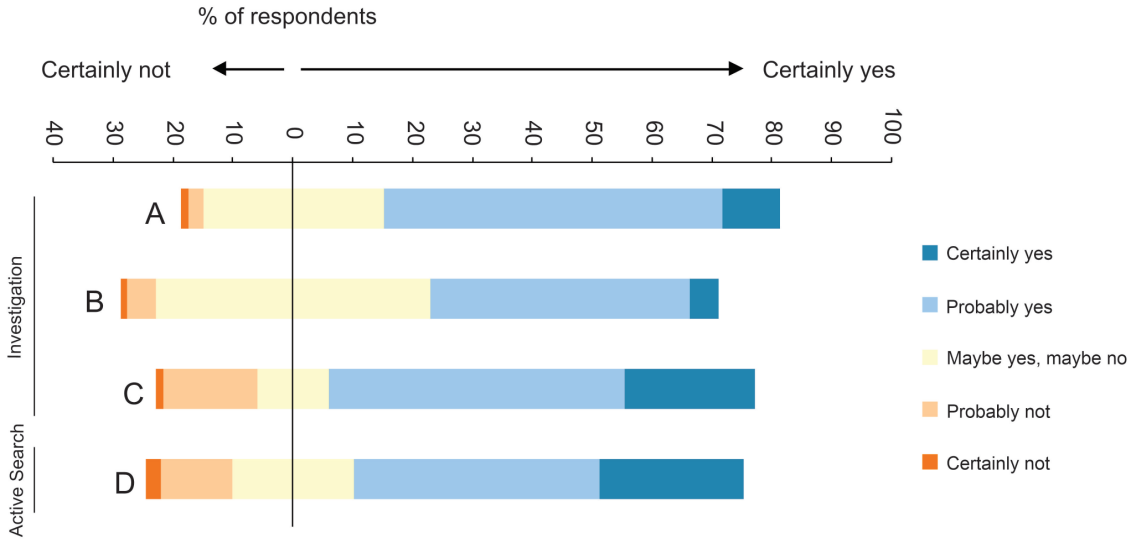
Figure 1. Difficulties reported by pharmacists in the best pharmacovigilance performance in Brazil.
%, percentage; *n*, number of respondents.

Regarding these concerns, Faustino *et al*. claim that more effective public policies, with the creation of indicators that should be closely monitored by health agencies, or on-site supervision of the development of such activities, may constitute a good response to the reported difficulties.[18] Thereby, we can highlight through our results the need to improve public policies that should reach undergraduate and graduate programs in healthcare, especially among pharmacists, since the majority of the population of this study were enrolled in a graduate program and numerous difficulties were reported related to professional training.

Despite this reality, the results obtained in the present study demonstrate that the pharmacovigilance system in Brazil has been shaping up to the reality of each region. There are activities designed by different methodologies for the identification of ADRs, case studies and notifications. Although the numbers demonstrate a small percentage of pharmacists involved in each of these steps, there is a portion of pharmacists performing quite specific activities that are stated in the literature as having a high impact on positive pharmacovigilance results, such as trigger tools.[20]

Moreover, the data collection is carried out in practically all steps involving information recording, stakeholder participation, laboratory results and literature research. ADR investigation has been developed by a broad range of pharmacists. The notification covers all hierarchical levels of pharmacovigilance. Thus, although there are relevant flaws and difficulties in the data collection, one of these steps is being developed in some region of the country. Also, this may be explained by the time of work in hospitals, graduation time and specialization level, which all were high in the studied population, or even by the highest number of respondents from Northeast Brazil, where pharmacovigilance began in the country and where the main pharmacovigilance centers are located.

From this standpoint and based on the reported difficulties, it seems that there is a need to develop tools to assist pharmacists in achieving better performance in pharmacovigilance. We believe that such tools should probably be related to active search at hospital beds, including medical prescription and patient's record, as well as causality analysis, and the notification that best suits the Brazilian reality.



	Certainly yes		Probably yes		Maibe yes, maybe no		Probably not		Certainly not	
Questions	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
A. Could you identify which drugs are suspected among prescribed drugs?	8	9.6	47	56.6	25	30.1	2	2.4	1	1,2
B. Could you tell whether the event was due to a drug or the patient's clinical condition?	4	4.8	36	43.4	38	45.8	4	4.8	1	1,2
C. Would you know where to look for the ADR incidence of the drugs being investigated?	18	21.7	41	49.4	10	12.0	13	15.7	1	1,2
D. Are you able to identify those patients who are at an increased risk for developing ADR?	20	24.1	34	41.0	17	20.5	10	12.0	2	2,4

Figure 2. Level of knowledge of Brazilian pharmacists in specific stages of investigation and active search of adverse drug reaction.
ADR, adverse drug reaction.

Although there are many tools already described in the literature that help these processes,[21–24] some are imprecise,[25,26] unavailable, or have no cross-cultural translation that meets the need and reality of Brazil and which seems to be indispensable.[27] According to the results obtained in the present study, these tools may be developed as systems or applications for mobiles, tablets or laptops; however, they should be able to operate in offline versions.

In addition to these findings, our results also indicate that there seems to be a need related to the prevention of ADRs or mitigation of these events. In this case, proposals related to ADR management protocols,[28] or description of risk factors for ADRs to characterize risk populations,[29] could support pharmacovigilance practices.

Regarding the pharmacist's ability to carry out pharmacovigilance, it was observed that the pharmacist's training, experience and knowledge (Table 1 and Figure 2) make this professional capable of developing such activities. However, there must be financial support in human and material resources at national, regional and local levels. As for human resources, health education tools may bring positive results.[30,31] Regarding material resources, the availability of tools for accessing information based on scientific evidence, such as those previously mentioned, and facilities for the development of pharmacovigilance activities might have immeasurable benefits.

Lastly, we believe that investments such as these may optimize the pharmacists' knowledge, help to disseminate the patient safety culture, improve

the pharmacist–patient relationship or that between professional healthcare teams, enhance medical record documentation and increase ADR notification in the country.

Limitations

This study should be analyzed based on its limitations. Although there was an effort to increase the sample size, the sample number is small; thus, we chose to discuss evidence of limitations for the consolidation of pharmacovigilance in Brazil, as these results may not be representative of the Brazilian population. In the studied population, most respondents were from Northeast Brazil, which may represent a confounding bias. Being part of a larger project involving pediatrics and having been presented to the respondents as part of it, the present study may have expanded access to pharmacists involved with pediatrics and limited access to other pharmacists. Also, because it did not reach a larger number of newly trained professionals, the study may not have presented all the difficulties of this population and, consequently, not be totally representative of it. Regarding the inherent limitations of the method, it is important to highlight the voluntary participation of pharmacists generally engaged with the subject (pharmacovigilance) that work directly in pharmacovigilance services or who used the questionnaire as a way to report problems observed in the daily life of this service. Despite efforts, the sample was not large enough to perform statistical analysis of association that could result in safer outcomes and, therefore, this was not shown in this study.

Conclusion

Brazilian pharmacists perform numerous activities relevant to the best performance of pharmacovigilance. However, some difficulties, especially those involving human resources, seem to stand out, followed by issues involving the work environment. Although they report such difficulties, there are indications that many Brazilian pharmacists are fit to perform pharmacovigilance, reporting, for the most part, that they have few obstacles with specific processes of research and active search. Regarding this, it is worth mentioning that most pharmacists had been previously enrolled in a graduate program and had greater involvement with the pharmacovigilance service. Access to information was considered very important by them, although they still have difficulties with this access in the work environment.

This study pointed out numerous challenges to pharmacovigilance practices involving pharmacists in Brazil. It is believed that the correction of certain difficulties, found in the present study, may impact on the better consolidation of pharmacovigilance activities in the country. However, regulatory agencies at all hierarchical levels of pharmacovigilance must work together to make it possible. Based on the findings of this study, it is possible to develop such activities with local changes, or with the effective participation of only one pharmacist. Nevertheless, all these strategies only affect a small percentage of the hospitals and, at national level, this impact continues below international expectations.

Conflict of interest

The authors declare that there is no conflict of interest.

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Supplemental material

Supplemental material for this article is available online.

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