Brazilian Journal of TRANSPLANTATION

ORIGINAL ARTICLE

Adverse Events in Cells, Tissues, and Organs Donation and Transplantation

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https://doi.org/10.53855/bjt.v25i2.461_en

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Section Editor
Ilka Boin

Received
Abr. 14, 2022

Approved:
Maio 3, 2022

Conflict of interest
Nada a declarar

How to Cite

Paim SMS, Roza BA, Schirmer J. Adverse Events in Cells, Tissues, and Organs Donation and Transplantation. BJT.2022. 25(02):e8222. https://doi.org/10.53855/bjt.v25i2.461.en

eISSN
2764-1589

Abstract: **Objective:** To characterize adverse events in cells, tissues, and organs donation, and transplantation notified in the state of São Paulo, Brazil. **Method:** Descriptive study with quantitative approach. Data provided by Transplantation Central of São Paulo from the "Individual notification form of adverse reactions in Biovigilance", of the FormSUS platform, between 2016 and 2019, and categorized according to the nomenclature recommended by the World Health Organization regarding nature and type of event, severity, and imputability. Analysis was performed using descriptive statistics. **Results:** Fifty-two notifications were characterized, 90.4% related to the recipient, 78.8% from allogeneic procedures, 48.2% related to organs, and 44.2% to hematopoietic stem cells. The causes of notifications were infections (55.7%), other ones (30.8%), and neoplasms (13.5%). Most of the events were moderate (44.3%), and 36.5% were confirmed. **Conclusion:** It was possible to identify the scenario of biovigilance in the state, visualizing that the main adverse events are related to the receptor from allogeneic procedures. In addition, the major cause of adverse events in the state of São Paulo are infections, especially those caused by *Mycobacterium tuberculosis* and *Klebsiella pneumoniae*. The characterization of these events can support the development of safety strategies to prevent recurrence, the realization of institutional training and public policies to encourage notification and expand the understanding of adverse events in this scenario, since it is only possible to ensure quality and safety in health care, especially in the context of donations and transplants, from the recognition of reality.

Descriptors: Biosurveillance; Transplants; Tissue and Organ Procurement; Cell Transplantation; Tissue Transplantation; Patient Safety; Nursing.

INTRODUCTION

Over the past few years, the subject of patient safety has gained increasing prominence. There are several protocols, guidelines, legislations, tools, and researches that bring information, safety improvement strategies, regulations, and important definitions to the subject.[1–3]

In transferring this discussion to the area of cell, tissue and organ donation and transplantation, another equally important concept is added: biovigilance. This is surveillance in the context of organs, tissues, cells, and human body parts from donation to transplantation in the recipient. It aims to identify information about risks and adverse events that may occur throughout the process.[4]

In Brazil, until February 2021, the notification of adverse events in donation and transplantation was carried out using an online form located in FormSUS.

FormSUS was an online form preparation system for use by the Brazilian Unified Health System (UHS) and partner public agencies. The "Form for individual notification of adverse reactions in biovigilance" could be found on this platform; however, the website suffered attempted cyberattacks, which compromised the security of the information, and, therefore, a decision to cancel this means of notification was made. Still, managers and registered professionals remained with access to old notifications and the ability to generate document with all the necessary details.[5,6] Currently, the notifications of adverse events are still performed by the individual adverse reaction notification form in biovigilance, but this is sent through the virtual platform LimeSurvey.[4]

Thus, in February 2020, the Collegiate Directive Resolution No. 339 was published by the National Health Surveillance Agency (Anvisa), which provides for the establishment of the National Biovigilance System, becoming an important milestone, bringing a new perspective and establishing the taxonomy for a new national scenario in biovigilance.[7]

Worldwide, initiatives regarding the notification of adverse events have been developed. An example is the Notify project, which gathers cases of adverse events and reactions and the lessons learned from each case.[8] The notification and analysis of adverse events, as well as the action plan to mitigate damage and prevent recurrence of these events, are relevant strategies to map the problems, ensure improvement in the quality of health services and patient safety, but there are still few studies published that portray this scenario, both locally and nationally or internationally.[9]

In view of the above, the need to identify the reality of biovigilance in the state of São Paulo through the identification and analysis of adverse events already reported was observed. Therefore, the aim of this study was to characterize the adverse events in cell, tissue, and organ donation and transplantation reported in the state of São Paulo.

METHODS

Descriptive study with a quantitative approach. The object of the study was the notifications of adverse events in donation and transplantation of hematopoietic stem cells (HSC), tissues and organs performed in the FormSUS electronic form in the state of São Paulo. The data from 2016 to 2019 were provided by the State Transplant Center of the state of São Paulo, which authorized its use in this research.

The study had the state of São Paulo as a scenario, since it is the Brazilian state with the highest number of transplants. In 2021, there were 2,676 solid organ transplants performed, 1,755 HSC transplants, and 4,980 eye tissue transplants. As for donation, the state reached the mark of 995 effective donors, while the national figure for solid organ transplants was 7,359, for ocular tissues 12,744, for HSC 3,826, and for effective donations 3,207.[10]

To obtain the study data, we used the document generated by FormSUS through the "Form for individual notification of adverse reactions in biovigilance." The notifications made in the system were used, and data were collected according to the fields to be filled in the notifications: date of procurement (when the adverse event related to the donor), date of the procedure (when the adverse event related to the recipient), type of procedure related to the adverse reaction, nature of the event (HSC, tissue or organ), date of detection, type of the adverse reaction, severity, correlation of the adverse reaction with the procedure involving cells, tissues and organs, description of the adverse reaction, description of measures in progress, date of notification, and observations.

All sensitive information, such as names of patients or professionals, institutions, birth dates, or any other information that could identify patients, was excluded before data collection. Therefore, data collection did not require the use of an informed consent form.

Fifty-six notifications made between the years 2016 and 2019 were available, and 52 were included in the study. The exclusion of four notifications was made because they presented incompatibility in the filling of important information, such as the date of the procedure and the date of detection of the adverse event. Therefore, it was understood that the remaining information could be compromised.

The information from the notifications was categorized according to the nomenclature recommended by the World Health Organization (WHO), the Brazilian Ministry of Health, and Anvisa,[1,4,7,9,11] originating the following categories of analysis: type of event (corresponding to the type of procedure related to the adverse reaction and the type of adverse reaction on the data collection form), nature of the event, severity, and imputability (equivalent to the correlation of the adverse reaction with the procedure involving cells, tissues, and organs).

The information contained in the other fields of the form, such as description of the adverse reaction, description of ongoing measures, and observations, served as support for the analysis of the information.

All data were analyzed with descriptive statistics, identifying the relative and absolute frequencies, obtaining a description of the biovigilance scenario in the state of São Paulo. For this, a Microsoft Excel spreadsheet was used. Data collection and analysis occurred between January and October 2021.

The research complied with Resolution No. 466/2012 and Resolution No. 510/2016, of the National Health Council, and was approved by the Research Ethics Committee, under opinion number 4,463,175, and Certificate of Ethics Appreciation Submission (CAAE) No. 39156020.7.0000.5505.

RESULTS

Fifty-two adverse event notifications were characterized in the state of São Paulo between the years 2016 and 2019, which will be presented according to the following categories: nature and type of event, severity, and imputability. Figure 1 illustrates the volume of adverse events notified per year.

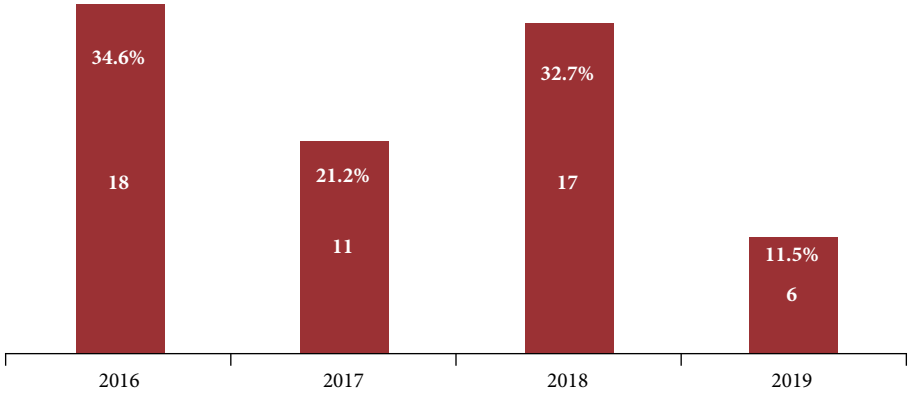

Figure 1. Adverse event notifications performed per year (n = 52). São Paulo, SP, Brazil, 2016–2019.

As for the nature of the event, of the 52 notifications, 90.4% (47) were events related to the recipient, while 9.6% (5) were related to the donor. Also, 78.8% (41) were allogeneic procedures, and 21.2% (11) were autologous procedures. Of the reports, 48.2% (25) were organ-related, 44.2% (23) HSC-related, 3.8% (2) tissue-related, and 3.8% (2) tissue and organ-related.

Regarding the type of event, 55.7% (29) of the notifications were linked to infections, 30.8% (16) to other causes (Table 1), and 13.5% (7) to neoplasms (Table 2).

Table 1. Relationship between adverse event notifications classified as other, nature of the event, severity and imputability (n=16). São Paulo, SP, Brazil, 2016-2019.

Causes of notification	n	%	Nature of the event	Severity	Imputability
Disease recurrence	3	18.5	HSC	Moderate, Moderate and severe	Discarded, discarded and confirmed
Perioperative complications	3	18.5	HSC, lung and kidney	Death	Discarded, confirmed and confirmed
Probable mobility of the dressing	1	6.3	Skin	Mild	Unlikely
Late graft loss	1	6.3	HSC	Moderate	Discarded
Severe allergic reaction	1	6.3	HSC	Severe	Likely
Lack of control in sending the organ	1	6.3	Liver	Death	Discarded
Hepatitis B	1	6.3	Liver	Moderate	Possible
Transfusion reaction	1	6.3	HSC	Mild	Possible
Lowered level of consciousness	1	6.3	HSC	Mild	Possible
Hemorrhagic cerebrovascular accident	1	6.3	Heart	Death	Unlikely
Possibility of infection	1	6.3	Pancreas and kidney	Moderate	Confirmed
Convulsion	1	6.3	HSC	Moderate	Possible
Total	16	100			

HSC: hematopoietic stem cells.

Table 2. Relationship between adverse events reported as neoplasms, nature of the event, severity and imputability (n = 7). São Paulo, SP, Brazil, 2016–2019.

Nature of the event		Severity	Imputability
Receiver	Kidney	Death	Possible
Receiver	Kidney	Severe	Likely
Receiver	Heart	Moderate	Inconclusive
Receiver	HSC	Moderate	Confirmed
Receiver	HSC	Moderate	Discarded
Receiver	HSC	Moderate	Discarded
Donor	Heart, liver and cornea	Moderate	Confirmed

HSC: hematopoietic stem cells.

With regard to severity, the majority (44.3%, 23) were notifications classified as grade 2 (moderate); 25% (13) as grade 4 (death); 19.2% (10) as grade 3 (severe); and 11.5% (6) as grade 1 (mild). With regard to imputability, 36.5% (19) were confirmed, 26.9% (14) discarded, 15.4% (8) possible, 9.6% (5) inconclusive, 7.7% (4) unlikely; and 3.9% (2) likely. Table 3 presents the relationship between severity and determined imputability of the reported cases.

Table 3. Relationship between severity and imputability of reported adverse events (n = 52). São Paulo, SP, Brazil, 2016-2019.

Severity	Imputability	N	%
Grade 2: Moderate	Confirmed	9	17.3
	Likely	0	0
	Possible	4	7.7
	Unlikely	2	3.9
	Discarded	4	7.7
	Inconclusive	4	7.7
Total		23	44.3
Grade 4: Death	Confirmed	4	7.7
	Likely	0	0
	Possible	1	1.9
	Unlikely	1	1.9
	Discarded	7	13.5
	Inconclusive	0	0
Total		13	25
Grade 3: Severe	Confirmed	5	9.5
	Likely	2	3.9
	Possible	1	1.9
	Unlikely	0	0
	Discarded	2	3.9
	Inconclusive	0	0
Total		10	19.2
Grade 1: Mild	Confirmed	1	1.9
	Likely	0	0
	Possible	2	3.9
	Unlikely	1	1.9
	Discarded	1	1.9
	Inconclusive	1	1.9
Total		6	11.5
TOTAL		52	100

Regarding infection, the main type of adverse event reported (55.7%), 89.7% (11) of infections were caused by *Mycobacterium tuberculosis*, of which 91% (10) were moderate events and 9% (1) were severe events. As for the infectious agent *Klebsiella pneumoniae*, which accounted for 30.8% (8) of the notifications of infections, 37.5% (3) were deaths, 25% (2) were severe events, 25% (2) were moderate events, and 12.5% (1) were mild events.

Of the other infectious agents, *Pseudomonas aeruginosa* represented 7.7% (2) of the notifications, with 100% of the cases classified as severe, while the infectious agent *Escherichia coli*, also with 7.7% (2), presented one severe case and one death (50% each). The agents *Enterococcus faecalis* and *Acinetobacter baumannii* together represented 7.6% (2) of the notifications with severe outcomes and death, respectively. Only one infection by a fungal agent classified as *Candida* spp. was reported (3.4%), with death as the outcome. Three other notifications did not describe the infectious agent. Table 4 presents the relationship between the infectious agents causing the adverse events, nature of the event, severity, and imputability.

Table 4. Relationship between the infectious agents causing the adverse events, nature of the event, severity and imputability (n = 29). São Paulo, SP, Brazil, 2016–2019.

Infectious agent n_{AI} (%)	Nature of the event (n_{NE})		Severity (n_G)	Imputability (n_I)
Mycobacterium tuberculosis 11 (89,7)	Receiver (9)	Organ (9)	Severe (1)	Confirmed (1)
			Moderate (8)	Confirmed (4)
				Inconclusive (2)
				Unlikely (2)
				Possible (1)
	Donor (2)	Organ (2)	Moderate (2)	Confirmed (1)
Klebsiella pneumoniae 8 (30,8)	Receiver (8)	HSC (4)	Death (2)	Discarded (2)
			Severe (1)	Confirmed (1)
			Mild (1)	Discarded (1)
		Organ (4)	Death (1)	Confirmed (1)
			Severe (1)	Possible (1)
			Moderate (2)	Confirmed (1)
				Inconclusive (1)
Pseudomonas aeruginosa 2 (7.7)	Receiver (2)	Organ (2)	Severe (2)	Confirmed (2)
Escherichia coli 2 (7.7)	Receiver (2)	HSC (2)	Death (1)	Discarded (1)
			Severe (1)	Confirmed (1)
Enterococcus faecalis 1 (3.4)	Receiver (1)	HSC (1)	Severe (1)	Discarded (1)
Acinetobacter baumannii 1 (3.4)	Receiver (1)	HSC (1)	Death (1)	Confirmed (1)
Candida spp. 1 (3.4)	Receiver (1)	HSC (1)	Death (1)	Discarded (1)
Unidentified agent 3 (10.3)	Receiver (3)	HSC (2)	Death (1)	Discarded (1)
			Mild (1)	Inconclusive (1)
		Tissue (1)	Mild (1)	Confirmed (1)

n_{AI}: sampling referring to the infectious agent; n_{NE}: *sampling the* nature of the event referring to the infectious agent; n_G: *sampling the* severity referring to the infectious agent; n_I: sampling the imputability referring to the infectious agent; HSC: hematopoietic stem cells.

DISCUSSION

The study presents the scenario of biovigilance in the state of São Paulo between the years 2016 and 2019, based on adverse events reported through the "Form for individual notification of adverse reactions in biovigilance," however some conceptual inconsistencies were identified. The form used for data collection denominates the notifications as "adverse reactions," however, according to the WHO definition used by the Ministry of Health, adverse reactions are unexpected damage caused by justified treatment in which all the correct process of execution was respected.[1,4,7,9,11]

Regarding the data that are reported in biovigilance, it is understood that using the term *incidents* is more appropriate, since it includes all events and the circumstances of these events that caused or could have caused harm to the patient. That is, it also includes events caused by human error or procedural and management problems in which some aspect of care may not have been performed correctly. When dealing with incidents with damage, the term *adverse events* is also used. [1,4,7,9,11] It is noteworthy that all notifications characterized in the study presented damage to patients.

As far as incidents with harm are concerned, these are classified according to severity, and can be: mild (loss of function, or symptoms are minimal and of short term), moderate (symptoms are more present in the affected patients and intervention is required, causing increased hospitalization time or permanent harm), severe (symptoms are severe and require major interventions, resulting in permanent harm, decreasing life expectancy or causing severe loss of function), or death (death was anticipated because of the incident).[4]

Still on the conceptual aspect, the "Form for individual notification of adverse reactions in biovigilance" presents as a field to be filled in: "Correlation of the adverse reaction with the procedure involving cells, organs and tissues." This is the definition of imputability, which relates the incident caused with the outcome presented by the patient. For the determination of this classification, careful clinical and procedural investigation is required.[4]

Imputability is classified as confirmed (when, after investigation, there is clear evidence that there was correlation of the incident with the injury), probable (when the evidence indicates this correlation but there is still doubt), possible (there is evidence that

the signs and symptoms may be associated with other causes, but the incident investigated cannot yet be discarded), unlikely (however much there is a possibility that the incident is not related to the injury, it is still not possible to rule it out), discarded (when the evidence indicates that there is no correlation between the incident and the injury), or inconclusive (when no evidence could be obtained after the investigation).[4]

In view of the above, the relevance of conceptual standardization in order to correctly identify and classify incidents is highlighted. This is to promote effective actions and strategies that change the security scenario, enabling the mitigation of damage and the prevention of adverse events recurrence. Standardization also allows results and strategies to be compared both nationally and internationally, seeking better results and data reliability, with the aim of improving the quality and safety of donation and transplantation processes.[12]

Despite the importance of knowing the adverse events in biovigilance, these data are still scarce. There are organizational, political, and institutional factors that can interfere with their collection and dissemination. Regarding the research, it was noticed a higher volume of notifications in the years 2016, 34.6% (18), and 2018, 32.7% (17), however in 2016 40,788 cell, tissue and organ transplants were performed, in 2017 41,693, in 2018 38,547 and in 2019 38,483.[12–16] That is, despite the high number of procedures performed, the rate of incident notifications is still low.

It is necessary that institutions are encouraged to report incidents, as well as develop strategies for mitigation and prevention. It is necessary to rethink management plans and training of teams and leaders in order to establish a culture of safety, understanding that this activity reinforces the institutional commitment to patients, families and the transplant system.[17] Regarding the nature of the events characterized in the study, most of them are related to allogeneic procedures and recipients. This data may be related to the fact that the transplant recipient is more vulnerable, corroborating another published study and the first report of adverse events data in biovigilance in Brazil.[12,18]

As for the severity of the adverse events under study, it is noted that in the state of São Paulo most notifications were classified as moderate, followed by deaths, severe, and mild. This information is not similar to that seen in the national report, since in Brazil the most common notifications are mild and moderate. This data demonstrates the more severe profile of the events reported in the state and suggests an important critical analysis of the processes, protocols and training of transplant teams, in order to understand the weaknesses of the services in the state and reverse the impact of severity in the affected patients.[18,19] However, in what concerns the imputability of the events, most of them were confirmed and discarded, showing that clinical investigation is carried out to understand the relationship between the damage presented by the patient and the incident. In the national report, most of the cases reported were also confirmed, but followed by probable and possible cases.[18] Besides providing greater assertiveness in the choice of conduct in the face of the adverse event, the effort to correctly determine the imputability of the cases is an ethical and responsibility issue.

After determining the general characteristics of the adverse events reported in the state of São Paulo, it is important to understand the causes of these reports. Regarding infections, the greatest cause of adverse events, it is known that the use of immunosuppressants by transplant patients causes a greater risk for the development of infections, whether community or opportunistic.[18,20]

In relation to *M. tuberculosis*, the infectious agent with the highest prevalence in reported cases, it is estimated that this infection in recipients is 20 to 74 times higher than in nontransplanted patients. Furthermore, it is possible to identify in the scientific literature that most cases in recipients are due to the activation of latent infection.[21]

Moreover, an important risk factor for the development of the disease is the geographic region of the donor or recipient. Regions with high incidence of tuberculosis cases, a disease caused by *M. tuberculosis* bacteria, present higher cases of this infection in transplant patients. It is noteworthy that the disease is prevalent in the state of São Paulo; in 2021, the incidence was between 31 and 50 new cases per 100,000 inhabitants.[22]

Although most cases of *M. tuberculosis* infection in the study were in recipients, two reports were related to donors. The bacterium in question can be transmitted through solid transplanted organs, and the geographical location of the donor is also an important risk factor. Symptoms in recipients of organs contaminated by the agent can be noticed immediately after transplantation or within the first few days, and it is important to evaluate the presence of fever up to three months after transplantation. If the symptom is present, it is urgent to perform tests for diagnosis and start treatment.[23]

Another relevant consideration in the case of transmission of the agent that causes tuberculosis is the intense evaluation and validation of the potential donor. It is important that clinical, community, and family histories be taken in order to identify where the donor lives, the donor's history of disease, and the presence of disease in family members or neighbors.[23] In cases of latent infection in the donor, transplantation is possible; however, prophylactic therapy is recommended for the recipient. Other situations of *M. tuberculosis* infection result in absolute contraindication for donation.[24,25]

The other prevalent infection in the studied reports was the one caused by the agent *K. pneumoniae*. This bacterium is responsible for respiratory tract infections, causing pneumonia, as well as urinary tract and bloodstream infections. It is a difficult agent to

control and treat, since it produces antimicrobial resistance enzymes. Moreover, it is present in hospital facilities and commonly infects hospitalized and immunocompromised patients.[26]

Klebsiella pneumoniae infections in patients receiving solid organs are on the rise. The same result identified in the study was observed in the first national biovigilance report regarding the prevalence of this type of infection.[18] Risk factors for *K. pneumoniae* infection include the use of immunosuppressants and previous use of broad-spectrum antimicrobials to previous long-term hospitalizations, use of mechanical ventilation, and the widespread presence of this bacterium in intensive care units and other hospital settings.[27]

In recipients of HSC transplantation, in addition to the aforementioned risk factors, infection by *K. pneumoniae* is even higher because of the consequences of the pathophysiology of hematologic diseases, such as chemotherapy-induced neutropenia and gastrointestinal mucositis.[28] It is noteworthy that mortality in these cases can range from 52 to 63%,[28] corroborating the results of this study, in which 50% of reported cases died.

In relation to other infections that cause adverse events, *P. aeruginosa* was not very prevalent, but had severe outcomes in the reported cases. In addition, it is one of the most lethal causes of bacteremia.[29] The post-transplantation hospital stay, the need for post-transplant dialysis, surgical site infection, and urinary tract infection were indicated as causes of colonization of kidney transplant recipients by this agent.[30]

The other adverse events reported involving infections were related to HSC transplantation. A study has shown that infections are the third leading cause of death in this transplant modality during the observation period, while in the post-transplant period they are the second leading cause of death.[31] Moreover, another research has shown that infections occurred in 93% of analyzed HSC recipients, with the agents *E. coli*, *E. faecalis* and *Candida* spp. also being identified.[32]

Regarding infection by the *A. baumannii* bacterium, other authors have also identified this agent as a cause of infection in HSC recipients. The results of this research identified high mortality in the same way as the present study.[33]

Confronting infections causing adverse events converges to the importance of developing intervention research in search of best practices both for the validation of potential organ and tissue donors and for the care of patients receiving transplants, including HSC, focusing on the prevention and treatment of infections, as well as for the development of screening strategies for risk factors and the improvement of appropriate treatments for this population.[31,32]

Besides infections, the second largest cause of adverse event notifications was classified as other, with 12 different entries in the "Form for individual notification of adverse reactions in biovigilance," as shown in Table 1.

The *Manual on Biovigilance of Human Cells, Tissues and Organs*, published in 2021 by Anvisa, recommends that adverse events include the following categories: infection, neoplasia, nonfunctioning graft, perioperative complications, genetic changes, and others.[4] Prior to this manual, there was a lack of more specific and described information regarding the categories, which may have created difficulty for the notifier to group and classify the adverse event data. The same challenge was visualized in the national biovigilance report and is presented as a limitation of the previous system.[18] This situation makes it difficult to compare data with those from other studies.

It is noteworthy that, among the notifications in this category, the events could have been classified as recommended by the manual, a challenge also identified in the national biovigilance report;[18] however, one of the notifications would have remained: "lack of control in sending the organ." This notification is related to the logistical issue of transplantation, especially in the packaging of the organ for transport. This is an important adverse event, because it impacts both the loss of the organ transported and the damage to the potential recipient, who will be prevented from performing the transplant.[34,35]

As for neoplasms, the third cause of adverse events reported, there is the limitation that none of the reported cases had the specification and description of the neoplasm. It is known that solid organ recipients have a significantly higher risk of developing epithelial tumors.[36–38] Moreover, the outcome of the neoplasm tends to be more aggressive, with higher morbidity and mortality rates. Besides the classic risk factors for the development of epithelial cancers, such as exposure to ultraviolet rays, in the case of transplant patients the use of immunosuppressants is an important risk factor.[36,37]

There are neoplasms that can be treated with the HSC transplant modality, but these cases present recurrence of the disease as a possible adverse event, the most common being acute myeloid leukemia, acute lymphoblastic leukemia, and Hodgkin's lymphoma.[39] In the study, most of the reported neoplasms were associated with HSC transplantation. In addition, the recurrences of neoplastic diseases in HSC transplantation were classified as "other," with three notifications with moderate and severe outcome.

Finally, after characterizing the biovigilance data from the state of São Paulo, the need to improve adverse event reporting systems is perceived, so that notifiers do not face challenges or barriers and the information is clear and respects the concepts recommended by the WHO and the Ministry of Health. Moreover, it is important that the teams that work in the transplant scenario are trained for the early identification of adverse events, as well as for the reporting and development of coping and treatment strategies,[8,19] thus seeking excellence in the care of transplant patients and ensuring the quality of services and patient safety.

CONCLUSION

The study allowed characterizing the data of adverse events in donation and transplantation of cells, tissues and organs reported in the state of São Paulo between the years 2016 and 2019. It was possible to identify the scenario of biovigilance in the state, visualizing that the main adverse events are associated with the recipient by allogeneic procedures.

The study shows that the major cause of adverse events in the state of São Paulo are infections, especially those caused by *M. tuberculosis* and *K. pneumoniae*. Therefore, it is suggested that intervention research be carried out in search of better practices in the care of both the evaluation and validation of potential donors and patients receiving solid organs, tissues and HSC, in order to optimize the diagnostic processes and the provision of specialized treatment to these patients. It is also important to strengthen hospital protocols and safety routines regarding the subject, with the goals of preventing the occurrence of infections and mitigating incidents.

The availability of data only from 2016 presents itself as a limitation of the study, since it was not possible to obtain a significant sample for possible correlations and inferences, however the availability of data until the year 2019 allowed isolated analysis of cases without conflict in relation to events linked to COVID-19. This allows future research to compare the data in two different healthcare settings.

The information obtained in this study can support governments, institutions and professionals in the development of safety and training strategies to prevent the recurrence of these incidents and encourage the reporting of adverse events. Furthermore, the data can be useful to other researchers in the area, for comparison and establishment of the national and global biovigilance scenario, as well as the development of intervention studies for the definition of evidence-based strategies. Furthermore, the recognition of the reality studied is relevant for the development of public policies aimed at preventing recurrence, training professionals, and developing institutional tools to support quality assurance and safety in donation and transplantation.

AUTHORS' CONTRIBUTION

Substantive scientific and intellectual contributions to the study: Paim SMS, Roza BA and Schirmer J; **Conception and design: Paim** SMS, Roza BA and Schirmer J; **Technical procedures: Paim** SMS and Schirmer J; **Data analysis and interpretation:** Paim SMS and Schirmer J; **Statistical analysis: Paim SMS** and Schirmer J; **Manuscript writing: Paim SMS**, Roza BA and Schirmer J; **Critical revision: Paim SMS**, Roza BA and Schirmer J; **Final approval: Paim SMS, Roza** BA and Schirmer J.

AVAILABILITY OF RESEARCH DATA

Data will be made available upon request.

FINANCING

Coordenação de Aperfeiçoamento de Pessoal de Nível Superior
[https://doi.org/10.13039/501100002322]
Grant No. 88887.506534/2020-00

ACKNOWLEDGEMENTS

Not applicable.

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