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Evaluation of adverse drug reactions notifications at a public hospital in Minas Gerais

Avaliação das notificações de reações adversas a medicamentos em um hospital público de Minas Gerais

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ABSTRACT

Introduction: Adverse drug reactions (ADR) are considered a serious public health problem, being responsible for an increase in morbidity and mortality and health costs. **Objective:** To know the occurrence profile and to describe the characteristics of the cases of ADR notified in a sentinel hospital in Minas Gerais. **Method:** Observational, descriptive and cross-sectional study, which used as a source the spreadsheet of suspected ADR reports from the hospital's risk management from January 2015 to December 2019. **Results:** 255 notifications were analyzed, the majority coming from active search (69.4%), involving 269 medications and 328 episodes of ADR. The sector with the highest number of notifications was the Medical Clinic (43.9%). The age range of the most affected patients was between 19-59 years (54.5%), predominantly male (50.6%) and white (54.1%). Most of the ADR were manifested through disorders in the integumentary system (36.3%), with mild severity (63.9%), mainly due to the use of systemic anti-infectives (44.6%). **Conclusions:** It is concluded that the notifications of ADR are recurrent in the hospital and their knowledge allows to outline their clinical profile, helping to prevent them and contributing to greater patient safety.

KEYWORDS: Pharmacovigilance; Notification; Adverse Drug Reactions

RESUMO

Introdução: As reações adversas a medicamentos (RAM) são consideradas um grave problema de saúde pública, sendo responsáveis pelo aumento da morbimortalidade e dos custos com a saúde. **Objetivo:** Conhecer o perfil de ocorrência e descrever as características dos casos de RAM notificadas em um hospital sentinela de Minas Gerais. **Método:** Estudo observacional, descritivo e transversal, que utilizou como fonte a planilha de notificações de suspeita de RAM da Gerência de Risco do hospital no período de janeiro de 2015 a dezembro de 2019. **Resultados:** Foram analisadas 255 notificações, sendo a maioria provenientes de busca ativa (69,4%), envolvendo 269 medicamentos e 328 episódios de RAM. O setor com maior número de notificações foi a clínica médica (43,9%). A faixa etária dos pacientes mais acometidos se situou entre 19-59 anos (54,5%), predominando o sexo masculino (50,6%) e a raça branca (54,1%). Grande parte das RAM manifestou-se por meio de distúrbios no sistema tegumentar (36,3%), com gravidade leve (63,9%), provindos principalmente do uso de anti-infecciosos sistêmicos (44,6%). **Conclusões:** As notificações de RAM são recorrentes no âmbito hospitalar e o conhecimento destas permite traçar seu perfil clínico, auxiliando na sua prevenção e contribuindo para a maior segurança do paciente.

PALAVRAS-CHAVE: Farmacovigilância; Notificação; Reações Adversas a Medicamentos

INTRODUCTION

Medicines are essential inputs in health care, being the most used form of treatment in the care of users, considered essential for improving the resolution of health services and preserving life[1]. However, for pharmacotherapy to be successful and to produce the expected results, it is essential that the drugs present quality, safety, efficacy, and that they are prescribed and used rationally[2].

Analyzes aimed at drug safety are performed in clinical trials before the drug is marketed. However, such studies have numerous limitations, such as: the restriction in the number of patients, the exclusion of patients at risk, the difficulty in detecting rare reactions, the short duration of the trials, a controlled environment, and the exclusion of associated therapies[3]. These limiting factors reinforce the need for continuous post-marketing drug monitoring and a risk/benefit assessment[4].

In this context, pharmacovigilance is inserted, a science that emerged from the need for early actions to promote the safe use of medicines in the population, aiming to monitor them throughout their life cycle, through activities related to detection, evaluation, understanding, and preventing of adverse events (AE) that may arise with its use[5]. In Brazil, the strategy to consolidate pharmacovigilance actions emerged from the creation of the Sentinel Hospitals Network, a project conceived by the Brazilian National Health Surveillance Agency (Anvisa), in 2001, with the objective of building a network of collaborators who would actively monitor the performance and safety of products used in health services[6,7].

Still active, the Sentinel Network remains open for any health care establishment, which at any time, requests its accreditation as a participating, collaborating institution, cooperation center, or reference center. In 2018, the network consisted of 259 hospitals spread throughout the national territory, 16 in the North region, 12 in the Midwest, 53 in the Northeast, 128 in the Southeast, and 50 in the South. The hospital participating in the study has been accredited to the network since 2008, becoming an active member in the dissemination of AEs that occurred in the institution[6,8].

AE is defined as the occurrence, in human beings, of any undesired effect, resulting from the use of products under sanitary surveillance, which may or may not be avoidable[9]. Among the different types of AEs involving pharmacotherapy, there is the adverse drug reaction (ADR), which is an intrinsic factor in the use of the drug itself and reflects a response that is harmful, unintended, and that occurs at doses normally used in humans for the prophylaxis, diagnosis, and treatment of diseases or for the modification of a physiological function[10].

Numerous factors can influence the onset of ADR, such as: age (due to physiological condition), gender (the difference in body composition between men and women can favor or hinder absorption, depending on the characteristics of the drug), pharmacogenetic factors (differences in the genetic profile, such as, for example, variability related to cytochrome P450 enzymes), liver and kidney failures (impaired drug metabolism and excretion), and self-medication[11].

The classification used for ADRs, proposed by Rawlins and Thompson in 1998, subdivides them into two groups: those that result from normal pharmacological effects, however with increased intensity, and those that have totally abnormal pharmacological effects. The former would be the result of an exaggerated pharmacological action and effect of a drug administered at usual therapeutic doses (type A). And the second are unexpected (bizarre), even considering the pharmacological properties of a drug administered in usual doses (type B). This classification was extended by the same authors, including types C (dose and time dependent), D (delayed reactions), E (withdrawal syndromes), and F (reactions that produce therapeutic failure)[12].

According to the World Health Organization (WHO), suspected ADRs are still analyzed and classified according to: causality (defined, probable, possible, conditional, and unrelated) and severity (mild, moderate, severe, and fatal). Regarding causality, an analysis must be performed to establish a causal relationship between the suspected drug and the reaction that occurred in the individual. Regarding severity, ADRs are evaluated according to the risk and damage they can cause to the individual[13,14].

ADRs are the fourth leading cause of death in the United States, with an estimated 100,000 people dying in hospitals each year for this reason. This high incidence can result in a higher mortality rate than those attributed to patients with AIDS, breast cancer, or being run over[15]. In general, international studies report a prevalence of 10% to 30% of these reactions during hospitalization. In Brazil, the epidemiology of ADRs during hospitalization is poorly investigated and published studies are generally limited to teaching hospitals[16]. Among some studies carried out in recent years that evaluated the occurrence of ADRs during hospitalization, their presence was identified in cases ranging from 46% to 85%, depending on the analyzed sample[17,18,19].

In the institution under study, the ADR cases identified are reported by any professional from the institution to the Risk Management sector by manually or virtually filling out an Adverse Incident Notification Form. After analysis and investigation of the occurrence by a pharmacist, Anvisa is informed of this occurrence through a notification system. Until the end of 2019, ADR notifications were registered at Anvisa through the Health Surveillance Notification System (Notivisa), however, in 2020, this system was replaced by VigiMed, a version of the VigiFlow System used by WHO, aiming to better organize the flow of notifications, enabling the creation of more accurate reports on ADRs and contributing to the monitoring of drug safety worldwide[20].

ADR notification appears as a fundamental regulatory instrument to feed the country's pharmacovigilance system and, thus, guide

the decisions of Anvisa and other competent regulatory bodies[20]. Among the various pharmacovigilance methods used in the hospital context, spontaneous reporting and active search stand out, the first being a type of passive surveillance and the second, active surveillance[21].

The spontaneous reporting system consists of the voluntary communication of health-related incidents, carried out by health professionals, who provide direct care and who are knowledgeable about the clinical situation of patients[22]. The active search method occurs through medical records reviews and interviews with patients and/or prescribers, in search of data that are used as triggers, markers, or flags of potential ADRs. Once found, they act as clues to conduct clinical investigation of ADR[23].

Although the retrospective review of medical records is considered the most appropriate method of data collection for the assessment of ADRs, it has as a limitation the difficulty of detecting incidents that are not reported by the health team or observed by those who review the records, which may underestimate the occurrence of incidents[15]. Spontaneous notifications offer many advantages, such as: ease of use, adaptation to different realities, the possibility of providing data on unknown incidents, in addition to the low cost of implementation and maintenance. However, the limitations of the method reside in the adherence and in the difficulty in establishing causality between the risk and the occurrence of incidents[24].

It is estimated that only 6% of all ADRs are reported, and underreporting is one of the major obstacles to greater effectiveness of this system[22]. This problem is based on the lack of knowledge about what an ADR is and its impact, the alleged difficulty in making a notification with the extent and nature of what must be reported, the type of notification system, the ease of sending it, and, mainly, the fear of punishment[1]. Underreporting can lead to false conclusions that a real risk is absent, revealing a problem that directly affects the patient's health[21]. A study carried out by Patel et al.[25] in 2016 showed that an average percentage of up to 45.11% is attributed to preventable episodes of ADR that lead to hospital admissions.

ADRs are considered a serious public health problem, since, in addition to being responsible for increasing morbidity and mortality among patients, they also prolong the length of hospital stay and, consequently, generate more expenses for health systems. Therefore, they cause a negative impact in the clinical, humanistic, and economic scope[26]. As an intervention strategy, several hospitals have implemented pharmacovigilance programs in order to detect, analyze and prevent ADRs. However, studies developed on the subject and the adherence of professionals to the notification system of suspected ADR are still scarce[14].

In this sense, it is important to know the profile of ADRs that occur in an institution, in order to detect possible problems related to the use of drugs, providing technical-scientific knowledge aimed at preventing or minimizing damage, as well as promoting safe and rational use of these drugs.

The present study aimed to know the occurrence profile and describe the characteristics of ADR cases reported in a sentinel hospital in the interior of the state of Minas Gerais, between 2015 and 2019.

METHOD

This is an observational, descriptive, and cross-sectional study, whose purpose was to analyze data from ADR notifications from a sentinel hospital in the interior of Minas Gerais.

The Antônio Dias Regional Hospital (HRAD) was adopted as a study setting, a public hospital institution linked to the Hospital Foundation of the state of Minas Gerais (FHEMIG), located in the municipality of Patos de Minas, Minas Gerais, regional reference in urgent and emergency care for a population of approximately 700 thousand inhabitants, distributed across the 33 municipalities of the Northwest Expanded Region[27].

Voluntary ADR notifications from an active search, registered in the Risk Management database of the hospital under study, were selected and analyzed, which included the following criteria: 1) having been notified between January 1, 2015, and December 31, 2019; 2) be derived from ADR used at the usual dose in humans; 3) having been notified by this sentinel hospital of reactions that occurred in an intra- or extra-hospital environment; and 4) contain the main information: origin of the notification, age, sex, drug suspected of triggering the ADR, clinical manifestation, and degree of harm to the patient. Notifications that did not meet these criteria would be excluded from the study.

The database containing the notifications was made available by the Risk Management after the consent of FHEMIG's Research Ethics Committee, together with the approval of the project submitted to Plataforma Brasil, according to opinion nº 4,197,048. Upon obtaining the ADR notification worksheet, a specific form was filled out, with the addition of the variables analyzed in the study: age, sex, race, origin of the notification, sector of occurrence, length of stay, year of notification, drug to which the adverse reaction was attributed, clinical manifestation of the ADR, degree of harm to the patient, and the outcome of the event. Once inconsistencies were identified in the filling out of the ADRs, it was decided to carry out a complementary search in the electronic medical records of the Hospital Management System (HMS), in order to avoid reducing the sample space by excluding incomplete notifications.

After collecting and compiling the data, the drugs involved were classified according to the first level of the Anatomical Therapeutic Chemical (ATC) code, which classifies drugs according to the anatomical, therapeutic, and chemical system[28], and the type of ADR according to the first level of the Adversion Reaction Terminology (ART) code, a WHO terminology for rational coding of ADR terms[29]. The data obtained were recorded in Microsoft Office Excel® 2016 spreadsheets and analyzed in terms of absolute numbers, percentages, medians, and prevalence,

with their respective confidence intervals of 95% (95%CI) and statistical significance level of 5%.

RESULTS AND DISCUSSION

From January 2015 to December 2019, 255 notifications of suspected ADR were made in the HRAD, 44 (17.3%) of which occurred in 2015, 40 (15.7%) in 2016, 74 (29.0%) in 2017, 35 (13.7%) in 2018, and 62 (24.3%) in 2019, resulting in an average of 51 notifications per year. No notification met the exclusion criteria and needed to be discarded.

The number of notifications obtained (n = 255) is considered high compared to other studies carried out in the same period. A survey carried out by Duarte et al.[16] in 2014 in a sentinel cancer hospital in Paraíba found a total of 171 notifications between 2008 and 2012. A lower number of notifications was also found in the study by Valdez-Ramírez, carried out in a Mexican hospital in the period from 2014 to 2019, in which only 137 notifications of cases of ADR were obtained[16,32].

The main method observed for detecting suspected ADR notifications was by active search (69.4%), with spontaneous notification corresponding to 30.6% of cases. In a similar study carried out in 2011 by Romeu et al.[15], this same trend was observed, in which, during the study period, 99.1% of notifications from active searches were analyzed. Most of the notifications made by the active search method were completed by the clinical pharmacy team, whose daily work is part of the detailed evaluation of the effectiveness and safety of the drugs, which facilitates the recognition of ADRs and a more in-depth analysis of the occurrences.

Notifications were made by all hospital care sectors, according to Table 1. The inpatient unit that most recorded ADR cases was the medical clinic (43.9%), followed by the emergency room (19.6%), and the adult intensive care unit (ICU) (14.5%). Other researchers pointed out the medical clinic as the main sector affected by ADRs in studies similar to the present study[30,18]. The higher frequency of notifications in this inpatient unit can be explained by the characteristics of the users of the sector, such as a greater number of chronic diseases and polymedication[31].

Table 1. Notifications of adverse drug reactions (ADRs) by sectors of the Antônio Dias Regional Hospital (HRAD).

Sector	Absolute frequency (n)	Relative frequency (%)
Medical clinic	112	43.9
Emergency service	50	19.6
Adult ICU	37	14.5
Orthopedics	32	12.5
General surgery	14	5.5
Pediatrics	5	2.0
Neonatal ICU	4	1.6
Surgical ward	1	0.4
Total	255	100.0

Source: Elaborated by the authors, 2021.
ICU: Intensive Care Unit.

The median length of stay of patients with ADRs was 18 days (95%CI = 14.2–21.8), with the shortest time being one day in the emergency room/observation and the longest being 166 days in the neonatal ICU. This result is close to that found in a study carried out at the Hospital das Clínicas, Faculty of Medicine, University of São Paulo, in which the mean hospitalization time was 17 days[30]. It is worth mentioning that the comparison between mean and median was necessary due to the fact that no studies were found describing the median length of stay of patients affected by ADR.

The large number of patients hospitalized due to different diagnoses and the susceptibility to injuries caused by long periods of care may justify the average number of days of hospitalization. However, the literature reinforces that ADRs are significant causes of increased length of hospital stay, generating a burden on the health system and increasing risks for the patient inherent to the hospital environment[34].

Regarding the profile of patients affected by ADRs, there was a minimal difference between sex, with male and female protagonists, respectively, in 50.6% and 49.4% of the reactions. This result was similar to that found in a study by Lobo et al.[35], in which 55.7% of ADRs occurred in men and 44.3% in women. A study carried out in a university hospital in Brazil also showed that ADRs were more frequent in males (55.0%) when compared to females (45.0%)[18].

However, some authors have reported that women are more susceptible to developing ADRs, possibly due to factors such as contraceptive use, hormonal changes, and a higher concentration of adipose tissue[36]. It is worth mentioning that in the medical clinic and general surgery sectors, 58.0% and 57.1% of ADR episodes, respectively, affected females.

As for the age of the patients affected by ADRs, for a better visualization of the results, a division was performed by age groups, being these between 0-18 years old (children and adolescents), 19-59 years old (adults), and 60 years old or more (elderly)[37]. All age groups were observed in the notifications, with a median age of 49 years (95%CI = 46.3–51.2), ranging from seven days of life to 91 years, similar to that found in a study carried out by Magalhães et al.[38] in 2017, in which the average age was 51.8 years. Also, no studies were found describing the median age of hospitalized patients affected by ADR, making a comparison between mean and median necessary.

Unlike most studies that stated that the elderly was the class most susceptible to ADRs due to physiological changes that determine pharmacokinetic and pharmacodynamic changes, in the present study, the age group that presented the highest number of ADRs was 19 to 59 years (54.5%), with the white race prevailing (54.1%) (Table 2). However, the elderly also

had a large participation in ADR episodes, representing 33.3% of cases.

A cross-sectional research carried out in a reference teaching hospital for the northwest of the state of São Paulo highlights the age group of 26-59 years as the most notified in the period from June 2012 to July 2014 (n = 64; 42.4%), consolidating with the most prevalent age group in this study[19]. It is noteworthy that the HRAD is a reference for trauma, in which the majority of hospitalized patients are male, with an age corresponding to the age group that presented the highest number of notifications of suspected ADRs.

It was also observed that most patients affected by ADR were white. It is known that different ethnic groups present different risks for ADRs, either due to a change in the genetic constitution or due to cultural factors that increase the risks of the occurrence of the events. As an example, black individuals using cardiovascular drugs are more susceptible to developing ADRs than non-blacks, according to a study carried out by McDowell et al.[39] in 2006.

The 255 ADR reports involved 269 drugs, corresponding to 97 different active ingredients. It is worth noting that in some cases of ADR, more than one drug was suspected, evidencing the difficulty in accurately detecting which one triggered the adverse reaction. These drugs, according to the classification of the first level of the ATC code, belong mainly to the class of general anti-infectives for systemic use (44.6%). About 13.8% of the episodes were associated with drugs that act on the nervous system and 11.2% with drugs that act on the blood and hematopoietic organs (Table 3). In 2011, Romeu et al.[15] also reported such classes as the main responsible for ADRs that occurred in a sentinel hospital in Fortaleza.

General anti-infectives for systemic use stand out as the main class responsible for causing ADR in several studies, such as the one carried out by Magalhães et al.[38] in a sentinel hospital in Fortaleza, in which 55.8% of ADR cases were the protagonists, corroborating the results found in this research. Many patients are exposed to prolonged treatment protocols, and most of them end up receiving some anti-infective during the hospitalization period, sometimes in polytherapy regimens, which becomes an aggravating factor for the occurrence of AE of this class, in addition to contributing to the emergence of microbial resistance[40].

In the sample universe evaluated, it can be observed that the most reported anti-infective was vancomycin (7.4%; n = 20), an antibacterial belonging to the glycopeptide class. In 2015, Loução et al.[18] carried out a study on ADRs in a hospital in Paraná and also reported vancomycin as the drug most related to suspected adverse reactions, with 8.3% of cases, equating to the result found in this research. This fact, which is repeated in other publications, may be related to the time of drug administration, which can generate pharmacodynamic mechanisms that lead to the release of histamine and contribute to the appearance of ADRs, mainly cutaneous[42].

Drugs that act on the nervous system as well as on the blood and hematopoietic organs also stood out in the ADR notifications of the present study, contributing with 13.8% and 11.2% of the cases, respectively. Research carried out by Basile at a university hospital in the state of São Paulo revealed that the drugs most commonly involved in ADRs were also those belonging to the pharmacological classes with activity in the nervous system (35.6%) and blood and hematopoietic organs (14.9%), showing a similarity with the results of this research[41].

Among the drugs that act on the nervous system, it can be observed that the most reported was dipyrone (27.0%), an analgesic and antipyretic widely used in Brazil, belonging to the

Table 2. Profile of patients present in the notifications due to the occurrence of adverse drug reactions (ADRs).

	Sex					
	Male		Female		Total	
Age (years)	n	%	n	%	n	%
0 to 18	22	71.0	9	29.0	31	12.2
19 to 59	69	49.6	70	50.4	139	54.5
60 or older	38	44.7	47	55.3	85	33.3
Total	129	50.6	126	49.4	255	100.0
Race/Color						
White	72	52.2	66	47.8	138	54.1
Brown	53	51.5	50	48.5	103	40.4
Black	2	22.2	7	77.8	9	3.5
Not informed	2	40.0	3	60.0	5	2.0

Source: Elaborated by the authors, 2021.

Table 3. Classification of reported drugs suspected of causing adverse drug reactions (ADRs) according to the first level of the Anatomical Therapeutic Chemical (ATC) classification.

ATC class	N	%
[J] Antiinfective for systemic use	120	44.6
[N] Nervous system	37	13.8
[B] Blood and blood forming organs	30	11.2
[M] Musculo-skeletal system	24	8.9
[A] Alimentary tract and metabolism	13	4.8
[G] Genito urinary system and sex hormones	13	4.8
[C] Casdiovascular system	12	4.5
[R] Respiratory system	06	2.2
[H] Systemic hormonal preparations	04	1.5
[V] Various	04	1.5
[D] Dermatologicals	03	1.1
[L] Antineoplastic and immunomodulating agents	02	0.7
[S] Sensory organs	01	0.4
Total	269	100.0

Source: Elaborated by the authors, 2021.

group of pyrazolones. A study carried out in a university hospital also showed dipyrone as one of the most reported drugs in the development of ADRs (6.7%)[18]. Regarding blood and hematopoietic organs, warfarin (33.3%), an antithrombotic vitamin K antagonist, was the drug most involved in cases of ADR, similar to the findings of the Reis study, in which warfarin appeared as one of the main drugs involved in the reactions that contributed to the hospitalization of the elderly (15.3%)[44].

It should be noted that most ADRs, triggered by drugs that have activity in the blood and hematopoietic organs, affected mainly patients over 60 years of age. Ribas and Oliveira evaluated the profile of drugs prescribed for the elderly in a Basic Health Unit and demonstrated that the aforementioned therapeutic group is often indicated in the treatment of cardiovascular diseases, one of the main causes of death in the elderly, which justifies the analogy[43].

Regarding the clinical manifestations of ADR observed in the study, it was found that the integumentary system was the most affected, accounting for 36.3% (n = 119) of the symptoms, with pruritus (42.0%, n = 50), skin rash (21.0%, n = 25), and erythema (16.0%, n = 19). Therefore, cardiovascular disorders (hyperemia, tachycardia, and thromboembolism) were reported, representing 13.7% (n = 45) of ADRs, followed by changes in the central and peripheral nervous system (brain ischemia/hemorrhages, tremors, and agitation), totaling 12.8% (n = 42) of the events (Table 4). In several cases, a single patient had more than one reaction, which resulted in a total of 328 ADR episodes in the study period, in which anti-infectives had a major contribution.

A similar reality was observed in a study carried out by Oliveira et al.[19] in 2018, in which the integumentary system was the most affected by ADRs, accounting for 33.1% of the symptoms. It is believed that dermatological reactions were predominant, probably because they were easy to see[19]. In 2010, a cross-sectional study conducted by Varallo[17] in a teaching hospital identified changes in the cardiovascular system (14.6%) as one of the main clinical manifestations resulting from ADRs, as well as a survey carried out with users in Portugal, which found most of the signs and symptoms of ADR linked to changes in the nervous system (14.4%)[45], data that corroborate with the present study.

Regarding the severity of ADRs, most incidents were classified as mild (n = 163, 63.9%), that is, reactions of little clinical importance and of short duration, which did not substantially affect the patient's life. It was also observed the appearance of 52 (20.4%) cases of moderate severity - which may have caused or prolonged hospitalization, requiring the use of antidotes, 23 (9.0%) severe - directly threatening the patient's life, possibly leaving permanent sequelae – and 12 (4.7%) fatal, resulting in deaths[13] (Figure).

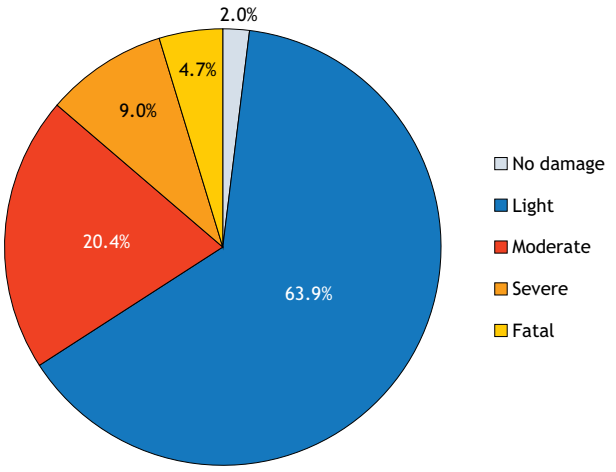
Loução et al.[18] evaluated the severity of ADR cases at a General University Hospital in the West of the state of Paraná, from January 2012 to December 2013, and also reported the prevalence of mild episodes (50.0% of cases), confirming the findings of this study. Despite the known underreporting, the act of notifying provides greater attention to the exposed reaction, allowing interventions and contributing to a lower risk of progression to a serious or fatal case[35].

In the analyzed period, 12 individuals who developed ADR progressed to the death outcome, mainly as a result of changes in the central nervous system, triggered by the use of drugs that act on the blood and hematopoietic organs, such as warfarin. This drug has been considered the main oral anticoagulant therapy for approximately 50 years, which is widely distributed by the Unified Health System throughout Brazil[46]. However, it is among the drugs most involved in ADRs, since it has a narrow therapeutic window, wide dose-response variety,

Table 4. Distribution of clinical manifestations of adverse drug reactions (ADRs), according to the affected system.

Organs and systems	n	%
Integumentary system disorders	119	36.3
Cardiovascular disorders	45	13.7
Nervous system disorders	42	12.8
Gastrointestinal disorders	25	7.6
Kidney and urinary disorders	20	6.1
General disorders	17	5.2
Blood and lymphatic system disorders	16	4.9
Respiratory disorders	13	4.0
Disorders at the site of administration	10	3.0
Endocrine disorders	10	3.0
Metabolic and nutritional disorders	10	3.0
Eye disorders	1	0.3
Total	328	100.0

Source: Elaborated by the authors, 2021.



Source: Elaborated by the authors, 2021.

Figure. Classification of adverse drug reactions (ADRs) by severity.

and high risk for bleeding, especially in the elderly, due to pharmacokinetic and pharmacodynamic changes resulting from aging[44].

It was also found that two patients manifested severe Stevens Johnson Syndrome (SJS), one of which was hospitalized for this reason and the drug suspected of causing the ADR was allopurinol, while in the other case, the patient developed the syndrome during hospitalization, with meropenem and/or ketoprofen possibly involved. However, despite the severity of SJS, both subjects had a recovered outcome. Although the etiopathogenesis of the disease is uncertain and it is probably an immunologically mediated process, one of the causes is exposure to drugs and medications, confirming with the work of Mockenhaupt[47], in which it was stated that the main SJS triggering drugs are anti-infectives, allopurinol and non-steroidal anti-inflammatory drugs (NSAIDs), corroborating the findings of this research.

The present research made it possible to trace the profile of pharmacovigilance notifications in the researched hospital, but some limitations compromised a greater performance and use of the results. Among them, the lack of information in some ADR descriptions, which made classification difficult and raised the need for a complementary search in the HMS electronic medical record, so that all the proposed variables were fulfilled.

Despite the fact that the number of notifications found in this research is higher than others previously reported, there is still a consensus on the existence of underreporting of ADRs in hospitals in general, which is a common phenomenon in all countries. It is difficult to fix it as its length is very variable[33]. In this follow-up, measures should be taken to actively disseminate among health professionals the importance of notifying an ADR, in order to contribute to the protection of public and patient health, as well as pay special attention to new drugs and new adverse reactions.

CONCLUSIONS

The study allowed the analysis and description of ADR notifications in patients treated at the HRAD during the years 2015 to 2019, pointing out a high prevalence of notifications from active search, carried out mainly by the clinical pharmacy team. There was a greater number of records in the medical clinic sector and ADR cases involving mainly male, white individuals aged between 19 and 59 years. The most reported therapeutic group were anti-infective agents for systemic use, with most ADRs manifesting through disturbances in the integumentary system, with mild severity and recovered outcome.

This theme shows the importance of pharmacovigilance in the detection of these ADRs and their notification, allowing robust knowledge about the effects of drugs, as well as the clinical profile of the undesirable episodes presented, and helping to improve public health. More studies similar to this one should be carried out to continue the statistics of ADRs at the aforementioned hospital and to be used as strategic instruments for decision-making that help in the prevention of ADRs, which would contribute to greater patient safety.

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Author's Contributions

Almeida PP, Resende DGO – Conception, planning (study design), and writing of the work. Lima TC – Conception, planning (study design), acquisition, analysis, data interpretation, and writing of the work. All authors approved the final version of the work.

Conflict of Interests

The authors inform that there is no potential conflict of interest with peers and institutions, politicians, or financial in this study.