

## EPIDEMIOLOGY OF MEDICINAL INTOXICATIONS REGISTERED IN THE NATIONAL SYSTEM OF TOXIC-PHARMACOLOGICAL INFORMATION 2012-2016

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**ABSTRACT:** In the universe of toxic substances, medicines are the most involved in intoxications. In 2016, they accounted for 34% poisonings in Brazil. The objective was to analyze drug intoxications recorded between 2012 and 2016, identifying the possible causes. It was a documentary study carried out using secondary data available at Sinitox and information contained in databases. The variables analyzed were: frequency by region, area of occurrence, sex, age, circumstance, evolution of cases, and frequency of deaths. The results showed that the southeast was the most prevalent region; the group most affected were women aged 20 to 49 years, followed by children aged 1 to 4 years; and attempted suicide as the main circumstance. The intention is to guide managers and health professionals in planning preventive actions, mitigating these incidents and promoting a better quality of life for the population.

**KEY WORDS:** Epidemiology; Poisoning; Pharmaceutical Preparations.

### EPIDEMIOLOGIA DAS INTOXICAÇÕES MEDICAMENTOSAS REGISTRADAS NO SISTEMA NACIONAL DE INFORMAÇÕES TÓXICO- FARMACOLÓGICAS DE 2012-2016

**RESUMO:** Dentre o universo de substâncias tóxicas, os medicamentos são os mais envolvidos em intoxicações. Em 2016, eles representaram 34% das intoxicações no Brasil. O objetivo foi analisar as intoxicações medicamentosas registradas entre os anos de 2012 a 2016, identificando as possíveis causas. Trata-se de um estudo documental realizado por meio de dados secundários disponíveis no sinitox e de informações contidas em bases de dados. As variáveis analisadas foram a frequência por região, a zona de ocorrência, o sexo, a faixa etária, a circunstância, a evolução dos casos e a frequência de óbitos. Os resultados mostraram que o Sudeste foi a região mais prevalente; o grupo mais atingido foi as mulheres de 20 a 49 anos, seguido de crianças de um a quatro anos; e a tentativa de suicídio como a principal circunstância. Pretende-se direcionar gestores e profissionais de saúde no planejamento de ações preventivas, amenizando esses incidentes e promovendo melhor qualidade de vida para a população.

**PALAVRAS-CHAVE:** Epidemiologia; Envenenamento; Preparações farmacêuticas.

## INTRODUCTION

Intoxications are adverse events in which chemical substances have harmful effects on living organisms, causing physiological changes and leading the individual to a pathological state<sup>1</sup>. These events can be identified by specific signs and symptoms and laboratory tests, so that through a careful assessment of this occurrence can guide correct treatment procedures in a timely manner for the patient, favoring a better prognosis<sup>1,2,3</sup>.

In the universe of toxic substances, medicines are the main agents involved in human intoxications. Many factors have contributed to this prevalence, such as the presence of several pharmaceutical formulations with questionable safety and efficacy in the retail market, the dissemination of pharmacies and drugstores that facilitate access to the drug, advertisements from the pharmaceutical industry, medical prescription errors and pharmaceutical dispensation, among other causes<sup>4</sup>.

The National System of Toxic-Pharmacological Information (Sinitox) has an annual statistical database related to human intoxications that occurred in Brazil. These data are collected from notifications made at all Toxicological Information and Assistance Centers (CIAT) present in several Brazilian states<sup>5</sup>. According to data from Sinitox, in 2016 alone, drugs accounted for approximately 34% intoxications in Brazil<sup>6</sup>.

In the State of Ceará, in 2002, there were 214 intoxications, 99 of which were caused exclusively by medicines<sup>7</sup>. Between 2010 and 2014, 1,362 cases of intoxications caused by medicines were notified by the Toxicological Assistance Center (CEATOX-CE)<sup>8</sup>.

The medicines frequently present in toxicological events are benzodiazepines, antidepressants, anticonvulsants, antimanic and mood stabilizer and over-the-counter medications such as analgesics, antipyretics, anti-inflammatories, among others<sup>9,10,11</sup>.

Given the above, drug intoxication is a public health problem, and despite being a generally preventable condition, has a high prevalence in Brazil and worldwide. Society is increasingly exposed to various types of medicines, with the growth of the pharmaceutical industry and pharmacies and drugstores<sup>12</sup>.

In this context, this study aimed to analyze the epidemiological profile of medicinal intoxications that

occurred in Brazil and reported to Sinitox between 2012 and 2016.

## METHODOLOGY

This was a documentary, quantitative and exploratory study, using secondary data. Information was collected from Sinitox about drug intoxications that occurred in Brazil between 2012 and 2016. The sample consisted of cases related to intoxications caused exclusively by medications.

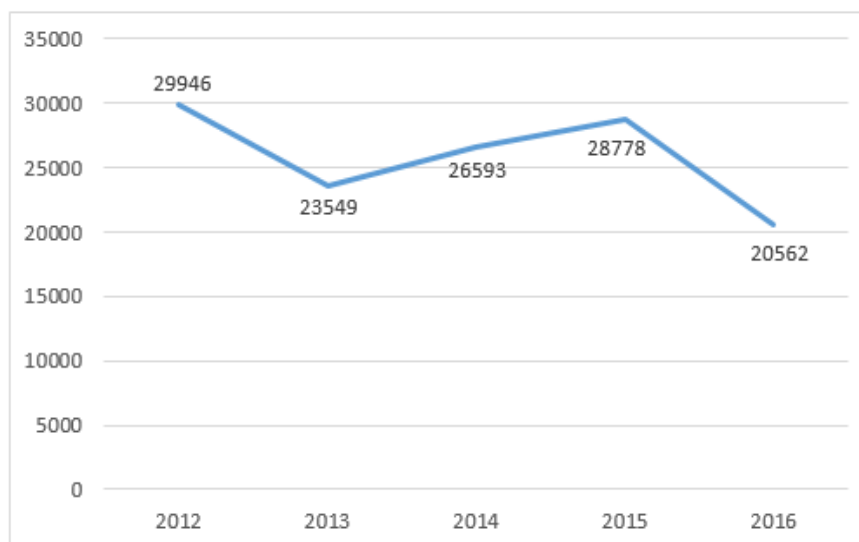
All occurrences of medicine poisoning duly reported to Sinitox during the period from 2012 to 2016 were included. Incomplete data were excluded from the study.

The variables analyzed were the distribution of cases according to the region of Brazil, the area of occurrence, sex, age group, circumstance and evolution of cases, as well as deaths from medicinal intoxications: distribution of deaths according to sex, age group and circumstance.

Data were collected from tables provided by Sinitox (<https://sinitox.icict.fiocruz.br>) on intoxications and poisonings occurring in Brazil. The information of interest is presented in graphs and tables, respecting the chronological order of the evaluated period, for calculation of absolute frequency of cases of medicinal intoxications and descriptive analysis.

## RESULTS

There were 129,428 cases of drug intoxications reported to Sinitox between 2012 and 2016 in Brazil. The year with the highest frequency of intoxications was 2012 with 29,946 cases (23%) (Graph 1).



**Graph 1.** Number of cases of drug intoxication according to the year. Sinitox data. Brazil.  
Source: Sinitox data

The Southeast region, in general, had the highest number of cases of human intoxication by drugs, with a total of 58,477 cases. Then, the South and Central-West regions, with 37,718 and 11,954 cases, respectively. The highest number of deaths was also registered in the Southeast with 138 deaths, followed by the South (87) and Northeast (66) regions.

Although the Southeast had the highest absolute number of deaths, the Northeast had the highest lethality

rate. In 2016, there were no records of drug intoxications in the North and South regions, thus impeding the real analysis of cases, especially in relation to the South, which maintained constant occurrence values between 2012 and 2015. Data in Table 1 list the number of cases, deaths and lethality according to the region between 2012 and 2016.

**Table 1.** Cases, deaths and lethality of drug intoxications that occurred in Brazil according to the region between 2012 and 2016 Brazil

Region		2012	2013	2014	2015	2016	Total
North	Cases (n)	236	383	202	263	-	1.084
	Deaths (n)	-	1	-	-	-	1
	Lethality (%)	-	0,26	-	-	-	0,26
Northeast	Cases (n)	2.257	1.804	1.736	1.939	2.459	10.195
	Deaths (n)	13	9	8	22	14	66
	Lethality (%)	0,58	0,50	0,46	1,13	0,57	3,24
Southeast	Cases (n)	14.253	7.778	13.496	15.826	7.124	58.477
	Deaths (n)	39	35	25	15	24	138
	Lethality (%)	0,27	0,45	0,19	0,09	0,14	1,14
South	Cases (n)	9.562	9.573	9.186	9.397	-	37.718
	Deaths (n)	23	21	21	22	-	87
	Lethality (%)	0,24	0,22	0,23	0,23	-	0,92
Central-West	Cases (n)	3.638	4.011	1.973	1.353	979	11.954
	Deaths (n)	22	12	7	3	4	48
	Lethality (%)	0,60	0,30	0,35	0,22	0,41	1,88

Source: Sinitox data

The urban area had the highest number of drug intoxications, totaling 112,929 cases. The number of occurrences in the rural area remained practically constant until 2014, but there was a decrease from 2015. It should also be considered that the number of ignored cases increased in the period from 2015 to 2016. Thus, it is not possible to affirm that there was a real drop in the number of intoxications in the rural area.

The prevalence of females was found in cases of drug intoxications. This is probably due to the higher consumption of medicines by women than by men and, consequently, by the appearance of adverse events; and also due to the higher frequency of suicide attempts in women. The sum of cases in women over the years considered in the study is 80,498 and in men, 48,200.

The most affected age groups were from one to four years, with 37,582 occurrences; 20 to 29 years, with 18,424 cases; and 30 to 39 years with 15,726 cases. There was a prevalence of medicinal intoxications in children aged one to four years, but when considering the age group of 20 to 49 years, which corresponds to the economically active period of people, this value exceeded the number of cases of child intoxication, with absolute frequency of 44,548 cases.

The prevalent occurrence in young people and adults suggests the common use of medicines for non-therapeutic purposes, but for intentional self-intoxications. With regard to the age group of 50 to 80 years, intoxications tend to decrease. The analyzed data are available in Table 2.

According to data in Table 3, the most frequent circumstance in medicinal intoxications that occurred during the study period was the attempted suicide with the cumulative total of 47,374 cases. Individual accident and therapeutic use also had significant values of cases in comparison to other circumstances, with a frequency of 43,182 and 18,348, respectively.

As seen in Table 4, most of the toxicological events of the studied period evolved to cure, with 62,568 cases. The non-confirmed cure was highlighted with 8,275 cases and the intoxications that evolved to death totaled 340 cases.

Among the 340 cases that occurred in the period, 161 deaths were female. The most affected age group

was 20 to 49 years (162), and the least affected was 80 years or more. The data from Sinitox does not provide a relationship between age and circumstance. However, according to the characteristics of fatal victims, it can be inferred that most deaths were caused by attempted suicide in individuals aged 20 to 49 years.

Suicide attempt was the circumstance with the highest prominence in all the years analyzed, totaling 199 cases (2012: 54 cases; 2013: 53 cases; 2014: 41 cases; 2015: 34 cases and 2016: 17 cases), followed by an accident that totaled 17 cases and therapeutic use (17 cases). There were no reports for collective accident, environmental, occupational accident, abstinence, food intake and abortion attempt. It is also important to consider that the ignored deaths had high values, making the real analysis of the data difficult.

**Table 2.** Cases of drug intoxication that occurred in Brazil, according to the age group between 2012 and 2016

Age group	2012	2013	2014	2015	2016	Total
< 1	844	642	868	1.103	1.005	4.462
01 – 04	8.129	6.772	9.167	7.831	5.683	37.582
05 – 09	2.185	1.640	1.739	2.033	1.568	9.165
10 – 14	1.856	1.391	1.214	1.329	1.049	6.839
15 – 19	2.826	2.324	1.952	2.303	1.510	10.915
20 – 29	5.034	3.793	3.448	3.909	2.240	18.424
30 – 39	3.906	3.017	3.166	3.483	2.154	15.726
40 – 49	2.631	1.854	2.055	2.431	1.427	10.398
50 – 59	1.333	1.038	1.228	1.671	1.185	6.455
60 – 69	482	417	552	1.079	868	3.398
70 – 79	296	214	346	783	636	2.275
80 ou +	131	108	156	375	375	1.145
Ign.	293	339	702	448	862	2.644

Source: Sinitox data

**Table 3.** Cases of drug intoxication that occurred in Brazil according to the circumstances in the period between 2012 and 2016

Circumstances	2012	2013	2014	2015	2016	Total
Individual accident	9.518	8.357	9.559	9.090	6.658	43.182
Collective accident	68	56	70	79	51	324
Environmental accident	8	8	2	1	2	21
Occupational	35	66	42	26	8	177
Therapeutic use	2.910	1.336	2.534	5.819	5.749	18.348
Inadequate medical prescription	148	157	134	53	48	540
Administration error	1.729	1.372	2.719	1.249	843	7.912
Self-medication	967	542	781	998	826	4.114
Abstinence	22	28	1	8	4	63
Abuse	538	219	234	211	179	1.381
Food intake	38	24	17	12	6	97
Suicide attempt	12.564	10.386	9.202	9.841	5.381	47.374
Abortion Attempt	53	19	28	40	21	161
Violence/Homicide	45	37	29	42	26	179
Misuse	389	237	352	320	152	1.450
Ignored	517	524	349	466	356	2.212
Other	397	185	540	523	252	1.897

Source: Sinitox data

**Table 4.** Evolution of cases of drug intoxications that occurred in Brazil in the period between 2012 and 2016

Evolution	2012	2013	2014	2015	2016	Total
Cure	19.336	13.895	8.404	18.581	2.352	62.568
Non-confirmed cure	4.446	4.256	4.511	4.532	530	18.275
Sequel	26	39	19	21	5	110
Death	97	78	61	62	42	340
Death other circumstance	38	9	11	7	4	69
Other	363	3.478	3.149	3.984	5.510	16.484
Ignored	5.640	1.794	10.438	1.591	12.119	31.582

Source: Sinitox data

## DISCUSSION

Medicines are significantly present in human poisonings in Brazil, being generally responsible for the largest number of cases in comparison with other toxic agents.

Several studies prove that drugs are the main agents involved in intoxications<sup>10,13,14</sup>. According to Silva and Costa<sup>14</sup>, drugs appear first as an agent involved in cases of exogenous intoxications, whereas drugs of abuse and pesticides appear second and third, respectively.

In the present investigation, when considering the regions of Brazil with the highest occurrence of drug intoxications, there was a higher incidence of cases in the Southeast region (58,477 cases), followed by the South and Central-West regions. The highest number of deaths was also registered in the Southeast (138 deaths) and the highest lethality rate is found in the Northeast (3.24%).

Such results are similar to the study by Mendes and Pereira<sup>15</sup>, in which the Southeast region prevailed with 65,421 cases, followed by the South and Central-West regions, adding up to 41,127 occurrences together. Regarding the lethality rate, the Northeast ranks first over the other regions.

The southeast, in general, has the highest number of cases and deaths. This can be explained by the excessive consumption of medicines in this region, since it is where approximately 50% of the country's official pharmacies and drugstores are present and where the largest pharmaceutical industrial pole is located; many Toxicological Information and Assistance Centers are also present, with an evident participation in the reporting of intoxications<sup>4</sup>.

Although the Northeast region does not have high rates of intoxication, it has a significantly high lethality rate. This is because health services are precarious and the population has limited access to medical care. In addition, there is a high population density and few CIATs, thus favoring the underreporting of many cases of drug intoxication<sup>16</sup>. As a result, it is understood that intoxication records are concentrated in more severe and even fatal cases, thereby increasing the mortality rate of the region.

Both the national and regional records showed a drop in the numbers of intoxications from 2013 and 2014, and these values increase gradually over the years 2015 and 2016. This decrease in occurrences may be related to the approval of the law 13021 of 2014, which, by means of article 5, makes mandatory the presence of a pharmacist in pharmacies of any nature<sup>17</sup>. Thus, the obligation of these professionals in pharmacies makes pharmaceutical care accessible to the general population, providing guidance mainly on therapy and the rational use of medicines.

The area of occurrence that stood out in the study was the urban area with 112,929 occurrences. Several studies corroborate this reality, which can be explained by the massive presence of pharmacies and drugstores in these areas, facilitating the access to medicines and, therefore, providing greater exposure<sup>9,18</sup>.

The large number of pharmacies in urban areas increases competition between these stores, contributing to the constant dissemination of promotional prices for medicines, and encouraging the purchase of these products, self-medication and the home stock of various drugs.

According to the present study, drug intoxications were predominant in female victims; youth and adults aged 20 to 49; followed by children aged one to four; and suicide attempt as the most frequent circumstance, followed by individual accident and therapeutic use.

When analyzing the distribution of occurrences according to gender, women prevailed with the highest number of cases in all the years evaluated in the study. This is similar to the data from several studies that aimed not only to analyze drug intoxications, but also acute exogenous intoxications caused by other agents<sup>18,19,20</sup>.

According to Morais et al.<sup>9</sup>, the prevalence of women in drug intoxications may be related to the culture of self-medication and to a higher frequency of suicide attempts than men. The common act of suicide attempts in women can be explained by the fact that women have greater intensity of depressive symptoms such as hypochondria, hysteria, hypomania.

Drug poisoning in children also gained prominence, being the second most prevalent group. The literature confirms this reality and points out that

the child audience is vulnerable to accidental poisoning occurring mainly in the domestic environment, where they find access facilitated by inadequate or careless storage by those responsible<sup>4,13,19</sup>.

Some characteristics make children one of the most vulnerable groups to drug intoxications, such as pharmacokinetic and pharmacodynamic differences, the risk of taking drugs due to lack of understanding, lack of information on the correct use of drugs and the wrong dose given by those responsible, inadequate storage, off label use and pharmaceutical presentations for adults, lack of development of specific drugs for children<sup>20</sup>.

Children in this age group are at the oral stage, that is, they bring to the mouth the objects they can catch. Also, many medications become attractive due to their colorful packaging and pleasant flavors, which combined with easy access (inadequate storage) can be major risk factors for intoxication occurrence<sup>21</sup>. Some social determinants may also favor intoxication in children caused accidentally by the parents, such as the young age of mothers, number of children and low education of parents<sup>22</sup>.

Suicide attempt is the most prevalent circumstance in both national and local data reported by CIATs. However, individual accidents and therapeutic use also concentrate a large number of cases<sup>4,19</sup>.

The occurrences, according to therapeutic use, can be related to medication errors, prescription and dispensing errors, lack of guidance on the correct use of the medication, among other occasions.

The medicine is the main choice in suicide attempts, due to its easy access. The causes that possibly point to this occurrence in young people and adults are depressed mood, family and social emotional problems, substance abuse, family history of psychiatric disorders, family rejection, and also physical and sexual abuse<sup>16</sup>.

The most used drugs in the most diverse circumstances were psychoactive drugs such as tranquilizers, antidepressants and anticonvulsants, followed by over-the-counter drugs such as dipyrrone, paracetamol, salicylates and digitalis<sup>3,11</sup>.

The frequent presence of neurological drugs in poisonings may be related to the considerable increase in recent years of mental health problems such as depression

and anxiety, considered as evils of modernity. In view of this, access to these drugs and knowledge about their high toxicological potential make them the main choice in suicide attempts<sup>23</sup>.

The research data referring to the evolution of the cases of drug intoxication demonstrated that there was emphasis on cure, totaling 62,568 occurrences, followed by unconfirmed cure, 18,275. The registered deaths corresponded to a total of 340, with 2012 being the year with the greatest number of deaths. It is important to note that ignored cases have grown over the years.

From the research data, the evolution of intoxications for healing outcome can be understood by the fact that many cases occurred in the age group from one to four years and probably caused by individual accidents or by therapeutic use, occasions that are often non-lethal compared to intoxications with suicidal motives. In addition, it is important to note that the majority of intentional self-intoxications do not result in death, as for each suicide there were several suicide attempts that were unsuccessful<sup>22</sup>.

Deaths from drug intoxication recorded during the years analyzed were prevalent in females (47.35%), aged 20 to 49 years (17.35%), and the main circumstance was suicide attempt (58.53%).

When analyzing deaths according to age, the frequency of cases was higher in young people aged 20 to 29 years, but the lethality rate was more significant in victims aged 50 years or older (0.41%) than in young people (0.32%).

From the findings of Veloso et al.<sup>24</sup>, the age group with the highest frequency in suicide was in individuals aged 20 to 29 years. However, the same authors point out that people aged 50 years or more were more effective in intentional intoxications, in which considering the total number of cases at that age, around 43% victims evolved to death, while in young people (20 to 29 years), this was only 10%.

Paula, Bochner and Montilla<sup>24</sup> analyzed hospital admissions among the elderly due to intoxications and adverse effects caused by medications in the period from 2004 to 2008, and identified that there was an increase in hospital admissions for the elderly due to drug intoxications in all age groups analyzed, ranging from

9.9% for the elderly aged 80 up to 88.7% for those aged 60 to 64 years. It was also identified that hospitalizations increase with advancing age.

The elderly is a group that is prone to drug intoxications in which there is a greater risk of evolving to death. It is in this age group that structural and physical changes occur in the organism, there is the appearance of chronic diseases characteristic of this age, such as cardiovascular, metabolic, psychiatric and neurodegenerative diseases and, consequently, the use of several drugs<sup>25</sup>.

In view of the above, several preventive and health promotion measures for the population should be adopted by authorities and health professionals, aiming to reduce these toxicological events and, consequently, the expenses related to the treatment of intoxicated people.

The improvement of healthcare is relevant, as its easier access for the population could diminish the culture of self-medication, in which many resort to this resource when they cannot get medical care for their health problems, and frequently need to face queues waiting to be treated<sup>26</sup>.

The most frequent victims of suicide attempts were young people and adults, especially females, there should be psychological monitoring of these groups, especially when they are seen in urgent and emergency services for intentional intoxications, since most of these people, usually, try suicide again<sup>21</sup>.

Another important measure would be for pharmaceutical professionals to be included in the teams of the women's health and family health (PSF) programs, so that they can develop pharmaceutical assistance, especially with regard to the storage and rational use of medicines, with special attention to the elderly, due to their fragile health, have several comorbidities and are generally polymedicated patients<sup>9</sup>.

The multiprofessional performance is an important factor with regard to patient care, as the exchange of information between professionals can be effective in preventing, diagnosing, treating, reporting and monitoring poisoning<sup>27</sup>.

Given the scenario of drug intoxications in Brazil, it is relevant to note that despite the high rates

of occurrence in the population, many cases are underreported. Authors report that most intoxications are attended and reported in units of medium to high complexity, indicating that the majority consisted of acute and severe intoxications, with mild and chronic conditions not being reported<sup>19,28</sup>.

Despite the underreporting of many cases of intoxication, data on toxicological events involving drugs are alarming, revealing that these products are used countless times in an irrational manner. This demonstrates the need for health promotion and protection actions to be reassessed and for more efficient preventive methods to be planned and implemented, which reach mainly the most frequent population groups in drug intoxications.

## CONCLUSION

Drug intoxications are a serious public health problem, demonstrating that drugs have been used beyond their therapeutic purpose, with frequent, irrational and indiscriminate use by a considerable portion of the population.

Thus, there are several causes for the occurrence of these aggravations in this profile. Among them, we can highlight: facilitated access to medicines; self-medication; polypharmacy; attempted suicide by drug intoxications due to psychological problems such as depression; failures in pharmaceutical assistance; medication, prescription and dispensing errors; childhood domestic accidents; and lack of development of drugs aimed at children.

Preventive actions are extremely important to reduce the occurrence of intoxications and reduce expenses related to events that can be avoided. The main preventive measure is the most effective pharmaceutical assistance, encouraging the rational use of medicines and informing about the risks of their incorrect use. However, specific protective measures should also be adopted, aiming to reach the most vulnerable groups.

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