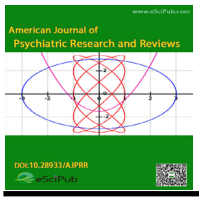
Research Article **AJPRR (2021) 4:31**



American Journal of Psychiatric Research and Reviews
(ISSN:2637-479X)

Epidemiology Of Exogenous Intoxication In A Triple Border Region Between The Years 2015 And 2019

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ABSTRACT

Objective: To characterize the profile of compulsory notifications of exogenous intoxication in Foz do Iguaçu, Paraná, in the five-year period 2015 to 2019. **Methods:** Documentary, quantitative-analytical study of the sociodemographic and epidemiological profiles, of notifications of exogenous intoxication. The variables were collected in Individual Notification Forms of the Notifiable Diseases Information System (SINAN) with a sample of 2799 evaluated records. The data were tabulated in spreadsheets, Microsoft Excel, and were analyzed using Sigma Plot, version 11.0. The results were expressed in absolute frequency and relative percentages. The analysis of associations between variables was performed using chi-square. **Results:** Regarding the socio-demographic and economic profile, it was found that the average age of victims of poisoning is higher for the male population, 33 years old (± 15.48), with a preponderance of intoxications among white, female individuals (n = 1174; 41.94%) and male (n = 736; 26.30%), with complete secondary education for women (n = 318; 11.36%) and incomplete primary education for men (n = 227; 8.11%), residing in urban areas, female (n = 1594; 56.95%) and male (n = 1069; 38.19%), whose occupation is in formal work, female (n = 270; 9.65%) and male (n = 178; 6.36%) respectively. Regarding epidemiology, drugs, especially anxiolytics, with digestive tract and evolution to cure were the characteristics most present in the notifications. **Conclusion:** Suicide attempts and abuse were the circumstances for their reports and the most recurrent ones, with drugs, especially anxiolytics and antidepressants, in the digestive tract being the most used. In the cases evaluated, the outcome of the cure without sequel predominated.

Keywords: Self-harm. Suicide attempt. Suicide. Drug intoxication. Exogenous Intoxication.

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How to cite this article:
Luciane Silvino Braz, Felipe Alexandre Zanutto Costa, Paola Fernanda Fedatto, Fátima Cividini, Isabel Fernandes de Souza, Ana Carolina Martins Gomes.Epidemiology Of Exogenous Intoxication In A Triple Border Region Between The Years 2015 And 2019. American Journal of Psychiatric Research and Reviews, 2021; 4:31.

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INTRODUCTION

Suicide is a social phenomenon of relevance in all societies. Increasingly, men and women go on the path of voluntary death, and why it is not always well understood[1].

It is a fact that the records of attempted suicide, have increased in recent years, especially among younger individuals, under 40 years old, which turns this fact into a worrying social problem, not only due to the effects on the person who commits it, but also for the psychological consequences on family members and people that are close[1].

An increase in the incidence of self-medication has been reported. This fact must be considered because it was demonstrated by the National Toxicological and Pharmacological Information System (SINETOX) that in Brazil, almost 30% of the intoxications that occurred are due to medications[2].

In this sense, risk factors for self-medication or incorrect use of drugs must be considered. Among them, the availability of the medication at home, inadequate storage, prescription errors and previous suicide attempts stand out[3]. This scenario is even more significant when considering that Brazil is one of the largest consumers of medicines in the world[3].

Therefore, the misuse of substances has the potential to generate intoxication. Such a picture consists of clinical manifestations, ranging from mild to severe, produced by intentional or unintentional medication intake[4].

Thus, the research mapped the sociodemographic and epidemiological profiles of suicide attempts by drug intoxication, registered in the Epidemiological Surveillance of a triple frontier city, between the years 2015 to 2019.

METHODS

A documentary and descriptive study of the epidemiological profile was carried out, with a quantitative approach, of suicide attempts by drug intoxication, from 2015 to 2019, in the city of Foz do Iguaçu, PR.

For this, the sociodemographic data and those related to the intoxication profile, contained in the Individual Notification Sheets of the Notifiable Diseases Information System (SINAN), were collected by the Epidemiological Surveillance sector at the Municipal Health Department. Data collection was carried out after approval by the Human Research Ethics Committee, by CAAE: 36547820.1.0000.0107.

The sample that composed this study consisted of the total number of medication poisoning notification forms, in the period and municipality mentioned above.

Included in this analysis were notifications that met the following inclusion criteria: legibility when filled in manually, information about gender, race, age, education, religion, occupation, region of residence (North, Northeast, Southeast, South and Midwest), year that occurred, category of the toxicological agent used in the attempt of intoxication (drugs, pesticides, home use, veterinary product, others, ignored), circumstance in which it occurred, the route of exposure / contamination (digestive, cutaneous, respiratory, ocular, parenteral , vaginal, trans placental, other, ignored), evolution of the case (cure without sequel, cure with sequel, death from exogenous intoxication, death from another cause, loss of follow-up, ignored), classification of the toxicological agent (medicated and non-medicated)) and among the drug toxicological agents which were the most used active principles for the suicide attempt. Such variables are contained in the Epidemiological Bulletin of the Health Surveillance Secretariat.

Notification forms that did not meet any inclusion criteria were excluded from the analysis, belonged to patients who did not live in Foz do Iguaçu at the time of the suicide attempt, and contained any illegible data.

The data on mapped suicide attempts included cases in which the variable “circumstance of exposure / contamination” was filled in as “suicide attempt” or ICD-10 group between X60 to X69 that characterize self-poisoning.

The data were tabulated in spreadsheets, Microsoft Excel, and were analyzed using the statistical software Sigma Plot, version 11.0. The form of consolidation was tabular. The results were expressed in absolute frequency and relative percentages, such as non-medicated and medicated toxicological agents. As for the sociodemographic / economic and epidemiological variables, in addition to the frequencies, the associations between the independent variables (sex) and the dependent ones were made with chi-square. Age was expressed as mean and standard deviation and the differences between the mean ages of females and males were calculated using ANOVA / DUNN'S

RESULTS

Between the years 2015 and 2019, a total of 5679 cases of exogenous intoxication were notified through the Individual Notification Form for Exogenous Intoxication of the Notifiable Diseases Information System (SINAN), at the Epidemiological Surveillance of Foz do Iguaçu, Paraná. Of this amount, a total of 2799 notification forms were included in this analysis, based on the inclusion and exclusion criteria determined.

From the analysis of the socio-demographic and economic profile, it was found that the average age of victims of poisoning is higher for the male population (md (female) = 31 ± 14.29; md (male) = 33 ± 15.48). In addition, it has been seen that there has been an increase in the number of poisoning records over the past five years, especially among the female population. Still, there is a preponderance of intoxications among individuals considered white [n (fem.) = 1174; 41.94% | n (male) = 736; 26.30%], regardless of gender, with complete high school for the female gender (n = 318 ; 11.36%) and incomplete elementary school for men (n = 227; 8.11%), residents in urban areas [n (women) = 1594; 56.95% | n (men) = 1069; 38.19%] and job occupation formal [n (fem.) = 270; 9.65% | n (male) = 178; 6.36%]. Such data are shown in Table 1.

Table 1. Distribution of data, from 2015 to 2019, related to socio-demographic and economic profiles, by absolute and percentage frequencies, of compulsory notification of exogenous intoxication, epidemiological surveillance, Foz do Iguaçu / PR, 2020.

Variant		**Female**		**Male**		**p-value**
		md	**dp**	***md***	**dp**	
Age		31	14.29	33*****	15.48	0.001
Variável	Category	*fi*	%	*fi*	%	p-value ******
Year	2015	181	6.467	84	3.001	0.001
	2016	180	6.431	77	2.751	
	2017	358	12.79	310	11.075	
	2018	412	14.72	419	14.97	
	2019	530	18.935	248	8.86	
Race	Caucasian	1174	41.944	736	26.295	0.001
	Brown	207	7.395	118	4.216	
	Black	65	2.322	64	2.287	
	Asian	18	0.643	5	0.179	
	Brazilian Natives	0	0.000	11	0.393	
	Ignored	180	6.431	193	6.895	
	Blank	17	0.607	11	0.393	
School Level	Unlettered	5	0.179	2	0.0715	0.001
	Incomplete Elementary	290	10.361	227	8.11	
	Complete Elementary	64	2.287	51	1.822	
	Incomplete High School	164	5.859	106	3.787	
	Complete High School	318	11.361	173	6.181	
	Incomplete University Education	60	2.144	23	0.822	
	Complete University Education	53	1.894	20	0.715	

	Not applied	20	0.715	15	0.536	
	Ignored	530	18.935	444	15.863	
	Blank	157	5.609	77	2.751	
Region	Urban	1594	56.949	1069	38.192	0.155
	Rural	16	0.572	15	0.536	
	Peri-urban	4	0.241	3	0.264	
	Ignored	3	0.107	2	0.0715	
	Blank	44	1.572	49	1.751	
Occupation	Formal Job	270	9.646	178	6.359	
	Unemployed	237	8.467	101	3.608	
	Entepreneur	75	2.680	75	2.680	
	Unformal job	49	1.751	55	1.965	
	Retired	33	1.179	26	0.929	
	State Worker	22	0.786	8	0.286	
	Chief	2	0.0715	4	0.143	
	Other	196	7.003	74	2.644	
	Ignored	451	16.113	466	15.934	
	Blank	326	11.647	171	6.109	

* The differences between the means (ANOVA) Women and Men, men have a higher average age (Dunn's Method) when compared with women; ** The association between sociodemographic variables and gender was made using the chi-square.

As for the epidemiological data, medication was the most reported toxicological agent [n (fem.) = 1091; 38.98% | n (male) = 366; 13.08%]. The circumstance of intoxication for the female gender was the suicide attempt (n = 1007; 35.98%) and for the male it was abuse (n = 478; 17.08%), with the digestive tract the most used [n (fem.) = 1440; 51.45% | n (male) = 924; 33.01%]. As for evolution, the cure was the most registered [n (fem.) = 1545; 55.20% | n (male) = 1040; 37.16%]. Other data in table 2.

Table 2. Distribution of data, from the period from 2015 to 2019, related to the epidemiological profile, by absolute and percentage frequencies, of compulsory notification of exogenous intoxication, epidemiological surveillance, Foz do Iguaçu / PR, 2020.

Variety	Category	Female		Male		p-value
		fi	%	*fi*	%	
Toxic Agent	Medicine	1091	38.978	366	13.076	0.001*
	Food and Drinks	166	5.931	335	11.969	
	Cleansing Products	105	3.751	24	0.857	
	Drugs Abuse	95	3.394	238	8.503	
	Pesticides	44	1.572	34	1.215	
	Rodenticides	40	1.429	17	0.607	
	Chemestry Products	32	1.143	38	1.358	
	Toxic Plants	10	0.357	18	0.643	
	Vet Products	7	0.250	6	0.214	
	Metal	2	0.073	5	0.179	
	Others	34	1.215	35	1.250	
	Ignored	0	0.000	0	0.000	
	Blank	35	1.250	22	0.786	
Circumstance	Suicide Attempt	1007	35.977	330	11.790	0.001*
	Abuse	231	8.253	478	17.078	
	Acidental	137	4.895	111	3.966	
	Automedication	57	2.036	33	1.179	
	Plain Use	51	1.822	59	2.108	
	Ingestion of food/drink	37	1.322	53	1.894	
	Therapeutic use	31	1.108	11	0.393	
	Taking in the wrong way	8	0.286	8	0.286	
	Violence or homicide	7	0.250	2	0.072	

	Abbortion Attempt	4	0.143	0	0.000	
	Environmental	4	0.143	2	0.072	
	Inadequate Prescription	1	0.036	1	0.036	
	Other	32	1.143	15	0.536	
	Ignored	28	1.000	19	0.679	
	Blank	26	0.929	16	0.572	
Via	Digestive	1440	51.447	924	33.012	0.001*
	Breathing	94	3.358	124	4.430	
	Cutaneous	55	1.965	23	0.822	
	Ocular	20	0.715	21	0.750	
	Parenteral	2	0.072	1	0.036	
	Vaginal	1	0.036	0	0.000	
	Transplacentaria	0	0.000	1	0.036	
	Other	0	0.000	2	0.072	
	Ignored	2	0.072	3	0.107	
	Blank	47	1.679	39	1.393	
Evolution	Cured	1545	55.198	1040	37.156	0.057**
	Cured with sequel	15	0.536	21	0.750	
	Death due to exogenous intoxication	12	0.429	4	0.143	
	Death due to other reasons	3	0.107	8	0.286	
	Lost of sequence	2	0.072	3	0.107	
	Other	0	0.000	0	0.000	
	Ignored	36	1.286	25	0.893	
	Blank	48	1.715	37	1.322	

The association between epidemiological variables and gender was made with the chi-square; * alpha test power> 0.80; ** alpha test power = 0.746.

As for non-medicated toxicological agents, food products and beverages were the most prevalent (n = 637; 62.57%) and as for medicated toxicological agents, the most recurrent belong to the classes of anxiolytics (n = 386; 28.89%) and various compounds (n =204; 20.04%) among which are antihypertensives, antihistamines, anti-inflammatories, drugs for the gastrointestinal tract, expectorants, diuretics, among others. Complete data on the pharmacological classes, most of which require medical prescription retention, listed in tables 3 and 4, and non-drug agents are shown in table 3.

Table 3. Distribution of data, from 2015 to 2019, medicated and non-medicated toxicological agents, by absolute and percentage frequencies, of compulsory notification of exogenous intoxication, epidemiological surveillance, Foz do Iguaçu / PR, 2020.

Variável	Categoria	*fi*	%
non-Medicated Toxicological Agents (n=1018)	Food products/beverages	637	62.574
	various compounds	204	20.039
	Poisonous substances	106	10.413
	Cleaning products	58	5.697
	Cosmetics	13	1.277
Medicated Toxicological Agents (n=1336)	Anxiolytic	386	28.892
	various compounds	300	22.455
	Antidepressant	260	19.461
	Antipsychotic	128	9.581
	Anticonvulsivant	115	8.608
	Analgesic and opioid	109	8.159
	Antibiotic	38	2.844

Table 4. Distribution of data, from 2019 to 2015, related to the pharmacological classes contained in the forms of compulsory notification of exogenous intoxication, consolidated by absolute and percentage frequencies, epidemiological surveillance, Foz do Iguaçu / PR, 2020.

Variety	Toxic Medicine Agent	*fi*	%
Anxiolytic (n=386)	Clonazepam	271	70.207
	Diazepam	66	17.098
	Zolpidem	16	4.145
	Alprazolam	9	2.332
	Bromazepam	7	1.813
	Midazolam	5	1.295
	Not specified	4	1.036
	Others	8	2.073
Antidepressant (n=260)	Fluoxetine	90	34.615
	Amitripityline	58	22.308
	Imipramine	37	14.231
	Sertraline	23	8.846
	Escitalopram	11	4.231
	Venlafaxine	10	3.846
	Citalopram	8	3.077
	Clomipramine	7	2.692
	Mirtazapine	3	1.154
	Bupropione	2	0.769
	Duloxetine	2	0.769
	Desvenlafaxine	2	0.769
	Others	6	2.308
	Not specified	1	0.385
antipsychotic (n=128)	Chlorpromazine	34	26.563
	Rispiridone	29	22.656
	Haloperidol	27	21.094
	Quetiapine	17	13.281
	Levomepromazine	13	10.156
	Olanzapine	6	4.688
	Others	2	1.563
anticonvulsant (n=115)	Cabamazepine	51	44.348
	Valproic Acid	35	30.435
	Phenobarbital	16	13.913
	Topiramate	4	3.478
	Fenytoina	4	3.478
	Others	5	4.348
analgesics and opioids (n=109)	Paracetamol +	68	62.385
	Dipyrone +	19	17.431
	Codeine	7	6.422
	Tramadol	6	5.505
	Morphine	2	1.835
	Others (Not opioids)	3	2.752
	Others (opioids)	2	1.835
	Not specified	2	1.835
Antibiotics (n=38)	Amoxicillin	12	31.579
	Metronidazol	6	15.789
	Cefalexin	4	10.526
	Azithromycin	3	7.895
	Ciprofloxacin	2	5.263
	Others	11	28.947

The main pharmacological agents of the drug classes are listed in table 4 with emphasis on the higher occurrence of notification of the use of Clonazepam (n = 271; 70.21%) in the case of anxiolytics, Fluoxetine (n = 90; 34.62%) in the case of antidepressants, Chlorpromazine (n = 34; 26.56%) for antipsychotics, Carbamazepine (n = 34; 26.56% for anticonvulsants,

Paracetamol + [representative sign of drug associations, such as caffeine, diclofenac, among others] (n = 68; 62.39%) and Codeine (n = 7; 6.42%) for analgesics and opiates, and, finally, Amoxicillin (n = 12; 31.58%) in the case of antibiotics

DISCUSSION

Suicide is a serious public health problem, and its incidence rate has been gradually increasing over the last 45 years[5]. The present research indicated a statistically significant increase for the female gender, with an increase of around one hundred in the quadrennium from 2016 to 2019.

In Brazil, suicide represents the third leading cause of death among young people aged 15 to 29 years[5]. In the study referring to the population of Foz do Iguaçu, it was observed that the average age was 31 for women, with a standard deviation of 14.3 (±), and 33 for men, with a deviation of 15.5 (±). Although the average was higher than the report of similar studies, the high standard deviation indicates the occurrence of cases in the younger population.

The use of self-medicating drugs represents about 30% of the cases recorded by the authors Leite and Monteiro (2018)[2]. In the present study, regarding the female gender, this percentage was higher, 39%, on the other hand, the male was lower, 13%. This corroborates with pre-existing data that indicate that in Brazil, medications are more used in suicide attempts than rodenticides, insecticides, pesticides, household cleaners, illicit drugs and foods unfit for consumption[6].

Other studies also indicate the relevance of the numbers related to drug abuse in notifications of exogenous intoxication, as reported by cases reported between 2000 and 2012 that exceeded 300,000 records in Brazil[6]. In 2019, about 27.86% of intoxications in Brazil were caused by drugs and 4.92% by domestic pesticides[4].

The use of drugs in an erroneous way or their use without indication, expose patients to the risk of intoxication. In this context, drug intoxication is one of the main causes of Brazilian mortality[7]. Therefore, the high rate of drug intoxication can be attributed to the great difficulty in implementing a policy of rational use of drugs[8]. This reality indicates the need for public health investment in pharmaceutical assistance and clinical pharmacy, considering that the drugs have potential-toxic dose-dependent[2].

In line with the authors Leite and Monteiro (2018), Chaves and collaborators (2017) point to the current public health challenge in notifying and assisting cases of human poisoning, especially when they are related to the misuse of medicines. This gained prominence due to the great ease of access to pharmaceutical products, together with the adoption of common popular practices, such as self-medication[2,3].

Regarding the toxic effects of medications, leading to the need for hospitalization or worsening, in some cases progressing to death, they may present in a dose-dependent manner or by high concentrations of the substance in the pharmaceutical form itself[2]. The dosage has a strong relationship with the outcome of the notification. In the present study, the significant majority evolved to cure, without sequel However, the percentage of deaths and cure with sequel were also recorded.

Thus, the role of the pharmacist is even more relevant when observing the data referring to the classes of drugs, with a higher incidence of intoxication by agent, whose retention of the prescription is mandatory[2].

In the study with epidemiological data from Foz do Iguaçu, in addition to drugs being the most used agent, the association with gender was statistically significant. This reality, also observed in the study by Assumpção, Oliveira and Souza (2018)[9].

The most common reasons that lead to the use of drugs in suicide attempts are situations of loss, frustration, emotional suffering, problems with family or emotional relationships and problems of a financial and / or marital

nature[10,11]. In this work it was demonstrated that among the main drug classes used for self-harm, those belonging to the class of anxiolytics and antidepressants are.

In this sense, it is important to emphasize that among the factors that motivate suicide, anxiety and depression are considered the most common mental disorders worldwide. Thus, it is estimated that this disease has already affected about 121 million Brazilians, with a higher prevalence in females, with at least 75% of those affected not having access to the most appropriate treatment[9]. In the present study, the circumstance of suicide was significant for women and abuse for men.

Agricultural pesticides lead the ranking with 41.22% of notifications with evolution to death[2]. In the present study, the agents, of non-medicated intoxication, were food products and beverages, followed by poisons - in which pesticides, insecticides, rodenticides, herbicides are included - and cleaning products and cosmetics.

In addition, a study has shown that the impact of the suicide attempt is not only on the individual, but for each victim, five to ten close people suffer serious psychological, economic and social consequences. Thus, this class of compulsory notification presents itself as a problem with high social impact[12].

CONCLUSION

Suicide attempts are significantly more recurrent among white women, with completed high school, living in urban areas and with formal occupation. Men have incomplete elementary education, with this demographic characteristic being different from theirs.

Regarding epidemiology, both sexes have more records of intoxication caused by a drug agent, in the digestive tract with evolution to cure. However, they differed as to the circumstance of intoxication, with suicide attempt for them and abuse for them. As for non-medicated agents, food products and beverages were the most recurrent. As for drug agents, anxiolytics and antidepressants were highlighted.

As future work and continuity of this epidemiological study, it is necessary to expand the analysis involving the other variables present in the compulsory notification form for exogenous intoxication and evaluation of the quality of filling out the said document.

REFERENCES

1. Ribas A, Mendonça A, Sabino D, Teixeira I, Dias H, Santos H. Tentativa de suicídio por intoxicação exógena na faixa etária de 10-19 anos no Brasil. Cad PUBLICAÇÕES UNIVAG. 2018;(9):69–74.
2. Leite MM de S, Monteiro ÁB. Análise das Intoxicações Medicamentosas no Estado da Paraíba-Brasil em 2017. J Biol Pharm Agric Manag. 2018;14(2):124–30.
3. Chaves LHS, Viana ÁC, Júnior WPM, Silva AL e, Serra L de C e. Intoxicação exógena por medicamentos: aspectos epidemiológicos dos casos notificados entre 2011 e 2015 no Maranhão. Rev Ciências Saberes [Internet]. 2017;3(99):477–82. Available from: http://www.facema.edu.br/ojs/index.php/ReOnFacema/article/viewFile/203/114
4. Brito ELB, Suchara EA. Caracterização das Intoxicações Medicamentosas Registradas em um Hospital Público. Rev Panorâmica On-Line. 2018;Edição Esp:113–28.
5. Moreira RMM, Félix TA, Flôr SMC, Oliveira EN, Albuquerque JHM. Análise epidemiológica dos óbitos por suicídio. SANARE, Sobral. 2017;16(1):29–34.
6. Santos GAS, Boing AC. Mortalidade e internações hospitalares por intoxicações e reações adversas a medicamentos no Brasil: análise de 2000 a 2014. Cad Saude Publica. 2018;34(6):1–14.
7. SINITOX B. SINITOX [Internet]. 2017 [cited 2020 Jun 11]. Available from: http://sinitox.icict.fiocruz.br/dados-nacionais
8. VILAS BOAS AC. Características Clínicas e Epidemiológicas das Entradas por Tentativas de Suicídio de um Hospital Público do Município de Rio Branco/AC no Período de 2007 a 2016 [Internet]. Universidade Federal do Acre (UFAC); 2018. Available from: http://dx.doi.org/10.1016/j.cirp.2016.06.001%0Ahttp://dx.doi.org/10.1016/j.powtec.2016.12.055%0Ahttps://doi.org/10.1016/j.ijfatigue.2019.02.006%0Ahttps://doi.org/10.1016/j.matlet.2019.04.024

%0Ahttps://doi.org/10.1016/j.matlet.2019.12725
2%0Ahttp://dx.doi.o

9. Assumpção GLS, Oliveira LA de, Souza MFS de. Depressão e Suicídio: Uma correlação. Pretextos - Rev da Grad em Psicol da PUC Minas. 2018;3(5):312–33.
10. Gondim APS, Nogueira RR, Lima JGB, Lima RAC, Albuquerque PLMM, Veras M do SB, et al. Tentativas de suicídio por exposição a agentes tóxicos registradas em um Centro de Informação e Assistência Toxicológica em Fortaleza, Ceará, 2013. Epidemiol e Serviços Saúde Rev do Sist Único Saúde do Bras. 2017;26(1):109–19.
11. Silva E de S, Marques Junior J, Suchara EA. Perfil de suicídios em município da Amazônia Legal. Cad Saúde Coletiva. 2018;26(1):84–91.
12. WHO WHO. World report on violence and health. Dahlberg LL, Biroux B, Stouthamer-Loeber M, Van Kammen WB, editors. Geneva: World Health Organization; 2002.