



**Acute poisoning in children and
adolescents admitted to the Pediatric
Emergency Unit of the Hospital de São
João (Porto, Portugal), 2014-2018**

Marta Sofia Resende Russo

**Dissertation for the Master's Degree in Forensic
Sciences and Laboratory Techniques**

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Dissertation for the Master's Degree in Forensic Sciences and Laboratory Techniques
Submitted to the University Institute of Health Sciences (IUCS)

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A Estudante

Marta Sofia Resende Russo

Aos meus Pais, Irmã e Avós Paternos
A vós dedico este trabalho!

“Aqueles que se sentem satisfeitos sentam-se e nada fazem. Os insatisfeitos são os únicos benfeitores do mundo” (Walter S. Landor)

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Scientific Production

Oral Communications in International Congresses

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Oral Communications in National Congresses

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Resumo

As intoxicações agudas ocupam o terceiro lugar como a principal causa de morte acidental na população infantojuvenil europeia e continuam a ser uma causa evitável de morbidade e mortalidade, em todo o mundo. As características e tendências das intoxicações nas populações pediátricas são de inegável relevância, uma vez que o desenvolvimento de estratégias preventivas e educativas direcionadas exigem o conhecimento profundo da prevalência específica e tipo de intoxicações numa determinada região. Em Portugal, a epidemiologia das intoxicações em crianças até aos 18 anos não foi estudada de forma abrangente. Desta forma, pretendemos analisar o padrão das intoxicações pediátricas admitidas ao Serviço de Urgência Pediátrica de um hospital terciário localizado no Norte de Portugal, para melhor compreender a epidemiologia do problema na região.

Esta análise retrospectiva incluiu pacientes com menos de 18 anos, internados no Serviço de Urgência Pediátrica do Centro Hospitalar de São João, Porto (Portugal), entre 2014 e 2018. Os dados relativos à idade, género e origem do paciente, ao agente tóxico envolvido e à intenção de intoxicação, à data e hora do internamento hospitalar, ao tratamento e ao resultado clínico, foram recolhidos dos registos médicos anonimizados dos pacientes.

Um total de 786 (0,20%) visitas por intoxicação, de um total de 389.913 admissões à urgência pediátrica, foram registadas durante o período de estudo. Através do estudo foi possível verificar que a principal via da administração do tóxico foi ingestão, e que a maioria das intoxicações ocorreram na faixa etária dos 13–18 anos. Da população estudada, 48,4% era do sexo masculino, não sendo também observadas diferenças significativas de género no padrão de intoxicação por diferentes agentes causais. As intoxicações por etanol (41,7%) e medicamentos (36,9%) lideraram as causas de intoxicação, seguidas dos produtos domésticos (9,2%) e drogas ilícitas (1,4%). A intoxicação por pesticidas representou menos de 1,0% dos casos. Enquanto 31,0% das intoxicações com produtos domésticos foram reportadas para crianças com idades até aos 2 anos, 63,0% das intoxicações com etanol ocorreram em adolescentes (13-18 anos). As intoxicações por fármacos também atingiram o seu pico nestas duas faixas etárias, relacionadas com a ingestão acidental exploratória de crianças e tentativas de suicídio, respetivamente. Os medicamentos mais comuns foram aqueles que atuavam no sistema

nervoso central. Não foram reportadas vítimas mortais durante os cuidados de urgência, mas 1,1% dos pacientes foram hospitalizados com prognóstico desconhecido.

Os registos mostraram uma maior incidência do número de intoxicações à sexta-feira, sábado e domingo.

As medidas preventivas para limitar o abuso de etanol e de outras substâncias psicoativas ilícitas devem ser reforçadas entre os adolescentes, no Norte de Portugal. A sensibilização da comunidade para eliminar os riscos relacionados com a ingestão exploratória de medicamentos e produtos domésticos no ambiente doméstico deve ser também reforçada, uma vez que esta continua a ser uma das principais causas de intoxicação na população pediátrica da região. Devem ser realizados estudos adicionais a nível nacional, para melhor compreender a epidemiologia das intoxicações em crianças e adolescentes portugueses.

Palavras-chave: Intoxicação; Pediatria; Epidemiologia; Etanol; Medicamentos.

Abstract

Acute intoxications rank third as leading cause of accidental deaths in European infant-juvenile population and remain an avertable cause of morbidity and mortality worldwide. The characteristics and trends of intoxications among paediatric populations are of undeniable relevance as the development of targeted preventive and educational strategies demands throughout knowledge on the specific prevalence and type of intoxications in a particular region. In Portugal, the epidemiology of intoxications in children aged up to 18 years has not been comprehensively studied. Herein, we intended to analyse the pattern of the paediatric intoxications presented to the Paediatric Emergency Department of a tertiary hospital located in the North of Portugal, to better understand the epidemiology of this problem in the region.

This retrospective analysis included intoxicated patients under the age of 18, admitted in the Paediatrics Emergency Department of the Hospital Centre of São João, Porto (Portugal), between 2014 and 2018. Data regarding age, gender and origin of the patient, the toxic agent involved and the intent of intoxication, the date and time of the hospital admission, the treatment and clinical outcome were collected from the patients' anonymized medical records.

A total of 786 (0.20%) visits due to intoxication from a total of 389,913 paediatric urgent admissions were recorded, during the study period. Through the study it was possible to verify that the main route of poison administration was by ingestion, and that most poisonings occurred in the age group 13–18 years old. From the studied population, 48.4% were male, with no significant gender differences being also observed in the pattern of intoxication caused by different causal agents. Intoxication by ethanol (41.7%) and pharmaceuticals (36.9%) led the causes of intoxication, followed by household products (9.2%) and illicit drugs (1.4%). Intoxication by pesticides represented less than 1.0% of the cases. While 31.0% of intoxications with household products were reported for children aging up to 2, 63.0% of ethanol intoxications occurred in adolescents (13-18 years old). Intoxications with pharmaceuticals also peaked in these two age groups, related to toddler exploratory self-accidental ingestions and attempts of suicide, respectively. The most common pharmaceuticals were those acting on the central nervous system. No fatalities were reported during emergency care, but 1.1% of the patients were hospitalised with unknown prognostic. Records have shown that there is a higher incidence of the number of poisonings between Friday, Saturday and Sunday.

Preventive measures regarding abuse of ethanol and illegal drugs should be strengthened among adolescents, in the North of Portugal. Community awareness to eliminate risks related to toddler exploratory ingestions of pharmaceuticals and domestic products in the household environment should also be reinforced as this is still a major cause of intoxication in the region's paediatric population. Additional studies should be conducted at the national level, to better understand the epidemiology of poisoning in Portuguese children and adolescents.

Keywords: Intoxication; Paediatrics; Epidemiology; Ethanol; Pharmaceuticals.

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Introduction

Poisoning represents a serious threat to public health (Azab *et al.*, 2016; Manini *et al.*, 2011). In the United States of America (USA), poisoning ranks second as the leading cause of death by injury (Mowry *et al.*, 2012). According to the American Association of Poison Control Center (AAPCC), more than one million poisonings occur every year in children under the age of 6 years-old (Hermanns-Clausen *et al.*, 2019), while figures of 140,000 and 170,000 are reported for children aged 6 to 12 years-old and adolescents aged 13 to 19 years-old, respectively (Gummin *et al.*, 2017; Mowry *et al.*, 2016). These indicators are however likely to be underestimated, considering that not all toxic exposures are clinically evaluated or reported to poison control centres (Gummin *et al.*, 2017; Mowry *et al.*, 2016). These intoxications negatively impact public wellbeing and represent a high economic expenditure to the USA Health Care System, with an estimated expense of nearly \$1,800 per poisoning (Corso *et al.*, 2006). In addition, according to the National Centre for Injury Prevention and Control, intoxications lead to more than 50,000 annual hospital visits among children under the age of 5 years-old, this costing the United States \$26 million in doctors alone and working time (Schwebel *et al.*, 2015).

In Europe, acute poisoning comes third as the cause of accidental death in children and adolescent population, similarly standing out as a preventable cause of injury and mortality (World Health Organization, 2008). Statistics from the World Health Organization (WHO) for Europe revealed more than 3,000 fatal poisonings occurred in 2004 among children and adolescents aged up to 19 years-old (World Health Organization, 2008). This number gets even higher when considering non-lethal poisonings, which encompass a frequent cause of hospitalisation in paediatric emergency rooms (Kearney, 2018; Pac-Kozuchowska *et al.*, 2016).

While acute voluntary intoxication with alcohol, drugs and medicines are the main cause of poisoning among teenagers and adolescents (Pac-Kozuchowska *et al.*, 2016; Pawlowska-Kamieniak *et al.*, 2018), most poisonings in toddlers occur through accidental ingestion (Mutlu *et al.*, 2010; Flanagan *et al.*, 2005) of pharmaceuticals and household products (Xiang *et al.*, 2012), in particular due to the lack of parental supervision and/or inappropriate storage of the domestic products (Schmertmann *et al.*, 2013). In this line, medicines, cosmetics, personal care products, bleach and cleaning products represent a significant risk for poisoning, since they are usually stored unsafely, in easy access

containers that are not childproof (Pac-Kozuchowska *et al.*, 2016; Pawlowska-Kamieniak *et al.*, 2018). In addition, in rural areas or other regions where agricultural work is predominant, exposure to insecticides, rodenticides and herbicides is also prevalent (Pac-Kozuchowska *et al.*, 2016; Pawlowska-Kamieniak *et al.*, 2018).

In fact, poisoning patterns depend strongly on the location considered, and are also affected by socioeconomic status, agricultural practices, and industrial development (Pac-Kozuchowska *et al.*, 2016; Pawlowska-Kamieniak *et al.*, 2018). Overall, childhood poisoning is more prevalent in males at all ages, but a greater gender discrepancy is observed in older children, mainly attributed to differences in socialization and the ease to engage in risky behaviours (Pac-Kozuchowska *et al.*, 2016; Pawlowska-Kamieniak *et al.*, 2018). Deaths occur mainly in low/middle income countries, but substantial differences can also be observed within countries, between urban and rural areas (Pac-Kozuchowska *et al.*, 2016; Pawlowska-Kamieniak *et al.*, 2018).

The main causes, routes, and circumstances of intoxication in the paediatric population will be herein reviewed, as well as the impact of rurality, age and gender in the patterns described. The approaches adopted or recommended for the management and prevention of poisoning in children will be also discussed.

1.1. Intoxication agent

According to Dinis-Oliveira *et al.* (2015), an intoxication agent is “*a chemical that in sufficiently large amounts can cause toxicity*”, the intoxication being dependent on the dose administered (O’Malley and O’Malley, 2018). Among the intoxication agents involved in paediatric poisoning, ethanol, medicines, illicit substances, and household products are the most frequent (Belchior, 2016; Warner *et al.*, 2011), but exposure to carbon monoxide or pesticides, and plant ingestion are also often described.

1.1.1. Ethanol

Ethanol poisoning is the most common cause of intoxication in teenagers, being broadly categorised based on the Blood Alcohol Concentration (BAC) (Tönisson *et al.*, 2013). In the case of young children, alcohol consumption is rare, but in such cases, severity is higher, with coma being easily achieved at low BAC (Gunja, 2012).

A report released by the British Broadcasting Corporation (BBC) in November 2018, indicates that more than 300 children have been hospitalized for alcohol poisoning in the Northern Ireland in the past six years (Kearney, 2018), while a 5-year retrospective study between 2006 to 2010, conducted at the Paediatric University Hospital in Białystok, Poland, revealed that of the 489 children hospitalized for poisoning, 244 (49.9%) were due to alcohol intoxication (Pawlowicz *et al.*, 2013). A similar number was recently given by Vrkić-Boban *et al.* (2018), on the Department of Paediatrics at the University Hospital of Split, Croatia, between January 2008 to December 2015 (Vrkić-Boban *et al.*, 2018). In a total of 24,651 hospitalised children, 488 were admitted to the emergency room due to acute intoxication, of which 272 (55.7%) for alcohol intoxication (Vrkić-Boban *et al.*, 2018). These statistics compare to those early presented by the same department, between November 1997 to October 2007, as from the 29,506 cases of children hospitalised, 594 were diagnosed by intoxication, of which 239 (40.2%) were due to alcohol poisoning (Bitunjac and Saraga, 2009). In a multicentre study with about 55 Paediatric Emergency Departments of the Spanish Society of Emergency Medicine, conducted between 2008 and 2017, in Bilbao, Spain, in a total of 749,803 cases identified in paediatric emergencies of all units, 1,749 cases were diagnosed as poisoning, of which 168 (9.6%) were due to ethanol (Santiago *et al.*, 2020).

Alcohol consumption by adolescents often occurs in relaxed environments, in the presence of their peers, who use the drug to feel better and relaxed (Gunja, 2012), "*to have a lot of party fun*" (Tönisson *et al.*, 2013), to abstract themselves from problems in their family relationships, or as a suicide attempt (Gunja, 2012).

In Estonia, around 85.9% of adolescents aged 13-16 years-old on average, have already consumed alcohol (Markina and Šahverdov-Žarkovski, 2007). A study conducted from 2005 to 2008, in the two main paediatric hospitals of the country, revealed 156 cases of children intoxicated by alcohol (mean age 14.2 years; between 8.4 and 17.9 years-old). Of these, 94.9% related to male (Tönisson *et al.*, 2013). Also, in Białystok, Poland, between 2006 to 2010, males, mainly between 16-18 years-old, were more poisoned by ethanol than females (Pawlowicz *et al.*, 2013).

An 8-year retrospective study between 2004 to 2011, at the Medical University of Vienna, Austria, reported that 249 children were hospitalized for acute alcohol intoxication, of which 132 were female (53%) *versus* 117 males (47%) (Binder *et al.*, 2016). The mean age was 15.3 years-old, and the mean BAC was 0.2% (Binder *et al.*, 2016). Although there were a few more cases of girls intoxicated on this study, they

consumed significantly less alcohol than boys (64 g vs. 90 g), but they reached the same BAC levels (girls: 0.19–0.49%; boys: 0.20–0.49%) due to the metabolism differences (Binder *et al.*, 2016). Results from this study highlighted a significant aspect regarding the relationship between gender and alcohol consumption, as it evidenced the girls' need of less alcohol to obtain the same BAC (Binder *et al.*, 2016).

In Lublin, Poland, a study between 2004 to 2013 demonstrated that there was a continuous increase in the children's admissions due to ethanol, from 27 children in 2004 to 53 in 2013, to the Department of Paediatrics of the University of Medicine (Pawlowska-Kamieniak *et al.*, 2018). This study found that, in addition to the increase in alcohol consumption by children and adolescents, which was more prevalent in females, the highest rate of alcohol consumers (64.2%) came from an urban environment (Pawlowska-Kamieniak *et al.*, 2018).

1.1.2. Pharmaceuticals

The inadequate consumption of medicines has been a medical and social problem of modern society, these agents being often involved in paediatric intoxications (Santiago *et al.*, 2020; Afukov *et al.*, 2019) related to toddler exploratory ingestions (Koh *et al.*, 2018) and to attempts of suicide in adolescents.

Accordingly, a retrospective study from 2009 to 2013 conducted in Cairo, Egypt, showed that unintentional poisoning by pharmaceuticals was responsible for most intoxications in (pre)school age groups (40.2%), while intentional poisoning by these substances predominated in adolescents (84%) (Azab *et al.*, 2016). Of note, male adolescents were mostly associated with accidental intoxications (6.3%), while females predominated in intentional intoxications (44.9%) (Azab *et al.*, 2016). The pharmaceuticals most frequently involved in intoxications in all age groups were non-opioid analgesics, antipyretics, and anti-inflammatory drugs (Azab *et al.*, 2016).

From 2016 to 2018, poisoning by pharmaceuticals increased about 2.5 times in the Toxicology Department of Nil Fyodorovich Filatov Clinical Hospital of the Children's City in Moscow, Russia (Afukov *et al.*, 2019). About 498 patients were admitted for intentional acute intoxication by pharmaceuticals, the predominant drug classes involved being psychopharmaceuticals (56%) and anti-inflammatory drugs (18.5%). Most of these intoxications related to female (85%) who pointed out family or social conflicts (47%), school problems (35%) and internet-related complaints (18%) as the main causes of self-

poisoning (Afukov *et al.*, 2019). Psychological tests performed in these patients revealed high levels of neuroticism (71%) and severe anxiety (57%) or depression (28%) (Afukov *et al.*, 2019).

In Italy, information on acute poisoning in children is scarce. A retrospective study at the Children's Emergency Service of the Regina Margherita Hospital, Turin, between 2012 and 2017, disclosed 1,030 children diagnosed with acute intoxication. From these patients, 55% were male, mainly between 1 and 4 years-old (mean age 2.2 years), and 41% were exposed to medication. The most common toxic agents were analgesics (20.8%), psychotropic (18.2%) and cardiovascular drugs (12.6%) (Berta *et al.*, 2020). From these poisonings with pharmaceuticals, 85% were accidental, 10.6% due to therapeutic error, 2.3% were suicide attempts, and 1.5% concerned use for recreational purposes (Berta *et al.*, 2020). Although Italy does not maintain statistics of poisoning in children constantly updated, the numbers are alarming and should be reduced.

A study by Agarwal *et al.* (2020) analysed all the 7,252 calls that were made to five poison centres in the USA, concerning unsupervised medicine exposure in children under 5 years-old, revealing that, from the 4,496 individuals that accepted to participate, 71.6% cases related to children aged up to 2 years-old, of which 47.6% corresponded to females and 92.8% corresponded to poisonings by a single drug (Agarwal *et al.*, 2020). About 33.8% of the poisonings occurred with prescription drugs and 62.7% from over-the-counter drugs (Agarwal *et al.*, 2020).

From the 15,069 children and adolescents under 18 years-old, admitted to the University Hospital of Olomouc, in Olomouc, Czech Republic for drug poisoning, from 1 January 2010 to 31 December 2012, about 55 were hospitalized for suspected acute intoxication by medication. These intoxications mainly occurred in females (72.7%), with children aged 0-3 years-old being the most prevalent group (36.4%), followed by school-age children (27.3%) and adolescents (14.5%) (Matalová *et al.*, 2019). Analgesics were the main agents involved in poisoning, especially ibuprofen (20%), followed by paracetamol (14.5%); the main route of exposure was *per os* (Matalová *et al.*, 2019). Solid drugs were involved in 72.7% of the cases, while liquids, including eye solutions and oral drops, were ingested in 23.6% cases. In 47.3% of the cases, the pharmaceutical agent was indicated to another person (Matalová *et al.*, 2019). Regarding the intent of the intoxication, in 58.2% were accidental, particularly among infants and preschool children (Matalová *et al.*, 2019). Suicide attempt was present in 32.7% patients, 94.4% corresponding to female adolescents, some of these cases relating to a second attempt; no

cases resulted in death (Matalová *et al.*, 2019). Paracetamol was the agent most involved in suicide attempts, followed by ibuprofen and antidepressants (mainly sertraline). Antihistamines, benzodiazepines and antipsychotics were also involved repeatedly (Matalová *et al.*, 2019).

Paracetamol is highly common as the agent of intoxication (Matalová *et al.*, 2019; Nistor *et al.*, 2017), capable of causing severe acute liver injury in children and adults, in the face of deliberate self-poison or accidental overdose (Chiew *et al.*, 2019). This medicine is widely used by paediatric against pain and fever, as it is highly safe when used at the recommended therapeutic doses. It was the most frequent single medicine between poisoning (23.1%), in a retrospective study conducted on a group of adolescents admitted for voluntary intoxication in the Emergency Department of St. Mary's Children's Hospital in Romania, during 2014 (Nistor *et al.*, 2017). In such a study, intoxication by pharmaceuticals (34.7%) was the most common, in a total of 219 adolescents admitted, with a predominance of females 56.3% over 15.5% of males, being observed (Nistor *et al.*, 2017). Benzodiazepines represented 19.2% of the intoxications, antiepileptics 15.4%, and antibiotics 13.5% (Nistor *et al.*, 2017). Suicidal attempt was admitted in 7.5% of the cases (5.8% in females), and in 3.7% of the cases the adolescents reported that this was the third attempt, while in one case it was the fourth (Nistor *et al.*, 2017). Self-inflicted poisoning is a common method in suicide attempts, this representing a serious health problem, so risk factors and signs need to be identified as early as possible to provide all necessary care (Nistor *et al.*, 2017).

Concerning analgesics, poisoning by the opioid tramadol is also frequent. A retrospective study on tramadol poisoning between 2010 and 2015 was conducted with all patients under the age of 18 years-old, admitted at the Noor and Ali-Asghar University Hospital, a renowned reference medical centre for the management of acute intoxications in Iran (Goudarzi *et al.*, 2020). From the 189 patients included in the study, 53.4% were males, with a mean age of 17 years-old. In all cases the route of exposure to the drug was oral, and the most common dosage was 100 mg, followed by 200 mg, the estimated mean dose of tramadol ingested being 1,126 mg (Goudarzi *et al.*, 2020). High school students represented 43.9% of the cases; in 93.1% of the cases intentional poisoning was reported (Goudarzi *et al.*, 2020).

According to data on the opioid exposure trends among children, provided by the Wisconsin Poison Control Center (WPCC), USA, calls for tramadol poisoning have increased among children aged 0-5 and 13-19-years-old, but calls for intoxication with

combinations of opioids/acetaminophen have decreased in proportion to opiate exposure (Creswell *et al.*, 2019). This is another wake-up call for the adult responsibility on the safe storage and for the implementation of new rules on the handling of prescription opioids, avoiding intentional or unintentional exposure of these substances to children and young people (Creswell *et al.*, 2019).

Kizilyildiz *et al.* (2018) reported 239 poisonings in Turkey, in children under 17 years-old in a period between June 2010 to November 2011, mainly by pharmaceuticals (57.3%), more specifically by antidepressants (29.9%). Also, from January 2008 to December 2015, 488 intoxicated children aged 0–18 years-old were hospitalized in the Department of Paediatric of the University Hospital of Split, Croatia. Of these, 28.9% children were diagnosed with poisoning by medications, such as anti-inflammatories, antipsychotics, antiepileptics, antihypertensives and anticoagulants (Vrkic-Boban *et al.*, 2018).

A case of particular interest concerns antibiotics, which are often prescribed to young children, based on the symptomatology. Improper use of antibiotics can cause serious problems and antimicrobial resistance (Tham *et al.*, 2020). In Malaysia, a retrospective study conducted at a tertiary hospital from January to May 2015, evaluated 549 children who presented symptoms such as fever and respiratory tract infections; a third of the children were discharged with antibiotic prescriptions (Tham *et al.*, 2020).

1.1.3. Illicit Drugs

The growing legalization of drugs, such as marijuana, hitherto considered illegal for recreational and medicinal purposes, increases exposure of children to the risk of intoxication (Denise, 2018). Data obtained by multiple paediatric emergency departments located worldwide, support this menace (Chen and Klig, 2019). Accordingly, a study conducted in paediatric emergency rooms of the main hospitals in France and analysed by the French Office of Drugs and Drug Addiction, identified 235 cases of children admitted for cannabis poisoning, during 2004–2014 (Claudet *et al.*, 2017a). Seventy one percent of these children were 18 months old or less (Claudet *et al.*, 2017a). The predominant form of the drug used was hashish (72%) – in 80% of these cases were observed resin sticks with 2–3 g, or balls with 2–4 g; the oral intake being the main route of exposure (75%) (Claudet *et al.*, 2017a). Most poisonings (72%) occurred at home (Claudet *et al.*, 2017a).

At particular risk of drug intoxication, are the children living in unsafe environments where heroine consumption is a frequent practice; these may experience mental health problems related to gestational exposure, accidental poisoning by opioids, and the dissolution of the family breast, which may end up in the child being institutionalized in orphanages or loss of parental figures by overdoses (Winstanley and Stover, 2019). Later in life, many of these children also experience drug use and dependence on illicit substances (Winstanley and Stover, 2019).

A case reported by the Hospital del Mar Paediatric Emergency Department, Barcelona, Spain, in 2011, concerned a 2-years-old girl who was admitted by respiratory symptoms for about 2 weeks (Papaseit *et al.*, 2011). Old clinical records showed that she was diagnosed with withdrawal syndrome, from which she had to undergo treatment (Papaseit *et al.*, 2011). They also found that the mother had substance-related disorders and was receiving treatment for heroin addiction (Papaseit *et al.*, 2011). After a series of tests and also in view of the mother's apparent behavior in the emergency room, the pediatricians concluded that both parents of the child were crack smokers, therefore the girl's hair was analysed (after washing to exclude external contaminants), and concluded that the main metabolite of cocaine, benzoylecgonine, appeared in segmented hair samples taken (from 0 cm to 3 cm, and 3 cm from the scalp) in very high amounts (1.9 ng/mg and 7.4 ng/mg, respectively) (Papaseit *et al.*, 2011). The analysis was also performed on the hair of the child's parents, revealing benzoylecgonine (mother 7.8 ng/mg and 6.4 ng/mg, respectively; father 13.6 ng/mg and 12.9 ng/mg, respectively) (Papaseit *et al.*, 2011). Based on this study, it was concluded that children experience more severe acute effects to chronic drug exposure, so conventional tests in blood, urine and capillary matrices should be done routinely in all children suspected of acute or chronic exposure to illicit drugs (Papaseit *et al.*, 2011).

In the USA, licit opioids are widely abused, especially among adolescents; from 1999 to 2010, the use had dramatically increased, along with the increased use of heroin and related fatalities (Knipper *et al.*, 2017). In this line, in Wisconsin, USA, in the last decade, overdoses and deaths by opioids have increased dramatically due to the higher consumption of illicit drugs, such as heroin, and prescription opioids (Creswell *et al.*, 2019). The increased availability of prescription and illicit opioids rises the risk of exposure of the infant/juvenile population to overdoses (Creswell *et al.*, 2019). According to data on the opiate exposure trends among children provided by the WPCC and the Wisconsin Central Hospital, 3,320 WPCC calls and about 2,275 admissions due to opiate

intoxication occurred between 2006-2016 (Creswell *et al.*, 2019). There was an increase in the rate of exposure to opioids, particularly in children aged 0-5 years-old and young people aged 13-19 years-old, where, in the majority of the cases, opioids had been prescribed to close relatives (Creswell *et al.*, 2019). However, during the study period, admissions involving heroin also increased dramatically among young people aged 13-19 years-old. Currently, in Wisconsin, overdose rates among the juvenile population continue to increase, part of which is due to heroin abuse, for which is necessary to implement prevention strategies to control both deaths and overdoses, and also rapid and effective treatments (Creswell *et al.*, 2019).

A study conducted in Poznań, Poland, from 1 January 2010 to 31 December 2012, reported 308 hospital admitted children by intoxication, in 46.75% of which the diagnosis was illicit drug intoxication. Females predominated, representing about 63.89% of the cases (Gontko *et al.*, 2013).

Although recreational drugs are consumed in relaxed and festive environments, for some adolescents, drug use is a risk factor for suicide (Ulseth *et al.*, 2019). In Norway, from 1 August until 31 July 2015, all cases of individuals up to 18 years-old who were admitted to the Department of Child and Youth Medicine of Sorlandet Kristiansand Hospital were studied (Ulseth *et al.*, 2019). From the 88 hospitalizations, less than 5% of the cases were due to drugs (Ulseth *et al.*, 2019). From these, about 22% of adolescents were considered suicidal – 94% of them declared self-mutilation as an objective of intoxication, and for this reason, they were followed by the Mental Health Department of the hospital; 54% of the adolescents received or had already received treatment in the Department of Child and Adolescent Psychiatry of the Hospital (Ulseth *et al.*, 2019). Even so, 20% of the cases were followed at the hospital's Psychiatry Department for substance abuse (Ulseth *et al.*, 2019).

A study between 2008 and 2017, in 55 Emergency Departments of the Spanish Society of Emergency Medicine, recorded 1,749 intoxicated children, the ingestion of illicit drugs being reported in 11.4% and accompanied by the consumption of ethanol (Santiago *et al.*, 2020).

The prevalence of abuse drugs is often difficult to determine, since the availability of new congeners is constantly evolving; the more changes in chemical structures, the more heterogeneity will exist in the physiological response and clinical symptoms, even if the drug is part of the group of some well-known classic drug (Wang and Hoyte, 2019). Prior knowledge of the adverse effects of a drug can provide important clues to the

doctors and caregivers and thus help in the treatment of intoxication and in limiting the harm to the child (Wang and Hoyte, 2019).

1.1.4. Household products

About a third of the more than 1.1 million annual consultations with the Centres for Intoxication Control in the USA reported in children under 5 years of age, were regarding poisoning by exposure to household products, such as cosmetics, hygiene products and cleaning substances (Schwebel *et al.*, 2015).

Among the household products most involved in this children intoxication are the detergent capsules for clothes and dishwashers (The National Safety Council, 2020). Laundry and dish detergent capsules are quite attractive to children, as these are colourful, soft and even a good product for teething problems, but they are also a threat to the child's health. Only in 2018, the AAPCC, USA reported that children under 5 years-old ingested, instilled or were exposed through contact with eyes or skin, to cloth washing capsules more than 9,000 times (The National Safety Council, 2020). These capsules are associated with many poisonings in children and can be more toxic than the classic laundry detergents (Claudet *et al.*, 2014). In fact, the toxicity elicited by a detergent capsule is substantially more severe, as it contains higher concentrations of ethoxylated tensioactives and alcohols, and a very high viscosity and hydrotropic powers (Claudet *et al.*, 2014). It is important to continue warning parents to keep the concentrated capsules out of the reach of children, contributing to the reduction of poisoning cases by household products (Claudet *et al.*, 2014).

A retrospective study from 1 January 2002 to 30 June 2013, conducted by the Paediatric Emergency Departments of the Children's Hospital of Toulouse in France, assessed and compared symptoms and severity after exposure to classic laundry detergents, with those elicited by new concentrated laundry capsules, in the paediatric population admitted to the tertiary-level Paediatric Emergency Departments (Claudet *et al.*, 2014). In the study period, 89 children were admitted, the mean age was 2.1 years-old, of which 65% of the cases were children under the age of 2 years-old and the predominant gender was male – representing about 60% of the cases (Claudet *et al.*, 2014). Of note, 57% of the children were symptomatic, in the majority with digestive symptoms (75%). When compared the cases between classic laundry detergents and concentrated capsules, it was concluded that children intoxicated by capsules were more

symptomatic (96%), than those who were intoxicated with classic detergents (51%), also having more digestive symptoms, often presenting bronchospasm, and there was a higher risk of eye injury, the degree of severity being higher (92% vs. 59%), compared to classic detergents (Claudet *et al.*, 2014).

In Turkey, a retrospective study on the cases of children aged 0 to 18 years-old admitted between 1 January and 31 December 2017, in the Paediatric Emergency Department of Faculty of Medicine Izmir Katip Celebi, revealed 211 cases of intoxication by household cleaning products (46.6%) (Gokalp, 2019). The data of this study evidenced that 286 (45.8%) of the products involved in these intoxications were not stored in their original packaging, while 95% of those that remained in the original packaging were not locked, potentiating accidental poisoning (Gokalp, 2019).

Often, treatment for this type of intoxication requires hospitalization, sometimes even in intensive care units, its effects including vomiting, severe respiratory problems, burns of the oesophagus and coma, in addition to burns also in the eyes and skin when liquid detergents are used (The National Safety Council, 2020).

Several intoxications occur in the home environment. Often the objects that small children bring to the mouth contain compounds that not all caregivers can identify at first sight, as it is the case of propylene glycol, a chemical that is present not only in environmental products, cosmetics and medicines, but also in child products, such as cleaning wipes and diapers (Guillot *et al.*, 2002). Propylene glycol is capable of causing severe toxicity in children, as observed by the paediatric service of the Hospital de Lisieux in France, in a 2-year-old boy found by his parents one morning, presenting lethargy and only reacting to acute pain (Guillot *et al.*, 2002). At the hospital admission, the boy presented fever (38.5 °C), signs of fatigue and polypnea. Urine and blood tests and the anamnesis disclosed propylene glycol poisoning, metabolic acidosis, and a high propylene glycol serum concentration (Guillot *et al.*, 2002). The two-year-old chewed disposable cleaning wipes, which later caused him propylene glycol poisoning (Guillot *et al.*, 2002). In cases such of unknown metabolic acidosis, propylene glycol poisoning should be considered and studied to allow the correct treatment (Guillot *et al.*, 2002).

In Kandang Kerbau, Singapore, 1,208 cases were admitted to the urgency of paediatrics of the Kandang Kerbau Women's and Children's Hospital for intoxication between 1 January 2009 and 31 December 2013 (Koh *et al.*, 2018). The highest percentage of intoxicated population (76.9%) was composed of children aged between 1 and 4 years-old, the predominant route of exposure being oral (98%), and in most cases

intoxication was accidental (89.5%) (Koh *et al.*, 2018). Household products predominated in 510 poisonings (42.2%), with bleach, liquid detergent, floor, cleaning liquid and dishwashing liquids being the intoxication agent in 17.1% of the cases; and insecticides, insect bait, insect repellents and silica gel in 11.6%; and mothballs in 9.8%; body soaps, hand sanitizers, shower gels and shampoo in 8.0%; perfumes, skin tones and cosmetic creams in 4.9%; nail polish and nail polish remover in 4.3%; paint and thinners in 2.7%; and air fresheners in 2.2% (Koh *et al.*, 2018). There were also 27.1% cases of intoxication by other household products not identified in the study (Koh *et al.*, 2018). Antidotes were used as treatment in 7.7% of the cases, gastric lavage was used in 3.5% and activated carbon in 25% (Koh *et al.*, 2018).

Ethanol is often present in a number of household products, to which children have easy access, further resulting in intoxications (Rayar and Ratnapalan, 2013). In Canada, a study conducted in Ovid Medline databases to identify cases reported by ingestion of household products containing ethanol, which led to the intoxication or death of children up to 18 years-old, resulted in 17 publications, some of which reporting serious adverse events, including death, seizures, and hypoglycaemia (Rayar and Ratnapalan, 2013). In some cases, child-resistant closures seemed to have contributed to the decrease in the intake of ethanol (Rayar and Ratnapalan, 2013). This study highlights the need for legislation regulating alcohol content in household products to be reviewed and public re-education strengthened to prevent poisoning in children (Rayar and Ratnapalan, 2013).

Currently, the world is going through a chemical phase, with the SARS-Cov-2 pandemics imposing means of protection that go through continuous disinfection, using many types of hand sanitizing or washing products (Hanna *et al.*, 2020). This type of products rapidly became frequent at home, health care facilities, schools and shops frequented by children (Hanna *et al.*, 2020). In Australia, one case was reported by Sydney Children's Hospital in Australia, concerning a 6-year-old girl admitted to the emergency department, diagnosed with ethanol poisoning due to ingestion of hand disinfectant (Hanna *et al.*, 2020). The child arrived at the department 1h15 after ingestion with symptoms of diplopia and disjointed speech, the mother reported that the child felt dizzy, and her older sister stated that her breath smelled like hand sanitizer (Hanna *et al.*, 2020). At hospital admission the child vomited 2 times; toxicological tests were performed, disclosing an ethanol concentration of 41.1 nmol/L or 0.19% (Hanna *et al.*, 2020). Given the further persistence of vomiting and lack of breathing, she was intubated

and ventilated (Hanna *et al.*, 2020). The treatment underwent consisted of ceftriaxone intravenously because the patient was septic, and she was transferred to a tertiary paediatric intensive care unit (Hanna *et al.*, 2020). After 3 hours of sedation the child was released, new analyses were made and the ethanol concentration decreased to 14 nmol/L (0.06%). Once awake, the child said that she frequently ingested in recent months the sanitizer, including the night before, but did not know the amount ingested (the Anti-Venom Information Centre estimated it around 50 mL). She explained she liked the taste and the smell of the product (Hanna *et al.*, 2020). During the 3 months of confinement the Anti-Venom Information Centre saw the risk of child exposure to hand disinfectant increase twice, as compared to 2019 (Hanna *et al.*, 2020).

1.1.5. Pesticides

Pesticides are a broad term to define chemicals used to eradicate pests, such as herbicides, insecticides, rodenticides, bactericides, insect and animal repellents, antimicrobials, fungicides, and others, and therefore may be present in food, water, gardens and schools, imposing a special risk of exposure to children (Roberts *et al.*, 2012). Although acute pesticide poisoning is rare and more frequent in agricultural areas (Kapka-Skrzypczak *et al.*, 2019), chronic exposure is highly preoccupant due to the use of insecticides and rodenticides at home, herbicides and soil fertilizers in gardens, air freshener sprays, pump, and nebulizers, all leaving persistent residues on the surfaces (Roberts *et al.*, 2012; Leveau, 2016). Young children are highly exposed to this type of toxics, in face of the proximity to the contamination source (Salameh *et al.*, 2003), either by ingestion, inhalation of contaminated air or absorption through the surface of the skin (Roberts *et al.*, 2012). Therefore, even at exposures to low concentrations of pesticides, if the duration of contacts is sufficient, they can lead to serious, permanent complications that will limit their development (Kapka-Skrzypczak *et al.*, 2019). The low body mass of children in early stages of life and their exploratory profile (Kapka-Skrzypczak *et al.*, 2019), exhibiting repetitive hand-to-mouth behaviour (World Health Organization, 2017), result in an increased risk of intoxication and greater vulnerability to this type of intoxication (World Health Organization, 2017).

Since 2000, the WHO has been trying to combat the legacy that pesticides have left in terms of global public health (World Health Organization, s/d) but in 2008, pesticides were still responsible for 45% of poisonings in children and were considered

the ninth most common substance reported to poison control centres (Roberts *et al.*, 2012).

A study conducted in the Paediatric Emergency Department of Yüzüncü Yıl Hospital, Turkey considering all cases of acute intoxication admitted between 1 June 2010 and 30 November 2011, revealed that pesticides/insecticides accounted for about 38.2% of the cases, out of a total of 102 patients under 5 years-old, being considered the main non-pharmaceutical agents involved in poisoning (Kizilyildiz *et al.*, 2018). Of note, in the study period, a deadly case of acute pesticide poisoning was recorded (Kizilyildiz *et al.*, 2018). High rates of pesticide poisoning are extremely worrying since evidence indicates that children's exposure to pesticides results in increased level of DNA cord breakage, oxidative damage, and increased micronuclei in peripheral blood lymphocytes (Kapka-Skrzypczak *et al.*, 2019).

Paraquat is found in several of the pesticide poisoning cases. This is a cationic herbicide, with no specific antidote (Elenga *et al.*, 2018), that affects multiple body organs (Song *et al.*, 2019) and is related to high mortality rates. Between January 2010 and May 2017, 110 children were hospitalized with acute paraquat poisoning at the Second University Hospital of Western China (Song *et al.*, 2019). Of these, 34.6% were younger than 6 years-old; 60.5% of these were male. Regarding the intent of the intoxication, 63.9% related to accidental ingestion, while 36.1% were suicide attempts. Acute renal lesions were found in 38.2% of the intoxicated children (Song *et al.*, 2019). In these cases, timely treatment of acute kidney lesions avoided further complications and death (Song *et al.*, 2019).

In 2007, paraquat was withdrawn from the European Union market due to its high toxicity and lethality in the previous years, even when victims ingested small amounts (Song *et al.*, 2019). In the same year, the marketing of paraquat was also banned in French Guiana, South America (Elenga *et al.*, 2018). Nevertheless, the pesticide remained free on the neighbouring countries' markets, making it accessible to the population of French Guiana and thus explaining the occurrence of further paraquat poisonings (Elenga *et al.*, 2018). Accordingly, a study conducted in the three main hospitals of French Guiana, from 1 January 2008 to 31 December 2015, disclosed 62 intoxicated patients, of which 18 were children (the mean age was 13.4 years-old) (Elenga *et al.*, 2018). Children remained hospitalised longer (mean 15 days) than adults (mean 2 days), although having ingested smaller doses (48.8 mg/kg vs. 595.8 mg/kg) (Elenga *et al.*, 2018). Many of the paraquat poisonings were self-poisoning cases (84%), with 3 cases relating to criminal poisoning.

Of interest, 2 children aged 5 and 8 years-old were forced by their mother to drink paraquat with her; the mother died within 24 hours, but the children managed to survive. The other case of criminal poisoning concerned a man who was poisoned at work and died 14 days later, after consumption about 200 mL of paraquat. The mortality rate in children in this study was 22% (4 cases), while in adults it was about 65% (26 cases) (Elenga *et al.*, 2018).

In addition to paraquat, zinc phosphide is a rodenticide commonly used, for which there is no antidote (Sánchez-Villegas and Bárcena-Ruiz, 2017). A retrospective, observational study from 2005 to 2015 analysed the medical records of 36 patients admitted to paediatrics of the Centre for Toxicological Information and Care of the General Hospital Dr. Gaudencio González Garza, Mexico. From these, 66% were children between 1 and 2 years-old, and 8% were adolescents who used the compound for attempting suicide (Sánchez-Villegas and Bárcena-Ruiz, 2017). In all cases, exposure to zinc phosphide occurred at home, none of the patients died, but all presented symptoms such as nausea, vomiting, metabolic acidosis, abdominal pain, hypoglycaemia and hypotension (Sánchez-Villegas and Bárcena-Ruiz, 2017).

1.1.6. Other commons agents

Besides the toxic agents mentioned above, other compounds are involved in poisonings in children, although less frequently, such as carbon monoxide (CO) (Szponar *et al.*, 2012). In 2016, CO poisoning was responsible for 5,000 poisonings in children in Boston, posing a challenge to healthcare professionals (Baran *et al.*, 2018), particularly during the winter (Szponar *et al.*, 2012).

Other products frequently involved in children poisonings are plants. Plant poisoning in children younger than 6 years-old was ranked, in 2018, as the third most frequent cause of emergency calls to poison centres in Germany (Hermanns-Clausen *et al.*, 2019). In France, in 2010, this poisoning agents accounted for about 5% of all cases analysed at anti-poison centres (Laffargue *et al.*, 2011). Plants contain toxins that trigger adverse effects when ingested or when in contact with the skin. Children and animals are the most exposed to toxic plants since the environment is often the same (Poppenga 2010). Plant toxicity varies with the species considered (Poppenga 2010).

Poisoning by mushrooms also represents a serious public health problem in developing countries. There are about 5,000 species of wild mushrooms worldwide, of

which 100 are classified as poisonous and up to 10 are fatal (Mărginean *et al.*, 2019). A study at the Department of Paediatric Cardiology, University of Medicine, Pharmacy, Sciences and Technology, Târgu Mures, Romania, in 2019, evaluated the case of two siblings, a 9-year-old girl and a 5-year-old boy, who were hospitalized for having strong gastrointestinal symptoms 24 hours after ingesting wild mushrooms. Several tests were performed to reverse the effects, however, the condition of both children worsened, leading to the death of both (Mărginean *et al.*, 2019). Wild mushroom picking are part of Romania's culture and used for the subsistence of families with low economic income (Mărginean *et al.*, 2019).

1.2. Route of intoxication

As depicted in the intoxication cases described above, most intoxications occur from ingestion of poisons (O'Malley and O'Malley, 2018; Belchior, 2016), which is intrinsically linked to the curiosity of the children and the practice of bringing objects to the mouth as part of the object exploitation in toddlers (Ramos *et al.*, 2005; Repetto, 1997).

A study conducted in Egypt between 2009 and 2013, in which 38,470 children were admitted to the poisoning treatment centre of the Ain Shams University in Cairo, disclosed ingestion as the most prevalent route of intoxication (96.3%), followed by inhalation (2.0%); in 1.9% of the cases it was not possible to assess the intoxication route (Azab *et al.*, 2016). Similarly, ingestion was to the main route of intoxication (75%) observed in a 11-year study (2004–2014) involving twenty-four paediatric emergency departments of France (Claudet *et al.*, 2017b).

1.3. Circumstances of the intoxication

The circumstances in which poisoning occurs in children are different from those for adults (Belchior, 2016). Accidental or involuntary intoxications concerns those cases which the individual has no intention of getting into contact with the toxicant or those in which the individual has no intention of ingesting drug doses that would cause intoxication. Voluntary or intentional intoxications are considered all cases in which the

individual voluntarily ingested excessive drug doses, for instance, those cases of suicidal ideation or abuse of ethanol (Salvado, 2013).

Most adult poisonings are intentional and, while many intoxications in adolescents relate to cases of suicide attempts or voluntary ingestion of alcohol (O'Malley and O'Malley, 2018), most intoxications in younger children are accidental (Mowry *et al.*, 2015) either due to exploratory ingestions or therapeutic errors. Such a pattern was verified in the study conducted in Egypt, which involved about 38,470 children observed at the Department of Forensic Medicine and Clinical Toxicology, Faculty of Medicine, Ain Shams University, Cairo, between 2009 and 2013, and disclosed that most poisonings were considered accidental (99.6%) in the preschool and school age groups (Azab *et al.*, 2016). The unsupervised home environment is a real danger to children, most poisonings occurring due to the leaving of medication, bleach, detergents and other easy-opening products, within the reach of children (Belchior, 2016).

Regarding suicide attempts, such cases mainly involve ethanol and pharmaceuticals (e.g., over-the-counter drugs, paracetamol, and central nervous system medicines) (O'Malley and O'Malley, 2018). A study involving five Poison Control Centres in the USA from February to September 2017, evaluated all calls made to caregivers due to exposure to solid dose medications by children under 5 years-old, and found that over half of exposures (51.5%) concerned prescription medications that had previously been removed from the original packaging, while 20.8% involved over-the-counter medications (Agarwal *et al.*, 2020).

In what concerns the circumstances of the intoxication, it is also important to understand whether they occurred during vacation time, weekends, bank holidays, and at the school time. In Brazil, a study analysed 45 cases of accidental exogenic poisoning involving children and adolescents, in 2013, and found that most poisonings occurred on Fridays (22.2%) and weekends (55.5%) (Brito and Martins, 2015). These data are also compatible with the study conducted at the Department of Paediatrics, University Hospital of Split, Croatia, from 2008 to 2015, in which, from the 488 children admitted, about 81.6% of the poisoning cases occurred during the weekends and holidays (Vrkic-Boban *et al.*, 2018). In relation to the month, April (17.8%) and June (13.3%) had the highest incidence (Brito and Martins, 2015). Most of the poisonings occurred in the late afternoon and evening, which relate to periods at which children and adolescents are in the home environment, this also justifying the higher number of poisonings on the weekends (Brito and Martins, 2015).

1.4. Intoxications in urban *versus* rural environments

Childhood poisoning and related fatalities mainly occur in low- and middle-income countries (World Health Organization, 2008), but substantial differences might also be observed within countries, between urban and rural areas (Pac-Kozuchowska *et al.*, 2016; Pawlowska-Kamieniak *et al.*, 2018). In this regard, a study conducted at the Children's Hospital of Chongqing Medical University in China between January 2006 and December 2015, in a total of 586 cases of hospitalized children, revealed that 79.0% were from rural areas and, of these, 94.0% were hospitalized for accidental intoxication (Song *et al.*, 2017).

A study conducted by the Department of Paediatrics, Medical University of Lublin, Poland, aimed to characterise ethanol consumption in the 492 children admitted between 2004 and 2013, according to the environment in which they live (Pawlowska-Kamieniak *et al.*, 2018), revealed that the youngest child intoxicated by ethanol was a 7.6-year-old boy derived from a rural environment, as opposed to the older 18-year-old boy, who came from an urban area (Pawlowska-Kamieniak *et al.*, 2018). Although intoxications in children from rural locations usually occur for younger ages and urban areas are more related to intoxication in adolescents, no gender differences were generally observed (34.3% boys and 12.9% girls were from rural areas, *versus* 22.8% boys and 29.9% girls came from urban zones) (Pawlowska-Kamieniak *et al.*, 2018). Another study in the same country, conducted from July 2008 to December 2012, involved 848 cases of ethanol intoxicated children, most derived from the urban environment (64.5%) (Pac-Kozuchowska *et al.*, 2016). However, children under 5 years-old were the most prevalent in the rural population (Pac-Kozuchowska *et al.*, 2016). Overall, comparable numbers of children from urban and rural origin reveal that consumption of ethanol is no more prevalent in one environment than in the other (Pawlowska-Kamieniak *et al.*, 2018). It may be at stake, the fact that children in both environments have easy access to alcohol (Pawlowska-Kamieniak *et al.*, 2018).

In addition to alcohol, also intoxications by pharmaceuticals and household chemicals, occur more frequently in rural young children and are mostly accidental (Pac-Kozuchowska *et al.*, 2016). In this line, as previously explained, also poisoning by pesticides are very usual in the rural areas. Intentional intoxication by pesticides is related

to a large portion of suicides in adolescents, especially in rural areas of countries with low and medium economic income (World Health Organization, s/d).

1.5. Gender and age susceptibility

Exploratory ingestions in toddlers and children at an early age mainly occur at home by substances there held. In children under 5 years-old, intoxications are mostly accidental, while in adolescents, intentional intoxications are more frequent (Ani, 2013).

In Portugal, the epidemiology of poisonings in children aged 0–17 years has not been extensively studied, but data provided by Centro de Informação Antivenenos (CIAV) indicate that the prevalence of poisonings in children peaks at 1–4 years-old and mainly concerns males (Centro de Informação Antivenenos, 2017). Other studies also point this gender tendency at the same age group for poisonings caused by household products (Belchior, 2016; Gontko *et al.*, 2013; Koh *et al.*, 2018). The fact that more poisonings occur in males is argued by some authors that link to the fact that they tend to be more active (Belchior, 2016). On the other hand, the female gender is particularly linked to attempts of suicide in adolescents (Afukov *et al.*, 2019; Gontko *et al.*, 2013; Matalová *et al.*, 2019; Nistor *et al.*, 2017). In this regard, females play a predominant role in poisoning by pharmaceuticals at ages above 12 years (Dias, 2017; Matalová *et al.*, 2019; Nistor *et al.*, 2017; Pawlowska-Kamieniak *et al.*, 2018). Still, males predominate in cases of ethanol intoxication in adolescents (Dias, 2017; Flanagan *et al.*, 2005; Mowry *et al.*, 2015; Pawlowicz *et al.*, 2013), with high ethanol consumption occurring as early as at 13 years-old, including in Portugal (Belchior, 2016; Dias, 2017).

1.6. Guidelines for initial and general management of poisoning

Many of the poisonings in children occur at home, with a high number of cases being treated at the place, without any medical assistance (American Association of Poison Control Centers, 2017). This procedure is however unrecommended, the parents being advised to always contact a medical or poison control centre in the face of an intoxication (Poison Control, 2019). Poison information centres provide detailed information on intoxications both for the general population and health care

professionals, and educate for prevention (Krenzelok, 1995). In Portugal, data provided by CIAV indicate that approximately half of the 30,000 calls received by the helpline in 2016 concerned intoxications at the initial poisoning stage, allowing a significant decline of morbidity and mortality through appropriate guidance on the intoxication management, and a significant decline of hospital admissions in case of false alarm (Centro de Informação Antivenenos, 2017).

At the hospital, in order to adopt the necessary and correct therapeutic procedures, clinicians need to understand certain aspects of the intoxication and of the child/adolescent, such as the route and time of exposure; nature and dose of the toxic (including all medications/products that were potentially accessed or administered); age and weight of the patient; and other circumstances of the poisoning (Ani, 2013).

Some unspecific measures might be adopted, such as the entire gastrointestinal lavage, also called gastric lavage, which help eliminate ingested, unabsorbed drugs, but has a limited role in the treatment and should not be performed without a physician's supervision. Administration of activated charcoal is also usually recommended for most ingestions (Ani, 2013), although there are no effective guidelines in relation to its use (Zellner *et al.*, 2019). In case of children that do not show improvements, activated charcoal can be administered in greater quantity (Chiew *et al.*, 2019). In fact, activated charcoal plays a key role in both primary and secondary detoxification as its repeated administration do not cause any harm to the patient (Zellner *et al.*, 2019). Nevertheless, activated carbon does not result in cases of poisoning by base acids, alcohols, organic solvents, organic salts or metals (Zellner *et al.*, 2019). A 2016 study by the Department of Internal Medicine and Clinical Toxicology of the Poison Control Centre in Munich, Germany, reported that from the 178,425 cases of intoxication treated in German hospitals, 4.37% of the cases had recommendation to administer activated carbon. Activated charcoal is indicated for the treatment of poisonings from moderate to severe life-threatening (Zellner *et al.*, 2019) and it is more effective, when administered in the first hour after administration (Ani, 2013). The indicated dose to be administered is usually about 10-40 times of the dose of the intoxicating substance and should be applied repeatedly in the case of substances that persist longer in the stomach (Ani, 2013). For some agents, specific antidotes are available, whose administration may follow the determination of the serum drug levels to help in the decisions of treatment (Ani, 2013). For instance, in the case of patients who had overdosed on paracetamol, they should be given activated carbon to prevent the drug from being absorbed and in patients at risk of

hepatotoxicity, intravenous acetylcysteine should be given. For opioid poisoning, the most common antidote is naloxone; for exposure to organophosphate and carbamate pesticides, the use of atropine is extremely common, while for benzodiazepines, the best antidote is flumazenil (Bucarechi and Baracat, 2005).

In what concerns poisoning by illicit drugs such as cannabis/marijuana and ecstasy, the management of intoxication is relatively identical (Ani, 2013). The administration of benzodiazepines is essential to calm the stimuli and control the agitation of the patients; it is also essential to perform blood and urine tests, to confirm the existence of illicit substances (Ani, 2013). In addition, the support provided by the doctors consists of a constant follow-up, specially to assess the risk of hyperthermia, which is symptom present in children who are intoxicated by these illicit drugs, in special by amphetamines; and the hypertension or other complications that arise during intoxication (Ani, 2013). In the vast majority of cases, intoxications by illicit drugs are mild and therefore, few hours following the administration of benzodiazepines, the intoxication symptoms are eliminated, without requiring further measures (Ani, 2013). In the case of more severe intoxications that include respiratory, renal or cardiac complications, the clinician will determine the procedures that should be adopted (e.g., haemodialysis, respiratory assistance, etc.) (Pianca *et al.*, 2017).

In Turkey, a study conducted between June 1, 2010, and November 30, 2011, at the Paediatric Emergency Department of the Yüzüncü Yıl University of Van found that in 36.4% of the cases gastric lavage was performed; and activated charcoal was administered in 53% of the cases, the remaining 9.6%, received specific treatment, such as haemodialysis and/or antidotes, in addition to symptomatic treatment (Kizilyildiz *et al.*, 2018). Also, in the retrospective study of Goudarzi *et al.* (2020) on tramadol paediatric poisonings between 2010 and 2015, at the Noor University Hospital and Ali-Asghar, Iran, the first-line treatments administered to the 189 patients consisted of activated charcoal (87.3% of the cases), gastric lavage (59.3%), oxygen therapy with mask (46.6%), naloxone (11.6%), anticonvulsants (13.2%) and intubation and ventilation (5.3%) (Goudarzi *et al.*, 2020).

1.7. Prevention and child safety at home

In what concerns prevention and child safety, in particular at home, special attention should be paid to areas to which the child has privileged access, avoiding stored in these places of products such as medicines, cleaning and washing chemicals, pesticides, alcohol, bleach and other disinfectants, alcoholic beverages and hygiene products (Pitone, 2020; Ani, 2013; American Association of Poison Control Centers, 2017). For such products, unreachable storage alternatives should be considered, for example at high located places. If this option is not possible, it is important to keep the items on their original containers. For instance, in addition to the suitable, safe placing, it is important to maintain the medicines and other products in their original packaging, bearing in mind the number of pills contained inside each package (Pitone, 2020). It is important to note that adults often remove medicines from the original packaging, which can result in an accident as the child has easier access to the secondary packaging. Accordingly, a study by Agarwal *et al.* (2020) on the 7,252 calls concerning unsupervised medicine exposures in children under 5 years-old revealed that, from the 4,496 individuals that accepted to participate, 71.6% occurred in children younger than 2 years-old, for which more than half of the poisonings (51.5%) occurred because children had access to the secondary packaging of the drugs taken from the original packaging (Agarwal *et al.*, 2020). About 33.8% of these poisonings occurred with prescription drugs, 32.8% related to over-the-counter drugs with child-resistant packaging, and 29.9% from over-the-counter drugs without child-resistant packaging (Agarwal *et al.*, 2020). From this study it was evident that most paediatric intoxications were the result of adults removing the medications from the original packaging, which resulted in the placement of the drug in an unsafe package for children, making it more available to inappropriate use (Agarwal *et al.*, 2020).

Colored boxes for medication storage or placement of household products in bottles of soft drinks or food are also not advisable as it might lead to inadvertent administration (Agarwal *et al.*, 2020; Pitone, 2020). Also, danger toxicants should be deposited in child-proof containers or protected with child-resistant locks (American Association of Poison Control Centers, 2017). Even so, at no time should it be assumed that the child cannot open a package, even child-resistant packages, or that (s)he is not exposed to any product, child surveillance and supervision being of paramount importance (Pitone, 2020).

Moreover, one should be aware of all types of plants that are kept at home as, in case of poisoning by ingestion of any of the leaves, this information should be known.

Above all, education of the child to not eat the plants is highly recommended (Pitone, 2020).

It is important that parents create a habit of viewing each product label before using it (American Association of Poison Control Centers, 2017). Protect the house with the installing of a CO detector, can also help protect the whole family, especially in the colder months, since exposure to this colorless and odorless gas can lead to serious illness or even death (American Association of Poison Control Centers, 2017). If the child or adolescent self-medicate is important to check whether the dose ingested is adequate, and an adult should be present to supervise the time of intake (Pitone, 2020). Supervision of young children should never be neglected (The National Safety Council, 2020).

2. Aims

Although the number of child-poisoning deaths has fallen in the last decades, acute intoxication in children remains a matter of concern and embodies a frequent cause of admission in paediatric emergency units. In this context, the epidemiological surveillance for specific country locations is of utmost importance to establish the extent and characteristics of the problem, and to accordingly determine the preventive measures to be implemented.

In Portugal, the epidemiology of intoxications in children aged 0–17 years-old has not been comprehensively studied. As such, this research intended to provide a comprehensive assessment of the child-intoxication profile among children of specific aged groups in a tertiary hospital located the North Region of Portugal, by comparing age-, gender- and origin (urban or rural)-specific trends in cause-specific intoxication rates. Specifically, the dissertation aimed to retrospectively analyse the epidemiology of accidental and intentional poisoning in the child and adolescent population (0-17 years-old) admitted to the Paediatric Emergency Unit of the *Centro Hospitalar de São João*, E. P. E. (CHSJ), Porto (Portugal) from 2014 to 2018, to allow a better understanding of the epidemiology of this problem in the region and, therefore, public health authorities to identify priority areas for interventions.

3. Materials and Methods

3.1. Study Population

This study included all patients under 18 years-old who presented at the Paediatric Emergency Unit of the CHSJ, including those who were transferred from other hospitals, between 1 January 2014 and 31 December 2018. Patients who met these study requirements were further selected, by excluding those cases concerning i) food poisoning (as it was impossible to determine if toxins were present or the case related to a simple infection), ii) bites from venomous animals, and iii) incorrect diagnosis of poisoning [performed according to the international classification of diseases, ninth revision (ICD-9)] . Cases presenting a complete lack of data on the patient's file or other clinical file anomalies were also excluded. All the files of the patients admitted to this study were made available by the database of the CHSJ.

3.2. Ethical concerns

The research involved the processing of previously collected sensitive personal health data (secondary use). As such, previous approval of the study by the CHSJ Healthcare Ethics Commission was sought and granted in March 2019. In addition, authorization to access the clinical files was also solicited to the competent authority for the re-use of clinical data (*Responsável pelo Acesso à Informação*, RAI) – the entity that manages the access to the patient personal data and processes notifications/authorizations of the National Data Protection Commission (NDPC), which also emitted the DataREuseCertificate for Research (DARE) (Attachment 5 and 6).

3.3. Study design

Data on children referred to the Paediatric Emergency Unit of CHSJ with "Intoxication" as either the cause for admission or the ICD-9 diagnosis, were retrieved from hospital medical records. Data on the intoxication (time and type of intoxication, intent, the precipitating factor in cases of attempted suicide, the time elapsed between the exposure and hospital admission, the clinical symptoms and signs, the changes in the

biochemical tests, treatment, clinical outcome and discharge destination) and children characteristics (age, gender, school cycle, post code of residence, and place of origin in the case of patients referred from other hospitals) were collected. Although the National Institute of Child Health and Human Development (NICHD) paediatric terminology was followed, for simpler analysis and interpretation, patients were classified only into four age groups: i) 0–2 (neonates, infants, and toddlers); ii) 3–5 (early childhood); iii) 6–12 (middle childhood); and iv) 13–17 (adolescents).

3.4. Statistical analysis

Collected data were statistically analysed using the IBM Statistical Package for the Social Sciences (SPSS) Statistics 27[®] software.

4. Results and Discussion

From January 2014 to December 2018, 389,913 patients were admitted to the Paediatric Emergency Unit of the CHSJ to receive clinical assistance. Of these, all cases of poisoning, classified as such either in the admission or during the ICD-9 diagnosis, accounted for 928 cases (0.24%). From these, about 142 cases were excluded, as they failed to meet the selection criteria: 9 cases related to food poisoning and 133 lack data on the agent that triggered the poisoning. This represented a loss of 15.3% of the cases, as has occurred in similar studies which also encountered food poisoning cases (Dias, 2017; Koh *et al.*, 2018; Matalová *et al.*, 2019) or had incomplete data files (Azab *et al.*, 2016; Dias 2017; Koh *et al.*, 2018; Tham *et al.*, 2020; Tönisson *et al.*, 2013).

About 786 cases (0.2%) matched the criteria accepted for the study, yielding paediatric intoxication rates similar to a previous study performed in the same hospital between January 2010 and December 2014 (Dias, 2017), and to other studies performed in the Department of Paediatrics of the University Hospital Olomouc, Czech Republic between January 2010 and December 2012 (0.36%) (Matalová *et al.*, 2019) and in Spain (0.23%) by the Spanish Society of Paediatric Emergency Medicine, between 2008 and 2017 (Santiago *et al.*, 2020). In Egypt, in the Department of Forensic Medicine and Clinical Toxicology, Faculty of Medicine, Ain Shams University, between January 2009 and December 2013 (44.1%) (Azab *et al.*, 2016), and in the Paediatric University Hospital in Białystok, Poland and Department of Paediatrics, Medical University of Lublin, Poland between 2006 and 2010 (25% and 13%, respectively) (Pawlowicz *et al.*, 2013; Pac-Kozuchowska *et al.*, 2016), poisoning seems to represent a higher concern in the context of paediatric emergency admissions. The lower rates in the former cases might be partially explained by the previously improvement in the preventive and educational measures in such countries (e.g., through campaigns that increase the awareness of the caregivers on the dangers and that disseminated the availability of the helplines to assist in such incidents) (Dias, 2017; Vrkic-Boban *et al.*, 2018).

The majority of these paediatric cases admitted to the CHSJ, came on their own initiative and by their own means, similarly to the observed in other studies (Azab *et al.*, 2016). Toddlers (0–2 years) represented about 18.4% of the intoxicated patients (Table 1), while children in the early childhood (3–5 years) corresponded to about 9.9% of the total intoxications. The age group of 6–12 years corresponded to about 6.5% of the total

cases, being the age group with the lowest percentage of intoxications. On the other hand, adolescents represented 65.1% of the intoxicated paediatric population.

Regarding the type of intoxication (Table 1), it was possible to observe that poisoning by pharmaceuticals and household products were the most prevalent in the age groups 0–2 years (46.9% and 31.0%, respectively) and 3–5 years (65.4% and 20.5%, respectively). Intoxications with pharmaceuticals and household products in neonates, infants, and toddlers are highly evident in several studies (Abbas *et al.*, 2012; Azab *et al.*, 2016; Gontko *et al.*, 2013; Matalová *et al.*, 2019; Koh *et al.*, 2018) and are, as previously explained, a pattern explicated by their exploratory behaviour (Brito and Martins, 2015; Matalová *et al.*, 2019) and by the adults' removal of medicines and/or household products from the original packaging, resulting in accidents as children easily access the drugs through the secondary packaging (Agarwal *et al.*, 2020; Gokalp, 2019).

Table 1. Distribution of the agent involved in intoxication by age group.

		Age group				
		<2	3–5	6–12	13–18	Total
		145 (18.4%)	78 (9.9%)	51 (6.5%)	512 (65.1%)	786 (100%)
		N (%)	N (%)	N (%)	N (%)	N (%)
Cause of intoxication	Ethanol	2 (0.3)	1 (0.1)	2 (0.3)	323 (41.1)	328 (41.7)
	Pharmaceuticals	68 (8.7)	51 (6.5)	26 (3.3)	145 (18.4)	290 (36.9)
	Household products	45 (5.7)	16 (2.0)	8 (1.0)	3 (0.4)	72 (9.2)
	Other	19 (2.4)	5 (0.6)	2 (0.3)	9 (1.1)	35 (4.5)
	Gases	6 (0.8)	4 (0.5)	13 (1.7)	8 (1.0)	31 (3.9)
	Ethanol & illicit drugs	0 (0.0)	0 (0.0)	0 (0.0)	14 (1.8)	14 (1.8)
	Illicit drugs	1 (0.1)	0 (0.0)	0 (0.0)	10 (1.3)	11 (1.4)
	Pesticides	4 (0.5)	1 (0.1)	0 (0.0)	0 (0.0)	5 (0.6)

Pharmaceuticals were also the most prevalent agents of intoxication in the middle childhood (51.0%), in accordance with other reports (Flanagan *et al.*, 2005; Hoikka *et al.*, 2013; Ahmed *et al.*, 2015), being also explained by the easy access to the medication that is left within their reach and by therapeutic errors (Sahin *et al.*, 2011). In this regard, drugs acting on the CNS were the main agents involved in poisoning by pharmaceuticals,

particularly in adolescents (37.9%) (Table 2). This can be explained by the fact that the Portuguese population has a high consumption of psychotropic drugs (Belchior, 2016). Intoxication by the simultaneous use of different pharmaceutical classes was also prevalent (8%), in line with the CIAV reports (Belchior, 2016).

Table 2. Influence of age on the pharmaceutical class used in the intoxication.

		Age group				
		<2	3–5	6–12	13–18	Total
		68 (8.6%)	51 (6.6%)	26 (3.3%)	145 (19.1%)	290 (36.9%)
		N (%)	N (%)	N (%)	N (%)	N (%)
Pharmaceutical class	Drugs acting on the CNS	15 (1.9)	9 (1.2)	5 (0.6)	55 (7.6)	84 (10.7)
	Other pharmaceuticals	45 (5.7)	36 (4.6)	18 (2.3)	44 (5.6)	143 (18.2)
	Multiple pharmaceuticals	8 (1.0)	6 (0.8)	3 (0.4)	46 (5.9)	63 (8.0)

In the case of adolescents (Table 1), both ethanol (63.1%) and pharmaceuticals (28.3%) prevailed, also in line with other studies (Gunja, 2012; Pawlowicz *et al.*, 2013; Vrkic-Boban *et al.*, 2018), including some performed in Portugal (Belchior, 2016; Dias, 2017). Such data are not surprising, as alcohol abuse is a cross-cutting problem in both adults and young people, especially in adolescence (Silva *et al.*, 2012) where young people consume under the influence of peers, believing that if they drink they would feel better and more relaxed (Sakoman *et al.*, 1999). According to WHO data, Portugal is one of the countries where alcohol consumption is higher (World Health Organization, 2014), this becoming a risk factor contributing to the occurrence of this type of intoxication (Belchior, 2016). These results also agree with national statistics on calls made to CIAV indicating that, during a ten-year study period, about 77 calls were made daily, from which 8,973 cases corresponded to intoxication in adolescents, mostly due to medications and drugs of abuse such as alcohol (Alves *et al.*, 2017).

We found that it is in the 13–18 age group that most poisonings are concentrated (Table 1), as observed in several studies (Dias, 2017; Goudarzi *et al.*, 2020; Malangu,

2008; Pawlowicz *et al.*, 2013). However, numerous other studies also observed higher prevalence of intoxications in younger children (<6 years-old) (Abbas *et al.*, 2012; Agarwal *et al.*, 2020; Azab *et al.*, 2016; Belchior, 2016; Claudet *et al.*, 2014; Flanagan *et al.*, 2005; Koh *et al.*, 2018; Oliveira and Suchara, 2014; Sharif *et al.*, 2003; Tsalkidis *et al.*, 2010; Z'Gambo *et al.*, 2016), which, as referred, is due to the child's curiosity and exploratory ingestions (Belchior, 2016). In adolescents, it can be explained by the high consumption of ethanol, as early as at 13 years-old (Dias, 2017).

In relation to gender (Table 3), it was possible to observe that 53.1% of the toddlers (0–2 years) corresponded to males, and 46.9% to females. In the case of early childhood (3–5 years), 56.4% were males *versus* 43.6% females, while the age group of 6–12 years and adolescents comprised about 54.9% and 45.1% of males, respectively, and 45.1% and 54.9% of females, respectively. Although no disparities were observed in our study, gender differences in the intoxication profile of children are frequently reported, where intoxications in males predominate (Agarwal *et al.*, 2020; Belchior, 2016; Claudet *et al.*, 2014; Hassan and Siam, 2014; Rodrigues *et al.*, 2018).

Table 3. Age crossed with gender

		Age group				
		<2	3–5	6–12	13–18	Total
		145 (18.4%)	78 (9.9%)	51 (6.5%)	512 (65.1%)	786 (100%)
		N (%)	N (%)	N (%)	N (%)	N (%)
Gender	Female	68 (8.7)	34 (4.3)	23 (2.9)	281 (35.8)	406 (51.7)
	Male	77 (9.8)	44 (5.6)	28 (3.6)	231 (29.4)	380 (48.3)

With regard to gender differences across the several types of intoxication (Table 4), our study indicate that females prevail in intoxications by pharmaceuticals (48.0%), in accordance with other studies (Afukov *et al.*, 2019; Gontko *et al.*, 2013; Matalová *et al.*, 2019; Nistor *et al.*, 2017), adolescents most contributed for such data. It was also possible to verify that male adolescents represented the most prevalent group in intoxications caused by non-pharmaceuticals, mainly ethanol (47.1%), as observed in other studies (Dias, 2017; Flanagan *et al.*, 2005; Mowry *et al.*, 2015; Pawlowicz *et al.*

2013), but also by household products (11.1%), gases (4.5%), ethanol and illicit drugs (3.2%), only illicit drugs (1.6%) and pesticides (1.1%).

Table 4. Distribution of the cause of intoxication by gender

		Gender		
		Female	Male	Total
		406 (51.7%)	380 (48.3%)	786 (100%)
		N (%)	N (%)	N (%)
Cause of intoxication	Ethanol	149 (19.0)	179 (22.8)	328 (41.7)
	Pharmaceuticals	195 (24.8)	110 (14.0)	305 (38.8)
	Household products	30 (3.8)	42 (5.3)	72 (9.2)
	Gases	14 (1.8)	17 (2.2)	31 (3.9)
	Ethanol & illicit drugs	2 (0.3)	12 (1.5)	14 (1.8)
	Illicit drugs	5 (0.6)	6 (0.8)	11 (1.4)
	Pesticides	1 (0.1)	4 (0.5)	5 (0.6)
	Other	10 (1.3)	10 (1.3)	20 (2.5)

In our study, it was observed that there was no significant variation in the number of poisonings per year (Table 5) between 2014 and 2018, as in the case of the study conducted in Egypt between 2009 and 2013 (Azab *et al.*, 2016). Regarding the seasonality, it was also not possible to verify a significant variation (Table 5), contrary to other studies that observed that intoxications peak in the spring, such as that conducted in Department of Paediatrics, Mackay Memorial Hospital, Taipei, Taiwan between 1996 and 2007 (36.7%) (Cho *et al.*, 2008); or winter, such as in Department of Forensic Medicine and Clinical Toxicology, Faculty of Medicine, Ain Shams University, Egypt between 2009 and 2013 (40%) (Azab *et al.*, 2016). In Poland children intoxications peak in the months of September (10.7%), October (11.7%), and December (11.0%) (Gontko *et al.*, 2013), while in Brazil, April (17.8%) and June (13.3%) seem to be more critical months (Brito and Martins, 2015). Regarding the days of the week in which the majority of the poisonings occurred, it was not possible to observe a large discrepancy in our study, in ages below 13, but in the age group 13–18 years-old there is a higher percentage of poisonings on Fridays (8.9%), Saturdays (14.6%) and Sundays (15.0%), which is

consistent with the studies conducted in Brazil, in the Emergency and Primary Care, in 2013 (Brito and Martins, 2015) and in Croatia, in the Department of Paediatrics, University Hospital of Split, from 2008 to 2015 (Vrkic-Boban *et al.*, 2018). Unequal distributions either in the season or days/months might be partially explained by the school periods and leisure time, as intoxications in children usually match holidays and weekends, while adolescents are mostly intoxicated (specially by ethanol and illicit drugs) during the weekend, New Year's Eve and specific holidays, when they party with their peers (Vrkic-Boban *et al.*, 2018).

Table 5. Distribution of the year, day of week, season and school holiday by age group.

		Age group				
		<2	3–5	6–12	13–18	Total
		145 (18.4%)	78 (9.9%)	51 (6.5%)	512 (65.1%)	786 (100%)
		N (%)	N (%)	N (%)	N (%)	N (%)
Year	2014	34 (4.3)	16 (2.0)	7 (0.9)	102 (13.0)	159 (20.2)
	2015	32 (4.1)	14 (1.8)	16 (2.0)	87 (11.1)	149 (19.0)
	2016	25 (3.2)	22 (2.8)	14 (1.8)	113 (14.4)	174 (22.1)
	2017	27 (3.4)	14 (1.8)	4 (0.5)	95 (12.1)	140 (17.8)
	2018	27 (3.4)	12 (1.5)	10 (1.3)	115 (14.6)	164 (20.9)
Day of the week	Monday	14 (1.8)	11 (1.4)	9 (1.1)	62 (7.9)	96 (12.2)
	Tuesday	17 (2.2)	12 (1.5)	6 (0.8)	57 (7.3)	92 (11.7)
	Wednesday	16 (2.0)	8 (1.0)	11 (1.4)	50 (6.4)	85 (10.8)
	Thursday	25 (3.2)	11 (1.4)	5 (0.6)	40 (5.1)	81 (10.3)
	Friday	17 (2.2)	11 (1.4)	6 (0.8)	70 (8.9)	104 (13.2)
	Saturday	29 (3.7)	10 (1.3)	4 (0.5)	115 (14.6)	158 (20.1)
	Sunday	27 (3.4)	15 (1.9)	10 (1.3)	118 (15.0)	170 (21.6)
Season	Winter	39 (5.0)	17 (2.2)	23 (2.9)	135 (17.2)	214 (27.2)
	Spring	36 (4.6)	17 (2.2)	11 (1.4)	128 (16.3)	192 (24.4)
	Summer	31 (3.9)	22 (2.8)	7 (0.9)	129 (16.4)	189 (24.0)
	Fall	39 (5.0)	22 (2.8)	10 (1.3)	120 (15.3)	191 (24.3)
School holiday	Yes	0 (0.0)	15 (1.9)	11 (1.4)	202 (25.7)	228 (29.0)
	No	0 (0.0)	63 (8.0)	40 (5.1)	310 (39.4)	413 (52.5)
	No Data	145 (18.4)	0 (0.0)	0 (0.0)	0 (0.0)	145 (18.4)

In the course of this study, it was not possible to confirm if neonates, infants, and toddlers were enrolled in any educational establishment (Table 6), as it was not possible to confirm whether they were on school holidays (Table 5). In the ages of 3 to 5 years-old, it was possible to verify that all attended preschool education and that only 19.2% were on school holidays, when admitted to the emergency department. In the case of middle childhood (6–12 years-old), 62.8% attended the first cycle, 17.6% attended the second cycle and 19.6% attended the third cycle, and only 21.6% were in school holidays, when admitted to the emergency department. As for adolescents, 11.7% attended the third cycle and 87.9% attended secondary school, and 39.4% were on school holidays, when admitted to the emergency department. It should be noted that the data show that there were more intoxications when the children were in school periods (52.5%) than in vacation (29.0%).

Table 6. School cycle distribution by age group.

		Age group				
		<2	3–5	6–12	13–18	Total
		145 (18.4%)	78 (9.9%)	51 (6.5%)	512 (65.1%)	786 (100%)
		N (%)	N (%)	N (%)	N (%)	N (%)
School cycle	Preschool	0 (0.0)	78 (9.9)	0 (0.0)	0 (0.0)	78 (9.9)
	1st cycle	0 (0.0)	0 (0.0)	32 (4.1)	0 (0.0)	32 (4.1)
	2nd cycle	0 (0.0)	0 (0.0)	9 (1.1)	0 (0.0)	9 (1.1)
	3rd cycle	0 (0.0)	0 (0.0)	10 (1.3)	60 (7.6)	70 (8.9)
	Secondary education	0 (0.0)	0 (0.0)	0 (0.0)	450 (57.3)	450 (57.3)
	No data	145 (18.4)	0 (0.0)	0 (0.0)	2 (0.3)	147 (18.7)

In what concerns the intent, it is intrinsically linked with the agent of intoxication (Figure 1). It was possible to observe that most of the intoxications were voluntary (35.6%; Table 7).

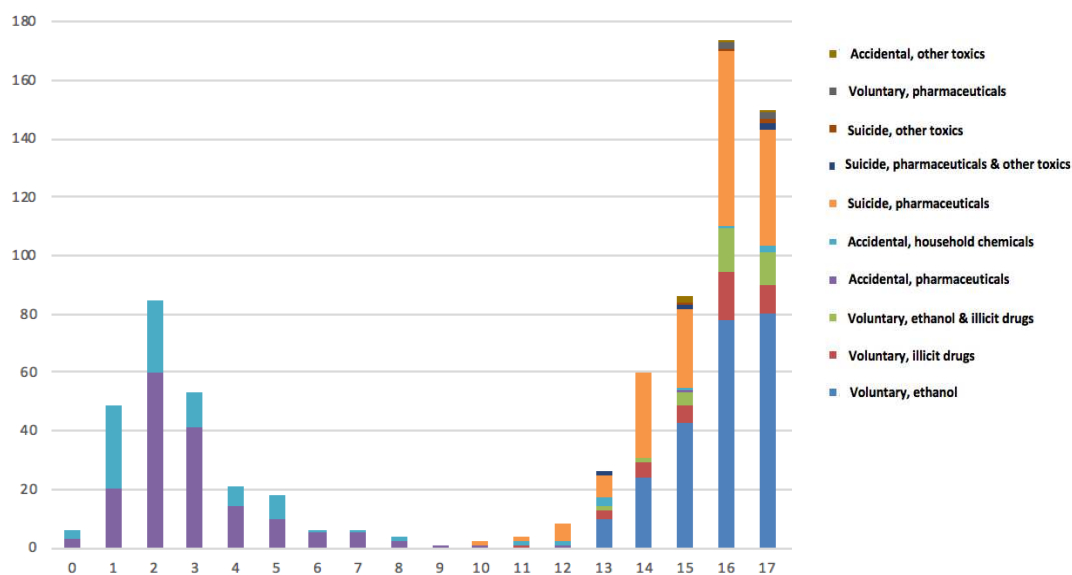


Figure 1. Distribution of the intent by age.

Table 7. Agent crossed with the origin of intoxication.

		Origin			
		Accidental	Intentional	No data	Total
		237 (30.2%)	280 (35.6%)	269 (34.2%)	786 (100%)
		N (%)	N (%)	N (%)	N (%)
Agent	Ethanol	2 (0.3)	274 (34.9)	51 (6.5)	327 (41.6)
	Other pharmaceutical	77 (9.5)	0 (0.0)	66 (8.4)	143 (18.2)
	Others	94 (12.0)	2 (0.3)	21 (2.7)	117 (14.9)
	Drugs acting on the CNS	21 (2.7)	1 (0.1)	62 (7.9)	84 (10.7)
	Multiple Pharmaceuticals	11 (1.4)	2 (0.3)	50 (6.4)	63 (8.0)
	Carbon monoxide	22 (2.8)	0 (0,0)	5 (0.6)	27 (3,4)
	Ethanol & illicit drugs	7 (0.9)	0 (0,0)	7 (0.9)	14 (1,8)
	Illicit drugs	3 (0.4)	1 (0.1)	7 (0.9)	11 (1.4)

The analysis of all age groups shows that intoxications were accidental in only 30.2% cases (Table 8), a different analysis from other studies showing that intoxications are mostly accidental (Azab *et al.*, 2016; Belchior 2016; Berta *et al.*, 2020; Brito and Martins 2015; Dias 2017; Gokalp, 2019; Goudarzi *et al.*, 2020; Hassan and Siam, 2014; Koh *et al.*, 2018; Kizilyildiz *et al.*, 2018; Matalová *et al.*, 2019), while in 35.6% of the cases the intention was voluntary. In the case of intentional intoxication in adolescents and according to the results obtained in Table 7, these occur mostly by pharmaceuticals, which is in line with many other studies (Belchior, 2016; Berta *et al.*, 2020; Brito and Martins, 2015; Gokalp, 2019; Gontko *et al.*, 2013; Gunja, 2012; Kizilyildiz *et al.*, 2018; Matalová *et al.*, 2019; Nistor *et al.*, 2017; Pawlowicz *et al.*, 2013; Sahin *et al.*, 2011; Ulseth *et al.*, 2019; Winstanley and Stover, 2019). It was also evident that more young females tried to commit suicide than young males (Table 9) (Gontko *et al.*, 2013; Kizilyildiz *et al.*, 2018; Matalová *et al.*, 2019; Nistor *et al.*, 2017; Xiang *et al.*, 2012). Still, it may not be representative, since in our study, there are a high amount of cases to which intention of intoxication was not specified (34.2%). In some of these patients, the cases represented a second, third or even fourth suicide attempt (Nistor *et al.*, 2017). Suicide attempts represent a serious public health problem (Xiang *et al.*, 2012) that deserve specialised attention to understand the motivations behind the practise of such self-inflicted injuries, in view of identifying preventable factors in advance to ensure adequate preventive care and apply more focused interventions (Nistor *et al.*, 2017).

Table 8. Distribution of administration route and intent of intoxication by age group.

		Age group				
		<2	3–5	6–12	13–18	Total
		145 (18.4%)	78 (9.9%)	51 (6.5%)	512 (65.1%)	786 (100%)
		N (%)	N (%)	N (%)	N (%)	N (%)
Administration route	Ingestion	101 (12.8)	54 (6.9)	22 (2.8)	147 (18.7)	324 (41.2)
	Inhalation	5 (0.6)	1 (0.1)	8 (1.0)	3 (0.4)	17 (2.2)
	Injection	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
	No data	39 (5.0)	23 (2.9)	21 (2.7)	361 (45.9)	444 (56.5)
Origin	Intentional	0 (0.0)	0 (0.0)	2 (0.3)	278 (35.4)	280 (35.6)
	Accidental	116 (14.8)	60 (7.6)	29 (3.7)	32 (4.1)	237 (30.2)
	No data	29 (3.7)	18 (2.3)	20 (2.5)	202 (25.7)	269 (34.2)

Table 9. Influence of gender in the origin of the intoxication.

		Gender		
		Female	Male	Total
		406 (51.7%)	380 (48.3%)	786 (100%)
		N (%)	N (%)	N (%)
Origin	Intentional	125 (15.9)	151 (19.2)	276 (35.1)
	Accidental	106 (13.5)	131 (16.7)	237 (30.2)
	Suicide attempt	4 (0.5)	0 (0.0)	4 (0.5)
	No data	171 (21.8)	98 (12.5)	269 (34.2)

With regard to the route of administration, it was possible to observe that ingestion was the most frequent at all ages (41.2%) (Table 8), as observed in many other studies (Azab *et al.*, 2016; Dias 2017; Goudarzi *et al.*, 2020; Hassan and Siam, 2014; Koh *et al.*, 2018; Matalová *et al.*, 2019; Mowry *et al.*, 2015; Mutlu *et al.*, 2010). Still, about 2.2% occurred by inhalation and in 56.5% of the cases no information could be collected.

Table 10. Influence of agent involved in the administration route.

		Administration Route				
		Ingestion	Inhalation	Injection	No data	Total
		324 (41.2%)	17 (2.2%)	1 (0.1%)	444 (56.5%)	786 (100%)
		N (%)	N (%)	N (%)	N (%)	N (%)
Agent	Ethanol	36 (4.6)	0 (0.0)	0 (0.0)	291 (37.0)	327 (41.6)
	Drugs acting on the CNS	61 (7.8)	0 (0.0)	0 (0.0)	23 (2.9)	84 (10.7)
	Other Pharmaceutical	97 (12.3)	0 (0.0)	1 (0.1)	45 (5.7)	143 (18.2)
	Others	84 (10.7)	1 (0.1)	0 (0.0)	32 (4.1)	117 (14.9)
	Multiple pharmaceuticals	41 (5.2)	0 (0.0)	0 (0.0)	22 (2.8)	63 (8.0)
	Carbon monoxide	0 (0.0)	15 (1.9)	0 (0.0)	12 (1.5)	27 (3.4)
	Ethanol & illicit Drugs	2 (0.3)	1 (0.1)	0 (0.0)	11 (1.4)	14 (1.8)
	Illicit drugs	3 (3.8)	0 (0.0)	0 (0.0)	8 (21.8)	11(1.4)

Regarding the presentation of symptoms at the time of hospital admission, neonates, infants, and toddlers (42.7%), and adolescents (85.0%), were the groups with the highest percentage of symptomatic intoxications, as observed in other studies (Claudet *et al.*, 2014; Dias 2017), while the remaining children were asymptomatic, also in line with other studies (Matalová *et al.*, 2019). During diagnosis and treatment (Table 11), most children with ages up to 12 years-old were medicated and subjected to biochemical and radiological exams. However, it was in adolescents that most biochemical analysis and pharmaceutical treatments were required.

Table 11.Exams by age group.

			Age groups				
			<2	3–5	6–12	13–18	Total
			145 (18.4%)	78 (9.9%)	51 (6.5%)	512 (65.1%)	786 (100%)
			N (%)	N (%)	N (%)	N (%)	N (%)
Exams	Medication	Yes	82 (10.4)	41 (5.2)	34 (4.3)	445 (56.6)	602 (76.6)
		No	63 (8.0)	37 (4.7)	17 (2.2)	67 (8.5)	184 (23.4)
	Biochemical analysis	Yes	41 (5.2)	31 (3.9)	24 (3.1)	408 (51.9)	504 (64.1)
		No	104 (13.2)	47 (6.0)	27 (3.4)	104 (13.2)	282 (35.9)
	Radiologic exams	Yes	6 (0.8)	1 (0.1)	4 (0.5)	28 (3.6)	39 (5.0)
		No	139 (17.7)	77 (9.8)	47 (6.0)	484 (61.6)	747 (95.0)

No deaths were reported in our study, as observed in the studies by Brito and Martins, (2015), Dias, (2017), Koh *et al.*, (2018) and Matalová *et al.*, (2019), with most patients being referred home after diagnosis. However, at ages over 6, particularly in adolescents, there was a significant percentage of patients who were referred to other hospitals, mainly in the cases of attempted suicide, where they were referred to psychiatric hospitals.

5. Conclusions

A total of 786 cases were analysed between 2014 and 2018, intoxications peaking at adolescence and in children under 4 years of age. Poisoning in preschool children was mainly unintentional and usually due to pharmaceutical agents and household products, which indicate the need for the use of child safety locks and education of caregivers with preventive measures. The highest prevalence of intoxications, however, concerned adolescents, who were voluntarily intoxicated with ethanol – mainly males, and for this reason it is necessary to continue to make progress to society becomes aware of this issue. In addition, stricter laws must be implemented, and preventive measures taken to avoid consumption. In addition to ethanol, poisoning by pharmaceuticals is also common in adolescents, mostly resulting from voluntary ingestion in females that attempted suicide. Most of the poisonings were severe but there were no fatal cases.

Previous studies conducted in the same hospital indicate exactly the same trends, so the profile of intoxications seem to be maintained over the years. Nevertheless, studies must be done in different regions of the country, to elucidate if the paradigm found in norther of Portugal translates at the national level, thus allowing local preventive measures to be extended nationally.

Of note, the most relevant limitation identified in this study concerned the poor quality of information in the records, since in many cases no information was available on the circumstances of the intoxication, on the amount of drug found in the blood, or even on the intoxication agent. Regarding the poisoning agent, it was not possible to quickly identify the compound, as well as a correct association of the classes to which the compounds belonged, which made the overall analysis difficult.. In addition, the lack of information about the intention was also observed. The importance of a correct information recording is paramount since it is a fundamental part of a physician's duties to provide patient care and the information contained in medical records should be documented daily and in a chronological order, demonstrating continuity of care and response to treatment. The information should be comprehensive enough to allow any colleague to follow up the case.

The implementation of protocols that help in the diagnosis of intoxications is also a possible way forward.

As verified in this study, it is important to realize the reality of poisoning anywhere in the world, because it is through these studies that forensic sciences can detect harmful

agents to the body, which encompasses analyses of biological material and that lead to the result of changes and damage caused and even the cause of death of the individual, which can happen by several factors , such as poisoning, drug abuse and suicides, where are involved a number of professionals trained to investigate and realize all the necessary requirements to reach a conclusion.

6. Bibliography

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Attachments

Attachment 1. Oral communication - Fifteenth - Young European Scientist – Meeting

Attachment 2. Oral communication - *L Reunião Sociedade Portuguesa de Farmacologia*

Attachment 3. Poster communication (Abstract) - *IV Congresso da Associação Portuguesa de Ciências Forenses*

Attachment 4. Poster communication - *IV Congresso da Associação Portuguesa de Ciências Forenses*

Attachment 5. Approval by the National Data Protection Commission

Attachment 6. Certificate of Reuse of Data for Research

Attachment 1. Oral communication - Fifteenth - Young European Scientist – Meeting

PAEDIATRIC INTOXICATIONS IN THE NORTH OF PORTUGAL BETWEEN 2014 AND 2018

Marta Russo^{1,2}, Luís Almeida Santos^{3,4}, Félix Carvalho², Rui Guimarães⁵, Ricardo Jorge Dinis-Oliveira^{1,2,6}, Diana Dias da Silva^{1,2}

¹ IINFACTS – Institute of Research and Advanced Training in Health Sciences and Technologies, Department of Sciences, University Institute of Health Sciences (IUCS-CESPU), Gandra, Portugal. ² UCIBIO, REQUIMTE, Laboratory of Toxicology, Faculty of Pharmacy, University of Porto, Rua Jorge Viterbo Ferreira 228, Porto, 4050-313, Portugal. ³ Department of Gynecology-Obstetrics and Pediatrics, Faculty of Medicine, University of Porto, Alameda Prof. Hernâni Monteiro, 4200-319 Porto, Portugal. ⁴ Pediatric Intensive Care Unit, UAG-MC, Centro Hospitalar Universitário de São João, Porto, Portugal. ⁵ MEDCIDS - Department of Community Medicine, Information and Health Decision Sciences, Faculty of Medicine, University of Porto, Alameda Prof. Hernâni Monteiro, 4200-319 Porto, Portugal. ⁶ Department of Public Health and Forensic Sciences, and Medical Education, Faculty of Medicine, University of Porto, Alameda Prof. Hernâni Monteiro, 4200-319 Porto, Portugal

Introduction: Acute intoxications rank third as leading cause of accidental deaths in European infant-juvenile population [1], and remain an avertable cause of morbidity and mortality worldwide. In Portugal, the epidemiology of intoxications in children aged 0–17 years has not been comprehensively studied.

Aim: Herein, we intended to analyse the epidemiological pattern of the paediatric intoxications presented to the Emergency Department (ED) of a tertiary hospital located in the North of Portugal, to better understand the epidemiology of this problem in the region.

Methods: Retrospective analysis of patients under 18 years old admitted to the ED of Hospital de São João, Porto (Portugal) due to intoxication, between 2014–2018.

Results: There was a total of 928 (0.24%) ED visits due to intoxication from a total of 389,913, during the study period. From the studied population, 48.49% were male, and no significant sex differences were observed in the pattern of intoxication caused by different causal agents. Intoxication by ethanol (37.82%) and pharmaceuticals (29.42%) led the causes of intoxication, followed by household products (10.99%) and illicit drugs (7.54%). Intoxication by pesticides represented less than 1% of the cases. While 72% of intoxications with household products were reported for children aging 0–3, 98% of ethanol intoxications occurred in adolescents (13–17 years-old). Intoxications with pharmaceuticals also peaked in these two age groups, related to toddler exploratory ingestions and attempts of suicide, respectively. The most common pharmaceuticals were those acting on the central nervous system. No fatalities were reported during emergency care, but 20.37% of the patients were further hospitalised.

Conclusions: Preventive measures regarding abuse of ethanol and illegal drugs should be strengthened among adolescents, as well as community awareness to eliminate risks related to toddler exploratory ingestions of pharmaceuticals and domestic products in the household environment.

References: [1] World Health Organization (2008). The global burden of disease: 2004 update. <http://www.who.int/iris/handle/10665/43942> (accessed November 30, 2019).

This work was supported by UID/MULTI/04378/2019 through FCT/MCTES funds. The authors declare that there are no conflicts of interests.

Attachment 2. Oral communication - *L Reunião Sociedade Portuguesa de Farmacologia*

PAEDIATRIC INTOXICATIONS IN THE NORTH OF PORTUGAL BETWEEN 2014 AND 2018

Marta Russo^{1,6}, João Viana^{2,3}, Luís Almeida Santos^{4,5}, Rui Guimarães², Félix Carvalho⁶, Ricardo Jorge Dinis-Oliveira^{1,6,7}, Diana Dias da Silva^{1,6}

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Introduction: Acute intoxications rank third as leading cause of accidental deaths in European infant-juvenile population [1], and remain an avertable cause of morbidity and mortality worldwide. The characteristics and trends of intoxications among paediatric populations is of undeniable relevance as the development of targeted preventive and educational strategies demands throughout knowledge on the prevalence and type of intoxications in a particular region. In Portugal, the epidemiology of intoxications in children aged 0–17 years has not been comprehensively studied. Herein, we intended to analyse the epidemiological pattern of the paediatric intoxications presented to the Emergency Department (ED) of a tertiary hospital located in the North of Portugal, to better understand the epidemiology of this problem in the region. **Methods:** Retrospective analysis of patients under 18 years old admitted to the ED of Hospital de São João, Porto (Portugal) due to intoxication, between 2014–2018. **Results:** There was a total of 928 (0.24%) ED visits due to intoxication from a total of 389,913, during the study period. From the studied population, 48.49% were male, and no significant sex differences were observed in the pattern of intoxication caused by different causal agents. Intoxication by ethanol (37.82%) and pharmaceuticals (29.42%) led the causes of intoxication, followed by household products (10.99%) and illicit drugs (7.54%). Intoxication by pesticides represented less than 1% of the cases. While 72% of intoxications with household products were reported for children aging 0–3, 98% of ethanol intoxications occurred in adolescents (13–17 years-old). Intoxications with pharmaceuticals also peaked in these two age groups, related to toddler exploratory ingestions and attempts of suicide, respectively. The most common pharmaceuticals were those acting on the central nervous system. No fatalities were reported during emergency care, but 20.37% of the patients were further hospitalised. **Conclusions:** Preventive measures regarding abuse of ethanol and illegal drugs should be strengthened among adolescents, as well as community awareness to eliminate risks related to toddler exploratory ingestions of pharmaceuticals and domestic products in the household environment. Additional studies should be conducted at the national level, to better understand the epidemiology of poisoning in Portuguese children and adolescents.

References: [1] World Health Organization (2008). The global burden of disease: 2004 update. <http://www.who.int/iris/handle/10665/43942> (accessed November 30, 2019).

This work was supported by UID/MULTI/04378/2019 through FCT/MCTES funds. The authors declare that there are no conflicts of interests.

Attachment 3. Poster communication (Abstract) - IV Congresso da Associação Portuguesa de Ciências Forenses

POISONING IN CHILDREN: SCALE OF THE PROBLEM

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Introduction: Acute poisoning ranks third as leading cause of accidental deaths in European infant-juvenile population [1], and remains an avertable cause of morbidity and mortality worldwide. Statistics from the WHO for the European Region disclosed the occurrence of more than 3,000 fatal intoxications per year in children and adolescent aged 0–19 years old [1]. This number gets even higher when considering non-lethal intoxications, which embody a frequent cause of admission to paediatrics' emergency rooms. According to the American Association of Poison Control, more than 1 million of poisonings occur per year in the United States, in children younger than 6, while numbers as high as 140 thousand and 170 thousand are reported for children aging 6–12 and teenagers aging 13–19 years old, respectively [2]. Noteworthy, these indicators are even likely to be underestimated, considering that not all toxic exposures are clinically evaluated or reported to poison control centres. These hospitalizations accounts to a vast health and economic burden, with an estimated expense of nearly 1.8 thousand dollars per intoxication for the US Health System [3].

Aims: Herein, we intended to summarize the state of the art of paediatric intoxications.

Methods: For such purpose, systematic literature search and review was conducted using PubMed and Web of Science databases, until March 2019.

Results: Intoxication patterns heavily depend on the region and country considered, being also affected by factors such as socioeconomic status, agricultural practices, industrial development, among others. Overall, childhood poisoning is more prevalent in males than females at all ages, but a higher gender discrepancy is observed in older children, mainly attributed to differences in socialization and ease to engage in risky behaviours. Fatalities mainly occur in low-income and middle-income countries, but substantial differences might also be observed within countries, between urban and rural areas. Pharmaceuticals, household products, and pesticides are listed among the most common substances involved in exploratory ingestions in toddlers. These accidents in children at an early age mainly occur at home, where these substances are held. Medications, cosmetics or other personal care products, bleach and cleaning agents represent a significant risk for intoxication as they are usually stored unsafely, under easy access or in non-child-proof containers. Also, in rural areas or other zones where agriculture work is predominant, exposure to insecticides, rodenticides and herbicides is prevalent. Paraffin and kerosene used for eating and cooking are also frequently involved in poisonings, as well as carbon monoxide from the combustion of hydrocarbon fuels, in particularly during winter. Acute intoxication with alcohol is a rising public health concern in adolescents, and binge drinking is increasing in younger age groups. Further, the misuse of drugs and medicaments are also common in older children. In Portugal, the epidemiology of intoxications in children aged 0–17 years has not been comprehensively studied. Most data on intoxications are provided by the Poison Information Centre (*Centro de Informação Anti-Venenos*, CIAV) and indicate that the prevalence of poisoning in children peak at 1–4 years old. Approximately half of the 30,000 calls received by the helpline per year concerns intoxications at the initial poisoning stage, allowing a significant decline of morbidity through appropriate guidance on the intoxication management and of hospital admissions in case of false alarm.

Conclusions: The characteristics and trends of poisoning among paediatric populations is of undeniable relevance as the development of targeted preventive and educational strategies, either through legislation or community awareness to eliminate risks in the household environment, demands throughout knowledge on the prevalence and type of intoxications in a particular region.

References:

1. World Health Organization. (2008). The global burden of disease : 2004 update. Geneva : World Health Organization. <http://www.who.int/iris/handle/10665/43942> (accessed March 31, 2019)
2. Gummin DD, Mowry JB, Spyker DA, Brooks DE, Fraser MO, Banner W (2017) 2016 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 34th Annual Report. *Clinical toxicology* 55(10):1072-1252 doi:10.1080/15563650.2017.1388087
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Attachment 4. Poster communication - IV Congresso da Associação Portuguesa de Ciências Forenses

XI JORNADAS CIENTÍFICAS DO DEPARTAMENTO DE CIÊNCIAS DO INSTITUTO UNIVERSITÁRIO DE CIÊNCIAS DA SAÚDE
IV CONGRESSO DA ASSOCIAÇÃO PORTUGUESA DE CIÊNCIAS FORENSES

POISONING IN CHILDREN: SCALE OF THE PROBLEM

Marta Russo^{1*}, Ricardo Jorge Dinis-Oliveira^{1,2,3}, Rui Guimarães³, Diana Dias da Silva^{1,2}

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³Department of Public Health and Forensic Sciences, and Medical Education, Faculty of Medicine, University of Porto, Alameda Prof. Hernâni Monteiro, 4200-319 Porto, Portugal

*Email: marta.r18@gmail.com

Introduction and aims:

Acute poisoning ranks third as leading cause of accidental deaths in European infant-juvenile population [1], and remains an avertable cause of morbidity and mortality worldwide. Statistics from the WHO for the European Region disclosed the occurrence of more than 3,000 fatal intoxications per year in children and adolescent aged 0–19 years old [1]. This number gets even higher when considering non-lethal intoxications, which embody a frequent cause of admission to paediatrics' emergency rooms. According to the American Association of Poison Control, more than 1 million of poisonings occur per year in the United States, in children younger than 6, while numbers as high as 140 thousand and 170 thousand are reported for children aging 6–12 and teenagers aging 13–19 years old, respectively [2]. Noteworthy, these indicators are even likely to be underestimated, considering that not all toxic exposures are clinically evaluated or reported to poison control centres. These hospitalizations account to a vast health and economic burden, with an estimated expense of nearly 1.8 thousand dollars per intoxication for the US Health System [3]. Herein, we summarize the state of the art of paediatric intoxications.

Factors affecting intoxication patterns:

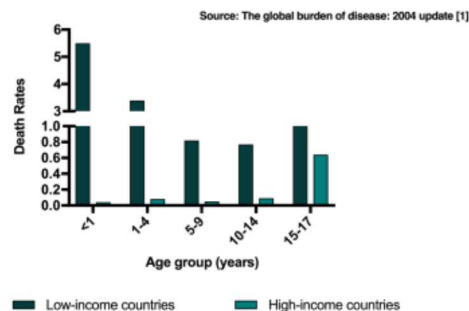
- Socioeconomic status
- Agricultural practices
- Industrial development
- Country income
- Gender
- Others



Gender

Childhood poisoning is more prevalent in males than females at all ages, but a higher gender discrepancy is observed in older children due to differences in socialization and ease to engage in risky behaviours

Age-standardized death rates from poisoning by age group with rate ratios for Low Income Countries and High Income Countries, WHO European Region



Poisonous agents

Toddlers

- Pharmaceuticals, cosmetics, personal care products, bleach, cleaning agents and other household products
- Insecticides, rodenticides, herbicides and other pesticides, particularly in rural areas
- Other agents (such as paraffin, kerosene, carbon monoxide)

Adolescents

- Alcohol (binging drinking is increasing in younger age groups)
- Misuse drugs
- Medications

In Portugal

- Most data on intoxications are provided by the Poison Information Centre (*Centro de Informação Anti-Venenos*, CIAV)
- The prevalence of poisoning in children peak at 1–4 years old
- Approximately half of the 30,000 calls received by the helpline per year concerns intoxications at the initial poisoning stage

Conclusions:

The characteristics and trends of poisoning among paediatric populations is of undeniable relevance as the development of targeted preventive and educational strategies, either through legislation or community awareness to eliminate risks in the household environment, demands throughout knowledge on the prevalence and type of intoxications in a particular region.

Acknowledgments:

FEDER POCI/01/0145/FEDER/007728 under the program PT2020 (UID/MULTI/04378/2013) and the framework of QREN (NORTE-01-0145-FEDER-000024) and COMPETE.

References:

1. World Health Organization. (2008). The global burden of disease: 2004 update. Geneva: World Health Organization. <http://www.who.int/lis/handle/10665/43942> (accessed March 31, 2019).
2. Gammon DJ, Mowry JB, Spiller SA, Brooks DE, Frazer MD, Banner W (2007) 2016 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 34th Annual Report. Clinical toxicology 55(10):1072-1252 doi:10.1080/15563650.2017.1388087
3. Selfert J. Incidence and economic burden of injuries in the United States. J Epidemiol Community Health. 2007;61(10):926. doi:10.1136/jech.2007.059717

Attachment 5. Approval by the National Data Protection Commission

Unidade de Investigação
Tomar conhecimento. Nada a opor. À DC.
25 de Junho de 2019
A Coordenadora da Unidade de Investigação

(Prof.ª Doutora Ana Azevedo)


SÃO JOÃO

n.º 183 / 19
DIREÇÃO CLÍNICA
26/6/2019
Centro Hospitalar São João
Ao CA

Centro Hosp. Univ. São João
Maria João Baptista
Diretora Clínica

ATM
21.6.2019
LH
PEDIDO DE AUTORIZAÇÃO
Realização de Investigação

Exmo. Senhor Presidente do Conselho de Administração
do Centro Hospitalar de São João

Nome do Investigador Principal:

Marta Sofia Resende Russo

Título da Investigação:

Intoxicações agudas em crianças e adolescentes admitidos no Serviço de Urgência Pediátrica do Hospital de São João (Porto, Portugal), 2008-2018

Pretendo realizar no(s) Serviço(s) de:

Urgência Pediátrica

a investigação em epígrafe, solicito a V. Exa., na qualidade de Investigador/Promotor, autorização para a sua efetivação.

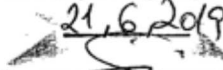
Para o efeito, anexo toda a documentação referida no dossier da Comissão de Ética do Centro Hospitalar de São João/Faculdade de Medicina da Universidade do Porto respeitante à investigação, à qual enderecei pedido de apreciação e parecer.

Com os melhores cumprimentos.

O Investigador/Promotor

Porto, 21 de Maio de 2019 . 

• Centro Hospitalar São João •
Centro de Epidemiologia Hospitalar

21.6.2019


CEH-SJ000

RESPONSÁVEL PELO ACESSO À INFORMAÇÃO



SÃO JOÃO

**Pedido de Reutilização de Registos Clínicos
para Investigação e Desenvolvimento (I&D)**

Exma. Senhor
Responsável pelo Acesso à Informação
(Anexo I da Lei n.º 27/2016 de 22 de agosto)
Dr. Rui de Mesquita e Silva Guimarães



SÃO JOÃO

Número do Pedido

11101082192

(A preencher pelo Gabinete de Apoio ao RAI)

AUTORIZADO

RAI Responsável pelo Acesso
à Informação e Centro
de Apoio ao RAI
(Lei n.º 26/2016 de 22/8)

15.06.18

1. Identificação do(s) Investigador(es) Preenchimento Obrigatório**1.1. Investigador Principal**Nome Marta Sofia Resende RussoContacto telefónico 913850667Endereço eletrónico martasrr18@gmail.com**1.2. Investigador(es) Associado(s)**Número Total: Nome Diana Cristina Dias da SilvaContacto telefónico 916589037Endereço eletrónico diana.dds@gmail.comNome Ricardo Jorge Dinis de OliveiraContacto telefónico 916240886Endereço eletrónico ricardinis@sapo.pt

Nome _____

Contacto telefónico _____

Endereço eletrónico _____@_____

1.3. Afiliação Institucional do Investigador Principal**1.3.1. Grupo Profissional**

Médico(a) Enfermeiro(a) Docente Estudante
 Outro. Qual? _____

1.3.2. Documento de identificação pessoal ou profissional

Cartão de Cidadão Bilhete de Identidade Célula Profissional
 Cartão de Docente Cartão de Estudante Outro. Qual? _____

Número de Documento 14869985**2. Enquadramento e Identificação do Trabalho de Investigação e Desenvolvimento** Preenchimento Obrigatório**2.1. Enquadramento da investigação**

Trabalho académico de investigação e desenvolvimento:
 Não conferidor de grau
 Conferidor de grau: Licenciatura Mestrado Doutoramento
 Projeto de investigação e desenvolvimento

2.2. Entidade(s) que tutela(m) a investigação

Centro Hospitalar de São João
Serviço: Urgência Pediátrica

Universidade do Porto
Faculdade/Instituto:

Outra Instituição. Qual? Instituto Universitário de Ciências da Saúde (CESPU)

Há alguma parceria entre instituições?

Não Sim. Qual(is)?

2.3. Orientador Dr. Aplicável

Contacto telefónico 916539037

Endereço eletrónico diana.dds@gmail.com

2.4. Título provisório

Intoxicações agudas em crianças e adolescentes admitidos no Serviço de Urgência Pediátrica do Hospital de São João (Porto, Portugal), 2008-2018

Deverá posteriormente indicar o título definitivo para emissão do Certificado de Reutilização pelo RAI - DATA REUse Certificate for Research - DARE através dos contactos disponíveis no fim deste formulário.

2.5. Acesso requerido

Ficheiro

Descrição do património informacional a que pretende ter acesso, identificando a informação a obter, i.e. nome, morada, diagnóstico, idade, códigos dos distritos, entre outros.

Consulta de processos clínicos em ambiente papel:

Bloco Consulta Externa Hospital de Dia Internamento MCDT Urgência

Deverá anexar ficheiro(s) contendo a identificação do pretendido, i.e. números de processos, episódios, números de utente, entre outros.

Anexar ficheiro(s) de acesso

Consulta de registos clínicos eletrónicos

Especificar os Sistemas de Informação:

Data previsível de fim de utilização das credenciais de acesso 2022 - 12 - 31

Outro Acesso. Qual?

2.3. Pareceres e Autorizações

Autorização da Hierarquia

Protocolo Científico Aprovado ¹

Parecer da Comissão de Ética para a Saúde (CES) ¹

Parecer do Centro de Epidemiologia Hospitalar ¹

Deverá anexar ficheiro(s) contendo cópia dos documentos referentes às opções selecionadas.

Anexar ficheiro(s) de acesso

¹ Caso se aplicável

3. Observações Preenchimento Opcional

4. Aceitação dos Termos e Condições da Reutilização

Cumulativamente com as obrigações decorrentes da lei já citada (n.º 2 e 3 do artigo 21 e o n.º 1 e 2 do artigo 12, ambos da Lei n.º 26/2016, de 22 de agosto) ao submeter o presente pedido concordo e fico ainda vinculado aos seguintes termos e condições:

- Comprometo-me a manter confidencial toda a informação à qual vou ter acesso;
- Não vou elaborar registos, susceptíveis de identificar ou tornar identificável a identidade das pessoas a quem os mesmos dizem respeito;
- Não vou elaborar, nem ficar na posse, de cópias de bases de dados utilizadas na recolha de informação;
- Comprometo-me a obter junto da Comissão Nacional de Proteção de Dados (CNPD) as necessárias autorizações, para eventuais bases de dados que venha a conceber e utilizar no âmbito da presente investigação;
- Comprometo-me a devolver ao Centro Hospitalar de São João, na pessoa do seu Diretor Clínico, as bases de dados e o resultado da investigação;
- Comprometo-me a ocultar os elementos de identificação da(s) pessoa(s) a quem os registos digam respeito, em futuras e eventuais publicações de resultados;
- Comprometo-me a consultar os processos clínicos nas instalações que me forem indicadas para o efeito;
- Comprometo-me a obter os necessários pareceres, quer da Comissão de Ética do Hospital, quer do Centro de Epidemiologia Hospitalar, sempre que necessário;
- Comprometo-me a citar as fontes sempre que publicitar o trabalho de investigação independentemente de requerer a Certidão de Reutilização (DATA REuse Certificate for Research - DARE);
- Tomei conhecimento, que a violação de qualquer dos compromissos aqui assumidos, resultará no apuramento de responsabilidades disciplinares, civis e penais e ainda, à impossibilidade futura de aceder a informação de saúde para fins de investigação.

5. Decisão do investigador sobre requerer a DATA REuse Certificate for Research - DARE Preenchimento Obrigatório

- Pretendo desde já requerer a Certidão de Reutilização (DARE) cujo sentido, valor e significado consulte em <http://portal-chsj.min-saude.pt/pages/710>.
- Não pretendo requerer a Certidão de Reutilização (DARE) cujo sentido, valor e significado consulte em <http://portal-chsj.min-saude.pt/pages/710>.

6. Assinatura

Nota 1: Se o presente pedido for submetido eletronicamente ou for assinatura digital qualificada ou posteriormente vem ao Centro Hospitalar de São João exibir o seu documento de identificação pessoal; ou no âmbito do seu espaço de liberdade e como manifestação expressa do seu consentimento envia cópia do referido documento, neste caso, concluído o processo ser-lhe-á devolvida ou eliminada a cópia do documento de identificação pessoal, conforme as indicações que dá.

Nota 2: Se o presente pedido for entregue presencialmente, assina e exibe o documento de identificação a quem recebe o pedido.

Data | 2019 | | | - | 05 | - | 17 |

Rafaela Russo
Investigador Principal

Em caso de dúvida no preenchimento contacte através dos endereços eletrónicos
rai.reutilizacao.id@chsj.min-saude.pt ou ruiguimaraes@chsj.min-saude.pt
ou pelos números de telemóvel 962 204 194 ou 918 880 299

SUBMITER



Questionário para submissão de Investigação

Exmo. Sr. Presidente da Comissão de Ética do Centro Hospitalar de São João/
Faculdade de Medicina da Universidade do Porto,

Pretendendo realizar a investigação infracitada, solicito a V. Exa., na qualidade de Investigador, a sua apreciação e a elaboração do respetivo parecer. Para o efeito, anexo toda a documentação requerida.

IDENTIFICAÇÃO DO ESTUDO

Título da investigação: Intoxicações agudas em crianças e adolescentes admitidos no Serviço de Urgência Pediátrica do Hospital de São João

Nome do investigador: Tanta Sofia Resende Nunes

Endereço eletrónico: maria.s.r.18@gmail.com Contacto telefónico: 913850667

Caracterização da investigação:

Estudo retrospectivo Estudo observacional Estudo prospetivo

Inquérito Outro. Qual? _____

Tipo de investigação:

Com intervenção Sem intervenção

Formação do investigador em boas práticas clínicas (GCP): Sim Não

Promotor (se aplicável): _____

Nome do orientador de dissertação/tese (se aplicável): Diana Cristina Dias de Sá

Endereço eletrónico: diana.dds@gmail.com

Local/locais onde se realiza a investigação: Centro Hospitalar de São João, EPE

Data prevista para início: 01/09/2019 Data prevista para o término: 31/08/2022

PROTOCOLO DO ESTUDO

Síntese dos objetivos: Caracterização exhaustiva das intoxicações pediátricas registadas no Serviço de Urgência Pediátrica do Centro Hospitalar de São João, EPE, entre 2008-2018.

Fundamentação ética (ganhos em conhecimento/ inovação; ponderação benefícios/risgos):
Esta revisão é de natureza relizante para auxiliar as entidades reguladoras europeias na identificação de áreas prioritárias de intervenção, assim como na mobilização de recursos para redução do número de intoxicações pediátricas.

CONFIDENCIALIDADE

De que forma é garantida a anonimização dos dados recolhidos de toda a informação?

O investigador necessita ter acesso a dados do processo clínico? Sim Não

Está previsto o registo de imagem ou som dos participantes? Sim Não

Se sim, está prevista a destruição deste registo após o sua utilização? Sim Não

CONSENTIMENTO

O estudo implica recrutamento de:

Doentes: Sim Não Voluntários saudáveis: Sim Não

Menores de 18 anos: Sim Não.

Outras pessoas sem capacidade do exercício de autonomia: Sim Não

A investigação prevê a obtenção de Consentimento Informado: Sim Não

Se não, referir qual o fundamento para a isenção:

A investigação utiliza apenas registos electrónicos anonimizados.

Existe informação escrita aos participantes: Sim Não

PROPRIEDADE DOS DADOS

A investigação e os seus resultados são propriedade intelectual de:

Investigador Promotor Ambos Serviço onde é realizado

Não aplicável

Outro: _____

BENEFÍCIOS, RISCOS E CONTRAPARTIDAS PARA OS PARTICIPANTES

Benefícios previsíveis:

Não aplicável

Riscos/incómodos previsíveis:

Não aplicável

São dadas contrapartidas aos participantes:

· pela participação Sim Não Não aplicável

· pelas deslocações Sim Não Não aplicável

· pelas faltas ao emprego Sim Não Não aplicável

· por outras perdas e danos Sim Não Não aplicável

CUSTOS / PLANO FINANCEIRO

Os custos da investigação são suportados por:

Investigador Promotor Serviço onde é realizado

Não aplicável

Outro: _____

Existe protocolo financeiro? Sim Não

LISTA DE DOCUMENTOS ANEXOS

- Pedido de autorização ao Presidente do Conselho de Administração do Centro Hospitalar de São João (se aplicável)
- Pedido de autorização à Diretora da Faculdade de Medicina da Universidade do Porto (se aplicável)
- Protocolo do estudo
- Declaração do Diretor de Serviço onde decorre o estudo
(sendo um estudo na área de enfermagem deve anexar também a concordância da chefia de enfermagem)
- Profissional de ligação
- Informação dos orientadores
- Informação ao participante
- Modelo de consentimento
- Instrumentos a utilizar (inquéritos, questionários, escalas, p.ex.): _____
- Curriculum Vitae abreviado (máx. 3 páginas)
- Protocolo financeiro
- Outros:

COMPROMISSO DE HONRA E DECLARAÇÃO DE INTERESSES

Declaro por minha honra que as informações prestadas neste questionário são verdadeiras. Mais declaro que, durante o estudo, serão respeitadas as recomendações constantes da Declaração de Helsínquia (1960 e respetivas emendas), e da Organização Mundial da Saúde, Convenção de Oviedo e das "Boas Práticas Clínicas" (GCP/ICH) no que se refere à experimentação que envolve seres humanos. Aceito, também, a recomendação da CES de que o recrutamento para este estudo se fará junto de doentes que não tenham participado em outro estudo, nos últimos três meses. Comprometo-me a entregar à CES o relatório final da investigação, assim que concluído.

Porto, 21 de Maio de 2019

Nome legível: MARTA SOFIA RESENDE RUSSO

Marta Russo
assinatura

Parecer da Comissão de Ética do Centro Hospitalar de São João/FMUP

Emitido na reunião plenária da CE de 14, 06, 19

A Comissão de Ética para a Saúde
APROVA por unanimidade o parecer do
Relator, pelo que nada tem a opor à
realização deste projecto de investigação.


Prof. Doutor Filipe Almeida
Presidente da Comissão de Ética

Attachement 6. Certificate of Reuse of Data for Research

Parecer da Comissão de Ética para a Saúde do
Centro Hospitalar Universitário de São João / Faculdade de Medicina da Universidade do Porto

Título do Projecto: Intoxicações agudas em crianças e adolescentes admitidos no Serviço de Urgência Pediátrica do HSJ (Porto, Portugal), 2008-2018

Nome da Investigadora Principal: Dra. Marta Sofia Resende Russo, aluna do Mestrado em Ciências e Técnicas Laboratoriais Forenses, da CESPU

Onde decorre o Estudo: Na Urgência Pediátrica do CHUSJ. Dispõe de autorização do Prof. Doutor Luís Almeida Santos, que será também o profissional de ligação.

Objectivos do Estudo:

Este trabalho de investigação tem como principal objectivo a caracterização exhaustiva das intoxicações pediátricas registadas no Serviço de Urgência Pediátrica do CHUSJ entre 2008 e 2018.

Estudo realizado no âmbito do Mestrado em Ciências e Técnicas Laboratoriais Forenses do IUCS-CESPU, sob orientação da Prof.ª Doutora Diana Cristina Dias da Silva e do Prof. Doutor Ricardo Jorge Dinis de Oliveira.

Concepção e Pertinência do estudo:

A intoxicação aguda, ocupa o terceiro lugar como principal causa de mortes acidentais na população infantil-juvenil Europeia, e continua sendo uma causa evitável de morbidade e mortalidade em todo o mundo. As estatísticas da OMS para a Região Europeia revelaram a ocorrência de mais 3.000 intoxicações fatais por ano em crianças e adolescentes de 0 a 19 anos. Esse número fica ainda maior quando se consideram as intoxicações não letais, que representam uma causa frequente de internamento hospitalar. Em Portugal, a epidemiologia das intoxicações em crianças com idades compreendidas entre os 0 e os 17 anos não foi estudada de forma abrangente, mas os dados fornecidos pelo Centro de Informação Anti - venenos, CIAV, indicam que a prevalência de intoxicações ocorre nas crianças com idade entre 1-4 anos e diz respeito principalmente ao sexo masculino. Aproximadamente metade das 30.000 chamadas recebidas pela linha telefónica de assistência por ano refere-se a intoxicações na fase inicial de envenenamento, permitindo uma orientação adequada sobre a gestão da intoxicação.

Esta informação é de extrema importância para auxiliar as entidades reguladoras competentes na identificação de áreas prioritárias de intervenção, assim como na mobilização de meios para redução do número de intoxicações pediátricas.

Assim, o presente estudo incluirá todos os pacientes com menos de 18 anos de idade que se recorreram à Unidade de Emergência Pediátrica da CHSJ, incluindo aqueles que foram

transferidos de outros hospitais, entre 1 de janeiro de 2008 e 31 de dezembro de 2018. Todos os dados dos pacientes serão obtidos através da base de dados do hospital.

Apensa um pedido ao RAI para reutilização de registos clínicos para Investigação e Desenvolvimento.

Benefício/risco: NA

Confidencialidade dos dados:

Corretamente acautelado

Respeito pela liberdade e autonomia do sujeito de ensaio: NA

Curriculum da investigadora: Adequado à investigação.

Data previsível da conclusão do estudo: dezembro de 2022

Conclusão: Proponho um parecer favorável à realização deste projecto de investigação.

Porto, 14 de Junho de 2019

O Relator da CES,

