Clinical and demographical features of adult patients with acute intoxication admitted to a medical intensive care unit

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CLINICAL AND DEMOGRAPHICAL FEATURES OF ADULT PATIENTS WITH ACUTE INTOXICATION ADMITTED TO A MEDICAL INTENSIVE CARE UNIT

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1 INTRODUCTION

1.1 Acute intoxications

A drug that is poisonous by nature or dosage can cause acute intoxication, a diseased condition of the organism. It is a dynamic process that is frequently brief but severe and which can swiftly deteriorate and cause life-threatening problems. As a result, it is crucial that the emergency room implement the appropriate therapeutic strategy right away (1). Acute poisoning commonly manifests as cardiovascular instability, dysrhythmias, arterial hypotension, respiratory depression, hypothermia, unconsciousness, delirium, and multisystem organ failure. Many of these patients must be hospitalized to the intensive care unit (2).

1.2 Epidemiology of acute intoxications

According to the World Health Organization (3), poisoning is the third most prevalent way that people commit suicide worldwide each year, even though attempts to commit suicide by drug exposure occur significantly more frequently than successful suicides (4). The Annual Report of the American Association of Poison Control Centres' National Poison Data System (NPDS) in 2021 reported 2,080,917 human exposure cases. Compared to the Annual Report of 2020 this is a decrease of 2.22%. The top 5 substance classes most frequently involved in all human exposures were analgesics (11.2%), household cleaning substances (7.49%), cosmetics/personal care products (5.88%), antidepressants (5.61%), and sedatives/hypnotics/antipsychotics (4.73%). Intoxications with antidepressants increased most rapidly, by 1,663 cases/year (5).

According to what is now known, there are considerable regional differences in the frequency and kind of acute intoxication, which are linked to the population's cultural, religious, economic, and developmental traits. For instance, the abuse of pharmaceutical medications is the most frequent cause of acute intoxication in developed geographical areas (6). In contrast, insecticides are a popular class of drugs that cause acute intoxications in underdeveloped nations (7-9). To lessen the severe effects of acute poisoning, prompt diagnosis and poison identification are crucial.

Both intentional and inadvertent intoxications are possible. Suicide attempts are the most frequent cause of intoxication in the younger population, while iatrogenic events, which are linked to a higher risk of death, are the most frequent cause in the elderly. More than one medicine is taken in nearly half of the cases. The average age of patients admitted to the intensive care unit is 45 years old, and 83% of them are under the age of 70 (10). Regarding the paediatric population, research has revealed that intoxications in infants and young children are

mostly inadvertent; however, in adolescents, intoxications are typically intentional, and with a 46.3% suicide attempt rate, they are more common (11).

Although there are several papers outlining the epidemiology and clinical traits of acute intoxications, there aren't many studies that look at the type and incidence of acute intoxications. In some parts of the world, these studies are even lacking entirely. Although predictors of outcome connected to acute intoxications could be useful tools in management methods directed to reducing morbidity and death in acutely poisoned critical patients, studies describing such predictors are also limited in this area (12).

For the proper care of the acutely poisoned patient and for the reduction of morbidity and mortality, epidemiological data on the overall pattern of poisonings in each geographic location, local features of the clinical presentations, and outcome predictors are essential. Every geographical area needs greater knowledge regarding the types, prevalence, and prognoses of severely intoxicated individuals so that such patients can be better managed and have better outcomes (13).

1.3 Clinical features of acute intoxications

1.3.1 Clinical signs

Poisoning symptoms and signs vary widely and are often non-specific. Therefore, the key to diagnosis is clinical vigilance and history. Assessing and stabilizing key functions is crucial, especially in cases of acute poisoning (14). Patients arrive at the hospital's emergency room with a variety of symptoms, including dizziness (92.8%), headaches (89.4%), breathing problems (78.4%), irritability (77.3%), and vomiting (68.8%), while some (16.8%) are unconscious (15). In patients with ethanol intoxication, the clinical presentation is characterized by early dysphoria and disinhibition. There may be nausea, vomiting, and memory loss. However, it can also cause more severe problems such as nystagmus, stupor, coma, poor speaking, impaired coordination, and unstable walking. In such situations, respiratory depression and death are also possible outcomes (16).

1.3.2 Procedure in acutely intoxicated patients

If a person has been poisoned, he or she may contact a family doctor or the poison control centre. If a patient calls the poison control centre and is asymptomatic, has taken a known harmless dose of medication, and is seen as credible, they may be treated at home with support from the centre. Those who are symptomatic or who may have had an unclear exposure should be taken by ambulance to the emergency room. Patients who arrive at a doctor's office

with changed mental status, unstable vital signs, or who have intentionally overdosed should be transported straight to the emergency room. Only individuals with stable conditions who unintentionally consumed a known quantity of a medicine with a minimal risk of toxicity should be observed by a family doctor (17). The first aid for acute poisoning is based on the usual basic measures and should be carried out according to the ABCDE scheme. This enables an orderly assessment of the patient to be made. The A stands for Airway, the B for Breathing, the C for Circulation, the D for Disability and the E for Exposure (18). In the following, the individual points are described below:

Airway: The airway assessment is performed first. In the event of unconsciousness, the most important thing is to look for possible airway obstruction due to tongue retraction and aspiration of stomach contents or other foreign bodies (18).

Breathing: The second evaluation is a respiratory evaluation. Here, the respiratory rate is at issue. Under normal circumstances, the average breathing rate is 10-14/ min. If spontaneous breathing is present, the patient should be turned to the recovery position and be provided with appropriate oxygenation (a facial mask is preferred, possibly a nasal cannula in case of associated vomiting). If spontaneous breathing is inadequate, intubation and reanimation are indicated (18).

Circulation: In the next step, the patient's circulation must be assessed. In any scenario, the capillary refill time and pulse rate can be measured. Circulatory issues can be detected by looking at the skin. Signs of reduced perfusion include changes in colour, perspiration, and a loss of consciousness. Heart auscultation should be done if a stethoscope is available. Blood pressure readings and electrocardiography monitoring should both be done as soon as possible. An essential unfavourable clinical symptom is hypotension. By laying the patient flat and elevating their legs, it is possible to lessen the consequences of hypovolemia. As quickly as feasible, intravenous access should be established, and saline should be infused (19).

Disability: Next, the quality of consciousness is checked. The AVPU approach, where the patient is scored as alert (A), voice responsive (V), pain responsive (P), or unresponsive, can quickly determine the level of consciousness (U). Intubation might eventually be necessary (19).

Exposure: It is important to look out for signs of trauma, bleeding, skin responses (rashes), needle marks, etc. Clothing should be taken off to allow for a complete physical examination (19). The physical examination is explained in more detail in the chapter below.

1.3.3 Anamnesis

After stabilizing the patient's airway, breathing. and circulation, a detailed anamnesis of the patient is taken. Historical information should include the kind of toxin or toxin(s), time of exposure (acute versus chronic), volume consumed, and method of delivery (i.e., ingestion, intravenous, or inhalation). Also, it is crucial to know whether there is a history of mental illness or previous suicide attempts, as well as how the exposure happened (accidental, suicidal attempt, euphoric, or therapeutic misadventure). Also, it's critical to ask about any and all medications used, including prescription, over-the-counter, vitamin, and herbal treatments. People may misidentify the medications they have taken; for instance, they can call acetaminophen or ibuprofen by the wrong name. Patients who have been poisoned may not be trustworthy witnesses, especially if they are suicidal, psychotic, exhibit a changed mental condition, or are under the influence of recreational drugs. Information requested from friends and relatives may also be useful if the patient is unable to provide it (20).

1.3.4 Physical examination

Once the patient is stable, a thorough physical examination may reveal additional symptoms that point to a particular poison. Certain medication classes can cause certain classic appearances. However, even these well-known symptoms may not always be present, and their occurrence is dependent on the quantity that the patient has consumed, their premorbid condition, any additional medications they may have taken, and any complications that may arise during the poisoning. By observing the patient's vital signs, the doctor can frequently determine the type of medicine or toxin consumed. Particularly when patients show signs of a changed mental status, a thorough neurologic assessment is crucial. However, neither the GCS nor the AVPU scales are acceptable as predictor of outcome in the poisoned patient. However, they can both be used as instruments to communicate the degree of awareness and determine whether intubation is necessary. It is important to examine the skin closely. The patient's clothing should be taken off so that the skin can be examined for colour, warmth, dryness, and diaphoresis. Diaphoresis is a crucial clinical marker that distinguishes sympathomimetic toxicity from anticholinergic poisoning. Track marks on the skin, which indicate intravenous or subcutaneous cocaine or opiate misuse, are a common skin finding. Moreover, pharmaceutical patches, such as those containing opioids like fentanyl, should be looked for during the skin inspection. In circumstances of drug misuse, these patches might be found in odd places like the scrotum and vagina (20).

1.3.5 Laboratory diagnostics

Laboratory tests can provide information on whether an organ is damaged and whether life-threatening electrolyte disorders are present. Thus, liver and kidney values as well as muscle parameters (creatine kinase, myoglobin) should be determined, and a coagulation test (partial thromboplastin time) should be performed. To detect liver damage, blood levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), and gamma-glutamyl transferase (GGT) must be determined. Abnormal kidney parameters are an indication of kidney damage and should provide information about organ function through the values of creatinine and urea (21). In people with alcohol intoxication, it is important to know that there are several metabolic abnormalities that acute alcohol intoxication is known to cause, including hypoglycaemia, lactic acidosis, hypokalaemia, hypomagnesemia, hypoalbuminemia, hypocalcaemia, and hypophosphatemia. That is the reason why it is also important to carry out a blood gas analysis with determination of the anion gap and quantification of serum electrolytes (22).

1.3.6 Instrumental diagnostics

A quickly accessible clinical tool like an electrocardiogram can assist doctors in treating poisoned individuals. If intoxication is suspected, it is taken for granted to write a 12-lead electrocardiogram, as it provides important information such as prolonged QT times, block images, arrhythmias, and widened QRS complexes. In the field of clinical toxicology, classic ECG abnormalities may indicate ion channel blockage, changes in adrenergic tone, or dysfunctional metabolic activity of the myocardium (23). In the case of altered mental status in the patient, a head computed tomography should be performed (24).

1.3.7 Toxidromes

Toxic syndromes are a collection of symptoms and signs connected to a particular group of poisons. If a toxidrome is present, quick identification of it can aid in identifying the toxin or type of toxin in question. Some typical toxidromes are anticholinergic toxidrome, cholinergic toxidrome, opioid toxidrome, and sympathomimetic toxidrome (25).

Anticholinergic toxidrome: Many drugs have anticholinergic side effects, and anticholinergics are easily available. The antagonization of the neurotransmitter acetylcholine is the mode of action of anticholinergic substances. The bulk of these agents are taken orally. The archetypal anticholinergics from which other anticholinergics are derived are the naturally occurring substances atropine, hyoscyamine, and hyoscine. Atropine is a therapy for bradyarrhythmias and an antidote for cholinergic toxicity caused by organophosphates and

nerve agents (26). Patients, especially the elderly, who have ingested a large amount of anticholinergic substances, usually show symptoms ranging from disorientation, delirium, and serious cognitive decline to dry mouth, constipation, and visual impairments (27). Anticholinergic poisoning is typically treated with nothing more than supportive care (26).

Cholinergic toxidrome: Acetylcholinesterase inhibitors and some other substances like organophosphates stimulate the neurotransmitter acetylcholine and are the cause of cholinergic toxidrome. In the parasympathetic nervous system, acetylcholine is the main neurotransmitter. Muscle contraction and glandular secretion are triggered by the stimulation of muscarinic and nicotinic receptors by acetylcholine. A surplus of acetylcholine in the receptor synapse causes overly strong parasympathetic effects, which is known as cholinergic toxicity (28). Salivation, lacrimation, urination, defecation, gastric cramps, and emesis are symptoms that typically manifest acutely between minutes to hours after ingestion of increased amounts of cholinergic substances. Yet, some patients experience delayed effects, either after a period of severe cholinergic symptoms and signs in the beginning or after a period of little to no clinical features (29). Atropine, oxime-derivatives (pralidoxime and obidoxime), and possibly diazepam are the pillars of the medical treatment. In order to reduce the negative consequences of too much acetylcholine at the receptor site, atropine works by competitively blocking the acetylcholine receptor, mostly at the muscarinic sites. The nerve agents are removed from the acetylcholinesterase enzyme by oxime-derivatives such as pralidoxime, allowing it to start hydrolysing acetylcholine once more (30).

Opioid toxidrome: Opioids can act on opioid receptors as agonists, partial agonists, or agonist-antagonists. The opiates that are now on the market reduce both pain sensation and perception. Opiate receptors come in a variety of forms in both the central and peripheral nervous systems. The stimulation of these receptors causes the perception of pain to be suppressed. Patients with opiate overdoses may frequently appear lethargic or have a low degree of consciousness. Other side effects of opiate overdose include miosis, generalized central nervous system (CNS) depression, and respiratory depression. Additionally, it is well recognized that the majority of opiates cause peripheral vasodilatation, which may lead to mild to severe hypotension (31). An effective treatment for opioid overdose is the antidot naloxone, which reverses the action of opioids (32).

Sympathomimetic toxidrome: Poison's impact on the suppression of norepinephrine and dopamine reuptake at the preganglionic synapse is connected to the genesis of acute sympathomimetic toxicity. As a result, the postsynaptic terminal and synaptic space have an

overabundance of norepinephrine and dopamine. Due to the end organ being impacted, this prolonged exposure is what results in the majority of the adverse consequences of sympathomimetics. Tachycardia, hypertension, and vasoconstriction, which cause cardiac ischemia and dysrhythmias, are some of the cardiac consequences. Vasoconstriction, stroke-like symptoms, and intracranial bleeding are all potential neurological side effects (33). This may be brought on by any of the sympathomimetics, with cocaine, amphetamines, and MAO-inhibitors serving as the typical drugs. A benzodiazepine is the principal drug used to relieve symptoms. This medication treats and aids in the prevention of seizures, as well as calming the agitated patient; as a result, it aids in the prevention of excited delirium. Intravenous fluids to aid with hydration, renal elimination of any metabolic breakdown products, and passive cooling to maintain a normal body temperature are further adjuncts (34).

1.4 Therapy

After the stabilization of vital parameters and the identification of the ingested toxin are completed, the elimination of the toxin is indicated. The following points below describe the different ways in which a toxin can be eliminated.

1.4.1 Gastric lavage

Most intoxicated patients require further treatments, such as gastrointestinal cleansing and strategies to improve excretion of the ingested poison. The attending physician typically suggests gastric lavage. Patients who have consumed a toxic dose that poses a serious risk to their lives are most likely to benefit from gastric lavage. A gastric lavage is a technique for suctioning the contents of the stomach to eliminate the unabsorbed toxins and gastric content (35). According to some experts, gastric lavage should only be done 30 to 60 minutes after ingesting a hazardous amount of medicine or poison. In most cases, later lavage offers no clinical advantage (36). Poor outcomes have frequently occurred when stomach lavage was skipped or delayed, according to our experience (37). Loss of protective airway reflexes (unless the patient is first intubated tracheally), ingestion of a strong acid or alkali, ingestion of a hydrocarbon with a high aspiration potential, or danger of gastrointestinal bleeding owing to an underlying medical or surgical condition are all contraindications for gastric lavage (38).

1.4.2 Charcoal

Charcoal has been used for decades to treat drug poisonings because it is affordable, secure, and easily accessible. Medical charcoal works through two different mechanisms. By

inhibiting poison's absorption in the digestive system, it reduces the initial plasmatic concentration of poison. Moreover, it improves substance clearance by stopping enterohepatic circulation or binding substances that have been reintroduced into the digestive system via passive or active transport (enteroenteric circulation) (39). When gastrointestinal decontamination of an ingested toxin is indicated in poisonings, an oral suspension of activated charcoal should be taken into consideration. Given within an hour of ingesting the poison, activated charcoal works best. When using activated charcoal as a treatment, the contraindications should be carefully taken into consideration (40). Impaired consciousness combined with the risk of aspiration in a patient whose airway has not yet been secured is a significant contraindication. In situations of poisoning with acids or bases, alcohols, organic solvents, inorganic salts, or metals, activated charcoal is useless or just partially effective. The recommended dosage is 10 to 40 times the amount of the intoxicating chemical, or 50 g for adults and 0.5-1 g/kg body weight for children (41).

1.4.3 Urine alkalinization

The process of urine alkalinization, which involves giving intravenous sodium bicarbonate to make urine with a pH of at least 7.5, accelerates the removal of some poisons (42). Urine alkalinization is the first-line therapy for individuals with severe salicylate poisoning who do not meet the requirements for haemodialysis. As active charcoal administration provides a superior option, urine alkalinization is no longer advised for treating barbiturate toxicity. Moreover, it is no longer advised for individuals who have methotrexate poisoning and are now treated with glucarpidase or folinic acid (43). The most frequent complication of urine alkalinization, hypokalemia, can be treated with potassium supplements (44).

1.4.4 Antidotes

Antidotes are substances that work to reverse the effects of a poison or toxin. Antidotes block the effects of the toxin by either restricting absorption, joining with the toxin and neutralizing it, reversing the effects of the toxin on end organs, or preventing the toxin's transformation into more dangerous metabolites. Antidote delivery may lessen the amount of free or active toxin as well as the effects of the toxin on end organs via techniques like competitive inhibition, receptor blocking, or direct antagonism of the toxin (45). Regarding the effectiveness of antidotes in acute emergency settings, a study showed that with antidote treatment in the emergency room, more than 96% of the acute poisoning cases achieved improvement in their systemic results, whereas 3% did not demonstrate any improvement.

Concerning the accessibility of certain antidotes, the hospitals in the study offered activated charcoal, atropine, calcium chloride, calcium gluconate, flumazenil, insulin, magnesium, sodium bicarbonate, and vitamin K (46). The appropriate antidotes to be administered in each case of intoxication are described in the lower chapter "*Most common intoxications*".

1.4.5 Haemodialysis

Haemodialysis and hemoperfusion, two extracorporeal removal procedures, significantly improve toxin clearance. Haemodialysis works by diffusing substances across a semi-permeable membrane along a concentration gradient (47). In the past few years, the indications for haemodialysis became very narrow. First and foremost, it must be a potentially life-threatening poisoning with a hydrophilic, non-protein-bound noxious substance with a low volume of distribution in order to be dialyzable. Examples of such noxious agents are arsenic, methanol, ethanol, ethylene glycol, propanol, salicylates, lithium, thallium salts, metformin, valproic acid, etc. The indications for extracorporeal removal of toxins are also affected by advancements in supportive care, modifications in gastrointestinal decontamination methods, and the development of relevant antidotes (48).

1.4.6 Hemoperfusion

Hemoperfusion represents one of the most effective extracorporeal elimination procedures. Blood is pumped through a cartridge filled with polymer-coated activated carbon, which can bind small molecules. Limiting factors here are also a high protein binding affinity and a large distribution volume of the absorbed noxious substance. Areas of application for hemoperfusion are severe poisoning with theophylline, carbamazepine, paracetamol, quinidine, colchicine, alkyl phosphates, and Amanita phalloides mushroom (49).

1.5 Most common intoxications

1.5.1 Ethanol

The most prevalent intoxication with alcohols is intoxication with ethylic alcohol, which is also the oldest and most often misused substance. Alcohol is mostly consumed and abused in western civilization. Adolescents and young adults are the groups most likely to show signs of acute intoxication from alcohol. Although some alcohol is also absorbed from the stomach, the small intestine is the location where the majority of alcohol is absorbed into the blood. Because absorption happens more quickly than metabolization and removal, alcohol builds up in the blood. If the stomach was previously empty, the concentration peaks between 30 and 90

minutes after intake. A big part of the ingested alcohol is metabolized mainly in the liver, where alcohol dehydrogenase converts ethanol to acetaldehyde. Alcohol exerts its effects through several mechanisms. The central nervous system is where acute poisoning manifests itself since it enhances inhibition and decreases excitement in the CNS. The main inhibitory neurotransmitter in the CNS is gamma-aminobutyric acid (GABA). Chloride can enter the cell when GABA attaches to receptors, reducing neuronal excitability. Strong GABA receptor binding by alcohol causes the inhibitory cascade to be activated, causing drowsiness, impaired cognitive function, and loss of coordination (50).

When a person consumes more alcohol than their liver can process, acute ethanol intoxication results. This accumulation of alcohol's metabolites is characterized by early dysphoria and disinhibition. There may be nausea, vomiting, and memory loss. However, it can also cause more severe problems such as nystagmus, stupor, coma, poor speaking, impaired coordination, and unstable walking. In such situations, respiratory depression and death are also possible outcomes (16). No antidote exists for acute alcohol intoxication; instead, supportive and symptomatic therapy, alcohol withdrawal prevention, and treatment of concurrent psychiatric problems and comorbidities are recognised and successful globally. Only very rarely is gastric decontamination advised. Treatment for moderate-to-severe intoxication (blood concentration > 1 g/L) should start with dextrose, thiamine, folic acid, and sufficient crystalloid replacement. Magnesium, potassium, and multivitamin supplements are recommended on an individual basis. If other reasons, such as head injury and cerebral haemorrhage, have been ruled out, antiemetics should be administered to patients who are experiencing nausea and vomiting. It is also necessary to properly monitor arterial blood gases, blood pressure, body temperature, glycemia, electrolytes, ketonemia, and ketonuria (51).

1.5.2 Benzodiazepines and sedatives

At the moment, benzodiazepines are used to treat anxiety, seizures, withdrawal symptoms, insomnia, and agitation, and are frequently used for procedural sedation. Since their creation several decades ago, benzodiazepines have been widely prescribed and used illicitly due to their wide range of uses and addictive qualities. The primary inhibitory neurotransmitter in the central nervous system, the gamma-aminobutyric acid A (GABA-A) receptor, is modulated by benzodiazepines to have its effects. The binding of benzodiazepines to the GABA-A receptor ultimately increases the flow of chloride ions via the GABA ion channel, causing postsynaptic hyperpolarization, which lowers the ability to generate an action potential. This results in symptoms like drowsiness, slurred speech, ataxia, and decreased consciousness.

Intoxications with benzodiazepines are treated with fluid replenishment, electrolyte correction, gastric lavage, activated charcoal, and the antidote flumazenil (52).

1.5.3 Antipsychotics

Poisoning with neuroleptics manifests itself in pronounced CNS effects, characterized by a delirious state up to a deep coma. Unconsciousness may lead to aspiration and, subsequently, the need for mechanical ventilation. Depending on the severity, there may be a loss of brainstem reflexes and, in combination with other centrally depressant substances, respiratory depression and even apnea. Furthermore, vegetative disturbances such as α-adrenergic-mediated vasodilation, low blood pressure, tachycardia, facial flushing, dry skin, and dry mucous membranes become apparent. In general, one can speak of an anticholinergic syndrome. The ECG shows QT time prolongation, which can lead to a life-threatening tachycardic arrhythmia (53).

Since no specific antidote exists, therapy is purely symptomatic. The first crucial step in treating intoxication with antipsychotics is the immediate discontinuation of the offending neuroleptic. Supportive medical therapy is thereafter the cornerstone of management. Since most patients are dehydrated during the acute stage of the illness, vigorous volume replacement is recommended. Electrolyte monitoring and rebalancing are crucial. Renal failure may be avoided by drinking alkalinized liquids or adding bicarbonate to food. Physical cooling techniques are crucial when someone is suffering from acute hyperthermia. It is recommended to keep patients under close observation for coagulopathies, aspiration pneumonia, renal failure, and other consequences of cardiorespiratory failure (54).

1.5.4 Antidepressives

Antidepressants are divided into selective serotonin reuptake inhibitors (SSRIs), selective serotonin and noradrenaline reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), 5-HT2 receptor antagonists, tetracyclic and monocyclic antidepressants, and monoamine oxidase inhibitors (MAOIs) (55). In principle, the intake of 10 – 20 mg/kg of most antidepressants can lead to moderate to severe disturbances. This can range from mild vigilance reductions to coma. Furthermore, dangerous functional impairments of the cardiovascular system may occur. Slight overdoses of antidepressants lead to mydriasis, sinus tachycardia, dry mouth, and warm and dry skin. Severe intoxications are characterized by coma and hypoventilation, as well as life-threatening cardiac effects. Inhibition of the sodium channel in the myocardium causes delayed stimulus conduction, which promotes the occurrence of ventricular arrhythmias. This blockage then leads to a disruption in the sodium-calcium

exchange, which leads to a reduced calcium concentration in the myocardial cell, which in turn is associated with reduced contractility of the heart muscle. Since the potassium channel is also affected, the repolarization of the myocardium is prolonged. Treatment of intoxication with tricyclic antidepressants includes general symptomatic supportive measures, gastric lavage, application of activated charcoal, maintenance of the airway, and monitoring of heart function. To prevent cardiotoxicity, sodium bicarbonate is given in a dose of 1 mEq/kg intravenously as a bolus and then in a continuous infusion, and in cases of severe hypotension, norepinephrine is administered. In cases of convulsions, benzodiazepines are used. Physostigmine, antiarrhythmics of groups 1A, 1C, and III, as well as flumazenil, should not be used (56).

1.5.5 Paracetamol and ibuprofen

N-acetyl para-aminophenol (APAP), generally known as paracetamol or acetaminophen, is one of the most popular over-the-counter analgesic and antipyretic medications (57). Its precise mechanism of action is still unknown, but because it inhibits the cyclooxygenase (COX) pathways, it has previously been grouped alongside NSAIDs. Acetaminophen possesses analgesic and antipyretic effects, just like NSAIDs. Acetaminophen, however, lacks peripheral anti-inflammatory effects, according to researches. Although it does not affect peripheral tissues, acetaminophen may inhibit the COX pathway in the central nervous system (58). Paracetamol is used in adults in doses of 650 to 1000 mg every 4-6 hours, up to a maximum of 4 g per day. Toxic effects are seen at a dose of 7.5 to 10 g per day, or 140 mg/kg. It is quickly absorbed through the gastrointestinal tract and achieves a therapeutic effect after 30 minutes to two hours. In the case of intoxication, vomiting, pain in the right upper quadrant of the abdomen, hypotension, failure of liver function with the development of encephalopathy, blood coagulation disorder, and haemorrhagic diathesis can be observed (59).

The basis of treatment for acetaminophen toxicity is the antidote N-acetylcysteine (NAC). If administered within 8 hours of acetaminophen use, NAC is practically always successful in treating potentially hepatotoxic dosages of paracetamol. With only minor changes in effectiveness, NAC may be administered orally or intravenously. The most widely utilized regimens are the 72-hour oral dosage protocol and the 21-hour IV protocol. When it is applied orally within the 72-hour protocol, the starting dosage is 140 mg/kg, followed by 17 doses of 70 mg/kg every 4 hours. If applying it intravenously within the 21-hour protocol, the loading dose is 150 mg/kg in 200 ml of 5% glucose solution within 60 minutes, followed by 50 mg/kg in 500 mL of 5% glucose solution within 4 hours, and 100 mg/kg in 1000 mL of 5% glucose solution within 16 hours (60). Additionally, activated charcoal should be provided to the patients (61).

1.5.6 Illicit drugs

Cocaine: Due to its sympathomimetic, vasoconstrictive, and local anaesthetic properties, acutely intoxicated patients with cocaine mostly present with signs such as tachycardia, hypertension, and agitation. Mydriasis, diaphoresis, hyperthermia, and tachypnea are common additional physical examination findings (62). According to some studies, benzodiazepines work best as a first-line treatment for agitation and cardiovascular toxicity by reducing CNS sympathetic output. It has been demonstrated that calcium channel blockers like diltiazem and verapamil effectively lower blood pressure. Benzodiazepines work best for treating agitated people, but antipsychotics like haloperidol and olanzapine may also be helpful. It has been demonstrated that combining benzodiazepines and antipsychotic medications is more effective than monotherapy in patients intoxicated with cocaine (63).

Heroin: Commonly referred to as diacetylmorphine, it is a prodrug that is much more effective than morphine. Heroin, which may be smoked, snorted, or injected, is seeing a rise in consumption that is partly attributable to initiatives to lessen the abuse of prescription painkillers (64). Due to its opioid receptor agonism, intoxicated patients typically show lessened respiratory effort and rate, sedation, and narrowed pupils. If rapid rescue efforts are not implemented, a significant overdose can develop into apnea with coma, which is followed by minutes by cardiac arrest and death (65). An opioid overdose can be reversed with the use of the opioid receptor antagonist drug naloxone. It acts by quickly interacting with opioid receptors and blocking heroin from activating them (66). The initial dose recommended is 2 mg or 4 mg IN or 0.4 mg or 2 mg IM/SC, to be repeated after 2-3 minutes if necessary (67).

1.5.7 Carbonmonoxide

The incomplete combustion of carbonaceous materials produces carbon monoxide (CO), which has a wide range of origins. Usually, victims are made unconscious before they are aware that they have been poisoned because it has no flavour, odour, or colour. CO toxicity's impact on haemoglobin's ability to bind oxygen accounts for its etiology. Because CO has a 220% higher affinity for haemoglobin than oxygen, it binds to hemoglobin to create carboxyhemoglobin (COHb). Cellular hypoxia results from hemoglobin's reduced ability to deliver oxygen as a result of this. Additionally, CO inhibits mitochondrial respiration by attaching to the heme moiety of the cytochrome c oxidase in the electron transport chain (68). When the COHb concentration is between 15% and 30%, the earliest symptoms of CO exposure include headache, nausea, dizziness, exhaustion, and decreased ability to maneuver. Loss of consciousness and ultimately death result from COHb concentrations between 30% and 70% (69).

Identification of concurrent drug ingestions is necessary for the management of these patients, particularly when intentional poisoning, fire-related toxic gas exposures, and inhalational injuries are present. There is no available antidotal therapy, and conventional therapy is only available with normobaric and hyperbaric oxygen. Despite the fact that hyperbaric oxygen considerably lessens the long-term neurological and emotional effects of CO poisoning, some survivors nonetheless experience significant morbidity. Therapies that aim to combat the inflammatory and oxidative side effects of CO poisoning have had some early success. The development of new strategies, such as CO scavenging agents, to specifically target the hazardous effects of CO is ongoing (70).

1.5.8 Pesticides

Pesticides are a class of chemicals that have greatly benefited humanity in the agricultural, industrial, and medical fields, but their toxicity to both people and animals has always been a worry (71). Organophosphorus substances are frequently used as pesticides due to their low cost, but due to their high toxicity, they pose a serious risk to the public's health, particularly in cases of occupational exposure in agriculture, during pesticide-assisted suicide attempts, and as nerve agents in warfare. There are a lot of cases of organophosphate poisoning due to their strong permeability through ingestion, absorption, and cutaneous exposure, and their frightening fatality rates are a result of this (72). Organophosphate molecules can enter the body through the skin, by inhalation, or through the digestive system. After being absorbed, the substance attaches to an acetylcholinesterase molecule found in red blood cells, rendering the enzyme inactive. Acetylcholine builds up excessively in synapses and neuromuscular junctions as a result of this. Fasciculations and myoclonic jerks can occur when nicotinic receptors at neuromuscular junctions are overstimulated. Due to the depolarizing block, this eventually results in flaccid paralysis (73). Although atropine continues to be the basis of therapy, numerous attractive new treatments are now being developed. Oximes are frequently used to treat organophosphorus poisoning. Additional promising therapy options include magnesium sulfate, calcium channel blockers (nimodipine), plasma alkalinizing drugs, nicotinic receptor antagonists, clonidine, and lipid emulsions. However, in order to prove their effectiveness, substantial phase III trials are needed (74).

1.6 Clinical features of acute intoxications in the southern regions of Croatia

According to current knowledge, there is significant variability in the incidence and type of acute intoxication depending on the geographical region, which is related to the cultural, religious, economic, and developmental characteristics of the population. For example, in developed geographical regions, the most common cause of acute intoxications is pharmaceutical drug abuse; on the contrary, in developing countries, insecticides are a common group of substances involved in acute intoxications. Timely diagnosis and recognition of the poison are of key importance in reducing the severe consequences of acute poisoning. Epidemiological data on the general pattern of poisonings in each geographic region, local characteristics of the clinical presentations, and outcome predictors are vital issues for the correct treatment of the acutely poisoned patient, and for the reduction of morbidity and mortality. It is necessary for every geographic region to have more information about the type, incidence, and outcomes of acutely intoxicated patients, which could improve their management and outcomes.

Currently, there are no available data to address such important data on acute poisonings among adults in the southern regions of Croatia. University Hospital of Split is a 1500-bed hospital, the largest hospital centre on the eastern Adriatic coast, and the central health institution in the entire southern region of Croatia. The hospital, with over 50,000 patients hospitalized per year, serves about one million citizens of the Republic of Croatia, about 500,000 residents of the southern part of Bosnia and Herzegovina, and about 500,000 tourists during the summer season.

2 OBJECTIVES

2.1 Objectives of the study

The main aims of the presented study were:

1. To assess the demographic characteristic of acute intoxications admitted to a medical ICU.
2. To assess clinical features of acute intoxications.
3. To assess outcome predictors of acute intoxications.

Hypotheses of the study:

1. There are significant gender differences in clinical features and outcomes in acutely poisoned patients.
2. There is a significant influence of poison type on clinical presentation and outcome.
3. There are significant differences in demographics, clinical presentation, and outcomes between suicidal and non-suicidal intoxications.

3 SUBJECTS AND METHODS

3.1 Study design

We conducted an observational retrospective cross-sectional study to investigate the clinical characteristics and epidemiological patterns of acute poisoning leading to medical ICU admissions. The study took place in the eight-bed medical ICU of the Internal Medicine Department, Division of Emergency and Intensive Medicine with Clinical Pharmacology and Toxicology, University Hospital of Split. This ICU is dedicated primarily for adult medical patients and refers critical patients for various conditions, including severe acute intoxications. The ICU is part of a larger department for intensive internal medicine with toxicology, and represents a regional toxicological and pharmacological centre. The study protocol was approved by the Ethics Committee at the University Hospital of Split with ethics code of 500-03/22-01/198; date of approval: November 28, 2022.

3.2 Study population

The study population consisted of all acutely poisoned adult patients who were admitted to the medical intensive care unit (ICU) of the Department for Urgent and Intensive Medicine with Clinical Pharmacology and Toxicology of the University Hospital of Split, Croatia, during one-year period, from November 1st, 2021, to November 1st, 2022.

Including criteria were patients aged over 18 years admitted to the ICU due to accidental, overdose, or intentional acute poisoning or drug exposure. Exclusion criteria included acute intoxication with concomitant additional acute or critical pathology, or a stay in the ICU for less than 4 hours. Poisoned patients in the emergency department (ED) were examined and treated by the physicians on duty. Depending on the severity of symptoms, the patients were discharged after management in the emergency department or transferred to our ICU. Criteria for ICU admission were live-threatening and severe acute intoxication, potentially lethal exposure, seizure, CNS depression, respiratory failure, or hemodynamic instability. The decision for ICU admission was responsibility of the attending physician, based on toxin amount, clinical severity, clinical demonstration, and potential postponed effects of the poison.

Patient's data were collected from central electronic hospital records and including medical history, demographic characteristics, toxin(s) (presumed or by toxicological analysis proved), the route of exposure, the cause of poisoning (accidental, overdose, intentional, exposure), vital signs, laboratory tests, electrocardiogram findings, treatment in ED/ICU and outcome (in-hospital mortality, discharge, length of stay) data. Electrocardiographic (ECG) abnormalities at admission time were also studied and were defined as follows: tachycardia as

heart rate greater than 100 beats/min, bradycardia as heart rate less than 60 beats/min, prolongation of QRS interval greater than > 100 ms, prolongation of QTc >more than 420 ms, left ventricular hypertrophy if the S wave in V1 plus the R wave in V5 or V6 is greater than 35 mm; and other ECG abnormalities according to standard criteria.

3.3 Statistical analysis

Descriptive statistics calculations and data were presented as number (percentages) for qualitative variables, and for quantitative variables are expressed as arithmetic mean ± standard deviation if normally distributed, or median (interquartile range) if non-normally distributed. Kolmogorov-Smirnov test was used for estimation of the normality of quantitative variables distribution. Qualitative data between groups were compared with Chi-square and Fisher's exact tests, as appropriate. Quantitative data were compared using unpaired Student's -t test or one-way ANOVA. Mann–Whitney test and Kruskal-Wallis tests were employed to analyse and compare quantitative variables with non-normal distribution. Correlations between quantitative data were calculated as significance of Pearson correlation coefficient for normally distributed variables or Spearman's rho coefficient for variables with a non-normal distribution. *P* values < 0.05 were considered significant. Statistical analysis was performed with SPSS software for Windows (IBM SPSS Statistics for Windows, version 26.0, Armonk, NY, USA).

4 RESULTS

During the 1-year observation study period, in our medical ICU, in total, 541 critical adult patients were admitted, of whom 81 cases (26 females, or 32.1%, and 55 males, or 67.9%) of acutely poisoned patients met inclusion study criteria. Those 81 participants admitted to our ICU represented 14.97% of annual ICU admissions. The mean age of the acutely intoxicated cohort was 43.16±14.77 years. Most cases (75 or 92.59%) of all intoxications were committed by oral ingestion of the poison. Demographics, clinical presentation on admission, management, and outcome of all subjects are shown in Table 1, along with sex differences. The gender and age distribution of participants are demonstrated in Figure 1a and 1b.

Table 1. Subjects demographics and clinical presentation on admission to the ICU, with management and outcome.

	All patients (N=81)		Females (N=26)		Males (N=55)		*P*
Age (years)	43.16±	14.77	45.69±	17.98	41.96±	12.99	0.146
Number of toxins in a patient	2.00	(1.00)	2.00	(1.00)	2.00	(1.00)	0.137
SatO2 (%)	92.86±	8.56	95.40±	3.70	91.58±	9.95	**0.031**
pCO2 (kPa)	5.75±	1.47	5.04±	0.73	6.08±	1.60	**0.006**
Glasgow coma score	8.46±	2.72	9.08±	2.21	8.16±	2.90	0.079
Urea (mmol/L)	4.93±	2.22	4.53±	2.25	5.11±	2.20	0.138
Creatinine (mmol/L)	89.43±	49.40	67.35±	19.24	99.87±	55.66	**0.002**
C-reactive protein (mmol/L)	2.80	(9.85)	1.50	(7.53)	3.30	(13.20)	0.085
Sodium (mmol/L)	138.49±	4.34	138.92±	3.08	138.29±	4.83	0.272
Potassium (mmol/L)	3.84±	0.52	3.83±	0.64	3.85±	0.45	0.450
Chloride (mmol/L)	101.80±	4.06	103.12±	3.54	101.14±	4.17	**0.023**
Bicarbonate (mmol/L)	23.66±	3.92	23.84±	3.59	23.58±	4.12	0.413
Heart rate (/min)	93.51±	22.34	93.77±	24.20	93.39±	21.63	0.472
Systolic blood pressure (mmHg)	116.41±	24.87	114.12±	22.06	117.45±	26.18	0.291
Diastolic blood pressure (mmHg)	70.98±	16.69	71.16±	14.54	70.89±	17.71	0.474
Length-of-stay in ICU (days)	2.00	(2.00)	2.00	(1.00)	2.00	(2.00)	**0.027**
Length-of-stay in hospital (days)	6.00	(2.00)	10.50	(12.75)	3.00	(15.00)	**0.007**
Suicidal self-poisoning (N, %)	56	(69.14)	25	(96.15)	31	(56.36)	**<0.001**
Benzodiazepines/Hypnotics (N, %)	43	(53.09)	18	(69.23)	25	(45.45)	**0.038**
Antidepressives (N, %)	14	(17.28)	6	(23.08)	8	(14.55)	0.259
Opioids (N, %)	18	(22.22)	1	(3.85)	17	(30.91)	**0.004**
Ethanol (N, %)	14	(17.28)	1	(3.85)	13	(23.64)	**0.023**
Antipsychotics (N, %)	62	(76.54)	7	(26.92)	12	(21.82)	0.404
Past psychiatric disorders (N, %)	62	(76.54)	22	(84.62)	40	(72.73)	0.186
Electrocardiogram abnormalities (N, %)	41	(50.62)	10	(38.46)	31	(56.36)	0.088
Vasopressors (N, %)	6	(7.40)	1	(3.85)	5	(9.10)	0.305
Antidotes (N, %)	27	(33.33)	9	(34.62)	18	(32.73)	0.529
Gastric lavage (N, %)	41	(50.62)	15	(57.69)	26	(47.27)	0.315
Activated charcoal (N, %)	39	(48.15)	13	(50.00)	26	(47.27)	0.503
Haemodialysis (N, %)	3	(3.70)	1	(3.85)	2	(3.64)	0.693
Oxygen in therapy (N, %)	58	(71.60)	13	(50.00)	45	(81.82)	**0.007**
Mechanical ventilation (N, %)	9	(11.11)	1	(3.85)	8	(14.55)	0.146
Transfer to psychiatric ward (N, %)	40	(49.38)	19	(73.08)	21	(38.18)	**0.003**

Legend: SatO2: peripheral oxygen haemoglobin saturation, pCO2: partial pressure of carbon dioxide, ICU: intensive care unit. Data are shown for the whole patient population as well as for the two subgroups, sex differences is calculated (Student's -t test for independent samples or Mann-Whitney test for nonparametric data, and Fisher's exact test for qualitative data), *P* for significant differences are bolded. Data is presented as arithmetic mean± standard deviation or median (interquartile range) for continuous variables and as count (percent) for qualitative variables.

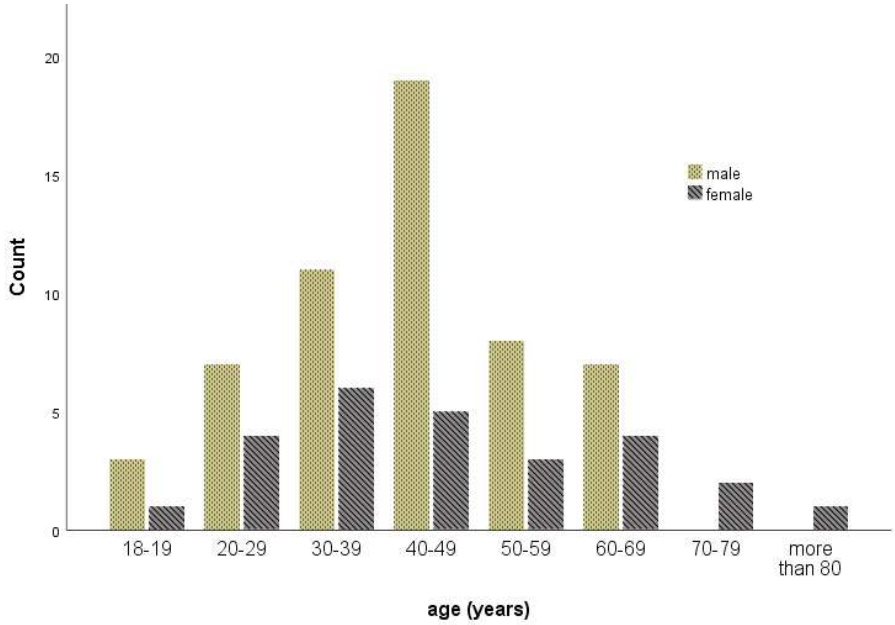

Figure 1a. Gender and age distribution of participants (N=81).

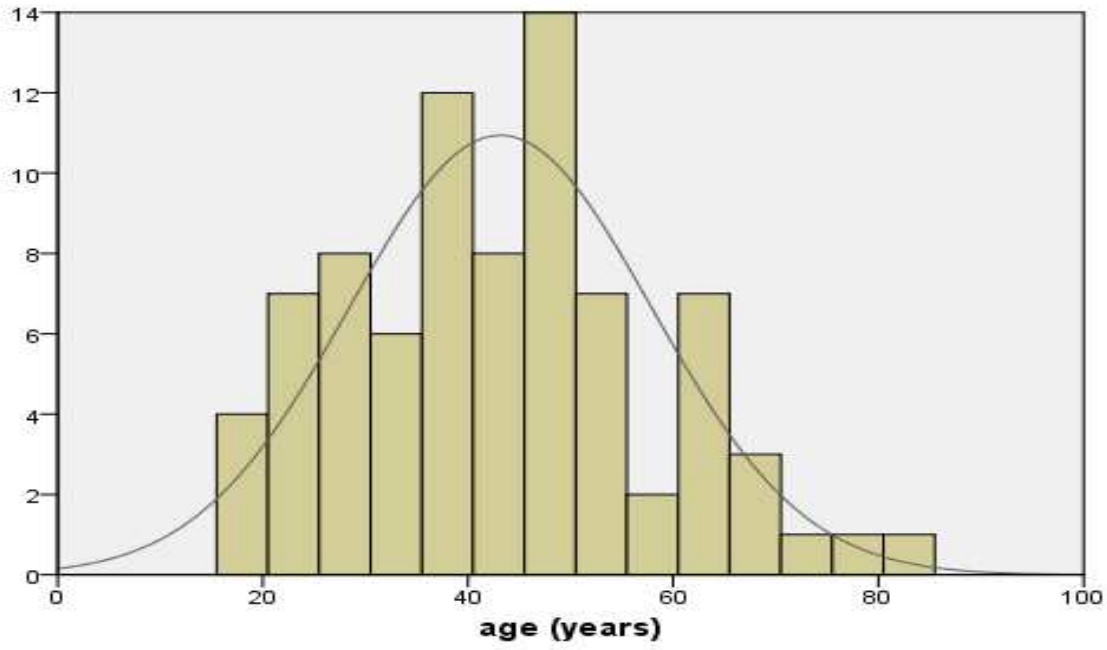

Figure 1b. Age distribution of participants (N=81).

Before admission, psychiatric disorders were established in 62 (76.5%) subjects. After recuperation and discharge from our ICU, 40 subjects (49.4%) were instantly transferred to the psychiatric department of our hospital as a continuation of hospital treatment. Among all cases, 56 (69.1%) of all acute intoxications were classified as suicidal, and 25 (30.9%) were overdoses, abuse, or accidental intoxications. Non-suicidal subjects (N=25) significantly differed from subjects committed to suicidal self-poisoning (N= 56) in age (3.36±9.71 vs. 45.75±15.93 years; *P* =0.009), in pCO2 (6.38±1.78 vs. 5.50±1.26 kPa; *P* =0.020), in length-of-stay in ICU (median 1.00, interquartile range 1.00 vs. median 2.00, interquartile range 2.00 days; *P*= 0.022) and in length-of-stay in hospital (median 2.00, interquartile range 2.00 vs. median 10.50, interquartile range 15.25 days; *P*=<0,001). Among suicidal subjects 55.36% were males (χ^2 = 13.099; *P* <0.001), 25.00% ingest antidepressives vs. 75.00% did not (χ^2 = 7.556; *P* =0.003), only 8.9% were poisoned with opioids (χ^2 = 18.55; p<0.001), only 10.71% with ethanol (χ^2 =5.48; *P* =0.024), 33.93% suicidal subjects ingest antipsychotics (χ^2 =11.08; *P* <0.001), 89.29% had previous psychiatric disorders (χ^2 =16.41; *P* <0.001), 70.91% suicidal patients were subjected to the gastric lavage (χ^2 =26.21; *P* <0.001), 67.86% were treated with activated charcoal (χ^2 = 28.23; *P* <0.001), and 66.07% (χ^2 =20.22; *P* <0.001) were transferred to the psychiatric ward after ICU treatment.

Only 3 (3.7%) patients died in our ICU as a consequence of severe acute intoxication or late complications. In one case of death, the toxin was ethanol, in the second case, the toxins were (combination) promazine, clozapine, and buprenorphine; and in the third case, the poisons were ziprasidone, alprazolam, pregabalin, and quetiapine. The vast majority of all cases (76, or 93.8%) included acute intoxication with one or more psychoactive substances (pharmaceutical and non-pharmaceutical, including illicit substances). Pharmaceutical psychoactive drug intoxication was the most common cause of acute intoxication; of these, diazepam was the most frequent (16.8%), followed by ethanol (9.0%) and alprazolam (7.8%) (Table 2).

Table 2. Frequency and number of the agents involved in acute intoxications, as a single substance or in combination.

A type of poison	N	%
Diazepam	28	16.8
Ethanol	15	9.0
Alprazolam	13	7.8
Methadone	11	6.6
Quetiapine	7	4.2
Clozapine	6	3.6
Pregabalin	6	3.6
Clonazepam	5	3.0
Sertraline	5	3.0
Methamphetamine	4	2.4
Olanzapine	4	2.4
Promazine	4	2.4
Amlodipin	3	1.8
Buprenorphine	3	1.8
Cannabis	3	1.8
Escitalopram	3	1.8
Lamotrigine	3	1.8
Opioids	3	1.8
Paroxetine	3	1.8
Buprenorphine+Naloxone	2	1.2
Cocaine	2	1.2
Hyoscine	2	1.2
Ibuprofen	2	1.2
Indapamide	2	1.2
Perindopril	2	1.2
Ramipril	2	1.2
Zolpidem	2	1.2
Amitriptyline	1	0.6
Amlodipine	1	0.6
Amphetamines	1	0.6
Bisoprolol	1	0.6
Bupropion	1	0.6
Carbamazepine	1	0.6
Chlorthalidone	1	0.6
Cihalotrin (Insecticide)	1	0.6
Ethylen Glycol	1	0.6
Fluvoxamine	1	0.6
Heroin	1	0.6
Ketoprofen	1	0.6
L-thyroxin	1	0.6
Levodopa+Benzerazid	1	0.6
Lithium	1	0.6
Mirzaten	1	0.6
Organophosphates	1	0.6
Paracetamol	1	0.6
Phenprocoumon	1	0.6
Rosuvastatin	1	0.6
Trazodone	1	0.6
Ziprasidone	1	0.6

After grouping poisons into classes, it can be assumed that toxins from the benzodiazepines/hypnotics class were the most common (48 agents, 28.7%), followed by antipsychotics (22 or 13.2%), opioids (21 or 12.6%), antidepressants (15 or 9.0%) and ethanol (15 or 9.0%) (Figure 2).

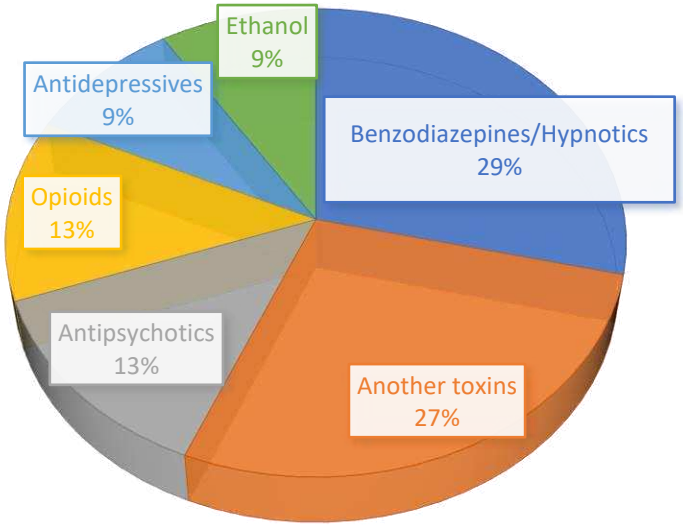

Figure 2. Distribution of poison classes participated in intoxications (as single toxin or in combination).

The largest number of cases were intoxications with more than one poison (55 subjects, or 67.9%): 2 substances were responsible for intoxication in 38 subjects (46.9%), 3 substances in 9 subjects (11.1%), 4 substances in 3 subjects (3.7%), 5 substances in 2 (2.5%) subjects, 6 substances in 1 (1.2%) and 7 substances in 2 (2.5%) subjects (Figure 3).

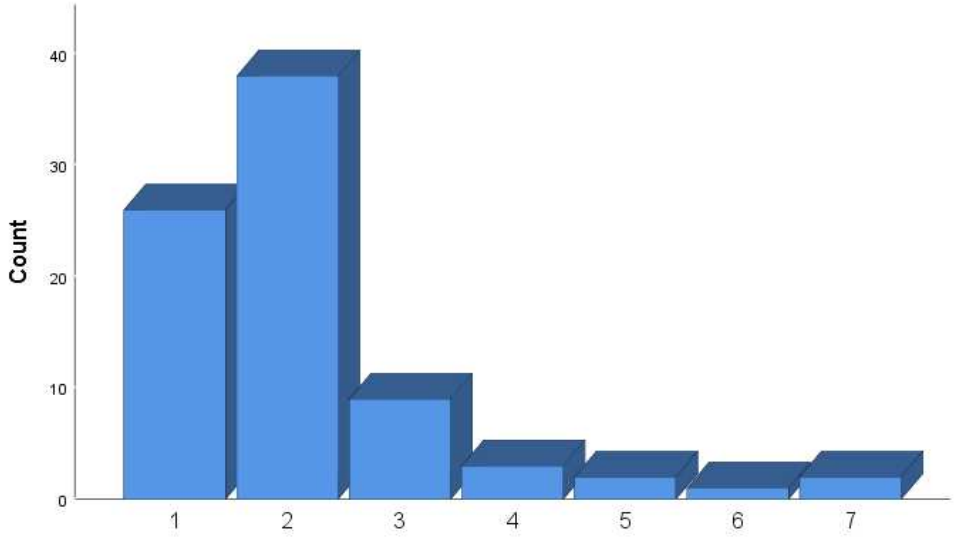

Figure 3. Distribution of number of poisons among intoxicated subjects.

When indicated, an antidote was used. Flumazenil was used in the largest number of cases (16 subjects, 50% of all antidote applications), followed by naloxone (11 subjects, and 34.4% of antidote applications). In 2 cases, atropine was used, and in 1 case, konakion, N-*acetylcysteine* (NAC), or pralidoxim were used (Figure 4).

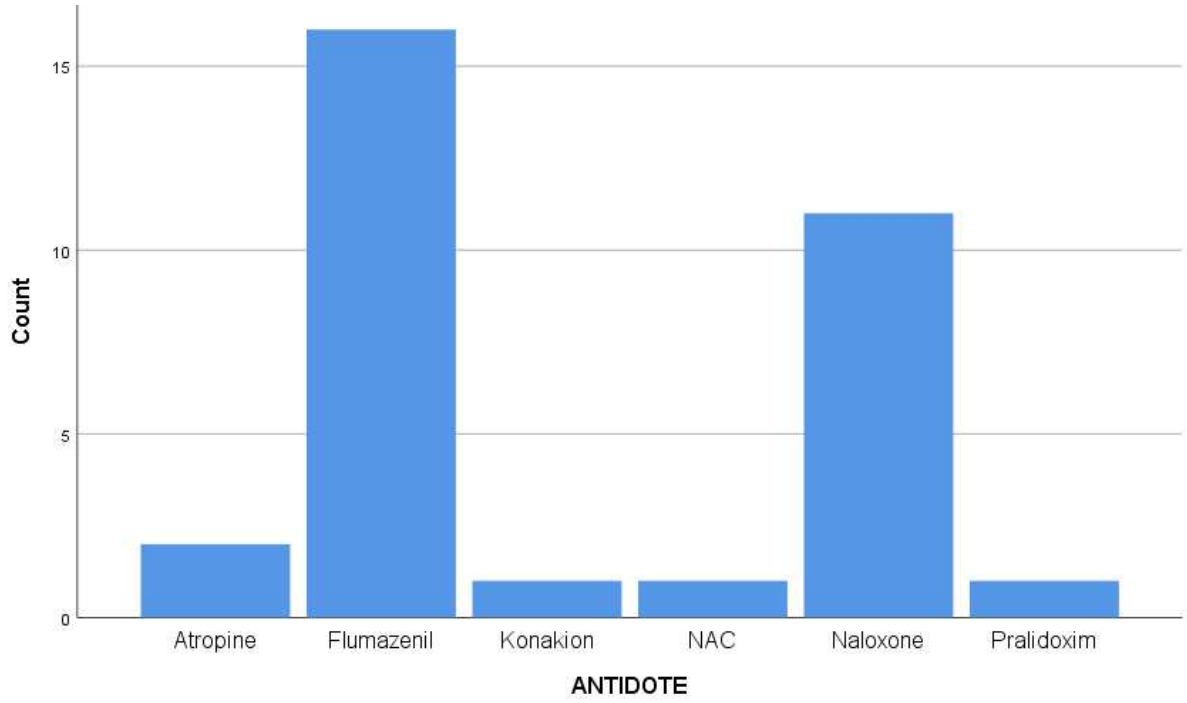

Figure 4. Number of antidotes used.

Electrocardiogram, performed at admission time was considered abnormal in 41 subjects (50.62%), and the most common recorded abnormality was sinus tachycardia (23 cases), followed by incomplete right bundle branch block (2 cases), QT interval prolongation (2 cases), complete bundle branch block (3 cases), supraventricular or ventricular extrasystoles (3 cases), AV blocks (2 cases), biphasic or negative T wave (3 cases), ST depression or elevation (2 cases), and reduced R wave in precordial leads with QS inferior (1 case) (Figure 5).

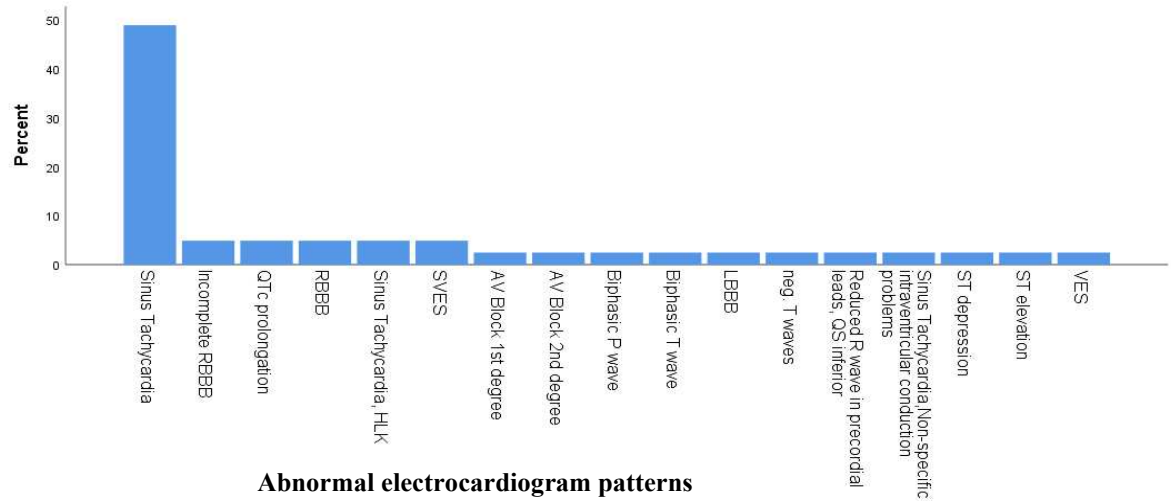

Figure 5. Distribution of abnormal electrocardiogram patterns.

Differences between patients poisoned with one toxin and patients poisoned with more than one toxin are shown on Table 3. Differences between patients treated with mechanical ventilation and patients no mechanically ventilated are shown on Table 4.

Table 3. Differences between patients poisoned with one toxin and patients poisoned with more than one toxin.

	One toxin (N=26)		**More than 1 toxin (N=55)**		*P*
Age (years)	47.27±	17.12	41.22±	13.24	**0.043**
SatO2 (%)	93.97±	6.54	92.36±	9.34	0.224
pCO2 (kPa)	5.86±	1.85	5.70±	1.27	0.354
Glasgow coma score	8.62±	2.43	8.38±	2.86	0.360
Urea (mmol/L)	4.57±	2.24	5.10±	2.21	0.161
Creatinine (mmol/L)	80.15±	28.03	93.82±	56.48	0.124
C-reactive protein (mmol/L)	1.05	(4.38)	3.30	(12.40)	0.064
Sodium (mmol/L)	137.42±	2.58	139.00±	4.90	0.064
Potassium (mmol/L)	3.98±	0.73	3.78±	0.37	0.052
Chloride (mmol/L)	100.88±	3.42	102.24±	4.29	0.089
Bicarbonate (mmol/L)	22.56±	4.98	24.20±	3.24	0.080
Heart rate (/min)	91.31±	15.40	94.57±	25.07	0.272
Systolic blood pressure (mmHg)	128.96±	22.40	110.71±	24.00	**0.001**
Diastolic blood pressure (mmHg)	78.56±	13.68	67.53±	16.90	**0.003**
Length-of-stay in ICU (days)	2.00	(3.00)	2.00	(2.00)	0.056
Length-of-stay in hospital (days)	13.00	(15.00)	3.00	(11.00)	**0.003**
Suicidal self-poisoning (N, %)	18	(69.23)	38	(69.09)	0.601
Benzodiazepines/Hypnotics (N, %)	8	(30.77)	35	(63.64)	**0.006**
Antidepressives (N, %)	1	(3.85)	13	(23.64)	**0.023**
Opioids (N, %)	7	(26.92)	11	(20.00)	0.334
Ethanol (N, %)	1	(3.85)	13	(23.64)	**0.023**
Antipsychotics (N, %)	5	(19.23)	14	(25.45)	0.375
Past psychiatric disorders (N, %)	24	(92.31)	38	(69.09)	**0.017**
Electrocardiogram abnormalities (N, %)	11	(42.31)	30	(54.55)	0.192
Vasopressors (N, %)	1	(3.85)	5	(9.09)	0.479
Antidotes (N, %)	12	(46.15)	15	(27.27)	0.077
Gastric lavage (N, %)	11	(42.31)	30	(54.55)	0.170
Activated charcoal (N, %)	12	(46.15)	27	(49.09)	0.497
Haemodialysis (N, %)	1	(3.85)	2	(3.64)	0.693
Oxygen in therapy (N, %)	18	(69.23)	40	(72.73)	0.421
Mechanical ventilation (N, %)	2	(7.69)	7	(12.73)	0.399
Transfer to the psychiatric ward (N, %)	19	(73.08)	21	(38.18)	**0.003**

Legend: SatO2: peripheral oxygen haemoglobin saturation, pCO2: partial pressure of carbon dioxide, ICU: intensive care unit. Student's -t test for independent samples or Mann-Whitney test for nonparametric data, and Fisher's exact test for qualitative data, *P* for significant differences are bolded. Data is presented as arithmetic mean± standard deviation or median (interquartile range) for continuous variables and as count (percent) for qualitative variables.

Table 4. Differences between patients treated with mechanical ventilation and patients no mechanically ventilated.

	No mechanical ventilation (N=72)		**Mechanically ventilated (N=9)**		*P*
Age (years)	42.81±	15.47	46.00±	6.80	0.272
Number of toxins in a patient	2.00	(1.00)	2.00	(1.50)	0.108
SpO2 (%)	94.59±	5.70	79.54±	14.29	**<0.001**
pCO2 (kPa)	5.55±	1.11	6.79±	2.53	**0.009**
Glasgow coma score	8.92±	2.38	4.78±	2.54	**<0.001**
Urea (mmol/L)	4.80±	2.00	5.96±	3.55	0.071
Creatinine (mmol/L)	81.03±	25.51	156.67±	113.59	**<0.001**
C-reactive protein (mmol/L)	2.50±	(7.95)	5.80	(97.80)	0.188
Sodium (mmol/L)	138.42±	4.40	139.11±	3.95	0.327
Potassium (mmol/L)	3.84±	0.51	3.82±	0.58	0.454
Chloride (mmol/L)	102.08±	3.92	99.78±	4.68	0.056
Bicarbonate (mmol/L)	24.01±	3.81	21.99±	4.23	0.081
Heart rate (/min)	91.23±	21.69	111.56±	20.04	**0.005**
Systolic blood pressure (mmHg)	119.76±	21.02	90.00±	36.89	**<0.001**
Diastolic blood pressure (mmHg)	73.41±	14.10	51.78±	23.37	**<0.001**
Length-of-stay in ICU (days)	2.00	(2.00)	10.78	(9.16)	**0.002**
Length-of-stay in hospital (days)	5.50	(13.50)	13.00	(16.50)	**0.044**
Suicidal self-poisoning (N, %)	51	(70.83)	5	(55.56)	0.282
Benzodiazepines/Hypnotics (N, %)	39	(54.17)	4	(44.44)	0.420
Antidepressives (N, %)	12	(16.67)	2	(22.22)	0.486
Opioids (N, %)	13	(18.06)	5	(55.56)	**0.023**
Ethanol (N, %)	12	(16.67)	2	(22.22)	0.486
Antipsychotics (N, %)	17	(23.61)	2	(22.22)	0.646
Past psychiatric disorders (N, %)	55	(76.39)	7	(77.78)	0.646
Electrocardiogram abnormalities (N, %)	33	(46.48)	8	(88.89)	**0.018**
Vasopressors (N, %)	1	(1.39)	5	(55.56)	**<0.001**
Antidotes (N, %)	22	(30.56)	5	(55.56)	0.131
Gastric lavage (N, %)	35	(49.30)	6	(75.00)	0.158
Activated charcoal (N, %)	35	(49.30)	4	(44.44)	0.548
Haemodialysis (N, %)	1	(1.39)	2	(22.22)	**0.031**
Transfer to psychiatric ward (N, %)	37	(51.39)	3	(33.33)	0.253

Legend: SatO2: peripheral oxygen haemoglobin saturation, pCO2: partial pressure of carbon dioxide, ICU: intensive care unit. Student's -t test for independent samples or Mann-Whitney test for nonparametric data, and Fisher's exact test for qualitative data, *P* for significant differences are bolded. Data is presented as arithmetic mean± standard deviation or median (interquartile range) for continuous variables and as count (percent) for qualitative variables.

Correlations between the Glasgow Coma Scale, main haemodynamic parameters, outcomes; and demographical/clinical parameters are demonstrated on Table 5, 6 and 7.

Table 5. Correlations between Glasgow Coma Scale (GCS) and clinical parameters.

	correlation coefficient	*P*
Age	0.043	0.352
Urea	-0.102	0.182
Creatinine	-0.330	**0.001**
C-reactive protein	-0.161 (rho)	0.076
Sodium	-0.018	0.436
Potassium	0.076	0.250
Chloride	0.210	**0.036**
Bicarbonate	0.147	0.149
Heart rate	-0.208	**0.032**
Systolic blood pressure	0.246	**0.014**
Diastolic blood pressure	0.260	**0.010**
Length-of-stay in ICU	-0.293 (rho)	**0.004**
Number of toxins	-0.056 (rho)	0.309
Length-of-stay in hospital	-0.075(rho)	0.252
SatO2	0.469	**<0.001**
pCO2	-0.326	**0.007**

Legend: SatO2: peripheral oxygen haemoglobin saturation, pCO2: partial pressure of carbon dioxide, ICU: intensive care unit. Spearman's rho or Pearson correlation coefficient), one tailed, significant correlations are bolded.

Table 6. Correlations between main haemodynamic parameters and clinical parameters and outcomes.

	Heart rate		**Systolic blood pressure**	
	Pearson Correlation coefficient	*P*	Pearson Correlation coefficient	*P*
Age	-0.064	0.288	0.096	0.198
SatO2	-0.253	**0.013**	0.331	**0.002**
pCO2	-0.056	0.340	0.221	0.051
Urea	0.079	0.243	-0.049	0.334
Creatinine	0.233	**0.019**	-0.362	**<0.001**
C-reactive protein	0.195	**0.042**	-0.256	**0.011**
Sodium	0.117	0.150	-0.022	0.425
Potassium	-0.077	0.249	-0.002	0.492
Chloride	0.018	0.439	-0.087	0.229
Bicarbonate	-0.087	0.271	-0.035	0.403
Heart rate	1.000	/	-0.125	0.136
Systolic blood pressure	-0.125	0.136	1.000	/
Diastolic blood pressure	-0.026	0.409	0.847	**<0.001**
Length-of-stay in ICU	0.270	**0.008**	-0.262	**0.009**
Length-of-stay in hospital	0.092	0.208	-0.198	**0.039**

Legend: SatO2: peripheral oxygen haemoglobin saturation, pCO2: partial pressure of carbon dioxide, ICU: intensive care unit. Pearson correlation coefficient, one tailed, significant correlations are bolded.

Table 7. Correlations between outcomes and clinical parameters.

	Length-of-stay in ICU		**Length-of-stay in hospital**	
	Correlation Coefficient	*P*	Correlation Coefficient	*P*
Age	0.337	**0.001**	0.329	**0.001**
Number of toxins in a patient	-0.093	0.205	-0.265	**0.008**
SatO2	-0.222	**0.025**	-0.015	0.449
pCO2	-0.187	0.081	-0.240	**0.036**
Urea	0.181	0.053	0.148	0.094
Creatinine	0.063	0.287	0.018	0.437
C-reactive protein	0.012	0.459	-0.200	**0.036**
Sodium	0.073	0.260	-0.055	0.314
Potassium	0.034	0.381	0.044	0.348
Chloride	-0.088	0.226	-0.101	0.194
Bicarbonate	-0.146	0.150	-0.198	0.080
Heart rate	0.153	0.087	0.047	0.338
Systolic blood pressure	-0.073	0.261	0.012	0.457
Diastolic blood pressure	-0.009	0.468	0.073	0.259
Length-of-stay in ICU	/	/	0.672	**<0.001**
Length-of-stay in hospital	0.672	**<0.001**	/	/

Legend: SatO2: peripheral oxygen haemoglobin saturation, pCO2: partial pressure of carbon dioxide, ICU: intensive care unit. Spearman's rho, one tailed, significant correlations are bolded.

A linear correlation plot between SatO2 and GCS is demonstrated on Figure 6. Linear correlation plots between systolic blood pressure and SatO2 and creatinin are demonstrated on Figures 7, and 8.

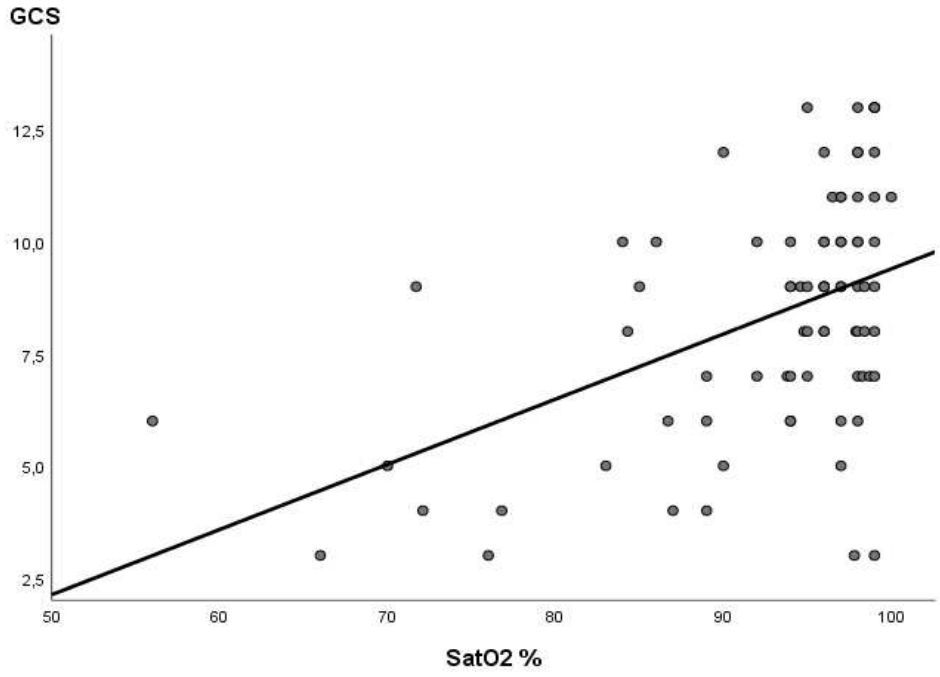

Figure 6. Linear correlation plot between Sat O2 and GCS (r=0.469; *P* <0.001).

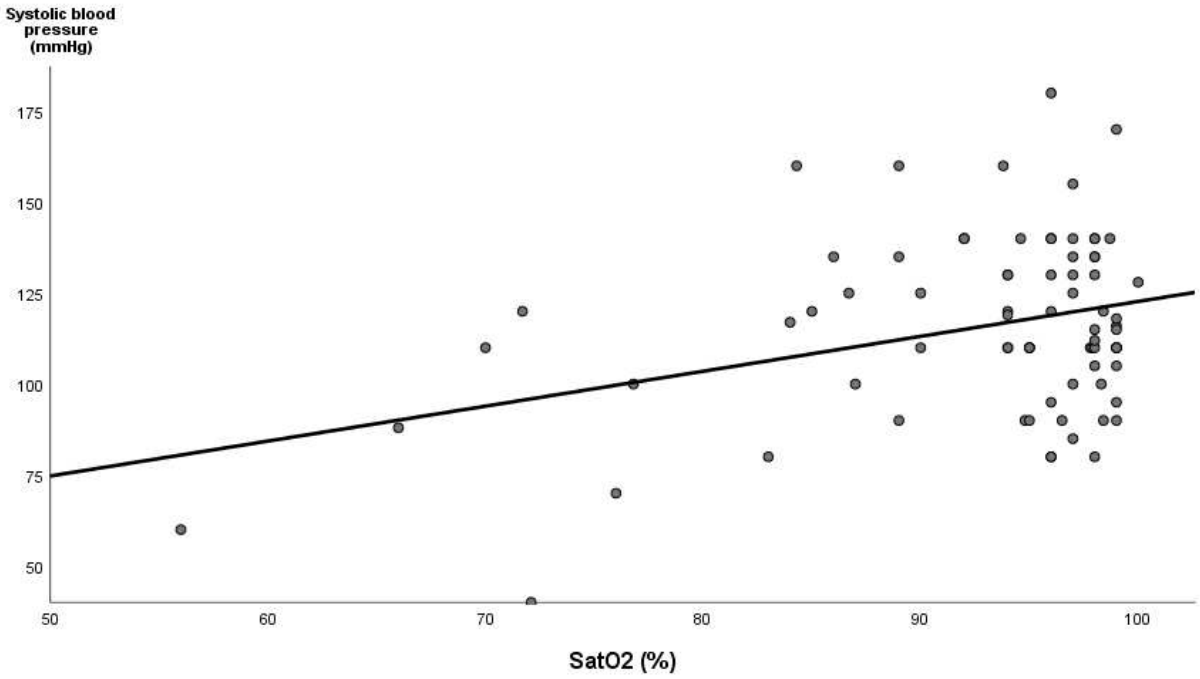

Figure 7. Linear correlation plot between Sat O2 and systolic blood pressure (r=0.332; *P*=0.002).

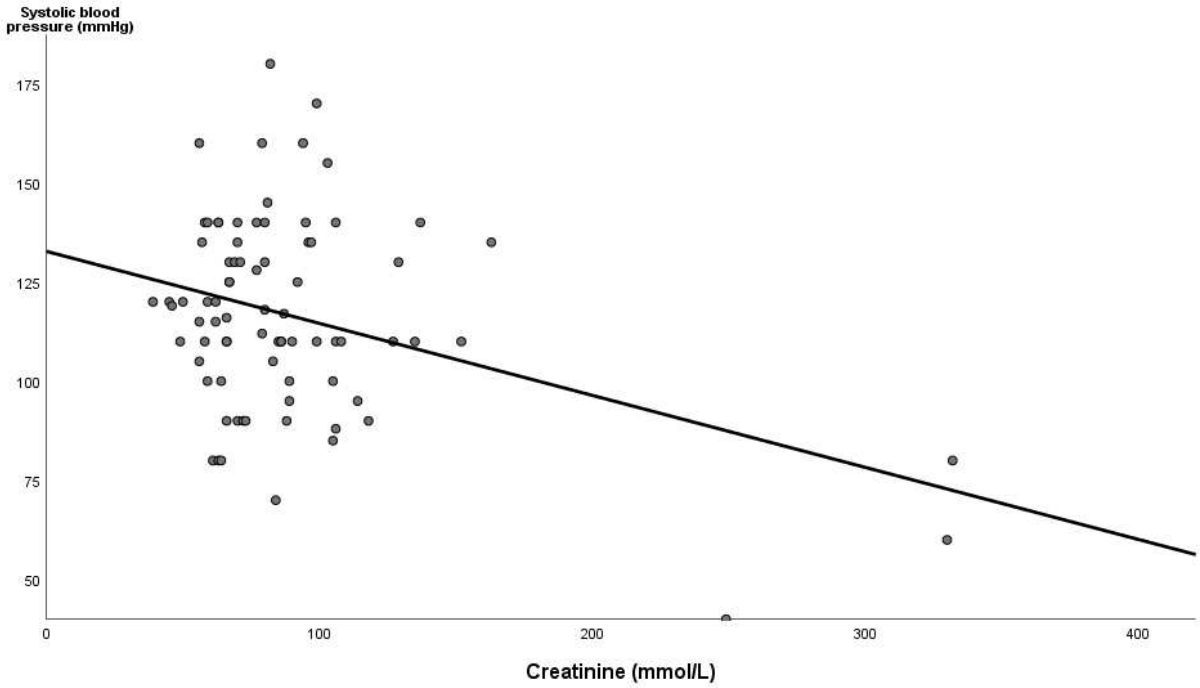

Figure 8. Linear correlation plot between Sat O2 and serum creatinine (r=-0.362; *P* <0.001).

Length-of-stay in hospital was significantly correlated with toxins number (Spearman's rho=-0.265; *P*=0.008), but length-of-stay in ICU was not correlated with toxins number (rho=-0.093; *P* =0.205). The age was positively correlated with length-of-stay in hospital (r=0.249; *P*=0.012). Numbers of toxins at a patient was significantly correlated with C-reactive protein (rho=0.219; *P*=0.025), systolic blood pressure (rho=-0.318; *P*=0.002) and diastolic blood pressure (rho=-0.262; p=0.009). C-reactive protein was significantly correlated with age (rho=0.277; *P*=0.006), SatO2 (rho=-0.410; *P* <0.001) and pCO2 (rho=0.230; *P*=0.042). Differences between groups poisoned with one toxin, two toxins and poisoned with more than two toxins are shown on Table 8.

Table 8. Differences between groups poisoned with one toxin, two toxins and poisoned with more than two toxins.

	one toxin (N=26)	two toxins (N=38)	more than 2 toxins (N=17)		
	Mean± Std. Deviation	Mean± Std. Deviation	Mean± Std. Deviation	F or Chi-Square*	*P*
Age (years)	47.27± 17.12	39.97± 14.07	44.00± 11.03	1.966	0.147
SpO2 (%)	93.97± 6.54	93.19± 9.58	90.56± 8.78	0.836	0.437
pCO2 (kPa)	5.86± 1.85	5.83± 1.30	5.37± 1.20	0.449	0.640
Glasgow coma score	8.62± 2.43	8.66± 2.81	7.76± 2.95	0.695	0.502
Urea (mmol/L)	4.57± 2.24	4.89± 1.78	5.56± 2.97	1.033	0.361
Creatinine (mmol/L)	80.15± 28.03	88.05± 45.22	106.71± 76.03	1.533	0.222
C-reactive protein (mmol/L)	11.32± 22.72	9.52± 23.86	18.41± 31.64	4.113*	0.128
Sodium (mmol/L)	137.42± 2.58	138.53± 3.29	140.06± 7.36	1.943	0.150
Potassium (mmol/L)	3.98± 0.73	3.76± 0.39	3.81± 0.31	1.403	0.252
Chloride (mmol/L)	100.88± 3.42	102.06± 4.37	102.63± 4.22	1.026	0.364
Bicarbonate (mmol/L)	22.56± 4.98	24.62± 2.55	23.27± 4.40	1.472	0.240
Heart rate (/min)	91.31± 15.40	93.00± 26.46	98.00± 22.10	0.473	0.625
Systolic blood pressure (mmHg)	128.96+ 22.40	113.00± 22.76	105.59± 26.57	5.770	**0.005**
Diastolic blood pressure (mmHg)	78.56± 13.68	68.11± 15.46	66.24± 20.23	4.131	**0.020**
Length-of-stay in ICU (days)	3.42± 3.76	2.47± 3.25	4.29± 6.34	3.798*	0.150
Length-of-stay in hospital (days)	13.23± 9.25	9.63± 14.70	8.35± 10.68	7.550*	**0.023**

Legend: SatO2: peripheral oxygen haemoglobin saturation, pCO2: partial pressure of carbon dioxide, ICU: intensive care unit. One-way ANOVA or Kruskal-Wallis test for nonparametric data), *P* for significant differences are bolded.

5 DISSCUSION

This 1-year observational study offers in-depth insight into the demographic and clinical characteristics of acute intoxications admitted to a medical ICU in the Split-Dalmatia region of Croatia. Data on the demographics, types, and clinical aspects of acute intoxications are highly relevant because our hospital covers a region with around 1,5 million residents (and an extra 500,000 tourists during the summer). Information on acute intoxications in adults in this area is completely lacking as of now.

The analysis showed that 14.97% of all annual ICU admissions in our local medical ICU and toxicology centre were due to acute intoxications. The percentage of patients admitted to critical care as a result of acute poisoning varies significantly by geographic location; for instance, it was 2.3% in a German ICU-based study, or 8.9% in a Turkish study by Yaylaci et al. (75, 76). An analysis of all ICU hospitalizations over a 6-month period in New York City, USA, found that acute intoxications accounted for 19% of all admissions (77).

The most frequent poisoning agents, as determined by our findings, were diazepam, ethanol, and alprazolam. Additionally, 28.7% of all cases of acute intoxications involved the benzodiazepine/hypnotic drug class, which is similar with other studies from France and Belgium, where benzodiazepines were the most frequently used drug class in cases of self-poisoning (78, 79). Analgesics and antidepressants, however, made up the vast majority of acute poisonings involving suicide in the USA and the UK (80, 81). Opioids are a significant and frequent cause of acute poisoning in New York City, USA, according to Hamilton et al. (82). Antipsychotics, opioids, antidepressants, and ethanol were the most significant categories of medications in our investigation after benzodiazepines. Serotonin reuptake inhibitors came in second place behind benzodiazepines in a French study by Beaune et al. that was done in the Paris metropolitan region on patients who had self-injured themselves and were admitted to a university hospital. Antipsychotic medications came in fourth place (83).

In a research published in Dutch, Bosch et al. found that acute intoxication with antidepressants accounted for 33.3% of all acute intoxication admissions to the ICU, 2.4% of all ICU admissions, and 2.7% of the overall intoxication group mortality (84). A one-year observational study in an emergency outpatient clinic in Oslo, Norway, found that ethanol (58%) was the most common toxin, followed by heroin (19%), benzodiazepines (18%), amphetamine (9%) and other substances, with 31% of poisonings including more than one toxin (85). An ICU-based retrospective study from urban India reported a similar pattern of acute intoxication: benzodiazepines were the first agents (29.7%), followed by alcohol (24.63%) and opioids (7.2%) (86). Organic solvents were the first class of toxic agents in a study that investigated acute poisoning admissions in Malaysia (20.2%), followed by pesticides (16.4%)

(87). Similar to this, agrochemicals, including aluminium phosphide and organophosphates, were responsible for 77.1% of instances of acute poisoning in an ICU-based investigation carried out in Tirana, Albania (88). From these studies, the pattern of intoxications can be discerned: in developing countries, the most common form of acute intoxication is poisoning with agrochemicals, while in developed countries, acute intoxications mainly occur with psychoactive substances, including alcohol and opiates. In an ICU-based study from New York City, the United States, Orsini et al. discovered that 35% of patients had ethanol in their serum, as well as opiates (18.33%), cocaine (13.24%), methadone (12.22%), benzodiazepines (10.18%), and marijuana (9.16%) in their urine toxicology screens (77).

The majority of the subjects in our study were male; acute intoxications in males were more severe (longer length of stay in ICU and significantly disordered blood gas analysis), despite the fact that females had a longer total hospital length of stay due to significantly more frequently transferring to the psychiatric ward. Although females were poisoned more frequently with the class of benzodiazepines/hypnotics, intoxications with ethanol and opiates were more common in males. Our study's most important finding was evidence that the most common poisons were pharmaceutical psychoactive drugs. The average GCS consciousness level was 8.46±2.72 points. We presume that the high proportion of psychoactive substance intoxications in our cohort was caused by the high number of mentally ill patients among our subjects (76.5%), as well as the fact that 69.1% of all cases were deemed to be suicidal. For example, 94.1% of acutely intoxicated patients admitted to an ICU in Turkey, according to a similar ICU-based study, were suicidal (76).

In our study, participants with psychiatric disorders had a significantly higher in-hospital length of stay, probably because a significant percent of these subjects were transferred to the psychiatric department as a continuation of hospital care. We believe that the easy accessibility of these medicines and their abuse were caused by the widespread use of benzodiazepines and other sedatives, as well as the liberal use of antipsychotics and antidepressants. It is common knowledge that people with mental disorders receive significantly more prescription medications than the general population (89). Given that people with mental illness may attempt suicide by ingesting their own medications, such prescriptions for drugs significantly increase the risk of multidrug exposure (90). In contrast, in our study, we were not able to establish a connection between previous psychiatric illness or suicidal intent and multidrug exposure in acutely intoxicated patients. Moreover, among the patients who were poisoned with only one agent, there were more subjects with a previous psychiatric disorder.

Our research also revealed that a significant portion of the cases (67.9%) involved multiple drug exposures. We demonstrated that multiple drug exposure was correlated with arterial hypotension at admission time. Our findings are consistent with the growing worry about multidrug poisoning (91). Beaune et al. showed a similar result of 53% poisonings resulting from multiple drug exposures, and this result was explained by the high percentage of patients who self-poisoned and had prior psychiatric illnesses, which is similar to our study (83). According to our data, an antidote was administered in 33.33% of instances, most frequently flumazenil and then naloxone. Activated charcoal was used in 48.15% of the instances. We believed that the appropriate administration of antidotes and activated charcoal in the ED and ICU could lower the morbidity and mortality linked to severe poisonings (92). According to a Belgian study by Hendrix et al., activated charcoal was administered in 70% of the cases (79).

In our report, 11.11% of the patients required mechanical ventilation and an intubation. A ventilated group of participants had significantly worse arterial gas analysis and level of consciousness, with more prevalent tachycardia, arterial hypotension, and the need for dialysis and vasopressors. Consecutively, in-hospital and ICU length of stay were significantly increased in the ventilated group of participants. Intoxication with opioids was more prevalent in the ventilated group compared to the non-ventilated group.

According to Mehrpour et al., 41.2% of highly intoxicated patients admitted to an ICU in a rural hospital in Iran required intubation (93). On the other hand, studies in Turkey and Greece revealed 2,7% and 4,5% of the patients intubated due to respiratory failure in acute poisoning, respectively, which is in line with our findings (94, 95). In a Turkish cohort of acutely intoxicated patients admitted to the ICU, Yaylaci et al. reported no fatality and just 3,3% mechanical ventilation due to respiratory failure (76). These variations in the proportion of patients receiving mechanical ventilation could be attributed to regional variations in exposure types and in ICU admission procedures. The bar for ICU admission is substantially lower in rich countries than it is in less developed ones. Even if they present with mild symptoms at admission, some institutions regularly admit all acutely intoxicated patients to the ICU (96). Antipsychotic poisoning, for instance, may cause delayed cardiovascular events, which would necessitate ICU admission even if vital functions were originally normal (97).

In our study, mechanical ventilation was correlated with hypoxia and hypercarbia, a lower degree of consciousness, tachycardia, and lower blood pressure at presentation. The need for mechanical ventilation was associated with the need for vasopressors and renal replacement therapy. In the group of patients who were treated with mechanical ventilation, intoxication

with opiates was significantly more common. The level of consciousness at admission time was lower in the group needing mechanical ventilation. Both hospital and ICU lengths of stay were prolonged in mechanically ventilated patients (83).

In our study, we reported a 3.7% death rate. Previous research in a medical ICU in a Croatian metropolis found a 2.6% fatality incidence in a group of 149 patients (4.6% of all ICU admissions), which had the diagnosis of self-poisoning (98). Similar ICU-based studies in Germany and Hong Kong found that intoxicated patients admitted to the ICU had fatality rates of 0.7% and 3%, respectively (6, 99). According to a Norwegian study, there are 3% fatal acute poisonings and a 1.1% in-hospital mortality rate (100). But in an ICU-based study carried out in eastern Iran, the mortality rate was 19.5% (93). Opioids and pesticides were the most frequently exposed substances in this study, and once again, local variances in toxin type and ICU admission requirements may account for such wide variations in fatality rates among nations.

The presented study has some limitations, mostly due to its retrospective design and data from a single centre, despite the centre is main toxicology referral institution in the region. Additionally, poisons and agents reported in the study were partly or not systematically confirmed by toxicological analysis.

6 CONCLUSION

This work describes the acute poisoning trends observed in Croatia's Adriatic region. Pharmaceuticals used in psychiatry made up the majority of the agents. The typical pattern of acute intoxication involved multiple drug exposure. The low death rate and low proportion of patients on mechanical ventilation highlight the significance of patient care in both outpatient and hospital emergency departments and the importance of early application of activated charcoal, gastric lavage, and antidotes. We believe that the widespread availability of legally prescribed psychoactive drugs has a major impact on drug addiction and the types of acute poisonings that occur. Therefore, it is necessary to introduce measures to limit access to the psychoactive drugs. Intoxication with opioids, initial poor gas findings in arterial blood, tachycardia, arterial hypotension, and a decreased level of consciousness are predictors of the need for mechanical ventilation. Multiple drug exposure was correlated with arterial hypotension at admission time.

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8 SUMMARY

Objectives: The objective of study was to assess the demographics, clinical parameters and outcome of acute intoxications among adult patients admitted in medical ICU (intensive care unit) in southern Croatia.

Subjects and Methods: An observational retrospective study was conducted during one-year period. Subjects were patients admitted to the ICU due to acute poisoning.

Results: 81 subjects (32.1% females) aged 43.16±14.77 years were admitted in ICU due poisoning (14.97% of total annual ICU admissions). Psychiatric disorders were previously established in 76.5%, and 69.1% of all acute intoxications were classified as suicidal. Non-suicidal subjects differed from suicidal subjects in age (37.36±9.71 vs. 45.75±15.93 years; *P*=0.009), in pCO2 (6.38±1.78 vs. 5.50±1.26 kPa; *P*=0.020), in length-of-stay in ICU (median 1.00, interquartile range 1.00 vs. median 2.00, interquartile range 2.00 days; *P* = 0.022) and in length-of-stay in hospital (median 2.00, interquartile range 2.00 vs. median 10.50, interquartile range 15.25 days; *P* =<0.001). Three (3.7%) patients died. Pharmaceutical psychoactive drug intoxication was the most common cause of acute intoxication, of these, diazepam was the most frequent (16.8%), followed by ethanol (9.0%) and alprazolam (7.8%). Benzodiazepines/hypnotics class was the most common group (28.7%), followed by antipsychotics (13.2%). The largest number of cases were intoxications with more than one poison (67.9%). Toxins number was significantly negatively correlated with length-of-stay in hospital (rho=-0.265; *P* =0.008), systolic blood pressure (rho=-0.318; *P* =0.002) and diastolic blood pressure (rho=-0.262; *P* =0.009). Electrocardiogram was considered abnormal in 50.62%.

Conclusion: The most common agents of acute intoxications were psychiatric pharmaceutical drugs. Multidrug exposure was a typical pattern of acute intoxication and was correlated with arterial hypotension at admission time.

9 CROATIAN SUMMARY

Naslov rada: Kliničke i demografske osobitosti akutno otrovanih odraslih bolesnika u internističkoj intenzivnoj jedinici.

Cilj istraživanja: Cilj ovog istraživanja bio je procijeniti demografske i kliničke osobitosti, te ishode akutnih intoksikacija kod odraslih bolesnika primljenih u internistički JIL (jedinicu intenzivnog liječenja) u južnoj Hrvatskoj.

Ispitanici i metode: Opservacijska retrospektivna studija provedena je tijekom jednogodišnjeg razdoblja. Ispitanici su bili odrasli bolesnici primljeni u internističku jedinicu intenzivnog liječenja zbog akutnog trovanja.

Rezultati: 81 ispitanik (32.1% žena) u dobi od 43.16±14.77 godina primljen je u JIL zbog trovanja (14.97% od svih godišnjih prijema u JIL). Psihijatrijski poremećaji prethodno su utvrđeni u 76.5% ispitanika, a 69.1% svih akutnih intoksikacija klasificirano je kao suicidalno. Nesuicidalni ispitanici razlikovali su se od suicidalnih po dobi (37.36±9.71 naspram 45.75±15.93 godina; p=0.009), po pCO2 (6.38±1.78 naspram 5.50±1.26 kPa; *P*=0.020), po duljini boravka u JIL (medijan 1.00, interkvartilni raspon 1.00 naspram medijan 2.00, interkvartilni raspon 2.00 dana; *P* = 0.022) i u duljini boravaka u bolnici (medijan 2.00, interkvartilni raspon 2.00 vs. medijan 10.50, interkvartilni raspon 15.25 dana; *P* =<0.001). Tri (3.7%) bolesnika su umrla. Trovanje psihoaktivnim lijekovima je najčešći uzrok akutne intoksikacije, od čega je najčešći bio diazepam (16.8%), zatim etanol (9.0%) i alprazolam (7.8%). Najčešća skupina bili su benzodiazepini/hipnotici (28.7%), a zatim antipsihotici (13.2%). Najveći broj slučajeva bile su intoksikacije s više od jednog otrova (67.9%). Broj toksina značajno je negativno korelirao s duljinom boravka u bolnici (rho=-0.265; *P* =0.008), sistoličkim krvnim tlakom (rho=-0.318; *P* =0.002) i dijastoličkim krvnim tlakom (rho=-0.262; *P* =0.009). Elektrokardiogram se smatra abnormalnim u 50.62%.

Zaključci: Najčešći uzročnici akutnih intoksikacija bili su psihijatrijski lijekovi. Trovanje sa više tvari bilo je tipičan obrazac akutne intoksikacije te je bilo udruženo sa arterijskom hipotenzijom u trenutku prijema.