

Original Article

Acute Respiratory Distress Syndrome in Drug and Chemical Poisoning: A Cross-sectional Study



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Article info:

Received: 17 May 2025

Accepted: 21 Jun 2025

Keywords:

Acute respiratory distress syndrome (ARDS), Drug poisoning, Chemical poisoning

ABSTRACT

Background: Poisonings are a major medical emergency, contributing to 15-20% of hospital visits. Acute respiratory distress syndrome (ARDS), defined by acute hypoxemia and non-cardiogenic pulmonary edema, presents significant challenges in diagnosis and management.

Objectives: This study investigates the incidence of ARDS in patients with drug and chemical poisoning hospitalized at Shah Vali Hospital in Yazd City, and Shahid Beheshti Hospital in Taft City, Iran from 2014 to 2023.

Methods: We conducted a descriptive cross-sectional study involving patients with drug and chemical poisoning presenting to the emergency departments of the two hospitals. After obtaining ethical approval, we reviewed medical records of eligible patients. Data were analyzed using SPSS software, version 25, presenting qualitative data as frequencies and percentages, and quantitative data as Mean±SD. The chi-square test assessed statistical significance, with P<0.05 deemed significant.

Results: Our analysis included 61 patients, comprising 77% men and 23% women, with a mean age of 46.1 years and an average hospitalization duration of 9.7 days. The primary cause of poisoning was suicide, accounting for 49.2% of cases, predominantly through oral ingestion (96.7%). Methadone was identified as the most common poisoning agent. Notably, 68.9% of patients had a history of addiction, and 27.9% required dialysis, while sepsis was present in 31.1% of cases. Among patients with ARDS, 21.3% had pre-existing pulmonary conditions. Elevated urea and creatinine levels were observed in 85.2% of cases, and metabolic acidosis was noted in all patients. Seizures occurred in 32.8% of individuals, with an overall mortality rate of 59%. Although no significant differences in mortality were

Citation Ghorbani S, Owliaey H, Aghazadeh-Habashi K, Razavi F, Rostami N, Rafatmagham S, et al. Acute Respiratory Distress Syndrome in Drug and Chemical Poisoning: A Cross-sectional Study. *Pharmaceutical and Biomedical Research*. 2025; 11(4):339-346. <http://dx.doi.org/10.32598/PBR.11.4.1366.2>

doi <http://dx.doi.org/10.32598/PBR.11.4.1366.2>

associated with addiction history ($P=0.310$), a strong correlation was found with the type of poisoning agents ($P<0.001$).

Conclusion: The study found 59% mortality rate among ARDS patients due to drug and chemical poisoning, emphasizing the need for effective management strategies. A significant proportion of cases were involved with addiction, primarily to methadone, yet no mortality correlation with addiction was observed. The findings underscore the complexities of treating ARDS in the context of poisoning, necessitating a diverse approach to improve patient outcomes.

Introduction

In Iran, poisoning is a significant public health concern, resulting in approximately 5600 fatalities every year. Notably, over half of these deaths are attributed to substance abuse and the consumption of stimulants. Other major causes of poisoning include exposure to pesticides, rodenticides, rice tablets (aluminum phosphide), alcohol, cyanide, lead, drug overdoses, and carbon monoxide [1, 2].

Drug-related poisonings constitute about 46% of hospital admissions for poisoning. The predominant substances involved are those that impact the central nervous system (CNS), particularly benzodiazepines, which account for approximately 30-50% of cases. Antidepressants and antipsychotics also contribute significantly, while non-opioid analgesics represent around 20% of drug-related poisonings. Among opioid-related cases, tramadol and methadone are the leading culprits, responsible for 65-70% of cases, followed by opium (20%) and crystal meth (6%), with other substances such as hashish, heroin, and morphine making up the remainder [2, 3].

Drug poisonings can manifest in various symptoms, one of the most severe one is acute respiratory distress syndrome (ARDS) [4-6]. First characterized in 1967 through clinical observations in critically-ill patients, ARDS is defined by acute hypoxemia, decreased lung compliance, and heightened respiratory effort [7]. The condition involves significant inflammatory insult to the alveolar-capillary membrane, resulting in increased permeability and diminished oxygenation [8].

ARDS can be categorized into two types. Pulmonary ARDS results from direct injury to the lung epithelium, but extrapulmonary ARDS occurs due to indirect injury to the vascular endothelium from an acute systemic inflammatory response. Pneumonia is the most common cause of pulmonary ARDS, while sepsis leads in cases

of extrapulmonary ARDS [9, 10]. Other less frequent causes include acute pancreatitis, transfusion-related acute lung injury, near-drowning incidents with aspiration of freshwater or saltwater, hemorrhagic shock or reperfusion injury, smoke inhalation, and drug-induced lung injury [11].

Two primary mechanisms contribute to drug-induced lung injury: Pump failure due to suppression of CNS or weakened respiratory muscle function and lung injury resulting from vascular, airway, or parenchymal damage. These mechanisms can interact; for instance, CNS depression may lead to aspiration or aspiration pneumonia, which can further result in respiratory muscle fatigue and hypoventilation. Additionally, substance abuse can impair the function of other organ systems, exacerbating respiratory failure [12]. The clinical presentation varies based on the substance involved, the duration of exposure (acute or chronic), any concomitant medications taken by the patient, and whether substances were used in isolation or in combination [13, 14]. Symptoms such as vomiting, sedation, obstruction, coma, or seizures heighten the risk of aspiration of oral or gastric contents, potentially leading to extensive chemical pneumonitis and subsequent ARDS [12].

Despite notable advances in intensive care management over recent years, ARDS is still associated with high mortality rates, with studies indicating a mortality rate as high as 40%. Current primary treatment strategies include fiberoptic bronchoscopy and mechanical ventilation support [15]. In cases of severe and refractory ARDS where conventional mechanical ventilation proves inadequate, extracorporeal membrane oxygenation is considered an alternative therapeutic option [16].

While many individuals with ARDS may experience improvements in lung function within a few months to two years, some patients face persistent respiratory challenges that can last a lifetime [17].

Given the importance of ARDS and the limited studies regarding its association with poisoning, this study aims to investigate the prevalence of ARDS and factors affecting its prognosis, in patients with drug and chemical poisoning referred to [Shah Vali Hospital](#) in Yazd City and [Shahid Beheshti Hospital](#) in Taft City, in Iran from 2014 to 2023.

Materials and Methods

Study design

This is a cross-sectional descriptive study aimed at investigating the prevalence of ARDS in patients with drug and chemical poisoning who presented to the emergency departments of [Shah Vali Hospital](#) in Yazd and [Shahid Beheshti Hospital](#) in Taft from 2014 to 2023.

Inclusion and exclusion criteria

The inclusion criteria for the study encompassed all patients presenting to the Emergency Department with a diagnosis of drug or chemical poisoning who subsequently developed ARDS during their hospital stay. The diagnosis of ARDS in these patients was confirmed by a specialist internal medicine physician with a subspecialty in pulmonology based on clinical symptoms, arterial blood gas analysis, chest X-ray, and chest CT scan. Patients were excluded from the study if their medical records were incomplete, if they could not be accessed to complete the information, or if ARDS developed due to reasons unrelated to drug or chemical poisoning.

Data collection

In compliance with the Helsinki Declaration and maintaining confidentiality, the study was approved by the University's Ethics Committee. Medical records of individuals diagnosed with poisoning during the specified time frame were reviewed in the medical records department to identify those meeting the inclusion criteria. The required research data included demographic information (age, gender, marital status, education level, field of study), type of drug poisoning, amount of drug consumed, presence of substance abuse or misuse, dialysis, sepsis, seizures, history of pulmonary disease, and laboratory test results extracted from the patients' medical files.

Data analysis

Data were entered into SPSS software, version 26. The frequency distribution of qualitative data was presented

as counts and percentages, while quantitative data were shown as Mean±SD. The chi-square test was utilized for statistical analysis. A $P < 0.05$ was considered statistically significant.

Results

The present study examined 61 patients with ARDS resulting from drug and chemical poisoning, who were referred to [Shah Vali](#) and [Shahid Beheshti](#) hospitals between 2014 and 2023. The average age of the patients was 46.14 years, with a range from 9 to 85 years. The average length of hospital stay was 9.65 days, varying from a minimum of 5 days to a maximum of 28 days.

Demographics and background

Among the patients, 48 were married (78.7%) and 13 were single (21.3%). In terms of educational background, 51 patients (83.7%) had an education level below high school, 8 patients (13.1%) had a high school diploma, 1 patient (1.6%) held an associate degree, and another patient (1.6%) had a bachelor's degree or higher. The gender distribution included 47 males and 14 females.

Mortality and toxic substances

Of the 61 patients, 36(59%) died, while 25(41%) survived. Methadone was the most commonly associated toxic substance, accounting for 68.9% of cases, followed by organophosphate compounds (6.6%) and opium (4.9%). Overall, opioids, particularly methadone, were the most frequently involved substances in poisoning, followed by chemical compounds (11.5%) and other pharmaceuticals (9.8%). [Table 1](#) provides comprehensive details about the toxic substances.

Addiction and substance use

Regarding the motivations for substance use, 30 individuals (49.2%) reported suicide as their primary reason, while 29(47.5%) cited misuse, and 2(3.3%) indicated accidental use. The predominant method of substance consumption was oral, with 59 patients (96.7%) using this method, while only 2(3.3%) reported injectable use. A total of 42 patients (68.9%) had a history of substance abuse, highlighting a considerable prevalence of addiction among those with ARDS. Furthermore, there was a significant difference in the frequency distribution of addiction history based on types of poisoning ($P < 0.001$), with 81.2% of individuals with a history of addiction reporting opioid use. Notably, among the 39 individuals

Table 1. Distribution of poisoning agents among ARDS patients

Type of Poisoning Agent	No. (%)
Methadone	42(68.9)
Heroin	2(3.3)
Organophosphates	4(6.6)
Crystal meth	1(1.6)
Opium	3(4.9)
Colchicine	1(1.6)
Tricyclic antidepressants	2(3.3)
Tramadol	1(1.6)
Propranolol	1(1.6)
Gasoline	1(1.6)
Citalopram	1(1.6)
Rice tablets	2(3.3)
Total	61(100)

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addicted to opioids, 34 were methadone users. However, there was no significant difference in the relative frequency of mortality based on addiction history ($P=0.31$).

Respiratory history, sepsis, and seizures

In terms of respiratory disease history, 48 patients (78.7%) reported no prior conditions. Among the remaining patients, 1 patient (1.6%) had asthma, and 12 had chronic obstructive pulmonary disease (COPD) (19.7%). Sepsis was present in 19 patients (31.1%). Additionally, seizures were noted in 20 patients (32.8%) of those with ARDS, while 41(67.2%) did not experience seizures. No significant differences were found in the frequency distribution of seizures based on gender ($P=0.302$), mortality ($P=0.317$), patient age ($P=0.080$), or types of poisoning agents ($P=0.63$).

Laboratory findings

Laboratory results indicated elevated blood urea and creatinine levels in 52 patients (85.2%). Among the ARDS patients, 44 individuals (72.1%) did not require dialysis, while 17(27.9%) did. There was no significant difference in the distribution of dialysis frequency based on types of poisoning agents ($P=0.270$), gender ($P=0.197$), age ($P=0.270$), or mortality ($P=0.98$), indicating no significant relationship between dialysis needs and both the

types of poisoning and demographic factors. Moreover, ABG analysis (demonstrated in Table 2) revealed a complete prevalence of low pH and increased pCO_2 among ARDS patients, with abnormal bicarbonate levels (either elevated or reduced) observed in 67.2% of patients.

Discussion

This study aimed to determine the prevalence of ARDS in patients with drug and chemical poisoning referred to Shah Vali and Shahid Beheshti hospitals in Yazd and Taft cities from 2014 to 2023. Over this 10-year period, 10000 patients with drug and chemical poisoning were treated, with 61 diagnosed with ARDS, indicating a prevalence of approximately 0.61%. The average age of these patients was 46.14 years, and the average length of stay was 9.65 days, ranging from 5 to 28 days.

Types of poisoning and substance abuse

Methadone overdose emerged as the most prevalent type of poisoning among ARDS patients. Previous studies on opioid-related poisoning have rarely reported acute lung injury or ARDS, which aligns with our findings [5, 18]. Although the pathophysiology of ARDS following opioid overdose remains unclear, probable mechanisms include direct drug toxicity, hypoxia, acidosis, and increased pulmonary capillary permeability [19].

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Table 2. Arterial blood gas parameters in ARDS patients

Parameter	Level	No. (%)
pH	Decreased	61(100)
Bicarbonate level	Normal	20(32.8)
-	Increased	3(4.9)
-	Decreased	38(62.3)
Total	-	61(100)
PCO ₂ Level	Increased	61(100)

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The distribution of addiction history revealed that 16.8% of ARDS patients had a substance abuse history. No significant correlation was found between addiction prevalence and mortality rates; however, a marked variation was observed based on the type of poisoning, with methadone being the most common substance. This trend is consistent with findings by Zarei et al. [20] and Ehsaei et al. [21]. Also, the high prevalence of methadone in Iran may be due to the availability of opioid addiction clinics offering it as maintenance therapy [22].

Comparison with other studies

Our study's low prevalence of ARDS among drug-poisoned patients is similar to a Japanese study from 2004 to 2011, which identified only 27 ARDS cases attributed to drug use out of 197 total cases [23]. We also found no significant correlation between poisoning agent type and patients' age or gender, aligning with the findings of Ghaffourian et al. [24]. This finding contrasts with research by Ala et al. [25] in northern Iran, which linked demographic factors to poisoning agents. The difference may be due to sample size, as Ala's study involved 200 patients compared to our 61 ARDS cases. Notably, while their study identified alcohol as the primary agent, our study highlighted methadone as most significant.

Mortality rates and risk factors

The mortality rate among poisoned ARDS patients in our study was 59%, which is consistent with Bhadade et al.'s report of 57% and Summers et al.'s finding of 75.3% in ARDS patients [26, 27]. Although none attributed ARDS specifically to drug use. We also found no correlation between the type of poisoning agent and mortality, reinforcing the notion that other factors may play a role in outcomes.

Risk factors for mortality in ARDS patients include multi-organ dysfunction, pre-existing pulmonary and non-pulmonary diseases, and metabolic acidosis. Our findings revealed elevated blood urea and creatinine levels in 85% of patients, suggesting renal failure is common in ARDS cases. Research by Panitchote et al. [28] indicates that factors such as age, illness severity, diabetes, and acidosis contribute to acute kidney injury (AKI) in ARDS patients. Pilarczyk et al. [29] reported a 70% prevalence of AKI linked to higher mortality rates, and a meta-analysis of COVID-19 patients with ARDS demonstrated a greater incidence of AKI compared to those without ARDS [30].

Renal failure and dialysis requirements

Furthermore, 28% of our patients required dialysis, highlighting the prevalence of severe renal failure within this group. Alenezi et al. [30] reported a 20% dialysis requirement among COVID-19 patients with ARDS, compared to just 1% in those without ARDS, illustrating a significant disparity. Mechanical ventilation may worsen AKI in ARDS patients, with studies indicating a threefold increase in risk associated with both conditions [31]. Elevated peak airway pressures have also been linked to more severe AKI [28]. However, our study did not find statistically significant differences in dialysis requirements based on age, gender, mortality, or poisoning type. The relatively young age of our patients and the impact of other organ-specific effects from poisoning may account for these findings.

Sepsis and underlying conditions

Our study revealed that 31.14% of patients had sepsis. According to Peek et al. [32], the incidence of sepsis resulting from ARDS in Western countries is approximately 6-7%. A study in Kurdistan reported a 6.18% incidence of ARDS due to sepsis. Targeted initial treat-

ment for severe sepsis or septic shock has been shown to reduce the need for mechanical ventilation, emphasizing the importance of managing underlying sepsis and identifying patients at risk for developing ARDS [33]. The discrepancies in sepsis-related ARDS incidence across studies may stem from variations in demographic factors, chronic disease histories, and other underlying causes. Notably, our research indicates that 19.7% of ARDS patients had a history of chronic COPD, while only 1.6% had asthma. This supports findings by Li et al [34], who identified COPD as a significant risk factor for ARDS in septic patients.

Acid-Base Imbalances

Blood gas analysis in our study showed that 62.3% of ARDS patients had low bicarbonate (HCO_3) levels, alongside elevated carbon dioxide (CO_2) and decreased pH. These results are consistent with findings of Yang et al. [35] and Bass et al. [36], who reported increased CO_2 in ARDS patients, and Edriss et al. [37], who documented metabolic and respiratory acidosis in cases of citalopram toxicity. Metabolic acidosis can result from the direct metabolism of toxic agents and the role of the lungs in lactate production in ARDS. Dai et al. [38] identified elevated lactate levels as indicative of metabolic acidosis. Overall, these findings underscore the frequent occurrence of acid-base imbalances in ARDS, particularly metabolic acidosis, which can lead to decreased cardiac output, hypotension, and arrhythmias, thereby increasing mortality risk [39].

Seizures in ARDS patients

In our study, 33.8% of ARDS patients experienced seizures, but no correlation was found between seizures and the cause of poisoning. Behnoush et al. [40] identified tramadol (31.5%) and antidepressants (14.7%) as common seizure triggers, while Aghili and Oliai [41] reported tramadol as the leading cause (74.15%), followed by benzodiazepine withdrawal and organophosphate toxins. Despite existing literature on drug-related seizures, the prevalence of seizures in non-cardiogenic pulmonary edema remains underexplored. For example, Nosaka et al. [42] described a 15-month-old patient with ARDS and seizures successfully treated with extracorporeal membrane oxygenation. Our study found no significant links between seizures and patient mortality, age, or sex, which aligns with findings from Traficant et al. [43] and Asadi et al. [44], suggesting that seizures are not influenced by these demographic factors.

Conclusion

Our study identified a 0.61% prevalence of ARDS among patients with acute poisoning, with a concerning mortality rate of 59%. Seizures occurred in nearly one-third of cases, accompanied by elevated creatinine and BUN levels and metabolic acidosis, while sepsis affected fewer than one-third. Despite significant histories of addiction, mainly to methadone, no correlation with mortality was found. Dialysis was needed in less than one-third of patients, with no significant associations observed with seizures, age, gender, or poisoning type. This study highlights the need for effective management of ARDS in poisoning cases and suggests future research should investigate individual factors contributing to ARDS in various poisoning types.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Research Ethics Committee of Yazd Branch, Islamic Azad University of Medical Sciences, Yazd, Iran, (Code: IR.IAU.YAZD.REC.1402.066).

Funding

This research did not receive any grant from funding agencies in the public, commercial, or non-profit sectors.

Authors' contributions

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Conflict of interest

The authors declared no conflict of interest.

Acknowledgments

The authors acknowledge the support of Shahid Saadoughi University of Medical Sciences and the cooperation of hospital staff at Shah Vali and Shahid Beheshti Hospitals in Yazd and Taft cities, Iran.

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