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Pattern and impact of antidotal administration in an Egyptian tertiary poison control center: A three-year retrospective study (2021–2023)

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ABSTRACT

Timely antidote administration is a critical step in acute poisoning management. Awareness of poisoning patterns and the essential antidotal requirement could improve patient care with better hospital resource allocation. This study investigates the pattern and impact of antidotal administration on patient outcomes in an Egyptian tertiary poison control center, providing insights to optimize the antidote stocking of essential antidotes. A three-year cross-sectional study was conducted at Tanta University Poison Control Center from January 2021 to December 2023. Demographic data, poisoning characteristics, causative agents, and administered antidotal data were retrieved. The initial Poisoning Severity Score (PSS), total hospitalization period, and patient outcomes were also recorded. The included 447 antidote-treated poisoned patients showed near equal gender distribution and median age of 25 years. Atropine, oximes, N-acetylcysteine (NAC), and naloxone were the top administered antidotes among patients (48.3 %, 25.7 %, 19.9 %, and 11.2 %, respectively). Mortality and complications were recorded in 5.15 % and 20.8 %, respectively. Administration of atropine, oximes, NAC, and L-carnitine significantly improved all outcomes ($p < 0.05$). Although HBO therapy significantly improved mortality, it substantially increased intensive care unit admissions ($p < 0.001$). Despite folic acid administration significantly improved mortality and complication incidences ($p < 0.05$), its therapeutic efficiency is still questionable. Availability constraints of the digibind and botulinum antitoxin could affect patient outcomes. Administration of atropine, oximes, NAC, naloxone, and sodium bicarbonate was significantly linked to prolonged hospitalization ($p < 0.001$). Accordingly, the emergency department in each institution should regularly update the antidotal stock based on a review of the list of essential and commonly used antidotes.

1. Introduction

Acute poisoning is a global health emergency, causing substantial morbidity and mortality rates [1]. Annually, the World Health Organization (WHO) records that approximately seven million people experience acute poisoning, with 250,000 deaths, mainly in developing nations [2]. Various pharmaceutical and non-pharmaceutical agents contribute to acute poisoning, with inconstant incidences based on geographical diversity [3]. Substantially, agrochemicals are the leading cause in developing countries compared to drug overdose in industrialized nations [4].

Among the treatment guidelines modalities of acute poisoning, antidotes have a crucial role in management as they can counteract a particular poison, reduce adverse outcomes, shorten the hospitalization period, as well as decrease the economic burden of using other supportive measures [5]. Notably, the timely administration of naloxone can reverse respiratory depression resulting from opioid overdose, mitigating the need for mechanical ventilation [6]. Furthermore, administering antivenom and botulinum antitoxin are lifesaving measures in snake envenomation and botulism food poisoning, respectively [7,8].

Antidotes were categorized into three classes according to their urgency: class A (immediate administration within 30 minutes), class B (available within one hour post-exposure), and class C (based on poisons

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presented in each locality and should be available within 4–6 hours) [9]. Accordingly, class A and B antidotes should always be readily accessible in all hospitals [6,10]. As a result, the American College of Medical Toxicology and the American Academy of Clinical Toxicology recommended 44 antidotes for stocking, of which 23 immediate antidotes (class A) and 14 antidotes (class B) should be available within 1 hour for administration [11]. Furthermore, they suggested performing a formal antidote hazard assessment for each hospital to provide optimum poisoned patient care.

However, shortages in the antidotal supply and inappropriate antidote stocking are universal concerns documented in many nations, even in well-equipped and qualified hospitals [3,12]. The insufficient antidotal storage is definitely attributed to the high cost of their development and purchase, as well as the short life span of some antidotes, making it challenging to justify stocking such antidotes to avoid wastage.

Globally, the insufficient local availability of essential antidotes directly impacted the patients' outcomes, especially in certain xenobiotics that are substantially linked to severe morbidity and mortality [13]. Notably, a lack of methanol antidotes in Saudi Arabia resulted in poor patient outcomes, including a greater mortality rate and visual impairments among methanol-poisoned patients [14,15].

Thus, the worldwide drug shortage is an issue that is being raised nowadays for allocating hospital resource settings and providing patients with the optimum antidote treatment at appropriate times [13]. Accordingly, comprehensive data should be collected to establish an antidotal bank, including local poisoning trends and frequently and urgently used antidotes. Since the poison control centers are antidote depots, they should analyze the types of poisonings encountered in their facility, the number of patients who may be admitted, and the amount of each antidote needed [16].

For the abovementioned reasons, gathering information about antidote usage patterns is crucial for optimizing resource allocation, refining clinical protocols, and improving all potential outcomes. To the best of our knowledge, no published Egyptian studies are dedicated to studying antidote usage patterns. Therefore, the current study aims to investigate the patterns of antidote administration at Tanta University Poison Control Centre (TUPCC), assess the impact of antidote use on patient outcomes, and identify deficiencies in current practices. The findings will provide insights to improve antidote management strategies and optimize antidote stocking based on local poisoning trends.

2. Patients and methods

2.1. Ethical considerations

This cross-sectional study was carried out with the approval of the medical research ethical committee of the Faculty of Medicine, Tanta University, Egypt (approval code: 36264PR722/6/24). Patient confidentiality was maintained throughout the data collection, anonymizing all identifying information before analysis. A waiver of informed consent was obtained due to the study's retrospective nature.

2.2. Study design and settings

A three-year retrospective cross-sectional study was conducted at TUPCC, Tanta, Egypt, during the period between January 2021 to December 2023. The TUPCC is the tertiary poison control center in the delta server of all Gharbia governorate rural and urban countries. Additionally, it provides all emergency measures with the possibility of transferring severe cases to the intensive care unit (ICU) in the main emergency hospital.

2.3. Eligibility criteria

2.3.1. Inclusion criteria

All acute poisoned patients were included if they had a confirmed diagnosis of poisoning, received at least one antidotal therapy, and had sufficient documentation (complete and detailed medical records of their clinical course and outcomes). Acute poisoning was defined as exposure to a toxic substance resulting in clinical manifestations within 24 hours of exposure [17]. The diagnosis of acute poisoning was based on patient history, characteristic manifestations for each category, and available routine and toxicological investigations. For example, muscarinic manifestations (miosis, salivation, lacrimation, and bronchospasm), as well as nicotinic presentations (muscle fasciculations and weakness), are characteristic manifestations, suggesting cholinesterase inhibitors poisoning [18,19]. The frequently administered antidotes in our locality include atropine, N-acetyl cysteine (NAC), naloxone, hyperbaric oxygen (HBO), L-carnitine, digibind, botulinum antitoxin, sodium bicarbonate ($NaHCO_3$), and deferoxamine.

2.3.2. Exclusion criteria

All patients with chronic poisoning (repeated or continuous exposure to a toxic substance over 6 months causing long-term adverse effects) [20], chronic diseases (such as diabetes, hypertension, chronic cardiac, kidney, and liver diseases), as well as coingestion were excluded from this study. Additionally, transferred or discharged patients before completing treatment and those with incomplete medical records were not included. Furthermore, we excluded administered antidotes for symptomatic treatment only (e.g., using sodium bicarbonate for treating metabolic acidosis and atropine for treating bradycardia and bronchospasm).

2.4. Sample size calculation

According to Abu Esba et al. [15], we included all eligible poisoned patients by convenience sampling. The sample size was calculated using OpenEpi software version 3.01 [21] with an average population of 1010. The margin of error was 5 %, and the effect size used for the sample size calculation was 0.5, assuming the highest variability in poisoning cases. With a 95 % confidence interval (CI) ranging from 0.45 to 0.55, the minimum estimated sample size was 279. However, we increased the included sample to 447 to enhance the statistical power and validity of the results.

2.5. Collected data

Data were extracted from patients' medical records and placed into a specially designated sheet to fulfill the study aims. The collected data included demographic information (age, gender, and residence), poisoning characteristics (causative agent, route of exposure, mode of poisoning, and delay period from exposure to hospital admission in hours). The causative agents were categorized into pharmaceutical and non-pharmaceutical substances. According to Persson et al. (1998), the Poisoning Severity Score (PSS) was assessed based on the most severe patient's clinical symptoms or signs. It has five grades: grade 0 (no observed symptoms or signs related to poisoning); grade 1 (mild transient with spontaneously resolving symptoms); grade 2 (pronounced or prolonged symptoms that require active treatment but are not life-threatening); grade 3 (severe or life-threatening symptoms requiring intensive care); and grade 4 (death) [22]. The antidote name, total administered dose, administration timing post-exposure, and duration of therapy were also collected in detail. In addition, the requirement of mechanical ventilation (MV) and ICU admission, potential outcomes (improvement, mortality, and complications), and length of hospital stay were recorded.

2.6. Statistical analysis

The analytical program was the R Statistical language (version 4.4.2; R Core Team, 2024) [23]. Descriptive statistics were used to summarize the demographic and toxicological characteristics of the study population. Continuous variables, such as age and delay period, were presented as medians with interquartile ranges (IQR). However, categorical variables, such as poisoning type and patient outcomes, were expressed as frequencies and percentages. The normality of continuous variables was assessed using the Shapiro-Wilk test, and non-normally distributed data were analyzed using non-parametric tests. The chi-square test was used to compare year-wise antidote administration patterns in pharmaceutical and non-pharmaceutical agents. Furthermore, the frequency of antidote administration among pharmaceutical categories and non-pharmaceutical agents was assessed using chi-square for goodness-of-fit test. The association between antidote administration and PSS was analyzed using the multinomial goodness-of-fit test by complete enumeration. The impact of antidote utilization on mortality, complications, ICU admission, and MV was assessed using the binomial test. The length of hospital stay was compared among various antidotes using the multinomial goodness-of-fit test. A p-value of < 0.05 was considered statistically significant.

3. Results

Out of 3021 poisoned patients, 447 met the eligibility criteria, as illustrated in Fig. 1. The median age (IQR) was 25 (19.0–35.0) years, with a nearly equal gender distribution (50.6 % female and 49.4 % male), as well as more than half (54.8 %) of the patients were from rural regions. Regarding poisoning data, non-pharmaceutical agents accounted for 59.9 %, predominating cholinesterase inhibitors poisoning (48.3 %). However, acetaminophen was the principal pharmaceutical causative agent (19.9 %). Most of the poisoned patients were intentionally exposed by ingestion route (63.5 % and 70.9 %, respectively). The median delay period before hospital admission was 4 hours, with no significant impact on patient outcomes among poisoning categories. The highest number of poisoned patients presented initially with a moderate PSS (43.2 %). Although most patients improved (74.05 %), 20.8 % had complications, and 5.15 % expired. The most reported complications were pneumonia and delayed neurological sequelae (5.36 % of each). Approximately one-quarter of patients (24.84 %) were admitted to ICU, and 16.78 % required MV intervention. Nearly half of the patients (48.3 %) were hospitalized for more than 96 hours, as revealed in Table 1.

Year-wise, antidotes distribution showed an upward increase of antidotal for non-pharmaceutical agents (atropine, oximes, HBO, folic acid, and botulinum antitoxin) as well as pharmaceutical agents (NAC, L-carnitine, deferoxamine) in 2022 compared to 2021, followed by a decline in 2023 owing to changing in poisoning pattern, as demonstrated in Figs. 2 and 3.

Regarding the general antidote utilization pattern, atropine, oximes, NAC, and naloxone were the top administered antidotes (48.3 %, 25.7 %, 19.9 %, and 11.2 %, respectively). Furthermore, among the prevalence of poisoning categories, atropine and oximes were the most frequently used in cholinesterase inhibitors poisoned patients (86.7 % and 46.1 %). At the same time, naloxone and NAC were the most common pharmaceutical antidotes used in 75 % of opioid toxicity and 70 % of acetaminophen-poisoned patients, respectively. Although there was a timely initiation of atropine, NAC, and folic acid treatment represented by a short median onset time for antidote administration (2 hours), there was a delayed onset of HBO administration (44 hours). The NAC had the highest total duration of antidotal therapy (72 hours) compared with

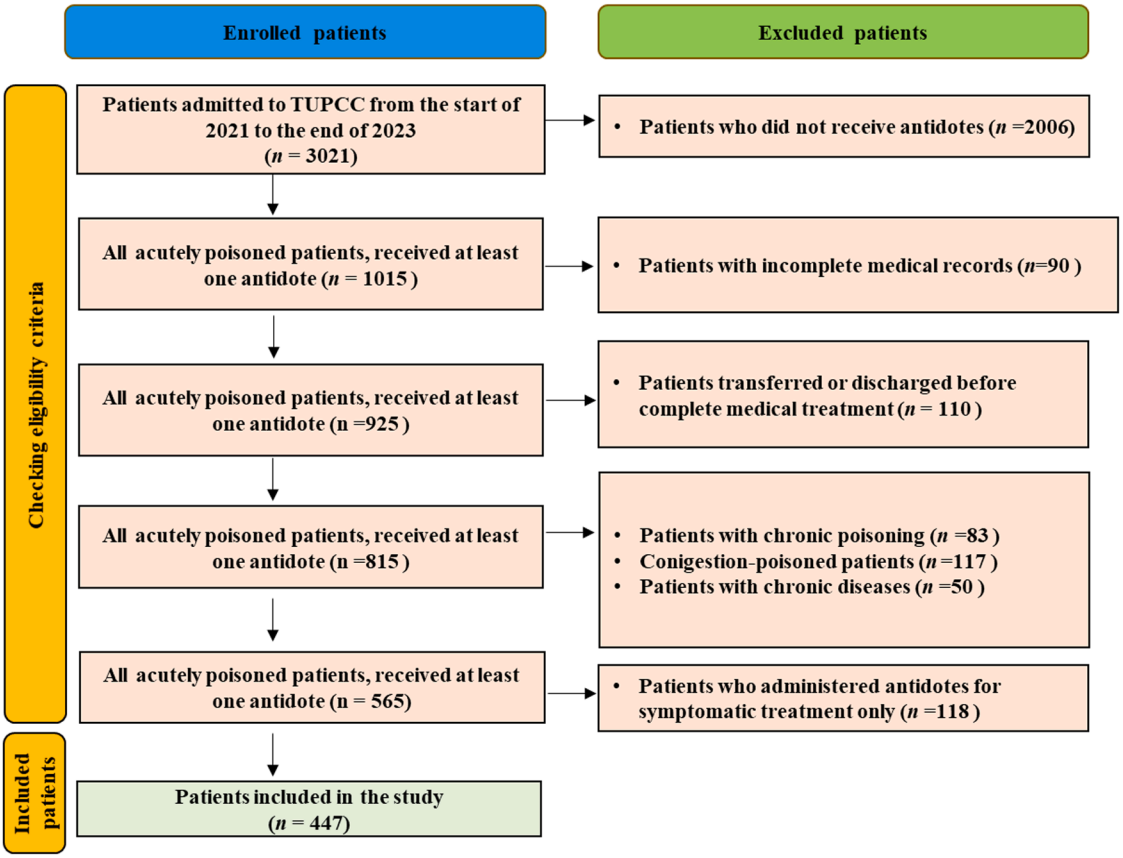

Fig. 1. Flowchart illustrating the recruitment process for enrolling patients administered antidotes in the Tanta University Poison Control Centre (TUPCC) during the study period (2021–2023).

Table 1
Demographic, toxicological characteristics, Poisoning Severity Score, patient outcomes, and hospitalization period of the study participants ($n = 447$).

Patient characteristics		*n* (%) / Median [IQR]
Demographic data		
	Age (years)	
	Median [IQR]	25.0 [19.0 35.0]
	Range	1.5–74.0
	Sex, *n* (%)	
	Female	226 (50.6 %)
	Male	221 (49.4 %)
	Residence, *n* (%)	
	Rural	245 (54.8 %)
	Urban	202 (45.2 %)
Toxicological data		
Poison type, *n* (%)		
	Non-pharmaceutical	268 (59.9 %)
	Pharmaceutical	179 (40.1 %)
Poison category, *n* (%)	Non-pharmaceutical	
	Cholinesterase inhibitors	216 (48.3 %)
	Botulism	2 (0.45 %)
	Methanol	6 (1.34 %)
	Carbon monoxide	46 (10.3 %)
	Pharmaceuticals	
	Acetaminophen	89 (19.9 %)
	Digoxin	8 (1.79 %)
	Antidepressants	20 (4.47 %)
	Anticonvulsants	9 (2.01 %)
	Opioids	50 (11.2 %)
	Iron	1 (0.22 %)
Mode of poisoning, *n*)%)	Accidental	163 (36.5 %)
	Suicidal	284 (63.5 %)
Route of poisoning, *n* (%)	Ingestion	317 (70.9 %)
	Inhalation	70 (15.6 %)
	Combined	47 (10.5 %)
	Injection	10 (2.24 %)
	Dermal	3 (0.67 %)
Delay period (hr)	Median [IQR]	4.0 [2.0 6.0]
	Range	0.5–27.0
Poisoning Severity Score, *n* (%)	Mild	99 (22.1 %)
	Moderate	193 (43.2 %)
	Severe	155 (34.7 %)
Patients' outcomes, *n* (%)	Complicated	93 (20.8 %)
	Died	23 (5.15 %)
	Improved	331 (74.05 %)
Complications, *n* (%)		
	No	354 (79.2 %)
	Pneumonia	24 (5.36 %)
	Respiratory failure	13 (2.8 %)
	Delayed neurological sequale	24 (5.36 %)
	Heart failure	15 (3.35 %)
	Seizures	17 (3.93 %)
ICU, *n* (%)		
	No	336 (75.16 %)
	Yes	111 (24.84 %)
Mechanical ventilation, *n* (%)		
	No	372 (83.22 %)
	Yes	75 (16.78 %)
Length of hospital stay (h), *n* (%)		
	< 24	125 (28.0 %)
	24–96	106 (23.7 %)
	> 96–168	216 (48.3 %)

n: number; ICU: intensive care unit; hr: hour; IQR: interquartile range.

other commonly used antidotes. Conversely, botulinum antitoxin and digibind had the least administered antidotes with the shortest therapeutic duration compared with other antidotes, as revealed in Table 2 and Figs. 4 and 5.

Table 3 depicts the association between the antidote administration and poisoning severity. Atropine, oximes, and L-carnitine administration were significantly noticed in patients with moderate PSS ($p = <$ 0.001, $<$ 0.001, and 0.014, respectively). However, HBO, naloxone, and digibind therapies were substantially predominant in patients with

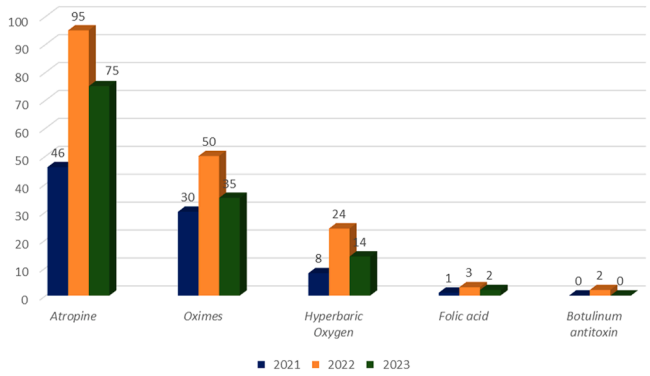

Fig. 2. Year-wise pattern of antidote administration in non-pharmaceutical agents demonstrates a nonsignificant upward increase in 2022 compared to 2021, followed by a decline in 2023 in atropine, oximes, hyperbaric oxygen (HBO), folic acid, and botulinum antitoxin using the chi-square test ($p > 0.05$).

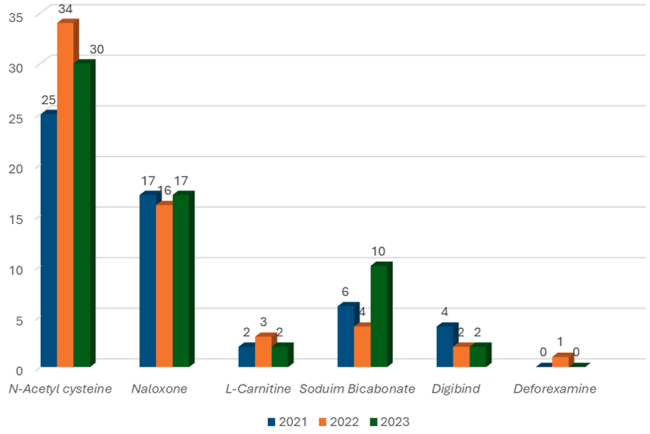

Fig. 3. Year-wise pattern of antidote administration in pharmaceutical agents demonstrates a nonsignificant upward increase in 2022 compared to 2021, followed by a decline in 2023 in N-acetyl cysteine (NAC), L-carnitine, and deferoxamine using the chi-square test ($p > 0.05$).

severe PSS ($p = <0.00$, <0.00, and 0.033, respectively).

Table 4 and 5 demonstrated that atropine, oximes, NAC, and L-carnitine administration significantly improved all patient outcomes ($p < 0.05$). Naloxone therapy was associated considerably with lessening mortality and requiring ICU admission and MV ($p < 0.001$ for each). Although HBO therapy significantly improved CO-related mortalities ($p < 0.001$), it noticeably increased ICU admission ($p < 0.001$). Administration of $NaHCO_3$ was considerably lower than the need for MV, with no recorded mortalities ($p < 0.001$ for each). Additionally, digibind and folic acid administration substantially reduced mortality and complications ($p < 0.05$). Accordingly, administration of atropine, oximes, NAC, naloxone, and $NaHCO_3$ was significantly linked to prolonged hospitalization ($p < 0.001$ for each), as revealed in Table 6.

4. Discussion

Antidote administration is a principal cornerstone in managing various xenobiotics poisoning by reducing, counteracting, and eliminating toxic effects [11]. Nowadays, antidote stocking is a major global challenge due to insufficient databases and limited resources, especially in developing countries [5]. Accordingly, medical implications have been raised due to suboptimal patient management and augmented adverse outcomes [1].

The geographical poisoning pattern diversity, the social concepts, and limited resource settings encounter logistical challenges that could

Table 2
Pattern of antidote utilization in acutely poisoned patients.

Antidotes	*n* (%)	Onset post-exposure (hours) Median [IQR] Range	Total dose # Median [IQR] Range	Total duration (hours) Median [IQR] Range
Atropine	216 (48.3 %)	2.0 [1.5–3.0] (0.5–6.0)	7.0 [3.0–11.0] (1.0–88.0)	24.0 [12.0–40.0] (2.0–300.0)
Oximes	115 (25.7 %)	3.0 [3.0–5.0] (1.0–6.0)	4.0 [4.0–7.0] (1.0–37.0)	40.0 [22.0–48.0] (4.0–200.0)
N- acetylcysteine	89 (19.9 %)	2.0 [1.0–3.0] (0.5–5.0)	121.0 [4.0–171.0] (0.5–200.0)	72.0 [48.0–72.0] (3.0–77.0)
Naloxone	50 (11.2 %)	3.0 [2.0–3.0] (1.0–5.0)	3.5 [2.0–10.0] (1.0–27.0)	13.5 [4.0–30.0] (1.0–97.0)
Hyperbaric oxygen	46 (10.3 %)	44.0 [12.0–65.0] (4.0–77.0)	3 [2.0–5.0] [1–5]	2 [2.0–2.0] 2 [1–5]
Sodium bicarbonate	20 (4.47 %)	4.0 [2.0–7.0] (1.0–8.0)	1.0 [1.0–1.0] (0.5–2.0)	2.0 [1.0–2.0] (1.0–4.0)
L-carnitine	9 (2.01 %)	6.0 [4.0–7.0] (2.0–8.0)	1.0 [1.0–1.0] (1.0–1.0)	2.0 [1.0–7.0] (1.0–8.0)
Digibind	8 (1.79 %)	6.5 [5.5–9.5] (5.0–12.0)	1.0 [1.0–1.0] (1.0–1.0)	2.5 [2.0–3.0] (2.0–3.0)
Folic acid	6 (1.34 %)	2.0 [2.0–3.0] (1.0–3.0)	10.0 [10.0–10.0] (10.0–10.0)	24.0 [24.0–24.0] (24.0–24.0)
Botulinum antitoxin	2 (0.45 %)	12.0 [12.0–12.0] (12.0–12.0)	1.0 [1.0–1.0] (1.0–1.0)	2.5 [2.0–3.0] (2.0–3.0)
Deferoxamine	1 (0.22 %)	6.0 [6.0–6.0] (6.0–6.0)	4.0 [4.0–4.0] (4.0–4.0)	8.0 [8.0–8.0] (8.0–8.0)

n (%): number and percentage of patients receiving each treatment; IQR: interquartile range; # total dose unit: atropine (ampoule), oximes (ampoule), N- acetylcysteine (sachet), naloxone (ampoule), hyperbaric oxygen (session), sodium bicarbonate (ampoule), L-carnitine (ampoule), digibind (vial), folic acid (tablet), botulinum antitoxin (vial), and deferoxamine (vial).

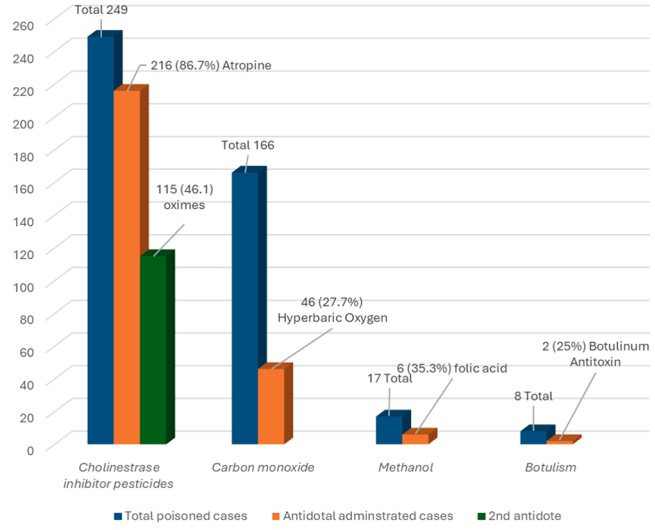

Fig. 4. Frequency of antidote administration among non-pharmaceutical categories. A Significant difference was observed among the administered antidotes where atropine and oximes are the most frequently used compared to other antidotes using the chi-square for goodness-of-fit test ($p < 0.001$).

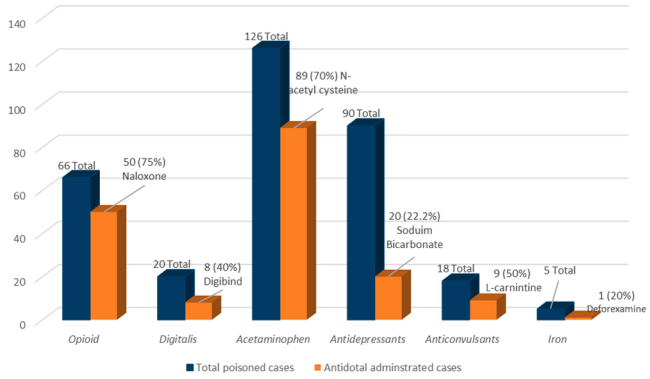

Fig. 5. Frequency of antidote administration among pharmaceutical categories. A Significant difference was observed among the administered antidotes where N-acetyl cysteine (NAC) and naloxone are the most frequently used compared to other antidotes using the chi-square for goodness-of-fit test ($p < 0.001$).

affect the types of antidote stocking in each hospital [24]. Hence, this study addressed the critical knowledge gap concerning a comprehensive analysis of antidote administration patterns and their impact on patient outcomes in our locality, highlighting challenges and regional variations in antidote availability for better resource allocation.

We observed a dramatic reduction of the included cases in our study (3021 patients) compared to the prior five-year epidemiological study at TUPCC by Rageh et al. [25] (9713 cases), which could be attributed to variance in the two studies' eligibility criteria, referral policies, restructuring of healthcare settings into hot and cold days, and implementation a hotline service. Substantially, Rageh et al., 2023 included all poisoned cases regardless of treatment strategies, whereas we included only all poisoned cases treated with specific antidotes.

The demographic profile of included patients reveals a median age (IQR) of 25 (19.0–35.0) with comparable gender distribution (50.6 % female and 49.4 % male). Likewise, a study recording antidotal utilization in Saudi Arabia by Abu Esba et al. [15] demonstrated a mean age (SD) of 30.9 ± 23 with 55 % females. Furthermore, Rageh et al. [25] recorded the predominantly young age group (36 %), with 55.9 % female percentages of acutely poisoned patients admitted to TUPCC in the preceding 5 years. However, many studies report significant gender differences in poisoning trends, with males often predominating in occupational exposure and females more prone to intentional poisoning [26,27].

We observed that the majority of poisoning cases occurred through the ingestion route for self-harm intention. Consequently, most of our patients had moderate to severe poisoning severity grades. Likewise, Lee et al. [28] demonstrated that suicidal mode and ingestion route were significant determinants of poisoning-related severity. Although Rageh et al. [25] reported shorter presentation times of < 2 hours, Eisa et al. [29] recorded a substantial association between the severity of

Table 3
Association of antidote administration with the Poisoning Severity Score.

Antidotes	Poison Severity Score (PSS)			
	Mild	Moderate	Severe	*p*-value*[a]
Atropine, *n* (%)	68 (31.5 %)	102 (47.2 %)	46 (21.3 %)	**< 0.001***
Oximes, *n* (%)	0 (0 %)	69 (60.0 %)	46 (40.0 %)	**< 0.001***
N-acetylcysteine, *n* (%)	25 (28.1 %)	40 (44.9 %)	24 (27.0 %)	0.081
Naloxone, *n* (%)	2 (4.0 %)	12 (24.0 %)	36 (72.0 %)	**< 0.001***
Hyperbaric oxygen, *n* (%)	0 (0 %)	18 (39.1 %)	28 (60.9 %)	**< 0.001***
L- carnitine, *n* (%)	0 (0 %)	7 (77.8 %)	2 (22.2 %)	**0.014***
Sodium bicarbonate, *n* (%)	4 (20.0 %)	10 (50.0 %)	6 (30.0 %)	0.291
Digibind, *n* (%)	0 (0 %)	2 (25.0 %)	6 (75.0 %)	**0.033***
Botulinum antitoxin, *n* (%)	0 (0 %)	0 (0 %)	2 (100.0 %)	0.333
Folic acid, *n* (%)	0 (0 %)	2 (33.3 %)	4 (66.7 %)	0.177
Deferoxamine, *n* (%)	0 (0 %)	0 (0 %)	1 (100.0 %)	1.000

Values are expressed as *n* (%), representing the number and percentage of patients receiving each antidote according to Poison Severity Score (PSS); [a]: percentages are calculated from rows; *p*-values are from the multinomial goodness-of-fit test by full enumeration; *: significance at $p < 0.05$.

poisoning and prolonged delay time (> 4 h) after ingestion. However, we did not detect a significant association between time to hospital admission and patients' outcomes in each poisoning category. Variance in sample size and poisoning-related factors could explain the lack of this association in our study.

Although most patients completely recovered in our study, the mortality rate was 5.15 %. Similarly, Rageh et al. [25] and Abu Esa et al. [15] demonstrated a comparable mortality rate (4 % and 4.5 %, respectively). However, Parmar et al. [30] reported higher fatalities

Table 6
Association of antidote administration with the hospitalization period.

Antidotes	Length of hospital stay (hours)			
	< 24 hours	24–72 hours	> 72 hours	*p*-value*[a]
Atropine, *n* (%)	50 (23.1 %)	0 (0 %)	166 (76.9 %)	**< 0.001***
Oximes, *n* (%)	0 (0 %)	69 (60.0 %)	46 (40.0 %)	**< 0.001***
N-acetylcysteine, *n* (%)	38 (42.7 %)	39 (43.8 %)	12 (13.5 %)	**< 0.001***
Naloxone, *n* (%)	10 (20.0 %)	31 (62.0 %)	9 (18.0 %)	**< 0.001***
Hyperbaric oxygen, *n* (%)	17 (37.0 %)	12 (26.1 %)	17 (37.0 %)	0.617
Folic acid, *n* (%)	0 (0 %)	4 (66.7 %)	2 (33.3 %)	0.177
L- carnitine, *n* (%)	4 (44.4 %)	1 (11.1 %)	4 (44.4 %)	0.415
Sodium bicarbonate, *n* (%)	6 (30.0 %)	14 (70.0 %)	0 (0 %)	**< 0.001***
Digibind, *n* (%)	0 (0 %)	5 (62.5 %)	3 (37.5 %)	0.085
Botulinum antitoxin, *n* (%)	0 (0 %)	0 (0 %)	2 (100.0 %)	0.333
Deferoxamine, *n* (%)	0 (0 %)	0 (0 %)	1 (100.0 %)	1.000

Values are expressed as *n* (%); representing the number and percentage of patients receiving each antidote based on the length of hospital stay; [a] : percentages are calculated from rows; *p*-values are from the multinomial goodness-of-fit test by full enumeration;*: significant *p*-values ($p < 0.05$).

Table 4
Impact of antidote utilization on acutely poisoned patient mortality and complications.

Antidotes	Mortality			Complications		
	No $n = 424$	Yes $n = 23$	*p*-value*[a]	Yes $n = 93$	No $n = 331$	*p*-value*[a]
Atropine, *n* (%)	201 (93.1 %)	15 (6.94 %)	**< 0.001***	34 (16.9 %)	167 (83.1 %)	**< 0.001***
Oximes, *n* (%)	100 (87.0 %)	15 (13.0 %)	**< 0.001***	35 (30.4 %)	66 (57.4 %)	**< 0.001***
N- acetylcysteine, *n* (%)	89 (100.0 %)	0 (0 %)	**< 0.001***	10 (11.2 %)	79 (88.8 %)	**< 0.001***
Naloxone, *n* (%)	44 (88.0 %)	6 (12.0 %)	**< 0.001***	18 (40.9 %)	26 (59.1 %)	0.291
Hyperbaric oxygen, *n* (%)	45 (97.8 %)	1 (2.17 %)	**< 0.001***	23 (51.1 %)	22 (48.9 %)	1.000
L-carnitine, *n* (%)	8 (88.9 %)	1 (11.1 %)	**0.039***	0 (0 %)	8 (100.0 %)	**0.008***
Sodium bicarbonate, *n* (%)	20 (100.0 %)	0 (0 %)	**< 0.001***	6 (30.0 %)	14 (70.0 %)	0.115
Digibind, *n* (%)	8 (100.0 %)	0 (0 %)	**0.008>***	2 (25.0 %)	6 (75.0 %)	0.289
Folic acid, *n* (%)	6 (100.0 %)	0 (0 %)	**0.031***	0 (0 %)	6 (100.0 %)	**0.031***
Botulinum antitoxin, *n* (%)	2 (100.0 %)	0 (0 %)	0.500	0 (0 %)	2 (100.0 %)	0.500
Deforexamine, *n* (%)	1 (100.0 %)	0 (0 %)	1.000	0 (0 %)	1 (100.0 %)	1.000

n (%): number and percentage of patients receiving each treatment; [a]: percentages are calculated from rows; *p*-values from Binomial test; *: significant *p*-values ($p < 0.05$).

Table 5
Impact of antidote utilization on ICU admission and mechanical ventilation of acutely poisoned patients.

Antidotes	ICU admission			Mechanical ventilation		
	No	Yes	*p*-value*[a]	No	Yes	*p*-value*[a]
Atropine, *n* (%)	175 (81.0 %)	41 (19.0 %)	**< 0.001***	190 (88.0 %)	26 (12.0 %)	**< 0.001***
Oximes, *n* (%)	74 (64.3 %)	41 (35.7 %)	**< 0.001***	89 (77.4 %)	26 (22.6 %)	**< 0.001***
N- acetylcysteine, *n* (%)	89 (100.0 %)	0 (0 %)	**< 0.001***	89 (100.0 %)	0 (0 %)	**< 0.001***
Naloxone, *n* (%)	40 (80.0 %)	10 (20.0 %)	**< 0.001***	40 (80.0 %)	10 (20.0 %)	**< 0.001***
Hyperbaric oxygen, *n* (%)	6 (13.0 %)	40 (87.0 %)	**< 0.001***	16 (34.8 %)	30 (65.2 %)	0.054
L-carnitine, *n* (%)	8 (88.9 %)	1 (11.1 %)	**0.039***	8 (88.9 %)	1 (11.1 %)	**0.039***
Sodium bicarbonate, *n* (%)	12 (60.0 %)	8 (40.0 %)	0.503	18 (90.0 %)	2 (10.0 %)	**< 0.001***
Digibind, *n* (%)	1 (12.5 %)	7 (87.5 %)	0.070	4 (50.0 %)	4 (50.0 %)	1.000
Folic acid, *n* (%)	4 (66.7 %)	2 (33.3 %)	0.687	4 (66.7 %)	2 (33.3 %)	0.687
Botulinum antitoxin, *n* (%)	0 (0 %)	2 (100.0 %)	0.500	2 (100.0 %)	0 (0 %)	0.500
Deforexamine, *n* (%)	1 (100.0 %)	0 (0 %)	1.000	1 (100.0 %)	0 (0 %)	1.000

Values are expressed as n (%), representing the number and percentage of patients receiving each antidote in relation to intensive care unit (ICU) admission and mechanical ventilation; [a]: percentages are calculated from rows and *p*-values from the Binomial test; *: significant *p*-values ($p < 0.05$)

(15.4 %) due to prolonged delay time till hospitalization, increased lethal snake envenomation and pesticide poisoning, referral of deteriorated cases from private hospitals, and lack of specific antidotes. Furthermore, Vaidya and Hulke [31] demonstrated 12 % mortality of acutely poisoned patients and recommended adequate providing specific antidotes as an effective measure to improve the patient's outcome.

Furthermore, we recorded a considerable portion of poisoned patients required ICU admission and MV (24.84 % and 16.78 %, respectively). Near similar findings, Shen et al. [32] and El-Sarnagawy and Hafez [33] recorded that 23 % and 23.4 % of intoxicated patients required MV, respectively. Conversely, other studies recorded lower MV and ICU admission rates [34,35]. Inconsistency in delay time, poisoning characteristics, treatment modalities, and antidote availability could affect patient outcomes.

Additionally, we recorded that 20.8 % of patients developed complications, and 48.3 % had prolonged hospitalization, highlighting the economic burden on hospital resources. In contrast, Rageh et al. [25] recorded that nearly half of the cases (52.2 %) were discharged within the first 24 hours of admission, based on family requests against medical advice (70.3 %).

Our study revealed that non-pharmaceutical agents constitute more than half of poisoning (59.9%), predominating cholinesterase inhibitors poisoning (48.3 %). The preponderance of pesticide poisoning is attributed to their wide accessibility in agriculture-based communities owing to their affordable price and uncontrolled purchase [36]. As a result, atropine and oximes were the top consumed antidotes in the current study (48.3 % and 25.7 %, respectively), which aligns with previous studies [30,37]. However, the variance in eligibility criteria could explain the predominance of phosphide rodenticides (80 %) in Rageh et al., 2023 study, which depends on supportive management without specific antidotes.

Furthermore, we recorded that acetaminophen and opioids were the most frequent pharmaceutical agents (19.9 % and 11.2 %, respectively). Similarly, an Iranian meta-analysis by Derhami et.al. [38] documented that opium and acetaminophen were the most common causes of poisoning. Subsequently, our study demonstrated that NAC and naloxone represented the most commonly used pharmaceutical antidotes administered in 70 % and 75 % of patients with acetaminophen and opioids poisoning, respectively. Conversely, naloxone was the least consumed antidote in Qatar General Hospital [39]. Differences in causative toxic substance accessibility and antidotal availability could affect the frequency of antidote usage.

Regarding the impact of antidotes on patient outcomes, we observed significant improvement in all patients' sequels with atropine, oximes, NAC, and L-carnitine administration. These favorable outcomes could be attributed to the rapid onset of atropine, oximes, and NAC administration (2–3 hours). Consistently, Reddy et al. [40] reported a significant reduction in intubation, MV, and short ICU stay in the group treated with atropine and pralidoxime due to alleviating peripheral and central respiratory symptoms during the acute cholinergic crisis. Furthermore, Downs et al. [41] concluded that promoting NAC within 8 hours prevented 91 % of adverse outcomes in massive acetaminophen overdoses. In addition, Gziut and Thanacoody [42] advocated using L-carnitine in the treatment of VPA-induced hyperammonemia in both acute and chronic valproic toxicities.

We also recorded that naloxone administration substantially reduced incidences of mortality, ICU admission, and MV requirement. Similarly, Chimbar and Moleta [43] and Choi et al. [44] documented decreasing fatalities with naloxone administration in opioid abusers. The naloxone's effectiveness in reversing opioid-induced ventilatory and central nervous system (CNS) depression could explain the lowering of ICU admission and MV rates [45]. However, the existence of severe opioid poisoning cases, together with concomitant naloxone side effects, such as pulmonary edema and cardiac complications, may explain the lack of association between naloxone administration and reducing opioid-related complications [46,47].

Additionally, our study revealed that tricyclic antidepressants (TCA) poisoned patients who administrated $NaHCO_3$ had a significantly lower need for MV with no recorded mortalities. Likewise, a prior study in TUPCC by Wahdan and Helal [48] did not record any fatalities in TCA-poisoned patients. Furthermore, Javadipour et al. [49] demonstrated gradual improvement in ECG abnormalities and outcomes following sodium bicarbonate therapy in TCA-poisoned patients [50].

The impact of HBO in treating carbon monoxide (CO) poisoning is still challenging. Although Huang et al. [51] and Rose et al. [52] reported lower delayed neurological sequels (DNS) incidences and mortality rates with HBO therapy, the meta-analysis by Ho et al. [53] did not demonstrate any significant improvement in HBO-treated CO-poisoned patients. Furthermore, a large nationwide cohort study in Taiwan showed higher DNS risks in patients who received HBO than those who did not [54]. Accordingly, we recorded significant improvement in CO–related fatalities, though there was a substantial increase in ICU admission in HBO-treated patients. The optimum benefit of HBO is attained with timely administration within 22.5 hours [55]. Therefore, the considerable rise in ICU requirements in HBO-treated CO-poisoned patients in the current study could be explained by a substantial delay until HBO treatment (44 hours). This extensive delay is due to logistical constraints of HBO booking sessions and transferring patients to specialized HBO units that are distant from our center. Furthermore, a considerable portion of HBO-treated patients had severe PSS (60.9 %), increasing the adverse outcomes probability.

Likewise, another concern was raised about the effectiveness of folate therapy [96]. Our study demonstrated that all methanol-poisoned patients treated with folic acid survived with no potential complications. Likewise, Theobald and Lim [56] suggested using folate therapy as adjuvant therapy in methanol-poisoned patients with metabolic acidosis, hypotension, and preexisting folate deficiency, as well as in outbreaks. However, Scanlon et al. [57] noted no additional benefit in folate therapy over the standard treatment in methanol-poisoned patients due to a concomitant fomepizole treatment that prevents methanol oxidation to formic acid [57].

Despite the effectiveness of fomepizole in methanol poisoning, it was unavailable in our locality. Accordingly, the cornerstone of methanol poisoning in TUPCC is hemodialysis, folic acid administration, and supportive therapy supported by Elbastawesy et al. [58]. Hence, further research is needed to assess the efficiency of folic acid as an adjuvant therapy in methanol poisoning.

Furthermore, botulinum antitoxin and digibind are limited available owing to their high cost and lower number of poisoning cases. Accordingly, we recorded that digibind and botulinum antitoxin were administered in 1.79 % and 0.45 % of patients, respectively. Although digibind was substantially administered in severe cases in our study, these patients survived, highlighting its potent effect. Likewise, Sheikh et al. [59] documented a more rapid reversal of toxicity, shorter intensive care unit lengths of stay, and lower mortality rates in the digibind-managed group.

In approximately similar instances, we noticed two botulism cases successfully treated with botulinum antitoxin. However, a prior study in TUPCC by Rageh et al. reported that botulism cases were referred to Ministry of Health specialized centers due to restricted accessibility. As a result, there was a substantial delay in administrating botulinum antitoxin (12 hours) due to the time required to request and transport the antidote to our center. Accordingly, a systematic review and meta-analysis by O'Horo et al. [8] concluded that early botulinum antitoxin therapy and high-quality intensive care are the cornerstones of botulism management for improving outcomes. Furthermore, Peñuelas et al. [60] highlighted the importance of early antitoxin administration for reducing hospitalization periods and adverse events.

From a risk/benefit standpoint, although there is an economic burden on healthcare institutions with atropine, oximes, NAC, naloxone, and $NaHCO_3$ in the form of prolonged hospitalization, it is tolerable compared to improving patient outcomes. However, poisoning centers

should have a minimum acceptable digibind and botulinum antitoxin antidotal stocking to treat severe poisoning cases exclusively due to their potent effect, limited availability, and expensive cost.

In Ethiopia, Kifle et al. [3] recorded a lack of essential antidotes in 80 surveyed pharmacies, emphasizing the necessity of implementing new strategies for antidote stocking. Furthermore, Al-Taweel et al. [5] reported the absence of complete stocking in all essential antidotes among 14 hospitals in Kuwait, highlighting the urgent need for expert consensus guidelines for restocking all essential antidotes. Accordingly, implementing a national antidote registry or local stocking guidelines is recommended to achieve the optimum antidotal effect with reasonable resource allocations.

5. Strength and limitations

This study is the first in our locality to provide insight into commonly used antidotes, emphasizing their association with poisoning severity and their impact on potential outcomes. We underscore the essential antidotes list to ensure the optimum antidote stocking in the emergency department and promote the ideal standardized management of acutely poisoned patients with hospital resource allocation. Furthermore, we highlight the potential defects in cases of unavailable or costly antidotes, emphasizing the necessity of their availability in a nearby stocking to attain optimal efficacy promptly. Although this study offers some guidance for antidote stocking and management, retrospective data collection from only a single poison center can not be applied to other emergencies. Furthermore, the limited study duration underestimated all necessary antidotes that should be available.

6. Conclusions

Our study assessed the pattern and impact of used antidotes in TUPCC, underscoring the importance of stocked essential antidotes. Atropine and oximes were the top administered antidotes in non-pharmaceutical poisoning, whereas NAC and naloxone were the most frequently used among pharmaceuticals. Administration of atropine, oximes, NAC, and L-carnitine significantly improved all outcomes. Furthermore, challenges were raised concerning the therapeutic efficacy of HBO and folic acid, as well as availability constraints in digibind and botulinum antitoxin. Prolonged hospitalization was considerably observed with atropine, oximes, NAC, naloxone, and $NaHCO_3$ therapy, highlighting the potential burden on healthcare institutions. However, timely antidotal administration substantially improved patients' prognosis, especially with atropine, oximes, and NAC therapy. Accordingly, we recommend customizing strategies for antidote stocking to achieve optimum antidotal effects. Furthermore, a national survey with an extensive database is suggested to capture all essential antidotes and to determine the minimum antidote stock levels, considering cost-effective issues before widespread implementation.

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Author statement

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CRediT authorship contribution statement

El-Sarnagawy Ghada N.: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Methodology, Formal analysis, Data curation, Conceptualization. **Abd Eldayem Yara B:** Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Formal analysis, Data curation, Conceptualization. **Sobeeh Fatma Gaber:** Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Formal analysis, Data curation, Conceptualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability

Data will be made available on request.

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