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Retrospective analysis of the poisoning cases in four different regions of the world

Hananeh KORDBACHEH[1,2], Lamis F. SHISHANI[1], Kübra KOLCI[1,3], Rim ALOMAR[1], Baraa HAMZE[1], Ahmet AYDIN[1*]

1 Department of Pharmaceutical Toxicology, Faculty of Pharmacy, Yeditepe University, Istanbul, Turkey.
2 Department of Pharmaceutical Toxicology, Faculty of Pharmacy, Eastern Mediterranean University, Famagusta, North Cyprus.
3 Department of Pharmaceutical Toxicology, Faculty of Pharmacy, Acıbadem Mehmet Ali Aydinlar University, Istanbul, Turkey
* Corresponding Author. E-mail: ahmet.aydin@yeditepe.edu.tr (A. A); Tel. +90 533 342 2565

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ABSTRATC: Poisoning remains a significant public health concern and continues to be one of the primary reasons for hospital admissions worldwide. Therefore, it is crucial to identify the most common causes of poisoning to reduce morbidity and mortality rates. This study aims to summarize and compare the frequency, patterns, causative agents, and gender distributions of poisoning among the most populous countries in the Middle East, North Africa, and South Asia regions, including Turkey, Jordan, Morocco, and India. The paper reviews literature on poisoning cases admitted to emergency departments between 2010 and 2020. A total of 20 relevant papers were included in the study. In Jordan, Turkey, India, and Morocco, 2545, 4441, 2895, and 3462 poisoning cases were identified, respectively. Ingestion was the primary route of exposure. In Jordan and India, the majority of poisoning cases were observed in males, while in Turkey and Morocco, females were more frequently involved. Non-pharmaceutical substances were the main cause of poisoning in Jordan, India, and Morocco, whereas medication was the primary cause of intoxication in Turkey. Except in Jordan, intentional exposure was the most common type of poisoning among the countries. To the best of our knowledge, there is no systematic review comparing the pattern of poisoning in these countries. The data extracted in this study can be utilized to enhance public awareness regarding both medication and non-medication intoxication.

Keywords: Intentional poisoning; Unintentional poisoning; Emergency departments; Frequency of poisoning; Exposure route.

1. INTRODUCTION

Poisoning is a qualitative term that denotes a chemical substance's ability to negatively affect the body. As Paracelsus famously stated, "all substances are poisons; there is none that is not a poison. The right dose differentiates a poison from a remedy." Human poisoning has emerged as a significant global health issue. Whether through accidental or deliberate exposure to man-made or natural agents, poisoning can result in significant mortality and morbidity [1]. Evidence suggests that poisoning ranks as the second leading cause of unnatural deaths, following closely behind traffic accidents across all age groups and is one of the most common reasons for hospitalization. In 2012, WHO reported more than 3 million poisoning cases worldwide, resulting in over 220,000 deaths annually [2]. However, the prevalence and types of poisoning vary between countries, strongly influenced by the availability of poisonous agents, environmental factors, and industrial and agricultural activities [1].

The absence of facilities for safe storage and disposal contributes to poisonings, which occur more frequently among young populations than adults. Peak poisoning frequencies are observed in low- and middle-income countries compared to developed ones [3]. According to the Global Burden of Disease study, approximately 86,353 people died from unintentional poisonings worldwide in 2015, with 78,054 (90%) deaths occurring in low- and middle-income countries. This disparity may stem from differences in population awareness, dietary factors, preventive measures, and regulatory policies [4].

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Pesticides, drugs, and alcohol are the most common toxic substances involved in poisoning cases. Drug poisoning can result from various substances, including prescription medications, over-the-counter drugs, illicit drugs, and chemicals. Central nervous system-affecting medications are frequently utilized for self-harm in developed countries. Unfortunately, many cases of drug poisoning go unreported or misclassified, leading to an inaccurate understanding of its true public health impact.

Recently, pesticide poisoning has garnered attention due to rising morbidity and mortality rates worldwide [3]. It's estimated that 370,000 people die annually due to deliberate pesticide ingestion, primarily observed in countries with agriculture-based economies [2,5]. However, the actual number of affected individuals may be much higher due to underreporting.

Hence, this study aims to identify and compare the trends of both medicinal and non-medicinal poisoning cases among the most populous countries in the Middle East, North Africa, and South Asia regions, including Turkey, Jordan, Morocco, and India. Understanding the general pattern of poisoning in a specific region can help identify risk factors and enable early diagnosis and management. The collection and analysis of data from toxic substance-related cases may aid in reducing poisonings [6]. Additionally, the data presented in this article can inform the development of appropriate intervention strategies to prevent both intentional and unintentional poisonings in the population. The main countries of the Middle East, North Africa, and South Asia regions were selected to estimate and compare the distribution of unintentional and intentional poisoning among all age groups. To our knowledge, no systematic review compares the patterns of poisoning in these countries. In this paper, a systematic literature search was conducted to gather all original reported poisoning cases in the four countries between 2010 and 2020. The authors utilized various keywords and combinations, such as intentional poisoning, unintentional poisoning, medication poisoning, non-medication poisoning, drug abuse, suicide, emergency departments (ED), hospitalization, pesticides, organophosphates, antipsychotic drugs, narcotics, and analgesic drugs.

2. RESULTS

Reviewed studies encompassed the total number of admitted patients to the Emergency Department (ED), including their age, gender, causative agents, and means of exposure. To collect these papers, we utilized various scientific databases and research engines, such as PUBMED, NCBI, and Google Scholar. Additionally, we accessed national data sources, including the websites of the Jordan National Drug and Poison Information Center (JNDPIC), The Pharmacy One™ Poisoning Call Center (P1PCC), the Moroccan Poison Control Center, tertiary care teaching hospitals in India, and the Ankara Branch of the Council of Forensic Medicine, as well as Antalya and Istanbul training and research hospitals.

Some studies were excluded from our review due to concerns regarding reliability, validity, and insufficient data. Therefore, this study included poisoning data from the periods 2014 to 2020 for Jordan, 2010 to 2020 for Turkey, 2010 to 2020 for India, and 2010 to 2020 for Morocco.

2.1. Poisoning Incidence in Jordan

Data from three national articles were extracted to evaluate poisoning statistics in Jordan. According to the P1PCC, 1,992 poisoning cases were reported in Jordan from 2014 to 2018. Unintentional poisoning was the most common cause of exposure (58.67%), followed by suicidal (25.33%) and therapeutic poisoning (5.33%), as indicated in Table 1. Ingestion (44.23%), dermal routes such as animal stings and bites (41.48%), and inhalation (11.63%) were the main routes of exposure. Conversely, ocular and parenteral routes were the least frequent (2.66%). Medication was the major cause of poisoning, accounting for 45% of reported cases.

Across all age groups, nonsteroidal anti-inflammatory drugs (NSAIDs) and paracetamol (28%) were the most commonly reported medications, followed by supplements and multivitamins (18%), antihistamines (10%), cardiovascular drugs (9%), antibiotics (8%), nervous system drugs (7%), and hypoglycemic agents (3%). Additionally, 14% of poisonings resulted from drug-drug interactions due to multiple drug ingestion. Co-ingestion of antipsychotic (25%), cardiovascular (12.5%), and analgesic (9.3%) medications led to severe medical outcomes [7].

P1PCC reported that among 900 patients poisoned by drugs, nearly half were male (52.22%), primarily within the age range of 21-50 years, followed by the age group of 5 years and under (34.0%). The majority of cases (98.33%) were reported from home [8]. Non-pharmaceutical agents were the second leading cause of poisoning, with animal bites (20%), household products (17%), heavy metals (4%), hydrocarbons (5%), pesticides (4%), and gases (2%) frequently involved, particularly in males.

Accidental poisoning was common among children under 5 years of age (22.62%), with unintentional poisonings (54.12%) and mild medical outcomes (61.45%) constituting the majority of incidents resulting from household product exposure [7].

Another study evaluated poisoning rates in Jordan during the COVID-19 lockdown, reporting that the majority of toxicity cases were due to home exposures, with no occupational exposures reported. Due to the lockdown, incidents of snake bites, stings, toxic plant exposures, and occupational hazards decreased. Most cases (75%) were unintentional exposures, while only 6% were suicidal. The most commonly reported agents were drugs (59%), followed by household agents (15%) and alcohol (7%). Toxic gases and toxic plant exposures were less common. Alcohol poisoning was predominantly observed in females, while drug and household agent poisonings were more prevalent in males. Exposures were reported across different age groups, with children aged 0 to 5 years being the most affected (61%). Notably, the age group of 11 to 15 years experienced a 275% increase in exposures, and those over 50 years experienced a 143% increase. Additionally, reports of toxic gas exposure from chlorine gas resulting from mixing bleach and other household chemicals increased during the lockdown period [9].

Table 1 summarizes the frequency of total cases, gender distribution, causative agents, manner, and route of exposure in poisoning incidents in Jordan.

Table 1. The frequency and proportion of poisoning cases in Jordan and the ratio of total evaluated cases in our study.

		2014-2018	2019-2020	Total evaluated cases in our study (%)
Reported case		1992	553	2545
Gender	**Male**	1156	310	1466 (57.6%)
	Female	836	243	1079 (42.4%)
Causative agents	**Medication**	900	462	1362 (53.52%)
	Non-medication	1092	367	1459 (57.33%)
Manner	**Intentional**	914	34	948 (37.25%)
	Unintentional	1078	519	1597(62.75%)
Route of exposure	**Ingestion**	1329	446	1775(69.74%)
	Other routes	663	87	750(29.47%)

2.2. Poisoning incidence in Turkey

Data from six national articles were extracted to evaluate poisoning statistics in various regions of Turkey from 2010 to 2020. A retrospective study examined a total of 839 poisoning cases among individuals aged 18 and over who were admitted to the Emergency Department (ED) between 2010 and 2015. Suicide attempts accounted for the majority of poisonings (54.4%), followed by accidental exposures (41.7%) and medication errors during treatment (3.9%). Drugs were the most common causative agents (55.4%), followed by carbon monoxide (24.5%), narcotics (14.2%), insecticides (2.4%), alcohol intake (1.2%), caustic substances (1.1%), and mushrooms (0.5%). Polypharmacy (46.8%) was the leading cause of drug poisoning, with paracetamol (9.7%) and selective serotonin reuptake inhibitor antidepressants (SSRIs) (7.8%) being among the most frequently reported medications [10].

In a study conducted between 2011 and 2016 at Antalya Training and Research Hospital, a total of 486 patients were admitted to intensive care units due to acute poisoning. Intentional exposure was predominant (82.7%), with drug ingestion being the primary method (74.3%) among suicide attempts. Multiple drug ingestion (56%) was the leading cause of poisoning, with antipsychotic and antidepressant medications having the highest rates of self-poisoning (21.9%) [11].

Another retrospective study examined 1,027 poisoning cases admitted to Uşak University Medical Faculty Education and Research Hospital between 2015 and 2017. Forty percent of cases were unintentional, while 60% were intentional exposures. The majority of cases (56.8%) occurred in females, with drugs being the most common causative agents (58.4%) [12].

During the period of 2015 to 2019, a total of 148 intentional poisoning cases were admitted to intensive care in Aksaray, with the highest incidence observed among individuals aged 21 years and younger (49.4%). Paracetamol (34.5%) and NSAIDs (14.2%) were among the most common causative agents [13].

Another retrospective study reported 597 poisoning cases between 2015 and 2020, including children aged 0-18 and adults over 19 years old. The majority of cases (56%) occurred in women, with suicide attempts being the leading cause (51.6%). Drugs were the most common causative agents (67.9%) [14].

Finally, a study conducted between 2016 and 2017 reported 1,344 patients admitted to the ED, with intentional poisoning accounting for the majority of cases (55.7%). Recreational substances (21%) and psychiatric drugs (19.4%) were among the most common causative agents [15].

Table 2 summarizes the frequency of total poisoning cases, gender distribution, causative agents, manner, and route of exposure in poisoning incidents in Turkey.

Table 2. The frequency and proportion of poisoning cases extracted from six studies in Turkey and the ratio of total evaluated cases in our study.

		2010-2015	2011-2016	2015-2017	2015-2019	2015-2020	2016-2017	Total (%)
Reported case		839	486	1027	148	597	1344	4441
Gender	**Male**	402	218	444	98	263	671	2096 (47.2%)
	Female	437	268	583	108	334	673	2403 (54.11%)
Causative agents	**Medication**	588	361	600	123	416	769	2857 (64.33%)
	Non-medication	251	125	427	25	181	575	1584 (35.67%)
Manner	**Intentional**	456	402	616	148	181	749	2552 (57.46%)
	Unintentional	350	84	411	0	333	595	1773 (39.92%)
Route of exposure	**Ingestion**	634	316	897	148	543	575	3113 (70.10%)
	Other routes	205	170	130	0	54	769	1328 (29.90%)

During the 2015-2020, 93 of poisoning cases were unknown.

2.3. Poisoning incidence in India

In order to evaluate the pattern of poisoning, India was divided into five main areas: North, South, West, North-east, and South-western regions during the period of 2010-2020. Six studies were included in this review.

During the period of 2010-2014, 505 poisoning cases were reported to the Emergency Department (ED) in the North-eastern region of India. The majority of cases (63.96%) were due to suicide attempts, followed by accidental exposure (24.55%). Pesticides, mainly organophosphates (61.38%), were the most common causative agents [16].

A cross-sectional retrospective study conducted in Western India from 2013 to 2015 reviewed a total of 1,010 patients. Poisoning was more prevalent in males (56.24%) than females (43.76%), with household and agricultural products (56.4%) being the most common agents [17].

Another hospital-based cross-sectional study in the South-western region of India in 2014 evaluated 306 poisoned patients. Suicide attempts accounted for 67% of cases, with pesticides (49%) being the primary agents involved [18].

In 2017, a retrospective study in the Northern region of India assessed 379 poisoned patients admitted to the ED. Pesticides, especially organophosphates, were the main cause of poisoning (25.07%), followed by snake bites (20.32%) and aluminum phosphide (18.73%) [19].

An observational study in the Southern region of India from 2018 to 2019 analyzed 278 acute poisoning cases reported to the ED. Organophosphorus compounds (41%) were the most common agents involved, with suicide attempts (79%) being the main reason for poisoning [20].

During the pandemic, a study in North India reviewed data from 100 patients with a history of poisoning. Corrosive agents (34%) were the most common poison consumed, with a higher mortality rate among males (84.8%) [21].

Another study evaluated 417 poisoning cases in North India. Snake bites (29.4%) and organophosphates (9.3%) were the most common types of poisoning among males, while snake bites (21.3%) and organophosphates (15.4%) were predominant among females. Suicide attempts accounted for 65.2% of cases [22].

Table 3 summarizes the frequency of total poisoning cases, gender distribution, causative agents, manner, and route of exposure in poisoning incidents in India.

Table 3. The frequency and proportion of poisoning cases extracted from six studies in India and the ratio of total evaluated cases in our study.

		2010-2014	2013-2015	2014	2017	2018-2019	2020	Total (%)
Reported case		505	1010	306	379	278	417	2895
Gender	**Male**	298	568	184	227	161	248	1686 (58.24%)
	Female	207	442	122	152	117	169	1209 (41.76%)
Causative agents	**Medication**	21	109	38	20	100	36	324 (11.19%)
	Non-medication	484	901	268	359	178	381	2571 (88.81%)
Manner	**Intentional**	323	539	205	260	221	272	1820 (62.87%)
	Unintentional	19	442	101	119	57	145	883 (30.5%)
Route of exposure	**Ingestion**	359	702	206	302	231	308	2108 (72.82%)
	Other routes	146	308	100	77	47	109	787 (27.18%)

2.4. Poisoning incidence in Morocco

Five studies were reviewed to analyze poisoning patterns in Morocco during the period of 2010 to 2020.

In 2014, a retrospective study reported 2,690 cases of pesticide poisoning, with an average age of 24.63 ± 10.29 years. Suicide attempts accounted for 98.4% of cases, with females being the most commonly affected group. Ingestion was the primary route of exposure (97.8%), with pesticides, including insecticides, rodenticides, herbicides, and fungicides, being the main causative agents [23].

Between 2010 and 2012, a total of 201 poisoned patients were admitted to the Emergency Department (ED) in the North region of Morocco Fez. Women comprised 74.1% of cases, with suicide being the most common mode of poisoning (85%). Pesticides, medications, carbon monoxide, and caustic agents were the most frequent toxic agents involved [24].

A retrospective study from 2012 to 2016 described the epidemiology of benzodiazepine intoxication in Morocco, reporting 1,544 cases. Adults were more prone to benzodiazepine exposure, with females comprising 70% of cases [25].

Another retrospective study from 2014 to 2020 evaluated acute pesticide poisoning in Morocco, reporting 398 cases. Accidental exposure, especially in children, was predominant, with insecticides, rodenticides, and herbicides being the main causative agents [26].

In 2016, a study reported 180 poisoning cases in the South-East of Morocco, with adults and adolescents having the highest incidence of drug poisoning. Female patients experienced more poisoning cases than males, with antipsychotic drugs predominating in overdose cases [27].

Additionally, a retrospective study in 2017 reported 480 suicide cases in Northern Morocco, with hanging being the predominant method used. Men, unmarried individuals, and those residing in rural areas were most affected [28].

In 2020, a retrospective study reported 132 poisoning cases admitted to the pediatric ED, with animal bites being the main cause, including scorpion stings and snake bites. Among medicinal poisoning cases, antiepileptic and neuroleptic drugs were most common [29].

Table 4 summarizes the frequency of total poisoning cases, gender distribution, causative agents, manner, and route of exposure in poisoning incidents in Morocco.

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Table 4. The frequency and proportion of poisoning cases extracted from five studies in Morocco and the ratio of total evaluated cases in our study.

		2010-2012	2014	2016	2017	2020	Total evaluated cases in our study (%)
Reported case		201	2690	180	460	132	3462
Gender	**Male**	52	812	45	330	61	1248 (36.05%)
	Female	149	1742	135	130	69	2076 (59.97%)
Causative agents	**Medication**	45	0	180	31	22	233 (6.73%)
	Non-medication	156	2690	0	429	110	3229 (93.27%)
Manner	**Intentional**	171	2469	73	460	115	3117 (90.03%)
	Unintentional	30	221	101	0	14	336 (9.71%)
Route of exposure	**Ingestion**	189	2630	180	31	91	2932 (84.69%)
	Other routes	12	60	0	429	41	530 (15.31%)

3. DISCUSSION

This review analyzed 20 studies meeting the criteria for poisoning case analyses in Jordan, Turkey, India, and Morocco from 2010 to 2020. Table 5 summarizes the key findings.

A total of 2,545, 4,441, 2,895, and 3,462 poisoning cases were identified in Jordan, Turkey, India, and Morocco, respectively. Ingestion was the primary route of exposure across all countries, but the causative agents and intention of exposure varied.

Non-medication agents, including pesticides, household products, animal bites, caustic agents, and carbon monoxide gas, were predominant in Jordan (57.33%), India (88.81%), and Morocco (93.27%) [8,16,17,23,25]. In contrast, pharmaceutical drugs were the major causative agent in Turkey (64.33%) [10-13,15].

Male populations in Jordan (57.6%) and India (58.24%) were more vulnerable to poisoning, with a higher frequency of accidental poisonings. Unintentional poisonings, particularly due to animal bites, were notable, with India being significantly affected by snakebites, resulting in numerous fatalities [30].

Intentional poisonings were predominant in males in Turkey (57.46%), India (62.87%), and Morocco (90.03%). However, in Turkey and Morocco, a higher proportion of poisoning cases were observed among females (54.11% and 59.97%, respectively).

Studies from Northeastern Morocco and Southwest India highlighted pesticides, such as organophosphates and aluminum phosphide, as common causative agents in intentional poisoning cases, attributed to the agricultural nature and economic factors in these regions [20,28].

Pesticides remain the most common poisoning substances in India and other low- and middle-income countries, contributing to a significant portion of suicides globally [31]. Despite efforts by international regulatory bodies, such as the Environmental Protection Agency (EPA) and Codex Alimentarius Commission (Codex), variations in pesticide standards persist among countries [32].

Table 5. Comparison of various poisoning profiles in Jordan, Turkey, India and Morocco

Country	Year of study	Total cases	Male	Female	Medication	Non-medication	Intentional	Unintentional	Ingestion	Other-route
Jordan	**2014-2020**	2545	1466 (57.6%)	1079 (42.4%)	1362 (53.52%)	1459 (57.33%)	948 (37.25%)	1597 (62.75%)	1775 (69.74%)	750 (29.47)
Turkey	**2010-2020**	4441	2096 (47.2%)	2403 (54.11%)	2857 (64.33%)	1584 (35.67%)	2552 (57.46%)	1773 (39.92%)	3113 (70.10%)	1328 (29.90%)
India	**2010-2020**	2895	1686 (58.24%)	1209 (41.76%)	324 (11.19%)	2571 (88.81%)	1820 (62.87%)	883 (30.5%)	2108 (72.82%)	787 (27.18%)

Morocco	**2010-2020**	3462	1248 (36.05%	2076 (59.97%)	233 (6.73%)	3229 (93.27%)	3117 (90.03%)	336 (9.71%)	2932 (84.69%)	530 (15.31%)

In contrast to Southwest India, drugs were found to be the most causative agent among poisoning cases in Northern India [19]. This difference in the type of poisoning within the country may be attributed to variations in the patterns of use and availability of pesticides. This finding aligns with previously reported studies in Turkey, where poisoning cases are more common in women, and medication is the most common method of poisoning. In Turkey, medication accounted for 64.33% of total poisoning incidence, a significantly higher ratio compared to other studied countries. A study in the Anatolian region of Turkey reported that the majority of intentional poisoning cases were among females, with drugs, particularly paracetamol, being the most frequently used agents [13].

The high rates of suicide among women in certain Turkish regions could be attributed to early marriage and sociocultural pressure. Similar scenarios were observed in poisoning cases reported from other Turkish cities such as Istanbul, Eskisehir, and Afyonkarahisar [10,11,12]. Interestingly, the data also indicated a shift in the intent of poisoning over time. An epidemiological study in the South-East of Morocco between 2004 and 2016 reported a high proportion of intentional poisoning among females, with psycholeptic drugs being the most common causative agents [27]. Despite the need for prescription of such drugs in Morocco, their illegal sale in the contraband market contributes to rising drug misuse.

Data from Northern Morocco between 2017 and 2020 showed that the incidence of suicide is primarily concentrated among adult males who are typically unmarried, reside in rural areas, and have low levels of formal education, with hanging being the most common method [28]. Previous research has shown that unemployment rates significantly contribute to increased suicide rates during certain times [33].

The outbreak of the COVID-19 pandemic has had profound health, psychological, social, and economic consequences worldwide, potentially impacting the pattern and rate of poisoning. A meta-analysis study evaluating suicide incidence before and during the COVID-19 pandemic in 33 countries, including Turkey, the United States, and some European countries, found that although the overall rate of death by suicide remained relatively unchanged during the pandemic, suicidal ideation and suicide attempts were more prevalent, especially among the adult general population and clinical patients [34]. Studies in Jordan and North Cyprus also reported a decrease in suicidal exposure during the pandemic [35,36].

In contrast, the COVID-19 pandemic has had significant effects on the Indian population across various domains. Several studies have highlighted an increase in suicidal attempts due to economic crises among young Indian people. Additionally, mortality rates among poisoned cases have increased, possibly due to delayed presentation to hospitals during lockdowns and shortages of medical staff and facilities [30]. Data from India also show a high rate of unintentional poisoning by household products among children, similar to findings reported in Morocco [25]. Conversely, several studies in Turkey indicate that drugs are the primary cause of unintentional poisoning among children, often attributed to the lack of child-resistant covers and packaging, as well as inadequate child supervision. The frequency of poisoning cases in children has increased during the lockdown period, with hospital admissions mainly due to accidental exposure to scorpion stings and snake bites [34-36].

4. CONCLUSION

The aim of this study was to evaluate and compare the incidence of poisoning in Jordan, Turkey, India, and Morocco during the period of 2010 to 2020. However, several limitations hindered the precise and accurate estimation of poisoning incidence in these regions. The primary limitation was the lack of adequate information and the absence of good-quality and specific registry data. For example, in Jordan, data regarding poisoning cases between 2010 and 2014 could not be found. Therefore, the study period for poisoning incidence may vary among the countries. Additionally, compared to Turkey and India, sufficient reported poisoning cases could not be found for Jordan and Morocco.

It's important to note that not all individuals who experience poisoning seek medical care or report to poison centers. As a result, many cases remain underreported, leading to a potential underestimation of the true incidence of poisoning.

This study highlights that the pattern of poisoning can vary not only over time and between countries but also among different regions within the same country. Analyzing poisoning statistics provides evidence-based data to identify risk factors among different populations and improve overall quality of life.

In conclusion, the data extracted in this study can be utilized to increase public awareness regarding both medicinal and non-medicinal intoxications, ultimately contributing to preventive efforts and better management strategies. However, future research efforts should focus on addressing the limitations identified in this study to obtain a more comprehensive understanding of poisoning incidence in these regions.

5. MATERIALS AND METHODS

The systematic review protocol is reported accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines [6]. The research results yielded numerous articles that were then assessed for relevance based on their title and abstract. In overall, the total number of 41 papers were retrieved among which 20 relevant papers were included in the study. All studies that have reported the total number of admitted patient to hospital, gender, age, causative agent and poisoning attempt were eligible to participate in this review. Relevant epidemiological and clinical observations were recorded in a standard proforma and were entered in Microsoft® Excel 2016. The research methodology is summarized in Figure 1.

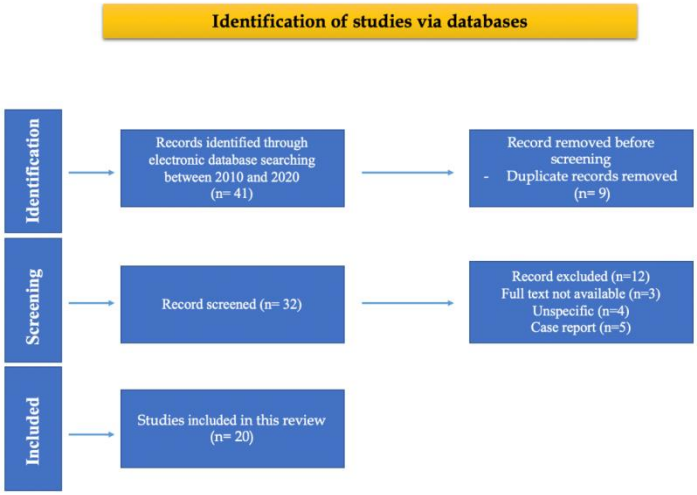

Figure 1. PRISMA diagram for the research methodology used in the review

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