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Clinical characteristics and treatment outcomes of acute phenoxy herbicide poisoning: a systematic review of published cases

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Abstract

Background: 2,4-Dichlorophenoxyacetic acid (2,4-D) is a widely used chlorophenoxy herbicide that causes significant systemic toxicity following acute ingestion. Despite an increase in the number of poisoning cases reported, clinical features, treatment strategies, and prognostic variables are still not fully integrated. The purpose of this systematic review was to provide an overview of the clinical signs, therapeutic approaches, demographics, and results of acute 2,4-D poisoning.

Methods: A systematic review was conducted in accordance with the PRISMA 2020 guideline. English-language case reports and case series describing human acute 2,4-D toxicity were identified through structured database searches and manual reference screening across three databases, with no time restriction. The quality and risk of bias of included case reports and case series were assessed using the JBI Critical Appraisal Checklist, and those scoring ≥50% were considered to have a low-to-moderate risk of bias. The variables extracted were demographic parameters, exposure intent, formulation and dose, clinical aspects, complications, treatment interventions, and survival outcomes.

Results: We identified and included 30 cases from 24 articles, corresponding to 22 original case reports and 2 case series studies. The median age was 34.5 years (IQR: 22–50.8), with males accounting for 70% of cases. Coma occurred in 46.7% of patients, while respiratory failure and hypotension were observed in 20% and 46.7**%**of cases. Urinary alkalization was used in 66.7% of cases, mechanical ventilation in 33.3%, and renal replacement therapy in 26.7%. Overall survival was 66.7%, with death at 33.3%. Non-survivors were more frequently to have coma, shock, respiratory failure, and multiple organ failure.

Conclusion: 2,4-D poisoning is a potentially life-threatening condition characterized by multisystem involvement. Supportive care and urine alkalinization remain the cornerstone of management. However, interpret clinical manifestations with caution, as the included cases were largely based on clinical diagnosis without consistent toxicological confirmation, and outcomes may be influenced by variation in pesticide formulations, including mixed compounds and co-formulants.

Background and rationale

2,4-Dichlorophenoxyacetic acid (2,4-D) remains one of the most widely used phenoxy herbicides worldwide for weed control in cereal crops, turf management, and, increasingly, in herbicide-tolerant agricultural systems. Its ongoing regulatory acceptance in numerous jurisdictions reflects the view that, under limited use, the substance offers agronomic advantages with controllable environmental persistence (1, 2).

However, its widespread presence has inevitably led to both unintentional and deliberate human exposure. Emergency departments and intensive care units continue to encounter cases of acute 2,4-D poisoning. especially in rural areas where access to pesticides is not adequately controlled (3, 4).

Although organophosphates frequently dominate discussions of pesticide toxicity, phenoxy herbicides, such as 2,4-D, account for a significant number of mild to severe poisonings (4, 5). The association between agricultural utility and the risk of 2,4-D poisoning is of concern, as it is simultaneously toxicological, clinical, and public health-oriented (6, 7).

Ideally, clinicians treating 2,4-D intoxication should use a well-defined clinical spectrum, proven prognostic markers, and standardized treatment recommendations based on pooled human data. Studies have examined many processes, including mitochondrial malfunction, membrane instability, and skeletal muscle damage (8, 9).

Compared with organophosphate poisoning, which has well-established antidotal procedures and systematic management algorithms, 2,4-D lacks comparable consensus guidelines. As a result, local practice patterns rather than synthesized evidence are typically employed to inform management decisions, such as urinary alkalinization or extracorporeal elimination (4, 10).

Several studies have previously described the toxicity of phenoxy herbicides. Previous reviews included basic descriptions of clinical features and toxicokinetic, stressing neuromuscular toxicity and the potential role of enhanced elimination (4, 11). Other primary studies identify case-fatality patterns and identify central nervous system depression and refractory acidosis as indications of the severe extent of poisoning (12, 13). While these contributions are important, they are constrained by either aggregation across diverse substances or small sample sizes, which limit generalizability.

The current study fills this gap by thoroughly examining published case reports and case series documenting 2,4-D toxicity within a clinical-toxicological framework that includes exposure assessment, clinical manifestations, therapeutic methods, and complications. By focusing on individual-level case data, we aimed to find patterns in presentation, laboratory abnormalities, complications, treatment interventions, and survival outcomes.

Unlike previous reviews that primarily focus on toxicokinetic or aggregate herbicide classes, this study provides a patient-level synthesis of clinically reported cases of acute 2,4-D poisoning, enabling identification of patterns in clinical presentation, management strategies, and outcomes.

Methods

This systematic review was conducted following the PRISMA guidelines 2020 (14) (Figure 1). The protocol was submitted to the International Prospective Register of Systematic Reviews (PROSPERO 2025: CRD420251271328). Enhance transparency before data extraction and analysis. No major deviations from the registered PROSPERO protocol were made.

A systematic literature search was conducted to identify all published case reports and case series on 2,4-Dichlorophenoxyacetic Acid poisoning. The search was performed on PubMed, Scopus, and Google Scholar with no time limit. The search strategy combined Medical Subject Headings and free-text terms.

The PubMed search query was ("2,4-Dichlorophenoxyacetic Acid" OR "2,4-D") AND (poisoning OR intoxication) AND (“Case Reports” OR “Case Series” OR “case report” OR “case series”). The Scopus query was adapted accordingly. A manual snowballing search was also performed by reviewing the reference lists of retrieved articles. Where case series included multiple patients, each case was extracted and analyzed individually.

Two independent reviewers initially screened all records based on titles and abstracts, followed by a full-text assessment of eligible studies. Any disagreements arising during study selection or data extraction were resolved through discussion between the reviewers, and unresolved discrepancies were adjudicated by a third reviewer.

Studies were included if they met the following criteria: (1) documented cases of acute human poisoning with 2,4-D; (2) provided clinical characteristics, laboratory findings, or management details; and (3) were published in English.

Acute poisoning was defined as a single or short-duration exposure to 2,4-D resulting in clinical symptoms within hours to days of ingestion.

Exclusion criteria included animal studies, environmental exposure studies without clinical outcomes, and cases where 2,4-D was not the primary toxicant. Grey literature, including conference abstracts and non-peer-reviewed reports, was also not included.

Data synthesis and risk of bias assessment

References were managed using Zotero. The methodological quality and risk of bias of included case reports and case series were assessed using the JBI Critical Appraisal Checklist. Each study was evaluated against the checklist items, and those scoring ≥50% were considered to have a **low to moderate risk of bias** (**Supplementary Table 1**).

Extracted data were recorded in a standardized datasheet using Microsoft Excel 2019. Variables collected included publication details, patient demographics, formulation and dose of exposure, clinical presentation (including vital signs and Glasgow Coma Scale score), complications, and management strategies such as gastrointestinal decontamination, urine alkalinization, renal replacement therapy, mechanical ventilation, diuretics, and patient outcomes (**Table 2**).

Data synthesis was performed descriptively using IBM SPSS Statistics 27. Categorical variables were presented as frequencies and percentages, while continuous variables were reported as medians with interquartile ranges (IQR). Percentages were calculated based on available data, and discrepancies reflect missing or inconsistently reported variables.

A meta-analysis was not conducted due to heterogeneity across case reports and case series. The results of the quality appraisal are summarized in Supplementary Table 1.

Results

Most included studies were of moderate methodological quality, with common limitations including incomplete reporting of exposure details and outcomes (Supplementary Table 1).

The review included A total of 24 articles, comprising 22 case reports and 8 cases from 2 case series published reports, which together contributed 30 individual patient cases. (Table 2). The included case reports originated from 13 countries across Asia, Europe, North America, and Africa. The majority of cases were reported from India (12), Croatia (4), Ethiopia (3), Iran (2), Indonesia, Canada, Germany, Nepal, Belgium, the United States, the United Kingdom, Romania, and Denmark, each of which contributed one case. Patients ranged in age from 14 to 80 years. The median age was 34.5 years (IQR: 22–50.8 years).

[Insert Table 2]

Although dose reporting was inconsistent across case reports, higher ingested volumes were generally associated with more severe clinical manifestations, including coma, multiorgan failure, and death. However, due to heterogeneity in reporting and variability in formulation types, a quantitative dose–response relationship could not be established.

Most patients were male, accounting for 70% of reported cases. 86.7% of the exposures resulted from suicidal ingestion, while accidental poisoning was 10% (Table 3). Different formulations of 2,4-D were identified across studies. Ethyl ester formulations were the most frequently reported, followed by dimethylamine.

Table 3
Demographic and Exposure Characteristics of Included Cases (n = 30)

Variable	Category	Frequency (n)	Percentage (%)
Age group	< 15	1	3.3
	15–24	11	36.7
	25–44	6	20.0
	45–64	10	33.3
	≥ 65	2	6.7
Sex	Male	21	70.0
	Female	8	26.7
	Not reported	1	3.3
Intentionality	Suicidal	26	86.7
	Accidental	3	10.0
	Unclear	1	3.3
Formulation	Ethyl ester	9	30.0
	Dimethylamine salt	3	10.0
	Amine salt (including amine)	2	6.7
	Acid formulation	2	6.7
	Isooctyl ester	1	3.3
	Mixed/combination (2,4-D + others)	2	6.7
	Aqueous formulation	1	3.3
	Unspecified / Not reported	10	33.3

[Insert Table 3]

Clinical Characteristics and Complications

Neurological depression was the dominant clinical feature, with nearly half of the patients presenting with coma; Hemodynamic instability and renal complications were also common, particularly among non-survivors. Severe outcomes were predominantly associated with multisystem involvement rather than isolated organ dysfunction. (Table 4). Metabolic problems, specifically metabolic acidosis, were reported in 26.7%. Acute kidney injury occurred in a significant number of patients. The most common respiratory problem was respiratory failure, which accounted for 20% and required ventilatory support.

Most case reports show gastrointestinal symptoms such as vomiting, mucosal damage, and gastrointestinal hemorrhage.

Table 4
Clinical Characteristics and Complications (n = 30)

Variable	Category	Frequency (n)	Percentage (%)
Level of consciousness at presentation	Coma (GCS ≤ 8)	14	46.7
	Altered mental status/confusion	7	23.3
	Conscious	5	16.7
Hemodynamic status	Hypotension/shock	14	46.7
	Hemodynamically stable	19	63.3
Acid–base disturbance	Metabolic acidosis	8	26.7
Renal complications	Acute kidney injury (AKI)	9	30.0
Muscle toxicity	Rhabdomyolysis / markedly elevated CK	7	23.3
Neuromuscular manifestations	Hypertonia/fasciculations/twitching	7	23.3
Respiratory complications	Respiratory depression/failure	6	20.0
Gastrointestinal complications	GI bleeding/erosions / significant vomiting	10	33.3
Infectious complications	Sepsis/pneumonia / secondary infection	6	20.0
Multiorgan failure	Present	3	10.0

Abbreviations: GCS = Glasgow Coma Scale; AKI = Acute Kidney Injury; CK = Creatine Kinase; GI = Gastrointestinal.

[Insert Table 4]

Management Strategies and Outcomes

The primary treatment for acute 2,4-dichlorophenoxyacetic acid (2,4-D) poisoning was supportive therapy; 76.7% of patients received gastrointestinal decontamination, and 43.3% were mechanically ventilated. Urine alkalinization with sodium bicarbonate was the most commonly utilized targeted strategy, accounting for 66.7% (Table 5). However, documentation of urine pH monitoring varied across the study. Renal replacement therapy (RRT) was utilized in 26.7% of the cases. Additional therapies included antibiotic administration for 30% of patients with suspected or confirmed secondary infections.

Table 5
Management Strategies and Outcomes (n = 30)

Variable	Category	Frequency (n)	Percentage (%)
Gastrointestinal decontamination	Gastric lavage ± activated charcoal	23	76.7
Supportive care (IV fluids/monitoring)	Provided	30	100.0
Mechanical ventilation	Required	13	43.3
Urine alkalinization ($NaHCO_3$)	Performed	20	66.7
Diuresis with diuretics	Furosemide or mannitol	9	30.0
Urine pH monitoring	Monitored	9	30.0
Renal replacement therapy (RRT)	Performed	8	26.7
Vasopressor / inotropic support	Required	4	13.3
Antibiotic therapy	Administered	9	30.0
Outcome	Survived	20	66.7
	Died	10	33.3

Abbreviations: IV = Intravenous; $NaHCO_3$ = Sodium Bicarbonate; RRT = Renal Replacement Therapy.

[Insert Table 5]

The majority of cases occurred in the age group 14–24 (12 cases) and 45–64 (10 cases). The large number of deaths occurs between the ages of 14–24 and 45–64. Over all Of 30 patients, 10 died, while 20 survived (Fig. 2).

Prognostic Comparison Between Survivors and Non-survivors

A comparison of clinical characteristics by outcome revealed significant differences in illness severity between survivors and non-survivors. Male patients predominated, with survival rates of 80% and mortality rates of 50%, similar to those of female patients, suggesting that sex distribution did not alter prognosis (Table 6).

Table 6
Comparison of Survivors vs. Non-survivors in Acute 2,4-D Poisoning (n = 30)

Variable	Category	Alive (n = 20) n (%)	Died (n = 10) n (%)
Sex	Male	16 (80%)	5 (50%)
	Female	3 (15%)	5 (50%)
Level of consciousness	Coma (GCS ≤ 8)	9 (45%)	6 (60%)
	Not comatose (GCS > 8)	11 (55%)	0 (0%)
Hemodynamic status	Hypotension/shock	6 (30%)	8 (80%)
	Stable	14 (70%)	2 (20%)
Respiratory failure	Present	1 (5%)	5 (50%)
	Absent	19 (95%)	5 (50%)
Acute kidney injury	Present	4 (20%)	7 (70%)
	Absent	16 (80%)	3 (30%)
Multiorgan failure	Present	0 (0%)	3 (30%)
	Absent	20 (100%)	7 (70%)
Mechanical ventilation	Required	6 (30%)	7 (70%)
	Not required	14 (70%)	3 (30%)
Urine alkalinization	Performed	14 (70%)	6 (60%)
	Not performed	6 (30%)	4 (40%)
Renal replacement therapy (RRT)	Performed	6 (30%)	2 (20%)
	Not performed	14 (70%)	8 (80%)

Abbreviations: GCS = Glasgow Coma Scale; RRT = Renal Replacement Therapy.

There were differences in neurological status across the groups. Patients who died were more likely to have a decreased level of consciousness, accounting for 60%, compared with those with no altered mental status. Hemodynamic instability was observed in 80% of non-survivors, compared with 20% of hemodynamically stable patients. Acute kidney injury was also more common in non-survivors, occurring in 70% compared with those who had no AKI. Ester formulations were more frequently observed in severe or fatal cases, consistent with their higher lipophilicity and toxicity profile; however, this observation should be interpreted cautiously due to the limited sample size. Importantly, multiorgan failure occurred only in patients who died, and urine alkalinization was used in a higher proportion of survivors than in fatal cases.

[Insert Table 6]

DISCUSSION

This systematic review investigates acute 2,4-D poisoning to identify demographic patterns,

clinical manifestations, therapeutic techniques, and outcomes. The findings show that acute 2,4-D poisoning is a multisystem toxic exposure that is primarily caused by intentional ingestion and is characterized by neurological depression, metabolic abnormalities, and high mortality.

The prevalence of young adult males and intentional exposure observed in this analysis is consistent with the global epidemiology of pesticide poisoning. Large epidemiological research indicates that pesticide self-poisoning represents a large contributor to the global suicide burden, particularly in agricultural countries where herbicides are readily available (37, 38). 2,4-D herbicides are widely available worldwide, raising the danger of intentional ingestion despite comparatively low toxicity during occupational exposure when used properly (6).

The variety of formulations reported in this review is consistent with toxicokinetic evidence. indicating that ester and amine derivatives are promptly hydrolyzed after absorption to the corresponding active acids, resulting in identical systemic toxicity profiles regardless of formulation (4, 39).

The clinical manifestations observed in this review can be mechanistically linked to the known toxicological effects of 2,4-D. Mitochondrial dysfunction and uncoupling of oxidative phosphorylation result in impaired ATP production, which likely explains the high prevalence of neurological depression, muscle toxicity, and multiorgan failure(40, 41). The association between severe outcomes and metabolic acidosis or shock observed in our dataset aligns with these pathophysiological mechanisms.

Muscle toxicity and rhabdomyolysis found in some patients are strongly supported by mechanistic investigations indicating direct myotoxic effects mediated by oxidative stress, membrane instability, and disturbed calcium homeostasis in skeletal muscle fibers. (42, 43). The release of intracellular muscle components contributes to renal tubular injury, which explains the high frequency of acute kidney injury (AKI) reported in this review (44).

Cardiovascular instability, such as hypotension and shock, appears to indicate severe systemic poisoning. Experimental models imply that mitochondrial dysfunction and reduced oxidative metabolism limit heart contractility and vascular responsiveness, contributing to circulatory collapse in serious poisoning (45). In addition, metabolic acidosis also impairs heart function and exacerbates tissue hypoxia (46).

The multisystem involvement observed in these systematic reviews of reports reflects the pharmacokinetic features of 2,4-D: rapid gastrointestinal absorption, widespread distribution, and generally intact renal excretion (47).

One of the most clinically noteworthy findings of this study is the prevalence of urine alkalinization among surviving patients. Pharmacokinetic considerations offer strong support for the therapeutic rationale. 2,4-D is a weak acid, and renal elimination is significantly dependent on urinary pH (15, 28).

Urine alkalinization increases chemical excretion in controlled pharmacokinetic trials. Controlled pharmacokinetic investigations reveal that alkaline diuresis significantly increases renal clearance and decreases the elimination half-life of chlorophenoxy herbicides (28, 48). In the absence of contraindications, toxicology guidelines prescribe sodium bicarbonate therapy for mild to severe poisoning (49, 50).

However, the uneven urine pH monitoring seen in the included cases reveals a significant clinical gap. Evidence-based recommendations emphasize monitoring urine pH, electrolyte levels, and volume status to prevent complications such as hypokalemia or fluid overload (51, 52).

Renal replacement therapy (RRT) was employed in certain severe cases. Because 2,4-D has a low molecular weight and little protein binding at dangerous quantities, pharmacological research indicates that extracorporeal excretion may be beneficial (27). Hemodialysis may improve toxin clearance, especially in individuals with severe acidosis, renal failure, or protracted unconsciousness (53).

Nonetheless, evidence is insufficient, and extracorporeal treatment should be considered supplementary rather than first-line therapy until stronger comparative trials are conducted.

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A comparison of survivors and non-survivors indicates that early physiological derangement is more frequently observed among those who died. In this study, mortality was more frequently observed among cases with coma, hypotension or shock, AKI, and multiorgan failure.

These findings are consistent with broader poisoning outcome research, which shows that early neurological depression and circulatory instability are consistently predictors of death outcomes across toxic exposures. Multiorgan dysfunction is most likely the result of chronic mitochondrial injury and systemic metabolic failure, rather than isolated organ toxicity (54, 55).

The greater need for vasopressor medication and mechanical breathing among non-survivors is more indicative of the severity of the illness than of therapeutic failure. Crucially, the prognosis depends primarily on early detection and vigorous supportive care, as there is no specific antidote.

An important consideration in interpreting these findings is the limited availability of toxicological confirmation. Most included case reports relied on clinical diagnosis and exposure history rather than laboratory quantification of 2,4-D levels. Pesticide formulations frequently contain co-formulants such as solvents and surfactants, which may independently contribute to toxicity. In this review, a proportion of cases involved mixed formulations or lacked detailed compositional data, further complicating attribution of clinical effects solely to 2,4-D.

Strengths and Limitations

By combining disparate clinical data, this review offers a comprehensive overview of acute 2,4-D toxicity. However, relying solely on published clinical reports introduces heterogeneity and limits quantitative inference about treatment efficacy. Due to the limited number of case reports, we included one case without sociodemographic characteristics, and we did not strictly follow risk-bias assessment. Another limitation is the absence of consistent toxicological confirmation across included cases. Without laboratory verification, the possibility of misclassification or co-exposure cannot be excluded.

Additionally, publication bias is likely, as case reports tend to preferentially describe severe, unusual, or survivable cases, which may not reflect the full clinical spectrum of 2,4-D poisoning.

Future Directions

To identify optimal alkalinization strategies, define criteria, and identify prognostic biomarkers, prospective toxicology registries and multicenter observational studies are needed. The creation of consensus clinical recommendations in areas with substantial pesticide exposure has the potential to significantly enhance outcomes.

CONCLUSION

Acute 2,4-dichlorophenoxyacetic acid (2,4-D) poisoning is a potentially lethal toxicological emergency induced mostly by deliberate ingestion. The clinical course consists of altered mental status, metabolic abnormalities, and multisystem involvement; hypotension, acute kidney injury, and multiorgan failure are emerging as major markers of a poor prognosis. Focusing on early recognition, supportive care, and appropriate use of urine alkalinization should be promoted, particularly in resource-limited settings. Future prospective multicenter studies are essential to establish evidence-based treatment guidelines and improve patient outcomes.

Abbreviations

- **2,4-D**: 2,4-dichlorophenoxyacetic acid
- **AKI**: acute kidney injury
- **ARF**: acute renal failure
- **BP**: blood pressure
- **CK/CPK**: creatine kinase
- **Cr**: creatinine
- **GCS**: Glasgow Coma Scale
- **GI**: gastrointestinal
- **GL**: gastric lavage

- **HR**: heart rate
- **ICU**: intensive care unit
- **IV**: intravenous
- **LOC**: loss of consciousness
- **LR**: Lactated Ringer's
- **MOF**: multi-organ failure
- **MV**: mechanical ventilation
- **$NaHCO_3$**: sodium bicarbonate
- **NR**: not reported.
- **RRT**: renal replacement therapy

Declarations

1. **Ethical approval**: Not applicable as this study is a systematic review of previously published data.
2. **Consent to participate:** Not applicable.
3. **Consent for publication**: Not applicable.
4. **Clinical Trial Number**: Not applicable.

4. **Availability of data and materials**: Not applicable.

5. **Competing interests**: The authors declare that they have no competing interests.

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7. Author's contribution

S.G.W, and B.T.H: conceptualization, data curation, formal analysis, literature review, and drafting the manuscript. M.T.B: data curation, literature review, critical review, revision, and approval. E.E.M, W.W, and E.F.Y: data curation, critical review, revision, and approval.

R.S., M.K., M.K, N.K.W and G.B.A: conceptualization, data curation, and approval. T.K., S.F.M., T.G.G., M.M.T, G.D.A, and D.G.N: data curation, critical review, revision, and approval. All the authors have read and approved the final version of the manuscript.

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Table

Table 2 is available in the supplementary files section

Figures

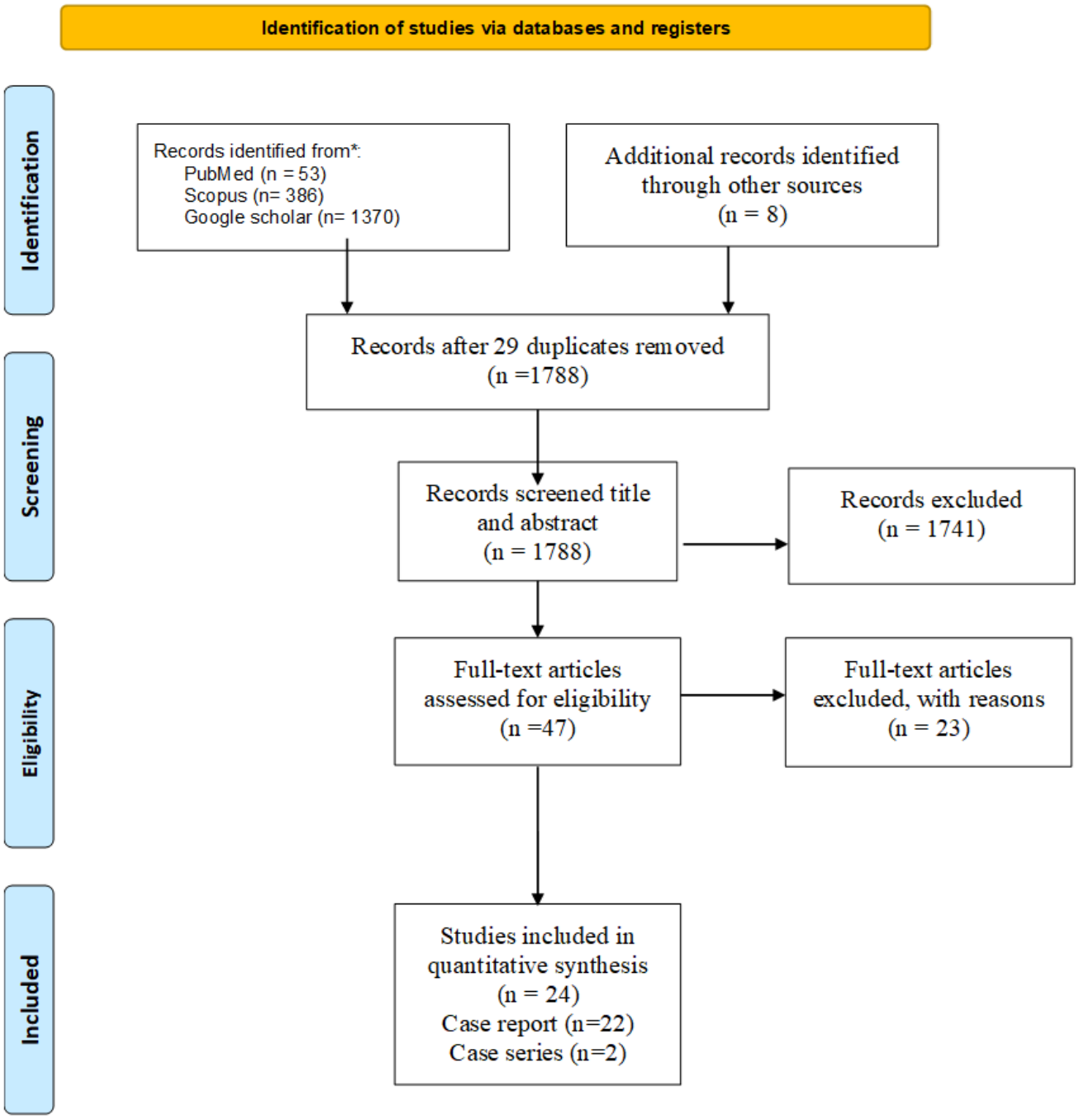


Figure 1

PRISMA flow diagram illustrating the systematic literature search and study selection process for cases of 2,4-dichlorophenoxyacetic acid (2,4-D) poisoning

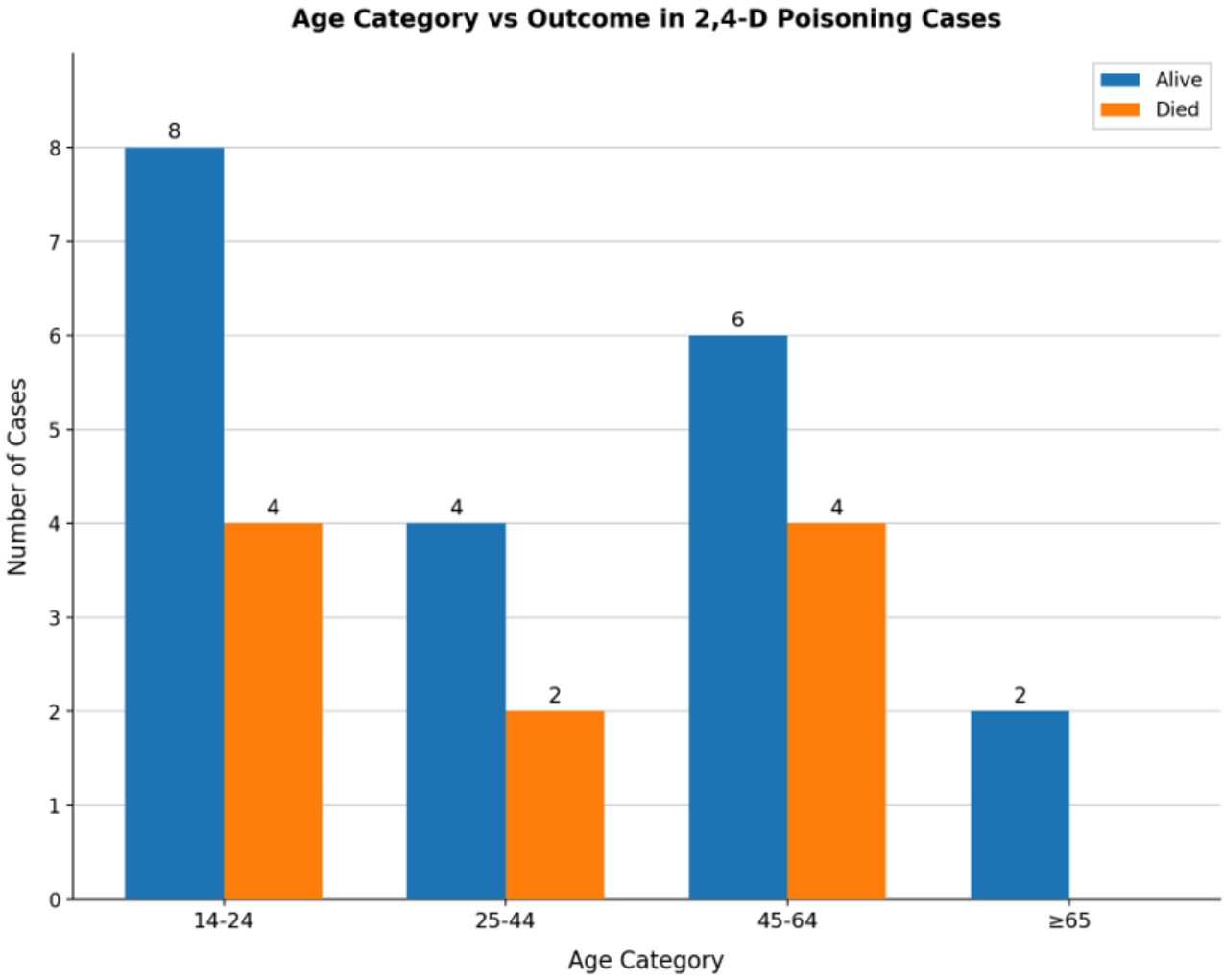


Figure 2

Distribution of age categories and clinical outcomes in acute 2,4-D poisoning cases (n = 30).

Supplementary Files

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- SupplementaryTable1.docx
- Table2.docx