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Perforated peptic ulcers in children: a systematic review

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Abstract

Background Perforated peptic ulcers (PPU) represent a significant complication of peptic ulcers, associated with high mortality. As no systematic review of the literature on PPU in children currently exists, this study aims to summarize findings from studies focusing on its risk factors, etiology, treatment modalities, and outcomes.

Methods A systematic review was conducted following the PRISMA guidelines. A literature search was performed on 24 November 2024, using four electronic databases: Web of Science, Scopus, PubMed, and ScienceDirect. The inclusion criteria were studies published in English, focusing on perforated peptic ulcers in paediatric patients. The exclusion criteria were: studies published in languages other than English; publication formats such as conference abstracts, personal communications, and single case reports; studies focusing on non-perforated peptic ulcers; studies involving participants > 18 years; and studies reporting ulcer perforations outside the stomach or duodenum.

Results Out of 1963 records identified, 12 studies met the inclusion criteria and were included in the review. A total of 239 children with perforated peptic ulcers were analyzed, with a median age of 11 years (range 3.2–16.5 years). The results indicate that ulcer perforations were more prevalent in males (74.8%). Furthermore, duodenal perforations (73%) were more common than gastric perforations (27%). The most commonly reported symptoms were abdominal pain ($n = 175$, 73.2%), vomiting ($n = 82$, 34.3%), peritoneal signs ($n = 79$, 33%), and fever ($n = 38$, 15.9%). Subdiaphragmatic free air was detected in 141 patients (58.9%). Of the total number of patients, 207 (86.6%) were treated surgically, while 32 (13.4%) received conservative treatment. Regarding the surgical approach, most patients underwent open surgery ($n = 143$, 69%) compared to laparoscopic repair ($n = 64$, 31%). Among the surgical procedures, 114 involved simple sutures, with or without an omental patch. Postoperative complications were reported in 30 children (14.5%). Reoperation was required in 4 patients (1.9%), and mortality was recorded in 9 patients (3.8%).

Conclusions PPU was more prevalent in males and predominantly located in the duodenum. Ulcer suturing, with or without an omental patch, was the most commonly utilized treatment modality, demonstrating a relatively low complication rate. Further studies are needed to provide more comprehensive and unbiased evidence on PPU in children.

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Keywords Peptic ulcer perforation, Peptic ulcer disease, Peptic ulcer, Perforation, Stomach ulcer, Duodenal ulcer, Children, Surgery, Laparoscopy

Introduction

Peptic ulcer disease (PUD) is a relatively rare but clinically significant condition in the pediatric population, characterized by mucosal injury of the stomach or duodenum resulting from an imbalance between aggressive luminal factors and mucosal defense mechanisms [1, 2]. Although peptic ulcers are more commonly diagnosed in adults, their incidence in children has increased over recent decades, largely due to improved access to endoscopic procedures [1–4].

Pediatric peptic ulcers are classified as primary, most often associated with *Helicobacter pylori* infection, or secondary, typically resulting from physiological stress, systemic illness, or the use of medications such as nonsteroidal anti-inflammatory drugs (NSAIDs) [5–7]. Among the potential complications of PUD, perforated peptic ulcer (PPU) represents a rare but life-threatening surgical emergency in children, associated with significant morbidity and mortality if not recognized and managed promptly [8–10].

Children with PPU may initially present with nonspecific symptoms of peptic ulcer disease; however, the onset of acute abdominal pain, peritoneal signs, and a systemic inflammatory response usually indicates perforation [8, 9]. The diagnosis is based on clinical suspicion and radiological imaging — most commonly plain radiographs demonstrating pneumoperitoneum — and is confirmed by computed tomography (CT) in equivocal cases [8, 11]. Surgical repair, typically performed via primary closure with an omental patch (Graham patch), remains the standard treatment, with laparoscopic approaches being increasingly utilized [12].

PPU in the pediatric population is infrequently reported in the literature, with most available data derived from isolated case reports, small case series, or retrospective studies with limited sample sizes. To date, no systematic review has synthesized the available evidence regarding the presentation, management strategies, and outcomes of PPU in children. Therefore, the aim of this systematic review is to summarize the current literature on PPU in the pediatric population, with a particular focus on epidemiology, clinical presentation, diagnostic modalities, treatment approaches, and patient outcomes.

Methods

Inclusion and exclusion criteria

Studies were included based on the following criteria: the study design had to be either retrospective (including case series and case-control studies) or prospective studies. Only articles published in English were considered. Eligible studies specifically addressed perforated peptic ulcers in the pediatric population, defined as individuals under 18 years of age. In addition, the anatomical site of the ulcer perforation had to be localized to the stomach and/or duodenum.

The exclusion criteria were: studies published in languages other than English; study formats such as conference abstracts, personal communications, and single case reports; studies focusing on non-perforated peptic ulcers; studies involving participants older than 18 years; and studies reporting ulcer perforations outside the gastric or duodenal regions.

Information sources and literature search strategy

A systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [13]. The search was performed by reviewer S.V. on 24 November 2024, using four electronic databases: Web of Science, Scopus, PubMed, and ScienceDIRECT. The Boolean logical operator expressions were used to search within databases, as follows:

PubMED: (children) AND (perforated ulcer OR perforation) AND (peptic ulcer OR gastric ulcer OR duodenal ulcer). The search was conducted with filters where the language was "English, and age was: "Child: birth-18".

Web of Science: TS=((children) AND (perforated ulcer OR perforation) AND (peptic AND ulcer OR gastric AND ulcer OR duodenal AND ulcer)). The search was conducted with filters where the language was "English".

Scopus: (children) AND (perforated AND ulcer OR perforation) AND (peptic AND ulcer OR gastric AND ulcer OR duodenal AND ulcer) AND (LIMIT-TO (LANGUAGE, "English")) AND (LIMIT-TO (DOCTYPE, "ar")).

ScienceDIRECT: (children) AND (perforated ulcer OR perforation) AND (peptic ulcer OR gastric ulcer OR duodenal ulcer). The search was conducted with filters where the language was "English," article type was research article, review article, subject areas were medicine and dentistry, and nursing and health professions. Access type was open access and open archive.

After completing the database search, reviewers S.V. and Z.P. manually examined the reference lists of the included articles to identify any further relevant studies.

Study selection and data extraction

Following the removal of duplicate records, two reviewers (S.V. and Z.P.) collaboratively screened the titles and

abstracts of all studies identified through the electronic database search. Studies that met the predefined inclusion and exclusion criteria were selected for full-text assessment. After reviewing the full-text articles, those that did not fulfill the eligibility criteria were excluded. Additionally, S.V. and Z.P. performed a manual search of reference lists to identify and include any further studies that met the inclusion criteria. For each study included in the systematic review, when possible, the following data were extracted: the first author of the article, year of publication, study period, study design, country, study period, total number of participants, number of participants by sex, age, localization of ulcer perforation, ulcer diameter, *Helicobacter pylori* presence, drug use, family history of perforated ulcer disease, symptoms, radiology findings, laboratory results, etiology of ulcer perforation, preoperative risk factors, type of treatment, type of surgical management, intraoperative complications, postoperative complications, reoperation/reintervention, length of hospital stay, postoperative treatment, follow-up period, and mortality. Data extraction was conducted by reviewers S.V. and Z.P.

Assessment of the methodological quality and the risk of bias of studies

Methodological quality and potential sources of bias in the included studies was assessed by S.V and Z.P. using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Case Series Studies [14]. JBI Critical Appraisal Checklist for Case Series Studies comprises nine questions: 'Q1 = Were there clear criteria for inclusion in the case series?'; 'Q2 = Was the condition measured in a standard, reliable way for all participants included in the case series?'; 'Q3 = Were valid methods used for identification of the condition for all participants included in the case series?'; 'Q4 = Did the case series have consecutive inclusion of participants?'; 'Q5 = Did the case series have complete inclusion of participants?'; 'Q6 = Was there clear reporting of the demographics of the participants in the study?'; 'Q7 = Was there clear reporting of clinical information of the participants?'; 'Q8 = Were the outcomes or follow-up results of cases clearly reported?'; 'Q9 = Was there clear reporting of the presenting site(s)/clinic(s) demographic information?'; and 'Q10 = Was statistical analysis appropriate?' [14].

Two independent reviewers (S.V. and Z.P.) responded to these questions with either 'Yes', 'No', 'Unclear', or 'Not applicable'. Disagreements between the reviewers at various stages of the review were resolved through discussion. A 'Yes' response contributed one point, while other responses did not contribute points. The total scores, ranging from 0 to 10 (case series studies), was the sum of all 'Yes' responses. The overall quality assessment score was calculated by dividing the total score by the maximum possible score, expressed as a percentage. Methodological quality was ranked as low (less than 33%), medium (33–66%), or high (over 66%).

Upon assessing the methodological quality of the studies, ten were found to be of high quality, while two were rated as medium quality according to the total quality assessment score (Table 1).

Statistical analysis

Nominal variables were descriptively presented as absolute and relative frequencies (percentages). The means of numerical variables were reported as arithmetic mean ± standard deviation in cases of normal distribution and as median and interquartile range for asymmetrical distributions. The normality of the distribution was assessed using the Kolmogorov-Smirnov test.

Results

Study selection

A search of the databases identified 1963 records, of which 184 were duplicates that were removed before the screening phase. Based on titles and abstracts, 1768 records were excluded during the screening phase. Subsequently, 11 papers were read in full, and 3 were excluded based on the inclusion and exclusion criteria. Additionally, four records were included after manually reviewing the reference lists of the selected records. Ultimately, 12 studies were included in the systematic review (Table 2). The PRISMA flow diagram of the literature search is presented in Fig. 1.

Study characteristics and summary of the included studies

All included studies were retrospective in design. A total of 239 children with perforated peptic ulcer (PPU) were analyzed. Sex-related data were available for 230 participants, of whom 172 (74.8%) were male and 58 (25.2%) were female. The median age was 11.0 years (range 3.2–16.5 years). The main characteristics of the studies included in this systematic review are presented in Table 2.

Four studies provided data on medication use in patients with perforated peptic ulcer (PPU), most commonly reporting the use of non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids. The most frequently reported clinical symptoms included abdominal pain ($n = 175$, 73.2%), vomiting ($n = 82$, 34.3%), peritoneal signs ($n = 79$, 33%), and fever ($n = 38$, 15.9%). Subdiaphragmatic free air was identified in 141 patients (58.9%) using radiography or computed tomography (CT). Data on the localization of the perforation were available for 222 patients, with duodenal perforations reported in 162 (73%) patients and gastric perforations in 60 (27%). Among the 239 children with PPU, surgical treatment was performed in 207 (86.6%), while 32 (13.4%)

Table 1 Methodological quality assessment of studies using JBI critical appraisal checklist for case series studies

JBI Critical Appraisal Checklist for Case Series Studies	Bülbül and Şalcı, 2024. [15]	Wang et al., 2023. [16]	Shen et al., 2023. [17]	Sayan et al., 2021. [18]	Yan et al., 2019. [19]	Reusens et al., 2016. [20]	Wong et al., 2015. [21]	Yildiz et al., 2014. [22]	Hua et al., 2007. [23]	Wong et al., 2006. [24]	Edwards et al., 2005. [25]	Dunn et al., 1983. [26]
Q1	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
Q2	Yes	Yes	Yes	Yes	Yes	U	Yes	Yes	Yes	Yes	Yes	Yes
Q3	Yes	Yes	Yes	Yes	Yes	U	Yes	Yes	Yes	Yes	Yes	Yes
Q4	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Q5	Yes	Yes	Yes	U	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Q6	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Q7	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Q8	No	No	Yes	No	Yes	U	U	U	No	No	Yes	No
Q9	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Q10	Yes	Yes	Yes	No	Yes	Yes	Yes	NA	Yes	NA	Yes	NA
The overall quality assessment score	90%	90%	100%	60%	100%	60%	90%	80%	90%	80%	100%	80%
Methodological quality of study	H	H	H	M	H	M	H	H	H	H	H	H

U = Unclear, NA = Not applicable, H = high, M = medium

were managed conservatively. Of those who underwent surgery, 143 (69%) were treated with open repair, whereas laparoscopic repair was performed in 64 (31%) cases. The majority of surgical procedures ($n = 114$) involved simple suturing or simple suturing combined with an omental patch. Postoperative complications occurred in 30 (14.5%) of the 207 surgically treated patients. Reoperation or reintervention was required in 4 patients (1.9%), and mortality was reported in 9 patients (3.8%).

A summary of family history of peptic ulcer disease, medication use, *Helicobacter pylori* status, clinical presentation, radiological findings, and laboratory results is provided in Table 3. Preoperative risk factors, surgical management, intraoperative and postoperative complications, reoperation or reintervention, and mortality are presented in Table 4. Finally, postoperative treatment, length of hospital stay, and follow-up data are summarized in Table 5.

Discussion

To date, this is the first systematic review of PPUs in the pediatric population. The analysis revealed that PPUs were more prevalent in males and were most commonly located in the duodenum. The most frequently reported clinical manifestations included abdominal pain, vomiting, signs of peritonitis, and fever. Additionally, subdiaphragmatic free air was the most commonly observed radiographic finding associated with PPU in children. In terms of medication use, NSAIDs and corticosteroids were the most frequently reported drugs associated with PPU. Regarding treatment approaches, primary ulcer suturing, either alone or reinforced with an omental patch, was the most commonly employed surgical technique, demonstrating a relatively low rate of postoperative complications.

Perforated peptic ulcers by sex

From an epidemiological perspective, the incidence of PPU has significantly changed since the 1980s, with studies worldwide reporting a decline in perforation rates [27–29]. A major contributor to this reduction has been the identification and medical treatment of *Helicobacter pylori*, including the use of proton-pump inhibitors [9, 27–29]. Over the years, a decrease in the incidence of PPU has been documented. However, when comparing incidence by sex, studies indicate an increase in the prevalence of perforated peptic ulcers among women. The initial male-to-female ratio of 4–5:1 has now shifted, in some countries, to approximately 1:1 [9, 29]. It has also been noted that in middle-income and low-income countries, men often exhibit a higher incidence of peptic ulcer disease and perforation compared to those in high-income countries [9, 29]. The results of studies included in this systematic review suggest that perforated PPU in

Table 2 Key characteristics of the studies included in the systematic review

Author	Study design	Country	Study period	Sample size	Sample (male/female)	Age
Bülbül and Şalcı, 2024. [15]	Retrospective	Turkey	June 2013–June 2023	11	9/2	16 (14–17)
Wang et al., 2023. [16]	Retrospective	China	January 2013–December 2021	30	21/9	3 (0.1–17)
Shen et al., 2023. [17]	Retrospective	China	January 2007–December 2021	45	35/10	13 (0.3–15)
Sayan et al., 2021. [18]	Retrospective	Turkey	January 2007–June 2020	9	N/A	15 (12–17)
Yan et al., 2019. [19]	Retrospective	China	January 2013–December 2016	20	17/3	6.6 (0.3–14)
Reusens et al., 2016. [20]	Retrospective	Belgium	1998–2015	5	3/2	11 (3–17)
Wong et al., 2015. [21]	Retrospective	China	2004–2014	13	9/4	15 (6–18)
Yildiz et al., 2014. [22]	Retrospective	Turkey	2005–2013	9	8/1	13.2 (6–17)
Hua et al., 2007. [23]	Retrospective	Taiwan	January 1986–June 2005	52	42/10	14.2 (2–18)
Wong et al., 2006. [24]	Retrospective	China	January 1999–February 2006,	17	15/2	14 (11–17)
Edwards et al., 2005. [25]	Retrospective	USA	January 1980–December 2003	29 (16 had perforated ulcer)	14/15 (perforated ulcer = 8/8)	3.5 (0.8–14.5) (patients with perforated ulcer = 4.3 (0.8–14.8))
Dunn et al., 1983. [26]	Retrospective	USA	1972–1982	39 (12 had perforated ulcer)	17/22 (perforated ulcer = 5/7)	Patients with perforated ulcer: 1.2 (0.1–17)

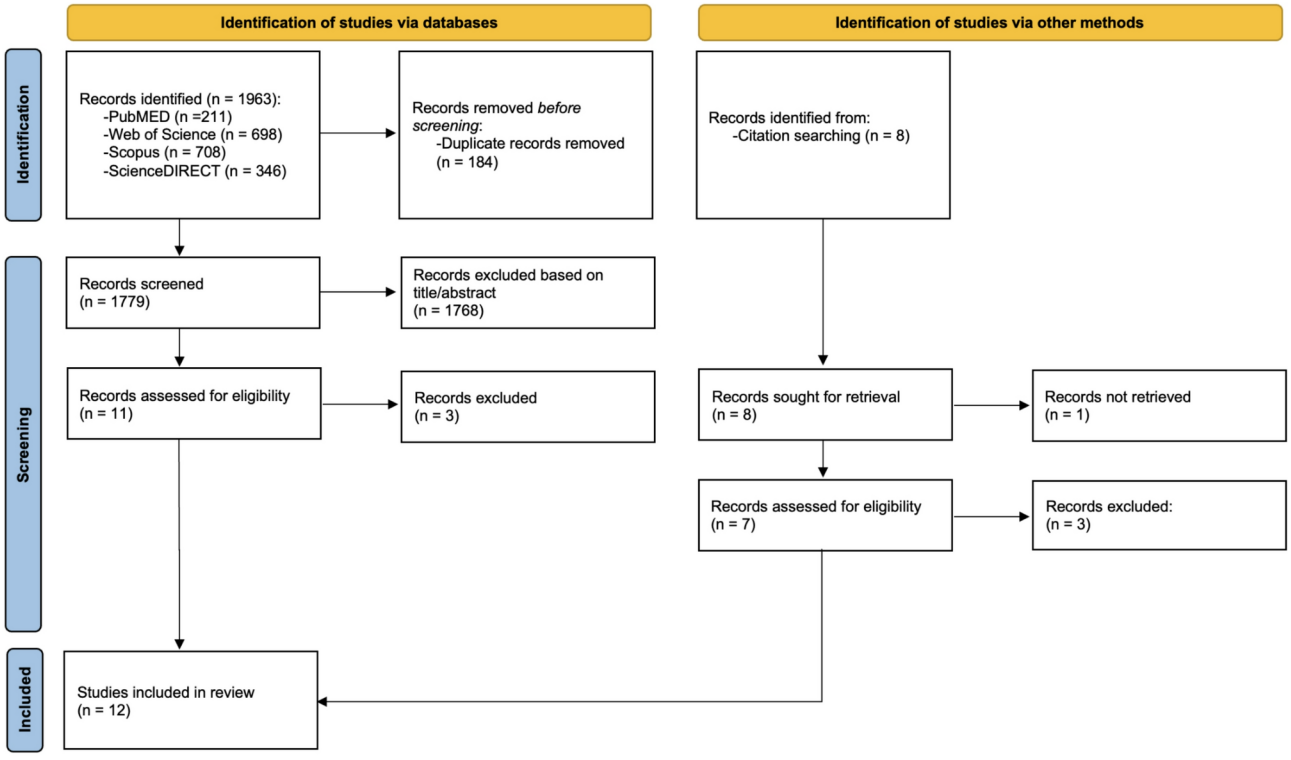

Fig. 1 PRISMA flow diagram of the literature search

Table 3 Family history, medication use, *Helicobacter pylori*, symptoms, radiology and laboratory findings of patients with perforated peptic ulcers

Author	Localization	Ulcer diameter (cm)	Family history	Medication use	H. pylori	Symptoms	Radiology findings	Laboratory findings
Bülbül and Şalcı, 2024. [15]	Gastric ($n=8$, 72.7%) Duodenal ($n=3$, 27.3%)	0.6 (0.5–1.0)	N/A	N/A	N/A	Abdominal pain ($n=10$, 90.9%), vomiting ($n=4$, 36,4%), and confusion ($n=1$, 9,1%)	Free air under the diaphragm was detected in all patients ($n=11$, 100%) on standing direct abdominal radiograph or computed tomography	N/A
Wang et al., 2023. [16]	Gastric ($n=21$, 70%) Duodenal ($n=9$, 30%)	Laparoscopy group (0.8 ± 1.7) Laparotomy group (1.0 ± 2.0)	N/A	N/A	N/A	Abdominal pain ($n=30$, 100%), peritoneal sign ($n=30$, 100%), and hypotension ($n=7$, 23.3%)	Free air under the diaphragm ($n=30$, 100%)	Laparoscopy group ($n=19$, 63.3%); CRP = 9.42 ± 39.42 Laparotomy group ($n=11$, 36.7%); CRP = 41.14 ± 40.64
Shen et al., 2023. [17]	Duodenal ($n=45$, 100%)	0.5 (0.2–1.0)	N/A	N/A	Surgery group ($n=8$, 62%), and conservative group (not specified)	Surgery group ($n=13$); abdominal pain ($n=13$, 100%), onset of abdominal pain within 24 h ($n=6$, 50%), vomiting ($n=10$, 76.9%), fever ($n=11$, 84.6%) Conservation group ($n=32$); abdominal pain ($n=32$, 100%), onset of abdominal pain within 24 h ($n=24$, 75%), vomiting ($n=24$, 75%), fever ($n=21$, 65.6%)	Free air under the diaphragm; standing direct abdominal radiograph ($n=15$, 33.3%)	CRP = 16.5 (8.75, 95) mg/dl Leukocytes ($\times10^9$/L) = 13.8 ± 4.52
Sayan et al., 2021. [18]	Duodenal ($n=9$, 100%)	All ulcers were < 2 cm	N/A	NSAID ($n=7$, 77.8%)	N/A	Abdominal pain ($n=9$, 100%), loss of appetite ($n=9$, 100%), and vomiting ($n=9$, 100%)	Free air under the diaphragm; standing direct abdominal radiograph ($n=6$, 66.7%)	N/A
Yan et al., 2019. [19]	Gastric ($n=9$, 45%) Duodenal ($n=11$, 55%)	0.6 (0.5–1)	$n=6$ (33.3%)	Corticosteroids ($n=2$, 10%)	$n=6$ (30%)	Abdominal pain ($n=10$, 50%) (duration of abdominal pain = 72 (5-120) hours), abdominal distension ($n=9$, 45%), vomiting ($n=13$, 65%), hematochezia ($n=3$, 15%), and melena ($n=2$, 10%)	Free air under the diaphragm; standing direct abdominal radiograph ($n=16$, 80%)	N/A
Reusens et al., 2016. [20]	Gastric ($n=4$, 80%) Duodenal ($n=1$, 20%)	N/A	N/A	N/A	$n=2$ (40%)	N/A	N/A	N/A
Wong et al., 2015. [21]	Gastric ($n=2$, 15.4%) Duodenal ($n=11$, 84,6%)	Laparoscopy group (0.5 ± 0.2) Laparotomy group (2.4 ± 0.5)	N/A	NSAID ($n=1$, 7.7%) Corticosteroids ($n=1$, 7.7%)	$n=2$ (15%)	Acute onset of abdominal pain ($n=13$, 100%)	Free air under the diaphragm; standing direct abdominal radiograph ($n=3$, 23.1%), and CT scan ($n=2$, 15.4%)	N/A
Yildiz et al., 2014. [22]	Duodenal ($n=9$, 100%)	N/A	$n=6$ (66.7%)	N/A	$n=5$ (urea breath test)	Abdominal pain ($n=6$, 66.7%)	Free air under the diaphragm; standing direct abdominal radiograph ($n=3$, 33.3%)	N/A

Table 3 (continued)

Author	Localization	Ulcer diameter (cm)	Family history	Medication use	H. pylori	Symptoms	Radiology findings	Laboratory findings
Hua et al., 2007. [23]	Gastric (*n* = 11, 21.2%) Duodenal (*n* = 41, 78.8%)	N/A	*n* = 8 (15.4%)	N/A	*n* = 4 (not specified how many were tested for H. pylori)	Abdominal pain (*n* = 52, 100%), peritoneal sign (*n* = 49, 94.2%), vomiting (*n* = 22, 42.3%), fever (*n* = 6, 11.5%), hematemesis (*n* = 4, 7.7%).	Free air under the diaphragm; standing direct abdominal radiograph (*n* = 43, 82,7%)	N/A
Wong et al., 2006. [24]	Gastric (n = N/A) Duodenal (n = N/A)	N/A	N/A	Corticosteroids (*n* = 1, 5.8%)	*n* = 16 (94.1%)	N/A	N/A	N/A
Edwards et al., 2005. [25]	Gastric (*n* = 5, 31.3%) Duodenal (*n* = 11, 68.7%)	N/A	N/A	NA/	*n* = 1 (four patients were tested)	N/A	N/A	N/A
Dunn et al., 1983. [26]	Duodenal (*n* = 12, 100%)	N/A	N/A	N/A	N/A	N/A	Free air under the diaphragm; standing direct abdominal radiograph (*n* = 12, 100%)	N/A

N/A = not available; NSAID = Nonsteroidal anti-inflammatory drugs

children have generally been more common in males. However, retrospective studies from the USA and Belgium have shown a similar distribution of perforated peptic ulcers between sexes in children. This finding aligns with evidence from some studies indicating that in socioeconomically more developed countries, sex-specific differences in the incidence of PPU are less pronounced [9, 28–30].

Medication use

Four studies included in the systematic review examined medication use and reported the utilization of NSAIDs and corticosteroids in some patients with perforated ulcers. The link between the formation of peptic ulcers and their subsequent perforation and the use of these medications can be explained by their mechanisms of action: NSAIDs inhibit cyclooxygenases, while corticosteroids inhibit phospholipase A2, both of which result in reduced prostaglandin synthesis [31, 32]. This reduction subsequently decreases the induction of bicarbonate and protective mucus production. Additionally, the diminished levels of prostaglandins contribute to dysregulation of mucosal microcirculation, resulting in reduced perfusion, which further impairs the reparative potential of the mucosa. Furthermore, lower prostaglandin levels may contribute to disinhibition of parietal cell activity, increasing hydrochloric acid synthesis, which exacerbates the risk of ulcer formation [32, 33]. NSAIDs may interact with the intestinal mucus layer and the phospholipid bilayer of cell membranes, disrupting these protective structures. Additionally, they uncouple mitochondrial oxidative phosphorylation, leading to increased intestinal permeability. This compromise in barrier function potentially heightens the likelihood of low-grade local inflammation, ultimately increasing the risk of developing peptic ulcers [34].

Helicobacter pylori

Helicobacter pylori is a gram-negative spiral bacterium capable of surviving in the acidic environment of the stomach due to its synthesis of urease, which breaks down urea into ammonia and carbon dioxide. Ammonia contributes to alkalinization, thereby protecting the bacteria from gastric acid [35, 36]. Notably, *Helicobacter pylori* synthesizes cytotoxins such as vacuolating cytotoxin A (VacA), the cytotoxin-associated gene A product (CagA), proteases, and phospholipases, which collectively contribute to the damage of the protective mucosal layer on the surface of the stomach and duodenum [36]. This damage is further exacerbated by synergistic local pro-inflammatory effects, increasing the likelihood of developing gastric and duodenal ulcers as well as the risk of complications such as PPU [36]. A systematic review and meta-analysis of 198 studies conducted over the past 30 years involving 152 650 patients established a global prevalence of *Helicobacter pylori* infection in children of 32.3% (95% CI, 27.3–37.8%) [37]. The studies included in our systematic review indicate that children with PPU exhibited a similar prevalence of *Helicobacter pylori* infection as children worldwide, according to the

Table 4 Preoperative risk factors, surgical management, intra/postoperative complications, reoperation, and mortality of patients with perforated peptic ulcer

Author	Localization	Preoperative risk factors	Surgical management	Intraoperative complications	Postoperative complications	Reoperation, reintervention	Mortality
Bülbül and Şalcı, 2024. [15]	Gastric (*n* = 8, 72.7%) Duodenal (*n* = 3, 27.3%)	N/A	Laparotomy (*n* = 11, 100%);	N/A	*n* = 3 (27.3%); opening in the wound, incisional hernia	*n* = 1 (9.1%)	*n* = 0
Wang et al., 2023. [16]	Gastric (*n* = 21, 70%) Duodenal (*n* = 9, 30%)	N/A	Laparotomy group (*n* = 11, 36.7%); simple suture (*n* = 11) Laparoscopy (*n* = 19, 63.3%); simple suture (*n* = 16), simple suture, omental patch repair (*n* = 2), and gastroscopic closure using clips (*n* = 1)	N/A	*n* = 3 (10%); based on Clavien-Dindo classification in the laparoscopy group: Grade 1 (*n* = 1) Grade 3b (*n* = 1) Laparotomy group: Grade 2 (*n* = 1)	N/A	*n* = 2 (6.7%) due to severe sepsis and multiple organ dysfunction syndrome, including one with fungal peritonitis
Shen et al., 2023. [17]	Duodenal (*n* = 45, 100%)	N/A	Laparotomy (*n* = 9, 20%); simple suture (*n* = 9) Laparoscopy (*n* = 4, 8.9%); simple suture (*n* = 4) Conservative treatment (*n* = 32, 71.1%)	N/A	*n* = 1 (7.7%); wound infection	*n* = 0	*n* = 0
Sayan et al., 2021. [18]	Duodenal (*n* = 9, 100%)	One patient had abdominal pain in the right lower quadrant, and vomiting that started four days ago (gangrenous appendicitis was detected, and an appendectomy was performed)	Laparotomy (*n* = 9, 100%); simple suture and omentum patch (*n* = 9)	*n* = 0	*n* = 0	*n* = 0	*n* = 0
Yan et al., 2019. [19]	Gastric (*n* = 9, 45%) Duodenal (*n* = 11, 55%)	Blunt trauma (*n* = 1), Bochdalek's hernia (*n* = 2), heterotopic pancreas (*n* = 1), Acute urticaria (*n* = 4), dexamethasone (*n* = 4), methylprednisolone (*n* = 1), Meckel's diverticulum (*n* = 1), R retrobulbar neuritis (*n* = 1), severe pneumonia (*n* = 1), pleural effusion (*n* = 1), Rotavirus gastroenteritis (*n* = 1)	Laparotomy (*n* = 13, 65%); simple suture (*n* = 6); simple suture, omentum patch (*n* = 2); simple suture, omentum patch, and resection of the Meckel diverticulum with enteroanastomosis (*n* = 1) Distal gastrectomy, gastrojejunal Roux-en-Y anastomosis (*n* = 3), simple suture, closed thoracic drainage, repair of pleura–peritoneal hiatus hernia, pleural decortication (*n* = 1) Laparoscopy (*n* = 7, 35%); simple suture (*n* = 7)	Gastroduodenal artery aneurysm rupture (GAAR) and upper gastrointestinal hemorrhage (UGIB) (*n* = 1) after Distal gastrectomy, gastrojejunal Roux-en-Y anastomosis	*n* = 2 (10%); adhesive ileus (*n* = 1), wound infection (*n* = 1)	*n* = 2 (10%); due to GAAR and UGIB	*n* = 0

Table 4 (continued)

Author	Localization	Preoperative risk factors	Surgical management	Intraoperative complications	Postoperative complications	Reoperation, reintervention	Mortality
Reusens et al., 2016. [20]	Gatric (*n* = 4, 80%) Duodenal (*n* = 1, 20%)	N/A	Laparoscopy (*n* = 5, 100%); simple suture and omentum patch (*n* = 5)	*n* = 0	*n* = 1 (20%); abdominal infection	*n* = 1 (20%); A patient with abdominal infection was treated with laparoscopic rinsing of the abdomen and placement of a drain	*n* = 0
Wong et al., 2015. [21]	Gastric (*n* = 2, 15.4%) Duodenal (*n* = 11, 84,6%)	Unstable hemodynamics (*n* = 4), and chronic use of steroids due to rheumatic disease (*n* = 1)	Laparoscopy (*n* = 7) Laparotomy (*n* = 6)	N/A	*n* = 0	*n* = 0	*n* = 0
Yildiz et al., 2014. [22]	Duodenal (*n* = 9, 100%)	N/A	Laparotomy (*n* = 9, 100%); simple suture, omentum patch (*n* = 9)	*n* = 0	*n* = 0	*n* = 0	*n* = 0
Hua et al., 2007. [23]	Gastric (*n* = 11, 21.2%) Duodenal (*n* = 41, 78.8%)	Respiratory tract infection (*n* = 1), salmonella sepsis (*n* = 1), history of esophageal reconstruction for corrosive injury, which resulted in stricture (*n* = 1), spinal injury at C2 (*n* = 1), a patient with burns (*n* = 1), astrocytoma (*n* = 1)	Laparotomy (*n* = 51 98.1%); vagotomy with pyloroplasty (*n* = 43), simple suture (*n* = 8) Laparoscopy (*n* = 1, 1.9%); simple suture (*n* = 1)	N/A	*n* = 9 (17.3%); wound infections (*n* = 3), jejunal perforation (*n* = 1), intraabdominal abscess (*n* = 1), adhesive ileus (*n* = 1) pancreatitis (*n* = 1)	N/A	*n* = 2 (3.8%) (time and cause of death is not specified)
Wong et al., 2006. [24]	Gastric (n = N/A) Duodenal (n = N/A)	One patient with Crohn's disease and oral steroid therapy with concomitant histamine2 blocker prophylaxis (*n* = 1)	Laparoscopy (*n* = 13, 76.5%); simple suture and omentum patch (*n* = 13) Converted to open repair (*n* = 4, 23.5%) due to technical difficulty (*n* = 2), and the large size of the ulcer (*n* = 2) (including the 1 patient with Crohn's disease).	*n* = 0	*n* = 0	*n* = 0	*n* = 0

Table 4 (continued)

Author	Localization	Preoperative risk factors	Surgical management	Intraoperative complications	Postoperative complications	Reoperation, reintervention	Mortality
Edwards et al., 2005. [25]	Gastric (*n* = 5, 31.3%) Duodenal (*n* = 11, 68.7%)	Congenital heart disease (*n* = 2), brain arteriovenous malformation (*n* = 1), meningitis (*n* = 1), cystic fibrosis (*n* = 1), hydrocephalus (*n* = 2), prematurity (*n* = 2), mental retardation, cerebral palsy (*n* = 2), chronic renal failure (*n* = 1), nephrotic syndrome (*n* = 1), end-stage renal disease (*n* = 1), asthma (*n* = 1), scleroderma (*n* = 1)	Laparotomy (*n* = 16, 100%); closure, duodenal ulcer (*n* = 3), closure, gastric ulcer (*n* = 2), closure with patch, duodenal ulcer (*n* = 6), closure, duodenal ulcer, pyloroplasty (*n* = 2), closure with patch, gastric ulcer (*n* = 3)	N/A	*n* = 11 (68.8%); wound infection (*n* = 3), wound dehiscence (*n* = 2), pneumonia (*n* = 2), breakdown of the repaired perforation site (*n* = 1), and persistent or recurrent bleeding (*n* = 2)	N/A	4 (14%); died between 1 day and 3 weeks after surgery. Related to: complex cyanotic heart disease (*n* = 2), cystic fibrosis with end-stage lung disease (*n* = 1), and severe prematurity and hydrocephalus (*n* = 1)
Dunn et al., 1983. [26]	Duodenal (*n* = 12, 100%)	N/A	Laparotomy (*n* = 12, 100%); simple suture and omentum patch (*n* = 9), simple suture, omentum patch, and pyloroplasty (*n* = 1), simple suture, omentum patch, and tube duodenostomy (*n* = 1), vagotomy and antrectomy (*n* = 1) was performed on 1-month-old female patient 1 with two large duodenal perforations.	N/A	N/A	N/A	*n* = 1

N/A = not available, GAAR = Gastroduodenal artery aneurysm rupture; UGIB = Upper gastrointestinal hemorrhage

Table 5 Postoperative treatment, length of hospital stay, and follow-up period of patients with perforated peptic ulcer

Author	Surgical management	Postoperative treatment	Length of hospital stay (days)	Follow-up period (months)
Bülbül and Şalcı, 2024. [15]	Laparotomy ($n=11$, 100%)	N/A	7 (4–10)	3 (0–24)
Wang et al., 2023. [16]	Laparoscopy ($n=19$, 63.3%), laparotomy ($n=11$, 36.7%)	N/A	Laparoscopy (13.8 ± 15.2) Laparotomy (16.1 ± 18.9)	N/A
Shen et al., 2023. [17]	Laparotomy ($n=9$, 69.2%), laparoscopy ($n=4$, 30.8%)	N/A	Surgery group (13.6 ± 5.60) Conservative group (14.8 ± 4.60)	8 (6–24)
Sayan et al., 2021. [18]	Laparotomy ($n=9$, 100%)	N/A	N/A	The mean postoperative follow-up period of the patients was 11.8 months. No complications or recurrence were observed.
Yan et al., 2019. [19]	Laparotomy ($n=13$, 65%), laparoscopy ($n=7$, 35%)	N/A	8 (7.0–9.3); gastric localization (8.5 ± 2.2), duodenal localization (12.5 ± 4.0)	The mean follow-up period was 18.5 months. No complications or recurrence were observed.
Reusens et al., 2016. [20]	Laparoscopy ($n=5$, 100%)	All patients ($n=5$) received general postoperative treatment, which consisted of antalgic treatment, antibiotics (cefazoline), and PPI.	6 (4–12)	N/A
Wong et al., 2015. [21]	Laparoscopy ($n=7$, 53.8%), laparotomy ($n=6$, 46.2%)	6 weeks after the initial surgery, upper endoscopy was performed in all patients ($n=13$) From all patients ($n=13$) antral biopsy was taken. H. pylori ($n=2$); successfully treated with eradication therapy (clarithromycin, amoxicillin, and PPI).	Laparoscopic group (6.4 ± 1.5) Laparotomic group (10.3 ± 4.4)	N/A
Yildiz et al., 2014. [22]	Laparotomy ($n=9$, 100%)	Triple therapy for H. pylori eradication; amoxicillin 50 mg/ kg/day, lansoprazole 1 mg/kg/day, and clarithromycin 15 mg/kg/day for 2 weeks	N/A	58 (3–94); abdominal pain 2 years after the therapy ($n=1$) (patient was administered a repeat course of conservative medical therapy)
Hua et al., 2007. [23]	Laparotomy ($n=51$, 98.1%), laparoscopy ($n=1$, 1.9%)	H2 blocker or proton pump inhibitor (PPI) $n=12$)	N/A	44 (84.6%) were available for follow-up. 22 had abdominal pain after the PPU episode and 6 patients had PUD recurrence confirmed by endoscopy. All of the patients with recurrent PUD were managed by "classic" surgery and 3 were given postoperative antacid treatment. No patient had PPU again
Wong et al., 2006. [24]	Laparoscopy ($n=13$, 76.5%), laparotomy ($n=4$, 23.5%)	Patients with H. pylori ($n=16$) received triple antibiotic therapy (PPI, clarithromycin, and amoxicillin)	The median was 7 days	The median was 32.6 months
Edwards et al., 2005. [25]	Laparotomy ($n=16$, 100%)	N/A	N/A	N/A
Dunn et al., 1983. [26]	Laparotomy ($n=12$, 100%)	N/A	N/A	N/A

N/A = not available

meta-analysis and systematic review by Yuan et al. However, it is noteworthy that studies included in our systematic review reporting the prevalence of *Helicobacter pylori* mention that testing for *Helicobacter pylori* was not performed on all patients [37]. Additionally, various diagnostic methods were applied (e.g., serology tests, urea breath tests, or stool antigen tests), which may contribute to a potential reduction in the consistency, internal validity, and reproducibility of the findings.

Symptoms, radiology, and laboratory findings

The most frequently reported symptoms in children with PPU were abdominal pain (primarily in the right lower quadrant), peritoneal signs, vomiting, and fever. This is consistent with the clinical presentation of perforated peptic ulcers described in adults [9, 29]. Gastroduodenal perforations are among the most common causes of pneumoperitoneum in adults, where the radiological finding of "free air" is highly indicative of perforated peptic ulcers [29, 38]. The results of studies included in this systematic review also indicate that free air was the most commonly reported radiological finding (with radiological modalities being standing direct abdominal radiographs and abdominal CT scans) in children with PPU. Additionally, the literature suggests the diagnostic use of ultrasonography in adults with PPU. However, the studies included in this systematic review did not report the use of this radiological method in children with PPU [39]. Regarding laboratory findings, two studies described elevated levels of CRP and leukocytes, which could be explained by accompanying inflammation or infection [29].

Treatment

The treatment of PPU is primarily surgical, with various suture techniques described for closure [29]. The results of studies included in this systematic review indicate that simple sutures or simple sutures with an omental patch were the most commonly used surgical methods for managing PPU in children. Both laparoscopic and open (laparotomy) approaches are used, with studies indicating an increased use of the laparoscopic approach [40, 41]. A meta-analysis by Zhou et al. (2015) compared laparoscopic and open repair of PPU in general population. The analysis included five randomized controlled trials and 24 non-randomized controlled studies, comprising a total of 5268 patients (laparoscopy = 1890, laparotomy = 3378). The results indicate that the laparoscopic approach is associated with a lower incidence of postoperative complications, reduced hospital mortality, earlier resumption of oral intake, less analgesic use, and a shorter hospital stay. Additionally, the findings showed a similar reoperation rate and operative time between the two approaches [42]. Regarding PPU in children, a study by Wang et al. (2023) comparing the operative time between laparotomy and laparoscopy groups found no statistically significant difference [16]. However, a study by Wong et al. (2015) reported that the length of hospital stay was shorter in the laparoscopy group compared to the laparotomy group, although the operating time was longer in the laparoscopy group [21]. Furthermore, in addition to surgical treatment, there is also non-operative management for PPU. The conservative "Taylor method" involves nasogastric suction, intravenous fluid administration, antibiotics, and repeated clinical assessments [29]. In our systematic review, only one retrospective study described the use of the conservative method in children with PPU. In this study, patients were successfully treated using this method without complications.

Intra/postoperative complications and reoperation

Retrospective studies included in this systematic review did not describe the occurrence of intraoperative complications in children with perforated peptic ulcers. However, these studies did report the occurrence of postoperative complications, the most common being wound infection and dehiscence, pneumonia, adhesive ileus, and intra-abdominal abscess. Studies suggest that postoperative complications in adults occur in approximately 30% of cases, with the most frequent being wound infection, intra-abdominal abscess, pneumonia, incisional hernia, ileus, and peritonitis [43, 44]. Furthermore, a more recent retrospective study by Wilhelmsen et al., conducted between 2011 and 2013 on 726 adult patients with PPU in Denmark, found that the most common postoperative complications were postoperative leak (5.9%) and wound dehiscence (4.7%). The study also revealed that around 1 in every 5 adult patients required reoperation due to postoperative complications [40]. In contrast, the findings from the studies included in our systematic review indicate a low incidence of reoperation in children with PPU. When reoperation was necessary, it was due to intraoperative complications (including upper gastrointestinal hemorrhage and gastroduodenal artery aneurysm rupture) and abdominal abscess [19, 20].

Mortality

The results of the studies included in this systematic review indicate that mortality in children with perforated peptic ulcers was low, with the highest incidence reaching 14% of the total sample. It should be emphasized that these retrospective studies involved small sample sizes and that patients with fatal outcomes generally had significant preoperative risk factors and comorbidities in addition to perforated ulcers. Studies describing the mortality rates of adults with PPU vary depending on geographic differences in causes, patient inclusion criteria, data collection methodologies, and other factors. For instance, Lau et al. (2011), through a systematic review and meta-analysis, determined that adults with PPU globally have an average 30-day mortality rate of 23.5% (95% CI: 15.5–31.0) [45]. Furthermore, a retrospective population-based study by Wang et al. (2010), using the Nationwide Inpatient Sample, which included a 20% stratified sample of all hospitalizations in the United States during 2006, reported a mortality rate of approximately 10.6% among adult patients with PPU [46]. Similarly, a retrospective population-based study by Bae et al. (2012), using the Korean National Health Insurance claims database, found a 30-day mortality rate of 3.15% among a sample of 4258 adults with PPU in 2006 [47]. A national prospective cohort study by Buck et al. (2014) included 2668

adult patients in Denmark who underwent surgery for PPU between 2003 and 2009. The study established a 90-day mortality rate of 27.7% following surgery [48].

Limitations

This systematic review included only 12 studies, all of which featured relatively small sample sizes. Furthermore, no retrospective cohort studies, prospective studies, or randomized controlled trials describing PPU in children were identified or included. Another limitation is that all the studies were single-centered. Additionally, while numerous variables were examined in this systematic review (as detailed in Methods 2.3 Study selection and data extraction), only a small number of studies reported most of these variables, further contributing to a limited comprehensive analysis, potential bias, and restricted generalizability of the findings. Moreover, due to the small number of studies and limited sample sizes, a meta-analytic approach to data synthesis was not undertaken, which contributed to a reduced quantitative synthesis, increased subjectivity, made it more challenging to identify patterns, and prevented the assessment of heterogeneity.

Conclusion

Studies indicate that perforated peptic ulcers were more prevalent in males and predominantly located in the duodenum. The most common symptoms included abdominal pain, vomiting, peritoneal signs, and fever, with subdiaphragmatic free air being the most frequently observed radiographic finding. Furthermore, NSAIDs and corticosteroids were the most commonly reported medications associated with these cases. Ulcer suturing, with or without an omental patch, was the most frequently utilized treatment modality, demonstrating a relatively low complication rate.

Future research should focus on conducting well-designed retrospective cohort studies, prospective studies, and randomized controlled trials, preferably involving multiple centers, to generate more robust and unbiased evidence regarding perforated peptic ulcers in children. The implementation of standardized methodologies and uniform reporting of key variables would enable more reliable comparisons between studies and support meta-analyses. Ultimately, such research is essential to improve the understanding of epidemiology, risk factors, and clinical outcomes, contributing to the development of more effective strategies for prevention and management in the pediatric population.

Abbreviations

CI	Confidence Interval
CRP	C-Reactive Protein
CT	Computed Tomography
GAAR	Gastroduodenal Artery Aneurysm Rupture
NASID	Non-Steroidal Anti-Inflammatory Drug
PPI	Proton-Pump Inhibitor
PPU	Perforated Peptic Ulcers
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PUD	Peptic Ulcer Disease
UGIB	Upper Gastrointestinal Hemorrhage

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Author contributions

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Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

All methods were carried out in strict adherence to the ethical principles outlined in the Declaration of Helsinki, a cornerstone document of the World Medical Association that provides guidelines for conducting medical research involving human participants.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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