

Progression from acute to chronic pancreatitis in children: a systematic review and meta-analysis

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Background: Most children recover after an initial acute pancreatitis (AP) episode; however, some progress to recurrent AP (RAP) or chronic pancreatitis (CP).

Purpose: We aimed to quantify progression rates and identify the risk factors associated with these transitions.

Methods: PubMed/MEDLINE, Embase, and Cochrane databases were searched on December 21, 2024, for pediatric studies reporting progression to RAP or CP (PROSPERO number: CRD420251086520). All observational studies were included, while case reports and case series were excluded. To evaluate the differences in RAP rates, we conducted subgroup analyses of etiology and severity. We also assessed clinical, structural, and genetic risk factors for disease progression. A random-effects model was used to pool proportions and odds ratios (OR) with 95% confidence intervals (CI). Heterogeneity was assessed using the I^2 statistic.

Results: A total of 68 studies met the inclusion criteria. After the first AP attack, RAP developed in 18% (95% CI, 16–22%; $I^2=76\%$; $k=39$ studies) and CP developed in 10% (95% CI, 6–16%; $I^2=67\%$; $k=5$ studies) of patients. Among children with RAP, 35% (95% CI, 24–49%; $I^2=78\%$; $k=7$ studies) progressed to CP. The RAP rates varied according to etiology and severity: hypertriglyceridemia, 33%; idiopathic, 28%; biliary, 19%; traumatic, 16%; drug-induced, 14%; virus-induced, 3%; severe, 39%; moderate, 24%; and mild, 21%. Structural abnormalities were associated with a higher risk of RAP (OR, 3.15; 95% CI, 1.51–6.56; $I^2=0\%$; $k=5$ studies). Pancreas divisum (OR, 2.64; 95% CI, 1.51–4.63; $I^2=17\%$; $k=7$ studies) and PRSS1 mutation (OR, 4.56; 95% CI, 3.06–6.80; $I^2=0\%$; $k=7$ studies) were associated with CP.

Conclusion: Approximately one in five pediatric AP episodes recurred, and over one-third of the RAP cases progressed to CP. The risk of RAP is influenced by the underlying etiology and severity of the initial episode, whereas structural and genetic factors are associated with later progression.

Key words: Acute, Recurrent, Chronic pancreatitis, Risk factor

Key message

Approximately 1 in 5 children with acute pancreatitis develops recurrent attacks, and over one-third of such cases progress to chronic pancreatitis. Progression is closely linked to genetic mutations, particularly PRSS1, and anatomical abnormalities, whereas demographic and routine clinical factors lack predictive value. These results support early genetic and anatomical assessments, enabling targeted follow-ups and timely interventions in high-risk pediatric patients.

Introduction

Once considered rare, acute pancreatitis (AP) in children is now recognized with increasing frequency, with incidence rates approaching those seen in adults.^{1,2} The incidence of childhood AP is in the range of 3–13 cases per 100,000 persons per year; on the other hand, the incidence of pediatric chronic pancreatitis (CP) is approximately 2 cases per 100,000 persons per year.³ While most pediatric

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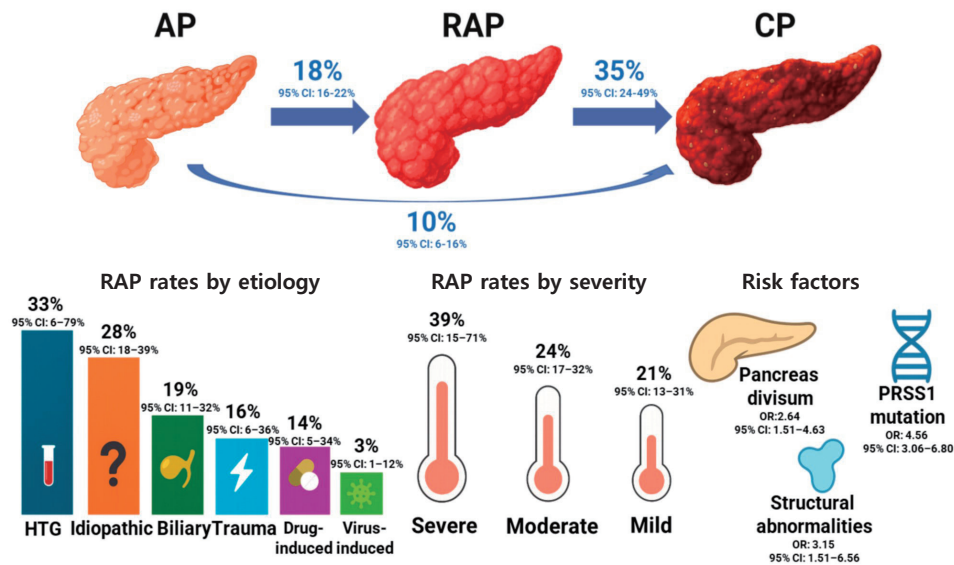
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Progression from acute to recurrent and chronic pancreatitis in children



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Graphic abstract. AP, acute pancreatitis; RAP, recurrent acute pancreatitis; CP, chronic pancreatitis; HTG, hypertriglyceridemia; OR, odds ratio; CI, confidence interval.

AP cases resolve without sequelae, a significant subset of patients experience progression to recurrent AP (RAP) and, subsequently, CP.²⁾ The natural history, risk factors, and outcomes of this progression remain incompletely understood, especially in the pediatric population, where etiologies and disease trajectories differ from those in adults.^{4,5)}

Major risk factors for pancreatitis progression in adults such as alcohol use and smoking are rarely implicated in children.⁶⁾ Instead, pediatric AP and its recurrence are often associated with genetic predispositions (such as pathogenic variants in PRSS1, CFTR, or SPINK1) and structural or metabolic factors (e.g., pancreas divisum, biliary anomalies, hypertriglyceridemia).⁶⁾ Given that the causes of pancreatitis in children diverge substantially from those in adults, applying adult data to pediatric cases may not be appropriate.⁶⁾ This underscores the need for pediatric-specific research on disease course and risk factors.

RAP and CP in children are associated with substantial morbidity, including chronic pain,⁷⁾ exocrine and endocrine insufficiency, and impaired quality of life.⁸⁾ Identifying children at risk for progression, understanding the timing and mechanisms of disease evolution, and recognizing modifiable and nonmodifiable risk factors are critical for optimizing management and improving long-term outcomes.^{2,5,9)} This meta-analysis aimed to synthesize current evidence on the rate of progression from acute to recurrent and CP in children, and to identify key risk factors associated with this progression.

Methods

We conducted our systematic review and meta-analysis in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) 2020 guidelines (Supplementary Table 1).¹⁰⁾ The study protocol was prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO, CRD420 251086520), and all analyses were carried out in full compliance with the registered protocol.

1. Eligibility criteria

We included studies based on predefined criteria structured using the CoCoPop¹¹⁾ (Condition, Context, Population) and PECO¹²⁾ (Population, Exposure, Comparator, Outcome) frameworks to address both progression rates and associated risk factors. Eligible studies included pediatric patients (under 18 years) diagnosed with AP, RAP, or CP. We included studies (prospective or retrospective observational studies, case series) that either reported the rate of progression from AP to RAP, AP to CP, or RAP to CP over time, or presented comparative data between disease groups relevant to potential risk factors for progression (e.g., age, sex, etiology, severity). Studies were excluded if they focused solely on adult populations, lacked extractable data for either outcome, or were published as case reports, reviews, editorials, in vitro and animal studies or abstracts.

To ensure methodological consistency, diagnostic defini-

tions were recorded as reported in the original studies. Among the 68 included studies, 76% used the International Study Group of Pediatric Pancreatitis: In Search for a Cure (INSPPIRE)¹³ criteria for pediatric pancreatitis, while 24% employed alternative frameworks, including other institutional criteria, ICD (International Classification of Diseases)-based definitions, or combinations thereof. According to INSPPIRE definitions, AP was diagnosed when ≥ 2 of the following were present: (1) abdominal pain compatible with AP; (2) serum amylase and/or lipase $\geq 3\times$ the upper limit of normal; (3) imaging findings consistent with AP. RAP was defined as ≥ 2 distinct episodes with complete resolution of pain (≥ 1 -month interval) or enzyme normalization between episodes.¹³ CP was defined as ≥ 1 of: typical pain plus characteristic imaging, exocrine insufficiency plus imaging findings, or endocrine insufficiency plus imaging findings.¹³ Disease severity was classified according to the 2012 Revised Atlanta Classification (mild: no organ failure or complications; moderate: transient organ failure < 48 hours or local complications; severe: persistent organ failure > 48 hours).¹⁴

Additionally no minimum follow-up duration was applied as an exclusion criterion; studies were included regardless of follow-up length to ensure comprehensive coverage of the available evidence.

2. Information sources and search strategy

We conducted a systematic search of 3 major medical databases, PubMed/MEDLINE, the Cochrane Library (CENTRAL), and Embase on December 21, 2024. The search was limited to studies published from 1992 onward and used the following search terms: *acute AND (chronic OR recurrent) AND pancreatitis*. To ensure methodological rigor, we followed the Cochrane Handbook guidelines for both study selection and data extraction.¹⁵ Although the INSPPIRE¹³ criteria are most commonly used in pediatric populations, they were established in 2012 and are diagnostically based on the original Atlanta Classification introduced in 1992.¹⁶ As the core diagnostic framework for AP (the 2-out-of-3 rule) was first formalized in the 1992 Atlanta criteria, we limited our search to studies published from January 1, 1992 onward to ensure consistency with standardized diagnostic definitions across studies.

3. Study selection and data extraction

All references were managed using EndNote 21 (Clarivate Analytics, USA), and duplicates were removed before screening. Two independent reviewers (EBG and ET) screened studies in 2 stages, first by title and abstract, then by full text. Disagreements at either stage were resolved through discussion with a third reviewer (MO). Cohen Kappa coefficient¹⁷ was calculated after each screening

phase to assess interrater agreement. Data were independently extracted by the same 2 reviewers (EBG and ET), with discrepancies resolved by the third reviewer (MO). Extracted information included first author, year of publication, geographic location, study period, study design, number of centers involved, sample size, age distribution, percentage of male participants, follow-up duration, and the proportion of patients progressing to RAP and CP, including breakdowns by etiology and disease severity. In addition, we extracted group-level comparative data (e.g., comorbidities, laboratory parameters, clinical features) for AP, RAP, and CP subgroups when such comparisons were available in at least 3 studies for a given parameter.

Where multiple studies reported data on potentially overlapping populations, we included only the study with the largest sample size. In cases of missing or unclear data, study authors were contacted for clarification.

4. Risk of bias

Two independent authors (EBG and ET) assessed the methodological quality of the included studies using the Joanna Briggs Institute Prevalence Critical Appraisal Tool (JBI)¹⁸ and the Quality In Prognostic Studies (QUIPS) tool,¹⁹ depending on the study type. The JBI tool was applied to studies that reported the progression of the disease, such as recurrence rates or progression rates to CP. In contrast, the QUIPS tool was used for studies that compared diagnostic groups (e.g., AP vs. RAP vs. CP) based on various clinical, demographic, or laboratory parameters. A third author (MO) resolved any disagreements that arose.

5. Data synthesis

All statistical analyses were performed using R v4.2.1 (R Foundation, Austria),²⁰ utilizing the meta²¹ and dmetar²² packages. To account for anticipated between-study variability, a random-effects model was employed for all meta-analyses. Heterogeneity was quantified using the I^2 statistic described by Higgins and Thompson,²³ and prediction intervals (PI) were reported when appropriate, following the recommendations of Inthout et al.²⁴ For proportion outcomes, the number of patients experiencing the event and the total sample size were extracted from each study, and pooled proportions with 95% confidence intervals (CI) were computed. For dichotomous comparisons, odds ratios (ORs) with 95% CIs were calculated by extracting event counts and group sizes for each comparator group. For continuous outcomes, the mean difference was used as the effect size, with the corresponding sample size, mean, and standard deviation collected from each study.

Forest plots were used to visually summarize the pooled results for outcomes reported in at least 3 studies. Funnel

plots and Peter tests were used to assess publication bias, but only for outcomes with a minimum of 10 studies.²⁵⁾ Additionally, leave-one-out sensitivity analyses were conducted to examine the influence of individual studies on overall estimates and heterogeneity. A 2-sided *P* value less than 0.05 considered significant.

Results

1. Search and selection

We identified 19,125 records through our systematic search. After screening titles, abstracts, and full texts, we included 68 studies in both the qualitative and quantitative syntheses. The selection process is shown in Fig. 1.

2. Basic characteristics of included studies

The full review identified 68 studies, 44^{2,5,9,26-65)} (Table 1) focusing on the progression of AP to RAP or CP, and 24 (Supplementary Table 2) comparing AP, RAP, and CP patient groups.

Of the 44 studies focusing on the progression of AP, 38 were retrospective and 6 were prospective, while 40 were single-center and 4 were multicenter. These studies enrolled patients between 1979 and 2022, were published between 1996 and 2024, and provided data on a total of 4,104 pediatric cases to our quantitative synthesis. Twenty-four studies were conducted in Asia (55%), primarily in China and India, 10 in Europe (23%), 6 in North America (14%), and 4 in the Middle East (9%), with none originating from South America or Africa. Sample sizes ranged from

11 to 371 participants; 29 cohorts enrolled fewer than 100 children, while 15 included 100 or more. Sex distribution was available in 41 cohorts, and boys predominated in 30 of them. Disease severity was reported in 12 cohorts, of which severe AP occurred in approximately 11% of index attacks.

3. AP progression rates based on etiology and severity

Using only articles with the INSPPIRE diagnostic criteria, RAP developed in 21% of children after initial AP (95% CI, 17%–24%; 95% prediction interval [PI], 9%–41%; $I^2=78\%$, $\tau^2=0.22$; $k=27$ studies, $N=2,837$ patients). When including all studies regardless of diagnostic criteria, the overall estimate was 18% (95% CI, 16%–22%; 95% PI, 7%–41%; $I^2=76\%$, $\tau^2=0.30$; $k=39$ studies, $N=3,587$ patients). Direct progression from AP to CP occurred in 10% (95% CI, 6%–16%; 95% PI, 3%–28%; $I^2=67\%$, $\tau^2=0.12$; $k=5$ studies, $N=727$ patients). Among RAP patients, 35% (95% CI, 24%–49%; 95% PI, 12%–69%; $I^2=78\%$, $\tau^2=0.24$; $k=7$ studies, $N=548$ patients) developed CP.

Etiology specific progression rates to RAP varied significantly ($\chi^2=25.74$, degrees of freedom=5, $P<0.001$ for subgroup differences), with hypertriglyceridemia-associated AP showing the highest rate of recurrence (33%; 95% CI, 6%–79%; 95% PI, 0%–99%; $I^2=0\%$, $\tau^2=0$; $k=3$ studies, $N=21$ patients), followed by idiopathic (28%; 95% CI, 18%–39%; 95% PI, 9%–61%; $I^2=68\%$, $\tau^2=0.28$; $k=8$ studies, $N=344$ patients) and biliary (19%; 95% CI, 11%–32%; 95% PI, 6%–50%; $I^2=54\%$, $\tau^2=0.23$; $k=7$ studies, $N=283$ patients) etiologies. Trauma-, drug- and virus-induced AP had lower progression rates (16%; 95% CI, 6%–36%; 95% PI, 5%–40%; $I^2=0\%$, $\tau^2=0$; $k=5$ studies, $N=49$ patients), (14%; 95% CI, 5%–34%; 95% PI, 3%–46%; $I^2=0\%$, $\tau^2=0.16$; $k=6$ studies, $N=78$ patients), and (3%; 95% CI, 1%–12%; 95% PI, 0%–20%; $I^2=18\%$, $\tau^2=0$; $k=4$ studies, $N=149$ patients), respectively) (Fig. 2; Supplementary Fig. 1). Disease severity showed a trend toward higher recurrence rates, although subgroup differences were not statistically significant ($\chi^2=2.60$, degrees of freedom [df]=2, $P=0.272$). Severe AP progressed to RAP in 39% (95% CI, 15%–71%; 95% PI, 2%–95%; $I^2=76\%$, $\tau^2=1.35$; $k=7$ studies, $N=85$ patients), compared with 24% for moderate cases (95% CI, 17%–32%; 95% PI, 17%–33%; $I^2=0\%$, $\tau^2=0$; $k=6$ studies, $N=206$ patients) and 21% for mild cases (95% CI, 13%–31%; 95% PI, 7%–47%; $I^2=67\%$, $\tau^2=0.15$; $k=6$ studies, $N=387$ patients) (Fig. 2; Supplementary Fig. 1).

4. Factors associated with disease progression

1) Patient characteristics and nonmodifiable factors

Anatomical abnormalities showed significant associations, with general structural anomalies associated with RAP (OR, 3.15; 95% CI, 1.51%–6.56; 95% PI, 1.26–7.87; $I^2=0\%$, $\tau^2=0$; $k=5$ studies, $N=575$ patients) (Fig. 3; Supplementary Fig.

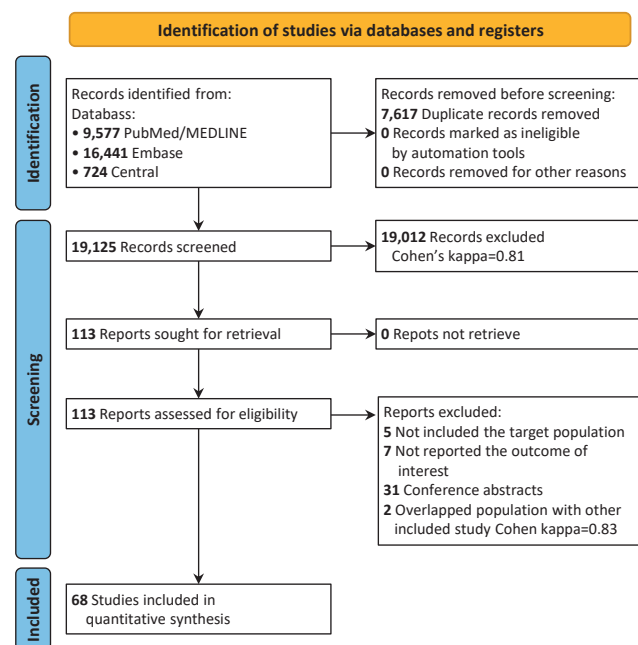


Fig. 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) flowchart of the article selection process.

Table 1. Characteristics of included studies focusing on the progression of acute pancreatitis

Study	Country	Study design	Centers	Study period	Follow-up time (mo) (mean or median)	Total cases (follow-up)	AP	RAP	AP to CP	Males, n (%)	Age (yr)	Severe patients, n (%)
Alabdulkareem et al. 2018 ²⁶⁾	Saudi Arabia	Retrospective	Multicentric	1994–2015	NR	50	41	9	NR	26 (52.0)	11.6	NR
Anafy et al. 2024 ²⁷⁾	Israel	Retrospective	Unicentric	2005–2019	NR	68	44	24	NR	37 (54.0)	15.3 (12–16.8) ^{a)}	NR
Anushree et al. 2022 ²⁸⁾	India	Prospective	Unicentric	2019–2021	NR	73	52	21	NR	43 (59.0)	8.4±3.2 ^{c)}	4 (5.5)
Appak et al. 2018 ²⁹⁾	Turkey	Retrospective	Unicentric	2014–2016	NR	41	32	9	NR	15 (36.6)	9.3±5.3 ^{c)}	NR
Badru et al. 2017 ³⁰⁾	USA	Retrospective	Unicentric	2007–2015	NR	48	39	9	NR	11 (22.9)	14.4 (1.7–17.8) ^{b)}	NR
Berney et al. 1996 ³¹⁾	Switzerland	Retrospective	Unicentric	1979–1993	NR	21	18	3	NR	9 (42.9)	10.8±3.5 ^{c)}	5 (24.0)
Bhanot et al. 2022 ³²⁾	UK	Retrospective	Multicentric	2013–2014	12.0	94	60	30	NR	48 (51.0)	11.2 (7.1–14.4) ^{a)}	NR
Bolia et al. 2015 ³³⁾	India	Retrospective	Unicentric	2001–2011	NR	87	68	19	NR	61 (70.1)	12 (1–18) ^{b)}	NR
Alvarez Calatayud et al. 2003 ³⁴⁾	Spain	Retrospective	Unicentric	NR	NR	31	25	6	NR	17 (55.0)	7.9 (2.1–5) ^{d)}	NR
Grzybowska-Chlebowczyk et al. 2018 ³⁵⁾	Poland	Retrospective	Unicentric	2004–2013	NR	51	39	12	NR	24 (47.0)	12.1 (1.7–18.0) ^{d)}	NR
Deveci et al. 2023 ³⁶⁾	Turkey	Retrospective	Unicentric	2010–2021	NR	108	85	23	8	54 (50.0)	10.0±4.8 ^{c)}	NR
Galai et al. 2019 ³⁷⁾	Israel	Retrospective	Unicentric	1995–2016	6	59	55	14	NR	34 (57.6)	11.3 (5.9–15.4) ^{a)}	NR
Geetha et al. 2012 ³⁸⁾	India	Prospective	Unicentric	2003–2010	NR	73	8	28	37	NR	NR	NR
Getsuwan et al. 2022 ³⁹⁾	Thailand	Retrospective	Unicentric	2000–2021	NR	155	134	18	14	NR	NR	NR
Guo et al. 2014 ⁴⁰⁾	China	Retrospective	Unicentric	2002–2012	NR	371	344	27	NR	178 (48)	NR	NR
Hao et al. 2016 ⁴¹⁾	China	Retrospective	Unicentric	2003–2015	55 (3–132) ^{b)}	159	114	45	9	NR	NR	NR
Al Hindi et al. 2021 ⁴²⁾	Bahrain	Retrospective	Unicentric	2006–2017	39 (4–59) ^{d)}	56	50	6	NR	33 (58.9)	Median, 8	NR
Kandula et al. 2008 ⁴³⁾	USA	Retrospective	Unicentric	1995–2004	NR	87	85	2	NR	45 (51.7)	1.7±0.7 ^{c)}	3 (3.4)
Kim et al. 2023 ⁴⁴⁾	Korea	Retrospective	Unicentric	2017–2022	NR	64	50	14	NR	38 (59.4)	11.9±4.8 ^{c)}	NR
Laugel et al. 2005 ⁴⁵⁾	France	Retrospective	Unicentric	1996–NR	NR	11	9	2	NR	7 (63.6)	10.1±3.6 ^{c)}	NR
López et al. 2013 ⁴⁶⁾	Spain	Retrospective	Unicentric	1988–2008	NR	27	24	3	NR	18 (66.0)	7.2 (6 mo–16 yr) ^{d)}	NR
Majbar et al. 2016 ⁴⁷⁾	UK	Prospective	Multicentric	2013–2014	NR	94	76	18	NR	48 (51.1)	11.2±3.4 ^{c)}	NR
Mengdi et al. 2022 ⁴⁸⁾	China	Retrospective	Unicentric	2017–2021	33 (5–55) ^{d)}	106	79	27	NR	57 (53.8)	Median, 7 yr	NR
Minen et al. 2012 ⁴⁹⁾	Italy	Retrospective	Unicentric	2007–2012	NR	45	34	11	NR	NR	NR	NR
Mirza et al. 2022 ⁵⁰⁾	India	Retrospective	Unicentric	2017–2019	NR	40	27	13	NR	25 (62.5)	9.3 (1–17) ^{d)}	3 (7.5)
Nasr et al. 2023 ⁵¹⁾	USA	Prospective	Unicentric	2013–2019	12	74	60	14	NR	40 (54.0)	NR	6 (8.1)
Nauka et al. 2018 ⁵²⁾	USA	Retrospective	Unicentric	2011–2016	NR	79	63	16	NR	46 (58.2)	14 (9.5–16) ^{d)}	17 (21.5)
Ohta et al. 2023 ⁵³⁾	Japan	Retrospective	Unicentric	2005–2022	46.5	29	19	10	NR	14 (48.3)	NR	9 (31.0)
Park et al. 2009 ⁵⁴⁾	USA	Retrospective	Unicentric	1994–2007	NR	215	182	33	NR	86 (40)	13.1±5.6 ^{c)}	NR
Pezzilli et al. 2002 ⁵⁵⁾	Italy	Retrospective	Unicentric	1998–1999	NR	50	36	14	NR	25 (50.0)	10.5±3.8 ^{c)}	NR
Poddar et al. 2016 ⁵⁶⁾	India	Retrospective	Unicentric	2003–2014	21.1±20.9 ^{c)}	140	132	8	24	98 (70.0)	NR	NR
Poddar et al. 2017 ⁵⁷⁾	India	Retrospective	Unicentric	2003–2015	25.5 (8.3–48) ^{b)}	88	NR	51	37	51 (54.8)	13 (10–14.5) ^{a)}	NR
Sağ et al. 2018 ⁴⁾	Turkey	Retrospective	Unicentric	2005–2016	68.1±24.3 ^{c)}	63	53	10	1	31 (49.0)	9.6±4.8 ^{c)}	11 (17.4)
Singh et al. 2017 ⁵⁸⁾	India	Prospective	Unicentric	2015–2016	NR	32	NR	22	10	22 (68.8)	14 (8–18) ^{d)}	2 (6.0)
Stringer et al. 2005 ⁵⁹⁾	UK	Retrospective	Unicentric	1994–2004	NR	33	25	8	NR	19 (57.6)	12.8±3.0 ^{c)}	NR
Sweeny et al. 2018 ⁵⁾	Usa	Prospective	Unicentric	2013–2016	21 (10.2–32.7) ^{a)}	115	95	20	NR	60 (52.0)	13.5 (9.3–15.9) ^{a)}	14 (12.3)
Tiao et al. 2002 ⁶⁰⁾	China	Retrospective	Unicentric	1986–2000	NR	61	52	9	NR	39 (63.9)	8.8±4.8 ^{c)}	NR
Volkan et al. 2023 ²⁾	Turkey	Retrospective	Multicentric	2010–2017	31.2±21.6 ^{c)}	165	107	51	21	74 (44.9)	9.6±4.5 ^{c)}	NR
Wang et al. 2022 ⁶¹⁾	China	Retrospective	Unicentric	2011–2020	NR	275	220	55	NR	140 (50.9)	12 (8–16) ^{a)}	28 (10.2)
Yeung et al. 1996 ⁶²⁾	China	Retrospective	Unicentric	1983–1992	NR	43	39	4	NR	23 (53.5)	9 (2–18) ^{b)}	NR
Zeng et al. 2022 ⁹⁾	China	Retrospective	Unicentric	2014–2021	NR	276	NR	140	136	129 (46.7)	NR	NR
Zheng et al. 2021 ⁶³⁾	China	Retrospective	Unicentric	2017–2020	17.9 (9.3–25.3) ^{a)}	96	66	30	NR	44 (45.8)	NR	NR
Zhong et al. 2021 ⁶⁴⁾	China	Retrospective	Unicentric	2013–2019	34.2±20.8 ^{c)}	130	111	19	NR	72 (55.4)	NR	4 (3.1)
Zhu et al. 2011 ⁶⁵⁾	China	Retrospective	Unicentric	2003–2009	NR	121	116	5	NR	67 (55.4)	6.8±3.4 ^{c)}	NR

AP, acute pancreatitis; RAP, recurrent acute pancreatitis; CP, chronic pancreatitis; NR, not reported.

^{a)}Median (interquartile range). ^{b)}Median (range). ^{c)}Mean±standard deviation. ^{d)}Mean (range).

2) and pancreas divisum to CP (OR, 2.64; 95% CI, 1.51–4.63; 95% PI, 1.16–6.02; $I^2=17\%$, $\tau^2=0.05$; $k=7$ studies, $N=977$ patients) (Fig. 4; Supplementary Fig. 2). Genetic mutations in PRSS1 were strongly associated with CP development (OR, 4.56; 95% CI, 3.06–6.80; 95% PI, 2.76–7.54; $I^2=0\%$, $\tau^2=0$; $k=7$ studies,

$N=1,068$ patients) (Fig. 4; Supplementary Fig. 2). In contrast, male sex, race (white or Hispanic), and family history of AP demonstrated no significant associations with progression to RAP or CP (Figs. 3 and 4; Supplementary Figs. 3 and 4).

Age at study inclusion did not differ significantly bet

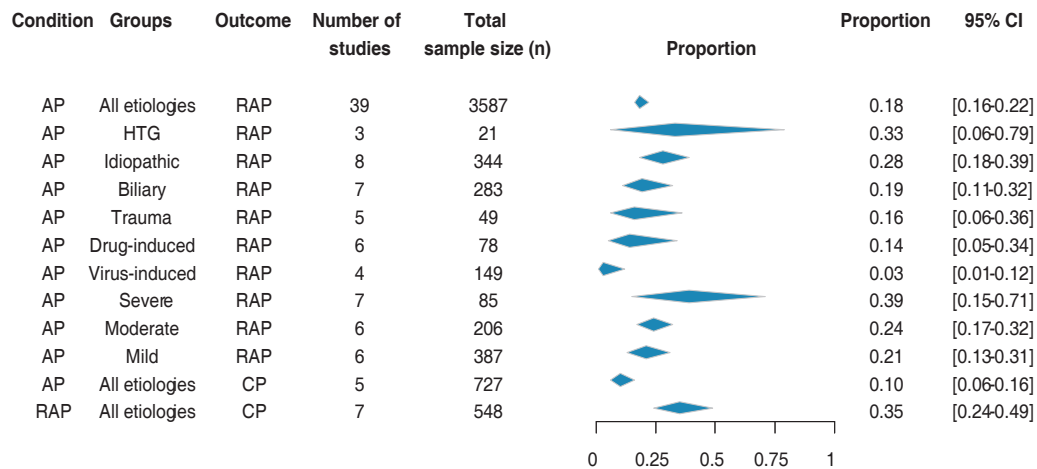


Fig. 2. Summary forest plot showing the recurrence rate of AP overall and stratified by etiology and severity as well as the progression rates of AP to CP after a single episode and after RAP. AP, acute pancreatitis; CI, confidence interval; CP, chronic pancreatitis; HTG, hypertriglyceridemia; RAP, recurrent acute pancreatitis.

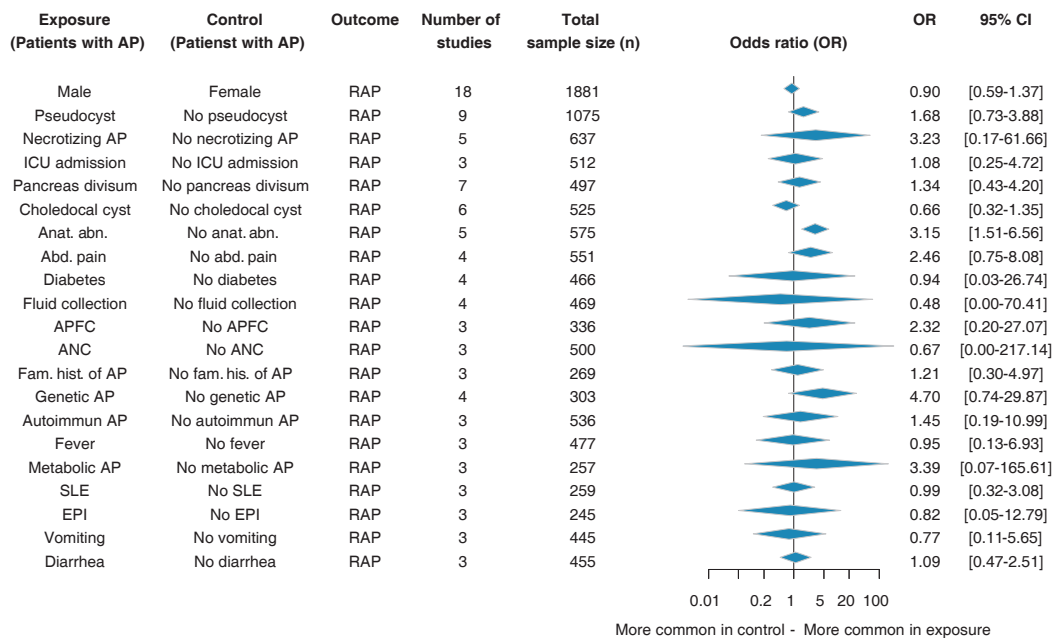


Fig. 3. Summary forest plot showing pooled odds ratios for proposed risk factors associated with recurrent AP after an index AP episode in children. abd., abdominal; anat. abn., anatomical abnormality; ANC, acute necrotic collection; AP, acute pancreatitis; APFC, acute peripancreatic fluid collection; CI, confidence interval; EPI, exocrine pancreatic insufficiency; ICU, intensive care unit; RAP, recurrent acute pancreatitis; OR, odds ratio; SLE, systemic lupus erythematosus.

ween AP and RAP or between CP and RAP. Clinical parameters, including length of stay, amylase, lipase, white blood cell count, and C-reactive protein (CRP) levels, showed no significant differences between the AP and RAP groups (Fig. 5; Supplementary Figs. 3 and 5). Other genetic variants (SPINK1, CFTR, and CTSC), broader genetic AP categorization, and anatomical features (choledochal cysts, annular pancreas, and maljunction) lacked statistical significance (Figs. 3 and 4; Supplementary Fig. 4).

2) Clinical and procedural factors

Medication-related AP was associated with a reduced

risk of CP (OR, 0.26; 95% CI, 0.07–0.91; 95% PI, 0–14.09; $P=0\%$, $\tau^2=0$; $k=3$ studies, $N=827$ patients). Exocrine pancreatic insufficiency (EPI) exhibited a robust association with CP (OR, 22.82; 95% CI, 9.26–56.25; 95% PI, 1.52–341.69; $P=0\%$, $\tau^2=0$; $k=4$ studies, $N=152$ patients). Interventional procedures significantly associated with CP included biliary sphincterotomy (OR, 4.16; 95% CI, 3.24–5.34; 95% PI, 0.32–54.36; $P=0\%$, $\tau^2=0$; $k=3$ studies, $N=956$ patients), biliary stenting (OR, 5.79; 95% CI, 4.42–7.60; 95% PI, 0.04–769.49; $P=0\%$, $\tau^2=0$; $k=3$ studies, $N=958$ patients), and pancreatic duct stenting (OR, 12.19; 95% CI, 3.16–46.97; 95% PI, 0.02–6822.01; $P=56\%$, $\tau^2=0.15$; $k=3$ studies, $N=957$ patients) (Fig. 4;

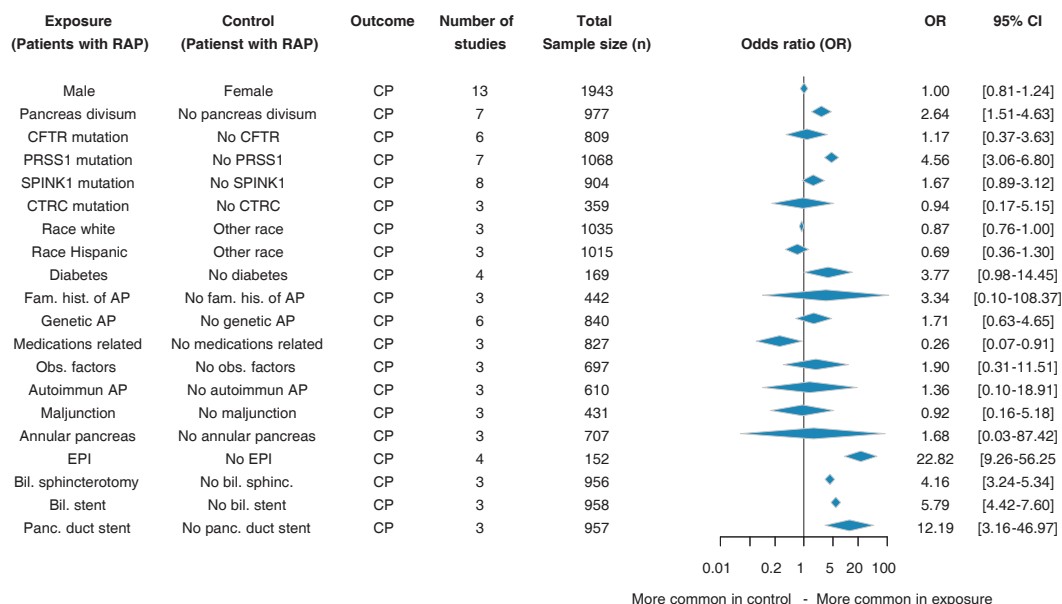


Fig. 4. Summary forest plot showing pooled odds ratios for proposed risk factors associated with progression from recurrent AP to chronic pancreatitis in children. AP, acute pancreatitis; bil., biliary; CI, confidence interval; EPI, exocrine pancreatic insufficiency; fam. hist., family history; obs., obstructive. OR, odds ratio; panc., pancreatic; sphinc., sphincterotomy.

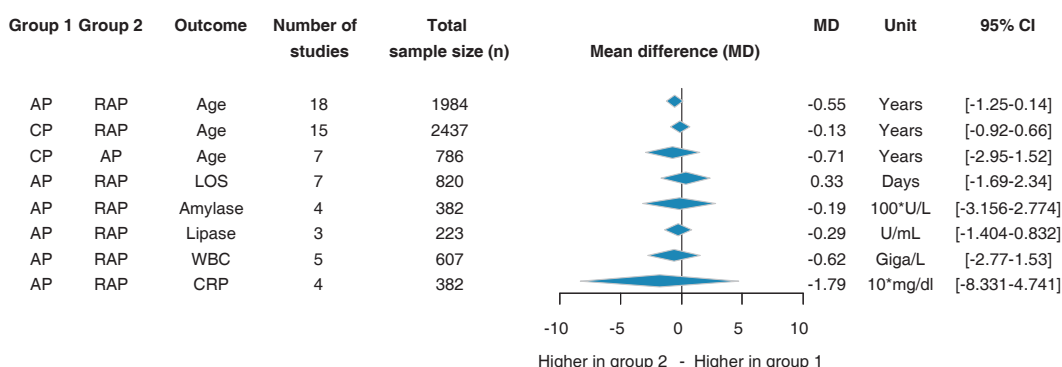


Fig. 5. Summary forest plot showing pooled mean differences for continuous clinical variables comparing disease groups in pediatric pancreatitis. AP, acute pancreatitis; CI, confidence interval. CP, chronic pancreatitis; CRP, C-reactive protein; LOS, length of hospital stay; RAP, recurrent acute pancreatitis; WBC, white blood cell count.

Supplementary Fig. 2). Conversely, autoimmune AP and metabolic AP showed no significant associations with RAP or CP (Figs. 3 and 4; Supplementary Fig. 5). Diabetes mellitus was not associated with RAP, but showed a nonsignificant trend toward an increased risk of CP (OR, 3.77; 95% CI, 0.98-14.45; 95% PI, 0.12-120.85; $I^2=0\%$, $\tau^2=0$; $k=4$ studies, $N=169$ patients) (Figs. 3 and 4; Supplementary Figs. 2, 4, and 6). The presence of systemic lupus erythematosus in AP patients was not associated with an increased risk of RAP. Clinical complications, including pseudocysts, necrotizing AP, abdominal pain, intensive care unit admission, gastrointestinal symptoms (vomiting, diarrhea), obstructive factors, fever, fluid collections, acute peripancreatic fluid collections, and acute necrotic collections, were not predictive of disease progression (Figs. 3 and 4; Supplementary Figs. 6 and 7).

5. Risk of bias assessment

We assessed study quality using the JBI tool for studies reporting the progression of AP and the QUIPS tool for comparison studies. Most studies had a moderate risk of bias, primarily due to small sample size in studies reporting the progression of AP and uncontrolled confounding in comparative studies. These limitations should be taken into account when interpreting our results. Detailed risk of bias assessments can be found in Supplementary Tables 3 and 4.

6. Publication bias and heterogeneity

We examined heterogeneity only for the overall recurrence rate from AP to RAP, as this was the only outcome with sufficient studies (≥ 10) for meaningful analysis. Several approaches were employed. First leave-one-out analysis was conducted but only marginally reduced the

substantial heterogeneity observed (Supplementary Fig. 8). Next, to address diagnostic heterogeneity, we performed sensitivity analyses stratifying studies by diagnostic framework (INSPPIRE vs. non-INSPPIRE) (Supplementary Fig. 9). We also compared studies with reported versus unreported follow-up duration (Supplementary Fig. 9), conducted a subgroup analysis stratified by follow-up length (<12 months, 12–36 months, and >36 months; Supplementary Fig. 10), and performed a meta-regression restricted to studies with documented follow-up to examine whether follow-up length was associated with RAP progression (Supplementary Fig. 11). Progression rates differed significantly by diagnostic framework ($P=0.019$), whereas follow-up reporting status had no significant impact ($P=0.161$), and subgroup analysis ($\chi^2=2.29$, $df=2$, $P=0.319$) with meta-regression confirmed no association between follow-up duration and progression rates ($P=0.976$) (Supplementary Figs. 9–11). When examining technical factors potentially contributing to heterogeneity, we found that smaller studies (sample size <100) reported significantly higher RAP rates compared to larger studies (21% vs 18%, $\chi^2=3.91$, $df=1$, $P=0.048$). Similarly, shorter study periods (<7 years) were associated with higher RAP proportions than longer studies (22% vs 16%, $\chi^2=3.98$, $df=21$, $P=0.046$) (Supplementary Fig. 12). Other factors, including study design, geographical region, single- vs multicenter setting, and gender distribution, did not significantly influence heterogeneity (Supplementary Fig. 13).

For publication bias assessment, both visual inspection of the funnel plot and Peter test ($P>0.305$) indicated no significant publication bias for the AP→RAP progression outcome specifically (Supplementary Fig. 14). Publication bias assessment was limited to this outcome due to insufficient studies (≥ 10) for other progression pathways.

Discussion

Our meta-analysis provides a comprehensive overview of the rate and risk factors for progression from AP to RAP and CP in the pediatric population. It is the first meta-analysis to specifically address this topic in children.

Our findings reveal a substantial risk of recurrence and chronicity in pediatric pancreatitis, with approximately one-fifth of children experiencing recurrence, one-tenth progressing to CP after an initial acute episode, and a 35% (CI, 24–49) transition rate from RAP to CP. This recurrence rate is comparable to that seen in adult populations, where recurrence rates of 20%–21%^{66,67} have been reported; however, the rate of progression to CP is slightly higher compared to the 8% (AP→CP) and 24% (RAP→CP) observed in the adult population.⁶⁸ Our analysis found no

significant association between follow-up duration and AP→RAP progression across multiple approaches ($P=0.161$ for reporting status, $P=0.319$ for subgroup analysis, $P=0.976$ for meta-regression). This suggests that most progression occurs within the first 1–2 years after initial presentation, consistent with clinical observations that children at risk typically experience recurrence early in their disease course.^{4,5,64}

Hypertriglyceridemia-associated pancreatitis showed the highest recurrence rate (33%; CI, 6–79), but this should be interpreted cautiously due to small number of studies, small sample size ($k=3$ studies, $N=21$ patients) and wide uncertainty (95% PI, 0%–99%). This finding is consistent with its known tendency to cause more severe inflammation through free fatty acid-mediated acinar cell injury and sustained metabolic derangement.⁶⁹ Idiopathic pancreatitis demonstrated the second-highest recurrence rate (28%; CI, 18–39). This underscores the importance of comprehensive evaluation, including genetic testing and advanced imaging such as endoscopic ultrasound and magnetic resonance cholangiopancreatography, in seemingly idiopathic cases.⁷⁰ A recent study reported that positive findings on endoscopic ultrasound were associated with a reduced incidence of recurrent idiopathic AP over a 1-year follow-up period.⁷¹ Biliary pancreatitis, the third most common cause, was associated with a 19% (CI, 11–32) risk of recurrence. This moderate rate likely reflects the effectiveness of definitive treatment, such as cholecystectomy for gallstones.⁷² However, recurrence remains a possibility, potentially due to retained common bile duct stones, microlithiasis, or underlying sphincter of Oddi dysfunction, highlighting the need for continued vigilance even after the primary biliary cause has been addressed.⁷² In contrast, etiologies representing a singular, often self-limited insult to the pancreas, such as trauma (16%; CI, 6–36), drug-induced (14%; CI, 5–34), and virus-induced AP (3%; CI, 1–12), were associated with the lowest risks of recurrence, aligning with clinical expectations. Similarly, medication-related (not drug-induced) AP was associated with a lower risk of CP (OR, 0.26; CI, 0.07–0.91), further strengthening that singular, self-limiting insults have smaller effects on the progression of AP compared to permanent risk factors.

Severe AP was associated with a nearly doubled risk of progression to RAP (39%; CI, 15%–71%) compared to mild cases (21%; CI, 13%–31%), however the severe AP estimate should be interpreted with caution due to the small sample size ($N=85$) and the wide prediction interval (95% PI, 2%–95%). This likely reflects the extent of necrosis-driven fibrosis, as severe episodes trigger robust inflammatory cascades and the activation of pancreatic stellate cells.⁷³ Histopathological studies confirm that

severe AP induces collagen deposition and ductal distortion, creating a profibrotic microenvironment.⁷³⁾ These findings underscore the importance of aggressive initial management to mitigate long-term sequelae.

PRSSI mutations were strongly associated with CP (OR, 4.56; CI, 3.06–6.80), highlighting the role of genetic predisposition in CP inflammation. PRSSI mutations cause aberrant trypsinogen activation, leading to sustained pancreatic inflammation and fibrosis.⁷⁴⁾ This finding aligns with research from the INSPPIRE consortium and the Chinese cohort reported by Zeng et al., which demonstrated a 3.48-fold increased risk of developing CP in children with gene mutations.^{9,75)} This underscores the importance of genetic screening, particularly in recurrent cases, to identify children who may benefit from genetic counseling and potentially preventive strategies such as lifestyle modifications and closer clinical surveillance. Interestingly, mutations in SPINK1, CFTR, and CTRC, which have been previously implicated in pancreatitis susceptibility, did not reach statistical significance in our analysis. This nonsignificance may reflect limited sample sizes or heterogeneous genetic backgrounds across studies and warrants further large-scale genetic epidemiological studies in pediatric populations.

Our analysis also showed that anatomical anomalies substantially influence the risk of progression. Structural anomalies in general (OR, 3.15; CI, 1.51–6.56) and pancreas divisum specifically (OR, 2.64; CI, 1.51–4.63) were associated with a significantly increased risk of RAP and CP, respectively. Pancreas divisum, previously debated as a pathogenic factor, is now increasingly recognized in pediatric pancreatitis, supporting recommendations for routine evaluation of anatomical abnormalities in children presenting with pancreatitis.⁷⁶⁾

The nonsignificant findings for demographic factors (male sex, race) and common clinical parameters (e.g., amylase, lipase, white blood cell count, and CRP) suggest that these variables might have limited utility as isolated predictive markers for progression. Similarly, clinical complications such as pseudocysts or necrotizing pancreatitis were not predictive, challenging the clinical assumption that early complication severity consistently predicts long-term outcomes. This may reflect effective acute-phase management, preventing long-term sequelae, or indicate the need for larger studies to clarify these associations.

Our analysis revealed strong associations between CP and both EPI (OR, 22.82; CI, 9.26–56.25) and interventional procedures such as biliary sphincterotomy (OR, 4.16; CI, 3.24–5.34), biliary stenting (OR, 5.79; CI, 4.42–7.60), and pancreatic duct stenting (OR, 12.19; CI, 3.16–46.97). These associations reflect advanced disease rather than causal relationships. EPI occurs only after extensive (>90%) loss

of pancreatic acinar tissue, making it a late consequence of CP rather than a predictive risk factor.⁷⁷⁾ Similarly, endoscopic interventions are typically performed in patients with more severe or complicated pancreatitis, representing therapeutic responses to advanced disease rather than risk factors for progression.⁷⁸⁾ Temporal analysis was limited as the studies did not specify whether procedures preceded or followed CP diagnosis. Emerging evidence suggests that timely endoscopic intervention in select cases, such as symptomatic pancreas divisum, might modify disease progression, although randomized controlled trials are lacking.⁷⁶⁾

1. Strengths and limitations

A major strength of this meta-analysis is its comprehensive scope. To our knowledge, this is the first study to systematically synthesize the rates and risk factors for progression from acute to recurrent and CP in the pediatric population. The inclusion of 68 studies, spanning diverse geographic regions and healthcare settings, enhances the generalizability of our findings. We employed a rigorous methodology, including a prospectively registered protocol, and robust risk of bias assessment using validated tools (JBI and QUIPS). The use of subgroup and sensitivity analyses enabled us to account for between-study heterogeneity and explore the impact of etiology, severity, and study design on progression rates. Despite these strengths, several limitations should be considered. First, since adjusted estimates were not available, all risk factor analyses were based on raw data extracted from the included studies and therefore represent unadjusted ORs. Most included studies were retrospective and single-center, with a moderate risk of bias, often due to small sample sizes or incomplete control for confounding variables. Heterogeneity among the included studies was considerable, driven in part by differences in sample size, study period, and diagnostic definitions of AP. However, regarding disease progression, variability in diagnostic criteria affected only the overall recurrence rate estimates, as all studies examining other progression pathways (AP→CP, RAP→CP) and subgroup analyses (etiology, severity) were based exclusively on INSPPIRE definitions. Although we performed subgroup analyses and leave-one-out sensitivity analyses, residual heterogeneity remains a limitation. Finally, the observational nature of the included studies precludes definitive conclusions on causality for most risk factors.

2. Clinical and research implications

The substantial risk of recurrence and progression to CP after an initial AP episode in children underscores the need for close follow-up and early risk stratification.

Moreover, the identified rates and risk factors enable patient risk stratification, offering an implication that can be applied immediately at the bedside.^{79,80)} Clinicians should maintain a high index of suspicion for RAP and CP, particularly in children with hypertriglyceridemia, idiopathic etiology, or severe initial episodes. The strong associations identified between PRSSI mutations and CP, as well as between anatomical abnormalities and both RAP and CP, support the routine use of genetic testing and cross-sectional imaging in children with unexplained or recurrent pancreatitis. Early identification of patients at risk may enable targeted interventions, genetic counseling, and more personalized surveillance strategies. Our study highlights the need for long-term, multicenter cohort studies to chart the natural history of pediatric pancreatitis. It emphasizes the urgency of randomized trials testing early, targeted interventions in high-risk children to modify disease progression.

In conclusion, this meta-analysis demonstrates that approximately 1 in 5 children with AP will experience recurrence, and more than one-third of those with RAP will progress to CP. Recurrence is most common after hypertriglyceridemic, idiopathic or severe index attacks, while progression is further promoted by structural anomalies and genetic mutations.

Footnotes

Supplementary materials: Supplementary Tables 1–4 and Supplementary Figs. 1–14 are available at <https://doi.org/10.3345/cep.2025.01879>.

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References

1. Mekitarian Filho E, Carvalho WB, Silva FD. Acute pancreatitis in pediatrics: a systematic review of the literature. *J Pediatr (Rio J)* 2012;88:101-14.
2. Volkan B, Akkelle BŞ, Bayrak NA, Tutar E, Kalaycık Şengül Ö, Polat E, et al. Long-term follow-up and outcome of pediatric acute pancreatitis: a multicenter study. *Turk Arch Pediatr* 2023;58:388-94.
3. Uc A, Husain SZ. Pancreatitis in children. *Gastroenterology* 2019;156:1969-78.
4. Sağ E, Kaya G, Bahat-Özdoğan E, Karahan SC, İmamoğlu M, Sarihan H, et al. Acute pancreatitis in children: a single center experience over ten years. *Turk J Pediatr* 2018;60:153-8.
5. Sweeny KF, Lin TK, Nathan JD, Denson LA, Husain SZ, Hornung L, et al. Rapid progression of acute pancreatitis to acute recurrent pancreatitis in children. *J Pediatr Gastroenterol Nutr* 2019;68:104-9.
6. Kumar S, Ooi CY, Werlin S, Abu-El-Haija M, Barth B, Bellin MD, et al. Risk factors associated with pediatric acute recurrent and chronic pancreatitis: lessons from INSPPIRE. *JAMA Pediatr* 2016;170:562-9.
7. Zsoldos F, Párnitzky A, Mosztbacher D, Tóth A, Lásztity N, Hegyi P. Pain in the early phase of pediatric pancreatitis (PINEAPPLE trial): pre-study protocol of a multinational prospective clinical trial. *Digestion* 2016;93:121-6.
8. Suzuki M, Minowa K, Isayama H, Shimizu T. Acute recurrent and chronic pancreatitis in children. *Pediatr Int* 2021; 63:137-49.
9. Zeng J, Zhang J, Hu Y, Wang X, Deng Z. Risk factors for the progression from acute recurrent to chronic pancreatitis among children in China. *Front Pediatr* 2022;10:908347.
10. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71.
11. Munn Z, Stern C, Aromataris E, Lockwood C, Jordan Z. What kind of systematic review should I conduct? A proposed typology and guidance for systematic reviewers in the medical and health sciences. *BMC Med Res Methodol* 2018;18:5.
12. Morgan RL, Whaley P, Thayer KA, Schünemann HJ. Identifying the PECO: a framework for formulating good questions to explore the association of environmental and other exposures with health outcomes. *Environ Int*

- 2018;121:1027-31.
13. Morinville VD, Husain SZ, Bai H, Barth B, Alhosh R, Durie PR, et al. Definitions of pediatric pancreatitis and survey of present clinical practices. *J Pediatr Gastroenterol Nutr* 2012;55:261-5.
14. Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, et al. Classification of acute pancreatitis–2012: revision of the Atlanta classification and definitions by international consensus. *Gut* 2013;62:102-11.
15. Higgins JPT, Green S. *Cochrane handbook for systematic reviews of interventions*. The Cochrane Collaboration, 2008.
16. Bradley EL. A clinically based classification system for acute pancreatitis. Summary of the International Symposium on Acute Pancreatitis, Atlanta, GA, September 11 through 13, 1992. *Arch Surg* 1993;128:586-90.
17. McHugh ML. Interrater reliability: the kappa statistic. *Biochem Med (Zagreb)* 2012;22:276-82.
18. Munn Z, Moola S, Lisy K, Riitano D, Tufanaru C. Methodological guidance for systematic reviews of observational epidemiological studies reporting prevalence and cumulative incidence data. *Int J Evid Based Healthc* 2015;13:147-53.
19. Hayden JA, van der Windt DA, Cartwright JL, Côté P, Bombardier C. Assessing bias in studies of prognostic factors. *Ann Intern Med* 2013;158:280-6.
20. R Core Team. *R: A language and environment for statistical computing*. Vienna (Austria): R Foundation for Statistical Computing, 2024.
21. Schwarzer G. *Meta: general package for meta-analysis*. GitHub, 2022.
22. Cuijpers P, Furukawa T, Ebert DD. Dmetar: companion R package for the guide doing meta-analysis in R. *dmetar*, 2020.
23. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med* 2002;21:1539-58.
24. Int'Hout J, Ioannidis JP, Rovers MM, Goeman JJ. Plea for routinely presenting prediction intervals in meta-analysis. *BMJ Open* 2016;6:e010247.
25. Harbord RM, Harris RJ, Sterne JA. Updated tests for small-study effects in meta-analyses. *Stata J* 2009;9:197-210.
26. Alabdulkareem A, Almahmoud T, Al-Tahan H, Javad S, Al Hatlani M. Etiology and clinical characteristics of pediatric acute pancreatitis in Saudi Arabia: a 20-year experience from a single tertiary center. *Int J Pediatr Adolesc Med* 2018;5:13-7.
27. Anafy A, Mirkin Y, Galai T, Ben-Tov A, Moran-Lev H, Yerushalmy-Feler A, et al. Acute pancreatitis in children with inflammatory bowel disease: risk factors, clinical course, and prognosis. *J Pediatr Gastroenterol Nutr* 2024;79:325-34.
28. Anushree N, Lal SB, Rana SS, Saxena A, Venkatesh V, Sharma AK, et al. Morphological and functional recovery following acute and acute recurrent pancreatitis in children: a prospective sequential 2-point evaluation. *Pancreatol* 2022;22:698-705.
29. Appak YC, Karakoyun M, Cetin G, Akmaz N, Baran M. Diagnosis and management of pancreatitis in childhood: a single-centre experience. *Inn J Pediatr* 2018;28:e62499.
30. Badru F, Saxena S, Breeden R, Bourdillon M, Fitzpatrick C, Chatoorgoon K, et al. Optimal timing of cholecystectomy in children with gallstone pancreatitis. *J Surg Res* 2017;215:225-30.
31. Berney T, Belli D, Bugmann P, Beghetti M, Morel P, Le-Coutre C. Influence of severe underlying pathology and hypovolemic shock on the development of acute pancreatitis in children. *J Pediatr Surg* 1996;31:1256-61.
32. Bhanot A, Majbar AA, Candler T, Hunt LP, Cusick E, Johnson PRV, et al. Acute pancreatitis in children - morbidity and outcomes at 1 year. *BMJ Paediatr Open* 2022;6:e001487.
33. Bolia R, Srivastava A, Yachha SK, Poddar U, Kumar S. Prevalence, natural history, and outcome of acute fluid collection and pseudocyst in children with acute pancreatitis. *J Pediatr Gastroenterol Nutr* 2015;61:451-5.
34. Alvarez Calatayud G, Bermejo F, Morales JL, Claver E, Huber LB, Abunaji J, et al. Acute pancreatitis in childhood. *Rev Esp Enferm Dig* 2003;95:40-4, 45-8.
35. Grzybowska-Chlebowczyk U, Jasielska M, Flak-Wancerz A, Więcek S, Gruszczyńska K, Chlebowczyk W, et al. Acute pancreatitis in children. *Prz Gastroenterol* 2018;13:69-75.
36. Deveci U, Ünsal SK, Dogan Y. A retrospective review of children followed up with the diagnosis of acute pancreatitis. *Niger J Clin Pract* 2023;26:1876-85.
37. Galai T, Cohen S, Yerushalmy-Feler A, Weintraub Y, Moran-Lev H, Amir AZ. Young age predicts acute pancreatitis severity in children. *J Pediatr Gastroenterol Nutr* 2019;68:720-6.
38. Geetha M, Saumya M, Balakrishnan V. Spectrum of pancreatitis in children and adolescents. *Indian J Gastroenterol* 2012;31:175-8.
39. Getsuwan S, Tanpowpong P, Lertudomphonwanit C, Junhasavasdikul T, Tim-Aroon T, Treepongkaruna S. Etiology and outcome of acute recurrent pancreatitis and chronic pancreatitis. *Pediatr Int* 2022;64:e15145.
40. Guo Q, Li M, Chen Y, Hu H, Hu W. Predictors for mortality following acute pancreatitis in children. *Pediatr Surg Int* 2014;30:1111-5.
41. Hao F, Guo H, Luo Q, Guo C. Disease progression of acute pancreatitis in pediatric patients. *J Surg Res* 2016;202:422-7.
42. Al Hindi S, Khalaf Z, Nazzal K, Nazzal O, Ahmed A, Alshai-bani L. Acute pancreatitis in children: the clinical profile at a tertiary hospital. *Cureus* 2021;13:e14871.
43. Kandula L, Lowe ME. Etiology and outcome of acute pancreatitis in infants and toddlers. *J Pediatr* 2008;152:106-10, 110.e1.
44. Kim HJ. Potential predictors of severe and recurrent pancreatitis in children: a single-center experience. *Pediatr Emerg Care* 2024;40:302-6.
45. Laugel V, Escande B, Entz-Werle N, Mazingue F, Ferster A, Bertrand Y, et al. [Severe acute pancreatitis in children receiving asparaginase: multicenter retrospective study]. *Arch Pediatr* 2005;12:34-41.
46. López MM, Herrero MM, Puente MH, Hernani MT, Sánchez CS, Calatayud G. Pancreatitis aguda: nuestra experiencia/acute pancreatitis: our experience. *Acta Pediatr Esp* 2013;71:3-8.
47. Majbar AA, Cusick E, Johnson P, Lynn RM, Hunt LP, Shield JP. Incidence and clinical associations of childhood acute pancreatitis. *Pediatrics* 2016;138:e20161198.
48. Mengdi LQ, Liang G. Predictive efficacy of BISAP, Pane 3

- and HAP scores in children with acute pancreatitis. *Chin J Pediatr Surg* 2022;43:993-1000.
49. Minen F, De Cunto A, Martelossi S, Ventura A. Acute and recurrent pancreatitis in children: exploring etiological factors. *Scand J Gastroenterol* 2012;47:1501-4.
 50. Mirza N, Mehta S, Kumar K, Malhotra S, Sibal A. Clinical profile of acute pancreatitis in children and adolescents from a single center in Northern India. *J Indian Assoc Pediatr Surg* 2023;28:35-40.
 51. Nasr A, Hornung L, Thompson T, Lin TK, Vitale DS, Nathan JD, et al. Prevalence of gastrointestinal symptoms and impact on quality of life at 1-year follow-up of initial attack of acute pancreatitis. *J Pediatr Gastroenterol Nutr* 2023;76:199-205.
 52. Nauka PC, Weinstein TA, Dolinger MT, Miller JM, Kohn N, Bitton S, et al. Validation of lipase and systemic inflammatory response syndrome as prognostic indicators in pediatric acute pancreatitis: a retrospective analysis. *J Pediatr Gastroenterol Nutr* 2019;68:389-93.
 53. Ohta K, Okanishi T, Sasaki M, Kawaguchi T, Murakami J, Maegaki Y. Tendency and risk factors of acute pancreatitis in children with severe motor and intellectual disabilities: a single-center study. *Brain Dev* 2023;45:126-33.
 54. Park A, Latif SU, Shah AU, Tian J, Werlin S, Hsiao A, et al. Changing referral trends of acute pancreatitis in children: a 12-year single-center analysis. *J Pediatr Gastroenterol Nutr* 2009;49:316-22.
 55. Pezzilli R, Morselli-Labate AM, Castellano E, Barbera C, Corrao S, Di Prima L, et al. Acute pancreatitis in children. An Italian multicentre study. *Dig Liver Dis* 2002;34:343-8.
 56. Poddar U, Yachha SK, Borkar V, Srivastava A, Kumar S. A report of 320 cases of childhood pancreatitis: increasing incidence, etiologic categorization, dynamics, severity assessment, and outcome. *Pancreas* 2017;46:110-5.
 57. Poddar U, Yachha SK, Borkar V, Srivastava A. Is acute recurrent pancreatitis in children a precursor of chronic pancreatitis? A long-term follow-up study of 93 cases. *Dig Liver Dis* 2017;49:796-801.
 58. Singh SK, Srivastava A, Rai P, Yachha SK, Poddar U. Yield of endoscopic ultrasound in children and adolescent with acute recurrent pancreatitis. *J Pediatr Gastroenterol Nutr* 2018;66:461-5.
 59. Stringer MD, Davison SM, McClean P, Rajwal S, Puntis JW, Sheridan M, et al. Multidisciplinary management of surgical disorders of the pancreas in childhood. *J Pediatr Gastroenterol Nutr* 2005;40:363-7.
 60. Tiao MM, Chuang JH, Ko SF, Kuo HW, Liang CD, Chen CL. Pancreatitis in children: clinical analysis of 61 cases in southern Taiwan. *Chang Gung Med J* 2002;25:162-8.
 61. Wang C, Fu B, Su D, Huang P, Fu X. Acute pancreatitis and recurrent acute pancreatitis in children: a 10-year retrospective study. *Gastroenterol Res Pract* 2022;2022:5505484.
 62. Yeung CY, Lee HC, Huang FY, Ho MY, Kao HA, Liang DC, et al. Pancreatitis in children--experience with 43 cases. *Eur J Pediatr* 1996;155:458-63.
 63. Zheng Q, Yan X, Ge L, Zhang S, Sun Y, Jia J, et al. Risk factors of recurrent acute pancreatitis after conservative treatment in pediatric population: a single-center study. *World J Pediatr Surg* 2021;4:e000209.
 64. Zhong R, Tan S, Peng Y, Xu H, Jiang X, Yan Y, et al. Clinical characteristics of acute pancreatitis in children: a single-center experience in Western China. *BMC Gastroenterol* 2021;21:116.
 65. Zhu YM, Liu F, Zhou XY, You JY, Xu ZY, DU YK. [Clinical characteristics of children with acute pancreatitis]. *Zhonghua Er Ke Za Zhi* 2011;49:10-6.
 66. Hajibandeh S, Jurdon R, Heaton E, Hajibandeh S, O'Reilly D. The risk of recurrent pancreatitis after first episode of acute pancreatitis in relation to etiology and severity of disease: a systematic review, meta-analysis and meta-regression analysis. *J Gastroenterol Hepatol* 2023;38:1718-33.
 67. Li S, Gao L, Gong H, Cao L, Zhou J, Ke L, et al. Recurrence rates and risk factors for recurrence after first episode of acute pancreatitis: a systematic review and meta-analysis. *Eur J Intern Med* 2023;116:72-81.
 68. Gagyi EB, Teutsch B, Veres DS, Pálincás D, Vörhendi N, Ocskay K, et al. Incidence of recurrent and chronic pancreatitis after acute pancreatitis: a systematic review and meta-analysis. *Therap Adv Gastroenterol* 2024;17:17562848241255303.
 69. Grisham JM, Tran AH, Ellery K. Hypertriglyceridemia-induced acute pancreatitis in children: a mini-review. *Front Pediatr* 2022;10:931336.
 70. Aronen A, Guilbert L, Hadi A, Kiudelis V, Panaitescu A, Wlodarczyk B, et al. Idiopathic acute pancreatitis (IAP)-a review of the literature and algorithm proposed for the diagnostic work-up of IAP. *Transl Gastroenterol Hepatol* 2024;9:71.
 71. Umans DS, Timmerhuis HC, Anten MGF, Bhalla A, Bijlsma RA, Boxhoorn L, et al. Prospective multicentre study of indications for surgery in patients with idiopathic acute pancreatitis following endoscopic ultrasonography (PICUS). *Br J Surg* 2023;110:1877-82.
 72. Abu-El-Haija M, Kumar S, Quiros JA, Balakrishnan K, Barth B, Bitton S, et al. Management of acute pancreatitis in the pediatric population: a clinical report from the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition Pancreas Committee. *J Pediatr Gastroenterol Nutr* 2018;66:159-76.
 73. Glaubitz J, Asgarbeik S, Lange R, Mazloun H, Elsheikh H, Weiss FU, et al. Immune response mechanisms in acute and chronic pancreatitis: strategies for therapeutic intervention. *Front Immunol* 2023;14:1279539.
 74. Whitcomb DC. Genetic risk factors for pancreatic disorders. *Gastroenterology* 2013;144:1292-302.
 75. Liu QY, Abu-El-Haija M, Husain SZ, Barth B, Bellin M, Fishman DS, et al. Risk factors for rapid progression from acute recurrent to chronic pancreatitis in children: report from INSPPIRE. *J Pediatr Gastroenterol Nutr* 2019;69:206-11.
 76. Lin TK, Abu-El-Haija M, Nathan JD, Palermo JP, Barth B, Bellin M, et al. Pancreas divisum in pediatric acute recurrent and chronic pancreatitis: report from INSPPIRE. *J Clin Gastroenterol* 2019;53:e232-8.
 77. Struyvenberg MR, Martin CR, Freedman SD. Practical guide to exocrine pancreatic insufficiency - breaking the myths. *BMC Med* 2017;15:29.
 78. Husain SZ, Srinath AI. What's unique about acute pancrea-

titis in children: risk factors, diagnosis and management. *Nat Rev Gastroenterol Hepatol* 2017;14:366-72.

79. Hegyi P, Petersen OH, Holgate S, Erőss B, Garami A, Szakács Z, et al. Academia Europaea position paper on translational medicine: the cycle model for translating scientific results into community benefits. *J Clin Med* 2020;9:1532.
80. Hegyi P, Erőss B, Izbéki F, Párnitzky A, Szentesi A. Accelerating the translational medicine cycle: the Academia Europaea pilot. *Nat Med* 2021;27:1317-9.

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