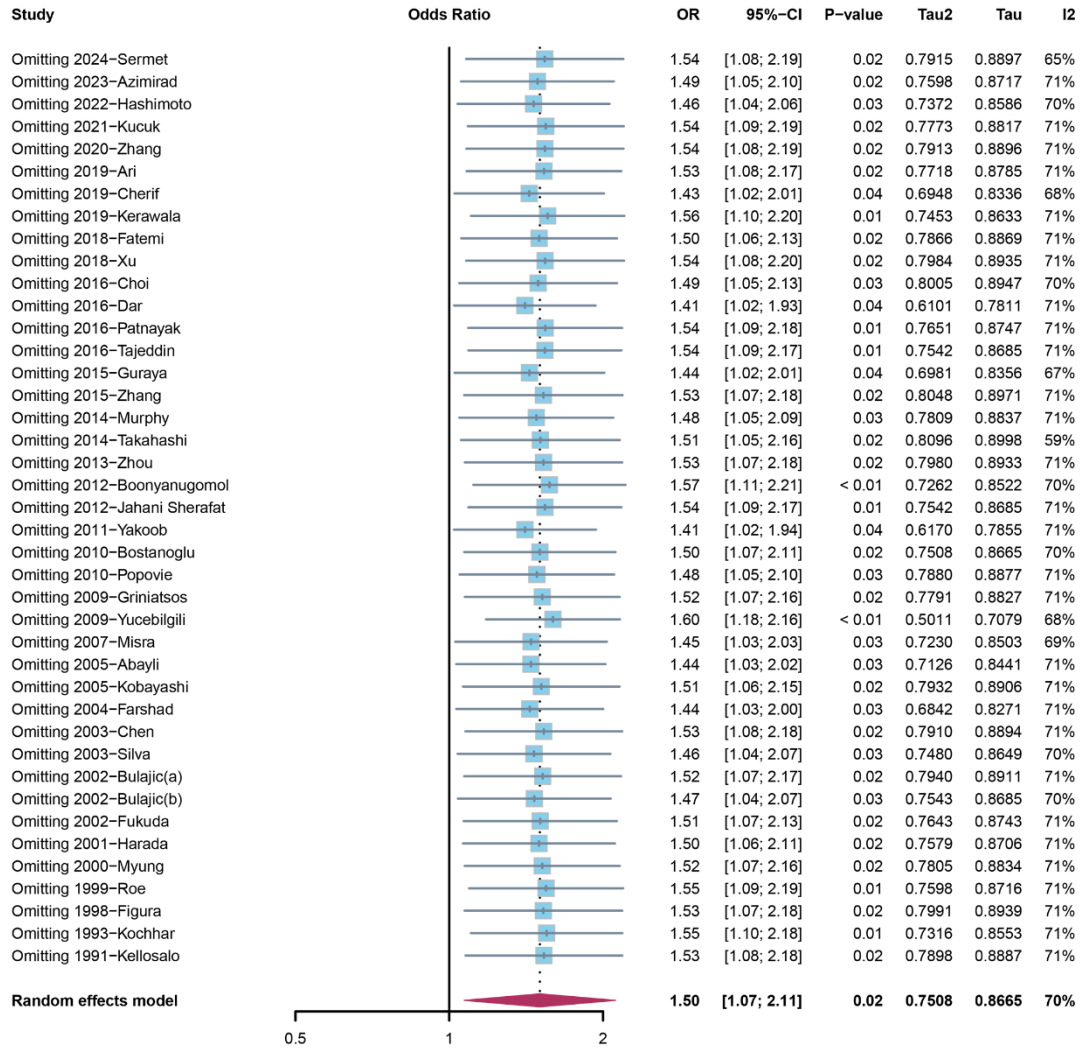


**Supplementary Figure 1** The funnel plot of the included 41 case-control and cross-sectional studies for the analysis of relationship between *Hp* infection and cholelithiasis risk. *Hp*: *Helicobacter pylori*



**Supplementary Figure 2** The results of sensitivity analysis by omitting one of the included case-control and cross-sectional studies

Supplementary Table 1 MOOSE Checklist

Criteria	Brief description of how the criteria were handled in the meta-analysis
<b>Reporting of background should include</b>	
Problem definition	<i>Helicobacter pylori</i> ( <i>Hp</i> ) infection in the biliary system has been reported in several studies, but the relationship between <i>Hp</i> and cholelithiasis remains controversial. Given their high prevalence, understanding the association between <i>Hp</i> infection and cholelithiasis is crucial for effective management of both conditions.
Hypothesis statement	<i>Hp</i> infection is associated with an increased risk of developing cholelithiasis.
Description of study outcomes	Cholelithiasis
Type of exposure or intervention used	<i>Hp</i> tested positive
Type of study designs used	The studies included were either case-control, cohort or cross-sectional in design.
Study population	No limitations were imposed.
<b>Reporting of search strategy should include</b>	
Qualifications of searchers	Each step was conducted by 2 investigators independently.
Search strategy, including time period included in the synthesis and keywords	We searched up to May 10, 2024, with the search strategy of “(( <i>Helicobacter pylori</i> ) OR ( <i>H. pylori</i> ) OR (HP) OR ( <i>Helicobacter</i> ) OR ( <i>Helicobacter species</i> ) OR ( <i>Helicobacter spp.</i> ) OR ( <i>Helicobacter genus</i> ) OR ( <i>Helicobacter pylori infection</i> ) OR ( <i>Helicobacter infection</i> ) OR ( <i>pylori</i> ) OR ( <i>enterohepatic Helicobacter spp.</i> ) OR <i>campylobacter</i> OR ( <i>campylobacter infection</i> ) OR <i>campylobacteriosis</i> OR ( <i>Campylobacter pylori*</i> OR <i>Campylobacter pylori subsp. Pylori</i> ) OR ( <i>campylobacter spp</i> )) AND ( <i>cholelithiasis</i> OR <i>cholecystolithiasis</i> OR <i>hepatolithiasis</i> OR <i>choledocholithiasis</i> OR <i>gallstone*</i> OR <i>gall*stone*</i> OR ( <i>gallbladder AND stone*</i> ) OR ( <i>gallbladder AND cholelith*</i> ) OR ( <i>gallbladder AND lithiasis</i> ) OR <i>bilestone*</i> OR ( <i>bile AND</i>

	stone*) OR (bile AND lithiasis) OR (bile AND cholelith*) OR (biliary AND calculus) OR (biliary AND stone*) OR (biliary AND cholelith*) OR (biliary AND lithiasis))”.
Effort to include all available studies, including contact with authors	We searched 4 major databases and applied no restriction other than the criteria mentioned in the Material and Methods section.
Databases and registries searched	PubMed, Embase, Web of Science, and Cochrane Library.
Search software used, name and version, including special features	We did not utilize any software for searching. EndNote was employed to screen retrieved citations and eliminate any redundancies.
Use of hand searching	We manually searched relevant studies for additional references.
List of citations located and those excluded, including justifications	The detailed search process is shown in Figure 2. The citation list could be provided if necessary.
Method of addressing articles published in languages other than English	Non-English studies were excluded.
Method of handling abstracts and unpublished studies	The studies unable to get detailed data and unpublished papers were left out.
Description of any contact with authors	None.
<b>Reporting of methods should include</b>	
Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	The Material and Methods section defined detailed inclusion and exclusion criteria.

Rationale for the selection and coding of data	The information was extracted including publication year, first author, region, types of cholelithiasis, sample sizes, sample sources and detection methods of <i>Hp</i> , and the <i>Hp</i> status of each group.
Documentation of how data were classified and coded	The decisions were made independently by 2 investigators. Any disagreement would be settled by a third investigator.
Assessment of confounding	It is in strict accordance with the Material and Methods section.
Assessment of study quality, including blinding of quality assessors; stratification or regression on possible predictors of study results	The methodologic index for non-randomized studies (MINORS) was used to assess the quality of included studies.
Assessment of heterogeneity	The heterogeneity was assessed by $I^2$ .
Description of statistical methods in sufficient detail to be replicated	The details of statistical analysis were described in the Material and Methods section.
Provision of appropriate tables and graphics	A flow chart, a pie chart, forest plots, a funnel plot, and tables were used in our article.
<b>Reporting of results should include</b>	
Graph summarizing individual study estimates and overall estimate	The pooled results were shown by forest plots.
Table giving descriptive information for each study included	Table 4 revealed the characteristics of included studies.
Results of sensitivity testing	Subgroup analyses were conducted according to regions.
Indication of statistical uncertainty of findings	The summarized odds ratios (OR) and hazard ratios (HR) were presented with a 95% confidence interval (CI) and we also performed the calculation of $I^2$ , and sensitivity analyses.
<b>Reporting of discussion should include</b>	

Quantitative assessment of bias	The funnel plot and Peters' test were used to evaluate the publication bias.
Justification for exclusion	We applied the exclusion criteria mentioned in the Material and Methods section.
Assessment of quality of included studies	The MINORS points of included studies were in the supplemental tables and the mean points were reported.
<b>Reporting of conclusions should include</b>	
Consideration of alternative explanations for observed results	We provided existing evidence of the underlying mechanisms of <i>Hp</i> -related cholelithiasis, the probable explanation of different results in various studies, and the possible source of heterogeneity.
Generalization of the conclusions	The pooled results indicated the <i>Hp</i> infection is positively associated with cholelithiasis especially in specific groups.
Guidelines for future research	Further studies are required to confirm the relationship between <i>Hp</i> infection and cholelithiasis as well as the mechanism behind this.
Disclosure of funding source	The funding source is presented in the manuscript.

**Supplementary Table 2** The detailed data of included studies for risk analysis

Year	First author	NO. of cholelithiasis	NO. of cholelithiasis	non-cholelithiasis +	cholelithiasis -	Non-cholelithiasis +	Non-cholelithiasis -	MINORS
2024	Loosen <sup>[1]</sup>	2394	34669	920	1474	10727	23942	18
2024	Sermet <sup>[2]</sup>	8753	5565	4599	4154	3052	2513	18
2023	Azimirad <sup>[3]</sup>	9	6	4	5	1	5	18
2023	Cen <sup>[4]</sup>	60	1132	34	26	492	640	16
2022	Higashizono <sup>[5]</sup>	23843	588087	1513	22330	28545	559542	14
2022	Hashimoto <sup>[6]</sup>	14	47	6	8	6	41	18
2021	Kucuk <sup>[7]</sup>	131	82	41	90	31	51	20
2020	Zhang <sup>[8]</sup>	935	935	428	507	453	482	17
2019	Kerawala <sup>[9]</sup>	45	45	34	11	39	6	17
2019	Cherif <sup>[10]</sup>	48	41	35	13	13	28	20
2019	Ari <sup>[11]</sup>	27	33	3	24	5	28	16
2018	Xu <sup>[12]</sup>	995	16976	432	563	7371	9605	18
2018	Fatemi <sup>[13]</sup>	52	25	46	6	20	5	17
2016	Tajeddin <sup>[14]</sup>	74	28	2	72	2	26	17

2016	Patnayak <sup>[15]</sup>	40	5	8	32	2	3	17
2016	Dar <sup>[16]</sup>	50	25	20	30	0	25	14
2016	Choi <sup>[17]</sup>	39	607	25	14	282	325	14
2015	Zhang <sup>[18]</sup>	882	9134	323	559	3087	6047	18
2015	Guraya <sup>[19]</sup>	95	30	75	20	12	18	16
2014	Takahashi <sup>[20]</sup>	694	14857	273	421	4220	10637	18
2014	Murphy <sup>[21]</sup>	10	214	10	0	188	26	18
2013	Zhou <sup>[22]</sup>	267	59	55	212	12	47	20
2012	Jahani Sherafat <sup>[23]</sup>	74	28	2	72	2	26	18
2012	Boonyanugomol <sup>[24]</sup>	53	103	22	31	62	41	14
2011	Yakoob <sup>[25]</sup>	89	49	21	68	0	49	16
2010	Popović <sup>[26]</sup>	3	204	3	0	139	65	18
2010	Bostanoglu <sup>[27]</sup>	47	3	0	47	0	3	14
2009	Yucebilgili <sup>[28]</sup>	41	27	2	39	13	14	15
2009	Griniatsos <sup>[29]</sup>	89	42	4	85	2	40	20
2007	Misra <sup>[30]</sup>	116	45	45	71	5	40	14
2005	Kobayashi <sup>[31]</sup>	30	27	17	13	14	13	14



2005	Abayli <sup>[32]</sup>	77	20	18	59	0	20	12
2004	Farshad <sup>[33]</sup>	33	40	6	27	0	40	12
2003	Silva <sup>[34]</sup>	46	18	18	28	2	16	16
2003	Chen <sup>[35]</sup>	70	52	22	48	17	35	14
2002	Fukuda <sup>[36]</sup>	15	23	1	14	1	22	18
2002	Bulajic(b) <sup>[37]</sup>	65	7	35	30	1	6	17
2002	Bulajic(a) <sup>[38]</sup>	63	26	37	26	15	11	16
2001	Harada <sup>[39]</sup>	53	16	1	52	0	16	14
2000	Myung <sup>[40]</sup>	30	13	26	4	11	2	14
1999	Roe <sup>[41]</sup>	11	21	3	8	9	12	14
1998	Figura <sup>[42]</sup>	112	112	92	20	90	22	17
1993	Kochhar <sup>[43]</sup>	3	15	0	3	8	7	17
1991	Kellosalo <sup>[44]</sup>	47	41	26	21	23	18	18

+: *Helicobacter pylori* positive; -: *Helicobacter pylori* negative. MINORS: Methodological index for non-randomized studies.

**Supplementary Table 3** The detailed data of included studies for phenotype analysis

Year	First author	Phenotype	Sample	Method for <i>Hp</i>	NO. Sample	of	<i>Hp</i> +	<i>Hp</i> -	MINORS
2001	Harada [39]	Choledocholithiasis	Bile	PCR	10		1	9	14
		Cholecystolithiasis	Bile/ epithelium	biliary PCR	23		0	23	
2005	Kobayashi [31]	Cholecystolithiasis	Bile	PCR	26		14	12	14
		Choledochocystolithiasis	Bile	PCR	4		3	1	
2010	Lee [45] a	Pigmented gallstones	gallstones	PCR	12		2	10	10
		Cholesterol gallstones	gallstones	PCR	10		0	10	
2013	Zhou [22]	Cholesterol	Gallbladder	PCR	82		14	68	20
		Pigment	Gallbladder	PCR	43		8	35	
2016	Dar [16]	Choledocholithiasis	Bile	PCR	19		9	10	14
		Cholelithiasis	Bile	PCR	18		4	14	
2016	Patnayak [15]	Pigment	Gallbladder	Immunostaining	27		6	21	17
		Cholesterol	Gallbladder	Immunostaining	3		0	3	
2016	Tajeddin [14]	Common bile duct stone	Bile	PCR	19		1	18	17
		Gallbladder stone	Bile	PCR	44		1	43	
		Cholesterol	Bile	PCR	47		1	46	
		Black pigment	Bile	PCR	23		0	23	
		Brown pigment	Bile	PCR	4		1	3	
2017	Seyyedmajidi [46] a	Cholesterol gallstones	Bile	PCR	87		10	77	12
		Black pigment stones	Bile	PCR	41		4	37	
		Brown pigment stones	Bile	PCR	22		2	20	
2021	Jahantab [47] a	Cholesterol	Bile	Antigen test	31		6	25	11

Pigment	Bile	Antigen test	101	28	73
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a: These studies are non-comparative studies. MINORS: Methodological index for non-randomized studies; *Hp*: *Helicobacter pylori*; PCR: polymerase chain reaction.

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