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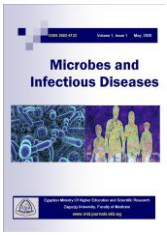

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Review article

Prevalence of occult hepatitis B in Southeast Asia: The first systematic review and meta-analysis

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ABSTRACT

Background: Occult hepatitis B infection is a significant public health concern in Southeast Asia. This systematic review and meta-analysis were conducted to provide detailed information about the pooled prevalence of OHB in Southeast Asia. **Methods:** A systematic search for articles describing the prevalence of OHB within Southeast Asian countries was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines. Our search returned fifteen (15) eligible articles involving 1864 OHB cases representing seven (7) Asian countries. A meta-analysis was performed on our eligible studies using the random effect model. A protocol was registered with PROSPERO (CRD42023422981). **Results**: The pooled prevalence of OHB in Southeast Asia was relatively high [10.5% (95% CI, 6.8% – 16.0%; I^2 = 98.37%; p < 0.001)]. Cambodia (51.2%, CI: 48.3 – 54.0%) had the highest estimate for OHB among the Southeast Asian countries. There was a significant difference in the prevalence of OHB with the year of study and types of study designs at p < 0.001. Between 2006 and 2010, studies had the highest pooled prevalence (25.0%, CI: 12.0 – 44.8%). There was a decrease in OHB pooled prevalence at the beginning of 2011. **Conclusion:** The findings of this review revealed a significant prevalence of OHB in Southeast Asia (10.5%) and a fall in the incidence of OHB over the last decade in Southeast Asia. The high prevalence of OHB in Southeast Asia, despite the drop in OHB incidence within the previous decades, stirs the need for an effective HBV prevention and control scheme.

Introduction

The hepatitis B virus is a significant public health concern globally [1], even after the introduction of the HBV vaccine[2]. A particular type of hepatitis B virus infection known as occult hepatitis B (OHB) is distinguished by the absence of hepatitis B surface antigen (HBsAg) in the serum despite the presence of viral DNA [3, 4]. This

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occurrence presents a severe problem for diagnosing and treating hepatitis B because people with occult infections may go unnoticed and pose a risk of spreading the disease [4,5]. Particularly in Southeast Asia, where hepatitis B infection is dominant, the prevalence and significance of concealed hepatitis B have attracted considerable attention [6]. This area has been classified as an OHB hotspot with a significant effect on public health [7].

In Southeast Asia, hepatitis B infection is a severe public health issue due to the high endemicity in several countries [7]. According to studies, some people in this region with chronic hepatitis B infection may also have occult hepatitis B [4, 8, 9]. Various populations have different OHB prevalence rates, which are impacted by variables like location, population demographics, and screening techniques[8, 10–12].

Numerous epidemiological studies have emphasised Southeast Asia's high prevalence of undetected hepatitis B. For instance, a Thai study found that among chronic hepatitis B patients who did not test positive for HBsAg, OHB prevalence was around 20%. Similarly, investigations in other Southeast Asian nations like Vietnam, Indonesia, and Malaysia have revealed prevalence rates ranging from 10% to 30% in various at-risk populations [4, 13–15].

Occult hepatitis B has critical clinical repercussions since it can lead to progressive liver damage and spread the HBV virus. Although people with OHB may have undetectable HBsAg levels, they frequently have detectable HBV DNA levels showing continuous viral replication [16, 17]. This ongoing viral replication can cause liver fibrosis, inflammation, and, ultimately, the emergence of hepatocellular cancer (HCC) [18].

Occult hepatitis B also presents a problem in the context of organ transplantation and blood transfusions [19]. Routine screening tests that do not detect HBsAg may unintentionally transmit occult HBV to vulnerable people, accelerating the disease's spread. Furthermore, the likelihood of the receiver contracting OHB after an organ transplant is increased, which could make the process more complex [19–21].

Several multifaceted, poorly understood mechanisms cause occult hepatitis B in Southeast Asia. Viral mutations, host immune responses, and co-infections are just a few theories explaining why hidden infections happen. The emergence of occult hepatitis B is heavily dependent on viral alterations. Point mutations in the HBV genome's pre-S or S region can lead to faulty or shortened HBsAg production, making it impossible to detect using standard serological techniques. These mutations may occur naturally or due to the host immune system or antiviral treatment exerting selection pressure [22].

Host immunological responses also influence the enduring presence of occult hepatitis B. As a result of the immune system's persistent strain on the virus in chronically infected people, escape mutants and concealed infection occur. The development of occult hepatitis B may also be influenced by host variables such as genetic differences in immune response genes and compromised cellular immunological responses [23, 24].

The development of hidden hepatitis B has been linked to co-infections, especially with other hepatitis viruses. HBV replication and expression can be altered by co-infection with hepatitis C (HCV) or the hepatitis D viruses (HDV), resulting in occult infection [25, 26]. The interaction between different viral infections may affect how the disease develops and how well treatments work [27].

Sensitive nucleic acid amplification methods are required for accurate occult hepatitis B diagnosis to identify low amounts of HBV DNA without HBsAg. Numerous techniques have been used to detect occult infection, including real-time polymerase chain reaction (PCR), nested PCR, and branched DNA tests. Variables like availability, cost-effectiveness, sensitivity, and specificity influence the selection of a diagnostic technique [13, 28, 29].

Southeast Asia is especially susceptible to the occult hepatitis B danger due to the region's high hepatitis B prevalence. The unusual epidemiology of OHB in the area results from the interaction of many elements, including co-infections, genetic variants, virus and host characteristics, and environmental factors. Effective disease management, prevention tactics, and public health initiatives depend on understanding the prevalence, clinical outcomes, and risk factors related to OHB in Southeast Asia [30, 31].

Despite the significant burden of OHB in Southeast Asian countries, the pooled prevalence of the occurrence of OHB in Southeast Asia is yet to be reported. This systematic review and meta-analysis

provide adequate information in that regard. To our knowledge, this systematic review and meta-analysis is the first of its kind. The findings of this study will provide baseline data on the pooled prevalence of OHB in Southeast Asia, and it will help healthcare providers and policymakers with practical OHB managerial tips and policies that will help reduce the associated OHB morbidity in Southeast Asia countries and entire Asia.

Methods

Study design and protocol

This systematic review and meta-analysis had a study protocol registered with the PROSPERO, a systematic review protocol database with the registration ID CRD42023422981. The PRISMA guideline was used as a checklist for this study **(Supplementary file K1)**.

Search strategy, inclusion, and exclusion criteria

A thorough search was conducted using various databases and search criteria to guarantee that no existing or ongoing reviews on "Occult hepatitis B in Southeast Asia" were duplicated. We first searched PROSPERO and the Database of Abstracts of Reviews of Effects (DARE) for ongoing or past reviews. PubMed, Scopus, Google Scholar, and ScienceDirect were searched among four international databases to learn more about the prevalence of occult hepatitis B in Southeast Asian nations.

Search phrases that best reflected the study were used as part of the search strategy for the PubMed database. OBI infection, occult hepatitis B, occult hepatitis B virus, and the names of specific Southeast Asian nations were among these labels (such as Brunei, Cambodia, Indonesia, Laos, Malaysia, Myanmar, Philippines, Singapore, Thailand, Timor-Leste, and Vietnam). Occult, hepatitis B, and infectious disease-related search phrases were added. The search method included MeSH terms and general keyword searches to find a wide range of pertinent papers. **File (K2)** of the supplemental materials contains the search methodology used for the databases.

The terms "Occult hepatitis B," "OBI," and "Southeast Asian countries" were used for the thorough search in databases other than PubMed. The titles and references of papers that satisfied the inclusion criteria were further examined as an extra search strategy. There were no language or publication year constraints on any of the searches. On February 23, 2023, the last search was conducted. Three authors separately searched the literature to reduce bias. Before screening titles and abstracts, all the included references were imported into the Mendeley Reference Manager, and duplicate entries were eliminated to assure accuracy.

Retrospective, cross-sectional, prospective , case-control, and randomised clinical trials were the study types used in this investigation. For inclusion, only first-person accounts of occult hepatitis B (OHB) in Southeast Asian nations were considered. Reviews, brief communications, comments, conference proceedings, editorials, studies reporting OHB outside of Southeast Asia, studies reporting OHB in non-HBV cases, studies with ambiguous OHB information, duplicate data, studies lacking clarity regarding the number of individuals examined, and studies with insufficient information (such as an unclear description of the detection method and type of sample) were all excluded from the study.

Data extraction and quality assessment

Three writers independently assessed the chosen studies' full text, abstract, and title during the screening process. They gathered pertinent data and organised it in a table. Any disagreements among the authors were settled by consensus after a fourth author assessed the findings. Title, abstract, and full-text screening were the three stages of the screening procedure. The first author's name, publication year, country, sample size, number of cases, occult hepatitis B (OHB) cases, detection technique, and study design type were all collected from each included study.

Three authors independently employed the Joanna Briggs Institute (JBI) prevalence data appraisal criteria **(Supplementary file K3)** to evaluate the studies' level of quality [32]. The nine parameters of this evaluation checklist set forth the standards for a typical research project. The results were scored using a "zero (0) for NO" and "two (2) for YES" coding scheme. Studies were graded from 0 to 18 according to the Joanna Briggs Institute's rigorous appraisal of prevalence data. Studies were deemed unacceptable for this study if their overall scores fell below fourteen (14) points. Studies that scored above fourteen (14) were considered high quality and included. **The supporting file (K4)** contains the evaluation of the quality score for each study. Three authors independently conducted the quality assessment. The reviewers' agreement was the basis for including papers in this investigation.

Data analysis

Two software packages were used for data analysis: Comprehensive Meta-Analysis software and OpenMeta Analyst version 3.1 (CEBM, 2022, Providence, RI, USA) (Biostat. inc, 2021, Englewood, NJ, USA) [33].

Subgroup analyses were carried out based on the study's type, country of origin, and year of sample collection to calculate the pooled prevalence of occult hepatitis B (OHB) in Southeast Asia. The random effects model was the most appropriate for this investigation because of the high diversity in sample collecting procedures, sample collection times, and detection techniques. This meta-analysis determined the pooled prevalence using the DerSimonian and Laird techniques [34].

A forest plot was built to evaluate the importance of each study, effect sizes, proportional prevalence, confidence ranges of predicted prevalence, and the level of heterogeneity. Logit transformation was used to transform all the data.

Utilising funnel plots and Egger's regression test, publication bias was investigated. The Inconsistency index Statistics (I^2) was used to measure the heterogeneity of study-level estimates, with values above 75%, 50%, and 25%, denoting strong, moderate, and low heterogeneity, respectively [35]. Heterogeneity was also assessed using the Cochrane Q test. If the Q ratio to the degree of freedom (df) is less than one (Q: df 1), non-significant heterogeneity would be allowed. A subgroup meta-analysis was carried out to pinpoint the causes of heterogeneity. The "Leave One Out" meta-analysis sensitivity test was used to analyse the overall impact of each study on the pooled prevalence and outcomes, as well as the between-study source of heterogeneity.

Results

Search results and eligible studies

Initially, 3973 abstracts were collected from the four worldwide electronic databases using a search strategy. Based on their titles and abstracts, 2186 papers were rejected after duplicates were eliminated—one hundred fourteen (114) papers qualified for full-text examination. However, 97 were disqualified because they didn't fit our inclusion requirements. The 16 q2 publications that comprised this comprehensive literature assessment and meta-analysis included 1864 OHB cases in 9006 Southeast Asian patients.

Characteristics of the eligible studies

The present study encompasses a comprehensive analysis conducted across seven Southeast Asian countries: Bangladesh, Indonesia, Laos, Thailand, Malaysia, Cambodia, and Vietnam. Sixteen articles from these countries met our inclusion criteria **(Table 1)**. Notably, Indonesia accounted for 37.5% (n=6) of the articles.

Across the sixteen studies, a total of 1864 cases of OHB were reported, with Cambodia documenting the highest number of cases (614 OHB cases), while Vietnam reported the lowest number (2 OHB cases) **(Table 1)**.

The articles encompassed three distinct study designs, namely cross-sectional, case-control, and retrospective studies. The cross-sectional design contributed significantly to the overall body of research, accounting for 81.3% (n=13), followed by case-control studies comprising 11.8% (n=2) and retrospective studies representing 5.9% (n=1) **(Table 1)**. Most study samples were collected between 2011 and 2015, comprising nine articles **(Table 1)**. A summary of included articles is provided in **Table (1)**.

Prevalence of OHB in Southeast Asia

There was a high pooled prevalence of OHB in Southeast Asia [10.5% CI: 6.8 – 16.0, I^2 = 98.37%, p <0.001]. The forest plot of all the pooled studies reveals the weight of the individual studies from different Southeast Asian countries, as shown in the forest plot represented in **Figure (2)**. The pooled prevalence of OHB in Southeast Asia was statistically significant at p<0.001. There was a publication bias among the included studies, as the standard error mainly tended towards the negative deviation. Egger's statistics were insignificant at p = 0.00876, as shown in **Figure (3)**.

The Leave one out sensitivity meta-analysis revealed no significant effect of the publication bias on the pooled prevalence. The included manuscripts were moderate to highly heterogeneous with evenly random weight distribution, as shown in **Figure (4)**.

Subgroup meta-analysis of OHB in Southeast Asia

There was a significant difference in the prevalence of OHB within Southeast Asian countries at p<0.001. Indonesia has the highest number of included studies (n =6) with a moderate OHB prevalence of 11.6% (CI: 5.3% - 23.2%). The included studies from Indonesia were highly

heterogeneous (I^2 = 97.15%). There was a significant measure of association (Q = 175.61) to the pooled prevalence and the occurrence of OHB in Indonesia at $\boldsymbol{p}$< 0.001. Cambodia, with only a single study, had the highest prevalence of OHB (51.2%, CI: 48.3% - 54.0%) among Southeast Asian countries compared to Bangladesh, with a single study and a low OHB prevalence (1.5%, CI: 0.5% - 4.5%). Studies from Thailand, Indonesia and Vietnam were highly heterogeneous (I^2 > 90.0%), as represented in **Table (2)**. The corresponding forest plot is shown in **Figure (5)**.

The type of study designed was also significant in association with the pooled prevalence of OHB in Southeast Asia. Case-control studies had the highest prevalence of OHB within Southeast Asian countries (15.4%, CI: 3.8% - 45.4%) compared to retrospective studies (2.3%, CI: 0.9% - 5.2%). Cross-sectional study designs had the highest number of studies (n =13) with a moderate prevalence (10.8%, CI: 6.6% - 17.4%), as represented in **Table (2)**. Cross-sectional and case-control studies were highly heterogeneous (I^2 > 80%) at $\boldsymbol{p}$<0.001. The corresponding forest plot is shown in **Figure (6)**.

Most included studies were from 2011 – 2015 (n =9). However, studies from 2006 – 2010 had the highest prevalence (25%, CI: 12.0% - 44.8%) compared to studies between 2021 and the present (0.7%, CI: 0.2% - 3.3%), as shown in **Figure (7)**. Studies from 2021 to the present had a moderate heterogeneity (I^2 = 65.2%) with a low measure of association (Q – 2.87) that was not statistically significant at $\boldsymbol{p}$ = 0.090, as represented in **Table (2)**. Studies from 2006 – 2020 were highly heterogeneous (I^2 > 95%) with high measures of association to the pooled prevalence of OHB within Southeast Asia at $\boldsymbol{p}$<0.001.

Table 1. Characteristics of all the included studies reporting OHB within Southeast Asia.

Name of Authors	Year of publication	Country of study	Type of study design	Total number tested	OHB positive
Ol et al. [36]	2009	Cambodia	Cross-sectional	1200	614
Thedja et al. [37]	2010	Indonesia	Cross-sectional	309	134
Utsumi et al.[38]	2010	Indonesia	Retrospective	222	5
Chiarakul et al.[39]	2011	Thailand	Case-control	56	4
Louisirirotchanakul et al.[40]	2011	Thailand	Cross-sectional	175	48
Peters et al.[41]	2013	Thailand	Cross-sectional	211	5
Khamduang et al. [42]	2013	Thailand	Cross-sectional	1682	404
Viet et al. [43]	2013	Vietnam	Cross-sectional	1200	298
Darmawan et al. [15]	2014	Indonesia	Cross-sectional	195	13
Jutavijittum et al. [8]	2014	Laos	Cross-sectional	906	99
Le et al. [44]	2015	Indonesia	Cross-sectional	376	49
Darmawan et al.[45]	2015	Indonesia	Cross-sectional	195	9
Hudu et al.[13]	2016	Malaysia	Cross-sectional	1000	55
Mardian et al.[46]	2017	Indonesia	Case-control	456	122
Chowdhury et al. [47]	2021	Bangladesh	Cross-sectional	200	3
Tung et al.[4]	2022	Vietnam	Cross-sectional	623	2

Table 2. A subgroup meta-analysis of the pooled prevalence of OHB in Southeast Asia in relation to the country, types of study designs and year of publication.

Variable	Number of studies	Prevalence (%)	95% CI	I^2(%)	Q	Heterogeneity test DF	*P*
Country							
Bangladesh	1	1.5	0.5 – 4.5	-	-	-	-
Thailand	4	12.7	6.5 – 23.6	92.56	40.31	3	<0.001
Indonesia	6	11.6	5.3 – 23.2	97.15	175.61	5	<0.001
Vietnam	2	3.3	0.0 – 76.3	97.64	42.37	1	<0.001
Malaysia	1	5.5	4.2 – 7.1	-	-	-	-
Laos	1	10.9	9.1 – 13.1	-	-	-	-
Cambodia	1	51.2	48.3 – 54.0	-	-	-	-
Overall	16	10.5	6.8 – 16.0	98.37	921.36	15	<0.001
Type of Study							
Cross-sectional	13	10.8	6.6 – 17.4	98.63	875.09	12	<0.001
Case-control	2	15.4	3.8 – 45.4	88.44	8.65	1	<0.001
Retrospective	1	2.3	0.9 – 5.2	-	-	-	-
Overall	16	10.5	6.8 – 16.0	98.37	921.36	15	<0.001
Year of Publication							
2021 - present	2	0.7	0.2 – 3.3	65.2%	2.87	1	0.090
2016 - 2020	2	12.7	2.4 – 46.9	99.1	110.86	1	<0.001
2011 – 2015	9	12.0	8.4 – 16.9	95.28	169.51	8	<0.001
2006 - 2010	3	25.0	12.0 – 44.8	97.3	73.94	2	<0.001
Overall	16	10.5	6.8 – 16.0	98.37	921.36	15	<0.001

Figure 1. Summary of the article selection process

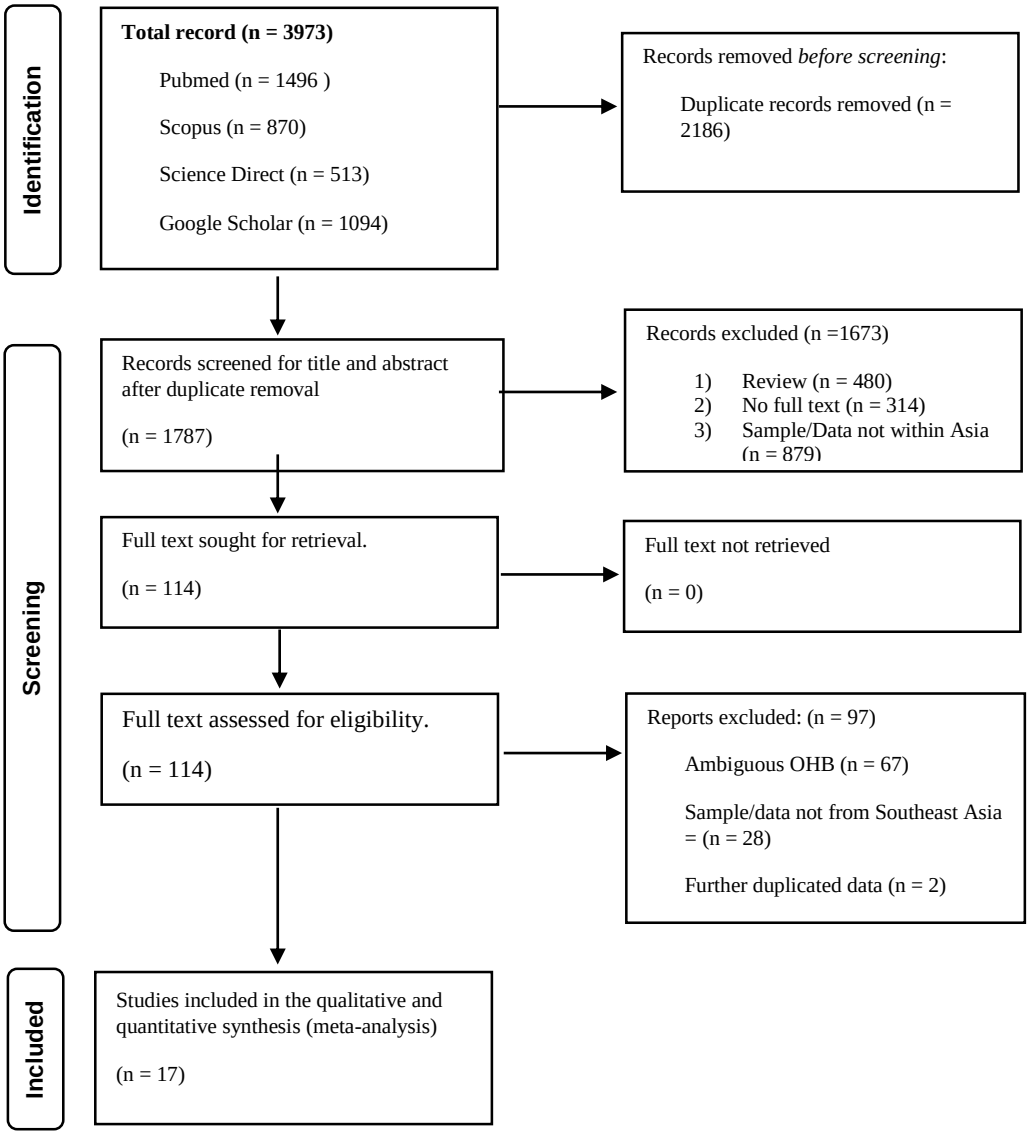


Figure 2. Forest plot showing the pooled Prevalence of OHB in Southeast Asia.

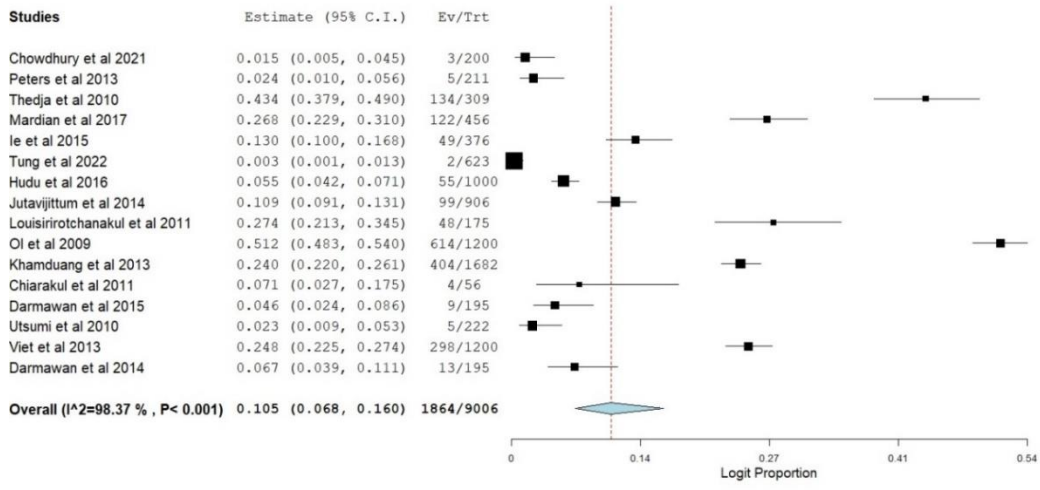
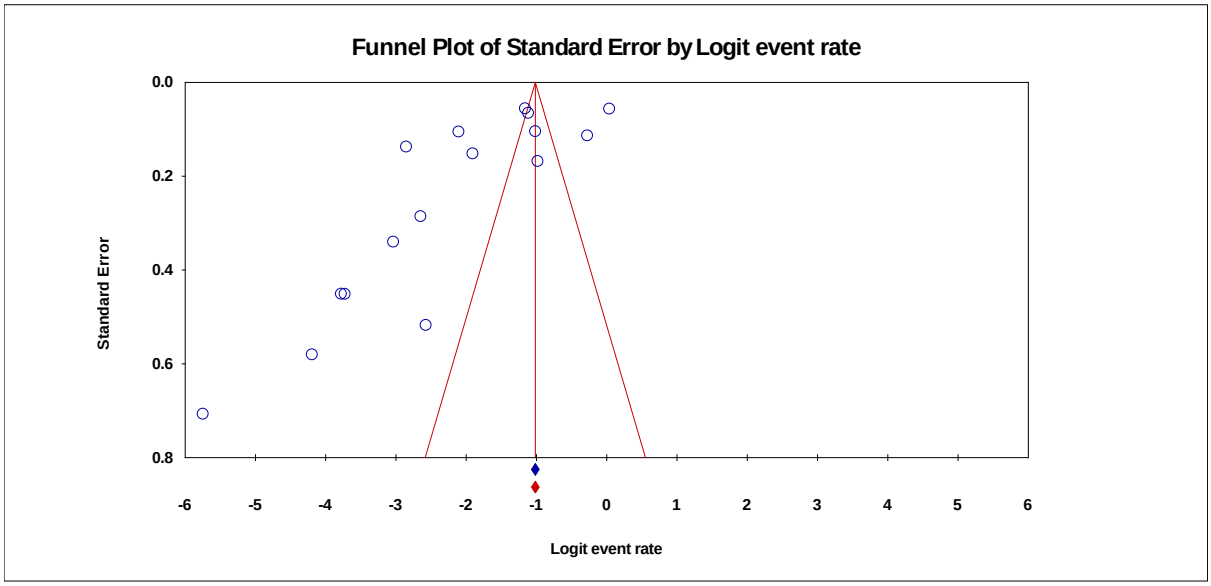


Figure 3. Funnel plot showing the publication bias of the pooled prevalence of OHB in Southeast Asia.



Egger's P = 0.00876

Figure 4. A forest plot showing the Leave one out sensitivity meta-analysis test for the pooled prevalence of OHB in Southeast Asia.

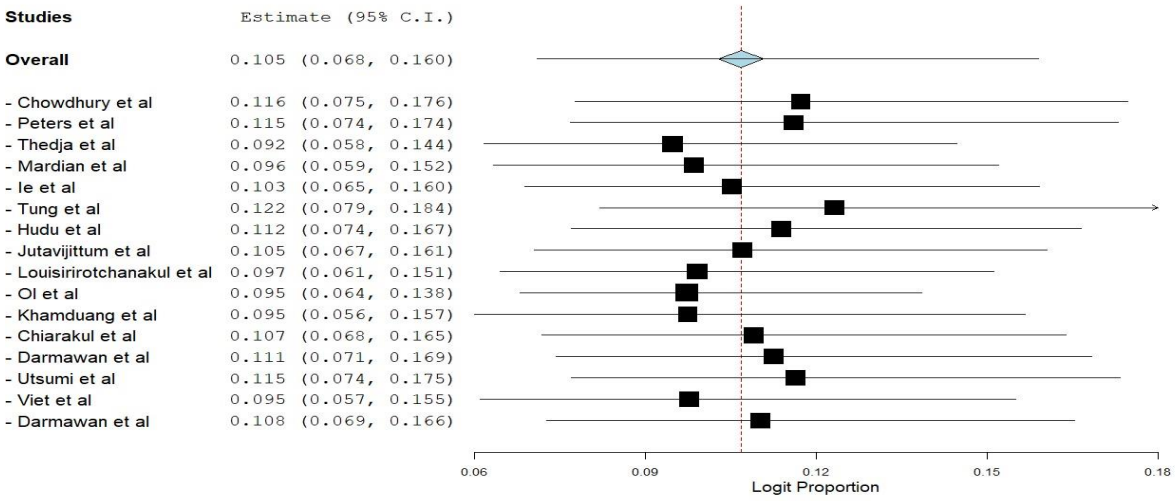


Figure 5. Subgroup meta-analysis forest plot showing the pooled prevalence of OHB in relation to Southeast Asian countries.

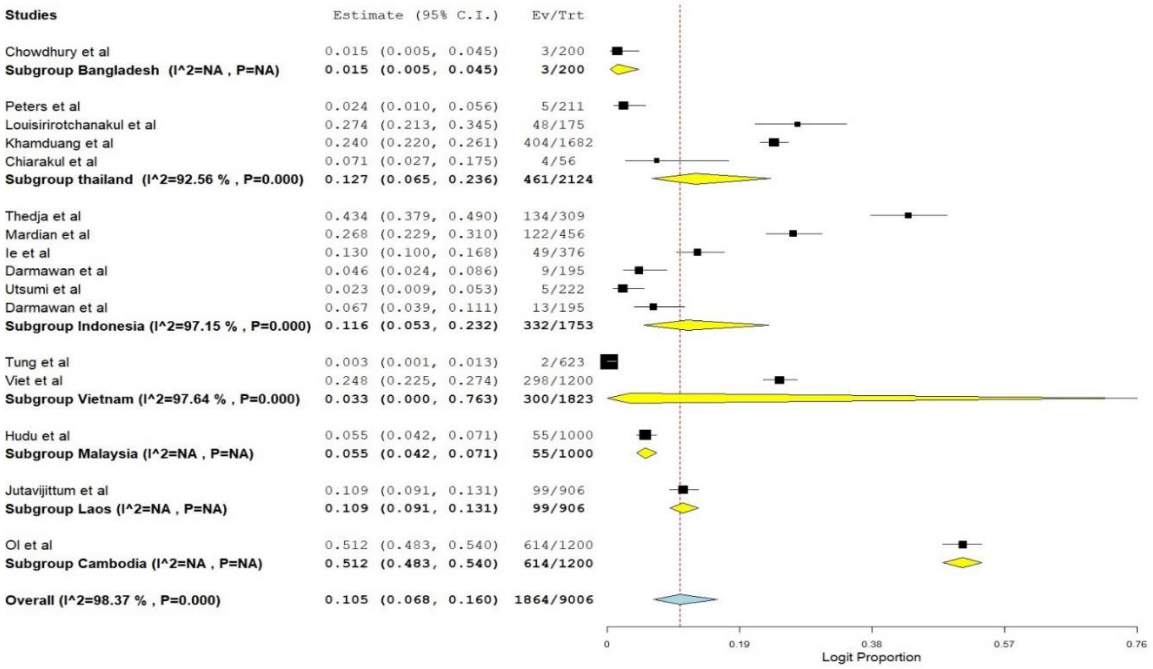


Figure 6. A subgroup meta-analysis forest plot showing the pooled prevalence of OHB in Southeast Asia in relation to their respective study designs.

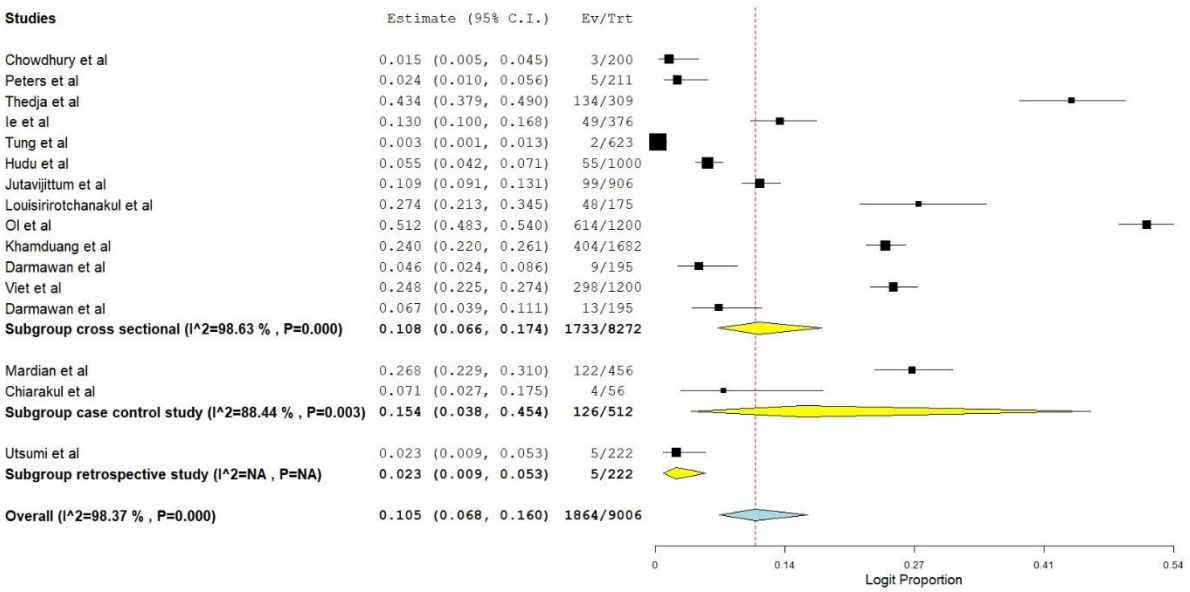
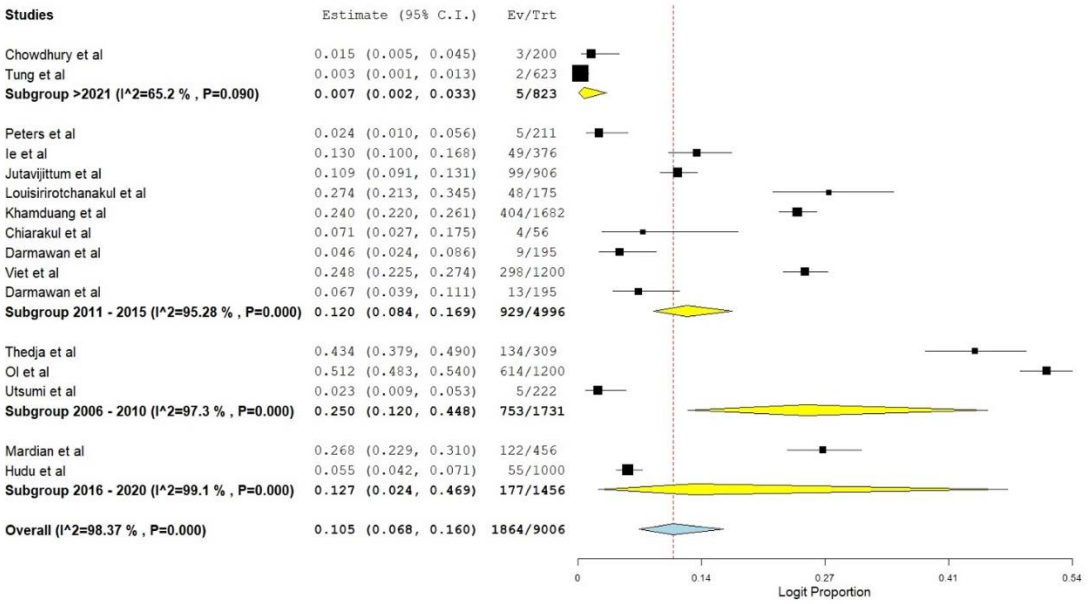


Figure 7. A subgroup meta-analysis forest plot showing the pooled prevalence of OHB in Southeast Asia in relation to their respective year of publication.



Discussion

The study reported the prevalence of OHB in Southeast Asia in a systematic review and meta-analysis. A comprehensive and extensive literature search was conducted across four databases to retrieve 3973 abstracts. After the initial screening of the title, abstract, and full text, sixteen (16) articles were included in the review. The included studies have 1864 OHB vases in a population of 9006 patients.

The pooled data from these publications were analysed to determine the prevalence of OHB in Southeast Asia. The findings of our study will contribute to the existing body of knowledge. Our study analysed studies from seven Southeast Asian countries (Laos, Bangladesh, Indonesia, Thailand, Malaysia, Cambodia, and Vietnam). Notably, Indonesia contributed most significantly to the study [37.5% (n = 6)]. The probable reason for the latter could be attributed to the high distribution of HBV cases in the country [48]. The report's findings concord with other reports [48–50]. The burden of HBV in Vietnam has reduced tremendously over the past two decades because of the HBV vaccine intervention and other awareness programs on HBV prevention and control and the latter could be implicated in the low incidence of OHB in Vietnam, and this finding complements other reports. The substantial variation in reported cases suggests that OHB risks and preventive measures may differ significantly within the region. Climate, working conditions, occupational health and safety practices, and cultural factors could contribute to these disparities [51, 52].

This systematic review and meta-analysis gave an insight into the different study designs in the included studies. Three study designs were encountered in the review (cross-sectional, case-control and retrospective studies). Cross-sectional studies were the most dominant, contributing 81.3% (n = 13) of the entire recruited study compared to case-control studies (11.8% [n =2]), indicating a notable, but comparatively more minor contribution to the study. The relatively limited presence of case-control studies implies that researchers have primarily focused on broader patterns and associations rather than isolating individual risk factors. Retrospective studies had the lowest morbidity (5.9% [n = 1]) among the included articles. The higher prevalence observed in case-control studies may be attributed to their ability to examine the association between OHB and potential

risk factors. The retrospective studies, although displaying a lower prevalence, provide valuable insights into OHB outcomes and long-term follow-up.

The probable reason for the low representation of the retrospective study design is unclear. Still, it could be attributed to the nature of the OHB, as there is no routine test in most clinical settings for detecting OHB occurrence within a study population. Our study's findings align with other reports [53, 54].

The subgroup meta-analysis reveals that most included articles were between 2011 and 2015. The reason for the high concentration of study within this period could be attributed to several factors, such as the availability of resources and emerging research interest, and specific events that triggered scientific research, as there was a surge of HBV incidence and the rise in vaccine escape HBV within Asia within the period. Our study's findings concur with other reports [55–57]. The temporal concentration of studies conducted between 2011 and 2015 further underscores the evolving nature of OHB infection within Southeast Asia.

Studies conducted between 2006 and 2020 exhibited a high degree of heterogeneity (I^2 = > 95%), indicating substantial variation in the prevalence of OHB across Southeast Asia during this period. Conversely, studies conducted between 2021 and the present showed moderate heterogeneity (I^2 = 65.2%). The latter suggests a potential shift or change in the patterns of OHB within the region. The findings of our report complement the reports of others [1].

Studies between 2006 -2010 had the highest pooled prevalence (25.0%) compared to studies between 2021 and the present (0.7%), with the lowest pooled estimate. The probable reason for the high prevalence of OHB in Southeast Asia within the period could be attributed to the sudden hike in HBV between 2006 – 2010 in some Asian nations. The findings of this study correspond with others' reports. The study presents a high pooled prevalence of OHB in Southeast Asia [10.5% (95% CI: 6.8 – 16.0). The statistical analysis also indicated significant heterogeneity among the included studies, as evidenced by an I^2 value of 98.37% and a p-value of less than 0.001. The forest plot highlights the contribution of each study to the overall pooled prevalence estimate. It is evident from the plot that the prevalence of OHB varied among the different countries, indicating potential regional differences in OHB incidence across Southeast Asian countries.

The potential effects of selective reporting of studies on the pooled prevalence estimate and publication bias were assessed. The standard error of the included studies tended to be negative, indicating a publication bias in the analysis. Notably, Egger's statistics produced a result with a non-significant p-value of 0.00876, showing publication bias.

The impact of publication bias was examined using a leave-one-out sensitivity meta-analysis. The analysis indicated that publication bias had no appreciable effect on the pooled prevalence estimate, indicating that the overall prevalence of OHB in Southeast Asia persisted even when individual research was disregarded. The included manuscripts showed moderate to high variability and a randomly distributed weighting. These findings highlight the necessity for focused interventions and education campaigns. Despite publication bias and heterogeneity, the findings are consistent with the idea that OHB is a significant burden in the region.

There was a significant variation in OHB prevalence among Southeast Asian nations (***p*** < 0.001). In the included studies, Indonesia showed a modest prevalence of OHB at 11.6% (CI: 5.3% - 23.2%). Cambodia had the highest incidence of OHB, with a pool prevalence of 51.2%, compared to Bangladesh, which had the lowest pooled estimate (1.5%). There was a substantial measure of association between the pooled prevalence of OHB in relation to countries. The probable reason for the significant correlation between the pooled prevalence of OHB and Asian countries could be attributed to the relatively heavy burden of HBV in Asia. The findings of our study correspond with the reports of other researchers in Cambodia [36], where they independently reported a significant burden of HBV prevalence [36]. The findings of our study highlight the significant variation in the prevalence of OHB among the Southeast Asian countries, with Indonesia, Cambodia, and Bangladesh exhibiting notable differences.

Strength and limitation

This study, however, has its strengths and limitations. The strengths of the study include the following: It is the first systematic review and meta-analysis reporting the pool prevalence of OHB in Southeast Asia, its comprehensive and extensive

search of literature across multiple databases, its critical meta-analysis of data, assessment of sources of publication bias and the impact of the bias to the generated pooled prevalence. Despite the strengths, there are, however, some limitations to the study. There was a low representation of Southeast Asian countries, as only seven were included in this study. There was insufficient documentation of OHB prevalence within Southeast Asia. Therefore, care needs to be taken in interpreting the results, as they might not represent the actual OHB burden in some Asian countries.

Conclusion

The prevalence of occult hepatitis B in Southeast Asia revealed a relatively high pooled prevalence of OHB (10.5%). Cambodia had the highest pooled prevalence (51.2%). The findings of this study will help healthcare providers and policymakers with practical OHB managerial tips and policies that will help reduce the associated OHB morbidity in Southeast Asian countries and the entire Asia.

Supplementary materials

K1: PRISMA guideline.

K2: Search strategy of OHB in Southeast Asia.

K3: JBI checklist for the prevalence data.

K4: Quality of included studies by JBI critical appraisal checklist for studies reporting prevalence data.

Author contributions

KEB and NM. Conceived and designed the study. Methodology: KEB, AAI, NM, WY, ZAD, AOM, OFO, ART, JER, IKJ, YL, SHM and RHS select and assess the quality of studies. KEB, WY, AAI, and RHS extracted and analysed data. Analysis and writing: KEB interpreted the results and drafted the manuscript. Writing review and editing: KEB, AAI, RHS, NM, and WY reviewed and edited the manuscript. All authors have read and agreed to the published version of the manuscript.

Institutional review board statement

Not applicable.

Informed consent statement

Not applicable.

Data availability statement

The data presented in this study are available in the supplementary material.

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Conflicts of interest

The authors declare no conflict of interest.

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