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Research article

Global outbreaks of foodborne hepatitis A: Systematic review and meta-analysis

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ABSTRACT

Hepatitis A Virus (HAV) is a significant threat in terms of food safety. A systematic literature search with the research question “What are the clinical outcomes of foodborne Hepatitis A virus infections?” was conducted. The pooled estimate of the outcomes-mortality, hospitalization, and severity rates, along with a 95% confidence interval (CI), was estimated. After screening, 33 studies were included for the data extraction and meta-analysis. The pooled prevalence of hospitalization among the HAV-positive patients was estimated to be 32% (95% CI 21–44), with high heterogeneity ($I^2 = 98\%$, $p < 0.01$). Australia had the highest hospitalization rate, with 82%, followed by Europe (42%). The hospitalization rate showed a significantly increasing trend (beta = 0.015, p=0.002) over the period. The pooled prevalence of mortality among the HAV-positive patients was estimated to be <1%, with low heterogeneity ($I^2 = 5\%$, $p = 0.39$). A wide range of food products were linked with the HAV outbreaks.

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1. Introduction

Foodborne diseases are a significant public health issue that can impact health, trade, and the economy. More than 200 diseases have been reported to occur due to consuming contaminated food with microorganisms or chemicals [1]. One in ten people globally becomes ill due to contaminated food consumption. The annual health burden of foodborne diseases has been estimated to be 600 million incident cases and 420000 fatalities. This morbidity and mortality resulted in a loss of 33 million healthy years of life [2]. The burden of foodborne diseases disproportionately affects the pediatric age group and the low- and low-middle-income countries (LMICs) [3]. An estimated 40% of fatalities from foodborne diseases are reported among children below five years of age [2]. The highest burden of foodborne illnesses is borne by the LMICs, wherein an estimated 1200–1300 DALYs per 100000 inhabitants have been reported [4]. Regarding economic impact, food safety-related incidents have been estimated to cost $7 billion in the United States of America (USA) [5].

A foodborne outbreak is "when two or more people get the same illness from the same contaminated food or drink" [6]. Bacteria, viruses and protozoans are implicated in foodborne infections and diseases due to microorganism contamination. Hepatitis A Virus (HAV) has been recognized as a major threat in terms of food safety, and it is responsible for multiple outbreaks across the globe [7]. HAV is classified as a Picornaviridae virus (family) and is kept under the Hepatovirus genus [8]. It is a single-stranded RNA virus which has five genotypes. Following an incubation period of two to seven weeks, HAV can progress into a symptomatic stage with flu-like presentations and gastrointestinal manifestations such as diarrhoea, vomiting, jaundice and abdominal pain [9]. Although sexual and blood transfusion routes have also been reported [10], the major route of transmission of HAV is the feco-oral route. The feco-oral transmission might be through direct contact with infected persons or indirectly through consumption of contaminated food and water. Countries have shown varied endemicity for HAV infection [11].

Foodborne HAV outbreaks have been known and reported since 1956 [7]. It is reported across the world, barring geographical and economic boundaries. Foods served and partaken at restaurants, parties and other social gatherings are the most common settings for HAV outbreaks [12]. Food products-fresh and frozen, raw and cooked, indigenous and imported, have been linked or found to be the source of the foodborne HAV outbreaks. Various food products, such as semi-dried tomatoes, onions, pomegranate arils, frozen berries, Shellfish, scallops, and baked items, have been reported as the potential source for the HAV outbreaks over the last 50 years. HAV contamination of the food can happen throughout the food chain, from cultivation to consumption [10]. HAV's clinical features and outcomes vary according to the age group, with the older population reporting severe forms of infection, including hospitalization and deaths [13]. Fulminant hepatitis, a rare but severe complication, recurrent hepatitis [14], and deaths have been reported from the HAV outbreaks. Extra-hepatic complications such as neurologic, renal and cardiovascular complications have also been observed rarely [10]. Hospitalizations and complication management (Liver transplantation) associated with HAV could substantially burden the healthcare systems [15,16]. Based on the systematic literature search conducted by the authors, comprehensive literature on the characteristics of foodborne HAV outbreaks and pooled estimates of their health outcomes was lacking at a global level. Hence, the index study was undertaken.

2. Materials and methods

2.1. Eligibility criteria

The present study was conducted with the research question, "What are the clinical outcomes of foodborne Hepatitis A virus infections?". The study followed the "preferred reporting standard for systematic reviews and meta-analyses (PRISMA)" checklist to ensure comprehensive reporting (Table S1). The relevant studies were identified through a systematic search process guided by the criteria outlined in Table S2. Furthermore, the meta-analysis protocol was registered with the "International Prospective Register of Systematic Reviews (PROSPERO)", ensuring transparency and accountability in the research process, with reference ID CRD42023432798.

2.2. Systematic search and duplicates removal

The search for relevant studies was conducted on June 05, 2023 across four databases: PubMed, Web of Science, Embase, and ProQuest. The search strategy involved the use of keywords such as "hepatitis A," "HAV," "foodborne," "outbreak," and "epidemic." A manual search of the references in eligible primary research papers and reviews was performed to identify additional studies meeting the inclusion criteria. The search results from each database were obtained using the respective search strategies, and the findings are presented in Table S3. In order to manage the identified articles, Mendeley Desktop V1.19.5 software was utilized.

2.3. Selection of the eligible studies

All studies that reported confirmed cases of foodborne hepatitis A were included. People of all age groups and gender were included in the analysis. Articles reporting suspected or probable patients of hepatitis A were excluded. No geographic restriction was applied. Only the studies published in the English language were included.

2.3.1. Title abstract screening

The titles and abstracts of the articles obtained through the systematic search were independently reviewed by two investigators

(APG and MAM) based on the predefined eligibility criteria. Any discrepancies or disagreements regarding the inclusion of an article for full-text review were resolved through discussion and mutual consensus between the investigators.

2.3.2. *Full-text screening & data extraction*

Two investigators independently evaluated the eligibility of the eligible full-text publications and further extracted the required data from the selected articles in Microsoft Excel (MB & AP). Disparities in the full-text review and data extraction between the investigators were removed at a consensus meeting that was held after the independent extraction. Any inconsistencies that could not be addressed were settled by the third investigator (APG). Information such as the outbreak period, country, method of HAV diagnosis, food products linked to the outbreak, total HAV-positive cases, age of the affected people, number of hospitalized patients, fatalities and severe cases were extracted from the final eligible articles. In order to ensure scientific accuracy, a PRISMA flow chart was utilized to document the overall process (Fig. 1).

2.4. *Quality assessment*

The quality of the studies was independently assessed by two investigators (MB&AP) using the "National Heart, Lung and Blood Institute" (NHLBI) quality assessment approach for case series.

2.5. *Data analysis*

The pooled estimate of the outcomes-mortality, hospitalization and severity, as proportions along with 95% confidence interval (CI), was estimated. Only the studies determined as fair or good quality were included in the sensitivity analysis. The I^2 test was used to evaluate the heterogeneity between the studies. An $I^2>50\%$ was regarded as having substantially high heterogeneity. A random effects regression model (DerSimonian & Laird estimation) was used to calculate the pooled estimate if the studies had significant heterogeneity. Each outcome's prediction interval (PI) was also determined [17]. We conducted the following subgroup analysis to identify the source of heterogeneity: Geographical factors (according to the continent of the study) and period (pre-2000 vs 2000–2010 vs Post-2020). Meta-regression was undertaken based on the year of publication and the male-to-female ratio. Doi plots and the LFK index were used to evaluate the publication bias if there are at least five studies in an outcome. Statistical significance was considered to exist at a p-value less than 0.05. All of the statistical analysis was done in R studio following standard codes [18].

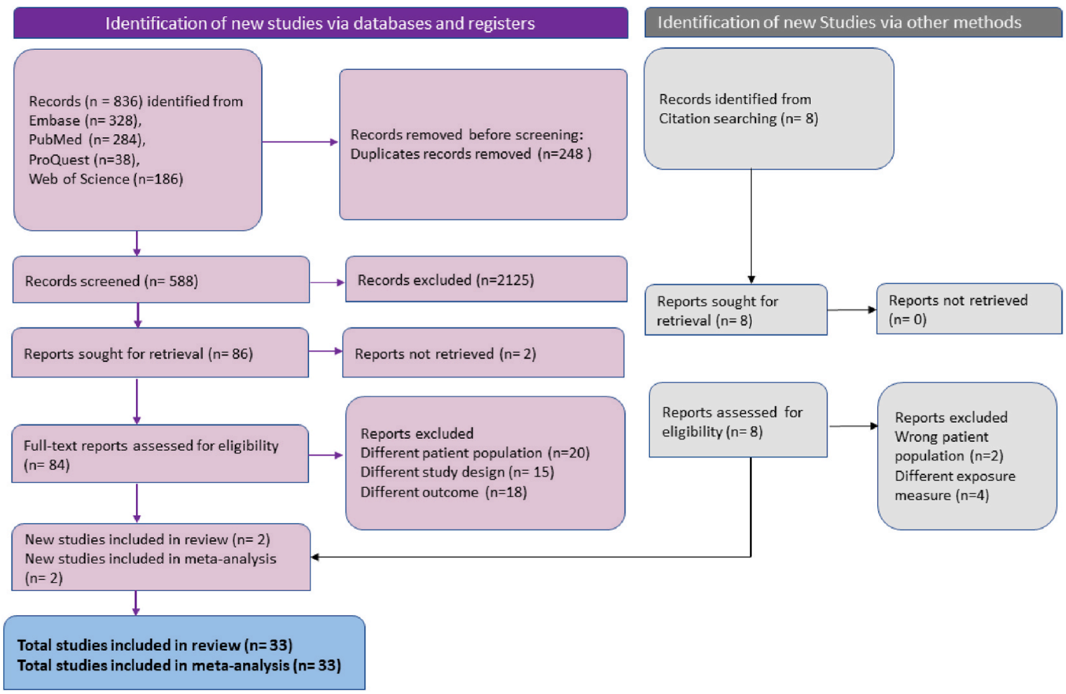

Fig. 1. PRISMA flow chart showing the search and screening process undertaken in the study.

Table 1
Characteristics of the included studies (N = 33).

Author et al., (year)	Year(s) of outbreak	Country	Method of HAV diagnosis	Food product linked	Imported/ Indigenous	HAV positive cases (nos)	No hospitalized (Nos)	No of deaths (nos)	Age (Mean/ Median)
Beller et al. (1992)	1988	USA	IgM ab +	Beverages	Indigenous	57	3	0	18
Calder et al. (2003)	2002	New Zealand	IgM ab+	Raw Bluberries	NR	81	18	1	23
Carvalho et al. (2012)	2011	UK	Genetic sequence	Semi dried Tomato	NR	7	4	0	–
CDC (1990-92)	1990	USA	IgM ab+	Lettuce	NR	110	0	2	–
CDC 2003	2003	USA	IgM ab+	uncooked/min heated green onion	NR	207	0	3	34
Ciesla et al. (2020)	2018	Poland	IgM ab+	Apple, peers, meals	NR	39	20	0	34.5
Collier et al. (2014)	2013	USA	IgM ab +	frozen pomegranate arils	Imported	165	69	0	47
Dentinger et al. (2001)	1998	USA	IgM ab +, PCR	green onion	NR	43	14	0	34
Desenclos et al. (1991)	1988	USA	IgM ab+	Oyster	Indigenous	53	17	0	31
Epson et al. (2016)	2013	USA	IgM ab+	Frozen organic berry-pomegranate aril	NR	147	64	0	48
Fitzgerald et al. (2014)	2013	Ireland	IgM ab+	Frozen berries	Indigenous	21	12	0	35
Franklin et al. (2018)	2018	Australia	Genetic sequence	Frozen Pomegranate arils	Imported	30	25	1	30.5
Gallot et al. (2010)	2010	France	IgM ab+	Tomatoes	Imported	59	28	0	31.5
Gassowski et al. (2018)	2018	Europe	Genetic sequence	NR	NR	55	0	1	31
Guillios-Becel et al. (2009)	2007	France	IgM ab+	Shellfish	Indigenous	111	28	0	40
Gurav et al. (2019)	2017	India	IgM ab+	not any food item in specific but a meal	Indigenous	73	0	3	
Hayashi et al. (1988)	1986	Canada	IgM ab+	Salads and Cooked food	Indigenous	15	3	1	43
Howitsz et al. (2005)	2005	Denmark	IgM ab+	Ice cream, Dried fruit	NR	29	3	0	52
McClure et al. (2022)	2019	USA	IgM ab + or PCR	Fresh Blackberries	Imported	20	11	0	50
O'Neill et al. (2022)	2021	Australia	IgM ab + or PCR	fresh Medjool dates	Imported	6	4	0	26
Petrignani et al. (2010)	2010	Netherlands	PCR	Semi-dried tomatoes	Indigenous	11	0	0	–
Prato et al. (2005)	2002	Italy	(HAV) IgM	various food products from a store	Indigenous	26	2	0	26
Reid et al. (1987)	1983	Scotland	IgM ab +	Frozen raspberries	Indigenous	24	5	0	–
Ruscher et al. (2020)	2019	Germany	PCR	frozen strawberries	Imported	65	50	0	48
Sane et al. (2015)	2013	Multi-country (Europe)	IgM ab + or PCR	strawberries or mango	Indigenous	107	71	0	36
Scavia et al. (2017)	2014	Italy	PCR	frozen berries	Imported	246	212	0	38

(continued on next page)

Table 1 (*continued*)

Author et al., (year)	Year(s) of outbreak	Country	Method of HAV diagnosis	Food product linked	Imported/ Indigenous	HAV positive cases (nos)	No hospitalized (Nos)	No of deaths (nos)	Age (Mean/ Median)
Schmid et al. (2008)	2008	Austria	IgM ab +	NR	NR	21	12	0	–
Schwarz et al. (2008)	2006	France	IgM ab +	liver pate	Indigenous	10	3	0	–
Severi et al. (2015)	2014	Multi-country (Europe)	IgM ab + or PCR	frozen berries	NR	1589	1102	2	36
Swinkels et al. (2014)	2012	Canada	IgM ab + or PCR	frozen fruit blend, cherries or pomegranate seeds	Imported	6	2	0	32
Vilaplana et al. (2021)	2021	UK	Genetic sequence	Medjool dates	Imported	31	25	0	60
Viray et al. (2018)	2016	USA	IgM ab +	Scallops	NR	292	74	2	40
Weltman et al. (1996)	1994	USA	IgM ab +	sugar-glazed baked goods	Indigenous	79	4	0	32.5

NR: Not Reported; UK: United Kingdom; USA: United States of America; IgM ab: Immunoglobulin M Antibody.

3. Results

3.1. Eligible studies

The selection process for the index SRMA is shown as a PRISMA flow chart in Fig. 1. After 248 duplicate items were removed, the

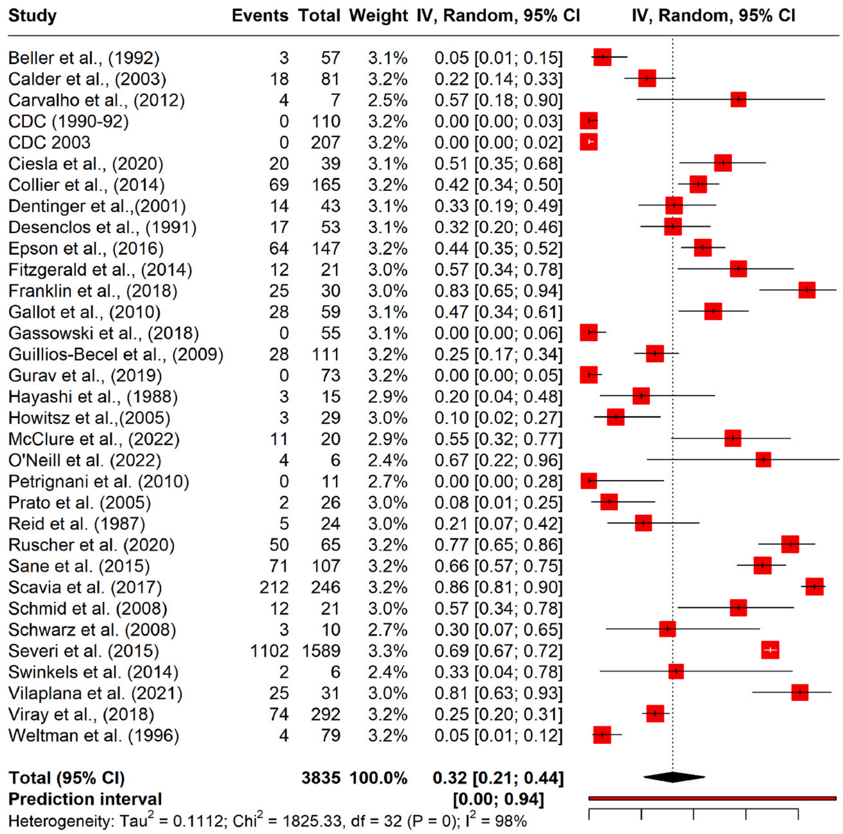

Fig. 2. Forest plot showing the pooled prevalence of hospitalization rate among the foodborne HAV infections.

systematic search yielded 588 unique articles. A total of 86 publications were included for full-text examination after the title abstract screening. In the full-text review, 53 articles were excluded since they had not reported our outcomes of interest (18) or they were of different study designs such as qualitative studies, policy, case reports, reviews and Opinion reports (15) or the study population was different from the objective, i.e. not confirmed cases of foodborne HAV (20). Two studies were identified by hand-searching of the references of the eligible studies. Finally, 33 studies were included (Fig. 1). The studies were conducted over a period from 1983 to 2022. Majority of the studies were from USA (10) [19–28], followed by France (3) [29–31], and other countries [32–51]. Continent-wise, North America (17) and Europe (12) reported 88% of all included studies. Risk of bias assessment revealed that all the studies were either fair or good quality. (Table S4).

3.2. Characteristics of the included studies

Diagnosis of the HAV in the included studies was undertaken through IgM antibody, polymerase chain reaction or genetic sequencing. A wide range of food products were linked with the HAV outbreaks. They included beverages [21], fruits (blueberries, apples, pears, frozen pomegranates, frozen berries, blackberries, frozen raspberries, frozen strawberries, mango) [22,25,26,32,34–36,45–47,49,50], vegetables (onion, lettuce & tomatoes) [19,20,29,33,42], dates [41,51], shellfish [30], scallops [27], Oysters [24], baked foods [28], salads [39], and ice-creams [40]. Nine among the 33 studies reported the HAV outbreak linked to an imported food product [22,26,29,36,41,45,47,50,51], while 12 of them were indigenous food-related outbreaks [21,24,28,30,35,38,39,42–44,46]. The mean age of the patients infected with HAV ranged from 18 to 60 years (Table 1). Male to female ratio of the patients included in the studies ranged between 0.40 and 12.25. The genotypes of the HAV reported in the outbreaks were IA, IB, IIA and IIIA. Four studies reported data on HAV infection among children (<18 years) [22,34,38,51], while two studies reported on the geriatric population (>60 years) within the overall infected population [22,51]. Four of the included studies reported the potential transmission of HAV to the patients through the food from the food handlers [20,28,43,48].

3.3. Hospitalization rate

The hospitalization rates across the eligible studies ranged from 0% to 86%. The pooled prevalence of hospitalization among the HAV-positive patients was estimated to be 32% (95% CI 21–44), with high heterogeneity ($I^2 = 98\%$, $p < 0.01$). The PI for the estimated outcome showed huge variation between <1% and 94% (Fig. 2).

Meta-regression revealed that the hospitalization rate had a significantly increasing trend over the period (beta = 0.015, p=0.002) (Fig. 3a). However, the male-to-female ratio among the cases included did not significantly impact the hospitalization rate. (beta = −0.023, p=0.395) (Fig. 3b). Diagnostic tests revealed no outliers among the included studies (Fig. S1). No significant change in the heterogeneity ($I^2 = 98\%$) and the pooled estimates (30–34%) was observed in the leave-one-out analysis (Fig. S2).

The results of the sub-group analysis have been depicted in Table 2. Although the sub-group analysis did not eliminate the

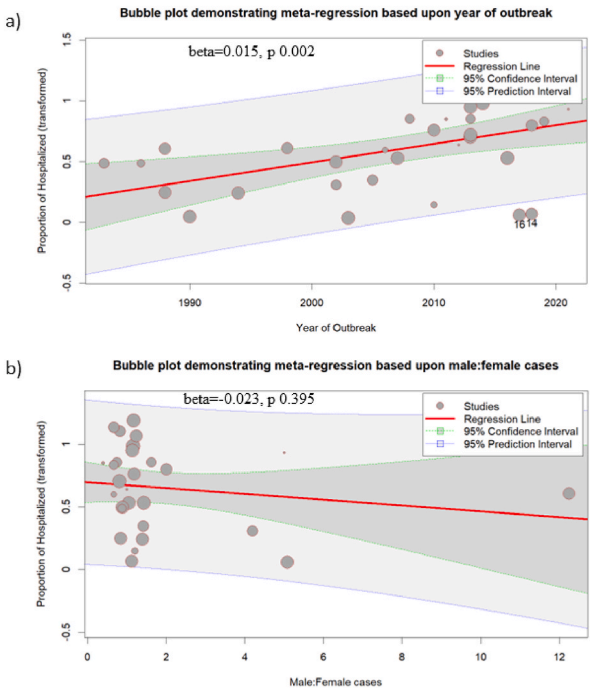

Fig. 3. Bubble plots showing meta-regression based upon year of outbreak and male:female ratio among the cases in the studies.

Table 2
Subgroup analysis of the studies reporting hospitalization rate according to geography.

Continent	No. of studies	Pooled estimate (95% CI)	I^2	p value
North America	12	19% (7-35)	97%	<0.001
Europe	17	42% (25–60)	97%	
Australia	2	82% (0–100)	0%	
Asia	1	<1% (0–5)	–	
Oceania (New Zealand)	1	22% (12–33)	–	

heterogeneity, it revealed a significant difference in hospitalization among the HAV patients in various continents. Among the regions, Australia had the highest hospitalization rate, with 82%, followed by Europe (42%). Publication bias evaluated by the Doi plot showed an asymmetrical plot, which revealed a potential publication bias. This was statistically confirmed by the LFK index value of −3.69, indicating a publication bias towards the studies reporting lower hospitalization rates. (Fig. S3).

In terms of the severity of the HAV infection, four studies reported on fulminant hepatitis and liver failure. Two cases of fulminant hepatic failure were reported by Collier et al. [22], and two cases of liver failure requiring liver transplantation were reported by Petrignani et al. [42].

3.4. Mortality rate

The majority of the studies reported no deaths among foodborne HAV patients. The mortality rates across the eligible studies ranged from 0% to 7%. The pooled prevalence of mortality among the HAV-positive patients was estimated to be <1%, with low heterogeneity ($I^2 = 5\%$, $p = 0.39$). The PI for the estimated mortality was between <1% and 1% (Fig. 4).

4. Discussion

Globally, there is a significant rise of HAV incidence, with a 13.9% increase in 2019 compared with 1990 [52]. Albeit the change in the epidemiology of HAV incidence owing to vaccinations and food safety protocols, specifically in developed countries, sporadic but significant outbreaks are still reported [10]. The index meta-analysis found a pooled hospitalization rate of 32% among the patients

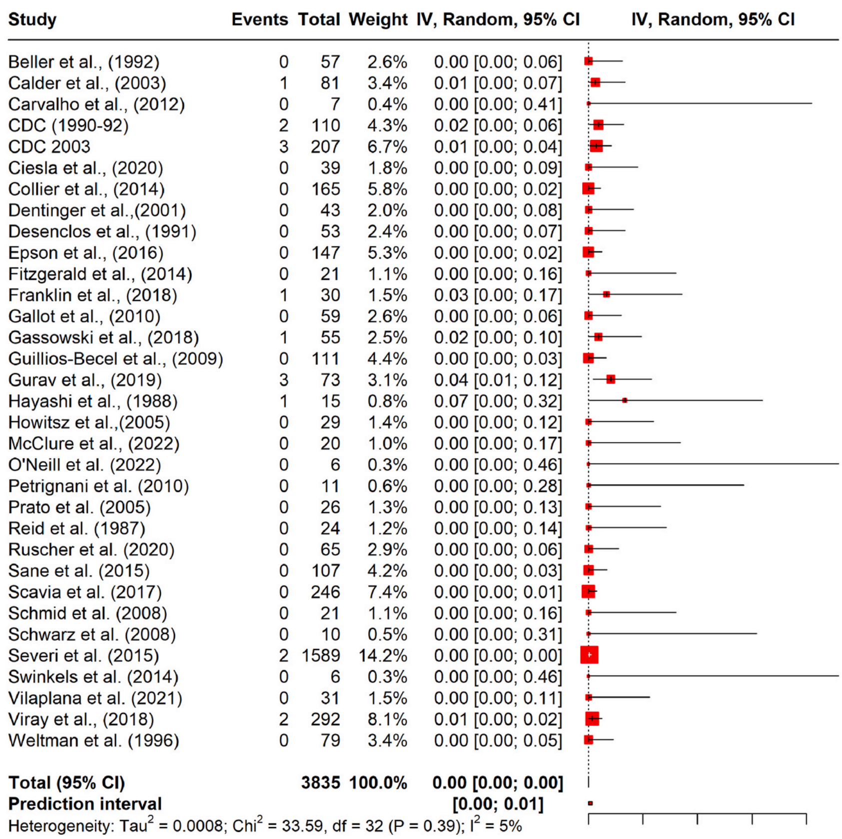

Fig. 4. Forest plot showing the pooled prevalence of mortality rates among the foodborne HAV infections.

infected with foodborne HAV. This indicates the higher severity among the patients and the burden HAV outbreaks mount on the existing healthcare system. The mean hospitalization cost for HAV patients has been estimated to be $16,232 in the USA, translating to more than $300 million dollars for HAV hospitalizations between 2016 and 2020 in the country [53]. Hepatitis has been reported as the most severe outbreak among all the foodborne virus related illness outbreaks from USA [54]. The present analysis found that hospitalization rates showed a significant increase over the period, which indicates a rising trend in the severity of the infection.

The hospitalization rates varied significantly across the continents, with studies from Australia reporting the highest rate of 82%, while North American studies reported as low as 19%. The geographical variations might be due to the varied severity in the patients infected with foodborne HAV. The geographical concentration of the studies from North America and Europe points towards the lacunae in the studies on foodborne HAV infection in low and low-middle-income countries. The high heterogeneity in the hospitalization rates found between the studies included in the current meta-analysis warrants exploration of the further potential factors contributing towards this. Studies from the USA, Europe and India have reported low hospitalization rates, including reports with nil hospitalizations [19,20,37,38,42]. However, mortality was reported in these studies, with the study from India reporting a mortality rate of 4% [38]. This indicates a gap in the timely identification and management of HAV cases. It might also be due to the severity of the infection, especially in developed countries.

A study from Italy reported the highest hospitalization rate of 86% among HAV patients. The duration of hospitalization also ranged up to 60 days, with a median of 7 days, further elaborating the healthcare burden posed by the outbreak [47]. The largest among the included studies, which had 1589 confirmed cases, reported that more than two-thirds were hospitalized. Most of the hospitalized patients in the study were adults in the productive age group, leading to indirect costs on the individuals and the economy [49]. Another multi-country outbreak from Europe also reported a high hospitalization rate of 66%. High hospitalization might also indicate underlying milder infections that do not reach health care or public health surveillance systems and hence are not reported [46]. Thus, the actual burden of HAV infections in these settings might be higher. Frozen berries were the most implicated food product in these high hospitalization rate outbreaks. This might be due to high chances of contamination owing to multiple exposure points, from their cultivation to consumption, especially for the imported berries [47].

Inadequate information on foodborne illness has been identified as a major concern in food safety among low-income countries [55]. Sex did not significantly affect the hospitalization rate among foodborne HAV-infected patients. This is in line with the analysis of HAV patients (from any source) from three states of the USA, which reported a similar rate of hospitalization among males and females [56].

The case fatality rate among foodborne HAV patients was <1%. The overall mortality rate from any source of HAV infections has been reported to be 0.01%–0.04% in the USA between 2016 and 2020 [57]. However, higher age had relatively higher mortality among the HAV patients [57,58]. A fall in the trends of mortality among HAV patients has also been reported globally [52]. The most severe adverse outcome of the HAV infection is fulminant hepatitis, which has a mortality rate of 80% [58]. The index analysis found four studies reporting cases of fulminant hepatitis and liver failure among foodborne HAV patients.

While hospitalization among foodborne HAV has shown an increasing trend, the mortality rates have declined over the past three decades [52]. The major reasons for these favourable mortality trends might be effective vaccination programs, health care quality and increased liver transplantation procedures [52,59]. Additionally, mortality has been reported to have unequal reduction between the countries owing to the variation in the implementation and distribution of the above factors [52,60].

The index review enumerates that HAV infections were associated with a wide variety of food products and beverages-processed, semi-processed, fresh, frozen, raw, cooked, and baked items. It has been estimated that 2–7% of all HAV outbreaks across the globe are foodborne [10]. With the ever-increasing globalization, the transmission of HAV from imported food items has also been reported among the nine of the included studies in the analysis. The role of food handlers in foodborne HAV transmission has been explored in past studies.

Adopting Water Sanitation and Hygiene (WASH) practices at all levels of the food chain-production, processing, preparation, and consumption can reduce foodborne HAV infection [12]. Genotype IB followed by IA has been the most common among the studies that have reported on the genotype of foodborne HAV in the current analysis. Past studies have reported I & III as the most common genotypes among HAV infections [61,62].

4.1. Strengths & limitations

The present analysis is the first to pool foodborne HAV infection's characteristics and clinical outcomes. The risk of bias in the included studies was evaluated using standard tools to ensure quality in the pooled estimates. Publication bias was explored by doi plot. However, the index analysis is not without limitations. High heterogeneity was present among the studies reporting the hospitalization rate. The heterogeneity was explored by meta-regression and sub-group analysis. Yet, the specific factor(s) responsible for the heterogeneity could not be identified from the current analysis. Patient characteristics such as ethnicity, comorbidities, age, and timing of outcome measurements could have contributed to the heterogeneity in the current study [63]. Although continent-level sub-group analysis was done to explore the heterogeneity, ethnicity could not be factored in owing to a lack of data. Thus, due to high heterogeneity, the pooled estimate must be taken with the caveat. The persistent heterogeneity was presented employing prediction interval in the current analysis. Although PI does not eliminate heterogeneity, it enables the peers to understand the extent of heterogeneity in terms of the outcome (hospitalization rate) [17], thus empowering them to take either the pooled or context-specific study-wise estimates. Publication bias also limits the interpretation of the meta-analysis's pooled estimates since most HAV outbreaks that could have a foodborne source are not detected or reported. Few studies did not report the potential source of foodborne HAV outbreaks.

5. Conclusion

The hospitalization rate among foodborne HAV infections is high, with an increasing trend over the period. However, the presence of reporting bias warrants a cautious interpretation of the findings from the index meta-analysis. Due to this preventable cause, the healthcare system burden might be high, which may strain the resources for other healthcare services. Mortality due to foodborne HAV is low. It is imperative to undertake food safety and surveillance to prevent foodborne HAV outbreaks. Vaccination can be an effective strategy against HAV occurring from any source. Adopting WASH practices at individual and institutional levels of the food industry can also reduce foodborne HAV outbreaks, reducing hospitalization and mortality.

Declarations

Conflict of interest

None.

Ethical statement

Review and/or approval by an ethics committee was not needed for this study because it was a systematic review and meta-analysis of the data from published literature.

5.1. Source of the funding

There was no funding source for this study. All authors had full access to all the data in the study and had the final responsibility for the decision to submit for publication.

List of Supplementary Files.

Data availability statement

The original contributions and raw data presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

CRediT authorship contribution statement

Aravind P. Gandhi: Writing – review & editing, Writing – original draft, Visualization, Validation, Resources, Methodology, Conceptualization. **Mohammed AL-Mohaithef:** Writing – review & editing, Methodology, Formal analysis, Conceptualization. **P. Aparnavi:** Writing – review & editing, Validation, Data curation. **Monika Bansal:** Writing – review & editing, Validation, Data curation. **Prakasini Satapathy:** Writing – review & editing, Validation, Data curation. **Neelima Kukreti:** Writing – review & editing. **Sarvesh Rustagi:** Writing – review & editing. **Mahalaqua Nazli Khatib:** Writing – review & editing, Formal analysis, Conceptualization. **Shilpa Gaidhane:** Writing – review & editing, Validation, Methodology, Data curation. **Quazi Syed Zahiruddin:** Writing – review & editing, Validation, Data curation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e28810.

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