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Zoonotic and Food-Related Hazards Due to Hepatitis A and E in Africa: A Systematic Review and Meta-Analysis

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ABSTRACT

INTRODUCTION: Foodborne infections are caused by a wide spectrum of microbial pathogens, and they pose a significant global health threat, resulting in millions of cases and thousands of fatalities annually. Among these pathogens, human viruses, including Hepatitis A virus (HAV) and Hepatitis E virus (HEV), play a significant role in foodborne viral outbreaks, especially in Africa. This systematic review determined the prevalence of these viruses in livestock and produce in Africa.

METHOD: A systematic search strategy was implemented following the PRISMA guidelines. Databases such as African Journal Online, Web of Science, Scopus, and PubMed were searched from their inception until November 30, 2023. Descriptive statistics and a proportional meta-analysis utilising a random-effects model with a 95% confidence interval were employed in the data analysis. The Cochrane risk-of-bias tool (ROB2) was utilised to evaluate the potential for bias in each study.

RESULTS: The search identified 27 articles that met the inclusion criteria, among which seven focused on HAV, comprising a total of 309 samples, whereas 20 studies focused on HEV, comprising a total of 4238 samples. Egypt had the highest number of studies, followed by Cameroon and Nigeria. The meta-analysis revealed an overall prevalence of 33.8% (95% CI: 17.0–50.6) for HAV in ducks and shellfish and 22.0% (95% CI: 12.1–31.8) for HEV in various livestock. Genotype 3 was identified as the predominant genotype, for both HAV and HEV.

CONCLUSION: This review revealed a high prevalence of HAV and HEV in livestock populations in Africa, shedding light on the potential risks associated with zoonotic and/or food-related infections. There is a need for continued surveillance and monitoring of these viruses in both animals and food products to mitigate the risk of foodborne outbreaks and protect human health.

KEYWORDS: Hepatitis A, Hepatitis E, zoonotic, domestic animal, transmission, prevalence, Africa, food safety, swine

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Introduction

Every year, foodborne infections affect approximately 600 million people globally, resulting in nearly 420 000 preventable deaths.¹ These diseases stem from various harmful agents, including bacteria, viruses, and parasites, that can taint food and make it hazardous to eat.² Notably, human-afflicting viruses are significant contributors to health issues and economic impacts.³ Hepatitis A virus (HAV) and Hepatitis E virus (HEV) cause approximately five million cases of acute viral hepatitis worldwide each year.⁴

Although both viruses are classified as small RNA viruses, they have distinct genetic differences and structures.⁵ HAV is a small, positive-sense RNA virus belonging to the *Hepatovirus* genus within the *Picornaviridae* family.⁵ It presents in two distinct forms: nonenveloped virions found in faeces and quasi-enveloped virions (eHAVs), which exit infected cells without causing cell damage.⁶ These eHAV virions can be detected in the blood of infected individuals and in the supernatant of infected cell cultures.⁷ Contaminated shellfish, poor sanitation, and close contact with infected individuals are

common transmission routes of HAV.^{8,9} HAV causes acute liver infection, which is characterised by liver inflammation, with symptoms ranging from mild to severe.¹⁰ Prolonged jaundice and itching due to bile flow obstruction can also occur.¹¹ Children under six years of age typically remain asymptomatic.¹² However, individuals with compromised immune systems and expectant mothers are at an increased risk of experiencing severe clinical hepatitis.¹³

HEV, on the other hand, has a single-stranded RNA genome with positive polarity and is enveloped within capsid proteins, forming an icosahedral structure.¹⁴ It belongs to the *Hepeviridae* family, which comprises two main genera: *Parabepevirinae*, which includes *Piscihepevirus*, such as the cutthroat trout virus, and *Orthohepevirinae*, which is further divided into four species.^{15,16} These species include (I) *Paslahepevirus*, which encompasses HEV variants found in humans, pigs, wild boars, deer, mongooses, rabbits, and camels, (II) *Avihepevirus*, which is found in chickens, sparrows, and little egret, (III) *Rocahpepevirus*, which includes HEV variants from rats, greater bandicoots, Asian musk shrews, ferrets,



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and minks, and (IV) *Chirohepevirus*, which is found in bats.^{15,16} Five genotypes of HEV can infect humans, with HEV-1 and HEV-2 being prevalent in Africa, Asia, and the Middle East, and primarily transmitted through the consumption of faeces-contaminated water.^{17,18} The primary reservoirs for the zoonotic strains HEV-3 and HEV-4 include deer, wild boars, and pigs,¹⁹⁻²¹ whereas HEV-7 has been found in camels.^{22,23} Recently, *Rocabepevirus ratti* strains have been found to be capable of infecting humans. These strains are carried primarily by rats, which frequently come into contact with pigs on swine farms.²⁴

The consumption of undercooked or raw meat products, including sausages, liver, and unpasteurised milk, has led to reported cases of HEV-3 and HEV-4 infections in developed nations.^{25,26} Similarly, outbreaks have occurred periodically in developing nations across Asia and Africa through the faecal-oral route, often involving the consumption of contaminated pork.^{18,27,28} Using pigs as a model for HEV infection, Yadav et al.²⁹ revealed that infectious HEV was present in sperm, suggesting a potential route of sexual transmission. In one human study in Egypt, however, HEV RNA and HEV Ag were not found in the semen of infertile men and acute Hepatitis E (AHE) patients, although HEV markers were present in the urine of HEV-1 patients.³⁰ However, a recent study in Germany detected infectious HEV-3 in patients' ejaculate³¹; similarly, HEV RNA was found in 28.1% of semen samples from Chinese infertile men, with all the isolates belonging to the HEV-4 variant,³² suggesting that HEV-positive ejaculate may pose a risk of transmission to sexual partners.

HEV causes chronic liver disease and severe complications, with symptoms including fever, fatigue, loss of appetite, nausea, vomiting, abdominal pain, dark urine, and jaundice.³³ Acute kidney injury and glomerulonephritis have also been reported in some HEV cases.^{34,35} The study by Elkhawaga et al.³⁶ represents the first report of abnormal renal function in AHE Genotype 1 infection in Egypt, based on an evaluation of kidney function tests (KFTs) in affected patients. While HAV vaccines are easily accessible and recommended for travelers to regions with high HAV prevalence, individuals with chronic liver disease, and other vulnerable groups,^{37,38} there is only one recombinant HEV vaccine, Hecolin, which is currently exclusively available in China and Pakistan.³⁹ Despite the significance of HAVs and HEVs in relation to zoonotic and food-related infections, a systematic review on the subject in Africa that provides comprehensive information to guide preventive, control, and management efforts has not been performed. This systematic review, therefore, evaluated the prevalence of HAV and HEV in major livestock species and produce in Africa.

Methods

PRISMA guidelines

To guarantee a methodical and transparent approach to our literature search and evaluation, we adhered to the Preferred

Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria.⁴⁰ A thorough checklist and flow diagram for record identification, screening, and evaluation are provided by the PRISMA standards.

Search strategy

We conducted an extensive literature search using African Journal Online, Web of Science, Scopus, and PubMed to gather all published studies evaluating the prevalence of HAV and HEV in Africa published from inception to November 30, 2023. Additionally, we explored the reference lists of pertinent articles to identify any additional studies for inclusion in our review. The search terms used included ("hepatitis A," OR "hepatitis E") AND ("foodborne" OR "animals" OR "livestock" OR "vegetables" OR "fruits") AND ("Algeria" OR "Angola" OR "Benin" OR "Botswana" OR "Burkina Faso" OR "Burundi" OR "Cabo Verde" OR "Cameroon" OR "Central African Republic" OR "Chad" OR "Comoros" OR "Congo" OR "Cote d'Ivoire" OR "DR Congo" OR "Djibouti" OR "Egypt" OR "Equatorial Guinea" OR "Eritrea" OR "Eswatini" OR "Ethiopia" OR "Gabon" OR "Gambia" OR "Ghana" OR "Guinea" OR "Guinea Bissau" OR "Kenya" OR "Lesotho" OR "Liberia" OR "Libya" OR "Madagascar" OR "Malawi" OR "Mali" OR "Mauritania" OR "Mauritius" OR "Mayotte" OR "Morocco" OR "Mozambique" OR "Namibia" OR "Niger" OR "Nigeria" OR "Reunion" OR "Rwanda" OR "Saint Helena" OR "Sao Tome and Principe" OR "Senegal" OR "Seychelles" OR "Sierra Leone" OR "Somalia" OR "South Africa" OR "South Sudan" OR "Sudan" OR "Tanzania" OR "Togo" OR "Tunisia" OR "Uganda" OR "Western Sahara" OR "Zambia" OR "Zimbabwe"). We did not place any restrictions on population groups or outcome measures to ensure the inclusion of all relevant studies.

Inclusion and exclusion criteria

To identify relevant studies, a thorough two-step screening was conducted. The first step involved assessing titles and abstracts to remove any duplicates or unrelated studies. The second step was a more in-depth evaluation of the remaining full-text research articles, which determined their suitability for inclusion in the review. The studies were evaluated on the basis of predefined inclusion and exclusion criteria. Eligible studies included those that reported the prevalence of HAV and HEV in livestock in Africa, as well as studies investigating the presence of HAV and HEV in plants, fruits, and vegetables. On the other hand, studies reporting the prevalence of HAV and HEV in humans, studies focusing on waterborne transmission of HAV and HEV, and reviews were excluded. The screening process involved two independent reviewers, and Mendeley Desktop, Version 1.19.8, was used to manage the search results and identify any duplicate records from the databases.

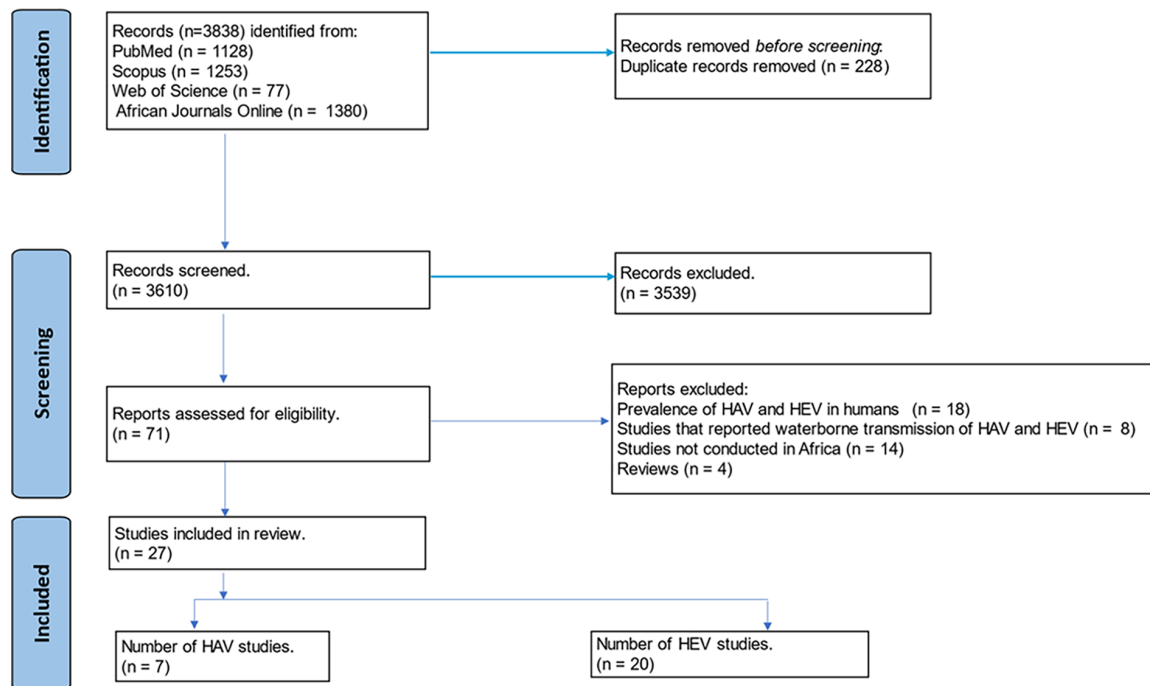


Figure 1. The PRISMA flow diagram for the study selection process.

Data extraction

The data from the reviewed studies were organised and managed using Microsoft Excel 2019, Version 2405. The extracted information included various details about the articles, such as the author(s), year and country, sampling location, sample collected, species or population type, diagnostic assays used for HAV and HEV detection, target genomic regions, number of positive cases, prevalence (%), and identified HAV and HEV genotypes. To ensure accurate extraction of relevant data related to the study characteristics and outcomes of interest, two authors independently utilised a predesigned data abstraction format created in Microsoft Excel 2019, Version 2405.

Evaluation of bias

The Robvis tool⁴¹ was used to visually represent the outcomes of the risk-of-bias assessment conducted on each study using the Cochrane risk-of-bias tool (ROB2).⁴² This assessment focused on five key bias domains: randomisation, deviations from interventions, missing outcome data, outcome measurement, and the selection of reported results. Each of these domains was given a classification of low-risk, high-risk, or some concerns. A study was considered low-risk if all domains received a low-risk designation, high-risk if at least one domain was labeled high-risk, and some concerns if there were concerns in one or more domains.

Statistical analysis

Descriptive statistics and a proportional meta-analysis with a random chance model were employed for the data analysis.

The analysis was conducted using R software, Version 4.3.3 (2024). The metaprop package was used to calculate the overall prevalence, accompanied by a 95% confidence interval. Pooled prevalence ratios were estimated using a random-effects analysis, and differences in the data were evaluated using a Chi-square test. Unfortunately, conducting a subgroup analysis was not feasible because of the inclusion of studies with mixed animal populations. To evaluate publication bias, the “metabias” command and a funnel plot were used.

Results

Search results

The initial online database search yielded a total of 3838 publications from the inception of the databases up to November 30, 2023 (Figure 1). After removing duplicates, 3610 records remained and were screened on the basis of their titles and abstracts. A total of 3539 articles were excluded because they did not meet the established inclusion criteria for the review. Next, 71 full-text articles were assessed for eligibility, and 27 articles met the inclusion criteria for the review. These 27 articles⁴³⁻⁶⁹ provided information on the detection of HAV and HEV in various animal populations, including swine, cattle, goats, chickens, rabbits, monkeys, camels, ducks, shellfish, fruits, and vegetables, in Africa (Supplemental Tables S1 and S2).

Study distribution

A total of 12 out of 58 African countries have investigated the detection of HAV and HEV in animal populations and produce. Figure 2 illustrates the distribution of these studies across different countries. Egypt had the greatest number of studies,



Figure 2. Distribution of included studies across countries in Africa.

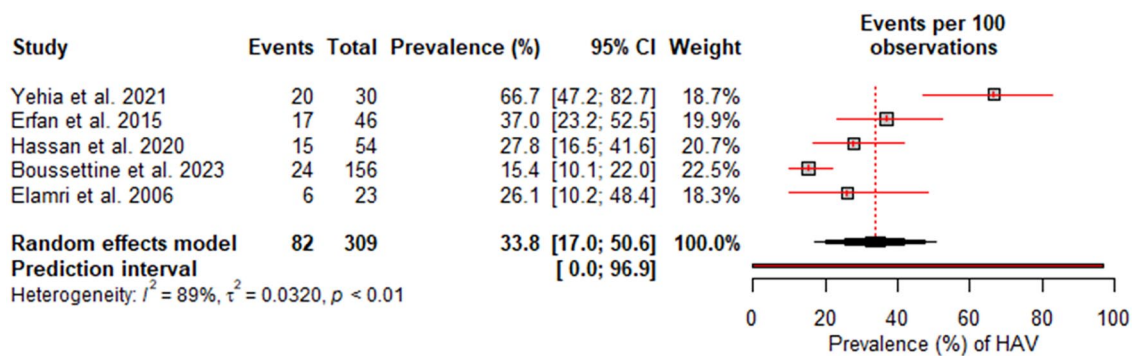


Figure 3. Forest plot for the pooled prevalence (%) of HAV in ducks and shellfish.^{44-47,49}

with a total of eight, followed by Cameroon, with four studies, and then Nigeria, with three studies.

Detection and prevalence of HAV

Seven studies (26%) detected the presence of HAV, all in North African countries, including Egypt, Morocco, and Tunisia.⁴³⁻⁴⁹ Among these studies, four focused on ducks^{43,44,47,49}, two focused on shellfish,^{45,46} and one identified HAV in fruits and

vegetables.⁴⁸ HAV was detected via RT-PCR, which primarily targets the VP1 gene. The identified HAV genotypes included Genotype 1 and Genotype 3. Prevalence data were available in five studies,^{44-47,49} comprising a total of 309 samples, 82 of which tested positive for HAV. The meta-analysis indicated that the overall prevalence of HAV in ducks and shellfish was 33.8% (17.0–50.6, 95% CI), with a random effect and a *p* value of <.05 (Figure 3). An *I*² value of 89% indicated significant heterogeneity among the studies.

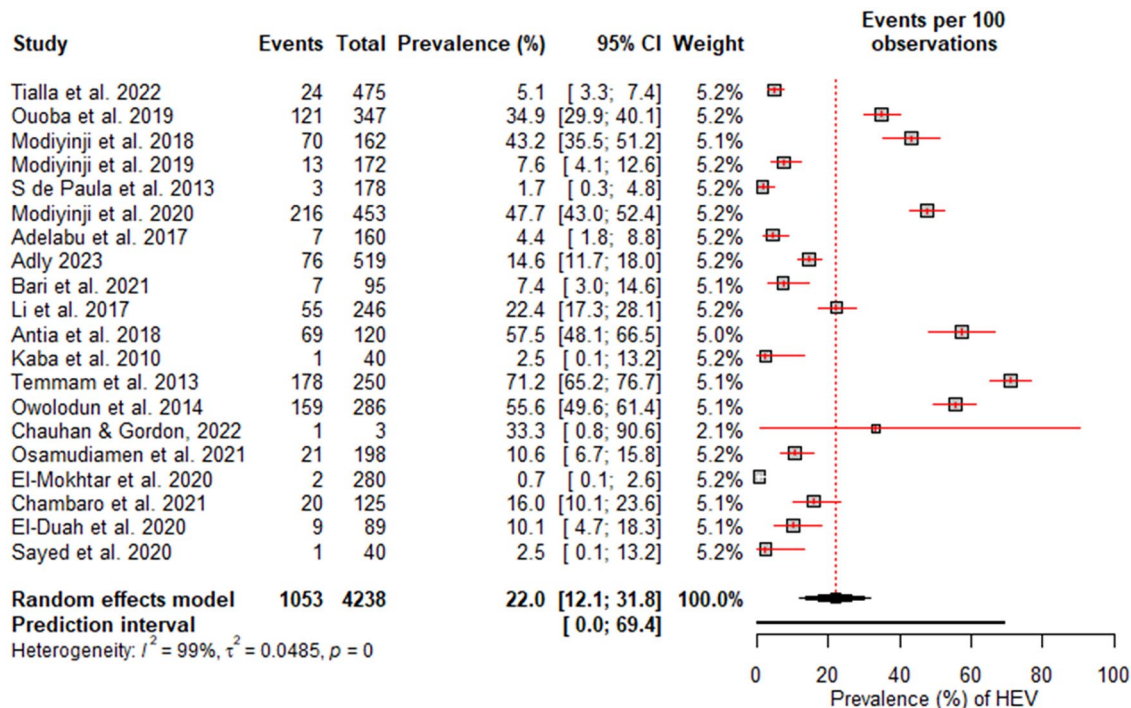


Figure 4. Forest plot for the pooled prevalence (%) of HEV in various livestock (pigs, chickens, rabbits, hares, cattle, sheep, goats, cows, camels, and monkeys).⁵⁰⁻⁶⁹

Detection and prevalence of HEV

The majority of the studies in this review, 20 (74%)⁵⁰⁻⁶⁹ detected the presence of HEV in livestock, primarily in western Africa. Ten of these studies^{50,52,53,58,60,61,65-68} focused on pigs, whereas the remaining studies focused on rabbits, hares, cattle, cows, sheep, goats, chickens, camels, and monkeys. Four studies used ELISA^{53-55,59}, six used RT-PCR (targeting the ORF1, ORF2, and ORF3 regions),^{52,56,60,61,63,67} and the others used both methods for the detection of HEV. Genotype 3 was the most prevalent genotype, identified in 18 studies,^{50-56,58-62,64-69} with one study⁶³ identifying Genotype 2. Prevalence data from 20 studies⁵⁰⁻⁶⁹ and 4238 samples revealed an overall HEV prevalence of 22.0% (12.1–31.8, 95% CI) in various livestock (Figure 4). An I^2 value of 99% indicated high heterogeneity among the studies.

Publication bias

The funnel plot displayed a slight asymmetrical distribution upon visual examination (Supplemental Figures S1 and S2). The results of the Egger linear regression test were not statistically significant, providing support for the absence of small study effects. A regression-based Egger test with a p value $< .05$ indicated potential reporting bias.

Risk of bias

Figure 5 shows a comprehensive assessment of the risk of bias for the 27 studies included in this systematic review. The assessment categorises the risk of bias into three levels: low-risk (represented by green), some concerns (indicated by yellow), and

high-risk (shown in red). The predominance of low-risk ratings in all evaluated domains indicates that the studies demonstrate strong methodological integrity and reliability.

Discussion

This review focused on investigating the detection and prevalence of HAV and HEV in African countries. The meta-analysis revealed an overall prevalence of 33.8% for HAV in ducks and shellfish and 22.0% for HEV in various livestock. These results are comparable to those of a meta-analysis in Africa, which reported a 23.4% prevalence of HEV Immunoglobulin G antibodies in animals¹⁷ and higher than a global meta-analysis that reported a 2% prevalence of HEV in ruminants,⁷⁰ as well as a meta-analysis that reported a 12% prevalence of HAV in ducks in mainland China.⁷¹

Notably, the reporting of HAV cases in Africa remains low, with a predominant focus on HAV outbreaks in ducks, especially in North Africa. This indicates a geographical bias in the studies conducted on HAV in Africa. In addition to ducks, shellfish have also been identified as a potential source of HAV contamination.^{45,46} Moreover, a study conducted in Egypt reported the presence of HAV in strawberries and green leafy vegetables, suggesting a potential risk of produce contamination.⁴⁸ RT-PCR, which targets the VP1 gene, was commonly used as a method for HAV detection, probably because of its high sensitivity and specificity in identifying HAV RNA.⁷²

While the available studies had a limited focus on HAV, the majority of the studies focused predominantly on HEV. These studies detected the presence of the HEV in livestock,

Study	Risk of bias domains					Overall
	D1	D2	D3	D4	D5	
Mansour et al. [43]	-	+	⊗	+	+	⊗
Yehia et al. [44]	+	+	+	+	+	+
Bousettine et al. [45]	+	+	-	+	+	-
Elamri et al. [46]	+	+	-	+	+	-
Erfan et al. [47]	+	+	+	+	+	+
Elmahdy et al. [48]	+	+	⊗	+	-	⊗
Hassan et al. [49]	+	+	-	+	+	-
Chambaro et al. [50]	+	+	+	+	+	+
Tialla et al. [51]	+	+	+	+	+	+
Adelabu et al. [52]	+	+	+	+	+	+
Modiyinji et al. [53]	+	+	+	+	+	+
Antia et al. [54]	+	+	+	+	+	+
Ouoba et al. [55]	-	+	+	+	+	+
Bari et al. [56]	+	+	+	+	+	+
Li et al. [57]	+	+	-	+	+	-
Owolodun et al. [58]	+	+	+	+	+	+
Modiyinji et al. [59]	+	+	+	+	+	+
Kaba et al. [60]	+	+	+	+	+	+
S de Paula et al. [61]	+	+	+	+	+	+
El-Mokhtar et al. [62]	+	+	+	+	+	+
Osamudiamen et al. [63]	+	+	+	+	+	+
Adly [64]	+	+	+	+	+	+
Temmam et al. [65]	+	+	+	+	+	+
Modiyinji et al. [66]	+	+	+	+	+	+
Chauhan & Gordon [67]	-	+	⊗	+	+	⊗
El-Duah et al. [68]	+	+	+	+	+	+
Sayed et al. [69]	+	+	+	+	+	+

Domains:
D1: Bias arising from the randomization process.
D2: Bias due to deviations from intended intervention.
D3: Bias due to missing outcome data.
D4: Bias in measurement of the outcome.
D5: Bias in selection of the reported result.

Judgement
⊗ High
- Some concerns
+ Low

Figure 5. Risk of bias assessment of the 27 studies.⁴³⁻⁶⁹

primarily in western Africa. The use of both ELISA and RT-PCR for HEV detection demonstrates the different approaches employed to identify the virus, with ELISA being useful for detecting HEV antibodies.⁷³ We found that pigs were the primary focus, underscoring their importance as reservoirs for transmitting HEV to humans. Although we did

not conduct a subgroup analysis, the meta-analysis by Modiyinji et al.¹⁷ revealed a higher seroprevalence of immunoglobulin G antibodies of 37.8% among pigs in Africa. The primary mode of transmission of HEV is the faecal-oral route, which typically occurs when contaminated food or water containing faecal matter carrying the virus is consumed.⁷⁴ Swine

production practices in Africa exhibit considerable variation, ranging from large-scale commercial operations to small-scale communal systems.⁷⁵ In communal systems, in which pigs have the freedom to roam and access water sources, there is a high potential for water contamination with pig faeces and urine, creating a route for transmission to humans.⁷⁶

Our review revealed the existence of three prominent genotypes of the hepatitis virus: Genotype 1, Genotype 2, and Genotype 3. Interestingly, Genotype 1 was found only in HAV, whereas Genotype 2 was exclusive to HEV. The codetection of HAV Genotypes 1 and 3 implies the presence of both local and imported strains. Genotype 1 is commonly associated with human outbreaks, whereas Genotype 3 is often found in animal reservoirs.¹⁸ The varying genotypes of HAV and HEV found in these studies demonstrate the genetic variability of these viruses. Notably, Genotype 3 was the most common genotype detected, which aligns with its global distribution pattern.⁷⁰ The high occurrence of HEV Genotype 3 in African pigs highlights the potential for zoonotic transmission to individuals who come into contact with these animals. The first documented case of HEV Genotype 3 in South Africa involved a transplant patient with an underlying medical condition.⁷⁷ Several studies conducted in South Africa have investigated the presence of HEV in human populations. For example, a study by Madden et al.⁷⁸ revealed a high incidence of HEV (27.9% anti-HEV IgG) among patients aged 30 years and older without liver disease. Since these patients did not have any contact with pigs, it was suspected that the transmission might be foodborne, possibly through the consumption of pork.⁷⁸ While HEV in swine has been recognised as the primary source of human infection, HEV subtypes capable of infecting humans have also been found in goats.⁶² However, the extent of their contribution to the transmission of HEV to humans remains poorly studied. It is currently unclear whether goats act as natural reservoirs for the virus or if they become infected through inadvertent exposure to strains originating from pigs. Additionally, other domestic livestock, such as sheep, rabbits, hares, cows, chickens, camels, and monkeys, should not be disregarded as potential reservoirs of infection.

Our review revealed that HAV and HEV are increasingly acknowledged as significant pathogens in Africa; yet, there is a significant knowledge gap regarding their infection in animals, despite the availability of data on human outbreaks in most African countries.^{28,79} The potential zoonotic risk of HAV and HEV transmission from livestock in sub-Saharan Africa remains poorly understood due to a lack of sequence information.⁶⁸ This review underscores the need for continued surveillance and monitoring of HAV and HEV in animals and food products to prevent foodborne outbreaks. Implementing control measures, promoting good agricultural and hygienic practices, and prioritising vaccination are crucial for reducing the transmission of these viruses within the food chain, particularly among high-risk groups.⁸⁰ To protect public health and minimise the impact of HAV and HEV infections, it is essential to

prioritise these preventive measures and conduct further research to understand the dynamics of these viruses in animal reservoirs. Adopting a One Health approach, which considers the interconnectedness of humans, animals, and the environment, is vital to addressing the challenges posed by HAV and HEV infections in Africa.

This review has several strengths, including its comprehensive coverage, methodological consistency, genotyping information, and use of meta-analysis. However, there are a few limitations to consider. This review's focus on North African countries and Western Africa for HAV and HEV detection may limit the generalisability of the findings to other regions in Africa. Additionally, the emphasis on specific animal species, such as ducks and pigs, may overlook the potential presence of HAV and HEV in other animals. The significant heterogeneity among the included studies, resulting from variations in study design, sample sizes, geographic locations, and diagnostic methods, could affect the interpretability and generalisability of the results. Furthermore, publication bias may impact the overall interpretation and presentation of the prevalence and detection rates, as studies with positive or significant results are more likely to be published.

Conclusion

This review illuminates the findings of HAV and HEV detection across different regions of Africa and various animal hosts, indicating their zoonotic potential and foodborne transmission risk. The predominance of Genotype 3 across different animal hosts suggests a persistent and pervasive risk to both animal and human health, highlighting significant public health concerns. The high prevalence, coupled with notable heterogeneity among studies, underscores the need for targeted, and comprehensive interventions. These should include enhanced surveillance, public health measures, vaccination programmes, collaborative research initiatives, and improved environmental controls to effectively mitigate the transmission of HAV and HEV.

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Conceptualisation, E.S.D., F.C.N.K., and A.O.; methodology, A.O., E.S.D., I.B., F.C.N.K., and K.W.C.S.; validation, A.O., E.S.D., F.C.N.K., and K.W.C.S.; formal analysis, A.O., F.C.N.K., E.S.D., I.B., and K.W.C.S.; investigation, A.O., E.S.D., I.B., F.C.N.K., and K.W.C.S.; resources, A.O., E.S.D., I.B., and K.W.C.S.; data curation, A.O., E.S.D., I.B., and K.W.C.S.; writing—original draft preparation, A.O., E.S.D., I.B., F.C.N.K., and K.W.C.S.; writing—review and editing, A.O., E.S.D., I.B., F.C.N.K., and K.W.C.S.; visualisation, A.O., E.S.D., F.C.N.K., I.B., and K.W.C.S.; supervision, E.S.D. and K.W.C.S.; project administration, E.S.D., and A.O.; funding acquisition, E.S.D. All authors have read and agreed to the published version of the manuscript.

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Not applicable.


Consent for Publication

All the authors have given their consent for the publication of this manuscript.

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Availability of Data and Materials

All the supporting data are presented in the manuscript and supplementary files.

Supplemental Material

Supplemental material for this article is available online.

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