Underreporting of Hepatitis E virus infection in Tanzania: a systematic review

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Introduction: Hepatitis E virus (HEV) frequently causes acute hepatitis with water-borne outbreaks in endemic areas. Updated evidence is required in Tanzania to inform the policymakers and identify research gaps.

Objective: The aim of this study was to analyse publications on the epidemiology of HEV in Tanzania.

Methods: We systematically searched all available publications from the major research databases, and selected websites for unindexed studies, policies, and reports for data reporting on the epidemiology of HEV in Tanzania from inception to date.

Results: Five articles were found. There was only one study, performed in 1998, that reported the prevalence of HEV infection in the general Tanzanian population (0.2%). Three other studies reported prevalence's of 8%, 6.6% and 0% among HIV-infected pregnant women, reproductive-aged women (15-45 years), and HIV uninfected pregnant women respectively, with no identified associated factors for HEV infection. One last article described an outbreak that affected 690 people with children's predominance, only 49 samples were tested for HEV and 14 confirmed positive.

Conclusions: Our study showed that HEV infection appears to be markedly underreported in Tanzania as evidenced by a significantly lower reported prevalence compared to neighbouring countries with similar demographics. Increased awareness of this disease by health care professionals and further epidemiological studies to establish the baseline data of the disease are needed urgently.

Keywords: Hepatitis E, prevalence, epidemiology, review, Tanzania

INTRODUCTION

Hepatitis E virus (HEV) infection is one of the commonest emerging diseases. It has affected 20 million people with 3.4 million symptomatic cases worldwide. Approximately 56,600 people have died and 3,000 stillbirths have occurred worldwide in 2005 due to HEV-related conditions.[1] HEV genotypes 1 and 2 are endemic in developing countries, and the major route of transmission is faecal-oral usually through contaminated water. HEV-1 and HEV-2 usually cause epidemic hepatitis that occurs sporadically throughout the year. Clinical presentation varies widely from asymptomatic or non-specific symptoms through severe life-threatening fulminant hepatitis and acute liver failure. Pregnant women especially during the third trimester have increased risk with subsequent development of adverse foeto-maternal outcomes (fulminant hepatic failure, preterm delivery, low birth weight and foetal mortality.[2] Also, other co-infections such as Human Immunodeficiency Virus (HIV) and Hepatitis B virus (HBV) have been correlated with increased frequency and exacerbated effects of HEV infection.[3]

In Africa HEV seroprevalence varies greatly from 0%-94% in the general population and outbreaks, with the case fatality rates of 17.8% and 42.1% in the general

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population and pregnant women respectively. The largest outbreak in Africa was reported in Uganda in 2007, which led to an attack rate of 25% of the population.[4]

Tanzania, one of the most resource-constrained countries in Africa, has poor foeto-maternal outcomes and a high burden of HIV and HBV infections. Clear information on the actual extent of HEV infection is needed. In this study we reviewed the available literature on HEV infection to determine the current situation, and to identify future areas of study.

METHOD

All English full articles or abstracts that reported on HEV in Tanzania were reviewed. We searched PubMed, Web of Science and Scopus databases for the article titles and/or abstracts published from inception to 30 September 2019. There were no initial exclusion criteria, as we aimed to review all available articles related to HEV. However certain publications were excluded later as indicated in Figure 1. The following search term combinations were used: ("hepatitis E" or "HEV" or "non-a" or "non-b" or "viral hepatitis" or "enteric hepatitis") AND ("Tanzania" or "Zanzibar" or "Arusha" or "Dar es Salaam" or "Dodoma" or "Geita" or "Iringa" or "Kagera" or "Katavi" or "Kigoma" or Kilimanjaro" or "Lindi" or "Manyara" or "Mara" or "Mbeya" or "Morogoro" or "Mtwara" or "Mwanza" or "Njombe' or "Pemba" or "Pwani" or "Rukwa" or "Ruvuma" or "Shinyanga" or "Simiyu" or "Singida" or "Tabora" or Tanga" or "Unguja"). The latter is a list of all administrative regions in Tanzania. The relevant references from obtained articles were also reviewed. Gray literatures were also searched in the websites of Tanzania Ministry of Health, Community Development, Gender, Elderly and Children[5], Tanzania National Bureau of Statistics [6], World Health Organization's country office [7] and Google search engine.

A total of 127 studies were identified after removing the duplicates; 64 from PubMed, 49 from Web of Science, and 13 from Scopus and one webpage. Out of these, we excluded 121 articles mainly because they did not contain data on HEV; and so, four studies and one webpage report remained for qualitative synthesis (Figure 1).

RESULTS

Epidemiology of HEV

There was only one study assessing HEV prevalence in the general population of Dar es Salaam in 1998. In this study one 26-year old woman out of 403 healthy volunteers (0.2%) was found to be seropositive for HEV. [8] Another study, in women of childbearing age (15-45 years) in a rural population of Moshi, in the northern part of the country, reported the HEV seroprevalence of 6.6%. In this study there was a trend, albeit not statistically significant, of increasing rates of HEV positivity in women aged 35 years and older compared with the younger group (9% vs. 5%). Other socio-demographic factors including residence and number of children were not associated with HEV infection. [9] Menendez et al [10] reported that no evidence of HEV infection in 180 pregnant women tested during the third-trimester of pregnancy in Ifakara, in southern Tanzania. A more recent study in 2018 has shown a higher HEV seroprevalence of 8% among HIV-infected pregnant women in the third trimester and at 9-months post-partum in the urban population of Tanga City. In this follow-up study, the annual HEV incidence rate was 1% (confidence interval 0.2%-3.4%). The median ages of HEV infected and uninfected groups were 28.0 (IQR 24-31) years and 28.5 (IQR 24-30) years respectively (p>0.05). The gestation age and CD4 counts were comparable between the two groups.[11] More details of these studies are in Table 1.

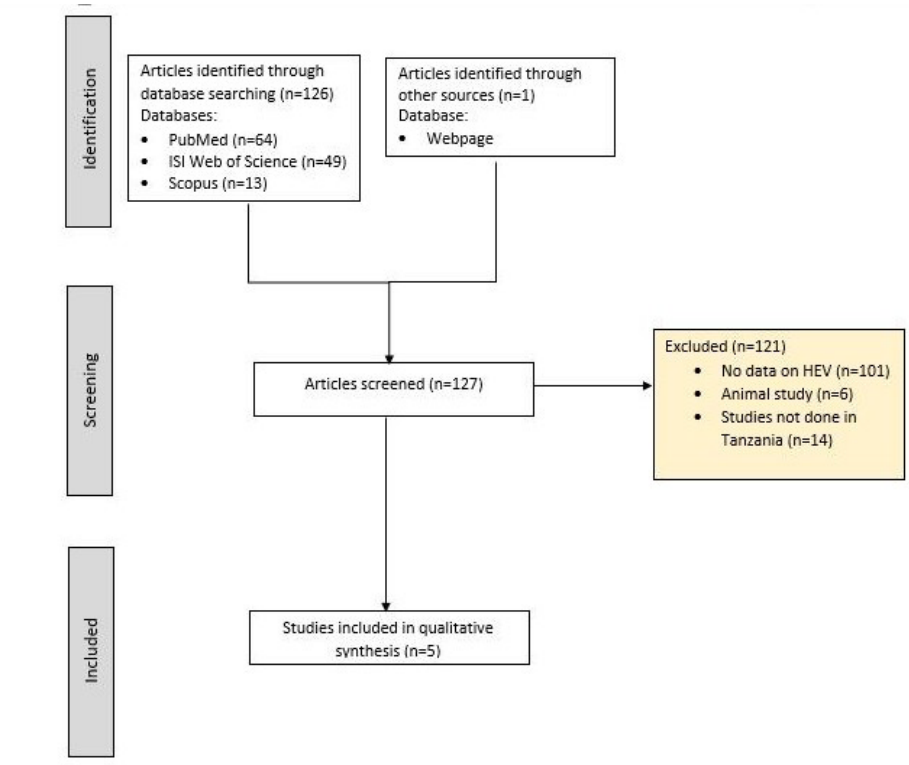

Figure 1. Flow diagram of the literature search and selection process.

Table 1. Characteristics of the studies selected for review

Author	Year of sampling/ publication	Region	Cohort	Sample size	HEV diagnostic method	Prevalence
Harritshoj, et al [11]	2006-2011/2018	Tanga	HIV-infected pregnant women	200	IgG$^{\alpha}$	8%
Stark, et al [9]	1996/2000	Kilimanjaro	Reproductive aged women	212	NS$^{\beta}$	6.6%
Menendez, et al [10]	1995/1999	Morogoro	Pregnant women	180	NS	0%
Miller, et al [8]	1992/1994	Dar es Salaam	Health volunteers	408	NS	0.2%

α IgG: Immunoglobin G βNS: Not stated

HEV outbreaks

One HEV outbreak was reported in 2013 in Buhingwe Kigoma, the western region of Tanzania. Six hundred and ninety patients were affected, most (61%) were children aged less than 15 years,; 54% were females. Most of the patients presented with general features: headache, fever, abdominal pain, general malaise, loss of appetite and vomiting. Jaundice and diarrhoea were rarely reported. The pregnancy state was not reported and there were no recorded deaths. In this outbreak, only 49 samples were actually tested, of which 14 were confirmed positive.[12]

DISCUSSION

High rates of HEV seroprevalence in the general population have been reported in neighbouring countries: Uganda (47.7%)[13], Zambia (42%)[14] and Kenya (18%).[4] We have identified one study[8], which reported only one case of HEV infection in the general Tanzanian population and a few other studies exclusively from female subjects. [9, 10, 11] These provide insufficient data to accurately represent the situation in Tanzania. This knowledge gap might arise from a low rate of routine HEV testing because of poor clinical awareness, unavailability of the resources and the tendency of diagnosing and treating for clinical malaria the patients that present with non-specific symptoms.[15] It is likely that significant HEV infection rates do occur in Tanzania given the recorded higher rates in neighbouring countries. The maternal complications associated with HEV infection cannot be neglected. Hence there is a need for updated information on the status and clinical presentations of the disease particularly in high-risk populations such as pregnant women. Also, adequate access and testing of these subjects should be advocated.

It is not uncommon for HEV outbreaks to occur in displaced communities and refugee camps due to poor hygienic conditions. Uganda and Kenya, on the northern border of Tanzania, have had major HEV outbreaks affecting about 14,000 people with fatality rates of 6.6% in the general population and 77.7% in pregnant women. [4] In both of these outbreaks, water contamination and person-to-person contact were the major sources of infection. Even though the Tanzanian experience in 2013 [13] was less devastating, vulnerability to more critical incidents should not be underrated. Therefore comprehensive health education on the improvement of general hygienic measures for patients presenting with general symptoms, and high- risk groups would be beneficial to reduce transmission. Also, an improved case detection in this population will lead to a better and timely supportive care.

CONCLUSION

Despite the indicators for its endemicity, our study suggests that the reported rates of HEV in Tanzania are considerably lower than neighbouring countries. This is probably due to poor clinical awareness in the presence of non-specific symptoms. The risk of misdiagnosis is increased with consequent inappropriate management. Thus, more studies in different population groups are required to provide the baseline status of the disease and to hasten the establishment and implementation of evidence-based control policies, which are currently not available.

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