ID Design Press, Skopje, Republic of Macedonia Open Access Macedonian Journal of Medical Sciences. https://doi.org/10.3889/oamjms.2019.143 eISSN: 1857-9655 **Review Article** 



# Hepatitis E Infection in Nigeria: A Systematic Review

Hilary I. Okagbue<sup>1\*</sup>, Muminu O. Adamu<sup>2</sup>, Sheila A. Bishop<sup>1</sup>, Pelumi E. Oguntunde<sup>1</sup>, Oluwole A. Odetunmibi<sup>1</sup>, Abiodun A. Opanuga<sup>1</sup>

<sup>1</sup>Department of Mathematics, College of Science and Technology, Covenant University, Ota, Nigeria; <sup>2</sup>Department of Mathematics, Faculty of Science, University of Lagos, Akoka, Lagos, Nigeria

#### Abstract

Citation: Okagbue HI, Adamu MO, Bishop SA, Oguntunde PE, Odetummibi OA, Opanuga AA. Hepatitis E Infection in Nigeria: A Systematic Review. Open Access Maced J. Med Sci. https://doi.org/10.3889/oamjms.2019.143

**Keywords:** Hepatitis E; Hepatitis B; Odd ratio; Logistic regression; Prevalence; Statistics

\*Correspondence: Hilary I. Okagbue. Department of Mathematics, College of Science and Technology, Covenant University, Ota, Nigeria. E-mail: hilary.okagbue@covenantuniversity.edu.ng

Received: 25-Feb-2019; Revised: 07-May-2019; Accepted: 08-May-2019; Online first: 29-May-2019

Copyright: © 2019 Hilary I. Okagbue, Muminu O. Adamu, Sheila A. Bishop, Pelumi E. Oguntunde, Oluwole A. Odetumbi, Abidun A. Opanuga. This is an openaccess article distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License (CC BV-NC 4.0)

Funding: This research was financially supported by Covenant University, Nigeria

Competing Interests: The authors have declared that no competing interests exist

**BACKGROUND:** Research done globally on hepatitis E virus (HEV) infection is far fewer compared with other types of hepatitis virus infection. Little is known on the prevalence of HEV in Nigeria.

**AIM:** The present study presents the prevalence of HEV infection in Nigeria from a few available research papers on HEV. The detailed statistical analysis was used to analyse the prevalence of HEV in humans and animals.

**MATERIAL AND METHODS:** A literature search in Web of Science, Scopus and PubMed databases was done, and a final 7 articles were selected. Minitab 17.0 was used to perform the correlational and binary logistic analyses.

**RESULTS:** Serum and faecal analysis of blood and stool samples of 1178 humans and 210 pigs (animals) were done, and the presence of anti-HEV IgG or HEV RNA in the study samples were 127 and 138 respectively. Further analysis showed the prevalence of HEV are 10.8% and 65.7% in humans and animals, respectively. Weak positive non-significant association (r = 0.327, p-value = 0.474) was obtained between the target (humans and animal) and the HEV infection (positive) groups. The application of binary logistic regression yielded an equation that can be used to predict the target group from the HEV positive humans or animals. Generally, the logistic model was not statistically significant (p-value = 0.376), and the model was able to explain 9.3% of the deviation or variability of the model. The odds ratio is OR = 1.0344 with 0.9550, 1.204 95% Confidence Interval (CI). Thus, in Nigeria, the odds of prevalence of HEV in animals are 1.0344 higher than humans.

**CONCLUSION:** The risk factors obtained from the few available articles are consistent with the global epidemiology of HEV infection. Food and animal handlers and those that consume unsafe water are the key people at risk of HEV infection in Nigeria.

# Introduction

Hepatitis E is an inflammatory liver disease caused by a non-enveloped positive-sense [1] and single-stranded ribonucleic (RNA) genome called the hepatitis E virus (HEV). The virus is in four different types identified as genotypes 1, 2, 3 and 4. Genotypes 1 and 2 have been isolated in humans while 3 and 4 are found in animals. HEV is transmitted mainly through faecal contamination of drinking water and uncooked foods. Generally, the risk factors of the disease include lack of access to cheap, safe and potable drinking water, unhygienic living conditions and indiscriminate disposal of human wastes, poverty, the insecurity that results to a strain on access to basic life amenities and limited access to quality health services [2]. Symptoms of the disease include mild fever, anorexia, nausea, jaundice, dark urine, pale stools and slight liver inflammation, although, rare cases have been reported to result to fulminant hepatitis in pregnant women [3], [4]. Diagnosis of HEV infection includes detection of the HEV in stool or serum samples and serological tests for identification of anti-HEV Ig G and Ig M [1]. Measures to be taken to eliminate the risk factors are consistent supply of clean and safe water, improving personal hygiene and ensuring proper disposal of human wastes.

Hepatitis E is one of five known human hepatitis viruses. Others are A [5], B [6], [7], C [8], [9], [10] and D [11]. The prevalence of HEV is very low compared with the others, especially hepatitis B virus (HBV). Numerous articles that investigated different aspects of HBV infections in Nigeria [12], [13], [14] and few papers are available for HEV infection.

This paper aims to present a statistical analysis of a few articles published on the prevalence of HEV infection in Nigeria. The few papers are traceable to the low prevalence of the disease in the world of which the studied country is a particular case. A similar investigation has been done and can be found in [15], [16], [17], [18], [19], [20], [21].

# **Material and Methods**

## Study Design

The study design is Web of Science, Scopus and PubMed databases. The keywords "Hepatitis E" OR "HEV" AND "Nigeria" were queried in Scopus, PubMed and Web of Science databases. PubMed, Scopus and Web of Science (WOS) returned 301, 66 and 11 articles respectively. Further evaluation showed that the articles in WOS are also contained in Scopus and are littered with hepatitis B and studies on areas not related to Nigeria. A final seven (7) articles were sieved out after all the unrelated articles were removed.

## Eligibility Criteria

The papers that contained the prevalence of HEV in their abstracts were included. Risk of bias was almost nonexistent since the sample size is small.

## Ethics Statement

No ethical rules were violated. All the sources of information were duly acknowledged.

## Statistical Analysis

The absence of numerous studies places undue restrictions on the use of different statistical techniques. The statistical techniques are needed to reveal hidden patterns as long as the sample size is appreciably high [22], [23], [24], [25], [26], [27], [28]. The 7 articles were analysed using Minitab version 17.0, binary logistic regression was used for the analysis, and this was as a result of splitting of the target groups into two distinct and non-overlapping classes. P-value of 0.05 was considered significant.

# Results

The summary of the data presentation of the 7 articles [29], [30], [31], [32], [33], [34], [35] are presented in Table 1. The publication span 10 years. It can be seen that (6/7) of both the methodology and diagnostics (tool for analysing serum and faecal samples) used in the articles are cross-sectional studies and enzyme-linked immunosorbent assay (ELISA) technique respectively.

Table 1:	Studies	on hepatitis	E virus	infection	in Nigeria
----------	---------	--------------	---------	-----------	------------

Author	Publication	Methodology	Target Group	Diagnost	Sample	HEV
	Year			ics	size	positive
[29]	2008	Observation	Hospitalized	Therapy	1	1
[30]	2013	Cross sectional	Non-hospitalized	ELISA	132	36
[31]	2014	Cross sectional	Pigs	ELISA	90	69
[32]	2014	Cross sectional	Non-hospitalized	ELISA	462	43
[33]	2015	Cross sectional	Non-hospitalized	ELISA	406	31
[34]	2018	Cross sectional	Pigs	ELISA	120	69
[35]	2018	Cross sectional	Non-hospitalized	ELISA	177	16

## Prevalence of HEV in the samples

HEV positive means the presence of anti-HEV IgG or HEV RNA in the study samples. The prevalence for each case is obtained using the dataset of Table 1, by dividing the total number of HEV positive and the total number investigated and multiplying by 100. This is presented in Table 2.

Table 2: Prevalence of the two types of HEV infection in Nigeria

	Humans	Animals
Total investigated	1178	210
HEV positive	127	138
Prevalence	10.8%	65.7%

## **Correlation Analysis**

Correlation coefficient was obtained between the target group (humans = 0, animal = 1) and the HEV positive and it was computed to be (r = 0.327, p = 0.474).

## **Binary Logistic Regression**

Binary logistic regression was performed to determine the association between the target group y (humans = 0, animal = 1) and the HEV positive (x).

#### Table 3: Deviance table

Source DF Adj Dev Adj Mean Chi-Square P-Value
Regression 1 0.7842 0.7842 0.78 0.376
Error 5 7.5915 1.5183
Total 6 8.3758

This is to determine if the prevalence of HEV can predict whether the target group is animal or human.

## Table 4: Model Summary

Deviance Deviance	
R-Sq R-Sq(adj) AIC	
9.36% 0.00% 11.59	

The details are presented in Tables 3 to 7, and the logistic regression equation is Exp(y) = -2.33+0.338x.

#### Table 5: Coefficient of the model

erm Coef SE Coef VIF
onstant -2.33 2.04
0.0338 0.0407 1.00

## Discussion

The few available studies on HEV infection in Nigeria is due to the less severe nature of the disease when compared with Hepatitis B infection. The low research activities on HEV can also be as a result of the low incidence of the disease, self-medication, the use of traditional or alternative medicine and nonhospitalization. Hospital records about the HEV infection will encourage cross-sectional and retrospective studies.

## Table 6: Odds Ratios for Continuous Predictors

Odds Ratio 95% CI	
x 1.0344 (0.9550, 1.1204)	

The risk factors available from the few articles are consistent with the global epidemiology of HEV infection. The risk factors are faecal contamination of water and food, improper disposal of human and animal wastes, poverty, unhygienic environment and inadequate access to quality healthcare services.

#### Table 7: Goodness-of-Fit Tests

Test DF Chi-Square P-Value
Deviance 5 7.59 0.180
Pearson 5 6.61 0.252
Hosmer-Lemeshow 4 4.60 0.330

Serum and faecal analysis of blood and stool samples of 1178 humans and 210 pigs (animals) were done, and the presence of anti-HEV IgG or HEV RNA in the study samples were 127 and 138 respectively. Further analysis showed the prevalence of HEV are 10.8% and 65.7% in human and animals, respectively. The high level of the prevalence in animals calls for urgent action to avoid infections to human via faecal oral transmission.

There is a weak positive non-significant

association between the target groups (humans and animals) and the HEV infection (positive). This is the outcome of the prevalence that showed that the prevalence of both groups is different; that is, high for animals and low for humans.

The application of binary logistic regression yielded an equation that can be used to predict the target group from the HEV positive humans or animals. Generally, the logistic model was not statistically significant (p-value = 0.376), and the model was able to explain only 9.3% of the deviation or variability of the dependent variable. The odds ratio was gotten to be; OR = 1.0344 (0.9550, 1.204) 95% CI. Thus, in Nigeria, the odds of prevalence of HEV in animals are 1.0344 higher than humans.

## Acknowledgement

The authors appreciate the efforts of the anonymous reviewers toward this publication. The support from Covenant University, Nigeria, is also deeply appreciated.

## References

1. Nicand E, Grandadam M. Hepatitis E virus. Virologie. 2003; 7(2): 87-96.

2. Assih M, Ouattara AK, Diarra B, Yonli AT, Compaore TR, Obiri-Yeboah D, Djigma F, Karou S, Simpore J. Genetic diversity of hepatitis viruses in West-African countries from 1996 to 2018. World J Hepatol. 2018; 10(11): 807-821. https://doi.org/10.4254/wjh.v10.i11.807 PMid:30533182 PMCid:PMC6280160

3. Lee EB, Kim JH, Hur W, Choi JE, Kim SM, Park DJ, Kang BY, Lee GW, Yoon SK. Liver-specific Gene Delivery Using Engineered Virus-Like Particles of Hepatitis E Virus. Scientific Reports. 2019; 9(1): Article number 1616. <u>https://doi.org/10.1038/s41598-019-</u> <u>38533-7</u> PMid:30733562 PMCid:PMC6367430

4. Vázquez-Morón S, Berenguer J, González-García J, Jiménez-Sousa MÁ, Canorea I, Guardiola JM, Crespo M, Quereda C, Sanz J, Carrero A, Hontañón V, Avellón A, Resino S. Prevalence of hepatitis E infection in HIV/HCV-coinfected patients in Spain (2012-2014). Scientific Reports. 2019; 9(1): Article number 1143. https://doi.org/10.1038/s41598-018-37328-6 PMid:30718554 PMCid:PMC6361883

5. Yamamoto C, Ko K, Nagashima S, Harakawa T, Fujii T, Ohisa M, Katayama K, Takahashi K, Okamoto H, Tanaka J. Very low prevalence of anti-HAV in Japan: high potential for a future outbreak. Scientific Reports. 2019, 9(1): Article number 1493. https://doi.org/10.1038/s41598-018-37349-1 PMid:30728377 PMCid:PMC6365493

6. Zong L, Peng H, Sun C, Li F, Zheng M, Chen Y, Wei H, Sun R, Tian Z. Breakdown of adaptive immunotolerance induces hepatocellular carcinoma in HBsAg-tg mice. Nature Comm. 2019; 10(1): Article number 221. <u>https://doi.org/10.1038/s41467-018-08096-8</u> PMid:30644386 PMCid:PMC6333806

7. Khadem Ansari MH, Rasmi Y, Abbasi L. Hepatitis B virus

Genotypes in West Azarbayjan Province, Northwest Iran. Open Access Maced J Med Sci. 2017; 5(7): 875-879. https://doi.org/10.3889/oamjms.2017.206 PMid:29362612 PMCid:PMC5771288

8. Hoofnagle JH. Course and outcome of hepatitis C. Hepatology. 2002; 36(5): S21-S29. <u>https://doi.org/10.1053/jhep.2002.36227</u> PMid:12407573

9. Youssef SS, Elemeery MN, Eldein SS, Ghareeb DA. Silencing HCV replication in its reservoir. Open Access Maced J Med Sci. 2018; 6(11): 1965-1971. https://doi.org/10.3889/oamjms.2018.372

10. Vila Brunilda H, Lila S, Erjona A, Silva B, Tefta R. Prevalence of hepatitis C virus in the population of Albania for the period 2007-2010. Open Access Maced J Med Sci. 2014; 2(3): 525-528. https://doi.org/10.3889/oamjms.2014.094

11. Ouedraogo HG, Kouanda S, Grosso A, Compaoré R, Camara M, Dabire C, Ouedraogo R, Traore Y, Baral S, Barro N. Hepatitis B, C, and D virus and human T-cell leukemia virus types 1 and 2 infections and correlates among men who have sex with men in Ouagadougou, Burkina Faso. Virology Journal. 2018; 15(1): Article number 194. <a href="https://doi.org/10.1186/s12985-018-1110-8">https://doi.org/10.1186/s12985-018-1110-8</a> PMid:30594218 PMCid:PMC6311018

12. Abiodun O, Shobowale O, Elikwu C, Ogbaro D, Omotosho A, Mark B, Akinbola A. Risk perception and knowledge of hepatitis B infection among cleaners in a tertiary hospital in Nigeria: A cross-sectional study. Clin Epidemiol Global Health. 2019; 7(1): 11-16. https://doi.org/10.1016/j.cegh.2017.12.001

13. Omotowo IB, Meka IA, Ijoma UN, Okoli VE, Obienu O, Nwagha T, Ndu AC, Onodugo DO, Onyekonwu LC, Ugwu EO. Uptake of hepatitis B vaccination and its determinants among health care workers in a tertiary health facility in Enugu, South-East, Nigeria. BMC Infect Dis. 2018; 18(1): Article number 288. https://doi.org/10.1186/s12879-018-3191-9 PMid:29954344 PMCid:PMC6027786

14. Agan TU, Monjok E, Akpan UB, Omoronyia OE, Ekabua JE. Trend and causes of maternal mortality in a Nigerian tertiary hospital: A 5-year retrospective study (2010-2014) at the university of Calabar teaching hospital, Calabar, Nigeria. Open Access Maced J Med Sci. 2018; 6(6):1153-1158. https://doi.org/10.3889/oamjms.2018.220 PMid:29983819 PMCid:PMC6026429

15. Popov GT, Pepovich R, Tsachev I. Hepatitis E Virus Infection in Bulgaria: A Brief Analysis of the Situation in the Country. Open Access Maced J Med Sci. 2019; 7(3): 458-460. <u>https://doi.org/10.3889/oamjms.2019.073</u> PMid:30834019 PMCid:PMC6390163

16. Baymakova M, Popov GT, Pepovich R, Tsachev I. Hepatitis E virus infection in Bulgaria: a brief analysis of the situation in the country. Open Access Maced J Med Sci. 2019; 7(3): 458-460. https://doi.org/10.3889/oamjms.2019.073 PMid:30834019 PMCid:PMC6390163

17. Pepovich R, Baymakova M, Pishmisheva M, Marutsov P, Pekova L, Tsachev I. Current knowledge on Hepatitis E virus infection. Vojnosanit Pregl. 2019; 76(7): https://doi.org/10.2298/VSP170815159P

18. Baymakova M, Sakem B, Plochev K, Popov GT, Mihaylova-Garnizova R, Kovaleva V, et al. Epidemiological characteristics and clinical manifestations of hepatitis E virus infection in Bulgaria: a report on 20 patients. Srp Arh Celok Lek. 2016; 144(1-2): 63-68. https://doi.org/10.2298/SARH1602063B PMid:27276860

19. Akanbi OA, Harms D, Wang B, Opaleye OO, Adesina O, Osundare FA, et al. Complete genome sequence of a hepatitis E virus genotype 1e strain from an outbreak in Nigeria, 2017. Microbiol Resour Announc. 2019; 8(1): e01378-18. https://doi.org/10.1128/MRA.01378-18 PMid:30637389 PMCid:PMC6318360

20. Wang B, Akanbi OA, Harms D, Adesina O, Osundare FA, Naidoo D, et al. A new hepatitis E virus genotype 2 strain identified from an outbreak in Nigeria, 2017. Virol J. 2018; 15(1): 163. https://doi.org/10.1186/s12985-018-1082-8 PMid:30352598 PMCid:PMC6199738 21. Ifeorah IM, Faleye TOC, Bakarey AS, Adewumi MO, Akere A, Omoruyi EC, et al. Acute hepatitis E virus infection in two geographical regions of Nigeria. J Pathog. 2017; 2017: 4067108. <u>https://doi.org/10.1155/2017/4067108</u> PMid:29387489 PMCid:PMC5745689

22. Oguntunde PE, Adejumo AO, Okagbue HI. Breast Cancer Patients in Nigeria: Data exploration approach. Data in Brief. 2017; 15: 47-57. <u>https://doi.org/10.1016/j.dib.2017.08.038</u> PMid:28971122 PMCid:PMC5612794

23. Adamu PI, Oguntunde PE, Okagbue HI, Agboola OO. Statistical data analysis of cancer incidences in insurgency affected states in Nigeria. Data in Brief. 2018; 18: 2029-2046. <u>https://doi.org/10.1016/j.dib.2018.04.135</u> PMid:29904711 PMCid:PMC5998707

24. Adejumo AO, Ikoba NA, Suleiman EA, Okagbue HI, Oguntunde PE, Odetunmibi OA, Job O. Quantitative Exploration of Factors influencing Psychotic Disorder Ailments in Nigeria. Data in Brief. 2017; 14: 175-85. <u>https://doi.org/10.1016/j.dib.2017.07.046</u> PMid:28795095 PMCid:PMC5537424

25. Adamu PI, Adamu MO, Okagbue HI. Data in support of high rate of pregnancy related deaths in Maiduguri, Borno State, Northeast Nigeria. Data in Brief. 2018; 18: 409-414. <u>https://doi.org/10.1016/j.dib.2018.03.038</u> PMid:29900198 PMCid:PMC5996266

26. Adejumo AO, Suleiman EA, Okagbue HI, Oguntunde PE, Odetunmibi OA. Quantitative Evaluation of Pregnant Women Delivery Status' Records in Akure, Nigeria. Data in Brief. 2018; 16: 127-34. <u>https://doi.org/10.1016/j.dib.2017.11.041</u> PMid:29201979 PMCid:PMC5699871

27. Adamu PI, Oguntunde PE, Okagbue HI, Agboola OO. On the Epidemiology and Statistical Analysis of HIV/AIDS Patients in the Insurgency Affected States of Nigeria. Open Access Maced J Med Sci. 2018; 6 (7): 1315-1321.

https://doi.org/10.3889/oamjms.2018.229 PMid:30087744 PMCid:PMC6062286

28. Adamu PI, Adamu MO, Okagbue HI, Opoola L, Bishop SA. Survival Analysis of Cancer Patients in North Eastern Nigeria from 2004-2017 - A Kaplan - Meier Method. Open Access Maced J Med Sci. 2019; 7(4): 642-649. <u>https://doi.org/10.3889/oamjms.2019.109</u> PMid:30894929 PMCid:PMC6420928

29. Panther E, Thimme R, Blum HE. Jaundice in an HIV-positive pregnant woman. Deut Mediz Wochen. 2008; 133(30): 1560-1562. https://doi.org/10.1055/s-2008-1081109 PMid:18642217

30. Ola SO, Odaibo GN, Olaleye OD, Ayoola EA. Hepatitis B and E viral infections among Nigerian healthcare workers. Afr J Med Medic Sci. 2013; 41(4): 387-391.

31. Owolodun OA, Gerber PF, Giménez-Lirola LG, Kwaga JKP, Opriessnig T. First report of hepatitis E virus circulation in domestic pigs in Nigeria Amer J Trop Med Hygiene. 2014; 91(4): 699-704. <u>https://doi.org/10.4269/ajtmh.14-0144</u> PMid:25002299 PMCid:PMC4183390

32. Junaid SA, Agina SE, Abubakar KA. Epidemiology and associated risk factors of hepatitis E virus infection in Plateau State, Nigeria. Virology. 2014; 5: 15-26. https://doi.org/10.4137/VRT.S15422 PMid:25512696 PMCid:PMC4251053

33. Ekanem E, Ikobah J, Okpara H, Udo J. Seroprevalence and predictors of hepatitis e infection in Nigerian children. J Infect Devel Count. 2015; 9(11): 1220-1225. <u>https://doi.org/10.3855/jidc.6736</u> PMid:26623631

34. Antia RE, Adekola AA, Jubril AJ, Ohore OG, Emikpe BO. Hepatitis E Virus infection seroprevalence and the associated risk factors in animals raised in Ibadan, Nigeria. J Immun Immunochem. 2018; 39(5): 509-520.

https://doi.org/10.1080/15321819.2018.1514507 PMid:30212262

35. Fowotade A, Akande O, Gbaja AT, Ogunleye VO, Ajayi A, Kehinde AO. Seroprevalence of hepatitis E among restaurant food handlers in Ibadan, Nigeria. Tanzania J Health Res. 2018; 20(3):1-7.