Hepatitis E Seroprevalence and Risk Factors in Humans and pig in Ghana

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Abstract

Background

Although Hepatitis E has significant negative impact on the health and wellbeing of underprivileged populations, the burden of HEV in Ghana is still unclear, despite widespread conditions that predispose people to the risk of infection.

Methods

A cross-sectional study was conducted to explore rates of HEV exposure and active infection, as well as risk factors in humans and domestic pigs in Ghana. The study involved 1365 community members, 105 pig farmers and 474 domestic pigs from four administrative regions of Ghana.

Results

Results showed overall seroprevalence and actual prevalence of 12.4% and 0.7% in community members and 15.2% and 2.9% in pig farmers respectively. There was no significant difference in seroprevalence between the two groups (Z = 0.851; p = 0.395). However, the prevalence in pig farmers was significantly higher than in other community members (Z = 2.412; p = 0.016). Age (OR = 1.369, CI = 1.243 – 1.508; p = 0.0000), gender (OR = 1.419, CI = 1.101 – 1.991; p = 0.043), and the region of residence (OR = 1.569, CI = 1.348 – 1.827; p = 0.0000) were significant risk factors for HEV seroprevalence in a multivariate regression model.

Introduction

Viral hepatites present a major threat to public health security, causing severe morbidities and high mortalities through acute and chronic infections (1). Hepatitis E is recognised as one of the primary causes of acute viral hepatitis in humans worldwide (2). It is a serious public health disease in many developing countries, especially in regions of high faecal contamination of drinking water supplies and poor sanitation (3). As a neglected tropical disease related to water, sanitation, and hygiene (WASH), Hepatitis E virus (HEV) infection has a huge burden on many underprivileged populations in developing countries but has gained insufficient attention in terms of control interventions, research, and treatment options (4, 5).

In Ghana, environmental risk factors for transmission of the infection to humans are ubiquitous: sanitation coverage is low at 15% with a 19% open defecation rate (6). Also, there is widespread faecal contamination of drinking water (7). Furthermore, domestic pigs, which are the primary host of the Hepatitis E virus are allowed to roam free in major pig production communities in Ghana; thus, serving as agents of environmental contamination by shedding the virus in faeces and urine.

The burden of this zoonotic infection is not well known in Ghana and there is a dearth of research data available. Results from a few localised serosurveys in various populations groups in Ghana such as pig handlers (8), blood donors (9, 10) and pregnant women (11, 12) highlight high HEV seroprevalence but the

actual prevalence and risk of transmission to the general public are not yet known. While the little research available research provides some insight into the problem of Hepatitis E in Ghana, several knowledge gaps remain: Previous studies featured small study areas and sample sizes and specific population groups rather than the general public. The prevalence of active infections, risk factors, and transmission routes were not explored (5).

To fill these gaps, a large cross-sectional study was conducted between October 2019 and October 2020 to investigate the contribution of zoonotic and WASH-related transmission routes to the burden of Hepatitis E in humans and domestic pigs in the South East of Ghana. HEV seroprevalence, prevalence, and associated risk factors are presented in this paper. These results enable us to better gauge the regional distribution and drivers of HEV seroprevalence and the national burden of disease, which are crucial for a better understanding of the epidemiology of the disease, improving awareness, and evidence-based decision making by policymakers in Ghana.

Materials And Methods

Sampling Frame and Study Sites

The sampling frame included all the 10 regions of Ghana, covering an area of about 240,000km^2. In each region, two (2) districts were randomly selected and, in each district, two (2) communities were purposely selected targeting the desire community types giving a total of forty (40) communities.

Although the study was initially a national survey including all the regions of Ghana, due to restrictions and logistical challenges as a result of the Corona Virus Disease (COVID-19) pandemic about half of the scope of the research was completed. The study, thus, covered four (4) out of the ten (10) former regions of Ghana including eight (8) districts and sixteen (16) communities.

The selected communities were a combination of "presence or absence of open defaecation (OD)" and "presence or absence of free-range pigs (PIG)" to explore the contribution of pigs and sanitation to the transmission of HEV. Thus, there were four categories of study communities: (1) Absence of both pigs and open defaecation (PIG- OD-), (2) Presence of both pigs and open defaecation (PIG+ OD+), (3) Absence of pigs and presence of open defaecation (PIG- OD+), and (4) Presence of pigs and absence of open defaecation (PIG+ OD-). The study sites are illustrated in Figure 1 below.

Study Design and Sample Size Estimation

A cross-sectional cluster survey method was employed for the study. CSurvey software version 2.0 was used to estimate sample sizes of 4,000 for humans and 3,200 for pigs at a desired level of precision of 0.05%. The estimation was done using HEV seroprevalence values of 37% and 85% for humans and pigs respectively determined from our previous study in Ghana (13). A minimum cluster size of 25 was determined which was adjusted to 40 to cover all communities in the sampling frame.

A sample size of 100 people was allocated to each community consisting of 75 community members and 25 pig farmers (1:3 ratio). However, in communities without pig farmers only community members were sampled;

thus, 100 community members. For pigs, since half of the communities (20) in the sampling frame included pigs, a sample size of 160 pigs was assigned to each community.

Table 1 shows the region, district, community, community status, and the number of research participants and pigs sampled from each study community.

Sampling technique.

A non-probability, purposive sampling technique was used to sample the study participants. Every male or female aged 1 and above and a resident of the study community was eligible to participate in the study. In each study community, pig farmers and community members were sampled representing occupationally exposure and unexposed population respectively, while free-range and confined pigs were sampled. To ensure that as many as possible pig farmers in the study communities participated in the study, engagement with their local association and snowballing were used to recruit them.

Table 1: Sampling Frame

Region	District	Community	Community Status	Community Members	Pig Farmers	Total Samples	Pigs
Accra	Ada East	Totimehkope	+OD PIG-	99	6	105	30
		Obane	+ OD PIG+	43	15	58	89
	Shai Osudoku	Odumase	+OD PIG+	91	3	94	83
		Lardor Wayo	-OD PIG+	80	4	84	-
Central	Ajumako	Turom	+OD PIG+	90	4	94	-
		Ola Estate	+OD PIG-	76	7	83	52
	Cape Coast Municipality	Breman Essiam	OD- PIG+	73	2	75	42
		Denkyira	-OD PIG-	104	0	104	-
Volta	Keta	Anlo Afiadenyigba	+OD PIG+	77	27	104	58
		Seva	+OD PIG+	92	12	104	32
	North Tongu	Bla	+OD PIG-	100	0	100	-
		Mepe	-OD PIG-	100	0	100	-
Eastern	Nsawam Adoagyire	Akwamu	OD+ PIG-	100	0	100	-
		Dzatsui-Newtown	-OD PIG-	100	0	100	-
	Fanteakwa	Bepoase	-OD PIG+	81	21	102	63
		Ehiamankyene	OD+ PIG+	59	4	63	25
Total				**1365**	**105**	**1470**	**474**

Data and sample collection and Processing

Blood samples (3-5ml) from human participants and pigs were collected by trained phlebotomists and veterinarians respectively and allowed to clot. The samples were then centrifuged at 3000rpm for 5 minutes for serum separation. The resulting serum samples were then transferred into labelled cryo-tubes and stored at -20^{o}C at the serology laboratory of the Noguchi Memorial Institute for Medical Research, University of Ghana.

Structured questionnaires containing closed and open ended-questions were administered to all consenting participants to obtain data on demographics, attitudes, and practices relating to sanitation water and hygiene, and contact with pigs and pork. This data was used to determine risk factors associated with HEV infection.

Serological methods

All serum samples from humans and pigs were tested for anti-HEV antibodies Immunoglobulin G (IgG) & Immunoglobulin (IgM) and Ab (total antibody) respectively using enzyme-linked immunosorbent assay (ELISA) and rapid immunochromatographic diagnostic kits (RDT). Samples testing positive for any of these tests were then tested for HEV antigens (HEV-Ag) using ELISA. The HEV-Ag ELISA is an inexpensive alternative to PCR that can qualitatively detect Hepatitis E virus antigen in serum or plasma samples. All the diagnostic test kits were manufactured by Wantai Beijing Biopharmaceuticals, China. Table 2 show the types of HEV markers and diagnostic test employed.

Table 2
HEV Markers and Test Used

	HEV Marker	Test	Number of Samples Tested
Humans	IgM	RDT	1470 (All samples)
	IgG	ELISA	1470 (All Samples)
	Ag	ELISA	178 (IgM & IgG Positives)
Pigs	Ab	ELISA	474 (All Samples)
	Ag	ELISA	296 (Ab Positives)

Data analysis

The data collected using the structured questionnaires and results of serological tests were entered into MS-Excel (2016). Statistical analysis was done using the Statistical Package for Social Sciences (SPSS) version 26.0 statistical software (IBM). Descriptive statistics of demographic parameters were computed and results presented as percentages. Binary logistic regression analysis was conducted in both univariate and multivariate models and odds ratios (OR) and their corresponding 95% confidence intervals (CI) used to determine risk factors associated with HEV infection. The Pearson chi-square (x^2) test was used to test the association between categorical variables while significant difference was tested using a Z test. Significance was accepted at the level of $P < 0.05$.

Results

Demographic Characteristics of Study Participants

Overall, 1470 participants were sampled from sixteen communities in four regions of Ghana. Of the total number of participants, 1365 (92.9%) were community members and 105 (7.1%) were pig farmers. A total of 877 of the participants were females (59.7%) and 593 (40.3%) males. The ages of the participants range from 1 to 92 years, with a mean age ± SD of 40.41 ± 22.24 years, a median of 40 years, and a mode of 60 years.

HEV IgG Seroprevalence in Humans

The overall seroprevalence indicating past or present exposure to HEV was 12.6%. Anti-HEV IgG antibody seroprevalence was higher in pig farmers (15.2%) than in community members (11.9%). However, the difference was not statistically significant (Z = 1.020; *p* = 0.308).

Similarly, HEV IgG seroprevalence was higher in males (13.3%) than females (11.3%), Table 3, but the difference was not statistically significant; Z = 1.173; *p* = 0.242. Anti-HEV IgG antibody seroprevalence increased quite consistently and significantly with increasing age; x^2= 67.021; *p* = 0.000. Figure 2 shows anti-HEV IgG Seroprevalence amongst the different age groups. The seroprevalence was lowest (0%) in the 1-4years age group and highest (20.8%) in the 40-49years age group.

Amongst the four regions, the seroprevalence range from 6.0% in the Eastern Region to 20.2% in the Central Region. HEV seroprevalence was significantly associated with region, x^2= 42.272; *p* < 0.00001. The seroprevalence in the Central Region (20.2%) and the Greater Accra Region (14.7%) were significantly higher than those in the Eastern Region (6.0%) and the Volta Region (8.3%). The regional distribution of HEV seroprevalence in humans is shown in Figure 3.

Seroprevalence significantly increased with the level of education with the lowest infections in persons with nursery education (1.7%) and the highest in persons with tertiary education (17.4%), (x^2= 15.747; *p* = 0.008). The seroprevalence amongst community types did not differ significantly; x^2= 4.485, *p* = 0.214; ranging from 9.9% in +OD PIG+ communities to 13.9% in -OD PIG+ communities.

The active HEV infection prevalence was 0.8%; the prevalence in pig farmers and community members was significantly different (2.9% vs 0.7%; Z = 2.412; p = 0.016). Prevalence and seroprevalence results are shown in Table 4.

Table 3
Demographics and HEV IgG Seroprevalence

Demographic Variables	N	Percentage (mean)	HEV (IgG) Seroprevalence	*P* Value
Gender				
Male	593	40.3%	13.3%	0.242
Female	877	59.7%	11.3%	
Age group				
1-4	44	3.0% (2.9)	0%	
5-9	91	6.2% (7.0)	2.2%	
10-14	87	5.9% (12.3)	3.4%	
15-19	110	7.5% (17.1)	3.6%	
20-29	196	13.3% (24.4)	5.6%	0.000
30-39	199	13.5% (34.8)	10.1%	
40-49	178	12.1% (44.3)	20.8%	
50-59	209	14.2% (54.1)	18.7%	
60+	356	24.2% (69.7)	17.4%	
Region				
Accra	341	23.2%	14.7%	
Eastern	365	24.8%	6.0%	
Volta	408	27.8%	8.3%	0.000
Central	356	24.2%	20.2%	
Educational level				
None	347	23.6%	16.7%	
Nursery	59	4.0%	1.7%	
Primary	346	23.5%	11.6%	
JHS	552	37.6%	10.5%	0.008
SHS	120	8.2%	10.8%	
Tertiary	46	3.1%	17.4%	
Population Group				
Community Member	1365	92.9%	11.9%	0.308
Pig Farmer	105	7.1%	15.2%	

Demographic Variables	N	Percentage (mean)	HEV (IgG) Seroprevalence	*P* Value
Community Type				
-OD PIG-	304	20.7%	13.8%	
-OD PIG+	261	17.8%	11.9%	0.214
+OD PIG-	388	26.4%	13.9%	
+OD PIG+	517	35.2%	9.9%	

Figure 2: HEV IgG Seroprevalence Amongst Age Groups

Table 4
HEV Prevalence and Seroprevalence in Community Members and Pig Farmers

HEV Test	Community Member (n = 1365)	Pig Farmer (n = 105)	Total (n = 1470)	Total Prevalence
Antibody				
IgM only	7 (0.51%)	0 (0%)	7	0.5%
IgG only	159 (11.6%)	16 (15.2%)	175	11.9%
IgM + IgG	3 (0.22%)	0 (0%)	3	0.2%
Total Prevalence	**12.4%**	**15.2%**	**185**	**12.6%**
Antigen				
HEV Antigen	(9) **0.7%**	(3) **2.9%**	12	**0.8%**

Demographic Risk Factors Associated with Anti-HEV Antibody IgG Seroprevalence in Humans

A univariate logistic regression model showed that age group, level of education, and region were significant demographic risk factors for HEV IgG seropositivity; *P* = 0.0000, P = 0.0009, and *P* = 0.0000 respectively, Table 5. There was 1.4 times more risk of being seropositive for HEV for each age group from the lowest age group to the highest (OR 1.365; 95% CI 1.252 - 1.488). Anti-HEV IgG seroprevalence increased from 0.0% in the 1-4 years age group to 17.4% in the 60+ years age group. Similarly, there was 1.2 times more risk of being HEV seropositive associated with each level of education from the lowest to the highest. Seroprevalence increased from 1.7% in persons with nursery education to 17.4% in persons with tertiary education. A 1.6 times more risk of HEV IgG positivity was associated with each region in this order; Eastern < Volta < Accra < Central. The risk factors for HEV seroprevalence in humans are shown in Table 5.

In a multivariate logistic regression model age group (*P* = 0.0000) and region (*P* = 0.0082) remained significant predictor of IgG seropositivity along with gender (*P* = 0.0433). Males were 1.4 times more likely to be seropositive for HEV than females (OR 1.418; 95% CI 1.011 - 1.991). However, the IgG seroprevalence in males and females was not significantly different (13.3% vs 11.3%; Z =1.173, *P* = 0.242). Age group was

significantly associated with HEV seropositivity; the odds of seropositivity increased from 1.4 times in the 1-4 years age group to 16.9 times in the 60+ years age group. The region of residence as a demographic risk factor significantly predicted HEV seropositivity with the highest risk in Central Region (OR 6.1), followed by the Greater Accra Region (OR 3.9) and the Volta Region (OR 2.5) with the lowest in Eastern Region (OR 1.7). Other demographic factors such as level of education, type of community, and population group did not show significant association with HEV seroprevalence.

Table 5
Logistic Regression of Demographic Risk factors for HEV (IgG) Infection in Humans

Univariate Logistic Regression								
Variable	**Coeff**	**StdErr**	P **Value**	**OR**	**(95% CI)**		**Overall Model Fit**	
					Low	**High**	x^2	P
Gender	0.1888	0.1612	0.2415	1.2078	0.8806	1.6567	1.3635	0.2429
Age Group	0.3110	0.0440	0.0000	1.3648	1.2521	1.4876	61.5476	0.0000
Level of Education	0.1648	0.0495	0.0009	1.1792	1.0701	1.2994	10.9089	0.0010
Category	0.2889	0.2841	0.3092	1.3350	0.7649	2.3300	0.9773	0.3229
Community Type	-0.1038	0.0693	0.1343	0.9014	0.7869	1.0326	2.2273	0.1356
Region	0.4786	0.0768	0.0000	1.6137	1.3883	1.8758	41.5532	0.0000
Multivariate Logistic Regression								
Variable	**Coeff**	**StdErr**	P **Value**	**OR**	**(95% CI)**		**Overall Model Fit**	
					Low	**High**	x^2	P
Gender	0.3496	0.1730	0.0433	1.4185	1.0106	1.9912		
Age Group	0.3144	0.0493	0.0000	1.3694	1.2433	1.5083		
Level of Education	0.0454	0.0570	0.4254	1.0465	0.9359	1.1702	104.166	0.0000
Category	0.2857	0.2992	0.3397	1.3307	0.7403	2.3919		
Community Type	-0.0361	0.0733	0.6225	0.9645	0.8354	1.1136		
Region	0.4506	0.0777	0.0000	1.5693	1.3477	1.8272		

HEV Seroprevalence in Pigs

A total of 474 pigs were sampled: 202 from the Greater Accra Region, 90 from Volta Region, 94 from Central Region, and 88 from Eastern Region. Free-range pigs were sampled from all four regions, whereas confined pigs were only available for sampling in the Greater Accra and Volta Regions. The sampled regions, number of pigs, and HEV seroprevalence as well as their *p* values are displayed in Table 6.

An overall HEV seroprevalence (HEV-Ab) of 62.4% and active infection prevalence (HEV-Ag) of 5.5% were recorded in the pigs. Seroprevalences amongst the free-range pigs from the various regions were significantly

different; x^2 = 113.4; *p* = 0.000. A significantly higher seroprevalence was demonstrated in pigs in the Greater Accra Region (85.7%) and the Volta Region (88.3%) than in the Eastern Region (18.2%) and the Central Region (51.1%); P < 0.00001 amongst free-range pigs. Also, seroprevalence in the Central Region was significantly higher than in the Volta Region (51.1% vs 18.2%; Z = 4.643, *P* < 0.00001). Amongst confined pigs, the seroprevalence was also significantly higher in pigs in Accra (89.4%) than in pigs in the Volta Region (6.7%); Z = 8.791, *p* < 0.00001. The regional distribution of HEV seroprevalence in pigs is displayed in Figure 3. Amongst the regions, seroprevalence between confined and free-range pigs was significantly different only in the Volta Region; 6.7% vs 88.3%; Z = 7.492; *p* < 0.00001, Table 6.

HEV antigen prevalence amongst both confine and free-range pigs ranged from 1.1% in the Eastern Region to 9.6% in the Central Region.

Table 6
HEV Seroprevalence in Pigs

Region	Husbandry	Number	Ab Seroprevalence	*P* Value	Ag Prevalence	*P* Value
Accra	Confined	104	(93) 89.4%	0.424	(9) 8.7%	0.093
	Free-Range	98	(84) 85.7%		(3) 3.1%	
Volta	Confined	30	(2) 6.7%	< 0.00001	0	0.297
	Free-Range	60	(53) 88.3%		(4) 6.7%	
Central	Confined	0	0	-	-	
	Free-Range	94	(48) 51.1%		(9) 9.6%	-
Eastern	Confined	0	0	-	-	
	Free-range	88	(16) 18.2%		(1) 1.1%	-
Total	**-**	**474**	**(296) 62.4%**		**(26) 5.5%**	

Figure 3: Regional Distribution of HEV Seroprevalence in Humans and Pigs

Risk Factors of HEV-Ab Seroprevalence in Pigs

HEV-Ab seroprevalence showed a significant association with husbandry and region for pigs in Accra and Volta region in both univariate and multivariate logistic regression models, Table 7. A significantly higher seroprevalence was found in free-range pigs compared with confined pigs (86.7% vs 70.9%); Z = 3.333; *p* = 0.0086. The odds of HEV seropositivity amongst free-range pigs was seven-folds higher than in confined pigs in the multivariate model (*p* = 0.0000). Also, the odds of HEV seropositivity was about 5times higher for pigs in Accra than pigs in the Volta Region (*p* = 0.0000).

Husbandry and region, however, were not significant predictors of HEV-Ag prevalence in both univariate and multivariate logistic regression models. Table 7 shows the univariate and multivariate logistic regression of risk factors associated with HEV seroprevalence in pigs.

Table 7
HEV Seroprevalence and Logistic Regression of Risk Factors in Pigs

		Univariate				Multivariate			
Husbandry (Accra and Volta)	**Anti-HEV Ab**	**OR**	**Low**	**High**	P **Value**	**OR**	**Low**	**High**	P **Value**
Confined	95 (70.9%)								
Free-range	137 (86.7%)	2.6782	1.4823	4.8388	0.0011	7.0506	3.5580	13.9716	0.0000
Region									
Accra	177 (87.6%)								
Volta	55 (61.1%)	4.5055	2.4831	8.1750	0.0000	4.6015	2.3003	9.2048	0.0000
Husbandry (Accra and Volta)	**HEV-Ag**	**OR**	**Low**	**High**	P **Value**	**OR**	**Low**	**High**	P **Value**
Confined	9 (6.7%)								
Free-range	7 (4.4%)	0.6439	0.2332	1.7780	0.3956	0.6663	0.2380	1.8653	0.4396
Region									
Accra	12 (9.0%)								
Volta	4 (2.5%))	1.3579	0.4257	4.3312	0.6052	1.2605	0.3888	4.0867	0.6997

Discussion

HEV Seroprevalence in Humans

In this study, HEV exposure, active infection, and risk factors for human and pig infection were explored to determine the burden of HEV and the contribution of zoonotic and WASH-related transmission routes to the disease in Ghana.

The results show an overall HEV seroprevalence of 12.6% and a prevalence of 0.8% in humans in Ghana. This level of HEV prevalence indicates endemic circulation of HEV in the study communities and Ghana at large which warrants action. There was no significant difference in seroprevalence between pig farmers and the general public in this study, as was found in previous studies: 38.1% in pig handlers (14), However, the

seroprevalence of 12.4% was higher than the 4.6% previously reported by Meldal, Sarkodie (10) in Ghana. The difference in seroprevalence between the two studies could be because this study covered a much broader population, age range, and regions in Ghana than the other. The effect of differences in time and diagnostics assays used could also be significant factors. Also, the overall exposure prevalence in community members in this study was much lower than the seroprevalence of 47.9% recorded in healthy people in Nigeria (15). The difference in seroprevalence between these two studies may be reflective of variation in sample size and age range of research participants. Moreover, differences in sanitation practices, socioeconomic status, and level of exposure of participants to risk factors of HEV infection could be possible reasons. In Asia, an HEV seroprevalence of 11% each was reported in healthy people in Taiwan (16) and Mongolia (17) which are very close to the seroprevalence in this study.

Seroprevalence of 15.2% was recorded for pig farmers in this study which is in between the previously reported 0% IgG and the 38.1% IgM by Adjei, Aviyase (14) in pig handlers in Ghana. It is unclear why Adjei did not record any anti-HEV IgG antibody but a high anti-HEV IgM antibody. Exposure of an HEV naïve population to infections for the first time could be the reason. As most of the participants had been working on the pig farm for less than a year and HEV infection was significantly associated with persons who had been working on the farm for less than one year.

Compared with other serosurveys in Africa, seroprevalence in pig farmers in this study was considerably lower than the 58.3% and 76% recorded in animal handlers in Nigeria and butchers in Burkina Faso respectively (15, 18). However, it is comparable with the seroprevalence of 14.1% reported in pig butchers in Madagascar (19). The dissimilarities in seroprevalence between occupationally at-risk persons in these studies may be influenced by the level of exposure of pig farmers to HEV-infected pigs and the level of prevalence of other predisposing factors for HEV transmission.

Ongoing HEV infection in this study seems to be low, as revealed by the overall active infection prevalence of 0.8% which is supported by the very low recent infection (IgM) of 0.5%. This could be characteristic of a low level of HEV transmission rate.

Demographic Risk Factors Associated with HEV (IgG) Seroprevalence in Humans

Demographic factors were explored in both the univariate and multivariate models to determine risk factors associated with HEV seropositivity. While age group, level of education, and region were associated with HEV seropositivity in the univariate analysis, gender, age group and region were significant predictors of HEV in the multivariate analysis.

Age group significantly predicted HEV IgG seropositivity; the trend of increasing HEV seroprevalence with increasing age in this study is consistent with many reports of HEV studies across the world; in India (20), Kenya (21), CAR (22), Indonesia (23), Taiwan (16), Spain (24), USA (25), and Germany (26). Since anti-HEV IgG is a marker of exposure and persists for long periods (up to 14 years) (27), the prevalence is bound to be higher in older than in younger individuals. Thus, seroprevalence increases with age as a consequence of accumulated infections over time.

While the risk of HEV infection was associated with increasing years/levels of education this observation is probably influenced by age since higher education level correlates with increasing age. This can be clearly inferred from the similarity in seroprevalence amongst the tertiary and none educated groups. The seroprevalence in persons without education was similar to those who had tertiary education, 17.4% vs 16.7%. All persons who were positive for HEV seroprevalence in the none educated category were adults aged 20years and above; education level appears to be a confounder.

Gender was significantly associated with HEV seropositivity in the multivariate analysis with a higher risk in males than in females. However, the odds ratio was not very high (1.4) and the difference in seroprevalence was not statistically significant, Z = 1.173; p = 0.242.

HEV IgG seroprevalence was significantly associated with the region of residence. The study communities in the Central and Greater Accra regions where seroprevalences were higher were more urban than communities in the Volta and Eastern region where seroprevalences were low. Many studies have found higher seroprevalence in rural than in urban areas (12, 15, 28, 29). In this study, however, it seems to be associated with increasing urbanisation as reported in studies in Gabon (30) and India (31). Overcrowding in urban areas puts pressure on sanitation and water facilities, creating unhygienic conditions which promote WASH-related HEV transmission. Such conditions are more prevalent in the Greater Accra and Central region than in the Eastern and Volta region.

HEV Seroprevalence in Pigs

Several serosurveys from many countries across the world have shown high HEV seroprevalence in domestic pigs with increased risk of infection in humans through direct contact and consumption of undercooked infected pork products (32). Unfortunately, studies investigating HEV seroprevalence in domestic pigs and the level of risk of zoonotic transmission from pigs to humans are lacking in Ghana. To the best of our knowledge, this is the first significant study and the third report of HEV seroprevalence in pigs in Ghana.

The high seroprevalence of 62.4% demonstrates clearly that HEV is endemic in pig populations in Ghana. The widespread practice of free-range pig husbandry in major pig rearing communities in Ghana exposes pigs to the risk of environmental HEV infections. Also, the practice of introducing free-range breeding stock to intensive farms introduces the disease to these systems.

Only a few seroprevalence studies of pigs are available in Ghana for comparison with the results from this study. The results support the high seroprevalence of 85% in our previous study in pigs from the Greater Accra and Upper East regions of Ghana. These results altogether enable us to gauge the national HEV seroprevalence as well as the regional distribution of HEV seroprevalence in pigs in Ghana. The seroprevalence of 62.4% in this study is lower than the 85% found in our previous serosurvey (13), and the 77.5% reported by El-Duah, Dei (33) in the Ashanti region of Ghana. However, the seroprevalence of 87.6% in this study and the 80% in our previous study both in the Greater Accra region are comparable.

When compared with HEV seroprevalence values in pigs from other African countries, our findings were comparable with results in Madagascar (19) and Nigeria (34).

HEV antigen is a marker of ongoing infection and was relatively low in pigs in Ghana at 5.5% compared with the 64.2% seropositive for anti-HEV antibodies. Other studies of HEV prevalence have used PCR on liver samples and so cannot be compared to this study which used antigen ELISA on serum samples. These studies recorded HEV prevalence of 0.9 – 10.1% (19, 33, 35, 36).

Conclusion

This study explored the seroprevalence of HEV and risk factors for infection in humans and pigs in Ghana. The results show that HEV infection is endemic in both occupationally at-risk persons and the general population in Ghana. HEV exposure prevalence (12.6%) was much higher than active infections (0.8%).

The results also show that HEV is endemic in domestic pig populations which serve as a HEV reservoir. The pervasive free-range pig production system predisposes roaming pigs to environmental HEV. Likewise, scavenging pigs can contaminate the environment by shedding the virus in faeces and urine. It is therefore important that authorities enforce the laws proscribing free-range pig production to prevent this and reduce the risk of HEV infection in pigs. Overall, this study helps define the burden of HEV in human and pig populations in Ghana. Although active infection seems to be minimal, the seroprevalence is a cause for concern.

Abbreviations

Ab: Antibody; CI: Confidence Interval; COVID-19: Corona Virus Disease; ELISA: Enzyme-Linked Immunosorbent Assay; HEV: Hepatitis E Virus; IgG: Immunoglobulin G; IgM: Immunoglobulin M; OD: Open Defaecation; OR: Odds Ratio; PCR: Polymerase Chain Reaction; RDT: Rapid Immunochromatographic Diagnostic; RNA: Ribonucleic acid; SPSS: Statistical Package for Social Sciences; WASH: Water, Sanitation, and Hygiene.

Declarations

Ethics approval and consent to participate

Ethical approval for the entire study was sought and received from the Ethics Committee of the College of Basic and Applied Sciences, University of Ghana (ECBAS 003/19-20) and the Ghana Health Services Ethical Review Committee (GHS-ERC013/10/19). Informed consent was acquired from all research participants. For minors and illiterate participants, informed consent was obtained from their parents/legal guardians, and pigs were sampled under the informed consent and supervision of their legal owners. All the activities carried out in the research were done following the guidelines and regulations of the Ghana Health Service.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Conceptualisation: HB, AOM, SCW & LB; Data collection and analysis: HB; Manuscript preparation: HB; Manuscript review and editing: HB, AOM, SCW & LB

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Figures

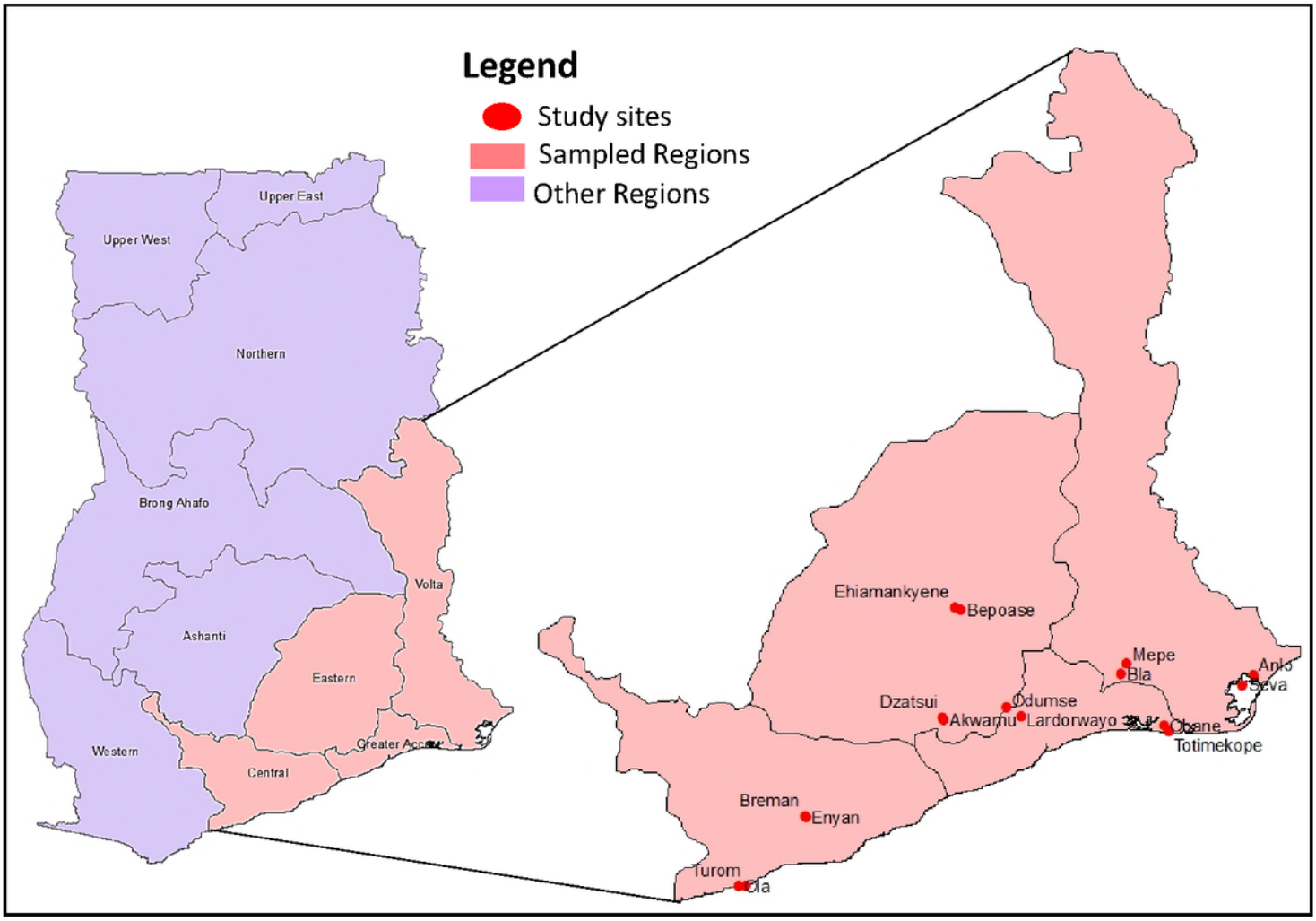

Figure 1

Study Sites

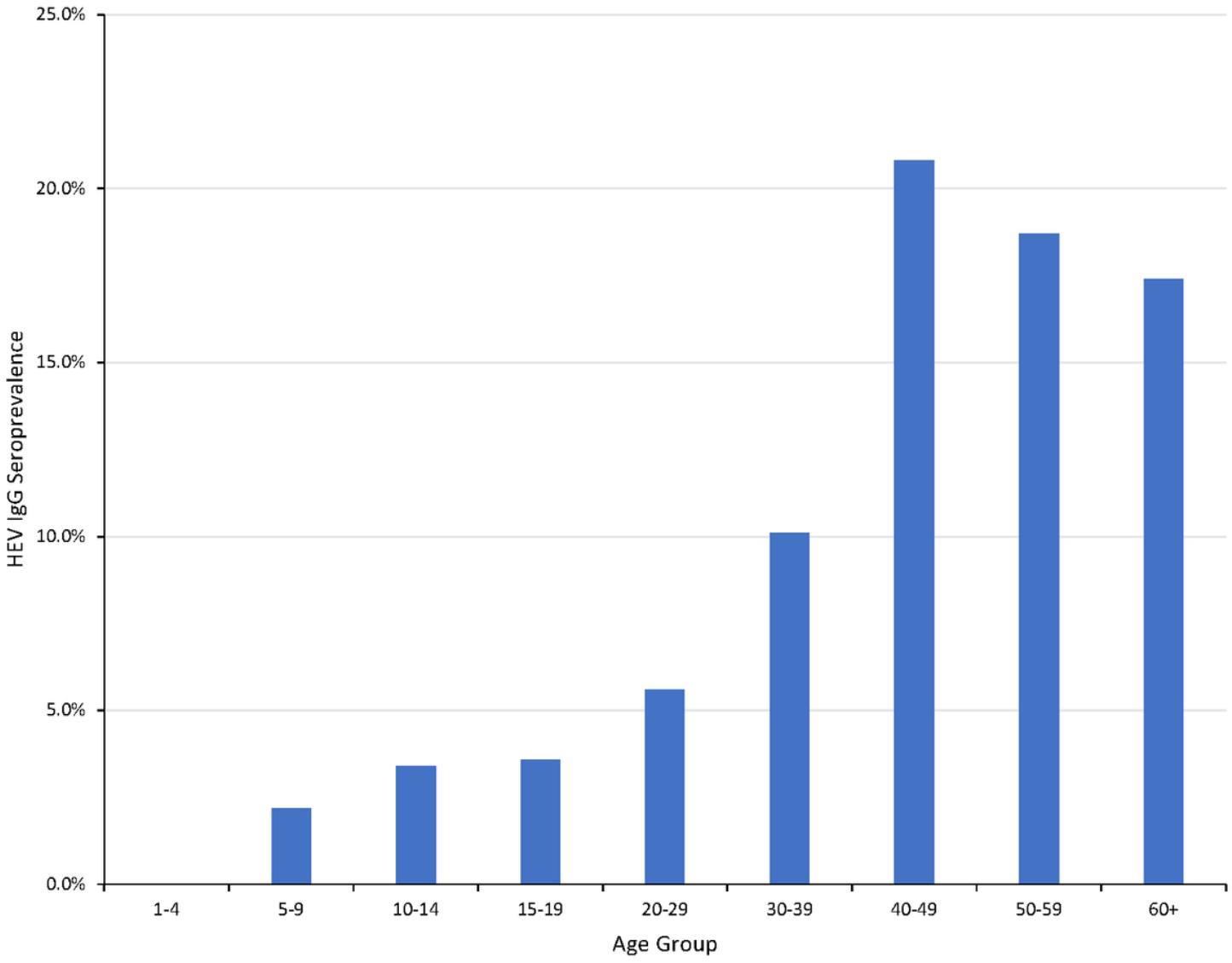

Figure 2

HEV IgG Seroprevalence Amongst Age Groups

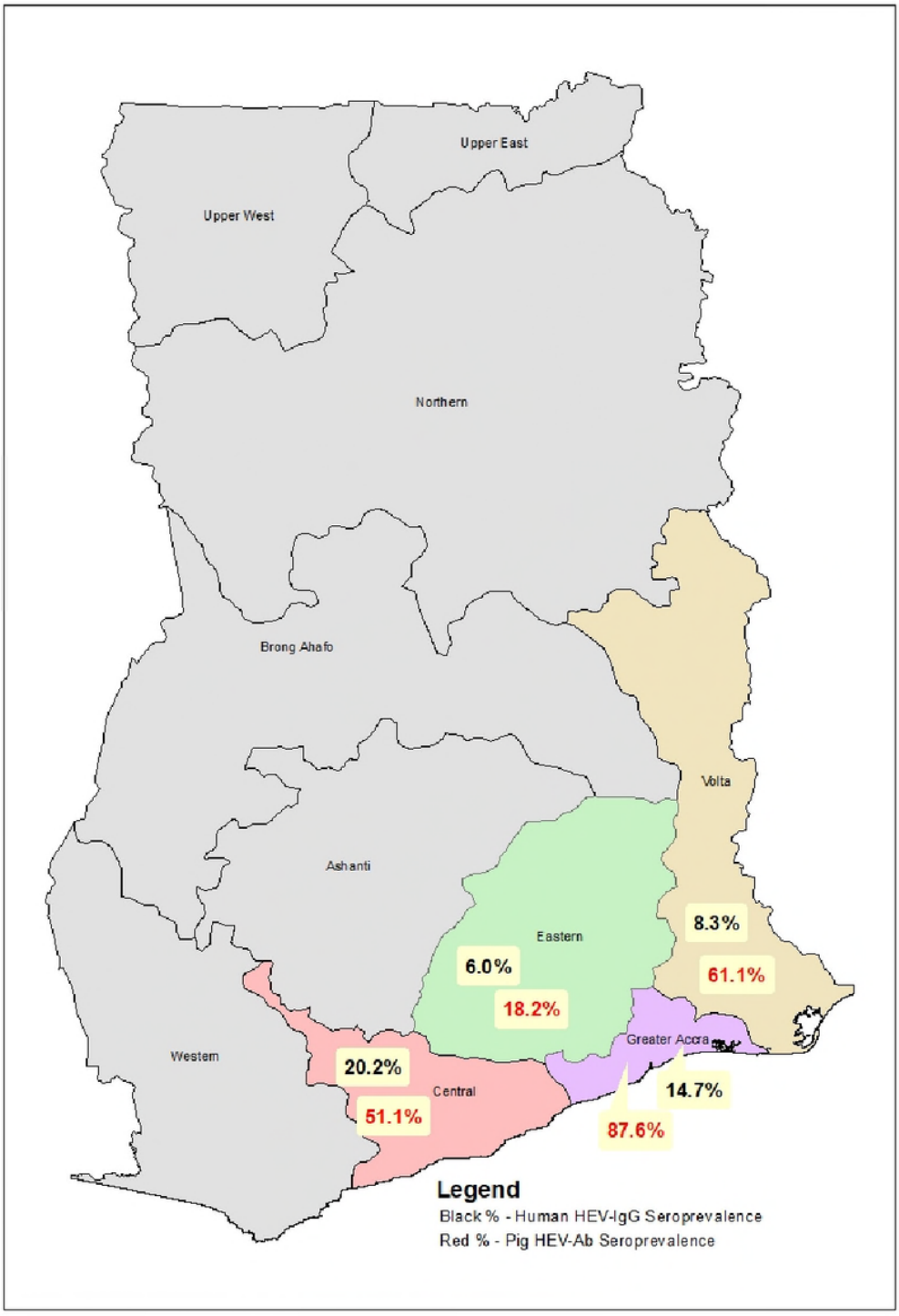

Figure 3

Regional Distribution of HEV Seroprevalence in Humans and Pigs