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Hepatitis E virus seroprevalence and associated risk factors in pregnant women attending antenatal consultations in Senegal

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Abstract: In West Africa, research on the hepatitis E virus (HEV) is barely covered despite the recorded outbreaks. The still low level of access to safe water and adequate sanitation is one of the main factors of HEV spread in developing countries. HEV infection induces acute or subclinical liver diseases with a mortality rate ranging from 0.5 to 4%. The mortality rate is more alarming (15 to 25%) among pregnant women, especially in the last trimester of pregnancy. Here, we conducted a multicentric socio-demographic and seroepidemiological survey of HEV in Senegal among pregnant women. A total of 1,227 consenting participants attending antenatal clinics responded to our questionnaire. Plasma samples were collected and tested for anti-HEV IgM and IgG by using the WANTAI HEV-IgM and IgG ELISA assay. HEV global seroprevalence was 7.9% with 0.5% and 7.4% for HEV IgM and HEV IgG, respectively. One participant's sample was IgM/IgG positive, while four were declared indeterminate to anti-HEV IgM as per the manufacturer's instructions. From one locality to another, the seroprevalence of HEV antibodies varied from 0 to 1% for HEV IgM and from 1.5 to 10.5% for HEV IgG. The data also showed that seroprevalence varied significantly by marital status ($p<0.0001$), by the regularity of income ($p=0.0043$) and by access to sanitation services ($p=0.0006$). These data could serve as a basis to setup national prevention strategies focused on socio-cultural, environmental and behavioral aspects for a better management of HEV infection in Senegal.

Keywords: Hepatitis E; Associated risk factors; Pregnant women; Environment; Prevention; Senegal

1. Introduction

Hepatitis E is geographically a very heterogeneously distributed disease, which is present in both developed and developing countries. Transmission is essentially by the

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faecal-oral route, causing generally asymptomatic infection [1-3]. To some extent, cases of mother-to-child transmission have also been reported [4-7], zoonotic transmission linked to ingestion of raw shellfish and undercooked pork [8-13], ingestion of fruits and vegetables contaminated by irrigation water [14, 15]. More generally, through contaminated water and crops, the environmental aspects seem to be a significant vector for the spread of HEV in developing countries [1, 16, 17].

Most infections are self-limited acute hepatitis in immunocompetent subjects. However, it can become severe with very high mortality rates in specific population groups, including pregnant women and immunosuppressed people [18-22]. Indeed, the mortality rate in the general population is around 0.5 to 4%, while pregnant women are likely to develop complicated forms of the disease that can lead to mortality rates ranging from 20 to 25% [4, 18, 19, 23]. High neonatal mortality and morbidity have also been reported [6, 7, 18, 24]. Therefore, HEV infection is considered as a promoting factor that can lead to hepatocellular carcinoma [23]. The WHO estimates that 20 million HEV infections and more than 3.3 million acute cases of hepatitis E are detected per year, with an estimated death of 56,600 cases [25].

In Senegal, a localized epidemic was declared in 2014 in the gold-bearing area of Kédougou located in the south-eastern region. Local health authorities reported nineteen deaths and that almost all of the infected individuals came from traditional gold panning sites; which concentrate a community of several workers from African countries, especially those bordering [26]. Since then, a very little epidemiological data is available at the national level. It should be noted that the diagnosis of hepatitis E is not done routinely, even less in pregnant women with symptoms that would suggest a potential infection. Furthermore, beyond the health, economic and environmental concerns, the issue of hepatitis E in West Africa is poorly covered, as evidenced by the very limited number of scientific studies [27, 28] . From a strategic point of view, obtaining new epidemiological data is necessary and will make it possible to fill this gap. For this, the main objective was to determine the seroprevalence and associated risk factors with hepatitis E virus infection in pregnant women attending antenatal consultations in Senegal.

2. Materials and Methods

Study sites, sampling and data collection

This prospective and multi-site study is part of a research program on the epidemiology of hepatitis E leaded by the GRBA-BE (Groupe de Recherche Biotechnologies Appliquées et Bioprocédés Environnementaux) / JEAI EPIVHE (Jeune Équipe Associée à l'IRD EPIVHE) and his collaborators. Except for Dakar, the capital city of Senegal which housed two sites, all the three other regions had only one (**Figure 1**). Regardless of geographic region, all inclusion sites are located in urban areas with relatively good attendance according to antenatal care providers. At the study design, the sampling plan forecasted around 200 pregnant women per site, or 1,000 participants over the enrolment period. In fact, according to the 2018 Demographic and Health Survey report, the coverage of prenatal care is estimated at 98%. Thus, almost all women aged 15 – 49 who delivered a child received prenatal care from a qualified provider, including midwives (91%). Six out of ten women made at least four prenatal visits (59%) and in 64% of cases, the first visit took place before the fourth month of pregnancy [29, 30]. However, disparities were mentioned according to place of residence, 71% in urban areas against 50% in rural areas. This rate is higher in urban areas 78% against 55% in rural areas [29].

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Figure 1. Map of Senegal with indication of the geographical sites of the study

The inclusion criteria were: pregnant woman from four weeks of amenorrhea confirmed by a pregnancy test and/or ultrasound, aged 18 or over, resident for at least 6 months in the targeted localities and consenting to participate in the study. Those with acute alcoholic hepatitis or drug-induced hepatitis and/or non-consenting were not included. On all the sites, a consecutive and non-redundant recruitment of participants was carried out over the period from March to July 2021. Socio-demographic and other relevant information to the study were collected with standardized survey forms and through individual and anonymous interviews. This consisted of collecting the address of the place of residence including trips over the past 12 months, access to sanitation and safe water supply services, individual and community hygiene (systematic hand washing after using the toilet, disinfection and rinsing of fruits and vegetables before consumption), age, education level, regular income linked to a professional activity and marital status. The data collected was entered directly into an excel file.

As the study was carried out in the context of COVID-19 pandemic, in accordance with the recommendations of the local health authorities, our field teams have taken all the necessary measures to prevent and fight against the spread of the SARS-CoV-2 infection.

For each participant, a whole blood sample was taken on EDTA tubes for laboratory analysis. Lymphocyte separation was performed within two hours after collection and the plasma was frozen at -80°C or stored at -20°C on site until processing. An individual identification code per site and per patient was assigned to each sample. A written and signed informed consent was obtained from each participant before the interview and sample collection. Ethical and administrative approvals were also obtained from the Senegalese National Ethics Committee for Health Research (N°000130/MSA/CNRES/Sec) and the Ministry of Public Health and Social Action (N°00000582/MSAS/DPRS/DR).

Anti-HEV antibodies detection

To detect anti-HEV IgM and IgG, we used Enzyme Linked Immunosorbent Assay (ELISA) from Wantai Biological Pharmacy Enterprise, Beijing, China (Wantai HEV-IgM ELISA and Wantai HEV-IgG ELISA) as per manufacturer's instructions. The specific HEV IgM and IgG antibodies was detected by adding recombinant HEV ORF2 antigens conjugated to the enzyme horseradish peroxidase (HRP-conjugate). The reported sensitivities and specificities are in the range of 97.10% - 98.40% for HEV IgM antibodies and 99.08% - 99.90% for HEV IgG antibodies respectively. In addition, the HEV-IgM represents the best marker for detecting the acute HEV infection, where RT-PCR cannot be performed [31]. Optical density was read using the MICRO READ 1000 ELISA Plate Analyser (Global

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Diagnostics B, BELGIUM). The tests were declared to be negative if IgM or the IgG index was <1, positive if the index was ≥1, and borderline if the index was = 0.9 - 1.1. All samples declared positive in the first tests have been re-tested in accordance with the manufacturer's instructions.

Statistical analyzes

Statistical analyzes were performed with JMP® Pro Version 15.0.0 software (SAS Institute Inc., Cary, NC, 1989–2021). To assess the sociodemographic and environmental factors associated with exposure to HEV infection, we performed bivariate analyses. With regard to the data of binary variables whose frequencies are less than 5, chi-square or Fischer's Exact tests were carried out. Was considered statistically significant, p-values < 0.05.

3. Results

A total of 1,227 pregnant women attending antenatal consultations were recruited through five health facilities across four different geographic regions. In Dakar, the recruitment was carried out at the Obstetrical Gynecology Center of the Aristid Le Dantec hospital (n=50) and at the Gaspard Kamara Health Center (n=116). At the other sites, we recruited 400, 397 and 264 participants respectively at the Regional Hospital Center of Saint-Louis, the Health District of Kédougou and the NEMA Health Center of Ziguinchor. The median age was 25 years [age range 18 – 50 years]. The distribution of age groups shows a greater representation of the [18 – 23 years] with 43.03%; [24 – 29 years] for 29.10% followed by the [30 – 35 years] with 29.10%. Participants aged 36 and above represented only 9.70%. Despite a relatively low number of participants in Dakar and Ziguinchor, the participation rate deemed very satisfactory at 122.7%. The overall and site-specific results of the survey relating to hand hygiene, the disinfection of unpackaged fresh fruits and vegetables before consumption and access to safe drinking water and sanitation services, educational level, marital status, regular income are summarized in Table 01.

In this study, 31.7% of the participants were without instructions, with higher rate observed in the locality of Kédougou (58.7%). Moreover, only 9% of them had reached a higher level of education. Unlike the other localities, 25.9% of the participants in the city of Dakar had reached a higher level of education. It should be noted that 92% of the participants in this study declared that they were married and only 18.7% had regular income (salaried or self-employed workers). On this last point, the highest rate was observed in Dakar (45.8%) which contrasts with that noted in Saint-Louis (11.8%).

Overall, 78.4% of pregnant women reported having access to safe drinking water. However, a remarkable low rate was noted in Ziguinchor (37.1%). Excepted in this locality, where 42.8% of participants declared that they did not have access to sanitation services, especially adequate toilets. The level of access for women residing in other localities was relatively acceptable and varied from 91.4% to 100%.

Regarding hand hygiene, overall, more than 90% of participants declared that they systematically washed their hands, especially after using the toilet. In addition, 71.3%, 87.7% and 100% of the participants respectively from Saint-Louis, Kédougou and Dakar declared that they proceeded to the decontamination of food matrices (fruits and vegetables), particularly those not wrapped and eaten raw. However, among respondents from Ziguinchor, almost 30% said they did not systematically decontaminate fruits and vegetables eaten raw (**Table 1**).

Table 1. Socio-demographic characteristics of patients and HEV markers

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Variable	Study sites									
	Saint-Louis (n=400)		Dakar (n=166)		Kédougou (n=397)		Ziguinchor (n=264)		All sites (n=1227)	
	Frequency (%)	Median	Frequency (%)	Median	Frequency (%)	Median	Frequency (%)	Median	Frequency (%)	Median
Range of age										
18 - 23	112 (28)	20	49 (29.5)	21	256 (64.5)	19	111 (42)	20	528 (43)	20
24 - 29	136 (34)	26	44 (26.5)	27	90 (22.7)	26	87 (33)	26	357 (29.1)	26
30 - 35	101 (25.3)	32	48 (28.9)	32.5	29 (7.3)	30	45 (17)	32	223 (18.2)	32
36 and above	51 (12.8)	36	25 (15.1)	37	22 (5.5)	38	21 (8)	39	119 (9.7)	38
Educational level										
None	62 (15.5)	.	25 (15.1)	.	233 (58.7)	.	69 (26.1)	.	389 (31.7)	.
Primary	170 (42.5)	.	46 (27.7)	.	82 (20.7)	.	77 (29.2)	.	375 (30.6)	.
Secondary	122 (30.5)	.	52 (31.3)	.	75 (18.9)	.	104 (39.4)	.	353 (28.8)	.
Higher	46 (11.5)	.	43 (25.9)	.	7 (1.8)	.	14 (5.3)	.	110 (9)	.
Marital status										
unspecified	11 (2.8)	.	0 (0)	.	16 (4.0)	.	4 (1.5)	.	31 (2.5)	.
Single	8 (2)	.	6 (3.6)	.	12 (3)	.	39 (14.8)	.	65 (5.2)	.
Maried	381 (95.3)	.	160 (96.4)	.	369 (93)	.	220 (83.3)	.	1130 (92)	.
Divorced or widowed	0 (0)	.	0 (0)	.	0 (0)	.	1 (0.4)	.	1 (0.08)	.
Regular income (paid work)										
unspecified	6 (1.5)	.	1 (0.6)	.	36 (9.1)	.	4 (1.5)	.	47 (3.8)	.
Yes	47 (11.8)	.	76 (45.8)	.	63 (15.9)	.	43 (16.3)	.	229 (18.7)	.
No	347 (86.8)	.	89 (53.6)	.	298 (75.1)	.	217 (82.2)	.	951 (77.5)	.
Access to safe water supply services										
unspecified	2 (0.5)	.	0 (0)	.	24 (6)	.	5 (1.9)	.	31 (2.5)	.
Occasionally	0 (0)	.	0 (0)	.	0 (0)	.	10 (3.8)	.	10 (0.8)	.
Yes	387 (96.8)	.	166 (100)	.	311 (78.3)	.	98 (37.1)	.	962 (78.4)	.
No	11 (2.8)	.	0 (0)	.	62 (15.6)	.	151 (57.2)	.	224 (18.3)	.
Access to sanitation services										
unspecified	1 (0.3)	.	0 (0)	.	12 (3)	.	5 (1.9)	.	18 (1.5)	.
Occasionally	0 (0)	.	0 (0)	.	0 (0)	.	5 (1.9)	.	5 (0.4)	.
Yes	388 (97)	.	166 (100)	.	363 (91.4)	.	141 (53.4)	.	1058 (86.2)	.
No	11 (2.8)	.	0 (0)	.	22 (5.5)	.	113 (42.8)	.	146 (11.9)	.
Disinfection of food products that are not wrapped and handled by hand (examples: Vegetables. fruits. etc.)										
unspecified	1 (0.3)	.	0 (0)	.	28 (7.1)	.	3 (1.1)	.	32 (2.6)	.
Occasionally	59 (14.8)	.	0 (0)	.	0 (0)	.	1 (0.4)	.	60 (4.9)	.
Yes	285 (71.3)	.	166 (100)	.	348 (87.7)	.	182 (68.9)	.	981 (79.9)	.
No	55 (13.8)	.	0	.	21 (5.3)	.	78 (29.5)	.	154 (12.5)	.
Systematic hand washing										
unspecified	0 (0)	.	0 (0)	.	16 (4)	.	4 (1.5)	.	20 (1.6)	.
Occasionally	0 (0)	.	0 (0)	.	0 (0)	.	6 (2.3)	.	6 (0.5)	.
Yes	392 (98)	.	166 (100)	.	350 (88.2)	.	206 (78)	.	1114 (90.8)	.
No	8 (2)	.	0 (0)	.	31 (7.8)	.	48 (18.2)	.	87 (7.1)	.
HEV markers seroprevalance										
HEV IgM Positive	2 (0.5)	.	0 (0)	.	4 (1)	.	0 (0)	.	6 (0.5)	.
HEV IgG Positive	42 (10.5)	.	7 (4.2)	.	38 (9.6)	.	4 (1.5)	.	91 (7.4)	.

The seroprevalence of HEV was 7.9% with 0.5% (n=6) and 7.4% (n=91) of participants were positive for IgM and IgG antibodies to HEV, respectively. Only one sample was IgM/IgG positive. A total of 4 samples were declared indeterminate to anti-HEV IgM despite having been re-tested according to the detection kit manufacturer's instructions. The observed prevalence rate of HEV varied from one geographic region to another. For anti-HEV IgM, no positive sample was identified in Dakar and Ziguinchor while it was 0.5 and 1% for Saint-Louis and Kédougou, respectively. The IgG seroprevalence was higher in the regions of Saint-Louis and Kédougou with 10.5% and 9.6% respectively, while in Dakar and Ziguinchor, it was 4.2 and 1.5%. Between sites, the differences observed were statistically significant only for the IgG seroprevalence ($p = 0.0133$) (Table 2).

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Table 2. Variability of HEV IgM and IgG serological markers according to age groups and localities

	IgM HEV		IgG HEV	
[Age groups] (%)	**n (%)**	**p-value**	**n (%)**	**p-value**
[18-23], n=528 (43)	1 (0.18)		28 (5.30)	
[24-29], n=357 (29.1)	2 (0.56)		26 (7.28)	
[30-35], n=223 (18.2)	2 (0.89)	**0.0372**	19 (8.52)	**0.0048**
≥36 years, n=119 (9.7)	1 (0.84)		18 (15.12)	
Total (n=1227)	6 (0.48)		91 (7.41)	
Location (Frequency)				
Saint-Louis (n=400)	2 (0.50)		42 (10.50)	
Dakar (n=166)	0 (0.00)		7 (4.21)	
Ziguinchor (n=264)	0 (0.00)	0.3293	4 (1.51)	**0.0133**
Kédougou (n=397)	4 (1.00)		38 (9.57)	
Total (n=1227)	6 (0.48)		91 (7.41)	

Furthermore, analysis of the aggregated data suggests a link between the age of the participants and exposition to HEV, (p-values were 0.0372 and 0.0048 for IgM and IgG respectively). With regard to age groups, this association is more remarkable among young adults [18 – 35 years], where more than 80% of infections were observed (Table 02). In addition, the marital status, the economic situation (regular income), and access to sanitation services (adequate toilets, appropriate wastewater disposal system), are significantly associated with exposure to HEV (**Table 3**).

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Table 3. Prevalance of HEV IgM and IgG markers and potential associated factors

		IgM HEV			IgG HEV		
Educational level	**Frequency (%)**	**n**	**Prevalence**	**p-value**	**n**	**Prevalence**	**p-value**
None	389 (31.7)	4	1.03	0.4655	32	8.23	0.4017
Primary	375 (30.6)	1	0.27		30	8	
Secondary	353 (28.8)	1	0.28		25	7.08	
Higher	110 (9)	0	0		4	3.64	
Marital status							
unspecified	31 (2.5)	0	0	0.9999	2	6.45	***< 0.0001***
Single	65 (5.2)	0	0		7	10.77	
Maried	1130 (92)	6	0.53		82	7.26	
Divorced or widowed	1 (0.08)	0	0		0	0	
Regular income (paid work)							
unspecified	47 (3.8)	0	0	1	1	2.13	**0.0043**
Yes	229 (18.7)	1	0.44		12	5.24	
No	951 (77.5)	5	0.53		78	8.2	
Access to the potable water supply service							
unspecified	31 (2.5)	1	3.23	0.1958	2	6.45	0.4001
Occasionally	10 (0.8)	0	0		0	0	
Yes	962 (78.4)	4	0.42		78	8.11	
No	224 (18.3)	1	0.45		11	4.91	
Access to sanitation services (Adequate toilets, appropriate wastewater disposal system)							
unspecified	18 (1.5)	0	0	1	2	11.11	**0.0006**
Occasionally	5 (0.4)	0	0		0	0	
Yes	1058 (86.2)	6	0.57		87	8.22	
No	146 (11.9)	0	0		2	1.37	
Disinfection of food products that are not wrapped and hand-handled (examples: Vegetables, fruits, etc.)							
unspecified	32 (2.6)	0	0	1	2	6.25	0.5984
Occasionally	60 (4.9)	0	0		6	10	
Yes	981 (79.9)	6	0.61		75	7.65	
No	154 (12.5)	0	0		8	5.19	
Systematic hand washing							
unspecified	20 (1.6)	0	0	0.4406	2	10	0.1950
Occasionally	6 (0.5)	0	0		0	0	
Yes	1114 (90.8)	5	0.45		87	7.81	
No	87 (7.1)	1	1.15		2	2.3	

4. Discussion

This study aimed to document the seroprevalence of the hepatitis E virus in pregnant women attending antenatal consultations in five health facilities distributed in four different geographical regions. The HEV seroprevalence was high (7.9%) with 0.4% (n=6) and 7.4% (n=91) of IgM and IgG respectively. Otherwise this global seroprevalence hides disparities between sites (Table 01). Similar prevalence has been reported in other studies conducted in pregnant woman especially in the 3rd trimester in Nigeria [32], among the

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HIV-1-positive pregnant women in central Africa [22] . Furthermore, our results differ from those of a multi-center study of 398 pregnant women in Ghana; where the seroprevalence of HEV was 12.20 and 0.2% respectively for IgG and for IgM [24]. Adjei et al. report higher prevalence of HEV IgM (64.40%) and HEV IgG (35.60); with positivity mainly observed in young adults [20 - 25 years] [33]. In Ethiopia, a study conducted among pregnant women revealed 42.4% and 0.9% positivity to anti-HEV IgM and IgG respectively [34]. HEV infection investigation among patients with acute febrile jaundice in Burkina Faso showed 2.6 % and 18.2% respectively for anti-HEV IgM and IgG among 900 patients [35].

Overall, an inter-site variability was observed both for the serological markers and for the associated sociodemographic factors. (Table 02 and 03). Similar results were also reported in a recent review dealing with viral hepatitis E outbreaks in refugees and internally displaced populations, sub-saharan Africa [17]. It is important to emphasize the differences between sites related to the participation rates and also the completeness or otherwise of the responses related to the questionnaire provided by pregnant women.

Hight rate of participation was obtained, which could be considered as indicative of good attendance at prenatal care structures. Compared to other regions, Dakar recorded lower participation rates (n=166, 41.5%). This situation could be linked to the fact that recruitment had taken place in the midst of a crisis due to the COVID-19 pandemic. Dakar, the capital city, concentrated more cases across the country and therefore its health facilities were rarely visited by the population for fear of contracting COVID-19. This low participation rate coincides with the fact that none of plasma samples tested revealed anti-HEV IgM positive, an indicator of acute infection, while 07 (4.2%) were positive for anti-HEV IgG antibodies indicating previous exposure to HEV. Previous studies carried out in Dakar also revealed rare cases of hepatitis E infections [36-38]. Access to adequate sanitation services and safe drinking water, including the participants' level of education (more than 50% reached the level of education equal to or higher than secondary school), could support the low seroprevalence of HEV observed in Dakar. The participant also declared systematically wash their hands after using the toilets, disinfect raw fruits and vegetables before consumption. In addition, among them, 45.8% of them had a regular income (Table 01). Similar results have been reported in studies conducted in Tunisia and Turkey showing that advanced age (>30), promiscuity, lower educational and income levels and rural residence were correlated with higher anti-HEV IgG positive values [39, 40].

The participation rate was also relatively low in Ziguinchor, where no case of anti-HEV IgM antibody positivity was detected and the seroprevalence of anti-HEV IgG was 1.5%, the lowest rate of all sites. Besides these reasons mentioned above, to try to explain these results; they are contradictory because 82.2% of the participants had no regular income related to work, 57.2% had no access to safe water and 42 8% also did not have access to toilets that met sanitary standards. In addition, 18.2% of pregnant women declared that they did not systematically wash their hands with soapy water after using the toilet and nearly 30% did not systematically decontaminate raw fruits and vegetables before consumption. Thus, this partial result of survey seems contradictory to serological tests obtained in Ziguinchor as for the other remaining sites. The same is true with data from the literature showing a link between these factors and the risk of HEV infection [24, 28, 34, 41].

In Kégoudou, the positivity rates for anti-HEV IgM (1%) and IgG (9.6%) in pregnant women contrast with those reported during the 2014 epidemic, where the prevalence rates of IgM and IgG in individuals who were identified in contact with people who tested positive for hepatitis E by RT-PCR and suspected based on symptoms were 38.8% and 27.5% for IgM and IgG, respectively. It should be noted that this study population had previously tested negative by RT-PCR. This study report that the risk of exposure was statistically higher in men (77.3%) than in women (22.7%). However, serious cases have been observed mainly in women, particularly those who are pregnant. Moreover, among them, two cases of death due to hepatitis E were noted during this study [26].

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Our work has also some limitations. First, the study sites are all located in urban areas. We were also unable to establish a link between seroprevalence of HEV infection and the pregnancy term. Another limitation is the lack of molecular data to confirm acute infection. This aspect is planned in further development of the project.

5. Conclusions

With a satisfactory participation rate (122.7%), this seroepidemiological survey confirms the circulation of HEV in Senegal and in particular contributes to a better understanding of hepatitis E virus infection in pregnant women with a national seroprevalence of 7.4%. Our data confirm that HEV is a poverty linked infection as evidenced by the significant association of seroprevalence with regular income and access to sanitation services. Means to mitigate this emerging infection should thus adopt a holistic intervention approach.

Author Contributions:

Conceived, get funding: AAMD, MP, CTK, AA
Coordinated the work, drafted the manuscript: AAMD, AA
Performed the work: AAMD, SL, CMG, AS, MN, NMPM, HS, SPM
Curation: AAMD
Formal analysis: AAMD, CMG, AA
Investigation: AAMD, AA, SL, NMM, FD, MEFD, BB
Supervision: AAMD, SL, CMN, HDN, NMM, FD
Validation: AAMD, CTK, MP, AA
Reviewed the manuscript: AAMD, SL, CMG, AS, HDN, NMM, FD, SD, MEFD, OT, BB, NMPM, FT, HS, GL, MN, SPM, ND, MD, ID, YD, CTK, MP, AA
All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement:

The study was conducted in accordance with the Declaration of Helsinki, and approved by the the Senegalese National Ethics Committee for Health Research (N°000130/MSA/CNRES/Sec, protocol code SEN20/31, date of approval: July, 05th 2020) and the Ministry of Public Health and Social Action (N°00000582/MSAS/DPRS/DR, protocol code SEN20/31, date of approval: July, 08th 2020).

Informed Consent Statement:
Informed consent was obtained from all subjects involved in the study.

Data Availability Statement:

Not applicable.

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Conflicts of Interest:

The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

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