**MODELLING TRENDS OF HEPATITIS E INFECTION**

**Abstract**

**Background**: Hepatitis E is prevalent in many individuals, particularly in developing regions. While the infection often results in a self-limited, acute illness, it has a high likelihood of progressing to a chronic condition. Chronic infections can occur in pregnant women, individuals with weakened immune systems (such as the elderly, those with underlying illnesses), and especially in individuals who have undergone solid organ transplants.

**Methods**: A comprehensive literature search on viral hepatitis E in children attending primary, secondary, and higher schools was conducted using various search terms. The focus on schools stems from the assumption that educational institutions should possess greater awareness of viral hepatitis E. A mathematical model was developed to describe the dynamic transmission of the virus, and sensitivity analysis was performed to assess the model's responsiveness to different parameters.

**Results**: The results indicate that oral consumption is the primary mode of transmission, especially in higher education settings. Sensitivity analysis demonstrated positive influences of all parameters associated with infection pathways. By utilizing the mathematical model of dynamic transmission, the projected infection rate can potentially be mitigated.

**Conclusion:** In conclusion, the projected infection rate as indicated by the model can be mitigated through the application of the dynamic transmission mathematical model. Implementing a range of strategies for targeted or widespread vaccination stands as a potent intervention for the improvement of public health.

**Keywords: Seroprevalence, Dynamic transmission, Modelling, Infection**

**Introduction**:

 Hepatitis E virus (HEV) infection is a significant global public health concern, accounting for over 50% of acute viral hepatitis cases. It is particularly prevalent in developing countries with inadequate access to clean water and sanitation. Large-scale hepatitis E epidemics have been reported in regions such as Asia, the Middle East, Northern and Central Africa, and Central America. However, sporadic cases of HEV infection have also surfaced in developed nations, including the USA and European countries.[1,2,3,4] Notably, recent studies have identified blood transfusions as a potential route of sporadic HEV infection.

Historical accounts suggest that HEV may not be an ancient disease [5], as it was initially categorized as an emerging ailment with an unclear origin. The designation "hepatitis E" was later assigned to this empirically transmitted disease. During the Afghanistan war in 1983, an outbreak of an unusual and unexplained hepatitis virus among Soviet soldiers was documented. Subsequent investigations revealed the presence of viral particles in the stools of affected soldiers through immune electron microscopy[6]. The viral genome was isolated from small samples of cloned bile obtained from experimentally infected macaques.

HEV, in its original form, comprises a minimum of four genotypes: 1, 2, 3, and 4. Genotypes 1 and 2 are exclusively found in humans, while genotypes 3 and 4 are present in several animal species, including pigs, wild boars, and deer. Interestingly, infected animals do not display any clinical symptoms but can transmit the virus to humans[7]. The virus enters the human body primarily through the colon, shedding in the feces of infected individuals. The main modes of transmission are the fecal-oral route and consumption of contaminated water. The virus typically follows a 2-6 week cycle. Symptoms of HEV infection commonly include jaundice, fever, anorexia, nausea, abdominal pain, vomiting, and liver enlargement. Severe cases can progress to fulminant hepatitis, severe liver failure, and even death. Diagnosis of HEV infection involves detecting specific IgM and IgG antibodies in the patient's blood[8].

Hepatitis E is widespread, particularly in developing regions, and may progress to chronicity, especially in high-risk populations such as pregnant women, immunocompromised individuals (e.g., the elderly and those with underlying illnesses), and solid organ transplant recipients. In some instances, HEV infection can be fatal, as reported in cases of fulminant hepatic failure[9].

Acute HEV infection affects approximately three million individuals annually, resulting in 70,000 deaths [10], with the majority of cases occurring in endemic regions. Recent increases in cases have been reported in low-endemic countries, driven by inadequate sanitation, compromised water supplies, and food contamination. High seroprevalence rates of HEV, ranging from 27% to 80%,[10] have been observed in developing nations like India and Southeast Asia. Surprisingly, industrialized countries like the United Kingdom and the USA have reported unexpectedly high seroprevalence rates of HEV (21-25%), potentially attributed to subclinical infections, animal exposures, cross-reactivity with other agents, or false-positive test results. Pregnant women and individuals with compromised immune systems face the highest mortality risks, ranging from 1% to 4%[10,11].

In Nigeria, limited investigations into HEV seroprevalence have shown varying results, with IgG and total antibody seroprevalence ranging from 7.0% to 66.75%. [12]Co-infection rates among Nigerian healthcare workers have indicated a 27.3% co-infection rate with hepatitis B virus (HBV) and human Epstein-Barr virus (HEV). Additionally, a seroprevalence of anti-HEV IgM antibodies ranging from 0.4% to 0.9% has been reported. HEV outbreaks have occurred in different regions of Nigeria, including Port Harcourt [12] and Bornu State [13], with varying genotypes involved. Consequently, further research and awareness efforts are essential to address the risks and provide projections to raise public awareness.

Recent research revealed a case of hepatitis E transmission through blood transfusion, originating from a donor who contracted the virus through zoonotic foodborne exposure [14]. This highlights the growing concern about the safety of blood transfusions regarding hepatitis E. Several countries, including Japan, the United Kingdom, Saudi Arabia, and France, have extensively documented cases of hepatitis E transmission through blood transfusions [14,15,16].

Hepatitis E virus (HEV), a single-stranded positive-sense RNA virus, primarily spreads through the fecal-oral route. Its genome comprises three open reading frames (ORF) flanked by untranslated regions at the 5' and 3' ends [17,18]. Typically, HEV infections manifest as acute, self-limiting hepatitis with an illness duration of 4-6 weeks, featuring symptoms like fatigue, appetite loss, nausea, and elevated serum ALT levels. However, in pregnant individuals, HEV infection can lead to fulminant hepatic failure, with a mortality rate as high as 20% [19,20]. Immunocompromised individuals, including solid organ transplant recipients and HIV/AIDS patients [21,22], may develop chronic hepatitis, liver fibrosis, cirrhosis, and extrahepatic symptoms such as neurological and kidney issues.

HEV comprises four main genotypes, with genotypes 1 and 2 exclusively affecting humans, [23,24] primarily through contaminated water sources in regions with poor sanitation, leading to widespread outbreaks. Consumption of meat from infected animals, especially pigs, occasionally results in HEV genotypes 3 and 4 infections in Western nations and China [17,18]. Furthermore, novel HEV strains, including HEV-3ra[26] from farmed rabbits in China in 2009[25] and HEV7 from Bactrian camels in 2016 [27], pose potential risks to human health. Additionally, rat HEV, genetically distinct from HEV1-8, has been found to infect humans, raising concerns about HEV exposure and interspecies transmission.

HEV is a significant concern, with infections causing violent outbreaks, particularly in areas with poor sanitation and contaminated water. [27] Zoonotic transmission plays a key role in clinical cases of hepatitis E in industrialized regions, often associated with consuming contaminated animal products or close contact with infected animals[28]. However, underreporting of HEV incidence is common due to limited diagnostics, variable incubation periods (2-10 weeks), and symptoms resembling other forms of acute viral hepatitis [29].

Animal models have been essential for studying HEV replication and pathogenesis, especially when efficient cell culture systems are lacking. These models help researchers understand virus-related pathology, host-virus interactions, and evaluate the effectiveness and safety of vaccines and therapeutics.

Expanding the understanding of HEV replication in various tissues may reveal the virus's pathogenic potential and its propensity to cause extrahepatic symptoms. Some HEV genotypes are associated with specific extrahepatic conditions, such as pancreatitis (genotype 1) and renal symptoms (genotype 3).

Four HEV genotypes have been identified, each with distinct characteristics. Genotypes 1 and 2 are responsible for epidemic hepatitis, primarily transmitted through water and the fecal-oral route. Genotypes 3 and 4 are prevalent in domestic and wild pigs. The extent of virus transmission and its clinical implications remain subjects of debate, with insufficient evidence to support universal screening recommendations [30,31,32].

The objective of this study was to model the prevalence of hepatitis E across educational institutions, from elementary schools to higher education, to assess the rate of dynamic transmission and provide projections for public awareness.

**Methodology**

The lack of widely recognized diagnostics and established operating methods for patient testing is a major factor in the exact incidence of HEV infection in many nations, leading to some linkage to formulate the model. Chronological Hepatitis E was adapted from (33).

Chronic Hepatitis E Virus Only a small proportion of individuals infected with HEV develop symptomatic episodes, with the majority experiencing asymptomatic seroconversion. The incubation period typically ranges from 3 to 8 weeks, with an average of 40 days [34]. In otherwise healthy individuals, HEV infections usually result in self-limiting acute viral hepatitis, accompanied by symptoms such as hepatomegaly, jaundice, and dark urine. [35] In rare cases, fulminant hepatitis can occur. Liver enzyme panels typically show elevated levels of alanine aminotransferase (ALT), aspartate transaminase (AST), alkaline phosphatase, -glutamyl-transferase, and bilirubin, with ALT levels typically higher than AST values [36].

Persistent Hepatitis E Virus

A significant clinical concern is the potential of HEV to progress into a chronic condition, particularly in individuals with compromised immune responses [37,38,39]. Chronic HEV infections have been observed in patients with conditions such as leukemia [17,40], HIV/AIDS, solid organ transplants, and immunosuppressive states. [41] Chronic infection is defined as persistent detection of HEV RNA for more than three months and can lead to cirrhosis, liver fibrosis, and, ultimately, liver failure necessitating a transplant. Symptoms may include fatigue, jaundice, weakness, abdominal pain, and fever [42]. Chronic HEV infections can also involve replication at extra-hepatic sites, potentially leading to mutations that increase virulence and transmissibility, making them of significant clinical concern [42,43].

Hepatitis E in Pregnancy

 Pregnant women contracting HEV during their second and third trimesters face increased morbidity and mortality, with mortality rates rising by up to 30% during outbreaks [44]. The precise causes of elevated mortality during pregnancy are not fully understood but are believed to involve genetic factors, hormonal changes, and immune responses [44,45]. Both the fetus and the mother face substantial risks, with a high rate of stillbirths, neonatal deaths, and maternal fatalities reported during HEV epidemics [46].

Hepatitis E Virus Strains Produced by Animals

Numerous HEV species have been identified in various animal species, some with zoonotic potential, while others remain non-zoonotic. Antibodies to HEV have been found in several animals, indicating the presence of HEV or related agents. However, conclusive evidence of HEV RNA in these animals is lacking. Some animal species, such as dairy cows in China, have been shown to be susceptible to genotypes 3 and 4 HEV infections, complicating the understanding of HEV strains in animals. Differentiating between distinct herpesviruses in these animals may require metagenomic data and virome characterization. HEV's transient viremia and often low viral RNA levels make this task challenging. Metagenomic sequencing of potential hosts from various locations and time periods may be necessary to avoid overlooking this frequently overlooked pathogen.

The most recent medical concern is the diversification of hepatitis E transmission routes, including organ transplants, blood transfusions, and blood, in addition to the traditional fecal-oral and zoonotic modes. Chronic HEV infection, particularly in transplant patients, has become more prevalent, surpassing the wide spectrum of infections, ranging from self-limiting to acute liver failure. Additionally, HEV's extra-hepatic manifestations affecting the kidneys, heart, pancreas, central nervous system (CNS), and other organs raise further concerns. However, advances in cell culture methods and animal models have improved our understanding of HEV's pathogenesis.

**Modelling Formulation**

Dynamic Transmission Hepatitis E epidemiology is rooted in the transmission of the virus through various pathways. The progression of the disease is modeled using the SEIR framework, representing susceptible, exposed, infectious, and recovered or deceased individuals [47]. This model encompasses human-to-human, animal-to-human, and environment-to-human transmission routes, while also accounting for control measures like vaccination and sanitation.

The population is divided into six distinct epidemiological classes: susceptible (S(t)), immunized (V(t)), infectious (IN(t)), animals (A(t)), and recovered (R(t)). Additionally, the model incorporates HEV pathogens in food or water denoted as K(t), V(t), A(t), and P(t).

Based on collected data, it is observed that restroom facilities in most areas are limited, with some people resorting to using open areas such as bushes, leading to contamination of water bodies during rainfall. Many individuals rely on streams for their water supply due to the scarcity of boreholes. The proportion of people with access to sanitation facilities or cisterns is denoted as 'h' to account for this phenomenon. Environmental transmission can also occur through contact with animals, influencing the rate of environmental pollution, which is represented as:

$$\frac{de}{dt}=θ\left( 1-h\right)In-e………………………………………………………………1$$

Where $θ$ is the transmission rate from infected humans *In* to the environment.

Here, θ represents the transmission rate from infected humans to the environment and *In* to the environment. Individuals with access to clean water are protected from waterborne infections unless exposed to infected humans or animals. The susceptible human population (S) is susceptible to HEV with a transmission rate of α and experiences mortality at a rate μ\_p. Those without access to boreholes have a higher risk of HEV transmission from the contaminated environment (e). Additionally, transmission from animals to humans (g) is considered.

The transmission by infected humans to the environment is denoted as 'r,' and virus decay is represented by 'f':

$\frac{dS}{dt}=μ-\left(1-m\right)αgeS$ +r-f…………………………………………………………..2

Upon successful infection, individuals move to the exposed class (E) and experience transmission to the environment (r) and virus decay (f). The incubation period is characterized by$\frac{1}{π}$ days:

$\frac{dE}{dt}=αge-\left(μ+π\right)-f$ ……………………………………………………………….3

 $\frac{dL}{dt}=rs-\left(μ+β\right)L$ …………………………………………………………………4

The class denoted as 'L' represents latent infections, experiencing transmission (rs) and natural death (μ + βL):

Following the incubation period, individuals become infectious (I), displaying various symptoms associated with HEV infection. Recovery occurs at a rate σ:

$\frac{dI}{dt}= πE-\left(μ+σ\right)I$ …………………………………………………………………..5

Some infected individuals may succumb to the infection or recover, transitioning to the immune class (R):

$\frac{dR}{dt}=\left(1-π\right)gI-μR$ ………………………………………………………………….6

Equations 1-5 form a system of equations describing the transmission between humans and their environment. The environment reaches a steady state before humans if environmental dynamics are faster. Equation 1 provides the quasi-stationary-state (QSS) equation:

$e^{\*}=θ\left(1-h\right)In$………………………………………………………..7

Substituting the steady state into the system equations yields the following equations:

$$\frac{dS}{dt}=μ-αg\left(1-h\right)\left(1-m\right)SIn-μS+r-f$$

$\frac{dE}{dt}=αg\left(1-h\right)θ-In-\left(μ+π\right)j-f$ ……………………………………………………..8

 $\frac{dI}{dt}=πβ-\left(μ+σ\right)I$

 $\frac{dR}{dt}=\left(1-ε\right)δI-μR$

According to [53, 54], in this system, the total population is represented as 1 = S + E + I + R + K. Therefore, data will be fitted to the system equations after analysis. The endemic steady state is defined by:

$S^{\*}=\frac{1}{Z\_{0}}$, $E^{\*}=\frac{μ(μ+σ)d}{παθ(1-h)(1-m)}(Z\_{0}-1)$ , $I^{\*}=\frac{μd}{αθ(1-h)(1-m)}(Z\_{0}-1)$

 $Z^{\*}=1-S^{\*}-E^{\*}-I^{\*}$- K\*

Where: $Z\_{0}=\frac{απθ(1-h)(1-m)}{(μ+π)(μ+σ)}$

which represents the HEV reproduction number. The transmission rate of HEV during the infectious period is expressed as

$\frac{απθ(1-h)(1-m)}{(μ+π)(μ+σ)}$ while the survival of the incubation period is denoted as $\frac{π}{μ+π}$.

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Table 1: Variables and Their Definitions for the HEV Dynamic Model, adapted from Korobrinkov, A., 2007

|  |  |
| --- | --- |
| Variable | Definition |
| S(t)L(t)In(t)R(t)V(t)P(t)K(t) | The number of susceptible humans at the time tThe number of latent humans at a time tThe number of infectious humans at a time tThe number of recovered (immune) humans at a time tThe number of vaccinated humans at a time tThe number of HEV pathogens at a time tThe number of non-vaccinated humans at time t |

Variable Definition S(t) The number of susceptible humans at time t L(t) The number of latent humans at time t In(t) The number of infectious humans at time t R(t) The number of recovered (immune) humans at time t V(t) The number of vaccinated humans at time t P(t) The number of HEV pathogens at time t is K(t).

Table 2: Parameters and their Definition for the HEV dynamic model

|  |  |  |  |
| --- | --- | --- | --- |
| Parameter | Definition | Value  | Source |
|  | Contact rate between S and other variables |  |  |
| $$s\_{h}$$ | 100 human/year | Assumed |
| $$α$$ | Transmission rate for Infectious humans | 0.01/year | Assumed |
| $$π$$ | Rate of pathogen release into food or water by infected persons | 0.02/year | Assumed |
| $$f$$ | Mortality rate of HEV pathogens | 1/7% per day | WHO |
| $$σ$$ | The natural pace of recuperation for contagious humans | 0.0238-0.1429$/day$ | WHO |
|   |
| $$g$$ | Transmission rate of animals to human beings | 0<a<1 | Estimated |
| $$b$$ | Rate of vaccination of susceptible people | 0.001/day | Assumed |
| $$μ$$ | Natural human mortality rate | 0.00156/year | WHO |
| $$δ$$ | Per capita rate of recovery from HEV | 1/12 per day | Estimated |
| $$β$$ | The speed at which latent individuals become infectious | 1/10/day | 60 |
|  |  |  |  |

Source: Author

**Protocol:**

We conducted an extensive literature search using various combinations of search terms related to viral hepatitis E and children in primary, secondary, and higher schools. Our primary focus was on schools since they are expected to have a better understanding of viral hepatitis E compared to other institutions. We developed a mathematical model to analyze the dynamic transmission of the virus, assuming uniform transmission lineages despite variations in dates. Sensitivity analysis was performed to assess the model's adaptability to different parameters.

Data for this analysis were primarily sourced from three secondary sources, which were documented by:

1. Emmanuel Ekanem et al. - Primary schools
2. (ii) MA Bugaje et al. - Secondary schools
3. (iii) Osanyinlusi et al. - Tertiary institutions
4. (iv) Chioma Ngozichukwu Pauline Mbachu (for data validation)

The laboratory examination procedure employed by most selected authors followed these steps:

Sample Collection: Five milliliters of blood were drawn into EDTA bottles at the University Medical Center and transported to the Microbiology Laboratory while being kept cold on ice packs.

Sample Processing: Within 24 hours of collection, whole blood samples were directly examined using an enzyme-linked immunosorbent assay (ELISA) kit (CTK Biotech, Inc. USA) to detect the presence of anti-HEV IgM antibodies. The assays were conducted following the manufacturer's guidelines, and the kit used in the study demonstrated high sensitivity, specificity, and accuracy, with values of 98.1%, 99.2%, and 98.9%, respectively. Anti-HEV IgM antibodies were considered indicative of recent or persistent HEV infection.

Data Analysis: The analysis of the collected data was performed using SPSS version 22 and E-views V10.

**RESULTS**

**Demographic Analysis of the respondent**

Table 3a: Age of respondents (Primary)

|  |  |  |  |
| --- | --- | --- | --- |
|  S/no | Age | Frequency | Percentage |
| 1 | 1 – 4 | 134 | 39.0 |
| 2 | 5 – 9 | 83 | 24.1 |
| 3 | 10 – 14 | 81 | 23.0 |
| 4 | 15 – 18 | 46 | 13.4 |
| Total | 344 | 100 |

Table 3b: Age of respondents (Secondary)

|  |  |  |  |
| --- | --- | --- | --- |
|  S/no | Age | Frequency | Percentage |
| 1 | 10 – 14 | 124 | 35.8 |
| 2 | 15 – 18 | 153 | 44.2 |
| 3 | 19 – 24 | 69 | 19.9 |
| Total | 346 | 100 |

Table 3c: Age of respondents (Tertiary)

|  |  |  |  |
| --- | --- | --- | --- |
| S/no | Age | Frequency | Percentage |
| 1 | 11 -15 | 103 | 38.6 |
| 2 | 16 – 20 | 152 | 56.9 |
| 3 |  21 – 25 | 12 | 4.5 |
| Total | 267 | 100 |

Table 4: Gender of respondents

|  |  |  |  |
| --- | --- | --- | --- |
|  Gender | Primary | Secondary | Tertiary |
| Male | 169 (49.1) | 243 (70.4) | 106 (39.7) |
| Female | 175 (50.9) | 103 (29.6) | 161 (60.5) |
| Total | 344 (100) | 346 (100) | 267 (100) |

Table 5: Use of Alcohol

|  |  |  |  |
| --- | --- | --- | --- |
|  Alcohol | Primary | Secondary | Tertiary |
| Yes | 1 (0.3) | 22 (6.4) | 31 (11.6) |
| No | 343 (99.7) | 324 (95.6) | 236 (88.4) |
| Total | 344 (100) | 346 (100) | 267 (100) |

Table 6: Blood Transfusion

|  |  |  |  |
| --- | --- | --- | --- |
| Transfusion | Primary | Secondary | Tertiary |
| Yes | - | 6 (1.7) | 9 (3.4) |
| No | 344 (100) | 341 (98.3) | 258 (96.6) |
| Total | 344 (100) | 346 (100) | 267 (100) |

Table 7: Type of Drinking water

|  |  |  |  |
| --- | --- | --- | --- |
|  Type | Primary | Secondary | Tertiary |
| Stream | 108 (31.4 ) | 17 (4.9) | 8 (3.0 ) |
| Borehole/well | 205 ( 59.6) | 217 (62.7) | 73 ( 27.3) |
| Sachet/bottle | 31 ( 9.0) | 112 (32.4) | 186 ( 69.7) |
| Total | 344 (100) | 346 (100) | 267 (100) |

Table 8: Contact with animals/rearing animals

|  |  |  |  |
| --- | --- | --- | --- |
| Contact | Primary | Secondary | Tertiary |
| Yes | 283 (82.3) | 73 (21.1) | 45 (16.9) |
| No | 61 (17.7) | 273 (78.9) | 222 (83.1) |
| Total | 344 (100) | 346 (100) | 267 (100) |

Table 9: Sanitation type

|  |  |  |  |
| --- | --- | --- | --- |
|  Type | Primary | Secondary | Tertiary |
| Bush | 76 (22.1) | 69 (19.9) | 4 (1.5) |
| Pit | 250 (72.7) | 245 (70.8) | 81 (30.3) |
| Cistern | 18 (5.2) | 32 (9.2) | 182 (68.2) |
| Total | 344 (100) | 346 (100) | 267 (100) |

 Table 10: Logistic Regression

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable/Institution** | **Primary** | **Secondary** | **Tertiary** |
| **Coefficients** | **Sig. level** | **Coefficients** | **Sig. level** | **Coefficients** | **Sig. level** |
| Age | 3.203 | 0.182 | 0.331 | 0.295 | 0.080 | 0.628 |
| Sex | 0.632 | 0.270 | 2.443 | 0.323 | 0.512 | 0.145 |
| Water | 0.594 | 0.081 | 0.643 | 0.019 | 0.240 | 0.004 |
| Blood Transfusion | 19.031 | 0.039 | 18.851 | 0.097 | 11.463 | 0.041 |
| Animals | 0.590 | 0.464 | 1.196 | 0.123 | 0.183 | 0.699 |
| Alcohol | 6.002 | 0.766 | 0.605 | 0.587 | 18.804 | 0.998 |
| Sanitation | 1.086 | 0.432 | 0.751 | 0.315 | 0.309 | 0.734 |
| Educational level | 7.042 | 0.048 | 6.878 | 0.031 | 9.317 | 0.011 |

Regarding gender (Table 4), a higher prevalence of hepatitis E virus (HEV) infection was observed among males (14.9%) compared to females (9.4%) across all three educational levels. In contrast to previous studies [48 & 49] that suggested an increased risk of HEV seropositivity based on the type of drinking water, our study revealed a higher prevalence of HEV infection among blood donors, with rates of 37.1% in primary, 24.4% in secondary, and 7.9% in tertiary education institutions. However, no statistically significant association with HEV positivity was found upon analysis.

It is worth noting that previous research has indicated that the primary route of HEV transmission is through the fecal-oral route [50]. In our study, we considered four different variables/observations. Table 10 illustrates the relationship between the type of institution and these variables. The table highlights that the type of drinking water is highly significant compared to other variables, with primary (p=0.081), secondary (p=0.019), and tertiary (p=0.004) institutions showing significant associations with HEV positivity. Notably, 74.77% of participants who tested positive had tap/well water as their source of drinking water (p<0.05), aligning with previous studies that have identified contaminated water as a primary source of HEV infection (reference 56). This may be attributed to inadequate water supply and poor sanitation conditions in the community.

In terms of contact with animals, our analysis did not yield any statistical significance across all three education levels (p>0.05). This finding does not support the hypothesis that zoonotic transmission is a significant route of HEV transmission.

ANALYSIS OF THE DYNAMIC MODEL

Figure 1 illustrates that as vaccination rates increase, the fraction of susceptible individuals decreases, resulting in fewer people exposed to the disease. Figure 2 demonstrates that higher vaccination rates are associated with a decrease in the number of infected individuals.

Improving sanitation practices can significantly reduce HEV infection rates. Initiatives such as water chlorination, blood transfusion screening, and improved personal hygiene practices can play a vital role in reducing the spread of the disease in the community. Figure 3 shows that enhancing sanitation and vaccination rates have a more pronounced impact on reducing the spread of HEV viruses. Eliminating the disease at the primary level could lead to its eventual disappearance by the time it reaches the tertiary level.



Figure 1: Impact of Sanitation Only



Figure 2: Impact of Vaccination Only



Figure 3: Impact of Both Sanitation and Vaccination

Sensitivity Analysis

Sensitivity analysis evaluates the model's responsiveness to changes in parameter values, which is crucial when dealing with data uncertainties and estimated parameter values. It helps identify which parameters are most influential and require intervention. In our analysis, we utilized Chitnis et al.'s methodology to determine a normalized forward sensitivity index, highlighting the most critical parameters.

A variable's normalized forward sensitivity index $μ$, which depends on a parameter g, is defined as $ψ\_{g}^{μ}= \frac{dμ}{dg} X \frac{μ}{g}$

For example, the sensitivity index of $R\_{k}$ (effective reproduction number) with respect to $s\_{h}$

 $ψ\_{g}^{R\_{k}}=\frac{∂R\_{k}}{∂s\_{h}} X \frac{s\_{h}}{R\_{k}}$

Table 11:  **Sensitivity indices of** $R\_{k}$

|  |  |
| --- | --- |
| Parameters | Sensitivity indices of $R\_{k}$ |
| $$s\_{h}$$ |  0.99866 |
| $$α$$ | 0.00786 |
| $$πc$$ | 0.00542 |
| $$f$$ | 0.00089 |
| $$σ$$ | 0.77623 |
| $$g$$ | -0.00586 |
| $$b$$ | 0.06554 |
| $$μ$$ | -0.09465 |
| $$π$$ | 0.08873 |

When $φ\_{s\_{h}}^{R\_{k}}>0$, it indicates that the value of c increases with an increase in $s\_{h}$, whereas when $φ\_{s\_{h}}^{R\_{k}}<0$, it signifies that c decreases as $s\_{h}$ decreases. The sensitivity indices' results are presented in the table below. Notably, parameters such as $s\_{h}$, α, π, f, σ, and b exhibit a positive correlation with $R\_{k}$, causing$R\_{k}$ to decrease as these parameters increase. On the other hand, variables like μ and g remain unaffected by changes in the generation of $R\_{k}$. Among all parameters, $s\_{h}$ emerges as the most sensitive, and parameters associated with the infection pathways consistently yield positive sensitivity indices.

**Forecasting of HEV from 2025 to 2040**

$$I\_{s}=F\_{s} x G\_{s}+α\_{s }$$

Where $I\_{s} $is the proportion of individuals infected in levels.

* $G\_{s}$ is the percentage of individuals in level s with access to clean water, sex drive
* $F\_{s}$ is the factor of HEV transmission in level s
* $α\_{s}$ is the transmission parameter in level s

Table 12: Projection from the table overtime

|  |  |  |
| --- | --- | --- |
| **Variable** | **Setting** | **Calendar Year** |
| **2025** | **2030** | **2035** | **2040** |
| **Drinking water** | Primary | 3 | 3 | 8 | 11 |
| Secondary | 17 | 19 | 21 | 27 |
| Tertiary | 1 | 2 | 6 | 8 |
| **Blood transfusion** | Primary | 1 | 1 | 1 | 2 |
| Secondary | 18 | 25 | 29 | 36 |
| Tertiary | 29 | 41 | 54 | 62 |
| **Contact with animals** | Primary | 1 | 1 | 1 | 2 |
| Secondary | 3 | 7 | 11 | 16 |
| Tertiary | 1 | 3 | 7 | 13 |

To the best of our knowledge, this current transmission model marks the first attempt to explicitly estimate the risk of developing hepatitis across different levels of schooling. However, it's important to note several limitations that require careful consideration. While the timeframes may vary, the model assumes that the transmission patterns remain consistent. Notably, Table 12 demonstrates a notably higher transmission rate among different genders at the tertiary level.

**Conclusion:**

In summary, the varying levels of HEV seroprevalence uncovered in this study highlight a concerning prevalence of HEV infection among blood donors in south-west Nigeria, underscoring the potential risk of HEV transmission through blood transfusions, which warrants further research. The mathematical non-linear dynamic model of transmission has been developed, incorporating vaccination and sanitation as control measures. The combination of sanitation and vaccination has demonstrated a more effective ability to minimize or eliminate the virus, thus preventing future outbreaks, as evidenced in the model.

The sensitivity analysis was conducted deliberately to assess the factors crucial to transmission. When devising an effective control strategy, parameters such as sh (contact rate) and σ (recovery rate) must be carefully considered. This dynamic model can serve as a valuable tool for public health interventions aimed at averting the projected figures from the forecast model, encompassing a range of targeted and general immunization strategies.

**Acknowledgement**: We acknowledge the following authors for using their raw data for application of the model. (i). Emmanuel Ekanem et al.- Primary

(ii). MA Bugaje et al. – Secondary schools

(iii). Osanyinlusi et al. - Tertiary Institution

(iv)**.** Chioma Ngozichukwu Pauline Mbachu (for data validation)

**Funding**: None

**Conflict of Interest**: We declare no conflict of interest.

**Ethical Approval:**

As per international standards or university standards written ethical approval has been collected and preserved by the author(s).

**Consent :** Authors understand and have read this research's description or had it translated. Authors understand that their participation is voluntary, and they know enough about the research study's purpose, methods, risks and benefits to judge that Author want to participate.

**Authors Contribution**: Semiu Ayinla (SA) Alayande is the principal investigator in charge of designing the study and write up. Onisile Deborah identified the needed data and Oboh Samuel did analysis of the data.

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