(International Print/Online Journal)

SJIF IMPACT FACTOR: 5.565
PUBMED-National Library of Medicine ID-101739732

ISSN (Print): 2209-2870
ISSN (Online): 2209-2862

International Journal of Medical Science and Current Research (IJMSCR)
Available online at: www.ijmscr.com
Volume 6, Issue 1 , Page No: 31-38
January-February 2023

IJMSCR

Estimation of Seroprevalence (IgG) of Hepatitis E virus Among Pregnant Women in South Chennai

[1]Akshaya Sathish, [2]Indrajith Devandra Balamurugan, [3]Jeyakumari Duraipandian, [4]Subha AM,
[1,2]MBBS, [3]MD (Micro), [4]MBBS, DGO, FICOG, DRM
[1,2]CRRI, [3,4]Professor & HOD
[3,4]Department of Microbiology
[3,4]JIPMER Karaikal (An Institute of National Health Importance)
[1,2]Tagore Medical College, Chennai- 127
(Affiliated to The Tamil Nadu Dr MGR Medical University, Chennai)

***Corresponding Author:**
Jeyakumari Duraipandian
Professor & HOD, Department of Microbiology
JIPMER Karaikal (An Institute of National Health Importance)

Type of Publication: Original Research Paper
Conflicts of Interest: Nil

Abstract

Background:

Hepatitis E virus (HEV) infection is a major public health issue in developing countries. HEV infection is an enterically transmitted, causing self-limiting acute viral hepatitis with high incidence and severe form of the disease in pregnant women. IgM antibody is an acute phase marker of HEV infection and IgG is used to study the exposure to HEV among the population. Our study aims to assess the seroprevalence (IgG) of HEV among the pregnant women in South Chennai.

Materials and Methods:

Healthy Pregnant women (n=200) attending the antenatal outpatient clinic of our hospital were included in the study. 2 ml of blood was collected and all the sera (n=200) were tested for anti-HEV IgG antibody by ELISA.

Results:

The prevalence of anti-HEV IgG antibody was found in 12 out of 200 samples (12/200) (6%). The mean age of our participants was 26.6± 3.8. The parity of our study population was primigravida (75%) and multigravida (25%). The gestational age was in 1st trimester (18%), 2nd trimester (30), and 3rd trimester (52%). All the positive pregnant women (100%) were primigravida and in the third trimester. Among the twelve positive subjects, 83% were urban dwellers belonging to the middle class, and they were literate.

Conclusion:

The seroprevalence rate of anti-HEV IgG among the pregnant women of our region is 6% (12/200) which is very low and this indicates better sanitation practices, safe water supplies, and an effective health system in south Chennai. The lack of protective antibodies warrants a vaccine to evade a potential HEV epidemic.

Keywords: Hepatitis E virus, IgG antibody, pregnant women, seroprevalence

Introduction

Hepatitis E virus (HEV) infection is a major public health issue in developing countries. The disease occurs either in the form of large epidemics or sporadic cases. HEV infection is enterically transmitted, causing self-limiting acute viral hepatitis. (1) The disease has distinctive and till now inexplicable epidemiological characteristics with repeated outbreaks, episodes of disease in the adult population, and high incidence and severe forms of

the disease in pregnant women. (2) HEV is one of the five major hepatotropic viruses, that primarily affects the liver. (3) It is an RNA-positive strand, a non-enveloped virus belonging to the family Hepeviridae. There are four genotypes of HEV 1-4; HEV 1 is largely associated with huge episodes in developing countries where conditions of hygiene and sanitation are poor. HEV is endemic in India, Africa, the Middle East, and Central America. It is the most common cause of acute viral hepatitis in the adult population in India. It is estimated that 2.3 billion people are infected globally.(4) The overall prevalence of anti-HEV antibodies in developing countries ranges between 20% and 40% in comparison with industrialized countries with 1% to less than 20%. (5,6) Rate of death in general during HEV infection is less than 4% which can reach 20 - 40% in pregnant women. (7,8) HEV mostly causes a self-limited disease but the nature of the disease in pregnant women is more severe. (9) The hormonal factors, immune and host susceptibility factors are proposed for the worse prognosis of HEV in pregnancy. Acute HEV infection is particularly severe during the second and third trimesters of pregnancy and may lead to fulminant hepatic failure and death in 30 –100%. The Prevalence of HEV infection in the second and third trimesters (19.4% & 18.4%) was found to be much higher than in the first trimester (8.8%) or in non-pregnancy females (2.1%) or males (2.8%). The fatality rate in pregnant women with fulminant hepatic failure has also been reported to be high (22.2%) with the greatest severity reported in the third trimester (44.4%). (10,11) IgM antibody to HEV is used as an acute phase marker of HEV infection and HEV IgG is used to study the exposure to HEV in a given population. The prevalence of anti-HEV IgG among the general population in India ranges from 4% in Kashmir and South India to as high as 29 -35% in Delhi. (12,13) Studies on the seroprevalence of HEV IgG among children and the general population are available from India but lacking data on Indian pregnant women. Hence, the present study was carried out to determine the seroprevalence of subclinical HEV infection in pregnant women attending the antenatal clinic of tertiary care hospital, in south Chennai.

Materials And Methods

Study Type : An institution based prospective and descriptive study conducted from August 2017 to December 2019.

Place Of Study : A tertiary care hospital in Kancheepuram district, Tamil Nadu.

Sample Size : Apparently healthy Pregnant women (n=200) attending antenatal outpatient clinic of our hospital. Sample size was calculated based on the seroprevalence of HEV in the previous study by using $n=4P(1-P)/d^2$ as a formula.

Inclusion Criteria:

All healthy asymptomatic pregnant women

Exclusion Criteria:

1. Pregnant women with the history of fever or jaundice
2. Confirmed cases of acute viral hepatitis either clinically or by laboratory tests

Ethical Consideration:

The study was approved by our Institute ethics committee. (Ref No: I EC No: 17/ June 2017) Informed written consent was obtained from all the participants after explaining the purpose of the study.

Sample Collection:

Demographic and clinical details were collected by preset Questionnaires. 2 ml blood was collected, while collecting blood for routine investigations. The sample was centrifuged and sera was separated and stored at -20°C.

Testing Method:

All the sera (n=200) were tested for anti HEV IgG antibody by ELISA (Third generation Enzyme Immunoassay, DIA PRO, Diagnostics Bio probes, Sesto San Giovanni (Milano) –Italy). The ELISA was done according to the protocols provided by the manufacturer. Test results were interpreted as ratio of the sample OD 450nm and cut –off value according to the following criteria given by the manufacturer.

Volume 6, Issue 1; January-February 2023; Page No 31-38

S/CO	INTERPRETATION
< **0.9**	Negative
0.9 -1.1	Equivocal
> 1.1	Positive

All the positive and equivocal samples were retested in duplicates and results were recorded. The results were analyzed using Epi Info version 7.2

Results

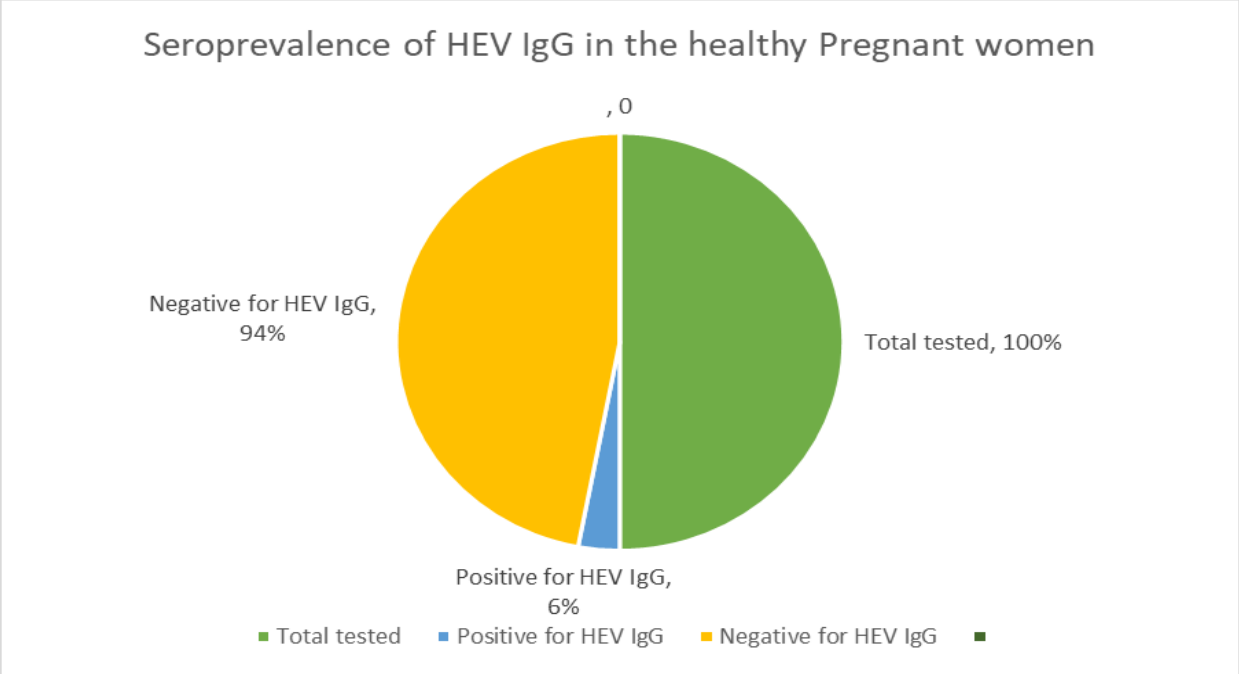
Table 1: Demographic characters and clinical status of the pregnant women

Variables	Subject (n=200)	Positive for IgG HEV (n= 12)
Age		
Mean ± SD Range	26.6 ± 3.8	26.6
	20 -41	23 -30
Live in		
Rural	40(20%)	2 (17%)
Urban	160 (80%)	10 (83%)
Socioeconomical satus		
High	5 (2.5%)	0
Middle	146(73%)	10(83%)
Low	49 (24%)	2(17%)
Education		
Literate	168(84%)	10(83%)
Illiterate	32 (16%)	2(17%)
Water source		
Can water/Aquaguard Pipe water	160 (80%)	10 (83%)
	30(15%)	2(17%)
Well water	10 (5%)	0
Sanitation		
Open defecation	0 (0%)	0
Closed system	200 (100%)	12 (100%)

Volume 6, Issue 1; January-February 2023; Page No 31-38

Parity		
Primigravida	150(75%)	12 (100)
Multigravida	50 (25%)	0
Gestational age		
1st Trimester	36(18%)	0
2nd Trimester	60 (30%)	0
3rd Trimester	104 (52%)	12(100%)
H/O Blood transfusion		
Yes	14(7%)	0
No	186 (93%)	
H/O Bad Obstetric history		0
Yes	18 (9%)	
No	182 (91%)	

Chart 1: Seroprevalence of (IgG) Hepatitis E virus in the healthy pregnant women



Volume 6, Issue 1; January-February 2023; Page No 31-38

Table 2: Seroprevalence of anti-hepatitis E virus IgG in India and other countries

Author	Year	Place	Total samples studied	Prevalence (%)	Population
Khuroo et al (26)	1994	Kashmir	40	5	Asymptomatic healthy children
Arankalle et al (17)	1995	Pune	1602	23.62	Healthy general population
Aggarwal et al (18)	1997	Lucknow	95	59.25	Asymptomatic general population
Das et al (27)	2000	New Delhi	500	35.6	General population sporadic AVH
Mathur et al (12)	2001	New Delhi	2070	26.25	Children with minor, non-hepatic illness
Mohanavalli et al (16)	2003	Chennai	185	8.6	Healthy children
Daniel et al (13)	2004	New Delhi	600	5.62	Blood donors, antenatalwomen, and individuals negative for HBsAg and Hepatitis c Virus antibody
Begum et al (14)	2009	New Delhi	300	33.67	Asymptomatic pregnant women
Andrew AA et al (28)	2009	Ghana	157	28.66	Asymptomatic pregnant women
Yahia et al (29)	2011	Egypt	116	46.7	Asymptomatic pregnant women
El- shety et al (30)	2014	Egypt	100	45	Asymptomatic pregnant women
Mamani et al (19)	2015	Iran	1050	7.4	
SivaSangeetha et al (15)	2016	Chennai	180	14	Asymptomatic pregnant women
Present Study	2017-2019	South Chennai	200	6	Asymptomatic pregnant women

The total participants of our study were (n=200). The mean age of our participants was 26.6± 3.8 and range was 20- 41years. The parity of our study population at the time of sample collection was primigravida (75%) and multigravida (25%). The gestational age of our study subjects was in 1st trimester (18%), 2nd trimester (30) and 3rd trimester (52%). Majority of the study subjects were belonged to middle class (73%) and 84% were Literate. **(Table - 1)** The prevalence of anti HEV IgG antibody was found in 12 out of 200 samples (12/200) (6%). **(Chart - 1)** The drinking water sources commonly used by the participants were water-can water (80%), pipe water (15%) and well water (5%). None of the pregnant women were using open sanitary practices. All (100%) have been using closed system of sanitation. The participants

Volume 6, Issue 1; January-February 2023; Page No 31-38

received blood transfusion was only (7%) and none of them were positive for anti HEV IgG. The bad obstetric history was observed in 18 pregnant women (9%) and they were negative for HEV IgG antibody. **(Table -1)** All the positive pregnant women (100%) of our study were primigravida and in third trimester. Among twelve positive subjects, (83%) were urban dwellers, belongs to middle class and they were literate. **(Table - 1).**

Discussion

HEV infection occurs either as an epidemic or in a sporadic form. It is an enterically transmitted, causing self-limiting acute viral hepatitis but severe infection with high mortality is observed in the pregnant women. It causes many outbreaks in the developing countries where personal hygiene and sanitary practices are poor. Detection of IgG antibody to HEV in healthy subjects has been used as a seroepidemiological tool to measure exposure to the virus. In developed countries, circulating antibodies to HEV have been present in smaller percentages, whereas in developing countries like India, the prevalence rates are higher with extensive variations in different regions. (Table - 2) The prevalence rate of anti-HEV IgG in our study is 6% (12/200) in pregnant women, which is very less in comparison to other studies in India like in New Delhi (33.67%), (14) Chennai (14%) (15). The study by Begum et al (14) New Delhi, stated that their study was done only in a primigravida with a higher prevalence rate, which is consistent with our study where all the positive cases were primigravida (100%). Also, the gestational age was analyzed with the seropositive rates and many studies showed higher rates in the third trimester, followed by the second and first trimesters. But on contrary, Begum et al, (14) affirmed that pregnant women are susceptible to HEV infection in early pregnancy. In our study, all positive subjects were in the third trimester.

The study by Siva Sangeetha et al (15) in Chennai, conducted in the same state like our study but in a different area, reported that the higher prevalence (14%) is attributed mainly to the water sources i.e., most of the pregnant women did not have drinking water facility, consumption of untreated water and many were non-vegetarians. We differ in these factors, as 83% of the positive cases (10/200) were using treated drinking water and closed sanitation practices.

A seroprevalence study done in southern states of India, more than a decade before, showed a less prevalence rate in the general population including children. The prevalence rates were 5.6% and 8.6 % by Daniel et al (13) and Mohana Valli et al (16) respectively. In converse, the seroprevalence of anti-HEV IgG was higher in northern states like New Delhi, Pune, and Lucknow at 35.6%, 23.62%, and 63% among the general population including both adults and children. (12, 17,18) Also, they conveyed that the higher the age, the more seropositivity was observed. In our study, the age ranges from 23-30 years among positive cases. (Table - 2)

Regarding the place of residence, urban dwellers showed a higher prevalence rate than rural residents in many studies. (13,14,16,19) This is like our study, where 10 out of 12 were from the urban city. But the study by Cevrioglu et al (20) reported a significant correlation between rural residence and higher anti-HEV positive values. Also, similar findings were observed by Stoszek et al (21) and they hypothesized that both zoonotic and anthroponotic transmission of a virulent (genotype3) strain of HEV has been occurring extensively in the villages. This emphasizes the need for extensive studies in rural, urban slums and urban cities simultaneously to make out the accurate exposure rates.

The blood and blood products are also capable of transmitting the viral infections and many healthy donors showed seropositivity to HEV. (22) But in our study, none of the positive cases have received any blood transfusion. The same findings were given by Khameneh RZ et al. (23)

The reason for the lower prevalence rate in southern states of India was analyzed from different perspectives. HEV is found to be excreted in low concentrations. (24) This factor could contribute to the lower efficiency of transmission of HEV, thereby lowering the seroprevalence of HEV in our region. Moreover, IgG antibody to HEV disappeared within 6- 12 months after they recovered from the disease. (25) The rapid decay of the level of antibodies IgG to HEV can also be a reason for the low prevalence of IgG in our region. Besides, the low seroprevalence rate may be due to the usage of safe drinking water and close sanitary practices in the majority of the

Volume 6, Issue 1; January-February 2023; Page No 31-38

participants of our study. But the widespread sanitary conditions in many urban slums and rural areas are far-off from satisfactory. Though there have been no major epidemics of HEV reported from southern states of India, it is anticipated that the water sources and sanitation of this region would aid the spread of these viral diseases i.e. feco–oral route.

Seropositivity has been underestimated owing to the rapid clearance of antibodies and this demands imperative considerations for vaccine implementation to avoid major outbreaks in the future. Nevertheless, before the execution of vaccination strategies, a critical call for the evaluation of circulating strains of HEV in south India is obligatory. Further extensive studies with low costs Immunoassays and molecular epidemiologic studies will help in localizing the loci of the spread of infection in this population.

Conclusion

The seroprevalence rate of anti-HEV IgG among pregnant women in our region is 6% (12/200). The prevalence rate is very low when compared to the other regions of our country. This indicates better sanitation practices, safe water supplies, and effective health system in south Chennai. The lack of protective antibodies warrants a vaccine to evade a potential HEV epidemic. Further studies are required with a higher sample size involving both urban and rural areas.

References

1. Khuroo MS, Khuroo MS. Hepatitis E: An emerging global disease – From discovery towards control and cure. J. Viral Hepat 2016; 23: 68-79.
2. Khuroo MS. Discovery of Hepatitis E: The epidemic non –a, non – b hepatitis 30 years down the memory lane. Virus Res 2011; 161:3-14.
3. Khuroo MS. Hepatitis E virus: Another addition to the existing alphabet of human hepatitis viruses. Ann Saudi Med 1996; 16:308-19.
1. 4. World Health Organisation. Viral hepatitis. Available from: URL:http//apps.who.int/gb/ebwha/pdf_files/A62/A62_22-en.pdf.
4. Vijay Kumar, Saumitra Das, Shahid Jameel. The biology and pathogenesis of hepatitis viruses. Current Science 2010; 98:10.
5. Aggarwal R. Hepatitis E and pregnancy. Indian J Gastroenterol 2007; 26: 3-5.
6. Khuroo MS. Study of an epidemic of non – A, non-B hepatitis possibility of another human hepatitis virus distinct from post transfusion non –A, non – B type. Am J Med 1980; 68:818 – 23.
7. Guthmann JP, Klovstad H, Boccia D etal. A large outbreak of hepatitis E among a displaced population in Darfur, Sudan, 2004 the role of water treatment methods.Clin Infect Dis 2006; 42: 1685 -91.
8. Labrique AB, Sikder SS, Krain IJ, West KP, Christian P, Rashid M etal. Hepatitis E, A vaccine preventable cause of maternal deaths. Emerg Infect Dis 2012; 18:1401- 04.
9. Dahiya M, Kumar A, Kar P, Gupta RK, Kumar A. Acute viral hepatitis in third trimester of pregnancy. Indian J Gastroenterol 2005; 24:128- 9.
10. Kumar A, Beniwal M, Kar P, Sharma JB, Murthy NS. Hepatitis E in pregnancy. Int J Gynae Obsts 2004; 85:240 - 44.
11. Mathur P, Arora NK, Panda Sk, Kapoor Sk, Jailkhani BL Irshad M. Sero -epidemiology of hepatitis E (HEV) in urban and rural children of north India. Indian Pediatr 2001; 38:461-75.
12. Daniel DH, Warier A, Abraham P, Sridharan G. Age-wise exposure hepatitis E virus in a southern Indian patient population without liver disease.AmJ Trop Med Hyg 2004;71:675-78.
13. Begum N, Devi GS, Husain AS, Kumar A, Kar P. Seroprevalence of subclinical HEV infection in pregnant women from north India: A hospital-based study. Indian J Med Res 2009; 130:709-13.
14. SivaSangeetha K, Geethalakhsmi S,Thatchinamoorthy G, Gouthami P, Jacob M. Seroprevalence of hepatitis E virus infection and their associated risk factors in pregnant women in Chennai, Tamilnadu. Open forum Infectious Diseases 2016; 3:423.
15. Mohanavaalli B, Dhevahi E, Menon T, Malathi S, Thyagarajan SP. Prevalence of antibodies to hepatitis A and hepatitis E virus in urban

Volume 6, Issue 1; January-February 2023; Page No 31-38

school children in Chennai. Indian Pediatr 2003; 40:328 - 31.
16. Arankalle VA, Tsarev SA, Chadha MS, Alling DW Emerson SU, Banerjee etal. Age –specific prevalence of antibodies to hepatitis A and E viruses in Pune, India, 1982 and 1992. J Infect Dis 1995; 171:447-50.
17. Aggarwal R, Shahi H, Naik S, Yachha Sk, Naik SR. Evidence in favour of high infection rate with hepatitis E virus among young children in India. J Hepatol 1997; 26:1425-26.
18. Mamani M, Zamani M, Hashemi HS, Keramat F. Seroprevalence of antibodies to Hepatitis E virus among pregnant women. Avicenna J clin Microb Infect 2015;2: e25339
19. Cevrioglu AS, Alrindis M, TanirHM, Aksoy F. Investigation of the incidence of hepatitis E virus among pregnant women in Turkey. J obstet Gynaecol Res 2004; 1:48-52.
20. Stoszek SK, Abdel – Hamid M, Saleh DA, El Kafrawy S, Narooz S, Hawash Y etal. High prevalence of hepatitis E antibodies in pregnant Egyptian women. Trans R Soc Trop Med Hyg 2006; 100:95-101.
21. Khuroo MS, Khuroo MS, Khuroo NS. Transmission of Hepatitis E Virus in Developing Countries. Viruses 2016; 8:253.
22. Khameneh RZ, Sepehrvand N, Khalkhali RH. Seroprevalence of Hepatitis E among Pregnant women in Urmia, Iran. Hepat Mon 2013; 13: e10931.
23. Ticehurst J, Popkin TJ, Bryan JP, Innis BL, Duncan JF, Ahmed A etal. Association of Hepatitis E virus with an outbreak of hepatitis in Pakistan: serologic responses and pattern of virus excretion. J Med Virol 1992; 36:84-92.
24. Goldsmith R, yarbough PO,Reyes GR, Fry KE, Gabor KA,Kamel M. Enzyme – linked immunosorbant assay for diagnosis of acute sporadic hepatitis E in Egyptian children.Lancet 1992;339:328-31.
25. Khuroo MS, Rustgi VK, Dawaon GJ, Mushahwar IK, YattooGN, Kamil S etal. Spectrum of hepatitis E virus infection in India. J Med Virol 1994; 43:281-86.
26. Das K, Agarwal A, Andrew R, Frosner GG, Kar P. Role of hepatitis E and other hepatotrophic virus in etiology of sporadic viral hepatitis virus in etiology of sporadic acute viral hepatitis: A hospital based study from urban Delhi. Eur J Epidemiol 2000; 16:937-40.
27. Andrew AA, Tettey Y, Aviyase TJ, Adu – Gyamfi CA, Obed S, Mingle JAA, etal. Hepatitis E virus infection is highly prevalent among pregnant women in Accra, Ghana. Virology journal 2009; 6:108.
28. Yahia Z, Mousa N, Shams M, Elewa A. Seroprevalence of subclinical HEV infection in asymptomatic apparently healthy, pregnant women in Dakahlya Governorate, Egypt. Asian J Transfus Sci 2011; 5:136-39.
29. El-Shety GA, Ali IA, Hammad SK, Kelany FY, Mostafa MT, Ali SM. Seroprevalence of subclinical Hepatitis E infection among pregnant women in rural Egyptians areas. AAMJ 2014; 12:162-76.

Volume 6, Issue 1; January-February 2023; Page No 31-38