



SEROPREVALENCE AND RISK FACTORS OF HEPATITIS E AMONG WOMEN OF REPRODUCTIVE AGE

Microbiology

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ABSTRACT

Background: Hepatitis E virus (HEV) is a major public health problem in developing countries and often fatal among pregnant women in the third trimester. And there is dearth of information about its prevalence among the women of reproductive age. **Objectives:** The aim of this study was to elucidate the prevalence, risk factors and pattern of HEV infection among the population of women of reproductive age. **Methods:** This descriptive-analytical study was conducted cross-sectionally on women of reproductive age who had visited the Shree Guru Gobind Singh Tricentenary Hospital located in Budhera, Gurugram during 2021 to receive routine cares. Data collection tool was a researcher-made questionnaire with items on participants' demographic characteristics, medical history, pregnancy profile, and source of drinking water. A blood sample was obtained from each participant and the titer of anti-HEV IgG was measured through the enzyme-linked immunosorbent assay (ELISA). Data were analysed using the SPSS software (v. 16.0). **Results:** This study was conducted on 150 women with an age mean of 31.1 ± 8.9 . The titer of anti-hepatitis E immunoglobulin G was positive in cases (36%). The prevalence of anti-HEV IgG seropositivity had no significant relationships with pregnancy and marital status, while it had significant relationships with the place of residence ($OR = 4.73$) and the source of drinking water ($P < 0.001$). To top it all Hepatitis E anti IgG was significantly lower with women of higher education level ($P = 0.004$) and significantly higher among the older extremes of age ($P = 0.018$). **Conclusions:** By the study finding the seroprevalence of hepatitis E is affected by educational level and residence. Hepatitis E virus infection was found to be related to personal, water and environmental hygiene.

KEYWORDS

Hepatitis E, Seroprevalence, Women, Public health, Reproduction

INTRODUCTION

Hepatitis E virus is a non-enveloped, positive sense single stranded virus of RNA genome. It causes the disease Hepatitis E which is a quite common cause of acute viral hepatitis among adults in India. The Human HEV, virus a member of family *Herpesviridae* and genus *Orthohepevirus*. In India the first case was discovered in New Delhi in 1955.^[1] The global epidemiology in terms specific for Hepatitis E indicates about 20 million new cases of hepatitis E virus (HEV) infections occur each year which includes 3.3 million asymptomatic cases. The most common mode of HEV transmission is a water and food-borne and it can lead to potential acute outbreaks with poor sanitation.^[2] Other modes of transmission which are document are zoonotic and transfusion-related transmission^[3]. Hepatitis E virus has four main genotypes (GT1-GT4). Amongst these humans are infected by GT1 and GT2, whereas GT3 and GT4 are naturally present in several mammalian animals such as pigs, and infrequently zoonotic transmission to humans.^[4]

The various genotypes have well defined geographical distributions and they have specific routes of transmission along with clinical scope of disease. That being the case the clinical and epidemiological features of infections caused by HEV in India are quite varied as compared to the developed nations like Europe & North America as the circulating genotype there is GT3, and in the East GT4 is more prevalent.^[4,5] In India, hepatitis E is solely caused by GT1 HEV, whether occurring in epidemic form^[6] or as sporadic cases.^[7] Clinical manifestation of HEV infection are nominal in the general population but can pilot to mortal conditions in immunocompromised patients, pregnant women, organ transplant recipient patients.^[8] The infections are self-limiting in nature and furthermore does not lead to chronic hepatitis or carrier stage. Pregnant women carry a substantial risk to advance to acute liver failure in contrast to non-pregnant females with hepatitis E.^[9] In computation, 20% - 25% of the cases, it can proceed to the unexpected death of the mother due to renal failure. Other complexity of HEV infection include fetal death, miscarriage, premature infant, and neonatal death.^[11] Hepatitis E infection notably with genotype 1, in the third trimester of pregnancy leads to is associated with more brutal infection and might progress to fulminant hepatic failure steering to maternal death.^[9] The maternal mortality rate in the above case is found to be around 15% to 25%^[10]. The definite mechanism of unreasonable severe liver injury in pregnant females is not yet explained, it is plausible that interaction of various hormonal and immunologic changes during pregnancy, along with a high viral load of HEV, exhibit the pregnant female more endangered. During pregnancy there is suppression of T-cell immunity because of the immunological changes to promote the preservation of the fetus in the maternal

environment, which exposes the pregnant female to HEV infection and in addition, the levels of the hormones such as progesterone, estrogen, and human chorionic gonadotropin rise as pregnancy advances creating an imbalance in the immune system and increase in viral replication.^[11] Although India is reported to be an endemic country for HEV, data on the prevalence of HEV infection among pregnant women is deficient and the epidemiology of HEV is not well defined in major parts of the country^[12,13]. Therefore, this study was conducted to elucidate the prevalence, risk factors and pattern of HEV infection among the population of women of reproductive age.

3. MATERIALS AND METHODS

This descriptive-analytical study was conducted cross-sectionally on women of reproductive age who had visited the Shree Guru Gobind Singh Tricentenary Hospital located in Budhera, Gurugram during 2021 to receive routine cares. The sample size was calculated using the following formula: $S = Z^2 \times P \times (1-P) / M^2$

Where, $Z = 1.96$ (for 95% confidence level) $P =$ Prevalence rate and $C = 10\%$ (Confidence interval) Using the convenience sampling method, the study subjects were selected from among women of reproductive age who visited the Obstetrics and Gynaecology Out Patient Department of Shree Guru Gobind Singh Tricentenary Hospital.

The inclusion criteria of the study included females of reproductive age group (15-49 years) with informed consent to participate in the study and visiting the clinic due to problems associated with women's health except for females presenting with acute signs and symptoms of hepatitis. The data involving the demographics such as age, place of residence, education level, occupation, and risk factors associated with hepatitis E (education level, place of residence, and type of drinking water) were collected by trained medical students. Afterwards, 5ml blood samples were taken from the cubital vein in a plain vial maintaining proper septic techniques. All the samples were allowed to clot for 45 minutes and blood was centrifuged for 15 minutes, at 3000rpm for separation of serum and stored at 2-8°C.

Then, the titer of the anti-HEV IgE was measured using a third-generation ELISA Kit manufactured by the DIA.PRO Diagnostic Bioprobe Srl, Sesto San Giovanni (Milano) Company. The collected data were analysed using SPSS-16 software by independent *t*-test. Further, odds ratios were estimated by the logistic regression model at a significance level of $\alpha = 0.05$. The ethical protocol of the research was approved by Institutional Ethical Committee of the university with ethics code SEC/FMHS/M.Sc/15/06/21-64.

RESULTS

In this study, 150 women of reproductive age with the mean age of 31.1 ± 8.9 were recruited in the study. The minimum age of the participants was 15 and the maximum age was 49. A total number of 20 subjects (13%) were pregnant and the rest were not. The prevalence of positive anti-HEV was determined as 36% ($n = 54$). The average age of women positive for hepatitis E infection was 33.5 ± 7.2 and the same for hepatitis E negative infection was 30.8 ± 6.9 . There was not much of a significant difference observed in the age of HEV positive and negative women ($P = 0.18$) acquiring hepatitis E infection was seen more in rural women around 4.73 times more as compared to the women habitating in urban areas. This difference was evident and statistically significant (Table 1). To include more factors, education also played an important role as higher education reduced the chance of acquiring HEV significantly in relation to illiterate subjects. Notably, the difference was also seen with division of education as college education reduced the chances further to primary level of education. The subjects who used untreated water were more likely to contract this disease as compared to subjects who consumed tap water.

DISCUSSION

In this study, the prevalence of HEV in women residing in peri-urban region of Gurugram district of Haryana who were within their reproductive age was 36% indicating the valuable presence of HEV in the study space. Having compared the results of the study with previous studies conducted, it had been ascertained that the prevalence of hepatitis E was higher in girls of reproductive age than within the general population (25%).^[14]

An identical study conducted in Iran reported the prevalence of positive anti-HEV as 11.7% among the women in reproductive age population.^[14] India as a developing country is endemic for hepatitis E. In an exceeding study conducted on Indian women within the northern region the seroprevalence of HEV was 33%^[15] that is sort of within to vary of our study. Most studies conducted in women in Iran and alternative elements of the globe have concentrated on pregnant women. The seroprevalence of anti-HEV was reported as 3.6%, in a study performed in Urmia.^[16] Also, the seroprevalence of HEV in pregnant females in the Ahvaz and Hamadan was reported as 5.2% and 7.4%, severally.^[12,17] In similar studies conducted in Gorgan and Isfahan, in women of fertility age the prevalence of anti-HEV was found as 6.3% and 4.2%, respectively.^[18, 19] Altogether of on top of declared studies, the prevalence of hepatitis E in women of reproductive age it had been less than the prevalence ascertained in our study. However, the prevalence is lower than the studies who reported 47.4%, 45% and 37% respectively in alternative parts of India. This disparity could be due to factors like degree of endemicity of HEV, socioeconomic standing additionally as variations within the hygienic conditions, availability of safe water resources, and healthful disposition within the regions beneath study.^[20]

In the present study, HEV positive subjects were younger than their HEV negative counterparts, and this distinction was statistically significant. Numerous studies by Stoszek et al. and Cevrioglu et al. observed that age encompasses a reference to the positive serology of HEV the link between age and also the positive serology of HEV will be a symbol of relationship between contact an infection.^[21]

Another space investigated during the study was the literacy level of the subjects. The results of the study revealed that the rate of prevalence of HEV infection declines with a rise in education level. This is in concurrence with most researches where women with tertiary educational status have the lowest seropositivity. This may be connected with the result of education and its influence on the practice and compliance to personal and environmental hygiene.^[22]

In addition, the results of this study suggested that there was a significant relationship between nature of drinking water, positive serology was also higher in subjects who consumed untreated water. In a study conducted in India and research performed by Cevrioglu et al., there was a significant relationship between the kind of drinking water and positive serology^[23,24] which was analogous to our study.

However, a research in Turkey observed a significant relationship between residence in cities and higher prevalence of anti-HEV.^[23] The components for such discrepancy may be the employment of unsafe water, particularly in rural areas, at the side of less hygiene and also the incompetent health system. In summation, the geographical conditions of the region and the season of sampling can be some other alternative

reasons for nonuniformity between the present study and other studies performed.

In the study we observed a significant association between socioeconomic status and HEV seropositivity, in order that pregnant women with low socioeconomic status tended to be more positive for HEV infection which was in concordance with some studies from Turkey and other parts of India^[21,22]

Hepatitis E is an crucial reason behind morbidity and mortality throughout pregnancy. The incidence of HEV in pregnant women all round the world was reported as 45% - 50%.^[24] The mechanism of hepatitis in pregnancy is not well understood. There are multiple factors resulting in liver damage in pregnancy associated with HEV. The steroid hormones are on the rise in pregnancy leading to a state of immune suppression and escalate virus multiplication. In inclusion to the above factors they even have an immediate inhibition on hepatocytes leading to liver disfunction and inhibiting its capability to fight numerous infectious agents. Meanwhile, the augment of pregnancy hormones such as of estrogen, progesterone, and HCG causes reduction in T-cell inflicting Th1 falling and Th2 rising and virus multiplication.^[25]

Additionally as declared on top of, HEV is prevalent in women who have low economic- social station or board in regions with low hygiene. In this respect, the change in immune status early in pregnancy at the side of malnutrition can be some of the dominant reasons.^[24] The seroconversion rate in the study was 60% in pregnant females (12/20) while it was 32% in non-pregnant females (54/130) which shows the seroprevalence is significantly higher in pregnant females in the reproductive age groups. Studies have shown that in India, HEV infection in pregnant females is associated with 60% chances of adverse maternal and foetal outcomes. Among these pregnant females the rate of fulminant hepatitis was 55% and this is 2.7 times higher as compared to HEV in non-pregnant females where this incidence is only 20%.^[26]

The unlike outcome of prevalence of HEV in different regions may be due to immunity, exposure to virus since childhood and most significantly the circulating genotype in various geographical regions leading to different virulence. The mortality in regards with HEV infection in pregnant women is high due to the hormonal changes during pregnancy and subsequent immunological changes.^[27] However, in this study outcome analysis was not performed since the study pertained concerning the seroprevalence of HEV.

CONCLUSION

HEV infection throughout pregnancy could be a health plight, However, a lot of time this importance is forsaken perhaps because of atypical observations on Hepatitis E complications among pregnant women in various geographical distribution over world. HEV surveillance in the whole wide world is required in order to provide significant public health recommendations and to reach an unanimity on this infection during pregnancy. The present findings suggest a high burden of HEV infection in pregnancy and the risk factors associated with it. In this study, there was a significant distinction in pregnant and non-pregnant women concerning the prevalence of HEV, it is steered that more studies be conducted with larger sample sizes. The strength of this work was investigating the serology of hepatitis E in both pregnant and non-pregnant women. The limitation of this study was not performing the molecular analysis of the samples.

Authors' contributions:

All the authors were involved in designing the study protocol and data analysis and interpretation; Ms Gimmi collected the data. Dr Ashima & Dr Manisha and wrote & revised the manuscript. All authors contributed to and read and accepted the final manuscript.

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Conflicts of interest: None declared.

Ethical approval: The study protocol was approved by the Institutional Ethical Committee of the university with ethics code SEC/FMHS/M.Sc/15/06/21-64 India and all participants gave written informed consent.

Table 1. The Chance of Contracting HEV Based on the Pregnancy Status, Education Level, the Type of Drinking Water and sanitation practices in Women Under Study

Variable name/ HEV	Positive frequency(p percentage)	Negative frequency(p percentage)	OR (95% C.I)	P Value
Pregnancy status				0.016
Pregnant	12(60)	8(40)	1.1 (0.55 - 2.21)	
Non pregnant	42(32)	88(68)	1	
Education level				0.01
College	16(10)	134(89)	1	
Primary school	37(25)	125(83.3)	3.01 (1.21 - 7.5)	
High school	31(21)	119(79)	1.54 (0.59 - 3.99)	
Illiterate	66(44)	85(57)	163.5 (40 - 667.9)	
Drinking water				0.0003
Municipal water	10(45)	12(55)	312 (95.6 - 1018.4)	
Filtered water	16(21)	61(79)	1	
Tube well water	28(55)	23(45)	163.5 (40 - 667.9)	
Sanitation practice				0.752(NS)
Personal toilet	53(37)	92(63)	1	
Public toilet	1(20)	4(80)	1.1 (0.55 - 2.21)	

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