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## Anti-Hev Antibody Prevalence in Three Distinct Regions of Turkey and its Relationship with Age, Gender, Education and Abortions\*

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**Abstract:** Hepatitis E virus (HEV) causes epidemics in developing countries such as India, Burma, Indonesia, Chad and China, but it causes sporadic cases in developed countries such as the U.S.A., Canada and the U.K. Turkey represents a bridge between HEV endemic and non-endemic areas, and HEV may cause epidemics in Turkey. In this study, the prevalence of HEV in three distinct regions of Turkey and its relationship with age, gender, education and abortions was investigated.

Nine hundred ten randomly selected cases from three cities in three geographic regions of Turkey (Manisa from the Aegean region, Elmadağ/Ankara from Central Anatolia and Diyarbakır from Southeastern Anatolia) were enrolled in the study. After informed consent was obtained, the subjects completed a detailed questionnaire including questions about age, sex, education, and the number of

pregnancies, abortions, stillbirths and live babies, and if there was a history of abortion from icteric pregnancy. We researched anti-HEV antibodies in the serum samples of subjects using ELISA.

The overall anti-HEV antibody seroprevalence rate was 6.3% (57/910). It was 2.7% in Elmadağ/Ankara, 3.8% in Manisa and 11.7% in Diyarbakır. There was a significant difference between Diyarbakır and the other two regions ( $p < 0.0001$ ). No significant difference was observed between the other parameters.

In conclusion, the overall anti-HEV antibody seroprevalence rate was 6.3% and these rates increased with age.

**Key Words:** Anti-HEV antibody, epidemiology, age, gender, education and abortion

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### Introduction

Hepatitis E virus (HEV) was first defined in an experimental infection model by I.V. infusion of feces filtrate of acute hepatitis cases caused by non-A non-B hepatitis viruses in 1983. It is a member of the Caliciviridae. It used to be called non-A, non-B hepatitis (NANBH) virus but developments in serological tests implied that there were at least two different viruses in NANBH viruses. One of them was named the hepatitis C virus and the other the hepatitis E virus (1-4). HEV spreads via the fecal-oral route, but may spread via the transfusion or transplacental route (5-7). It has a higher mortality rate in pregnant women (4,8-10) but anti-HEV seroprevalence rates are similar in pregnant and non-pregnant women (11,12). The reason for this high mortality rate is not well defined but the incidence of DIC in pregnant women is higher than that in non-pregnant women(4).

The disease is more prevalent in young adults and in middle-aged populations and rare in children and elderly populations (4,10,13). It causes epidemics in developing countries where hygienic conditions are poor. Since the 1950s, serious epidemics originating from contaminated drinking water have been reported (4,8-10,14-32). The results of epidemiological studies in Turkey have implied regional differences in anti-HEV antibody seroprevalence rates, i.e. it was higher in Eastern and Southeastern Anatolia (11,12,21,25,33-52). The rate in Southeastern Anatolia resembles that of high endemic areas of the world, but rates in other regions resemble those of developed countries.

In this study, we investigated anti-HEV antibody seroprevalence rates in three distinct regions of Turkey and their relationship with age, gender, education and abortion.

\* presented at the Biennial Meeting of IASL-2002.

## Materials and Methods

This study was carried out between March 1 2000 and May 15 2000 in Gülhane Military Medical Academy, Department of Infectious Diseases and Clinical Microbiology and Department of Immunology. Three cities from three geographic regions of Turkey were selected: Manisa from the Aegean region, Elmadag/Ankara from Central Anatolia and Diyarbakir from Southeastern Anatolia.

From Elmadag/Ankara, 148 males and 145 females (subtotal 293); from Manisa, 120 males and 172 females (subtotal 292); and from Diyarbakir 148 males and 177 females (subtotal 325), i.e. a total of 910 randomly selected subjects, were enrolled in the study.

The subjects were given detailed information about the study and written consent was obtained. They were asked about their age, sex, profession, birth place, duration of settlement, number in the household, and source of water. Females were also asked about their number of pregnancies, children and stillbirths, and age at the first pregnancy.

A 5 ml venous blood sample was drawn from each subject and centrifuged at 2000 rpm for 5 min. Serum was separated and 1 ml serum samples were stored at  $-80^{\circ}\text{C}$  until the anti-HEV antibody test was assayed. The serum samples were thawed and the anti-HEV IgG antibody test was assayed using a commercial kit (Genelabs Diagnostics, Switzerland) by an automated EIA device (TECAN, Italy) according to the manufacturer's manual.

The statistical analysis of the results was performed by chi-square test using SPSS.

## Results

Similar numbers of males and females were chosen, and there was no significant difference between the anti-HEV antibody seroprevalence rates of subjects grouped according to sex ( $p > 0.05$ ). Anti-HEV antibody seroprevalence rates in terms of certain conditions are given in the Table.

The overall anti-HEV antibody seroprevalence rate was 6.3%. There was a significant difference between the anti-HEV antibody seroprevalence rate found in Elmadag/Ankara and that in Diyarbakir and also between Manisa and Diyarbakir ( $p < 0.0001$ ), but there was

no difference between Elmadag/Ankara and Manisa ( $p > 0.05$ ).

There was a positive correlation between age and anti-HEV antibody positivity. There was significant difference between the 7 to 14 age group and the 25 to 64 age group ( $p < 0.01$ ) and between the 15 to 24 age group and the 25 to 64 age group ( $p < 0.05$ ) when anti-HEV antibody seroprevalence rates of age groups were compared.

When we compared anti-HEV antibody seroprevalence rates of subjects grouped according to their duration of education, there was no significant difference between the groups ( $p > 0.05$ ).

When we compared anti-HEV antibody seroprevalence rates versus duration of settlement, there was no significant difference between the groups ( $p > 0.05$ ).

For female subjects there was no significant difference between the parameters related to pregnancy ( $p > 0.05$ ).

When we compared anti-HEV antibody seroprevalence in terms of source of water, there was no significant difference between the groups ( $p > 0.05$ ).

## Discussion and Conclusion

HEV causes epidemics, especially in developing countries where hygiene is poor and many affected pregnant women suffer from fulminant hepatitis(8).

In our study, the anti-HEV antibody seroprevalence rate was 6.3% (57/910). In Turkey, the anti-HEV antibody seroprevalence rate varies from 3% to 34% in the literature (11,12,34,36,37,42,43,46,48). Aydın et al. (12) found an anti-HEV antibody seroprevalence rate of 3.0% in their 100-case study carried out in Trabzon. Özacar et al. (43) found a rate of 3.5% in their 112-case study in İzmir. Yavuz et al. (46) found a rate of 4.3% in their study of 91 health care workers (HCWs) in Van.

In three large-scale studies, serum samples were collected from different regions of Turkey. In a study (1580 cases) by Badur et al. (37) in four provinces of Turkey, they found an anti-HEV antibody seroprevalence rate of 5.3%. This rate was very close to our result. Another study was carried out by Thomas et al. (36). It was a 1350-case study including samples from İstanbul, Aydın, Ayvalık and Trabzon; the anti-HEV antibody seroprevalence rate was 5.9%. The third largest scale study was performed by Çetinkaya et al. (38) on 1351

Table. Anti-HEV Antibody Seroprevalence Rates.

CONDITIONS	Anti-HEV Antibody		
	Positive (n/%)	Negative (n/%)	
TOTAL (n = 910)	57 / 6.3	853 / 93.7	
Regions	Elmadağ/Ankara n = 293	8 / 2.7	285 / 97.3
	Manisa n = 292	11 / 3.8	281 / 96.2
	Diyarbakır n = 325	38 / 11.7	287 / 88.3
Professions	Student n = 183	4 / 2.2	179 / 97.8
	Civil Servant and Worker n = 296	22 / 7.4	274 / 92.6
	Health Care Worker n = 42	5 / 11.9	37 / 88.1
	Retired, Housewife n = 389	26 / 6.7	363 / 93.3
Age groups	7 to 14 n = 123	2 / 1.6	121 / 98.4
	15 to 24 n = 209	7 / 3.3	202 / 96.7
	25 to 64 n = 548	45 / 8.2	503 / 91.8
	Over 65 n = 30	3 / 10.0	27 / 90.0
Educational Characteristics	Uneducated n = 131	15 / 11.5	116 / 88.5
	8 years of education n = 439	21 / 4.8	418 / 95.2
	9 to 11 years of education n = 234	15 / 6.4	219 / 93.6
	Over 12 years of education n = 106	6 / 5.7	100 / 94.3
Duration of Settlement	0 to 5 years n = 247	12 / 4.9	235 / 95.1
	6 to 10 years n = 180	11 / 6.1	169 / 93.9
	11 to 20 years n = 217	10 / 4.6	207 / 95.4
	Over 21 years n = 266	24 / 9.0	242 / 91.0
Sources of Water	Network n = 869	54 / 6.2	815 / 93.8
	Well n = 41	3 / 9.3	38 / 92.7

healthy blood donors. The anti-HEV antibody seroprevalence rate in this study was 7.6%.

According to the results of these three large-scale studies and our study, the seroprevalence rate in Turkey may be considered to be 5% to 8%.

In the medical literature, no HEV epidemic has been reported from Europe, the developed countries of Asia, the U.S.A. or Canada. However, sporadic cases from the U.S.A., Italy, the U.K. and Australia have been reported; these patients had a history of travel to high endemic areas.

The anti-HEV antibody seroprevalence rate in healthy subjects and blood donors was 1.1% in Holland (53), 1.7% in Italy (54), 0% to 7.3% in Germany, 9.1% in Mexico, 2.3% in Wisconsin, and 4.4% in Alaska (55,56). In Spain, the anti-HEV antibody seroprevalence rate was 3.9% in a 863-blood donor study and in the same study it was 5.5% in 90 immigrants from sub-Saharan Africa (57). In a 374-case study from Mexico this rate was 10.5% (58). In a study performed in a low socioeconomic region of Brazil, the anti-HEV antibody seroprevalence rate was 2.6% in HCWs and 3% in blood donors (59).

Turkey has a lower anti-HEV antibody seroprevalence rate than developing countries but a higher rate than developed countries.

The anti-HEV antibody seroprevalence rates of the regions included in our study (Elmadağ/Ankara, Manisa and Diyarbakır) were 2.7%, 3.8%, and 11.7% respectively. The results from Elmadağ/Ankara and Manisa were significantly lower than those from Diyarbakır ( $p < 0.0001$ ), but the results from Elmadağ/Ankara and Manisa were similar to each other ( $p > 0.05$ ).

The anti-HEV antibody seroprevalence rate found in Diyarbakır was 11.7%. However, in other studies from the same region, Değertekin et al. (50) in a 220-case study, Hoşoğlu et al. (48) in a 156-case study, Yükselen et al. (47) in a 34-case study, Aydın et al. (52) in a 100-case study, and Ayaz et al. (11) in a 157-case study found this rate to be 7.7%, 17.3%, 23.5%, 29% and 34% respectively.

There was a significant difference between the anti-HEV antibody seroprevalence rates in the student group and in HCWs ( $p < 0.05$ ); but the students and HCWs were not evenly distributed. There were 22 subjects from Diyarbakır in the 42-case HCWs group and only 44 from Diyarbakır in the 183-case student group. Therefore, being a HCW is not a risk factor.

Hoşoğlu et al. (48) in a 102-case study involving laboratory staff from Diyarbakır found the anti-HEV antibody seroprevalence rate to be 19.6%; our rate was 22.7%. These two results were similar.

We also found no difference in anti-HEV antibody seroprevalence rates of professional groups ( $p > 0.05$ ). This shows that profession does not affect HEV transmission.

In our study, the anti-HEV antibody seroprevalence rate increased with age. Thomas et al. (36) found an anti-HEV antibody seroprevalence rate of 3.7% in the third decade and of 9.1% in the fourth decade. The 25 to 64 age group in our study included the third and fourth decades, and the anti-HEV antibody seroprevalence rate of this group was 8.2%, similar to that found by Thomas et al. (36).

Aldeniz et al. (60) performed a 812-case study in İstanbul and the results in terms of age groups were similar to ours. Alvarez-Muroz et al. (58), Fix et al. (61), and Khan et al. (62) stated that the anti-HEV antibody seroprevalence rate increased with age.

In our study, there was no difference between the anti-HEV antibody seroprevalence rates of groups in terms of duration of education, source of water, and duration of settlement. However, Thomas et al. (36) found significant differences.

Four hundred ninety-four of our cases were female and 62 of them were pregnant at the time of venipuncture. We found no differences between the anti-HEV antibody seroprevalence rates of groups when comparing parameters related to pregnancy ( $p > 0.05$ ).

#### **In conclusion,**

1. The overall anti-HEV antibody seroprevalence rate was 6.3%: 2.7% in Elmadağ/Ankara, 3.8% in Manisa and 11.7% in Diyarbakır.
2. There was a significant difference between the anti-HEV antibody seroprevalence rate of Diyarbakır and that in the other two regions, but there was no difference between Elmadağ/Ankara and Manisa.
3. The anti-HEV antibody seroprevalence rate in Diyarbakır (11.7%) in our study was lower than the rates found in previous studies carried out in the same region.
4. There was no difference between the anti-HEV antibody seroprevalence rates of and the groups in terms of duration of education, source of water, duration of settlement, and sex, and for women the number of pregnancies, age at the first pregnancy, icterus at pregnancy, stillbirth, abortion, etc.

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