Seroprevalence and risk factors of anti- hepatitis E virus antibody among healthy population in Baquba, Diyala province

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Abstract:

Background: An increasing attention has been noticed about the human infection by hepatitis E virus, especially in countries with low socioeconomic and poor sanitary standards.

Objectives: To determine the seroprevalence of anti-hepatitis E virus (HEV) IgG antibody among healthy population in Baquba (the center of Diyala province), and to investigate the impact of certain epidemiological factors.

Materials & methods: This study was conducted in the Public Health Laboratory for the period from October/2003 to August/ 2004.Serum samples were collected from 111 apparently healthy individuals, 50(45%) were males (mean age 25.1± 5.1) years, and 61(55%) females (mean age 23.2 ± 7.9) years. Additionally, information includes age, sex, residence, source of drinking water, family history of jaundice, and contact with domestic animals were recorded by personal interview. Similarly, 20 serum samples from chicken, 37 from sheep, 10 from cattle, and 10 from goats were also collected. All human and animal samples were submitted for anti-HEV IgG antibody detection using Enzyme-linked immunosorbant assay (ELISA). Collected data were statistically analyzed.

Results: The prevalence of anti-HEV IgG among healthy population was 18%, with significantly higher positivity rate in young adults (P= 0.006). The anti-HEV IgG positivity rate was slightly higher in males compared to females (20% *vs.* 16.4%). Individuals who were in contact with domestic animals had 2 times more risk to be anti-HEV IgG positive (Odd ratio 2). Participants from rural areas had higher positivity rate compared to those from urban areas (20% *vs.* 15.7%). Anti-HEV IgG positivity rate was slightly higher in those drinking municipal water (18.7 %) compared to those used river/wells water for drinking (15%). Likewise, family history of jaundice has insignificant effect on the prevalence of anti-HEV IgG. Non of the animal sera were positive for anti-HEV IgG.

Conclusion: Seroprevalence of anti-HEV IgG among healthy population in Baquba was comparable to those documented in endemic areas.

Key wards: Seroprevalence, Hepatitis E virus, Diyala.

Introduction:

Hepatitis E virus (HEV) is the major causative agent of water borne acute viral hepatitis formerly known as enterically transmitted non-A, non-B hepatitis. HEV is generally transmitted by the fecal-oral route, although other routes were also reported [1]. It is responsible for large epidemics and sporadic infections in developing and developed countries [2] .

The disease generally affects young adults that increased by age [3]. The clinical illness is similar to other forms of acute viral hepatitis except in pregnant women, in whom illness is particularly severe with high mortality rate [4] . Subclinical and inapparent infection may occur; however, chronic infection is unlikely [5].

The prevalence of anti-HEV IgG in endemic regions has been documented to be ranged between 3%-26%, while in non-endemic regions was 1%-3% [6,7]. Screening of healthy blood donors in Central Europe and North America has shown a prevalence of anti-HEV antibodies of 1.4%-2.5%, in South Africa 1.4%, in Thailand 2.8%, in Saudi Arabia 8.3%, and in Egypt 24% [8, 9, 10]. In another study, 18% of normal blood donors from eight US states were positive for anti-HEV IgG antibody [11].

It has been found that the seropositivity rate of anti-HEV IgG among different animal species were varied from 4.4% to 6.9% in cattle, 54.6%-74.4% in pigs, 2.1%-21.5% in rodents, 22.7% in dogs, but not goats [12,13]. Further reports have documented high prevalence of HEV infection among persons with occupational exposure to swine suggests animal-to-human transmission [14,15]. Isolation and characterization of HEV from certain animals that could infect human suggest that animal reservoir may exist and provide direct evidence for the zoonotic nature of the virus [16].

Materials & methods:

The present study was conducted for the period from October/2003 to August/2004 in the Public Health Laboratory in Baquba-Diyala province. The human group consists of 111 apparently healthy individuals. The age range was 9.5-53 years. 50(45%) were males with mean age (25.1± 5.1) years, and 61(55%) females with mean age (23.2 ± 7.9) years. Special questionnaire was filled by personal interview. The information includes age, sex, residence, source of drinking water, family history of jaundice, and contact with domestic animals. The human privacy was respected by taken the participants consent.

Additionally, 20 blood samples from chickens, 37 from sheep, 10 from cattle, and 10 from goats were also included. Four to five

milliliters of blood were aspirated aseptically from each participant by vein puncture (for animals the jugular vein was used). Samples were left at room temperature to clot. Sera were separated by centrifugation at 3000 RPM for 5 minutes. Sera were deep freezed (-20 ^{0}C) till use. Anti-HEV IgG antibody was detected using Enzyme-linked immunosorbant assay (Biokit, Spain), following manufacturer instructions. All data were statistically analyses.

Results:

The results showed that the prevalence of anti-HEV IgG among the study population was 18% with a 95% confidence interval (11.5%-26.7%). The anti-HEV IgG positivity rate was significantly higher in young adults (P= 0.006), table (1).

Although the anti-HEV IgG positivity rate was slightly higher in males compared to females (20% vs. 16.4%); however, this increment was statistically insignificant (P > 0.05). Males had 1.3 times more risk as that in females and the 95% CI was (0.5%-3.4%), table (2).

Table (1): Anti-HEV IgG positivity rate by age groups.

Age (years)	No.	Anti-HEV positive	
		No.	%
> 20	23	0	0
20-29	67	15	22.4
30 +	21	5	23.8

Table (2): Anti-HEV IgG positivity rate by gender.

Sex	No.	Anti-HEV IgG positive		Odd ratio	95% CI
		No.	%		
Male	50	10	20	1.3	0.5-3.4
Female	61	10	16.4	**Reference**	

The results also showed that contact with domestic animals insignificantly affects the anti-HEV IgG positivity rate (P> 0.05). Inspite of that, individuals with contact with domestic animals had 2 times more risk to be anti-HEV IgG positive (Odd ratio = 2), table (3).

Similarly, the effect of positive family history of jaundice on the rate of anti-HEV IgG positivity was statistically insignificant (P > 0.05), table (4).

Table (3): Anti-HEV IgG positivity rate by animal contact.

Contact with domestic animals	No.	Anti-HEV IgG positive		Odd ratio	95% CI
		No.	%		
Yes	46	11	23.9	2	0.7-5.2
No	65	9	13.8	**Reference**	

Table (4): Anti-HEV IgG positivity rate by family history of jaundice.

Family history of jaundice	No.	Anti-HEV IgG positive		Odd ratio	95% CI
		No.	%		
Yes	97	17	17.5	Reference	0.3-5.1
No	14	3	21.4	1.3	

The anti-HEV IgG positivity rate among participants who reside in rural areas was higher than that among those reside in urban areas (20% vs 15.7%); however, the difference was statistically insignificant (P> 0.05). The source of drinking water was divided into rivers/ wells and municipal water. Although the anti-HEV IgG positivity rate was slightly higher in those drinking municipal water (18.7 %) compared to those used river/wells water for drinking (15%); there was insignificant difference between the two groups (P > 0.05), table (6). The results also showed that all animal sera included in this study were negative for anti-HEV IgG antibody.

Table (5): Anti-HEV IgG positivity rate by residence.

Residence	No.	Anti-HEV IgG positive		Odd ratio	95% CI
		No.	%		
Rural	60	12	20	1.3	0.5-3.6
Urban	51	8	15.7	**Reference**	

Table (6): Anti-HEV IgG positivity rate by source of water supply.

Source of water supply	No.	Anti-HEV IgG positive		Odd ratio	95% CI
		No.	%		
River/well	20	3	15	Reference	
Municipal	91	17	18.7	1.3	0.3-4.9

Discussion:

Baquba and its peripheries where the present study conducted, besides harboring a relatively high infection rate of hepatitis B and hepatitis C particularly among risk population [17], it has witnessed several episodes of acute viral hepatitis, notably the last one was due to hepatitis E virus [18,19]. Based on the current results of anti-HEV IgG positivity rate and as far as the WHO categorization this region can be considered as endemic by HEV [6]. Of note, comparable rates of HEV infection have been reported from areas ranked as endemic by HEV [7,8,9].

High rates of HEV infection are usually seen in areas with low standard of living where major contamination of water supply is likely to occur [1,20]. Probably the presence of similar conditions in Baquba City may explain the high positivity rate of HEV infection. These conditions include, low standard of hygiene, lack of proper disposal system plus unsafe water supply . Under these conditions, it seems logic, to assume that the principal source of contamination in the present study are persons with subclinical infection who shed the virus with their feces, as occurs in other endemic areas [9,21,22].

The significantly high rate of anti-HEV IgG among young adults was consistent with most studies conducted in this field [6,23,24]. The most reasonable explanation is that, because HEV is not ubiquitous in nature, as the excretion of virus in stools during acute infection is low and is often in a degraded form [3], beside that the virus is extremely labile to the unfavorable environmental conditions [5]. So, when infections occur particularly during childhood are mostly asymptomatic or mild [6,25]. In spite, HEV is unlike HAV in that the provoked immunity is short lived, and therefore reinfection is likely to occur in later life [20,26]. The results revealed an insignificantly higher infectivity rate in males compared to females. However, controversial results have been reported in the literature [5, 21,26] .

The anti-HEV IgG was insignificantly higher among rurals as compared to urbans. On the other hand, municipality has insignificantly higher risk over that of rivers/wells. It is worth to mention that several reports have documented higher HEV infection in rural communities with low socioeconomic status [9,27,28]. On the contrary, outbreaks of HEV infection have been reported in urban areas that associated with major contamination of water supply [21,29,30]. These reports indicates that contamination of drinking water by the virus weather it is occur in rural or urban areas is the principal source of HEV that leads to the appearance of clinical disease.

The insignificant effect of previous family history of jaundice on the anti-HEV IgG positivity rate may be due to the fact that HEV infection is principally a water-borne disease and that person-to-person transmission is uncommon, although viral spread by contact has been reported in some epidemics [2,9,21].

Although HEV infection has been documented in certain animal species such as pigs, sheep, cattle and rodents as well as in sewage from animal origin mainly pigs [16,29,30] ; however, evidence of high prevalence of HEV infection in persons who were in contact with animals was not available in the literature, except among those who work with swine [15,18]. The insignificant effect of animal contacts on the infectivity rate seems likely, since non of animal sera were positive for anti-HEV IgG. This may be either due to the low concentrations of anti-HEV antibodies in animal sera which are beyond the sensitivity of the utilized assay, or another HEV strain may be circulating in Iraqi animals, that are different from that used in the preparation of utilized diagnostic materials.

References:

1-Purcell, R.H. Hepatitis E virus. In: Fields B.N.; Knipe, D.M. & Howley P.M. Fields Virology. 3rd. Ed. 1996, Lippencott-Raven. 2831-43.

2-Khuroo, M.S. Hepatitis E virus: Another addition to the existing alphabet of human hepatitis viruses. Ann.Saudi Med. 1996; 16 (3): 308-19.

3-Hall, A. J. Viral hepatitis: Control, Sero-epidemiology and surveillance. Trans. Roy. Soc. Trop. Med. Hyg. 1996; 90: 1-2.
4-Krawczynski, K.; Aggarwal, R. and Kamili, S. Hepatitis E. Infect. Dis. Clin. North Am. 2000; 14 (3): 669-87.
5-Aggarwal, R.; Kini, D.; Sofat,S. and Krawczynski, K. Duration of viremia and fecal viral excretion in acute hepatitis E. Lancet, 2000; 356: 1081-2.
6-World Health Organization, Department of Communicable Disease Surveillance and Response. Hepatitis E. Series No. CDS/CSR/ EDC/ 12, 2001 Geneva, Switzerland.
7-Kaur,H.; Oberoi, A.; Chander, R.; Pawae, G. and Verma, M. Epidemiology of hepatitis E and A in Ludhiana. Trop. Gastroenterol. 2002; 23(2): 76-8.
8-Al-Knawy, B; El-Mekki, A. and Yarbough, P. The role of hepatitis E virus infection among patients with acute viral hepatitis in Southern Saudi Arabia. Ann.Saudi. Med. 1997; 17 (1): 32-4.
9-Fix, A.D.; Abdel-Hamid, M.; Purcell, R.; Shehata,M.; Abdel-Aziz, F.; et al. Prevalence of antibodies to hepatitis E in two rural Egyptian communities. Am.J.Trop. Med.Hyg. 2000; 62 (4): 519-23.
10-Lin, C.C.; Wu, J.; Chang, T.; Chang, W.;Yu, M.; et al. Diagnostic value of immunoglobulin G (IgG) and IgM anti-hepatitis E virus (HEV) tests based on HEV RNA in an area where hepatitis E is not endemic. J.Clin. Microbiol. 2000; 38 (11): 3915-8.
11-Meng, X.J.; Wiseman, B.; Elvinger, F.; Guenette, D.; Toth, T.;et al. Prevalence of antibodies to hepatitis E virus in Veterinarians working with swine and in normal blood donors in the Unites States and other countries. J. Clin.Microbiol. 2002; 40 (1): 117-22.
12-Favorov, M.O.; Kosoy, M.; Tsarev, A.; Childs, G. and Margolis, H. Prevalence of antibody to hepatitis E virus among rodents in the United States. J.Infect.Dis.2000; 181:449-55.
13-Poel, W.; Verschoor,F.; Heide, R.; Herrera, M.; Vivo, A.; et al. Hepatitis virus sequences in swine related to sequences in humans, the Netherlands. Emerg.Infect.Dis.2001; 7(6): 970-6.
14-Drobeniue,J.; Favorov, M.; Shapiro, C.; Bell, B.; Mast, E.; et al. Hepatitis E virus antibody prevalence among persons who work with swine. J.Infect. Dis. 2001;184: 1594-7.
15-Meng, X.J. Zoonotic and xenozoonotic risks of hepatitis E virus. Infect. Dis. Rev. 2000;2: 35-41.
16-Tei, S.; Kitajima, N.; Takahashi, K. and Mishiro, S. (2003). Zoonotic transmission of hepatitis E virus from deer to human beings. Lancet, 362: 371-73.
17-Hasan, A.SH. Prevalence of hepatitis B and hepatitis C virus infections among healthcare workers. J. Diyala, 2003;15: 154-160.
18-Hasan, A.SH. Outbreak of hepatitis B virus infection in a rural community in Diyala. J. Diyala, 2004;18: 45-52.
19-Hasan, A.SH.; Al-Duliami, A.A. and Omer, A. R. Occurrence of an outbreak of hepatitis E infection in Baquba city. Iraqi J. Commun.Med. 2006 (in press).
20-Skidmore, S.J. Hepatitis E. Trans.Roy. Soc. Trop.Med. Hyg.1997; 91: 125-6.
21-Malik,I.A. and Tariq, W.Z. Hepatitis E in Pakistan. East. Medit. Health J.1996; 2(1): 121-8.
22-Nicand, E.; Grandadam, M.; Teyssou, R.; Rey, G. and Buisson, Y. Viremia and fecal shedding of HEV in symptom- free carriers. Lancet, 2001; 357: 68-9.
23-Aggarwel, R.; Kumar, R.; Pal, R.; Naik, S.; Semwal, S. and Naik, S. Role of travel as a risk factor for hepatitis E virus infection in a disease-endemic area. Indian J.Gastroenterol. 2002; 21(1): 14-8.
24-Goncales, N.S.; Pinho, G.; Moreira, R.; Saraceni, C.;Spina, A. Hepatitis E. virus immunoglobulin G antibodies in different population in Campinas-Brazil. Clin. Diag. Lab. Immunol. 2000; 7(5): 813-6.
25-Sidal,M., Unuvar, E.; Oguz, F.; Cihan,C.; Onel,D.and Badur, S. Age-specific seroepidemiology of hepatitis A,B, and E infections among children in Istanbul-Turkey. Eurp.J.Epidemiol. 2001; 17(2): 141-4.
26-Mathur, P.; Arora,N.; Panda,S.; Kapoor, S.; Jailkhani, B.and Irshad, M. Seroepidemiology of hepatitis E virus (HEV) in urban and rural children of North India. Indian Pediatr.. 2001; 38(5): 461-75.
27-Bradley, D.W. Hepatitis non-A, non-B viruses become identified as hepatitis C and E viruses. Prog. Med.Virol. 1990; 37: 101-35.
28-Isaacson,M.; Frean, I.; He, J.; Seriwatana, J. and Innis, B. An outbreak of hepatitis E in Northern Namibia, 1983. Am.J.Trop. Med. Hyg.2000; 62 (5): 619-25.
29-Valazquez, O.; Steller, H. and Avila, C. Epidemic transmission of enterically transmitted non-A, non-B hepatitis in Mexico. 1986-1987. JAMA. 1990; 263: 3281-5.
30-Pina, S.; Buti, M.; Cortina, M.; Piella, J. and Girones, R. HEV identified in serum from humans with acute hepatitis and in sewage of animal origin in Spain. J.Hepatol. 2000; 33 (5): 826-33.

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