Original Article

THE LIBYAN JOURNAL OF Infectious Diseases
The Official Periodical of the Libyan National Center for Infectious Diseases Prevention and Control
Vol. 1 No.1 Jan-2007

Seroprevalence of anti-hepatitis D antibodies in hepatitis B virus infected patients in Benghazi, Libya

Ahmed Elhassi[1], Abdul-Nasser Elzouki[1], Mohamed Arabi[1], Mustafa Alturki[1], Rajab Tobgi[2]

1-Department of Medicine, Faculty of Medicine, Garyounis University, Benghazi, Libya.

2-Department of Microbiology, Faculty of Medicine, Garyounis University, Benghazi, Libya.

ABSTRACT

Objectives: Hepatitis D virus (HDV) infection is considered to be high in the Mediterranean basin. Data regarding this infection in Libyan population are scance. The aim of the present study was to determine the seroprevalence of anti-HDV antibodies in hepatitis B virus (HBV) infected patients in Benghazi.

Materials and Methods: The study population comprised one hundred thirty-eight patients with chronic HBV infection who were attending the liver clinic, Aljamahiriya Teaching Hospital, Benghazi. The diagnosis of HBV infection in those patients was based on repeatedly positive HBsAg in the serum with other laboratory and / or radiologic featurse of liver disease. All patients were tested for the presence of Anti-HDV IgM antibodies and Anti-HDV IgG antibodies using ELISA techniques. At the same time the level of HBV-DNA was measured using polymerase chain reaction (PCR) techniques for both Anti-HDV antibodies positive and negative patients.

Results: Fifteen patients were positive for anti-HDV IgG antibodies (10.8%) and none was positive for Anti-HDV IgM antibodies (0%). The HBV-DNA levels were higher in HBV patients with Anti-HDV antibodies than in patients positive for Anti:HDV Anti- HDV antibodies (P=0.01).

Conclusion: HDV infection does not appear to be commonly prevalent in Libyan patients with HBV. In comparison to data from previous results from Mediterranean area, the seroprevalence of HDV in Libyan patients who were attending the liver clinic, Benghazi is considered to be intermediate.

Key words:
Coinfection, Hepatitis B virus, Hepatitis D virus, viral hepatitis.

INTRODUCTION

Hepatitis D virus (HDV) is a defective RNA virus of Hepadna family which is dependent on the presence of HBV for its replication and expression (1). It is estimated that more than 350 millions are HBV carrier worldwide, of them at least 15 millions (5%) are infected with HDV. The prevalence of HDV is estimated to be high in the Mediterranean basin and reaches up to 25% in some countries (1-3).

Corresponence and reprint request: **Ahmed Elhassi**
Department of Medicine, Faculty of Medicine
Garyounis University, Benghazi, Libya
Phone & Fax: 061-9095361
Email: ahmedl-hassi@yahoo.com
Received : 7 /6/ 2006, Accepted : 20 /11/ 2006

Infection with HDV takes place either at the same time of HBV infection and is called coinfection or acquired after infection with HBV and called superinfection. Its mode of transmission follows the same route of HBV infections but considered to be higher in drug addicts (4,5). Its clinical significance is due to the fact that coinfection with HBV carries high risk of fulminant acute hepatitis and super-infection associated with high rate of chronic liver disease as well as the suppressive effect of HDV on HBV replication (2,4,6-10).

Diagnosis is usually made by detection of antibodies against delta virus either IgM or IgG by serological assays (11). Many modalities, like stander interferon and pegylated interferon, had been tried for treatment of chronic HDV infection with low success rate (12). Over the last ten years the prevalence of HDV infections show significant decline especially in countries with previous high prevalence rate. This is attributed mainly to effectiveness of hepatitis B vaccination program as well as the applications of stander precaution used during handling of blood and other body fluids of HBV patients (3,13).

MATERIALS AND METHODS

The present study was conducted at Aljamahiriya Hospital, Benghazi, Libya, a 515-bed teaching hospital established in 1918. The hospital has a catchment population of approximately 500.000 persons and its liver clinic acts as a referral specialized clinic for patients of the Eastern part of Libya with chronic liver disease.

The cohort comprised 138 patients with HBV infection who were attending the liver clinic over a period of six months (September 2005 to February 2006). Patients with coinfection of HBV and Hepatitis C virus infection were excluded. The diagnosis of HBV infection was based on repeatedly positive HBsAg in the serum with other laboratory and/or radiologic features of liver disease. All patients sera were tested for the presence of Anti-HDV IgM and IgG antibodies using the enzyme linked immunosorbent assay (ELISA) techniques. At the same time the serum levels of HBV-DNA were measured for both Anti-HDV antibodies positive and Anti-HDV antibodies negative patients using the polymerase chain reaction (PCR)techniques. The threshold of detection was >35 copies/ml. Serum alanine aminotransferase (ALT) levels were measured in both Anti-HDV antibodies positive and Anti-HDV antibodies negative patients and the upper limit of normal value was 40 IU/L.

Statistical analysis was conducted using the statistica 5.0. A two tailed student's test and chi-square were used as appropriate. Results were considered significant if p value was less than 0.05.

RESULTS

Out of 138 Libyan patients enrolled in this study, 93 were males (67.4%) and 45 were females (32.6%), with male to female ratio of 2:1. The mean age was 46.4 ± 13.7 years with a range from 15- 79 years. Fifteen (10.8%) patients (12 males and 3 females) were positive Anti-HDV IgG antibodies whereas none of the patients was positive for IgM Anti-HDV antibodies. The mean HBV-DNA level was 150.000 copies/ml and 6.00.3000 copies/ml for Anti-HDV antibodies positive and Anti-HDV antibodies negative patients with chronic HBV infection, respectively (p=0.01). The mean value for ALT levels in Anti-HDV antibodies positives was 24±3 IU/ml and for Anti-HDV antibodies negative patients was 30±2 IU/ml (p>0.05).

Table 1 shows the characteristic features of both Anti-HDV antibodies positive and Anti-HDV antibodies negative patients.

Table 1. Characteristic features of Anti-HDV antibodies positive and Anti-HDV antibodies negative patients.

	Anti-HDV positives N=15	Anti-HDV negatives N=123	p-value
Sex:			
Males	12 (80%)	81 (66%)	
Females	3 (20%)	42 (34%)	
Age:			
Range (years)	22- 56	15- 79	
Mean ALT			
level (IU/L)	24 ±3	30 ±2	NS*
Mean			
HBV-DNA (copies/ml)	150.000	6.00.3000	<0.01

*NS=non-significant

DISCUSSION

Out of 138 HBV patients enrolled in this study 15 patients show anti-IgG reactivity for delta virus giving a seroprevalence rate of 10.8%. No reactivity for anti-IgM delta antibody indicating that there was no recent infection with HDV. It is difficult to assert that our results are either high or intermediate due to lack of previous data on Libyan patients with HBV infection. Indeed our compressive data have been taken from studies mainly done in the Mediterranean area which show at least double trend in the prevalence of HDV infection. In the late 1970s the prevalence rate reached up to 30% in the southern part of Europe (14,15), where as in the late 1990s the seroprevalence rate showed a sharp decline to reach 8.3 % This decline was attributed to effective HBV vaccination program as well as effectiveness of standerd precaution while handling of blood and other body secretions (13,16-18). In the far East where the prevalence of HBV is high the prevalence of HDV is low (5%) (19,20). In the northern part of Africa the prevalence reaches up to 23.5% (21,22), whereas in the Gulf area it reaches up to 8% (23-25). The lowest prevalence rate was observed in North America 1.6% (26). Regarding HBV-DNA level we found that the level of viremia is higher in HBV-delta negative antibody patients than in HBV-delta positive patients. This is a known fact due to the suppressive effect of delta virus on HBV replication (6,9). Normal mean ALT level was noted among each group of patient population although many studies showed increased ALT activities among patients who are HDV positive (7,9,14). This could be attributed to the small number of Anti-HDV positive patients in the present study.

In conclusion, HDV infection does not appear to be commonly prevalent in Libyan patients with HBV. In comparison to the data from previous results from the Mediterranean region, the seroprevalence of HDV in Libyan patients who were attending the liver clinic in Benghazi is considered to be intermediate.

REFERENCES

1. Elzouki A-N. Hepatitis D virus. Ann Saudi Med 1996;16:184-192.
2. Rizzetto M, Ponzetto A, Forzani I. Epidemiology of hepatitis delta virus. Prog Clin Biol Res 1991;364:1-12.
3. Navascues CA, Rodriguez M, Sotorrio NG, Sala P, Linares A, Suarez A, *et al.* Epidemiology of hepatitis D virus infection: changes in the last 14 years. Am J Gastroentrol 1995;90:1981- 1984.
4. Bonino F, Negro F, Baldi M, Brunetto MR, Chiaberge E, Capalbo M, *et al.* The natural history of chronic delta hepatitis. Prog Clin Biol Res 1987; 234:145-152.

5. Manghisi OG, Guglielmi V, Cozzolongo R, Buongiomo G, Cuppone R, Ragnini F, *et al.* The risk factors for hepatitis D viral infection in southern Italy. Minerva Gastroentrol Dietol 1996;42:11 -16.
6. Smedile A, Rosina F, Saracco G, Chiaberge E, Lattore V, Fabiano A, *et al.* Hepatitis B virus replication modulates pathogenesis of hepatitis D virus in chronic hepatitis D. Hepatology 1991; 13: 413- 416.
7. Smedile A, Farci P, Verme G, Caredda F, Cargnel A, Caporaso N, *et al.* Influence of delta infection on severity of hepatitis B. Lancet 1982;2: 945 -947.
8. Pasetti G, Calzetti C, Degli Antoni A, Ferrari C, Penna A, Fiaccadori F. Clinical features of hepatitis delta virus infection in a northern Italian area. Infection 1988;16: 345 -348.
9. Hadyziyannis SJ, Papaioannou C, Alexopoulou A. The role of hepatitis delta virus in acute hepatitis and in chronic liver disease in Greece. Prog Clin Biol Res 1991:364:51 -62.
10. Chen PJ, Chen DS, Chen CR, Chen YY, Chen HM, Lai MY, *et al.* Delta infection in asymptomatic carriers of hepatitis B surface antigen: low prevalence of delta activity and effective suppression of hepatitis B virus replication. Hepatology 1988;8:1121 -1124.
11. Aragona M, Macagono S, Caredda F, Criyelli O, Lavarini C, Maran E, *et al.* Serological response to the delta virus in hepatitis D. Lancet 1987; 1:478-480.
12. Niro GA, Rosina F, Rizzetto M. Treatment of hepatitis D. J Viral Hepatitis 2005; 12(1):2- 9.
13. Gaeta GB, Stroffolini T, Chiaramonte M, Ascione T, Stomaiulo G, Lobello S, *et al.* Chronic hepatitis D: a vanishing disease? An Italian multicenter study. Hepatology 2000;32:824- 827.
14. Ramalho F, Caevalho G, Bonino F. Clinical and epidemiological significance of hepatitis delta virus infection in chronic HBV carriers in Portugal. Prog Clin Biol Res 1987;234:409 -417.
15. Buti M, Esteban R, Jardi R, Allende H, Baselga JM, Guardia J. Epidemiology of delta infection in Spain. J Med Virol 1988;26:327 -332.
16. Sagnelli E, Stroffolini T, Asione A, Bonino F, Chiaramonte M, Colombo M, *et al.* The epidemiology of hepatitis delta infection in Italy. J Hepatol 1992;15:211 -215.
17. Balike I, Onul M, Tekeli E, Caredda F. Epidemiology and clinical outcome of hepatitis D virus infection in Turkey. Eur J Epidemiol 1991;7: 48-54.
18. Rosina F, Conoscitore P, Cuppone R, Rocca G, Giuliani A, Cozzolongo R, *et al.* Changing pattern of chronic hepatitis D in southern Europe. Gastroenterology 1999;117:161- 166.
19. Chakraborty P, Kailash U, Jain A, Goyal R, Gupta RK, Das BC, *et al.* Seroprevalence of hepatitis D virus in patients with hepatitis B virus-related liver disease. Indian J. Med Res 2005; 122: 254 -257.
20. Liaw, YF, Chiu KW, Chu CM, Sheen IS, Huang MJ. Heterosexual transmission of hepatitis delta virus in the general population of an area endemic for hepatitis B virus infection: A prospective study. J Infect Dis 1990;162:1170 -1172.
21. Darwish MA, Shaker M, Raslan OS, Abdel-Raouf T. Delta virus in Egypt. J Egypt Public Health Assoc 1992;67(1 -2):147- 161.
22. Roingeard P, Sankale JL, Dubbois F, Diouf A, Bacha A, Mboup S, *et al.* Infection due to hepatitis delta virus in Africa: report from Senegal and review. Clin Infect Dis 1992; 14:510 -514.
23. Toukan AU, Al-Kandari S. The role of hepatitis D virus in liver disease in the Middle East. Prog Clin Biol Res 1991;364:63 -68.
24. Al-Traifi, Ali A, Dafalla M, Al-Tamimi W, Qassem L. Prevalence of hepatitis delta antibody among HBsAg carriers in Saudi Arabia. Ann Saudi Med 2004; 24: 343- 344.
25. Rezvan H, Forouzandeh B, Taroyan S, Fadaiee S, Azordegan F. A study on delta virus infection and its impact in Iran. Infection 1990;18:26- 28.
26. Cheng HH, Wang DQ, Minuk GY, Anand CM, Stowe TC, Buchan KA. The prevalence of antibody to delta virus in western Canada. Clin Invest Med 1986; 9:156-159.