

Research Paper

The Prevalence of Hepatitis D Virus Infection amongst Patients with Chronic Active Hepatitis B Virus Infection in Duhok Governorate

Nawfal R. Hussein^{1,*}, Ziad A. Rasheed², Ali A. Taha³ and Sabri K. Shaikhow¹

¹ The Department of Internal Medicine, Faculty of Medical Science, School of Medicine, University of Duhok, Duhok, Kurdistan Region, Iraq

² Azadi Teaching Hospital, General Directorate of Health-Duhok, Duhok, Kurdistan Region, Iraq

³ The Department of Infection Control, General Directorate of Health-Duhok, Duhok, Kurdistan Region, Iraq

* Corresponding author, e-mail: (doctornrs@yahoo.com)

(Received: 25-3-15; Accepted: 29-4-15)

Abstract: *Hepatitis D virus (HDV) is a small RNA containing virus requiring concomitant infection with hepatitis B virus (HBV) for its survival and pathogenicity. The aim of this research was to study the prevalence of HDV in patients with chronic active hepatitis B in Duhok city, Iraq. Cases of chronic active HBV infection were selected retrospectively using case sheets in hepatitis unit in Azadi teaching hospital. Then, using ELISA, the anti-HDV IgM and IgG positivity was studied. Amongst 1500 registered patients, 158 cases met the criteria of chronic active HBV. The majority were male 113/158 (71.5%) and from Duhok district 105/158 (66.5%). Additionally, the majority of the patients were young with an age average of 30.5±13.8 years. HDV IgM and IgG positivity was studied in 46 randomly selected patients with chronic active HBV. It was found that 3/45 (6.6%) patients were positive for anti-HDV IgM. All these patients were male. None of the tested patients was positive for IgG. The prevalence of HDV in Duhok was lower than that found elsewhere in Iraq. More studies are needed to explore the prevalence of HDV in chronic carriers and in chronic active HBV but with larger sample recruitment.*

Keywords: HDV, HBV, Duhok.

1. Introduction:

Infection with HBV is a worldwide issue that is associated with a high rate mortality and morbidity (Aspinall *et al.*, 2011). Nowadays, 350 to 400 million people are suffering from chronic hepatitis B (CHB) infection (Aspinall *et al.*, 2011). The persistence of hepatitis B surface antigen (HBsAg) for more than 6 months is considered CHB (Aspinall *et al.*, 2011; Carey *et al.*, 2009). The development of chronicity after acquiring the infection depends upon different factors and varies from 90% in new born babies who acquire the infection vertically from their mothers to 5% in adults (Miriam, 2003; Giovanna, 2003). Subjects with HBV infection are vulnerable to another infection with HDV and therefore all patients should be examined for the co-infection (Miriam, 2003; Giovanna, 2003). HDV, which was discovered by Rizzetto *et al.* in 1977, is a defective RNA virus that depends entirely upon HBV infection for its replication and expression (Jacobson *et al.*, 1985; Rizzetto *et al.*, 1977). The infection with these two viruses can be either co-infection or super-infection. Co-infection occurs when the patients acquiring both HBV and HDV at the same time while super-infection occurs when the subjects suffer from HBV and acquire HDV afterward (Jacobson *et al.*, 1985; Rizzetto *et al.*, 1977). Worldwide, more than 15 million subjects are infected with HDV and a great variation in the prevalence amongst different geographical regions. The highest rate is found in Middle East, and Eastern Europe (Jacobson *et al.*, 1985; Fonseca, 2002). Both HBV and HDV are transmitted through the same routes including blood-borne, sexual, percutaneous and vertical (perinatal) transmission. It is worth mentioning that the risk of severe acute infection and fulminant hepatitis is higher with HBV-HDV co-infection and with increased risk of cirrhosis, and hepatocellular carcinoma (HCC) than those having HBV infection alone (Jacobson *et al.*, 1985; Fonseca, 2002). The aims of this research were to study the risk factors associated with HBV and prevalence of HDV in patients with chronic active hepatitis B in Duhok city.

2. Material and Methods

Study Design:

The data were collected retrospectively using hepatitis records in hepatitis unit, Azadi teaching hospital. 1500 case sheets were examined in three stages. In the first stage, patient's sheets of HBV were selected and isolated from other cases of hepatitis. In the second stage, HBV infection cases were classified into two groups: chronic carrier group and chronic active hepatitis group. In the third stage, cases of chronic active hepatitis were examined carefully for risk factors. The study setting was Azadi teaching hospital. This hospital is a tertiary referral hospital in which all the chronic active hepatitis cases were referred to.

Patients and Data Assessment

Patients with isolated HBsAg positivity during the previous 6 month period were considered as asymptomatic hepatitis B carriers. The diagnosis of chronic hepatitis B was based on HBsAg positivity, anti-HBcIgG positivity, a measured ALT level of 2 times the upper limit of normal in a single assessment plus a viral load of more than 20,000 U/ml. Data analysis was conducted by Excel 2010.

HDV Positivity

In this study, 45 patients were selected randomly and tested for anti-HDV IgM and IgG positivity prospectively. The IgM and IgG were studied by commercial DIA.PRO Diagnostic Bio probes ELISA kits (Italy) following manufacturer's instruction.

3. Results and Discussion:

Amongst 1500 recorded patient with hepatitis, 158 subjects met the criteria of chronic active hepatitis. Amongst them 113/158 (71.5%) were male. In addition, 73/158 (46.2%) of the involved patients were married. Majority of the patients were young with an age average of 30.5 ± 13.8 years. It was found that 4/158 (2.5%) of the subject were younger than 10 years old. The peak prevalence was found amongst patients within the age group of 21-30 years old (Table 1).

Table 1: Age distribution of patients with chronic active hepatitis

Age Groups	Patients No. (%)
(1-10) years	4(2.5)
(11-20) years	28(17.7)
(21-30) years	65 (41.1)
(31-40) years	29(18.4)
(41-50) years	14 (8.9)
(51-60) years	11(7.0)
> 60 years	7(4.4)
Total	158

Patients in this study were ratified according to the geographical residency. It was found that 105/158 (66.5%) of the patient resided Duhok district. This followed by Zakho district where 15/158 (9.5%) of patients lived there (Table 2). Qasrouk district was the least affected as 3/158 (1.9) subjects were from this city (Table 2).

Table 2: Geographical distribution of patients with chronic active hepatitis

City	Patients No. (%)
Dohuk	105 (66.5)
Zakho	15 (9.5)
Shingal	8 (5.1)
Amedi	7 (4.4)
Semel	8 (5.1)
Qasrouk	3 (1.9)
Other Cities	12 (7.6)
Total	158

Risk Factors of HBV

Amongst the patients with chronic active hepatitis, 42/158 (26.6%) gave a history of previous dental procedures. While 40/158 (25.3%) gave a history of surgical procedures, only 13/158 (8.2%) had a history of blood transfusion. All of HBs Ag positive donors denied any history of illegitimate sex and drug use (Table 3).

Table 3: The distribution of risk factors associated with HBV infection

Risk Factor	Patients No.	Patients Percentage (%)
Blood Transfusion	13	8.2
Dialysis	4	2.5
Drug User	0	0
Illegitimate Sex	0	0
Dental Surgery	42	26.6
Other Surgery	40	25.3
Tattoo	6	3.8
Needle Stick	1	0.6
Family History	14	8.9
Denied RF	38	24.1

HDV Positivity

Amongst 158 involved subjects, we examined 45 patients for anti-HDV IgM and IgG. It was found that 3/45 (6.6%) patients were positive for anti-HDV IgM. All these patients were male. None of the tested patients was positive for IgG.

HBV poses a risk on the society as it can be easily transmitted. Certain behaviors and risk factors are associated with such a transmission (Luo *et al.*, 2012). HDV is a small RNA containing virus requiring concomitant infection with HBV for its survival and pathogenicity (Pascarella and Negro, 2011). Since discovery of HDV in 1977 by Rizzetto in Italy, it is well documented that HDV is a widespread disease that has affected a large number of population with HBV infection in the world (Pascarella and Negro, 2011). Limited knowledge is available about the infection with this virus in Iraq.

In this study, we classified the patients according to the age into groups. Within the youngest group (under the age of ten), 4 patients were found with chronic active hepatitis B. These patients should have been covered by the expanded program of vaccination. It is recommended to conduct a study about the coverage and the success rate of vaccination in this age group. In addition, the highest prevalence was found in the age group of 21-30 years old. This age group should be targeted by health planners with a vaccination and education program. Additionally, the vast majority of patients were from Duhok district. Hence, any program tackling the issue of HBV should focus on this district.

The exposure to certain risk factors increases the chance of contracting HBV. Amongst these factors are the use of contaminated needle, drug users (Akselrod *et al.*, 2014), tattooing (Jafari *et al.*, 2010), sexually active heterosexuals or homosexuals (Corona *et al.*, 1991), infants born to infected mothers (Toussi *et al.*, 2007), healthcare workers (Hussein, 2015; Averhoff *et al.*, 2012; Singhal *et al.*, 2009), patients with chronic renal failure (Qadiet *et al.*, 2004) and patients with multiple blood transfusion (Omar *et al.*, 2011). It is worth mentioning that HBV can stay stable in the environment for up to seven days. Hence, blood contaminated household objects can pose a risk for transmission (Sypsa *et al.*, 2001). In our study, around 9% of HBV-positive subjects gave a positive family history of HBV infection. Lack of education about the method of transmission may have helped the spread of infection. Drug users and subjects with multiple sexual partners are at high risk of HBV (Parry, 2010). It was previously shown in Egypt that 28% of HBV positive cases gave a history of drug use or illegitimate sex (Awadalla *et al.*, 2011). None of patients recruited in this study gave a history of illegitimate sex or drug abuse. No efforts were saved to keep the privacy of the patients; however

admitting illegitimate sex or drug abuse is extremely difficult in the society due to the associated embarrassment.

Many studies have shown that using contaminated surgical instruments can be resulted in an outbreak of blood borne viral infection private clinics and hospitals (Redd *et al.*, 2007; Asthana and Kneteman, 2009; Parry, 2010). In this research, it was found that the majority of HBV subjects gave a history of visiting dentists and undergoing previous surgery. To confirm these results, a case control study is needed in the future to determine the risk factors associated with the transmission of HBV. If these results shown to be accurate, then this will warrant an urgent investigation about the infection control measures especially sterilization in all hospitals and private clinics particularly those of dentists. In addition, around 8% of patients with chronic active HBV gave history of blood transfusion. Nowadays, there are strict measures of examining the blood before transfusion. Probably, these patients contracted the infection before imposing such measures.

In this study, we examined the patients with chronic active hepatitis for anti-HDV IgM-as a marker of acute infection- and IgG- as a marker of chronic infection. It was found that 6.6% of our recruited patients were positive for IgM indicating an acute infection. When we checked the case sheets of these patients, it was found that these patients were all on 300 mg/day Tenofovir (Cipla, India)for the treatment of HBV. They had been stable on the treatment with sudden increase of ALT. Probably; such an increase was due to acute HDV infection. None of the patients showed positive result for Ant-HDV IgG. Previous studies have shown great variations in the anti-HDV seropositivity amongst patients with chronic HBV infected subjects ranging from 4.1-25.6% at different regions of the world (Zaki *et al.*, 2003; Gholamreza *et al.*, 2007; Ghadir *et al.*, 2012). Previous study conducted in Iraq recruiting 108 subjects showed that the overall prevalence of HDV amongst patients with chronic HBV infection was 16.6 % (Al-Hilli and Al-Ugaidy, 2002). In the same study, the prevalence of HDV amongst patients with chronic active hepatitis was 20.8% (Al-Hilli and Al-Ugaidy, 2002). In Iran, different studies showed different prevalence of HDV. The prevalence ranged from 2% in Qom province (Ghadir *et al.*, 2012) to 17.7% in Hamedan province (Alizadeh *et al.*, 2010). In Turkey, The seroprevalence of HDV in chronic active HBV patients ranged from 15% to 41% (Celen *et al.*, 2006). In a study conducted in Bangladesh, the prevalence of HDV positivity was 21% and 25% in asymptomatic carriers and patients with chronic liver disease, respectively (Zaki *et al.*, 2003). In addition, in a study conducted in India, 5.7% of patients with chronic active hepatitis showed positive results for anti-HDV (Jaiswal *et al.*, 1998).

Studying the risk factors associated with HBV in Duhok would give significant information to the infection control department and health planers to control the spread of such infections. Our study has limitations. Firstly, this study should be considered preliminary and to confirm the risk factors associated with HBV, a case control study should be conducted. In addition, the sample size used for studying the prevalence of HDV was small. It is recommended that a larger sample size should be included in any study in the future.

4. Conclusions

The prevalence of HDV in Duhok was lower than that found elsewhere in Iraq. More studies are needed to explore the prevalence of HDV in chronic carriers and in chronic active HBV but with larger sample recruitment.

References

- [1] H. Akselrod, L.E. Grau, R. Barbour and R. Heimer, Seroprevalence of HIV, Hepatitis B virus and Hepatitis C virus among injection drug users in Connecticut: Understanding infection and co-infection risks in a non-urban population, *American Journal of Public Health*, 104(9) (2014), 1713-1721.

- [2] H.A. Al-Hilli and Y.H. Al-Ugaidy, Prevalence of hepatitis delta virus super infection in chronic HBV infection, *IJGE*, 1(3) (2002), 30-33.
- [3] A.H.M. Alizadeh, M. Ranjbar, A.S.S. Tehrani, F. Keramat, M. Mamani, M. Rezazadeh and et al., Seroprevalence of hepatitis D virus and its risk factors in the west of Iran, *Journal of Microbiology, Immunology and Infection*, 43(6) (2010), 519-523.
- [4] M.J. Alter, Epidemiology of hepatitis B in Europe and worldwide, *Journal of Hepatology*, 39(2003), 64-69.
- [5] E.J. Aspinall, G. Hawkins, A. Fraser, S.J. Hutchinson and D. Goldberg, Hepatitis B prevention, diagnosis, treatment and care: A review, *Occupational Medicine*, 61(8) (2011), 531-540.
- [6] S. Asthana and N. Kneteman, Operating on a patient with hepatitis C, *Canadian Journal of Surgery*, 52(4) (2009), 337-342.
- [7] F.M. Averhoff, N. Glass and D. Holtzman, Global burden of hepatitis C: Considerations for healthcare providers in the United States, *Clinical Infectious Diseases*, 55(suppl 1) (2012), S10-S15.
- [8] H.I. Awadalla, M.H. Ragab, M.A. Osman and N.A. Nassar, Risk factors of viral hepatitis B among Egyptian blood donors, *British Journal of Medicine and Medical Research*, 1(1) (2011), 7-13.
- [9] W.D. Carey, The prevalence and natural history of hepatitis B in the 21st century, *Cleveland Clinic Journal of Medicine*, 76(Suppl 3) (2009), S2-S5.
- [10] M.K. Celen, C. Ayaz, S. Hosoglu, M.F. Geyik and M. Ulug, Anti-hepatitis delta virus seroprevalence and risk factors in patients with hepatitis B in Southeast Turkey, *Saudi Medical Journal*, 27(5) (2006), 617-620.
- [11] R. Corona, G. Prignano, A. Mele, G. Gentili, F. Caprilli, E. Franco and et al., Heterosexual and homosexual transmission of hepatitis C virus: Relation with hepatitis B virus and human immunodeficiency virus type 1, *Epidemiology and Infection*, 107(03) (1991), 667-672.
- [12] J.C. Fonseca, Hepatitis D, *Rev Soc Bras Med Trop*, 35(2) (2002), 181-90.
- [13] M.R. Ghadir, M. Belbasi, A. Heidari, S.S. Sarkeshikian, A. Kabiri, A.H. Ghanooni and et al., Prevalence of hepatitis D virus infection among hepatitis B virus infected patients in QOM province, Center of Iran, *Hepatitis Monthly*, 12(3) (2012), 205-208.
- [14] R. Gholamreza, S. Shahryar, K. Abbasali, J. Hamidreza, M. Abdolvahab, K. Khodaberdi and et al., Seroprevalence of hepatitis B virus and its co-infection with hepatitis D virus and hepatitis C virus in Iranian adult population, *Indian Journal of Medical Sciences*, 61(5) (2007), 263-268.
- [15] F. Giovanna, Natural history of hepatitis B, *Journal of Hepatology*, 39(2003), 50-58.
- [16] N.R. Hussein, Prevalence of HBV, HCV and HIV and Anti-HBs antibodies positivity in healthcare workers in departments of surgery in Duhok City, Kurdistan Region, Iraq, *Int. J. Pure Appl. Sci. Technol*, 26(2) (2015), 70-75.
- [17] I.M. Jacobson, J.L. Dienstag, B.G. Werner, D.B. Brettler, P.H. Levine and I.K. Mushahwar, Epidemiology and clinical impact of hepatitis D virus (delta) infection, *Hepatology*, 5(2) (1985), 188-91.
- [18] S. Jafari, R. Copes, S. Baharlou, M. Etminan and J. Buxton, Tattooing and the risk of transmission of hepatitis C: A systematic review and meta-analysis, *International Journal of Infectious Diseases*, 14(11) (2010), e928-e940.
- [19] S.P. Jaiswal, D.S. Chitnis, K.K. Artwani, G. Naik and A.K. Jain, Prevalence of anti-delta antibodies in central India, *Tropical Gastroenterology: Official Journal of the Digestive Diseases Foundation*, 20(1) (1998), 29-32.
- [20] Z. Luo, L. Li and B. Ruan, Impact of the implementation of a vaccination strategy on hepatitis B virus infections in China over a 20-year period, *International Journal of Infectious Diseases*, 16(2) (2012), e82-e88.
- [21] N. Omar, K. Salama, S. Adolf, G.S. El-Saeed, N.A. Ghaffar and N. Ezzat, Major risk of blood transfusion in hemolytic anemia patients, *Blood Coagulation & Fibrinolysis*, 22(4) (2011), 280-284.
- [22] J. Parry, At last a global response to viral hepatitis, *Bulletin of the World Health Organization*, 88(11) (2010), 801-802.

- [23] S. Pascarella and F. Negro, Hepatitis D virus: An update, *Liver International*, 31(1) (2011), 7-21.
- [24] A.A. Qadi, H. Tamim, G. Ameen, A. Bu-Ali, S. Al-Arrayed, N.A. Fawaz and W.Y. Almawi, Hepatitis B and hepatitis C virus prevalence among dialysis patients in Bahrain and Saudi Arabia: A survey by serologic and molecular methods, *American Journal of Infection Control*, 32(8) (2004), 493-495.
- [25] J.T. Redd, J. Baumbach, W. Kohn, O. Nainan, M. Khristova and I. Williams, Patient-to-patient transmission of hepatitis B virus associated with oral surgery, *Journal of Infectious Diseases*, 195(9) (2007), 1311-1314.
- [26] M. Rizzetto, M.G. Canese, S. Arico, O. Crivelli, C Trepo, F Bonino and et al., Immuno fluorescence detection of new antigen-antibody system (delta/anti-delta) associated to hepatitis B virus in liver and in serum of HBsAg carriers, *Gut.*, 18(12) (1977), 997-1003.
- [27] V. Singhal, D. Bora and S. Singh, Hepatitis B in health care workers: Indian scenario, *Journal of Laboratory Physicians*, 1(2) (2009), 41-48.
- [28] V. Sypsa, E. Hadjipaschali and A. Hatzakis, Prevalence, risk factors and evaluation of a screening strategy for chronic hepatitis C and B virus infections in healthy company employees, *European Journal of Epidemiology*, 17(8) (2001), 721-728.
- [29] S.S. Toussi, J. Abadi, M. Rosenberg and D. Levanon, Prevalence of hepatitis B and C virus infections in children infected with HIV, *Clinical Infectious Diseases*, 45(6) (2007), 795-798.
- [30] M.H. Zaki, G.L. Darmstadt, A. Baten, C.R. Ahsan and S.K. Saha, Seroepidemiology of hepatitis B and delta virus infections in Bangladesh, *Journal of Tropical Pediatrics*, 49(6) (2003), 371-374.