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Original Research Article

Prevalence of Hepatitis D in Jaundice Patients in Tertiary Care Hospital

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Conflict of interest: Nil

Abstract:

Background: In 1977, Rizzetto et al in Italy identified Delta or Hepatitis D virus. Hepatitis D virus is a small RNA virus. It is a defective virus in human in sense that it requires helper function of HBV genome. The objective of this study is to determine prevalence of hepatitis D in jaundice patients attending tertiary care hospital, Ahmedabad, to determine prevalence of hepatitis D in HBsAg reactive patients, To determine various age and sex specific prevalence of Hepatitis D, and To assess severity of infection in HBV and HDV.

Material & Methods: This study was carried out of 1571 patients, suffering from Jaundice, admitted at tertiary care hospital, Ahmedabad from December 2015 to July 2017. Each serum sample was tested for HBsAg antigen by enzyme immunoassay at our serology lab in microbiology department. Confirmed HBsAg reactive samples serum was collected immediately in plastic disposable vials to avoid contamination and stored in freezer at -20^0C. Each HBsAg reactive serum sample were tested for HDV Antigen ELISA & Anti-HDV Antibody ELISA.

Results: Among 1571 patients' prevalence of HBsAg Antigen reactive among jaundice patients was 11.2%. HD antigen detection in HBsAg reactive patients was 2.27%. total Anti-HD antibody detection in HBsAg reactive patients was 6.25%.

Conclusion: we conclude that the prevalence rate of hepatitis D virus infection was 0.7% in jaundice patient and 6.25% in hepatitis B reactive patients at tertiary care hospital, Ahmedabad. Male were more seen to be infected with HDV than females. This HDV prevalence can be decreased by global HBV vaccination, increasing awareness, improved preventive measures and changes in the socioeconomic conditions in a fast-developing country like India.

Keywords: HBV, HDV, HDV Antigen ELISA, Anti-HDV Antibody ELISA, Jaundice, Hepatitis.

Introduction

Hepatitis viruses are heterogeneous group of viruses that are taxonomically diverse (belong to different families) but all are hepatotropic; causes acute inflammation of the liver producing identical histopathologic lesion and similar clinical illness such as fever, nausea, vomiting and jaundice[1].Hepatitis viruses are classified into six types1;Hepatitis A virus (HAV): it causes infective hepatitis, Hepatitis B virus (HBV): it causes serum hepatitis., Hepatitis C virus (HCV): it is common cause of post transfusion replication., Hepatitis D virus (HDV): it is a defective virus, needs HBV for its replication., Hepatitis E virus (HEV): it is the agent of enterically transmitted Non-A Non-B hepatitis, Hepatitis G virus (HGV): it is not hepatotropic virus.

In 1977, Rizzetto et al in Italy identified Delta or Hepatitis D virus. Hepatitis D virus is a small RNA virus. It is a defective virus in human in sense that it requires helper function of HBV genome[2]. Its clinical course is varied and ranges from acute, self-limited infection to acute, fulminant liver failure. Chronic liver infection can lead to end-stage liver disease and associated complications (including accelerated fibrosis, liver decompensation, and hepatocellular carcinoma) [3]. HDV infection occurs only simultaneously or as super-infection with HBV.

The virus is transmitted through contact with the blood or other body fluids of an infected person. Vertical transmission from mother to child is rare. Currently there is no effective antiviral treatment for hepatitis D. Hepatitis D infection can be prevented by hepatitis B immunization[4]. Approximately 5% of the global HBV carriers are co-infected with HDV. Out of approximately 350 million carriers of HBV worldwide, 18 million people are infected with HDV[5].

In May 2016, the World Health Assembly endorsed the Global Health Sector Strategy (GHSS) on viral hepatitis 2016–2021. The GHSS calls for the elimination of viral hepatitis as a public health threat by 2030 (reducing new infections by 90% and mortality by 65%).

The report focuses on hepatitis B and C, which are responsible for 96% of all hepatitis mortality. It presents data along the five strategic directions (strategic information, interventions, equity, financing and innovation) – key pillars of the GHSS to facilitate monitoring of progress in countries, regions and globally, and to measure the impact of interventions on reducing new infections and saving lives between 2015 and 2030[6].

Aims and Objectives

- To determine prevalence of hepatitis D in jaundice patients attending tertiary care hospital, Ahmedabad. To determine prevalence of hepatitis D in HBsAg reactive patients.
- To determine various age and sex specific prevalence of Hepatitis D. To determine various risk factors for Hepatitis D virus infection. And to assess severity of infection in HBV and HDV.

Materials and Methods

This study was carried out of 1571 patients, suffering from Jaundice, admitted at tertiary care hospital, Ahmedabad from December 2015 to July 2017. Criteria for selection of patients: Patients were considered to be suffering from jaundice, if the following criteria were satisfied.

Clinical: Yellow Sclera, yellow urine, anorexia and abdominal pain are major indications. & Pruritus, nausea, vomiting, spider naive and palmar erythema are the subsidiary symptoms. & Biochemical: Serum bilirubin > 1 mg & SGPT > 35 IU / ml Each selected serum sample was tested for HBsAg antigen by enzyme immunoassay (Erba Lisa SEN HBsAg) at our serology lab in microbiology department. Confirmed HBsAg reactive samples serum was collected immediately in plastic disposable vials to avoid contamination and stored in freezer at -20^{0}C. After that Each HBsAg reactive serum sample were tested for HDV Antigen ELISA(Dia.pro diagnostic bioprobes) & Anti-HDV Antibody ELISA (DiaSorin ELISA kit)

Results and Observations

The study was conducted on patients, were attending tertiary care hospital, Ahmedabad. Patients selected for this study were suffering from jaundice. Patients had high serum bilirubin and SGPT level.

In each sample HBsAg ELISA was performed and from HBsAg reactive samples HD Antigen and Anti-HD Antibody ELISA were performed. Among 1571 total jaundice patients 176 (11.2%) were positive for HBsAg and from this 176, 4 (2.27 %)were positive for HD Ag and 11 (6.25 %) were positive for Anti -HD Ab.

Table 1: Distribution of HDV infection according to Age

Sr. No.	Age Groups	HBsAg Reactive patients	HD Ag Positive	Anti-HD Ab Positive	Total HDV Infection	Percentage
1	**0-10**	2	0	0	0	0.00%
2	**11-20**	16	0	0	0	0.00%
3	**21-30**	33	1	1	1	3.03%
4	**31-40**	38	0	3	3	7.89%
5	**41-50**	54	1	4	4	7.40%
6	**>50**	33	2	3	3	9.09%
	TOTAL	**176**	**4**	**11**	**11**	**6.25%**

Table 1 shows that there were no HDV infection in patients up to 20 years of age in this study.

In the present study, the prevalence of Anti-HD antibody was highest in the >50 years age group followed by 31-40 years age group and then by 41-50 years age group. A few patients (4) who had Anti- HD antibody also showed the presence of HDV antigen. Highest prevalence rate of HDV Infection was in old persons (> 50 year of age), which was 9.09%.

Above table shows Prevalence of HDV infection in HBsAg Reactive patient was 6.25 %. 4 patients show simultaneous detection of HD Ag and 11 pt shows Anti-HD Ab..

Table 2: Distribution of HDV infection according to sex

	HBsAg Reactive Patients	HD Ag positive	Anti-HD Ab positive	Total HDV positive	Total HDV Percentage
Male	130	2	9	9	6.92%
Female	46	2	2	2	4.35%
Total	176	4	11	11	6.25%

Looking at the sexual preponderance, out of 176 HBsAg reactive patients, 73.9% (n=130) were male and 26.1% (n=46) were females. Male: Female ratio was 2.82:1 Among 11 HDV positive patients, from which 9(6.92%) males and 2 (4.35%) were females. Prevalence rate amongst the male was found considerably high as compare to female.

Table 3: Distribution of HDV infection according to clinical groups

Clinical groups	HBsAg Reactive cases	HDV infection positive	HDV infection Percentage
Fulminant hepatitis	48	9	18.75%
Non- fulminant hepatitis	110	2	1.82%
Jaundice without S/S hepatitis	18	0	00%
Total	176	11	6.25%

As Shown in above table, prevalence rate amongst cases of fulminant hepatitis was as high as 18.75. % while in case of non- fulminant hepatitis, only 2 cases (1.82%) were found positive for HDV infection and from which one case was of chronic active hepatitis in which antigen and antibody both were positive. None of cases of only jaundice without signs and symptoms of hepatitis were found positive for HDV infection. This suggests that fulminant hepatitis is much more common in HDV infection.

Table 4: Distribution of HDV Infection according to risk groups

Risk groups	HBsAg Reactive Patients	HDV positive Patients	Percentage
Blood transfusion	35	3	8.57%
Surgery	29	1	3.45%
Multiple exposure	19	1	5.26%
AKT	7	0	00%
Others	86	6	6.97%
Total	176	11	6.25%

Above table shows that rate of positive cases was higher in cases with previous history of blood transfusion, which was 8.57 % and in cases with history of multiple exposure and surgery; it was 5.26%% and 3.45 % respectively. The group others include the cases with no other specific history or H/O drug addiction. In our study there was no case of drug addiction.

Table 5: Distribution of positive cases of HDV Infection in different age and sex groups.

Sr No	Age groups	Male	Female	HDV Infection
1	0-10	0	0	0
2	11-20	0	0	0
3	21-30	1(9.09%)	0	1(9.09%)
4	31-40	3(27.27%)	0	3(27.27%)
5	41-50	4(36.36%)	0	4(36.36%)
6	>50	1(9.09%)	2(18.18%)	3(27.27%)
	Total	9(81.82%)	2(18.18%)	11 (100%)

Above table shows Distribution of positive cases of HDV Infection in different age and sex groups, HDV infection was most common in males with age group 41-50 years followed by 31-40 years. The only two female cases that were positive for HDV infection were found in older age group (>50 years).

Result and Discussion

Table 1: Comparison of prevalence rate HBsAg reactive patients with other study:

Study	Jaundice positive patients	HBsAg Reactive patients	Prevalence (%)
Present study	1571	176	11.20%
Kumar S. et al, katiyar[16]2015	105	16	15.24%

In table 1: In present study prevalence rate (11.20%) of HBsAg reactive patients was slightly low as compared to Katihar study. Thus, difference may be due different study group. WHO data suggests the prevalence of Hepatitis B in South-East Asia Region among 2.0% of the general population[15]. The prevalence of Hepatitis B is much higher in present study as compare to WHO data that may be due to our study was conducted on jaundice patients attending tertiary care hospital, Ahmedabad.

Table 2: Comparison of prevalence rate of hepatitis D infection with different previous studies:

Study	HBsAg Reactive Cases	HDV positive cases	Prevalence (%)
Present study	176	11	6.25%
Angeles Castro et al. Spain[17] ,1989	175	34	19.40%
Valeri Kelly, London[18],1989	406	20	4.92%
L. Mathyssen et al., Netherland[19] ,1988	173	7	4.04%
Shaikh M A et al., Larkara[20] 2003-2008	774	183	23.6%
CD Alert, NICD, Mehsana[21]India 1997	17	3	17.65%
CD Alert, NICD, Shri Ganganagar[21] ·1997	70	6	8.57%
Banker DD. et al., Mumbai[22] 1992	331	124	37.46%
Mapara M. et al. Ahmedabad[7] -2002	169	10	5.91%
Chakraborty P. et al. New Delhi[10] 2004	123	13	10.60%
Shanmugam et al., Chennai[23] 2008	153	9	5.90%
Shah L. et al. Surat[24] 2010-2011	141	12	8.50%
Biswas Samrat et al Assam[25] 2014	89	1	1.12%

Table no 2: shows that there is great variation in prevalence of HDV in different studies. In studies, which were conducted outside India, prevalence rate varies from 4% (Netherland) to 23.6% (Larkara).

Above table shows studies which were conducted in different epidemics of India, prevalence of HDV ranged between 1.12% (Assam) to 18% (Mehsana).

Thus, the difference exists in different studies due to different geographical regions, ethnic, behavior groups and different study methodology. In our study prevalence of HDV infection is 6.25%. which was comparable with previous study done in Ahmedabad 2002 (5.91%). It was significantly low as compared to previous studies done in Mehsana, Gujarat 1997 (17.65%), and South Gujarat 2008 (8.50%). If we compare our study with different studies done across India, this study shows a low prevalence as compared to study done in Sri Ganganagar 1997 (8.57%) and in New Delhi in 2004 (10.60%).

This study shows a higher prevalence when compared to recent study was done in Assam in 2014(1.12%). Our study is comparable with study done in Chennai (5.90%)in 2008.

In India, the trend is much different from that other countries and HDV infection does not seem to be very common. It is suggested that the infection is switching towards low prevalence in this country[10].

Table 3: Comparison of HDV Infection in different age with different study:

Age group	M.V. Murhekar, SC segal[26] et. al.	Shah L[23] et. al.	Mapara M[7]. et. al.	Our study
0-10	0	0	0	0
11-20	1	0	0	0
21-30	0	2	2	1
31-40	5	5	4	3
41-50	2	3	2	4
>50	0	2	2	3
Total	8	12	10	11

Table No 3: shows the age wise distribution. From the table we observed positive cases of HDV Infection are among the adult and old age. In our study highest positive case of HDV infection was in 41-50 year age group as compare to other studies where it was highest in 31-40 year.

Table 4: Comparison of our study according to age /sex, clinical groups and risk factors:

Study/ Characteristic		Shah L[23]. et al.		Mapara M[7]. et al.		Our Study	
		HBsAg reactive Cases	HDV infection (%)	HBsAg reactive Cases	HDV infection (%)	HBsAg reactive Cases	HDV infection (%)
Sex	**Male**	111	10(9.0)	109	09(8.25)	130	9(6.92)
	Female	30	02(6.6)	60	01(1.66)	46	2(4.92)
Clinical groups	**Fulminant hepatitis**	53	08(15.09)	61	08(13.11)	48	9(18.75)
	Non- Fulminant Hepatitis	78	4(5.12)	98	02(2.04)	110	2(1.89)
	Jaundice without s/s of hepatitis	10	00(00)	10	00(00)	18	00(00)

Table 5: Comparison study for prevalence rate of HDV infection in different risk groups.

Study/ Risk group	Angeles Castro[11] et al.		Valorie Keely[12] et al.		Shah L[13]. et al		Mapara M[7]. et al		Present study	
	HBsAg reactive cases	positive (%)	HBsAg reactive cases	positive (%)	HBsAg reactive	positive (%)	HBsAg reactive	positive (%)	HBsAg reactive	positive (%)
Blood transfusion	15	2(13.3%)	24	0(0%)	60	6(10%)	52	4(7.69%)	35	3(8.57%)
Sexual	2	0(0%)	108	2(1.85%)	29	1(4.16%)	24	1(4.16%)	19	1(5.26%)
Others	158	32(20.25%)	274	18(6.56%)	107	5(4.67%)	93	5(5.37%)	122	7(5.73%)
Total	175	34(19.42%)	406	20(4.92%)	196	12(6.12%)	169	10(5.91%)	176	11(6.25%)

Looking at the sexual preponderance in all studies, HDV infection is higher in males. It may be due to, sharing injection equipment contaminated with HBsAg or engaging in high risk behaviour, such as unprotected sex. As shown in above table, prevalence rate of HDV infection amongst cases of fulminant hepatitis was as high as 15.09% in Shah L. et al and 13.11% in Mapara M. et al, which is comparable with our study (18.75%). All studies show low prevalence of HDV infection in non-fulminant hepatitis. No study shows HDV infection in jaundice patients without signs and symptoms of hepatitis. Our study suggests that HDV was more commonly associated with fulminant hepatitis. The study done by Gupta P, Kar Pet al[2] also shows that Hepatic Encephalopathy was seen in 75% of delta infected patients as compare to 13.88% of delta negative patients. There is a lot variation in the clinical course. More positivity of anti HD antibody in case having severe liver disease. There appeared to be a large variation in the reported HDV seroprevalence in Fulminant hepatic failure (12.6 to 63%)[6,7,8,9] from India. In non-fulminant hepatitis anti-HDV antibodies were found in 1.89 percent. In contrast, higher seroprevalence of 21.4 and 19 percent have been reported from Chandigarh and Mumbai, respectively[13]. Small number subjects evaluated in different studies (including the present study) limited the overall interpretation.

Above studies shows that variation in rate of positivity for HDV infection in different risk groups in different community. Our study shows the rate of HDV infection is highest in cases of blood transfusion (8.57%), which is comparable to Angeles Castro et al (13.33%), Shah L. et al (10%) and Mapara M. et al (7. 69%), while in Valore Keely et al study a, it was 0. It may be due to multiple blood transfusions and lacunae of blood screening before blood transfusion. Our study shows increased positive percentage in multiple exposed patient (5.26%) compare to other study and it is comparable to previous study Mapara M. et al. (4. 16%). This it may be due to unprotected sex. In present study, there was no case of drug addiction. The group others include the cases with surgical procedure and no other specific history or H/O drug addiction. In our study 1 case (3.44%) was positive for HDV infection in surgical risk group, it is comparable with Shah L. et al study in which 3.33 % HDV infection seen in surgical patients. Composition and risk factor distribution within the respective study groups may account for the apparent inter-study differences.

Conclusion

We conclude that The prevalence rate of hepatitis D virus infection was 0.7% in jaundice patient and 6.25% in hepatitis B reactive patients at tertiary care hospital, Ahmedabad. Male were more seen to be infected with HDV than females. Prevalence of HDV infection was more in old age (>50 years) than 31-50 years. In this study, there was zero HDV infection prevalence in children. Prevalence of HDV infection was high in previous blood transfusion patients. One of the common route of HDV transmission is hematologic, suggesting the need for blood screening for HDV particularly in groups with numerous blood transfusions. Clinician dealing with the Liver Disease should be made aware of the danger of twin infection with HBV and HDV. HDV infection may lead to fulminant hepatitis because highest prevalence seen in fulminant hepatitis patients. The HDV infection is not uncommon. Coexistent infection with Hepatitis B aggravates the course of liver disease. This HDV prevalence can be decreased by global HBV vaccination, increasing awareness, improved preventive measures and changes in the socioeconomic conditions in a fast-developing country like India.

Bibliography

1. Apurva Sankar Sanstry. Sandhya Bhat k, Textbook of Microbiology, First edition, 2016; 527-540.
2. Ananthanarayan R. and Panikar C.K. Jayaram, Textbook of Microbiology, Fifty edition, Pg. 508-516.
3. Praveen K Roy, MD, AGAF; Chief Editor: BS Anand, MD, Drugs & Diseases, Gastroenterology, Hepatitis D, Updated: Mar 16, 2017.
4. WHO, Hepatitis D Fact sheet, Reviewed July 2017
5. Abbas Z et al. Hepatitis D: Scenario in the Asia-Pacific region, World J Gastroenterol. 2010 Feb 7; 16(5):554-62.

6. WHO report, Global hepatitis report, 2017.
7. Mapara M et al. prevalence of hepatitis d jaundice patients, May 2002
8. Emmanuel Thomas, Masato Yoneda, and Eugene R. Schiff, Viral Hepatitis: Past and Future of HBV and HDV, Cold Spring Harb Perspect Med. 2015 Feb; 5(2).
9. Christian Trepo, A brief history of hepatitis milestones, Hepatology Unit, CROIX ROUSSE Hospital and INSERM U1052, Lyon, France, Liver International (2014) © 2013 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd. 30.
10. Chakraborty P, Kailash U, Jain A, Goyal R, Gupta RK, Das BC, Kar P. Seroprevalence of hepatitis D virus in patients with hepatitis B virus-related liver diseases. Indian J Med Res 2005; 122: 254-257.
11. Gimson A.E.S. O'Grady J.G. Ede R.J. et al. Late onset hepatic failure, Haematology, (1986), Pg. 288-294.
12. Bernuau J. Rueff B., Banhamou J.P. Fulminant and subfulminant liver failure, Liver disease, 1986; 97-106
13. Henryk Dancygier, clinical hepatology, principles and practice of hepatobiliary diseases. volume 2, 2009.
14. Harrison, Principal of Internal Medicine, acute viral hepatitis,16th edition, chapter 285, page 1822-1837.
15. WHO:http://www.who.int/mediacentre/factsheets/fs204/en1/ Reviewed , July 2017
16. Kumar Shambhu Nath, Vimal Kumar, D P Banerjee, Prevalence of Hepatitis B Surface Antigen and seropositivity Among Jaundice Chidren in katiyar, International Journal of Scientific and Research Publications, April 2015;5(4).
17. Castro Angeles and Pedreria Jose, Hepatitis Delta infection in North-West Spain, Lancet, March 1989; 665.
18. Kelly Valerie, Hepatitis Delta infection in South-east London, Lancet, January 1989; 45.
19. Matthyssen L. et al. Organon Scientific Development Group. Netherlands, Viral Hepatitis and Liver Disease, 1988; 409-411.
20. Majid Ahmed Shaikh, Wazir Muhammad Shaikh et al Frequency of Hepatitis D Virus Infection in Hepatitis B Surface Antigen-Positive Liver Diseases, Journal of the College of Physicians and Surgeons Pakistan. 2011; 21 (1): 23-25
21. CD Alert, NICD, Viral hepatitis, September 1997.
22. Banker DD, Desai P, Brawner TA, Decker RH. Hepatitis delta virus infection in Bombay. Trans R Soc Trop Med Hyg. 1992; 86: 424-425
23. Shanmugam et al, Seroprevalence of hepatitis delta virus infection among subjects with underlying hepatic diseases in Chennai, southern India. medical image analysis, august 2008;102(8): 729-840.
24. Shah LJ, Mulla et al. A. Prevalence of Hepatitis D Virus (Hdv) In South Gujarat. J Microbiol Immunol infects 2008; 41:227-230.
25. Biswas Samrat et al. Seroprevalence of Hepatitis D Virus in Patients with Hepatitis B Virus-Related Liver Diseases,2014, Assam, India, IJHRMLP, Vol: 02 No: 02, July 2016.
26. M.V. Murhekar, K.M. Murhekar, V.A. Arankalle, S.C. Sehgal. Hepatitis delta virus infection among the tribes of the Andaman and Nicobar Islands, India. Transaction of the Royal Society of Tropical Medicine and Hygiene. 2005; 99: 483-484.