Prevalence Of Hepatitis Delta Virus (HDV) Infection In Hepatitis Bvirus Surface Antigen (HbsAg) Positive Subjects.

Talib Hussain Talpur[1], Shohabuddin Rind[2], Riaz Hussain Khokhar[3], Safdar Ali Parvez Tunio[4], Ashok Kumar Lohano[5], Amir Shahzad Malik[6]

1. Talib Hussain Talpur, PG PMCH Nawabshah
2. Shohabuddin Rind, Senior registrar gastroenterology GMMC Sukkar
3. Riaz Hussain Khokhar, Consultant gastroenterology , HMC Nawabshah
4. Safdar Ali Parvez Tunio, Assistant Professor KMC Khairpur
5. Ashok Kumar Lohano, Assistant Professor, Department Of Medicine, PUMHSW, SBA
6. Amir Shahzad Malik Assistant Professor, Department Of Medicine, PUMHSW, SBA

Corresponding author:
Shohabuddin Rind Senior registrar gastroenterology GMMC Sukkar
dr.shahabrind@yahoo.com

OBJECTIVE: To work out the pervasiveness of hepatitis delta virus infection amongst HBsAg (Hepatitis B virus surface antigen) positive patients.
Setting: Current research was piloted in Department of Medicine at Peoples University hospital Nawabshah.
Duration: Six Months (from September, 2017 to March, 2018).
Study design: Current study was a Cross sectional. Subjects and Method: After approval of study from the school of Physicians and Surgeons of Pakistan, a written consent was taken from the 155 subjects attending inpatient or outpatient department of internal medicine in PMCH Nawabshah. Demographic detail (including name, age and gender) were obtained. All those that fulfill the inclusion criterion were included in study otherwise were excluded. Exclusion criteria were followed strictly to avoid confounding variables. Brief history regarding hepatitis B and D and duration of hepatitis B and D were taken. The appropriate investigations of the subjects like serum anti-HDV by ELISA also as HBsAg (Hepatitis B surface antigen) were send to the institutional laboratory.
RESULTS: The average age of the subjects was 44.6±10.2 (20-60) years. Out of total 155 subjects 54.2% (84) were male subjects and 45.8% (71) were female subjects. 127 (81.9%) HBV patients had delta hepatitis virus.
Conclusion: It is concluded that prevalence of hepatitis D disease is high in subjects affected by hepatitis B infection.
KEY WORDS: hepatitis B, Hepatitis D virus, hepatitis B Surface Antigen, co-infection.

How to cite this article:. Talpur TH[1], Rind S[2], Khokhar RH[3], Tunio SAP[4], Lohano AK [5], Malik AS[6.] **Prevalence Of Hepatitis Delta Virus (HDV) Infection In Hepatitis B virus Surface Antigen (HbsAg) Positive Subjects. .** JPUMHS:2020;10(02)103-109.
http://doi.org/10.46536/jpumhs/2020/10.02.299

INTRODUCTION:

Globally the cirrhosis accounts for about 5-10% of cases and is that the seventh important explanation for morbidity and mortality [1,2.] The prevalence of co-infection of HDV with HBV carriers is around 5% affecting nearly 10-15 million people worldwide [2]. Co-infection is related to more devastating complications and thus mortality due to hepatic failure is up to 20% [3-5]. Hepatitis Delta Virus infection is uncommon in the most industrialized nations and is usually seen in subjects using intravenous (IV) substance abuse or male-to-male sex. In Pakistan, Das et al published an outsized sample size study that showed 16.6% sero-positivity of HDV infection and disease was more common in central part of country [6]. However Abbass et al in their study found that 26% of hepatitis B cirrhotic patients having HDV[7].

Subjects presenting with personality changes, turbulences in sleep, misperception, difficulty in concentration, unusual manners, somnolence and coma is regarded as having Hepatic encephalopathy [8,9]. It is a significant complication related to more than ammonia that affects brain which then end in different manifestation of hepatic encephalopathy [9.]

Studies on incidence of decompensated cirrhosis or hepatic encephalopathy secondary to hepatitis B with concomitant hepatitis D infection are infrequent [9-13]. Amini et al has found the occurrence of HDV infection among decompensated or hepatoma patients to be 53.77% [14.] Gu et al in his cohort study has also found statistically significant association of HDV with gastrointestinal hemorrhage, hepatic encephalopathy and ascites (p value <0.01) [15].Poor prognosis of the patients has been seen within the patients with decompensated cirrhosis with resulting

increased mortality. In the advanced nations and also worldwide the co infection incidence is declining possibly due to vaccination facilities. In contrary, in Pakistan, previous studies showed increasing prevalence rate therefore screening for anti HDV should be done to patients with HBV in order that appropriate measures should be done to scale back associated morbidity and mortality. In a study on 200 subjects positive for HBsAg by rapid device method, only 96 (48%) subjects were reactive by ELISA method, out of these 96 HBsAg reactive subjects, in 80 (88.80%) subjects Anti- HDV were detected by ELISA [12].

Hepatitis B virus (HBV) Infection is worldwide community health problem. It is a big reason for morbidity and mortality, particularly in the growing nations and also the available data shows variable results. Study by gupta showed, that 10% (4/40) of the subjects suffering from cirrhosis related to HBV had anti-delta antibodies reactive [5]. On other hand research by Zaidi G showed that 48% were reactive for HBsAg. Out of those HBsAg, 88.8% were anti-HDV positive [12]. Thus the rationale of my research is to work out the burden of delta viral infection in hepatitis B positive patients within the local population reporting at Peoples University Hospital Nawabshah, in order that appropriate strategies might be developed to avoid further complications

OBJECTIVES:

Determine the occurrence of HDV (hepatitis delta virus) infection amongst HBsAg (Hepatitis B virus surface antigen) positive subjects.

OPERATIONAL DEFINITION

- Hepatitis D virus: Presence of small circular enveloped RNA virus on ELISA.
- Hepatitis B Virus: HBsAg positive on ELISA.
- Anemia Hb< 10mg/dl
- Smoking: Smoker is defined as a person who smokes at least 5 cigarettes a day for more than 1 year.

MATERIAL AND METHOD

Setting: Current research was piloted in Department of Medicine at Peoples University Hospital Nawabshah. Duration: Six months (from September, 2017 to March, 2018). Study design: Current study was a Cross sectional. Sample Size: The sample size was n=155, the software (Raosoft) for "Sample size calculation" was used for sample calculation with 95 % confidential interval and 5 % margin of error. Sample Technique: Non-probability Consecutive sampling technique was applied.

Inclusion Criteria:-

• Age 20 years to 60 years
• Either gender
• HBsAg on ELISA positive.

Exclusion Criteria:-

• Subjects with Hepatitis C virus (HCV) or HIV, other high risk groups such as subjects with hemophilia, blood dyscrasia , regularly blood/blood product transfusions, chronic kidney disease and subjects on hemodialysis or peritoneal dialysis as per medical history of patient.
• I/v drug abusers.

Data Collection Procedure:-

After approval of study from the College of Physicians and Surgeons of Pakistan, a written informed consent was taken from all the subjects attending inpatient or outpatient in department of general medicine at PMCH Nawabshah. Demographic detail (including name, age and gender) were obtained. All those who fulfill the inclusion criterion were included in study otherwise were excluded. Exclusion criteria were followed strictly to avoid confounding variables. Brief history regarding hepatitis B and D and duration of hepatitis B and D were taken. The appropriate investigations of the subjects like serum anti-HDV by ELISA also as HBsAg (Hepatitis B surface antigen) were send to the institutional laboratory. Pro-forma is designed to record the findings of the research by the researcher.

Statistical analysis

All the collected data were analysed by using the computer based software SPSS version 20. All the quantitative variables such as age, BMI, Hb level and duration of hepatitis B were intended for the mean and SD. Frequencies and percentage were computed for qualitative variables like sex, residential status, anemia, smoking status, anti-HDV on ELISA. Effect modifiers like gender, age, BMI, anemia, smoking status, residential status and duration of hepatitis B were organized by stratification. Chi-square test with significant $P<0.05$ was applied to ascertain the effect of those on outcome variable.

RESULTS

Total 155 subjects fulfilling selection criteria were recruited. Descriptive statistics of patient's characteristics were presented in

table 1. The mean age (in years) of the subjects was 44.6±10.2 (20-60), Mean BMI was 23.9±6.3(19.5-18.9), mean Hb level was 9.7±2.6 (7.8-12.6) and 4.2±1.5(2-8)years was mean duration of HBV disease. Distribution of gender was stated, in table 2, where 84(54.2%) patients were male, 71(45.8%) patients were female. Distribution of residence was stated, in table 2, where 88(56.8%) patients were resided in urban areas, 67(43.2%) patients were in rural areas. Distribution of anemia was stated, in table 2, where 92(59.4%) patients had anemia, 63(40.6%) patients were non anemic. Distribution of smoking status was stated, in table 2, where 75(48.4%) patients were smoker, 80(51.6%) patients were non-smokers. In table 2 distribution of outcome which was presence of HDV (hepatitis delta virus) in HBV (Hepatitis B virus) subjects was stated, 127(81.9%) patients had hepatitis delta virus. In table 3-4 stratification for HCV in HBV patients was stated with respect to effect modifiers, significance checked by applying chi-square test with $p < 0.05$ as significant most of the outcomes shows significance difference.

Table: 1 Descriptive statistics of patient's characteristics (n=155)

Variables	n	Minimum	Maximum	Mean	Standard Deviation
Age(in years)	155	20	60	44.6	10.2
BMI(kg/m^2)	155	19.5	28.9	23.9	6.3
HB level	155	7.8	12.6	9.7	2.6
Duration of HBV (in years)	155	2	8	4.2	1.5

Table: 2: Frequency & Percentages of Percentages variables (n=155)

Sex	Frequency	Percentages
Male	84	54.2%
Female	71	45.8%
Urban	88	56.8%
Rural	67	43.2%
Anemia Yes	92	59.4%
Anemia No	63	40.6%
Smoker	75	48.4%
Non-smoker	80	51.6%
HDV Yes	127	81.9%
HDV No	28	18.1%
Total	155	100%

Table 3. Stratification for HDV in HBV patients in relation to age, Gender Residence & Duration of HBV(n=155)

Stratification for HDV in HBV patients in relation to age		HDV		Total	P-value
		Yes	No		
Age groups	<40 years	42	19	61	0.001
		68.9%	31.1%	100.0%	
	≥40 years	85	9	94	
		90.4%	9.6%	100.0%	
Total		127	28	155	
		81.9%	18.1%	100.0%	
Stratification for HDV in HBV patients in relation to gender		HDV		Total	P-value
		Yes	No		
Gender	Male	66	18	84	0.23
		78.6%	21.4%	100.0%	
	Female	61	10	71	
		85.9%	14.1%	100.0%	
Total		127	28	155	
		81.9%	18.1%	100.0%	
Stratification for HDV in HBV patients in relation to Residence		HDV		Total	P-value
		Yes	No		
Residence	Urban	73	15	88	0.71
		83.0%	17.0%	100.0%	
	Rural	54	13	67	
		80.6%	19.4%	100.0%	
Total		127	28	155	
		81.9%	18.1%	100.0%	
Stratification for HDV in HBV patients in relation to Duration of HBV		HDV		Total	P-value
		Yes	No		
Duration of HBV	≤5 years	38	20	58	0.001
		65.5%	34.5%	100.0%	
	>5 years	89	8	97	
		91.8%	8.2%	100.0%	
Total		127	28	155	
		81.9%	18.1%	100.0%	

Table 4. Stratification for HDV in HBV patients in relation to BMI, Anemia & smoking status (n=155)

		HDV		Total	P-value
		Yes	No		
BMI	≤25	80	10	90	0.008
		88.9%	11.1%	100.0%	
	>25	47	18	65	
		72.3%	27.7%	100.0%	
Total		127	28	155	
		81.9%	18.1%	100.0%	
Stratification for HDV in HBV patients in relation to anemia		HDV		Total	P-value
		Yes	No		
Anemia	Yes	81	11	92	0.017
		88.0%	12.0%	100.0%	
	No	46	17	63	
		73.0%	27.0%	100.0%	
Total		127	28	155	
		81.9%	18.1%	100.0%	
Stratification for HDV in HBV patients in relation to smoking status		HDV		Total	P-value
		Yes	No		
Smoker	Yes	67	8	75	0.02
		89.3%	10.7%	100.0%	
	No	60	20	80	
		75.0%	25.0%	100.0%	
Total		127	28	155	
		81.9%	18.1%	100.0%	

Discussion

In Pakistan especially Sindh province occurrence of HDV infection is high. Earlier it was thought that the prevalence of HDV infection was higher and exists particularly to the rural areas this assumption is not sustained by current study as a large number of study belonged to the urban community, this suggests that high prevalence of HBV-HDV co-infection exists in the cities also. The number of participants in this research was not enough in comparison to the available studies. The outcomes of current study are very remarkable and motivating. This was a prime study on this subject from the local area where there is increased occurrence of dual HBV-HDV infection was observed. In current study there was increased rate of HDV in male gender in comparison to the female gender. Anti-HDV by ELISA was positive in 88.8% of HBV positive subjects; this prevalence rate is higher in comparison to the previous reports from Pakistan [11]. The outcome of current study further advocated that pervasiveness of HBV/HDV co-infection in Pakistan had amplified through the previous era. The active HDV infection rate is 30.00% in Pakistan as was analysed by reactive HDV RNA qualitative by PCR that is quite increased rate. Moreover the incidence of HDV infection is common in male gender in comparison to females. The risk behaviors of male gender are recognized for this increased HDV infection. The common public, and all the health related personal must be given awareness about the risk factors related to the HBV and HDV co-infection. The incidence of anti-HDV antibodies in HBsAg (inactive carriers) was 4% in our study. We did not observe the relationship of studied risk factors in relation to HDV infection, though likelihood of missing bias could not be ruled out. Subjects with clinical jaundice and raised enzymes had more prevalence of HDV as compared to the in-active carriers of HBsAg, this could be elucidated by observing more serious infection in patients with dual infection of HBV and HDV. Cancer is very frequent globally and Hepatocellular carcinoma is the at the number fifth place and biologically about six percent of total recently confirmed malignancies, the occurrence of liver cancer vary place to place immediately.[13] HBV and HCV, HBV and HDV as super added or as co-infection, Non Alcoholic Fatty Liver Disease (NAFLD), (ALD) Alcoholic Liver Disease are the main threat factors are for Hepatocellular carcinoma mainly these identified risk factors direct to the development, which then proceed further to hepatic cirrhosis later on.[14] One of the few human oncogenous recognized viruses is that of HBV.[10] In nations with HBV endemic the incidence of HCC is observed increased. The hazard of HCC development increases with HDV co-infection.[15] This research was conducted to conclude the comparative occurrence between subjects affected by viral hepatitis due to viral hepatitis B and their associated various risk agents present in these patients. Many times there are multiple risk factors and their repeated exposures in these patients. Patients visiting gastroenterology / hepatology clinic/departments in the above said institutions, that what is the valid position in relation to viral hepatitis B and their associated risk factors, so that timely detection and management may lead to the dropping of associated burden of disability and death. Saravanan S et al [16] researches showed the subjects of chronic hepatitis group, suffering from viral hepatitis B and are chronically ill, antibodies against Hepatitis D Virus were present in approximately 5.7% of diseased persons, leading to the generally chronic liver disease (Cirrhosis) in about 5.9% patients. In subjects suffering from chronic hepatitis B, antibodies against HDV were detected in about 05.7%, leading to cirrhosis in 05.9% subjects respectively. [16]Worldwide about 48 to 60 million persons had HDV infection in HBV infected subjects. The universal occurrence of HDV in general population is about 0.80% and 13.02% in HBsAg reactive carriers. The worldwide prevalence of HDV in a latest study is reported 0.98% [17]. The difference with the former literature can basically be endorsed to the stratification for diverse inhabitants and the elimination of non-representative populaces such as IDUs, HIV and liver ailment subjects. Thus the criticism of overestimation made in previous studies can be avoided [18,19]. Many factors are attributed to the raising universal burden of HDV. HDV was previously regarded as the satellite virus of HBV. Current studies have demonstrated that other than HBV can act as helper virus for HDV [20]. The HCV can support the assembly and secretion of HDV infectious particles in subjects, as was observed by raised occurrence rate and three fold raises in odds for HDV infection in double infected subjects with HBV and HCV, but more confirmatory investigations are needed [20.] The frequency of HDV infection is tremendously raised amongst HBV-positive IDUs. Hence, current research fits with former work presenting the significance of injection drug practice in

transmission of HDV infection [21, 17]. Intravenous drug users and HIV exposure are also contributing factors for increasing burden of HDV [23,24]. The burden of HDV occurrence can be reduced by reducing the transmission from intravenous drug users. There is a significant variation in the HDV prevalence among different geographical parts of the world. HDV infection prevalence is high in Tunisia, Mongolia, and Niger (15.33%, 8.31% and 5.04%) respectively. In eighteen countries over the globe the prevalence of HDV is over 1.0%, and more than half the nation's from Africa, however Latin America has fair count of high prevalence countries. In HBsAg positive carriers the incidence of HDV is 10% to 20% in 23 countries, between 20%-30% in 10 countries and in 23 countries the incidence remains above 30% respectively. The previous data analyzed high prevalence rates of HDV infection in Asia (central), Europe (eastern), Latin America (tropical and central) and sub-Saharan Africa [17]. Asia and Africa are both major reservoirs of HBV infection; the findings suggest that Asia (44.41% to 56.55%) and Africa (22.30% to 38.37%) have the large inhabitants hit by infection due to HDV [25]. Rind S et al in ISRA hospital concluded that prevalence of hepatitis D disease is sort of high in subjects affected by hepatitis B infection. Failure to acknowledge HDV can cause improper treatment of patients affected by HBV. Complete and proper implementation of HBV vaccination should be wiped out the overall population to scale back the burden of combined HDV illness in coming future.[26] The prevalence of HCC was 33.34% in subjects with dual infection of chronic HBV and HDV in comparison to single chronic HBV infection with occurrence of 20.80% [27.]

CONCLUSION

We concluded that prevalence of hepatitis D disease is sort of high in subjects affected by hepatitis B infection. Failure to acknowledge HDV can cause improper treatment of patients affected by HBV. Complete and proper implementation of HBV vaccination should be wiped out the overall population to scale back the burden of combined HDV illness in coming future.

The consequences of the present research describe an increased incidence of HDV-HBV dual infection in Pakistan that has been enlarged in excess of time. Our country is an epidemic region for infection of HDV.

Limitation

The restrictions of current study comprises the consumption of retrospective data collection by many of the clinicians by dissimilar laboratory methods. Inadequate facts administration organizations had proscribed an evaluation of Hepatitis Delta Virus testing through the research centers. HBV subjects were not usually experienced for anti-HDV antibodies and HDV RNA were not tested in most of the seropositive subjects, so partial testing reporting marks the situation probable that more or less patients with HDV-infection were not find out.

Funding: No Funding From Any Organization

Conflict Of Interest: No

Acknowledgment: we are thankful to all the persons who cooperated for the organization and compilation of this study

Author contribution: The authors of this research had contributed from design to data and from results and analyses to discussion.

REFERENCES

1. Kim MY, Choi H, Baik SK, Yea CJ, Won CS, Byun JW, et al. "Portal hypertensive gastropathy: correlation with portal hypertension and prognosis in cirrhosis". Dig Dis Sci 2010;55(12):3561–7.
2. Ramachandran S, Zhai X, Thai H, Campo DS, Xia G, GanovaRaeva, et al. Evaluation of intrahost variants of the entire hepatitis B virus genome. PLoS One. 2011;6(9):e25232.
3. Gu XH, Chen Z, Dai RY, Zhang ML, Tang HM, Chen LB,etal.Analysis on the clinical features of 507 HDV-infected patients.CellBiochemBiophys. 2014 Dec;70(3):1829-32. doi:10.1007/s12013-014-0137-8
4. Sundaram V, Shaikh OS. Hepatic encephalopathy: pathophysiology and emerging therapies. Med. Clin. North Am. 2009;93(4):819–36, vii.
5. Gupta P, Kar P, Chakravarty A, Jain A. Delta virus infection in cirrhotics in a north Indian hospital. J Assoc Physicians India. 1993 Aug;41(8):503-4.
6. Das K, Ali H, Mahmood T, Munir SM, Ahmed T, Farooq MU. Comparative analysis of disease activity in patients of chronic Hepatitis B virus. J Ayub Med CollAbbotabad. 2008;20(2):39–42.
7. Abbas Z, Qureshi M, Hamid S, Jafri W. Hepatocellular carcinoma in hepatitis d: does it differ from hepatitis b monoinfection? Saudi Journal of Gastroenterology : Saudi J Gastroenterol. 2012 Jan-Feb;18(1):18-22. doi: 10.4103/1319-3767.91731.
8. Randolph C, Hilsabeck R, Kato A, Kharbanda P, Li YY, Mapelli D et al. . "Neuropsychological assessment of

hepatic encephalopathy: ISHEN practice guidelines". Liver Int.2009;29(5):629–35.
9. Guan R, Lui HF. Treatment of hepatitis B in decompensated liver cirrhosis. Int J Hepatol. 2011;2011:918017. doi: 10.4061/2011/918017. Epub 2011 Jun 23.
10. Bajaj JS. The modern management of hepatic encephalopathy. Aliment PharmacolTher. 2010 Mar;31(5):537-47.
11. Mumtaz K, Hamid SS, Adil S, Afaq A, Islam M, Abid S. Epidemiology and clinical pattern of hepatitis delta virus infection in Pakistan. J GastroenterolHepatol 2005;20:1503-7.
12. Zaidi G, Idrees M, Malik FA, Amin I, Shahid M, Younas S, et al. Prevalence of hepatitis delta virus infection among hepatitis b virus surface antigen positive patients circulating in the largest province of Pakistan. Virol J. 2010 Oct 26;7:283.
13. B. Heidrich, C. Yurdaydin, G. Kabacam, B.A. Ratsch, K. Zachou, B. Bremer, et al.Late HDV. RNA relapse after peginterferon alpha-based therapy of chronic hepatitis delta. Hepatology, 60 (1) (2014), pp. 87-97
14. European association for the study of the liver: easl clinical practice guidelines: management of chronic hepatitis b virus infection. J. Hepatol., 57 (2012), pp. 167-185
15. Gupta P, Biswas D, Shukla I, Bal A. Need for Routine Screening of HBV and HDV in Patients with Cirrhosis of the Liver. Ind J Med Microbiol. 2005;23:141–142. doi: 10.4103/0255-0857.16060.
16. 16.Carmo-Fonseca JC. Hepatitis D. Rev Soc Bras Med Trop. 2002;35:191–90.
17. .Rizzetto M, Hoyer B, Canese MG, Pureell RH, Gerin JL. Delta agent association of Delta antigen with hepatitis B surface antigen and RNA in serum of Delta infected chimpanzees. Proc NattAcadSci USA. 1989;77:6124–6128. doi: 10.1073/pnas.77.10.6124.
18. Hsieh TH, Liu CJ, Chen DS, Chen PJ. Natural course and treatment of hepatitis D virus infection. J Formos Med Assoc. 2006;105:869–81. doi: 10.1016/S0929-6646(09)60172-8.
19. Seetlani NK, Abbas Z, Raza S, Yakoob J, Jafri W. Prevalence of Hepatitis D in HBsAg positive patients visiting liver clinics. JPMA. 2009;59:434.
20. Chakraborty P, Kailash U, Jain A, Goyal R, Gupta RK, Das BC. Seroprevalence of hepatitis D virus in patients with hepatitis B virus-related liver diseases. Indian J Med Res. 2005;122:254–7.
21. Deertekin H, Yalçin K, Yakut M. The prevalence of hepatitis delta virus infection in acute and chronic liver diseases in Turkey: an analysis of clinical studies. Turk J Gastroenterol. 2006;17:25–34.
22. Rizzetto M. Hepatitis delta: the virus and the disease. J Hepatol. 1990;11Suppl 1:S145–8.
23. Triki H, Said N, Ben Salah A, Arrouji A, Ben Ahmed F, Bouguerra A, et al. Seroepidemiology of hepatitis B, C and delta viruses in Tunisia. Trans R Soc Trop Med Hyg. 1997;91(1):11–4.
24. Djebbi A, Rebai WK, Bahri O, Hogga N, Sadraoui A, Triki H. [Serological markers, viral RNA and genotype of hepatitis delta virus in HBs antigen positive Tunisian patients]. PatholBiol (Paris). 2009;57(7-8):518–23. doi: 10.1016/j.patbio.2008.09.010.
25. Jenhani F, Ayed K, Gorgi Y, Zoulim F, Pichoud C, Trepo C. Delta infection in chronic HBs Ag carriers in Tunisia: high prevalence in chronic asymptomatic HBs Ag carriers and in HBs Ag positive cirrhosis. Ann Trop Med Parasitol. 1990;84(4):349–53.
26. Gaeta GB, Stroffolini T, Chiaramonte M, Ascione T, Stornaiuolo G, Lobello S, et al. Chronic hepatitis D: a vanishing Disease? An Italian multicenter study. Hepatology. 2000;32(4 Pt 1):824–7. doi: 10.1053/jhep.2000.17711.
27. Degertekin H, Yalcin K, Yakut M. The prevalence of hepatitis delta virus infection in acute and chronic liver diseases in Turkey: an analysis of clinical studies. Turk J Gastroenterol. 2006;17(1):25–34.
28. Huo TI, Wu JC, Lin RY, Sheng WY, Chang FY, Lee SD. Decreasing hepatitis D virus infection in Taiwan: an analysis of contributory factors. J GastroenterolHepatol. 1997;12(11):747–51.
29. Acharya SK, Madan K, Dattagupta S, Panda SK. Viral hepatitis in India. Natl Med J India. 2006;19(4):203–17.
30. Makuwa M, Caron M, Souquiere S, Malonga-Mouelet G, Mahe A, Kazanji M. Prevalence and genetic diversity of hepatitis B and delta viruses in pregnant women in Gabon: molecular evidence that hepatitis delta virus clade 8 originates from and is endemic in central Africa. J ClinMicrobiol. 2008;46(2):754–6. doi: 10.1128/JCM.02142-07.
31. Kushner T, Serper M, Kaplan DE. Delta hepatitis within the Veterans Affairs medical system in the United States: Prevalence, risk factors, and outcomes. J Hepatol. 2015;63(3):586–92. doi: 10.1016/j.jhep.2015.04.025.
32. Celen MK, Ayaz C, Hosoglu S, Geyik MF, Ulug M. Anti-hepatitis delta virus seroprevalence and risk factors in patients with hepatitis B in Southeast Turkey. Saudi Med J. 2006;27(5):617–20.
33. Rind S, Jamali AA, Hussain R. Hepatitis D Virus Infection in Hepatitis B Surface Anitgen Positive Cases at Isra University Hospital Hyderabad Ann. Pak. Inst. Med. Sci 13 (2), 173-176
34. Hussain R. Jamali AA, Rind S, Hepatocellular Carcinoma in Patients Suffering from Chronic Hepatitis B versus Co-Infection of Hepatitis B and D Virus. Journal of Islamabad Medical & Dental College, 2017,203-207