Poster Presentation Abstracts

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AN EXPERIENCE OF PEGYLATED INTERFERON IN PATIENTS WITH CHRONIC HEPATITIS D

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Background and aims: Hepatitis D is a difficult to treat infection. Standard interferon-alpha is not an ideal treatment. Recent few trials with pegylated interferon have shown better response. The aim of this study was to evaluate the local experience of the efficacy of pegylated interferon for the treatment of chronic hepatitis D.

Methods: An observational study. Data of the HDV RNA positive patients treated with pegylated interferon in the last two years was analyzed. Patients were treated for 48 weeks. Virological and biochemical responses were noted.

Results: Total number of patients treated so far is 65. Two patients decompensated during treatment. Twenty nine patients have completed the treatment. All are males. Median age 28 years (range 15-55). Sixteen patients received pegylated interferon alpha-2a and thirteen alpha-2b. Clinical cirrhosis was present in 12 (41%). End of treatment viral clearance was seen 13/29 (45%) cases. ALT normalization was seen in 12/29 (41%). Four patients have completed six months post-treatment. Two had sustained response, one relapsed and one became PCR negative. The treatment was well tolerated by most of these patients.

Conclusion: Patients of hepatitis D should be considered for treatment with Pegylated interferon as a significant proportion of patients do respond to treatment.

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INTERFERON FOR CHRONIC HEPATITIS D: A SYSTEMATIC REVIEW

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Background and aims: The aim of this systematic review was to evaluate the beneficial and harmful effects of interferon-alpha for the treatment of chronic hepatitis D.

Methods: Included in this analysis were randomised clinical trials evaluating interferon-alpha versus placebo or no intervention as well as combination therapy versus interferon monotherapy for chronic hepatitis D infection.

Results: Ten randomised trials fulfilled the inclusion criteria. 340 participants were analysed. Five trials compared standard interferon with no treatment. End of treatment virological response (ETR) was seen in 32.6% of the patients compared to 7.8% in the untreated controls (RR 0.76, 95% CI 0.66 to 0.87, P = 0.0001). Sustained virological response (SVR) was achieved in 17.4% of patients on interferon compared to 5.2% of controls (RR 0.89, 95% CI 0.80 to 0.98, P = 0.02). End of treatment ALT normalization was seen in 34.8% patients treated with interferon versus 1.3% in the controlled group (RR 0.69, 95% CI 0.59 to 0.80, P < 0.00001). ALT remained normal in 11.9% treated patients at six months post-treatment follow-up (RR 0.92, 95% CI 0.84 to 0.99, P = 0.04).There was histological improvement in 27.2% patients treated with interferon-alpha compared to 15.6% in controls % (RR 0.86, 95% CI 0.74 to 1.00, P = 0.06). Two trials comparing a higher dose with a lower dose of standard interferon achieved SVR in 23.3% with higher dose compared to 10% with the lower dose (RR 0.85, 95% CI 0.68 to 1.07, P = 0.16). Four trials compared interferon monotherapy with lamivudine, ribavirin or adefovir in combination with interferon. There were no significant differences in the ETR, SVR and biochemical responses.

Conclusions: Interferon is not an ideal agent for treating hepatitis D. Addition of an oral anti-viral agent does not improve the response rate and needs further evaluation.

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HEPATOCELLULAR CARCINOMA IN HDV: DOES IT DIFFER FROM HBV MONOINFECTION

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Background and aims: Hepatitis D superinfection in patients with chronic hepatitis B leads to accelerated liver injury, early cirrhosis and decompensation. It may be speculated that hepatocellular carcinoma (HCC) may differ in these patients from HBV monoinfection. This study aimed to compare clinical aspects of hepatocellular carcinoma in patients of hepatitis D with hepatitis B alone.

Methods: A total of 92 consecutive HCC cases seropositive for antibody against hepatitis D virus antigen (HDV group) were compared with 92 HBsAg positive but anti-HDV negative cases (HBV group). The clinical manifestations, Child Class, tumor characteristic, and staging were compared.

Results: The mean age was not different in both groups of patients (55.4 years in HDV group and 53.7 in HBV group). Other features including sex, presence of ascites, serum biochemistry, gross tumor appearance, Child Class and Okuda stage were not significantly different between the two groups. Decreased liver size was noticed more in cases of HDV group compared to HBV group where the liver size was normal or increased (p=0.000). HDV group had lower platelets (p=0.063) and larger varices on screening endoscopy (p=0.005). Multifocal tumors were more common in HBV group (p=0.057). TNM classification showed more stage III-IV disease in HBV group (p=0.000).

Conclusion: Decreased liver size and indirect evidence of more severe portal hypertyension and earlier TNM stage compared to HBV monoinfection indicate that HDV infection possibly causes HCC indirectly by inducing inflammation and cirrhosis.

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VIRAL HEPATITIS D AMONG HEMODIALYSIS PATIENTS: A WORLDWIDE UNDERESTIMATED PROBLEM

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Background: Hepatitis D virus (HDV) infection is a major concern among hemodialysis (HD_i) with HBs Ag positive; and HDV can be transmitted at serum dilutions as high as 10^{-11} and HBsAg-positive HD_i patients stand therefore a very high risk of becoming infected with HDV through blood contamination of the hemodialysis machinery or through transfusions. Despite the importance of the problem studies of HDV in HD_i are limited, the reported frequency of HDV infection among HD_i patients is different throughout the world and there is no definite standard protocol to manage disease in these patients.

Methods: We gathered all reports on HDV infection in HDi patients by an integrative search of MEDLINE from 1985 to August 2008.

Results: After a preliminary evaluation, we found only 18 articles that seemed relevant. These articles were analyzed in detail and the relevant data were gathered and summarized. Worldwide estimates on the frequency of HDV infection in HDi patients are inadequate in different parts of the world. European reports have suggested that HDV infection is rare or absent in HDi patients. HDV seems to be a serious problem in western Asian countries. Studies reported higher than 8% of HDV in HDi patients in Turkey, 7.7% in Oman and 12.5% Saudi Arabia had evidence of HDV infection Despite the concern raised by these studies which suggested that the prevalence of HDV in HDi was higher than the average global prevalence (5%), no other specific research has been carried out since 1994 in HDi patients in Middle East.

Conclusion: In conclusion, despite all aforesaid problems regarding HDV infection in HDi subjects, few studies have been carried out in developing countries to determine the prevalence of HDV in HDi patients. And we will present a standard protocol to manage disease in these patients.

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IMPORTANT PRESENCE OF CO-INFECTION OF HEPATITIS B GENOTYPE F AND HEPATITIS DELTA GENOTYPE 3 IN THE AMAZON REGION OF COLOMBIA

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The delta virus (HDV) is widely distributed and associated with fulminant hepatitis epidemics in areas with high prevalence of HBV. Few studies have been carried out to assess their epidemiologic impact in Colombia. Seven samples from patients who died of fulminant hepatitis in the Amazon Region of Colombia were sent to the laboratory for HBV diagnosis. These samples were positives for HBsAg by ELISA test. A fragment of 734 bp partially comprising HBsAg and Polymerase coding regions (S/POL) was amplified. For the detection of HDV RNA, an amplification of 403 bp was performed. Of the seven patients, five also were positive for HBV and five were positive for HDV. The sequences obtained in this study were genotyped by phylogenetic reconstructions using reference sequences from each genotype obtained from GenBank (Datasets HBV n=361; HDV n=57). These sequences were aligned using Clustal X software and edited in the SE-AL software. Bayesian phylogenetic analyses were done using Markov Chain Monte Carlo (MCMC) approach implemented in BEAST v.1.5.3. The MCC tree was obtained from summarizing the 10000 substitution trees using Tree Annotator v.1.5.3. The two samples successfully sequencing for HBV were subgenotypes F3 and F1b. The five samples positive for HDV were genotype HDV-3. Even if the sampling does not detailed information about the epidemiological behavior of these viruses, the presence of five positive samples for HDV shows an important presence of HDV in the region. This is the first study performed in Colombia where both HDV and HBV are characterized. These results invite a proposal of a greater control of co-infection and of HDV infection in the Amazon Region of Colombia and showed that the sequences found in this study, classified under group HDV-3, correspond to those already reported in South America, where this genotype has been shown to be prevalent.

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A POSSIBLE ROLE FOR HSP105 IN HDV REPLICATION

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Results obtained by 2DE MS-based quantitative proteomics analysis, showed that, in Huh7 cells expressing the large delta antigen (L-HDAg), the heat shock protein 105 (HSP105) suffered a decrease in its expression. Here the results were confirmed by western blot analysis and several assays were performed in order to understand how this protein could be involved in HDV replication. Immunoprecipitation assays were initially performed and have shown that HSP105 interacts with both forms of the delta protein with higher preference for the L-HDAg. HSP105 was then silenced using siRNAs and a 30% decrease of the expression of HSP105 was achieved leading to a 35% decrease in the expression of L-HDAg. As for RNA levels, qPCR was performed showing a 30% decrease in mRNA levels of HSP105 and 2-fold increase in the levels of HDV RNA. Immunofluorescence assays show that, although in low levels, HSP105 co-localizes with the delta antigen.

So it seems that in the presence of the large delta antigen there is a decrease in the expression of HSP105. On the other hand, by silencing HSP105, the large delta antigen expression decreases and the levels of HDV RNA increase, which is expected as the large form of the delta antigen has been shown to inhibit replication. These results and the fact that HSP105 and the large delta antigen seem to interact directly suggest that HSP105 is involved in HDV replication.

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VIROLOGICAL AND CLINICAL CHARACTERISTICS OF DELTA VIRUS INFECTION IN RURAL AND URBAN POPULATION OF SINDH, PAKISTAN

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Background and aim: Hepatitis “D” virus infection or delta hepatitis has been studied in various regions of Pakistan, but prospective data comparing rural and urban population with respect to clinical and virological characteristics is sparse.

Method: We prospectively investigated 426 the HBSAg positive patients at our Hepatology clinic belongs to all over Sindh except Karachi. We divided patients in urban and rural groups. All the participants under went testing for HBeAg, HBV DNA both qualitative and quantitative assays, delta antibody testing and delta RNA where appropriate. Both groups were matched in age, weight and BMI.

Results: Out of 426 patients, 193(45.3%) were reactive for delta antibody. In rural it was 37% and 8.2% in urban with p-value of 0.003. HDV RNA was tested in 140 anti HDV reactive patients. It was detected in 48/114 (42%) rural and 12/26 (46%) urban patients with p-value of 0.2. Hepatitis delta was significantly more prevalent in rural male compared to urban male with p-value of 0.01. No difference in female sex seen. More advance disease is seen in rural patients {Cirrhosis with anti HDV positive. Rural 72/158 (45.6%), urban 11/35 (31.4%) P-value < 0.001}. There was no difference in urban and rural groups with respect to presence of HBV DNA, HBeAg, anti HCV antibody and ALT levels in females.

Conclusion: Significantly higher anti HDV is prevalent (37%) in rural patients of Sindh province. HDV co infection is associated with increased morbidity of liver disease in both rural and urban patients.

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THE PREVALENCE OF HEPATITIS DELTA VIRUS INFECTION IN HEPATITIS B VIRUS-RELATED ACUTE AND CHRONIC LIVER DISEASES IN INDIA

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Background and aims: Several reports indicated a declining trend in the occurrence of hepatitis D virus (HDV) infection in some geographical areas. However, little information is available in India to confirm whether a similar epidemiological change is occurring in this part of the world. The present study was undertaken to evaluate the seroprevalence of HDV in patients with hepatitis B virus (HBV) related liver diseases attending a Government hospital in New Delhi, and to assess any change in its epidemiology by comparing the results with seroprevalence figures reported in the past.

Methods: A total of 246 patients with HBV-related liver diseases comprising 62 cases of acute viral hepatitis (AVH), 12 of fulminant hepatic failure (FHF), 74 of chronic hepatitis (CH), 88 of cirrhosis and 10 of hepatocellular carcinoma (HCC). All patients were evaluated for the presence of delta antibodies using commercially available ELISA kits. Both IgM and IgG anti-delta assays were performed to differentiate between active and convalescent infection.

Results: The mean age of the patients was 35.6 +/- 3.3 years with a male : female ratio of 11:5. Of the 246 patients, serological evidence of delta virus infection was seen in 27 subjects (10.9%); 18 (7.3%) had evidence of past infection (IgG positive, IgM negative) and the remaining 9 (3.6%) recent infection (IgM anti-delta antibody positive). Evidence of HDV infection in acute viral hepatitis, fulminant hepatitis, chronic hepatitis, cirrhosis and hepatocellular carcinoma groups was found in 3.1%, 20%, 8.1%, 15.2% and 33.3% patients, respectively.

Conclusion: Our results suggest that delta infection may not be very common in Indian patients with HBV-related liver diseases. It is also possible that HDV epidemiology in this part of the world may be undergoing a transition towards decreasing prevalence.

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IMPACT OF HEPATITIS DELTA VIRUS REPLICATION ON SEROEPIDEMIOLOGIC MARKERS OF CHRONIC HEPATITIS B INFECTION

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Introduction: The influence of hepatitis delta virus (HDV) infection on hepatitis B virus (HBV) associated antigens and antibodies may vary. The presence of HBV replication markers, hepatitis B e antigen (HBeAg) or HBV DNA, is associated with not only continuing hepatitis activity or intermittent hepatitis flares but also with subsequent disease progression, including hepatic decompensation and hepatocellular carcinoma (HCC).

Aim: To elucidate the changing seroepidemiologic profile of HBV in HDV infected patients, we examined for HBsAg and HBV DNA titers, HBeAg and anti-HBe status in our HBV/HDVpatients.

Methods: A group of 303 chronic HBV infected patients were involved into the study. Anti-HDV seropositivity was investigated in all patients. The anti-HDV positive cases were further tested for HDV RNA. Finally, HDV RNA positive patients were compared to HDV RNA negative cases in terms of HBV DNA, HBsAg titers, HBeAg and anti-HBe results.

Results: Of 303 chronic HBV cases, 136 patients were anti-HDV positive (44,9%). Totally 124 of 136 anti-HDV positive patients were tested for HDV RNA and 69 cases were found positive (55,6%). The HDV RNA positive patients showed lower HBV DNA levels with a significant difference (median: 9420 copies/ml, range: 5.8-1.9x10^8 ,n=69 and 33850 copies/ml, range: 212-5.5x10^9, n=55 respectively; p< 0.01). Mean HBsAg titer of the HDV RNA positive group was higher than that of HDV RNA negative group and the difference was also significant (313±56 ve 281±93, respectively; p= 0.04). HBeAg was positive in 8.1 % of HDV RNA positive and 7.3% of HDV RNA negative patients (p>0.05). Anti-HBe was positive in 41.1% HDV RNA positive and 35.5% of HDV RNA negative patients (p>0.05).

Conclusions: Our findings demonstrated that HDV replication has significant influence on HBV DNA and HBsAg titers, but not on HBeAg and anti-HBe positivity rates in chronic HBV patients.

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MODIFIABLE RISK FACTORS IN CHRONIC DELTA INFECTION

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Introduction: A growing body of literature indicates that the epidemiologic characteristics of chronic hepatitis delta infection can be influenced by a number of factors. Main risk factors of this infection can be evaluated as; a-) Family history of chronic hepatitis B, b- Dental therapy history, c-) History of sexual contact with suspected carrier, d-) Operation or transfusion history and e-) History of iv drug injection.

Aim: The aim of this study is to investigate the factors that have been suspected for their influence on higher incidence and exacerbation rate of HDV in our region.

Methods: A group of 303 chronic HBV infected patients was investigated for the study. The mean age of patients was 43.8±12.7 (between 18 and 73 years). HBeAg and anti-HBe positivity were 21.6% and 78.4%, respectively.

Results: Anti-HDV positivty was seen in 136 patients (44.9%). When the risk factors in study group were screened, anti-HDV positive group had family history of 74.9%, dental therapy history of 57.2%, sexual contact with suspected HBV carrier history of 7.3%, operation or transfusion history of 8.4% and iv drug injection history of 0.6%. Anti-HDV negative group had family history of 61.1%, dental therapy history of 63.2%, sexual contact with suspected HBV carrier history of 5.7%, operation or transfusion history of 7.3% and iv drug injection history of 1.4%. The family history was significantly higher in anti-HDV positive group (p=0.024) and it was only found to be an important risk factor for anti-HDV positivity in the study group (Odds ratio 1.34, 95% confidence interval 1.05 to 1.72).

Conclusion: Although a variety of potentially modifiable factors may influence the epidemiology of chronic HDV infection, family history seems to be the most important risk factor among them. A good understanding of the risk factors is important for proper management and counselling of HDV patients.

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EPIDEMIOLOGY OF HEPATITIS DELTA VIRUS (HDV) IN IRAN

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Background and aims: It is estimated that approximately 5 % of HBsAg carriers are infected with hepatitis D virus (HDV) worldwide. Data about the HDV incidence and prevalence are various in different parts of the world.

Methods: We reviewed all published reports on HDV regarding its prevalence (sero - and molecular epidemiology) as well as its risk factors in Iranian HBsAg positive individuals.

Results and conclusions: Of 3869 sample size studied, 293 (7.57%) were HDV - infected, 221(75.4%) of cases and 72 (24.6) were positive by HDV antibody and HDV RNA, respectively. Among 72 HDV RNA isolates that were investigated by molecular approaches, all contained genotype I which phylogenetically related to Turkish and Italian sequences obtained from the database. Tattooing, Phlebotomy, dental procedures, war, imprisonment, intravenous drug abusing, homo dialysis and living in urban areas are the major risk factors with high HDV prevalence.

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THE ROLE OF DELTA INFECTION IN SPLENOMEGALY ASSOCIATED WITH CHRONIC LIVER DISEASES

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Background: Chronic delta infection had been reported to have a substantial role in splenomegaly.

Aims of study: To asses the role of delta infection in cases of splenomegaly associated with chronic liver diseases

Methods: 93patients with histologicaly chronic liver disease were divided into three groups: Huge splenomegaly (37),moderate splenomegaly (29) and mild splenomegaly (27)were subjected to clinical examination,urine,stool &rectal snips analysis for Bilharziasis,Biochemical&virologic liver profile ,ultrasonography for size of liver and spleen and needle liver boispsy.

Results: 26 patients(70.2%)+ve delta lgG with huge,6(20.6%)with moderate with no cases in mild splenomegaly with significant value higher in huge than that in moderate splenomegaly(P< 0.001).+ve delta lgG of huge splenomegaly 26(70.2%) showed that19(51.3%)with +ve HBsAg and 7(19.9%) with -ve HBsAg ,+vedelta lgG of moderate splenomegaly 6(20.6%) sohwed that 2(6.8%) with +ve HBsAg and 4(13.7%)with -veHBsAg..HBeAg was -ve all positive delta and therefore it is presence may tend to preclude chronic delta infection

+ve HBsAg &-ve delta lgG patients 4(10.8%) of huge ,5(17.3%) of moderate,2(10.0%)patients of mild splenomegaly with no significant value .+ve anti HCV & +ve delta lgG patients and-ve anti HCV & +ve delta lgG patientswere13(35.%) of huge ,3(10.3%) of moderate,0of mild splenomegalywith significant value higher in patients with huge than that iwith moderate splenomegalyalsowith no significant value.

+veBilharzial ova by stool analysis and rectal snips in were[9(24.3%),10(27.02%)] in huge,11(37.9%),10(34.4%)] in moderate and [11(40.7%),11(40.7%)] with no significant value among the three groups .But schistosomiasis increased with the degree of cirrhotic activity ; there were +ve Bilharziassis in7(58.3%)with cirrhotic mild activity.18(94.7%)with moderate and6(100%) with severe activity with significant value higher in patients with moderate than cirrhotic mild activity.

Conclusion: Huge splenomegaly has been attributed to chronic delta infection and not to schistosomiasis even if HBsAg negative.But schistosomiasis has been reported to increase histopathological activity of cirrhosis due to impaired immunity.

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THE PREVALENCE OF HEPATITIS DELTA VIRUS AND DIFFERENT ETHNICAL GROUPS IN SIND, PAKISTAN

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Background and aims: In Asia-Pacific region HBeAg infection along with HDV is a major health concern. Approximately 18 million people are estimated to be involved in HDV infection. The trend of HDV disease is almost decreasing from the European region, but increasing in South Asia countries due to favorable spreading conditions for Hepatitis B and other related diseases. The true existing data are not available from most of the countries including the Pakistan. We studied the prevalence of HDV infection among different ethnical groups in Sind, Pakistan.

Method: The data collected from 533 total patients of the two major hospitals of two different cities of province Sind, Pakistan which were presenting the ISRA University, Hyderabad and Aga Khan University Karachi in last three years. Among them we found 480 patients of HBeAg with HDV positive DNA PCR detectable.

Results: We found in our study that the prevalence of HDV was 40% based on antibody results among the patients serum who were attending the tertiary care hospitals for detection of HBsAg. The mean age was 32.67 years (median 31.00 years, range 3- 80). Males were more affected 424 (79.5%) as compared to the female 109 (20.4%).The ethnically the Sindhi speaking were 67%,Urdu 14%,pathan 6.6%,Balochi 8.1% and rest were in the others. Moreover, the study showed that 415(77.8%) were literate people, we further divide the ethnic groups into two Sindhi and Non-Sindhi categories, among them 51 positive and 12 positive cases were found respectively on the bases of HDV RNA Qualitative test.

Conclusion: The Prevalence of HDV infection among our region of Pakistan seems to be very high and increasing in Sindhi rural areas, which is alarming situation. This infection occurred in all age groups particularly in the males because they are frequently exposed to the spreading risk factors.

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THE SIGNIFICANT DECREASE IN HDV-RNA OBSERVED IN HIV-HBV-HDV TRIPLE INFECTED PATIENTS TREATED WITH TENOFOVIR (TDF) IS NOT CORRELATED TO HBSAG QUANTIFICATION AND LIVER FIBROSIS REGRESSION

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Background and aims: Chronic hepatitis D is a difficult-to-treat infection for which very few therapeutic options are available, and virtually none are efficient in the context of HIV co-infection. It has been suggested that tenofovir might have an indirect effect on HDV-RNA level by decreasing the pool of HBsAg necessary for HDV replication.

Methods: Data from a prospective 3-year cohort including 158 HIV-HBV (9 HIV-HBV-HDV) co-infected patients treated with tenofovir as part of their HIV regimen were analysed. HDV-RNA and HBV-DNA were quantified at baseline and every year during treatment using a home-built real-time quantitative PCR assay and a real-time PCR technique from Roche diagnosis, respectively. HBsAg was quantified every 6 months using ARCHITECT System, Abbott and liver fibrosis was evaluated using Fibrometer®. Declines in HDV-RNA, HBV-DNA, HBs Ag and fibrosis score were assessed by mixed linear models.

Results: After a mean 23.6 months of TDF treatment, a positive correlation was found between HBsAg and HBV-DNA (ρ=0.68), but lower correlations were observed between HDV-RNA and HBV-DNA (ρ=0.44), and HDV-RNA and HBsAg (ρ=0.38). Significant declines in HBV-DNA and HDV-RNA were noted: -0.117 logUI/mL after 12 months (95%CI: -0.220; -0.013) and -0.064 log copies/mL per month (95%CI: -0.117; -0.011), respectively. Decline in HBsAg was mild (-0.016 logUI/mL per month, 95%CI -0.039; 0.008) and non significant (p=0.2). All patients were classified as cirrhotic according to liver fibrosis score, which did not vary over time.

Conclusions: HBsAg plasma level and liver fibrosis score were not significantly affected by TDF use in HIV-HBV-HDV co-infected patients, although significant HDV-RNA and HBV-DNA declines were noted. This might explain why HDV clearance very rarely happens in the context of HIV, even with the use of TDF.

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HEPATITIS B AND D: EVALUATION OF A CASE SERIES OF PATIENTS FROM THE WESTERN BRAZILIAN AMAZON

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Background and aims: The Brazilian Amazon region is characterized as one of the areas of the world of most increased occurrence of hepatitis B virus (HBV) and Delta (VHD) infection. Clinically both viruses can range from asymptomatic to fatal forms. We aimed to describe the main epidemiological and clinical aspects, as well as of the biology of HBV and HDV in patients from this specific region.

Methods: In a descriptive study of a serie of cases a clinical and epidemiological instrument was applied using medical records and governmental information from the National Information System for Notifiable Diseases (SINAN) regarding data collection as clinical aspects, epidemiological and serological data.

Results: This study evaluates 355 patients, 84% classified as chronic hepatitis showing a median age of 28 years. The cumulative incidence rate of acute hepatitis B ranged from 42/100,000 inhabitants / year to 117/100,000 inhabitants / year. We detected a reactivity of 55.6% for HBV and HDV coinfection. The occurrence of death was associated with HBV / HDV coinfection. Hepatitis B virus genotypes, most commonly found were A, F and D, genotype A been the most prevalent. HDV genotype III was found in all samples.

Conclusion: The HBV/HDV coinfection was present in all clinical forms. The detected association with past history of hepatitis and death in the family demonstrate the importance of HBV and HDV in the aethiology of acute icteric desease in this specific region.

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DELTA HEPATITIS VIRAL LOAD AND CLINICAL ASPECTS - EXAMPLES FROM THE WESTERN BRAZILIAN AMAZON

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Background and aims: The western Brazilian Amazon is known as a high prevalence area of hepatitis B and D infection. Since late 60's fatal cases of acute liver failure are describe within families in very small isolated villages. Although HBV vaccination program is running since 1989, high figures of chronic HBV carriage is still described. We reviewed cases of chronic liver disorders due to HBV and HDV coinfection during a compensated clinical phase referred to our outpatients' clinic aimed to estimate the influence of HDV viral load.

Methods: This is an evaluation of HBV and HDV coinfection clinical cases. Clinical evaluation included haematological and liver enzymes dosage; clinical and demographic data were recorded from the patient's medical record. Hepatitis D viral load count was done by qRT-PCR following a protocol developed by Kiesslich D, 2009. We selected only those with detectable HDV-RNA levels.

Results: We examined 21 patients, 9 females and 12 males with a median age of 29 years (21-49). Among those patients studied 7 (33.3%) had clinical diagnosis of chronic hepatitis and 14 (66.7%) of liver cirrhosis, all presenting, HBsAg reactive, HBeAg negative and total anti-HD reactive. The mean HDV load was 3.85 $\log_{10}$ copies/mL (2.27-5.57). Viral load showed association with age, mean RNA levels was 4.46 $\log_{10}$ copies/mL among those aged up to 25 years and 3.48 $\log_{10}$ copies/mL within those patients older ($p=0.03$). We could not describe any association with clinical diagnosis, gender or variation of liver enzymes or haematological features.

Conclusion: The cases examined may indicate that HDV viral load could be of great importance in younger groups which may reflects early stages of infection when a course of antiviral therapy may be mostly needed. Older patients or those with end-stage liver disease, HDV viral load may reveal the natural course of illness.

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THE ROLE OF HDV IN THE NATURAL HISTORY OF THE PERSISTENT HBV INFECTION

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Introduction: The natural course of the persistent HBV infection is complex and dynamic with four main phases: immune-tolerance (IT), immune-clearance (IC), low-replicative/inactive-carrier (LR) and HBe-Antigen-negative hepatitis (ENH]. However, the role of HDV co-infection in the progression of the different phases of HBV infection is unclear.

Methods: 52 patients with hepatitis delta were followed for up to 14 years (median 3.41 years). None of them was receiving therapy at baseline; along follow up, 22 patients remained untreated. The baseline characteristics of this delta co-infected group was compared with a large HBV mono-infected untreated cohort comparing different phases of HBV mono-infection (Jaroszewicz, J Hepatol 2010).

Results: At baseline, 5 anti-HDV-positive patients were in the IT phase, 5 in the IC, 26 were LR and 16 had a ENH. Comparing HBV-HDV co-infected with HBV mono-infected patients, ALT activities were similar between the two groups in all four phases of HBV infection (median (IU/ml): HBV-HDV/HBV: IC 124/114; IT 46/32; LR 33/34; ENH 157/185). However, HBV-DNA was lower in all phases in the Delta group (median (log_{10} IU/ml): HBV-HDV/HBV: IC 3.56/7.47 [p=0.006]; IT 2.46/8.04 [p< 0.001]; LR 0.77/2.28 [p< 0.001]; ENH 3.05/5.92 [p< 0.001]). Of note, patients in the LR phase tested less often positive for HDV RNA than patients in the other three phases (42% vs. 83% [p=0.03]).

During follow up, 12 of the untreated patients (54%) did not progress to another phase of HBV infection. From the ten patients who switched HBV phase along follow up, 6 achieved the LR phase. Out of 10 HBeAg-positive patients, only 2 seroconverted, and no HBsAg seroconversion was detected.

Conclusions: Our data suggests that HDV alters the natural course of HBV infection, with a possible suppression of the dynamic course of the HBV infection, as well as an inhibition of the HBV's viral load in all phases.

EFFICACY OF 48 WEEKS OF PEGYLATED INTERFERON ALPHA-2A IN ROMANIAN PATIENTS WITH CHRONIC HEPATITIS D (CHD)

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Background and aims: Hepatitis D is considered to be the most severe form of viral hepatitis, causing more severe liver disease than HBV monoinfection; associated with accelerated fibrosis progression, earlier hepatic decompensation and increased risk for hepatocellular carcinoma development.

Interferon proved some efficacy in delta hepatitis in previous small studies. PegIFN alfa-2a demonstrated sustained benefits in HBV infection and it seems a possible therapeutic option for the most aggressive viral hepatitis. This study aim was to evaluate efficacy of PegIFN alfa-2a in delta chronic hepatitis patients.

Methods: The study was conducted in 8 centers: 31 patients (HBsAg, anti-delta and HDV RNA positive) were included in the analysis. Patients were evaluated at baseline, prior to initiation of a 48 wk course of PegIFN, also during therapy, at the end-of-treatment and at follow-up, after 24 weeks. Efficacy analyses included all patients who received at least one dose of study medication. The primary efficacy parameters were HDV RNA negativity and ALT normalization at the end of follow-up period. Secondary efficacy measures assessed HDV-RNA negativity at the end-of-treatment, suppression of HBV DNA levels at the end-of-treatment and after 24 weeks of follow-up.

Results: Primary efficacy parameters: 61.3% (19 out of 31 patients) had negative HDV-RNA and 17 patients had normal ALT levels (54.8%, n=31) at the end of follow-up.

Secondary efficacy measures: 64.5% (20 out of 31 patients) had negative HDV-RNA at the end-of-treatment. 83.9% of patients (26 out of 31 patients) achieved HBV DNA suppression at the end of follow-up period, suppression defined as $< 1x10^5$ copies/ ml. All confidence intervals presented are CI95%.

Conclusions: 48 weeks of PegIFN alfa-2a demonstrated very good efficacy in delta chronic hepatitis, with almost two thirds achieving HDV RNA negativity, confirming the value of this therapy as first-line option in chronic hepatitis delta.

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BASELINE FEATURES AND TREATMENT EVOLUTION AFTER 1 YEAR OF PEGINTERFERON ALPHA 2A IN A LOW RESOURCES SETTING

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Background and aims: The Amazon region has the highest prevalence rates of hepatitis B and delta virus infection in Brazil that considerably impacts the health care system. Low access to HDV and HBV molecular analyses is still important issues to be considered. So, physicians are forced to use alternative strategy. We performed a retrospective analyses of laboratory samples from Manaus patients to show the delta hepatitis impact and the treatment evolution after 1 year of pegylated interferon using ALT levels to monitor the therapy results.

Material and methods: in 2009, laboratory samples data from 7 patients were collected from The Tropical Medicine Foundation medical files retrospectively. Gender, age, serology/markers, liver biopsy, ALT levels and treatment information were analyzed.

Results: All patients were: HBeAg negative/total anti-HDV positive, young (< 30 years) and male. Almost half of patients have advanced liver disease with compensated cirrhosis (see the attached table).

HBeAg/Anti-HDV	ALT baseline levels (X ULN)	Baseline liver biopsy / clinical features
- / +	> 5 < 10	Cirrhosis /splenomegaly
- / +	> 10	Metavir A4/F3
- / +	> 5 < 10	Cirrhosis/splenomegaly
- / +	> 2 < 5	Metavir A2/F1
- / +	= 5	Inconclusive
- / +	> 5 < 10	Inconclusive /splenomegaly
- / +	> 2 < 5	Cirrhosis/splenomegaly

[Samples HBV/HDV information]

All patients received peginterfeon alfa-2a 180µg/week. After 1 year all patients showed ALT normalization with no signs of hepatic descompensation.

Discussion: Recently, HIDIT trial showed sustained virologic response measured in terms of undetectable serum HDV RNA after peginterferon alfa-2a. However, when there is a lack of resources the disease monitoring must use biochemical evaluations. These sample of patients showed that ALT levels measures could be an viable alternative in a low resources setting.

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DELTA HEPATITIS IN AMAZON REGION - THE IMPACT OF DISEASE AT JURUÁ RIVER CHANNEL

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Introduction: The Western Amazonia region has the highest prevalence rates of hepatitis B virus infection in Brazil and the Juruá river banks has a very high prevalence rate of hepatitis B and Delta. However, the population living there faces the challenge of lack of access to healthcare services.

Aims: We conducted a project to screen the population in Eirunepé, a small settlement located between Juruá and Purus rivers´ channels to check current hepatitis B and Delta epidemiological situation.

Methods: Samples from 316 Eirunepé patients were evaluated between July - December 2008 and were tested for Anti-HBsAg and total Anti-HBcAg. The total Anti-HBcAg positive samples were tested for the remainig HBV serologic tests/markers and total anti-HDV.

Results: In 316 samples: 14,5 % were HBsAg positive and 63% of those were total anti-HDV positive. Serologic data were available in the table bellow:

Age interval (in years)	Patients N	HBsAg+ N (%)	Anti-HBcAg+/Anti-HBsAg+ N (%)	Anti-HDV+ /Anti-HBc+ N (%)
0 - 19	139	10 (23)	31 (26)	5 (16)
20- 39	127	28 (61)	66 (55)	20 (62)
40 - 59	32	7 (15)	18 (15)	5 (16)
≥60	13	1 (1)	4 (3)	2 (6)
Unknown	5	0 (0)	1 (1)	0 (0)
Total	316	46 (100)	120 (100)	32 (100)

[Serologic information per patients age]

Discussion: The results from Eirunepé confirms the high circulation of hepatits B virus and a high prevalence of HDV co-infection in the Amazon region. The anti-HDV positive individuals among HBsAg positive at all ages possible indicates to different ways of transmission other than sexual or blood contamination such as the intra-familial route. Besides, almost 90% of them were less than 40 years old which

probably also indicates a lack of an effective anti-HBV vaccination program regarding the geographic and social barriers.

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DETECTION OF HEPATITIS DELTA VIRUS RNA IN DRIED BLOOD SPOTS (DBS) FROM USING REAL-TIME PCR IN BRAZILIAN REGIONS WITH DIFFICULT ACCESS TO HEALTHCARE

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Background and aims: The Amazon basin has the highest prevalence rates of hepatitis B virus infection in Brazil and delta hepatitis super-infection poses an additional threat in this region. However, collecting and transporting samples for nucleic acid analysis can be challenging, especially in situations where financial resources are limited. We developed a Real-Time PCR (qPCR) method for detecting Hepatitis Delta (HDV) RNA and successfully adapted it for use with dried blood spot (DBS) samples. The aim of this study was to define the sensitivity and specificity of this assay.

Material and methods: A qPCR for HDV RNA, an internal control and a calibration curve were developed, and the sensitivity, specificity and dynamic range of amplification were confirmed using a cloned virus with HDV, HIV and HCV fragments, and a panel of quantified HCV and a panel with HIV were used to infer the HDV quantitation. Plasma and DBS samples were collected from 29 anti HDV positive individuals from the Amazon basin and performed in parallel. Plasma samples were transported frozen whereas DBS were transported at room temperature for a distance over 3,000 km to the laboratory where assays were performed. We selected 10 samples with viral load values ranging from 5 $\log_{10}$ to 3 $\log_{10}$ and diluted them out to generate triplicate samples with values of 4 $\log_{10}$, 3 $\log_{10}$ and 2 $\log_{10}$ copies/mL to access repeatability.

Results: Twelve samples presented positive viral load ranging from 3.24 to 5.942 $\log_{10}$ copies/mL (r=0.97, ANOVA = 1.414E-20). Sensitivity, specificity and positive predictive value of detection RNA in DBS was of 100%. Standard deviation in repeatability assays were < 0.06.

Discussion: Detection and quantitation of HDV RNA in DBS is accurate and can be a cost-effective strategy for HDV diagnostic and treatment monitoring, especially in remote settings in which resources are limited.

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CLINICAL AND VIROLOGICAL CHARACTERISTICS OF BULGARIAN PATIENTS WITH CHRONIC HEPATITIS D

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Coinfection with hepatitis D virus (HDV) in patients with chronic hepatitis B (CHB) is important with respect to treatment response in Bulgarian patients.

The aim of this study is to evaluate the relationship between sex, age, transaminase activity and virological response in adult patients with CHB and HDV coinfection.

We analyzed the data of 18 patients (male/female ratio 14/4) aged from 22 to 59 years, treated in the clinic from 2003 to 2009.

Liver biopsy was not performed in 8 patients because of coagulation abnormalities. Liver cirrhosis was present in 10 patients. All cases were treated with Roferon A, and in 14 patients a significant decrease in HBV DNA was observed, followed by a drop in ALT and GGT. Age of patients did correlate neither with ALT nor with HBV DNA and stage of fibrosis. There was no correlation between HBV DNA, sex and stage of fibrosis. Furthermore, we did not observe correlation between ALT levels and HBV DNA, and with stage of fibrosis.

We treated a 36 year old patient with standard dose of Tamiflu for three months following treatment with Roferon A and a 0,4 log decrease in HDV RNA was observed.

A patient with chronic hepatitis B, D and C was treated with Roferon A and a decrease in B virus replication was proved.

In conclusion 3,75 % of Bulgarian patients with CHB have coinfection with HDV. The percent of people with significant level of replication of virus B is significant enough and has to be taken into account when treating. HBV DNA does not correspond with age, activity and severity of disease.

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PRESENCE OF PRETREATMENT SEROPOSITIVITY OF ANA AND P-ANCA MAY PREDICT PEG-INTERFERON RELEATED TRANSAMINASE FLARES IN PATIENTS WITH DELTA HEPATITIS

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Aim: Hepatitis D (delta) is a superimposed infection to Hepatitis B. Antiviral therapy with peg-interferons can be used in patients with chronic infection Serum autoimmunity may be seen in delta hepatitis. Aim of this case reports is to evaluate the importance of autoantibodies in patients with delta hepatitis and to establish their influence on peg-interferon treatment.

Methods:

Case 1: 20 years old male patient was diagnosed as delta hepatitis. There were no thrombocytopenia and prolonged prothrombin time. His liver transaminases were three fold higher than upper normal limit. A liver biopsy revealed advanced paranchimal disease (Knodell score:16 and fibrosis:2).

Case 2: 30 years old female patient was diagnosed as delta hepatitis. Her platelet count and prothrombin time were in normal limits. His liver transaminases were four fold higher than upper normal limit. A liver biyopsy revealed advanced paranchimal disease (Knodell score:17 and fibrosis:3).

Autoantibodies were researched by indirect immunofluorescence using dilution between 1:10 to 1:640. HDV RNA assays were performed by PCR methods. Both of cases had received peg-interferon alpha 2a at a dose of 180 µg/wk.

Results: Pretreatment, both of patients had p-ANCA seropositivity (1:20) and ANA seropositivity(1:100). At the fourth week of the treatment liver transaminases were ten fold elevated. At the sixth week of the treatment liver transaminases were returned to near normal levels.

Discussion: Presence of pre-treatment ANA and p- ANCA seropositivity may play a role in evalution of chronic hepatitis D patients and could be a predictor of pegilated interferon releated transaminase flares in patients with hepatitis delta. It was suggested that prevalence of the serum autoantibodies may influence treatment outcome, but large-scale studies are still pending.

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THE IMPACT OF CHILD-PUGH SCORES ON THE FREQUENCY OF GALLSTONES IN PATIENTS WITH CIRRHOSIS DUE TO HEPATITIS DELTA VIRUS

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Background and aims: HDV infection has been associated with severe liver diseases ranging from chronic hepatitis to cirrhosis. The objective of this prospective analysis was to assess the prevalence of cholelithiasis among patients with cirrhosis due to hepatitis D and to determine the correlation of Child-Pugh scores with gallstones.

Patients and methods: In this prospective study, 35 cirrhotic patients (M = 20, F = 15, mean age 58 years, SD +/- 15), observed from May 2009 to May 2010 were enrolled. Baseline demographic and clinical characteristics were similar in both groups.

Patients with histological or clinical diagnosis of cirrhosis divided into 2 groups depending on the hepatitis B or D status(Group A and B). Delta hepatitis associated cirrhosis was diagnosed in 19 patients. Severity of liver disease was classified by Child-Pugh score. Abdominal ultrasonography was performed for every patient. Anova analysis was used for comparing two groups.

Results: No significant differences in CTP scores, age and gender were found between the two groups. Eleven patients (31.4%) had gallstones in all groups. The frequency of gallstones was similar between the two groups (5/16, in group A, 31.2% vs. 6/19 in group B,31.6%;p=NS). Higher points of Child-Pugh score was associated with gallstones among group B patients($p < 0.05$).There was no correlation between gallstones and Child-Pugh scores in group A patients(p=NS).

Conclusions: Cirrhosis was associated with gallstones. Higher Child-Pugh scores were associated with increased gallstone formation in hepatitis delta virus linked cirrhosis.

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ASSESSMENT OF EFFECT OF HEPATITIS DELTA VIRUS ON PORTAL HEMODYNAMICS IN CIRRHOSIS

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Background and aims: HDV infection has been associated with severe liver diseases ranging from chronic hepatitis to cirrhosis. The evidence of HDV RNA positivity is closely related to serious liver disease in patients with Hepatitis B and can affect the natural course of cirrhosis as well as the findings of complications. Duplex ultrasonography was evaluated as a noninvasive technique of determining portal hemodynamic characteristics. The aim of this study was to evaluate the impact of HDV on the portal venous system in patients with cirrhosis.

Patients and methods: In this prospective study, 33 cirrhotic patients (M = 18, F = 15, mean age 54 years, SD +/- 15), observed from May 2009 to May 2010 were enrolled. Baseline demographic and clinical characteristics were similar in both groups. Patients with histological or clinical diagnosis of cirrhosis divided into 2 groups depending on the hepatitis B or D status(Group A and B). Delta hepatitis associated cirrhosis was diagnosed in 19 patients. Severity of liver disease was classified by Child-Pugh score. All patients had greater than 5 points of CTP score. Diameters of portal and splenic veins and spleen and portal blood flow were measured using a duplex ultrasound. Mann-Whitney U test was used for comparition of two groups.

Results: No significant differences in CTP scores, age and gender were found between the two groups.The mean (SD) diameters of portal and splenic veins and spleen were not different between two groups($p>0.05$). Futhermore the mean (SD) portal venous velocity was 15,843 cm/s in Group A and was 13,625 cm/s in group B and this parameter was not different in both groups($p>0.05$).

Conclusions: On the basis of these results, we may speculate that portal hemodynamics of patients with HDV associated cirrhosis does not differ statistically from patients with Hepatitis B associated cirrhosis.

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SEROPREVALANCE OF DELTA HEPATITIS IN HBSAG CARRIERS AT IZMIR TEPECIK EDUCATIONAL AND RESEARCH HOSPITAL

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Introduction: Hepatitis delta virus, an incomplete virus dependent on replicating hepatitis B virus (HBV) for its multiplication, can infect individuals with active HBV infection and can cause severe liver disease. Its prevalance is less than Hepatitis B virus, but it causes more serious clinical situations. In this study we investigated Anti-HDV seroprevalance and epidemiological features among HBsAg seropositive outclinic patients at Izmir Tepecik Educational and Research Hospital.

Materials and methods: Serum samples collected from outclinic patients at Izmir Tepecik Educational and Research Hospital between September 1st 2007 and 30th of August 2009 were evaluated. Anti-HDV assay was carried out by EIA (Diasorin-Italy).

Results: Out of 3094 HBsAg positive patients 79 had (% 2,5) Anti-HDV IgG seroprevalence. Fourty two of these 79 patients were inactive Hepatitis B carriers, 34 of them were chronic Hepatitis B, two had liver cirrhosis and one had hepatocellular carcinoma.

Discussion: Although super infection and co-infection of HDV are less prevalent, the prognosis is worse. The response to therapy is poor. Because of this patients with Hepatitis B should be evaluated further for HDV infection.

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PREVALENCE OF DELTA VIRUS INFECTION IN PATIENTS WITH HEPATITIS B VIRUS INFECTION

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Aim: Infection with HDV is considered to be high in Mediterranean basin our data regarding this infection in our HBV populations is deficient, our objective to estimate the seroprevalence of HDV in our HBV patients.

Method: One hundred thirty eight patients from viral hepatitis clinic Jamahiriya hospital were randomly selected and tested for the presence of anti-IgM and IgG anti-delta virus antibody, at the same time the level of HBV-DNA measured for both delta antibody positive and negative patients.

Result: Fifteen patients out of 138 tested positive for anti-Delta virus-IgG antibody (10.8%) and non for IgM-anti-Delta were positive (0 %), the HBV-DNA level was high in HBV negative Delta antibody where is for Delta positive were low.

Conclusion: HDV dose not appear to be commonly prevalent in Libyan patient with HBV. In comparison to data from previous result from Mediterranean area the seroprevalence of anti-Delta virus considered to be intermediate in our patients who were attending liver clinic , ideally we should have our national data to observe the effectiveness of hepatitis B vaccination on positive impact regarding HDV infection.

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MODELING OF EARLY VIRAL KINETICS IN CHRONICALLY HBV/HDV-INFECTED PATIENTS AFTER LIVER TRANSPLANTATION

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Viral kinetic models have become important for understanding the main biological processes which determine the dynamics of chronic viral diseases and for optimizing effectiveness of anti-viral therapy. We developed a new mechanistic viral kinetic model to investigate the Hepatitis-B-Hepatitis-D-host interplay in the first days after liver transplantation. Since hepatitis B immunoglobulin (HBIG) administration is the standard of care as prophylaxis of reinfection after liver transplantation for hepatitis B virus-related liver disease, it is of particular importance to assess the relation of HBsAg levels and the HBIG dose which is required for successful reduction of circulating HBsAg and raising of anti-HBs levels.

We analyzed serial quantifications of viral load (HBV and HDV), HBsAG levels, anti-HBs levels and HBIG dosing schemes in 26 coinfected patients undergoing liver transplantation and estimate model parameters by non-linear fitting.

Our findings show a strong correlation between HDV- and HBsAG-decline, anti-HBs increase and HBIG dosing schemes. In contrast to patients with daily HBIG administration, patients with intermittent HBIG administration demonstrated a plateau phase before elimination of HDV-RNA and HBsAg. This emphasizes the importance of continued HBV reinfection prophylaxis also enabling HDV-RNA clearance after liver transplantation. The results also suggest that this modeling approach may help to optimize HBIG dosing schemes and further anti-viral treatment in patients undergoing HBV/HDV-indicated liver transplantation.

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LEVEL OF VIRAL REPLICATION AND DISEASE PROGRESSION IN HBV-HDV CHRONIC INFECTION

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Background: The HDV infection may aggravate the outcome of patients with chronic HBV hepatitis. At our knowledge, there are no data about the rate of HBV-HDV liver disease progression depending on viral replication level.

Aim: To evaluate if different levels of viral multiplication could affect the progression of liver disease in HBV-HDV chronic hepatitis.

Methods: A cross-sectional study performed in 2006 in Bucharest area identified 223 patients with HBV-HDV double infection. HBV-DNA and HDV-RNA were measured in 2006, using PCR methods (an in-house qualitative reaction for HDV and a TaqMan Roche quantitative reaction for HBV).

Depending on replicate status of infections, we defined two groups of patients:

I. 28 patients with HDV-RNA present in serum and HBV-DNA more than 10000 c/ml

II. 195 patients with double infection HBV-HDV.

Results: There were no significant differences between the two groups regarding the distribution by gender (10:18 versus 97:98, p=.16), mean age and age groups (44.82 versus 44.51 years; p=.74) , the duration of the illness (10.9 versus 8.8 years, p=.25) ,the biological data: increased ALT (42.85% vs 42.05%, p=.93) or ALT over 2 x ULN (10.7% vs 18.4%, p=.31) ; prothrombin index less then 70%(14.28% vs 18.4%, p=.47) ; thrombocytes < 100 000/mm3 (10.7% vs 12.8%, p=.99). The number of patients with advanced illness (ESLD) didn't significantly differ neither at the begining of the study (2006): 7.1% vs 15.9%, p=.12 nor in the present (2010): 12% vs 18.5% (p=.23). The progression of the disease does't appear to be higher in group I : 0.013/patients x years vs 0.008/patients x years, p=.15.

Conclusion: Concomitant HBV and HDV significant viral replication doesn't appear to correlate with the present liver injury severity and it is not a prognostic marker for the progression towards ESLD on a short/medium term (3 years).

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HBV/HDV CO-INFECTION IN CARRIERS WITH UNUSUAL CLINICAL PICTURES, CORRELATIONS WITH DELTA AG VARIATIONS

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Background: Probably 5% of the HBV carriers have HDV superinfection. The risk of fulminant hepatitis, cirrhosis and hepatocelluler carcinoma is higher in superinfection than the settings when HBV is alone.

Methods: 86 HBsAg positive/HBeAg negative carriers with upper limit ranges of ALT and low or undetectable levels of HBV viral load who did not respond to HBV therapy were selected. After RT amplification of C-terminal region of HDV Delta antigen, direct sequencing was carried out to explore the genotype(s) and nucleotide/amino acid variations.

Results: 14 (16.2%), 12 (14%) and 12(4%) of patients were HDV RNA, Anti-HDV and both DNA RNA/antibody positive, respectively. The mean ALT level was higher in HDV positive patients (75.9 U/ML) than HBV-infected alone individuals. Genotype I was the only detected genotype. Phylogenetically, the most closely related isolates were of Turkish, Italian and Mongolian origin. Overall, of total 224 nucleotide changes, 128 (57.1%) were missense (amino acid altering) mutation. The mutation frequency (ratio between silent and missense mutations) was 0.67 indicated a positive selection pressure exerted on these antigens. In 2 isolates that were negative in HDV serology but positive by RT PCR, we found a combination of mutations in amino acid residues between 349 and 389 of Delta Ag.

Conclusion: The HDV molecular data were in accordance with other regions in The Middle East. HDV should be suspected in HBV carriers with unusual clinical and virological pictures.

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CLINICAL AND EPIDEMIOLOGICAL DISTRIBUTION OF HEPATITIS DELTA

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Background: In all approximately 20 mln people infected with HDV in the worldIn combination with HB virus HDV has the highest mortality rate of all hepatitis infections of 20% Both superinfection and coinfection with HDV results in more severe complications in compaire with HBV alone.

The aim is to show clinical and epidemiological distribution of patients with HDV in our clinic.

Methods: For period of 2008-2009 years we studied the epidemiological characteristics and clinical spectrum of 13 patients with HDV. 3 patients were women, 9 were HBeAg negative (69%) The median age was 32 years (8-56). Diagnosis of HDV infections were established during 6 month up to 20 years after suspecting exposure. Screening tests included: serological HBsAg, AntiDelta IgM, antiHBcor IgM and IgG, antiHCV, antiHIV, antiHAV IgM, virological HBV- DNA, HDV- RNA quantitative, biochemical as well as liver instrumental investigations.

Results: 9 patients were HBV-HDV, triple co-infected were 4, from which 2 patients HBV-HDV-HCV, 2 patients HBV-HDV-HIV. The ways of HDV transmission were the following: 8 patients were I/V drug users, 2 haemotransfusions, 1 haemodialisis, 1 intrafamily, 1 surgical manipulation. Clinical spectrum: 2 patients with acute mixt coinfection with severe liver failure, among which in 1 patient developed spontaneous clearance of both viruses, in other chronic delta hepatitis. In 7 patients HDV primary was diagnosed in stage of cirrhosis with following complications: ascites in 5 patients and liver encephalopathy in 2 patients with lethal outcome. (none of them was triple co-infected), 4 were with chronic hepatitis delta. HDV was the dominant virus in 9 patients.

Conclusions: HDV is rare in our country and is mostly associated with i / v drug use.In combination with HB virus HD results more severe complications including a grater likelihood of developing liver failure in acute infections and a rapid progression to liver cirrhosis.

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COMPARISON BETWEEN LIVER STIFFNESS VALUES OBTAINED BY TRANSIENT ELASTOGRAPHY IN PATIENTS WITH HEPATITIS B VIRUS MONO-INFECTION VERSUS HEPATITIS DELTA VIRUS CO-INFECTION

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Background and aims: Hepatitis D virus (HDV) is a defective RNA virus which leads to hepatitis delta only in hepatitis B virus (HBV) surface antigen (HBsAg)-positive individuals. Usually, chronic HDV infection is associated to a more severe liver disease than HBV mono-infection and with a higher risk to develop hepatocellular carcinoma. Our aim was to compare liver stiffness values in HBV mono-infected patients versus patients with HDV co-infection.

Material and methods: We performed a retrospective study on 476 patients with chronic hepatitis: 440 cases of HBV mono-infection (159 women, 281 men, average age 41.5±14 years) and 36 cases of HDV co-infection (16 women, 20 men, average age 40.5±11.6 years) registered in the Department of Gastroenterology and Hepatology, Timisoara during 2007-2009. Liver stiffness values were obtained by using transient elastography (FibroScan®-Echosens, Paris, France). Ten valid results were determined and mean value was expressed in kPa. We did not include in our study patients with liver cirrhosis.

Results: The frequency of HDV infection was 7.5% among HBsAg-positive patients (36/476). Valid liver stiffness values were obtained in 95.6% of cases and only few could not be determined due to abdominal obesity or narrow intercostals spaces. We observed that mean liver stiffness values were higher in patients with HDV co-infection compared to patients with HBV mono-infection from an extremely significant statistical point of view (8.4±2.6kPa versus 6.7±2.4 kPa, p=0.0003).

Conclusion: Patients with HDV co-infection who were evaluated non-invasively by transient elastography presented higher liver stiffness values compared to patients with HBV mono-infection. Further on, they should be treated and periodically evaluated, as they are likely to develop a more severe liver disease.

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ANA, SMA AND BCLA ANTIBODIES IN HDV-RELATED CHRONIC HEPATITIS

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Background and aims: Serum antinuclear (ANA) and smooth muscle autoantibodies (SMA), mainly with the “speckled” (ANAs) and “vessel” pattern (SMAv) respectively, may occur as an unspecific finding in many infectious disorders, including viral hepatitis. A particular autoantibody, termed BCLA and reacting with the Basal Cell Layer of squamous epithelia (rat oesophagus), was described in close association with HDV infection. Aim of this study was to evaluate prevalence and significance of ANA, SMA and BCLA in HDV-related chronic hepatis (CH).

Patients and methods: Serum from 27 patients with HDV-related CH and 25 patients with HBV-related HDV-unrelated CH (control group) was tested by IFL at 1:40 dilution on Hep-2 cells for ANA and on rat kidney and oesophagus sections for SMA and BCLA detection, respectively.

Results and conclusion:

	ANA+	SMA+	BCLA+
HDV-CH (27)	11 (41%), all ANAs	2 (7%), all SMAv	5 (18%)
HBV-CH (25)	7 (24%), 6 ANAs, 1 centromere	2 (8%), all SMAv	0

[Table 1]

HDV patients with and without autoantibodies were compared with respect to: sex, age, presence of cirrhosis, HCC, IgG or IgM anti-HDV, serum levels of HDV-RNA, HbsAg, HBV-DNA, transaminases, gamma-GT, AP, albumin, γ-globulin, bilirubin and a1-fetoprotein, INR and platelet count. No significant difference could be detected between BCLA as well as ANA and/or SMA positive and negative cases.

1. In HDV-related CH a spectrum of autoimmunity (ANAs and SMAv) can be detected which is shared by many infectious disorders. In particular, ANAs occurred at a higher frequency (41% vs 24%) in HDV than HBV-related CH.

2. By contrast, the BCLA reactivity seems to be specific for HDV-related CH, occurring in 18% HDV cases and never in HBV cases.

3. The presence of serum autoantibodies, either unspecific (ANAs, SMAv) or specific (BCLA) for HDV-related CH, does not affect the clinical and biochemical picture of the disease.

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CHARACTERISTICS OF HEPATITIS DELTA IN NORTHERN CALIFORNIA

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Aim: To assess the prevalence and demographics of HDV co-infected patients in our Northern California network.

Methods: In this study, 82 patients who were positive for HBsAg and hepatitis D virus (HDV) antibody were included. A cross-sectional approach reviewing chart and laboratory data was utilized.

Results: All hepatitis delta patients were extracted from a prior study conducted by this collaboration. In the study, there were 1,296 chronic HBV carriers. Of 1,191 chronic HBV patients with liver biopsies performed, 262 had cirrhosis (22 %).

82 patients (6.3%) were identified as HDV positive either by HDV antibody testing or by positive HDV antigen titers. Out of 82 HDV positive patients, 59 were male (71%) and 22 were female (27%). 44 patients were non-hispanic Caucasian (54%) and 23 were API (28%). 67 patients (82%) were tested for HCV by antibody testing: 23 of the 67 patients (34%) were co-infected with HCV, and 16 of the 23 (67%) had cirrhosis.

Conclusion: HDV affects individuals of all ages, primarily males. Individuals with HBV/HDV co-infection have higher rates of cirrhosis. Individuals with HBV/HCV/HDV co-infection have significantly higher rates of cirrhosis than individuals with either HBV/HDV co-infection or chronic HBV infection alone. Testing for HDV should be performed in all patients, especially those with advanced liver disease or high risk behavior.

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MOLECULAR CHARACTERIZATION OF HDV AMONG AMERINDIAN GROUPS FROM BRAZIL

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Background and aims: In Brazil, HBV infection is highly endemic in some Amerindian groups, sometimes also accompanied by HDV infection. In others South America countries, such as Peru, Ecuador and Venezuela, outbreaks of fulminant hepatitis caused by HDV in Amerindian people have been described and HDV-3 was identified in these cases. In Venezuela, among Amerindians chronically co-infected with HBV/HDV, HDV- 1 was identified in Amerindians from West (Yucpa) and HDV-3 in Amerindians from South (Yanomami). In Brazil, HDV-3 was also identified in non-Amerindians carriers from Eastern and Western Amazon Basin, but there is not any information about HDV genotype among Brazilian Amerindian groups. The aim of this study was characterized the HDV genotype circulating in two Amerindian groups (Yanomami and Kanamari) from western Amazon basin of Brazil.

Methods: A total of 26 anti-HD positive samples were analyzed (12 from Kanamari and 14 from Yanomami groups). Genotypes characterization was carried out by amplification and partial sequencing of the delta antigen region of the viral genome. HDV genotype was determined by phylogenetic analyses along with previously genotyped sequences retrieved from GenBank.

Results: HDV RNA was amplified and its sequence determined for 16 samples; HDV genotype 3 was found in all of them and the sequences grouped in specific clusters according to origin of sample (Kanamari or Yanomami group).

Conclusions: HDV-3 circulating among Amerindians groups in Brazil as in non Amerindian population of the same region. The sequences of each group were very closely related, what suggest recent introduction of the virus. These results suggest that HDV may have been recently introduced into those two Amerindian groups through non-Amerindian people, probably gold miners that in the least years have invaded Amerindian demarcated lands.

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HEPATITIS DELTA VIRUS (HDV) INFECTION IN HIV-HBV CO-INFECTED PATIENTS IN SÃO PAULO, BRAZIL

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Background and aims: Limited information is available about the seroprevalence of hepatitis delta virus (HDV) among HBV-HIV co-infected patients in Brazil. The aim of this study was to evaluate the prevalence of HDV in a group of HIV-HBV co-infected patients, followed at a single institution in 2007, in São Paulo.

Methods: 2,412 HIV positive patients were tested for HBV infection. Serological markers for HBV (HBsAg, HBeAg and total anti-HBc) were detected by ELISA. One hundred-twenty HBsAg positive patients (4.9%) were identified. Plasma specimens were obtained from 85 patients, comprising the study population that underwent further Anti-HD detection by ELISA, RNA detection by PCR and genotyping by sequencing.

Results: Only one (1.2%) anti-HDV positive patient was identified. Current HDV infection was confirmed by PCR and the genotype of this case was determined by phylogenetic analysis as HDV-1. The patient was a 37 years-old male patient that is a sex work, whom was born at Ceará (Northeast of Brazil) and lived in São Paulo for the last 20 years.

Conclusions: HDV is not frequent among HIV-HBV co-infected patients in the Southeast of Brazil. HDV-1 is not common in Brazil and this patient showed a high risk behavior. Furthermore, its sequence was closely related with European HDV-1 isolates, what suggests that this patient was infected through contact with people from this region, where HDV-1 is more prevalent.

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AFRICAN HEPATITIS DELTA GENOTYPE IN A BRAZILIAN PATIENT

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Background and aims: The hepatitis D virus (HDV) is endemic worldwide, but the prevalence of infection varies in different geographical areas. In the Brazilian Amazon Basin, HDV is endemic and represents a significant public health problem, but few studies have assessed its prevalence in other Brazilian regions. HDV is classified into eight genotypes (HDV-1 to HDV-8) that have a distinct geographic distribution: HDV-1 is found worldwide; HDV-2 in Japan, Taiwan, and Yakutia, Russia; HDV-4 in Taiwan and Japan; HDV-3 in the Amazon basin and HDV-5 to HDV-8 were recently isolated from patients of African origin. In this study we evaluated the soroprevalence of HDV in HBV chronically infected patients from Maranhão, in Northeast Brazil, and characterized viral genotypes in positive cases.

Methods: 100 HBsAg positive serum samples were tested by ELISA for antibody to HDV (anti-HD). Those with positive results were further analyzed to assess the presence of HDV RNA and genotype characterization by amplification and sequencing of a fragment of the delta antigen genomic region.

Results: Anti - HDV were positive in 2 samples (2%) and only one of them was positive to HDV RNA. Phylogenetic analyses of this HDV sequence showed that it clustered with previously characterized African HDV genotype (HDV-8). The patient was a 41 years-old male patient, living in rural area of city and did not report travel to outside of your city.

Conclusions: Our results point to a low endemicity of HDV in Brazilian Northeast population. Nevertheless, the detection of HDV RNA in one patient indicates that this virus can be transmitted to other HBV carriers from this region. This is the first description of the HDV-8 in non autochthonous African populations. This genotype may have been recently introduced or come with slaves brought to Brazil during the colonial period.

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RESULTS OF A FRENCH NATIONAL QUALITY CONTROL FOR HEPATITIS DELTA VIRUS RNA QUANTIFICATION

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Background: Hepatitis delta virus (HDV) is a highly pathogenic virus that causes acute and chronic liver diseases. HDV diagnosis relies on the detection of anti-HDV IgG and IgM antibodies. HDV replication is confirmed by the detection of serum HDV RNA. We developed a TaqMan-based real time RT-PCR quantification method capable of quantifying the 8 reported HDV genotypes over a wide dynamic range of values, from 10^2 to 10^8 copies/mL. This technique was used as the reference. We conducted a national quality control of HDV diagnosis in 18 different laboratories.

Methods: Four samples (1 negative and 3 IgG- and IgM-positive) were sent to the 18 participating laboratories for serological testing. Four additional samples were provided for molecular diagnosis to 6 of them having implemented HDV RNA testing by 'in house' real time PCR techniques: a negative control and 3 HDV RNA positive samples, with different genotypes and HDV RNA levels, i.e. HDV-1 with 4.5×10^7 copies/mL, HDV-7 with 2.1×10^5 copies/mL and a mixture of HDV-1 + HDV-7 with 2.4×10^7 copies/mL, respectively.

Results: The 18 laboratories reported identical results for anti-HDV IgG and IgM antibody detection, whatever the commercial kit used. In contrast, discordant results have been obtained for HDV RNA quantification. One laboratory underquantified all of the tested samples and the remaining 5 accurately quantified the HDV-1 sample, whereas HDV-7 RNA was underquantified by 4 out the 5 laboratories, both alone or mixed with HDV-1.

Conclusion: HDV RNA level quantification by real time RT-PCR is the tool of choice in the clinical management of patients with HDV infection. The genetic variability of the infecting strains is of great importance in the performance of the technique. This French national HDV RNA quality control highlights the need for improvement and international harmonization of HDV RNA quantification tools.

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PATTERNS OF T CELL RESPONSES AND CYTOKINE PRODUCTION IN HEPATITIS DELTA INFECTION

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Introduction: Infection with hepatitis D virus (HDV) may cause progressive chronic liver disease. However, not all patients develop liver cirrhosis and immune correlates for clinical outcomes are poorly defined. Aim of this study was to investigate both HDV-specific and HBV-specific T-cell responses and serum cytokine levels in a well defined cohort of HDV patients.

Methods: 23 individuals with HBV/HDV co-infection were included. PBMC were stimulated by overlapping peptides covering the entire hepatitis delta antigen and HBV-surface, HBV-core and HBV-polymerase antigens. T-cell-proliferation was investigated by 3H-Thymidin-incorporation. Production of interleukin-2, interleukin-10, interferon-gamma and interferon-gamma-induced-protein-10 was evaluated by CBA in cell culture supernatants, serum samples of HDV patients were additionally tested for interleukin-17A and interleukin-21.

Results: Significant levels of IL-10 (mean 11.49+/-3.36pg/ml) and IP-10 (220.15+/-220.12pg/ml) were detectable in sera of 22 (96%) and 23 (100%) patients with hepatitis delta. IFNgamma (5 patients; 8.86+/-15.84pg/ml) and IL-2 (1 patient,97.8 pg/ml) tested less frequently positive. IL-17 and IL-21 was found in 16 (70%; 26.29+/-16.89pg/ml) and 10 (43%; 66.84+/-83.36pg/ml) patients.

T-cell proliferative responses against HDV were detected in 4 patients and rather weak. In contrast, HBV-specific proliferative responses were more frequent, stronger and more often multispecific in hepatitis delta patients compared with HBV-monoinfected controls. HDV-infected patients with HBV-specific proliferative responses had lower HBsAg levels. HDV-specific IFNgamma production in cell culture supernatant was detected in 7/23 patients while HDV-specific IL-10, IP-10 and IL-2 responses were seen in only 2 or 3 patients.

Discussion/conclusion: High serum IP-10 levels indicate activation of the endogenous IFN-system in delta hepatitis which is paralleled by an anti-inflammatory IL-10 response in all patients and a Th-17 response in about half of the patients. Subsequently, antiviral effector cytokines and antigen-specific T-cell responses are rather weak in chronic HDV infection. Distinct adaptive immune responses towards HDV or HBV may determine different outcomes of the infection.

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DELTA HEPATITIS IN SOUTHEAST TURKEY, STILL OF CONCERN

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Background: HDV infection of chronically infected HBV-carriers may lead to fulminant acute hepatitis or severe chronic active hepatitis, often progressing to cirrhosis, may also lead to the development of hepatocellular carcinoma.

Methods: Serological markers of hepatitis B virus (HBsAg, HBeAg, Anti-HBe) and hepatitis Delta virus (HDV-IgM, HDVIgG) were analyzed. In laboratory, commercial kits based on the enzyme-linked immunosorbent assay (ELISA) E170 (Roche, Germany) and micro ELISA method (Triturus, Spain) was used. Serum hepatitis B virus DNA were analyzed with PCR.

Results: We found HDV ratio in 8% (34/422) of asymptomatic hepatitis B virus carriers, 15.3% (35/228) in chronic hepatitis B patients and in 58.3% (7/12) in cirrhotic patients. There was no statistically significant difference in patients with chronic HDV infections related to gender and age. Hepatitis delta virus infection showed a two fold increase in chronic hepatitis ($p< 0.01$) patients and seven folds in cirrhotic patients ($p< 0.001$).

Conclusion: This study shows the harmful impact of Hepatitis D infection in chronic and cirrhotic patients. Delta hepatitis continues to be a major cause of severe form of hepatitis and cirrhotic patients.

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REGIONAL SEROPREVALENCE OF HEPATITIS DELTA AND HEPATITIS E VIRUS IN AN ENDEMIC PART OF TURKEY

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Background: Hepatitis delta virus (HDV) infection is an acute and chronic inflammatory process involving the liver. Turkey is in the intermediately endemic region and Anti-delta seroprevalance was found to be nearly 6.7%. Hepatitis E virus (HEV) infection is the major cause of enterically transmitted Non-A Non-B hepatitis in many parts of the world and causes epidemics, especially in developing countries where hygiene is poor and many affected pregnant women suffer from fulminant hepatitis. In Turkey, the anti-HEV antibody seroprevalence rate varies from 3%-12%.

Methods: This study was conducted in Diyarbakir State Hospital between 01.01.2006-31.12.2009 for HDV, 01.01.2006-31.12.2008 for HEV. The serological markers of Anti Delta IgM, Anti Delta IgG, Anti HEV IgM, Anti HEV IgG were investigated retrospectively in serum samples sent from policlinics and clinics to microbiology laboratory. The gender distribution and mean age of patients were determined. In laboratory, commercial kits based on micro ELISA method (Triturus, Spain) was used.

Results: There was no significant difference between gender and HDV seroprevalence rates ($p>0.05$) but there was significant difference between age and HDV seroprevalence($p< 0.01$). Also, we found statistically significant difference between Anti HEV-IgM and age ($p< 0.001$). As seen in Table 1, the seroprevalence of hepatitis delta is increasing with years. These rates are higher than the other parts of our country. Anti HEV seroprevalence rates are similar when we compare with other studies conducted in urban and rural parts of the country.Table 1: Seroprevalence of Anti-HDV and Anti-HEV

	AntiDeltaIgM	AntiDeltaIgG	AntiHEVIgM	AntiHEVIgG
2006	38/5018 (0.7%)	216/5018 (4.3%)	4/540 (0.7%)	84/540 (15.5%)
2007	40/1541 (2.5%)	118/1541 (7.6%)	4/454 (0.8%)	49/454 (10.7%)
2008	65/1420 (4.5%)	202/1420 (14.2%)	56/387 (14.4%)	48/387 (12.4%)
2009	64/1555 (4.1%)	140/1555 (9%)	-	-

[Seroprevalence of Anti-HDV and Anti-HEV]

Conclusion: Results obtained in this study indicate that the high prevalence of delta hepatitis in southeastern Turkey is striking. Additional measures must be promptly taken in region and an intensive educational program to reduce risk behaviors should be continued. Awareness of the delta virus has become inevitable.

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GENERAL CHARECTERISTICS OF CHRONIC HEPATITIS DELTA VIRUS INFECTION

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Background and aims: Hepatitis delta virus (HDV) infection is a defective RNA virus that requires the hepatitis B virus (HBV) for transmission and replication. It is still health problem in Turkey that can cause cirrhosis and hepatocellular carcinoma .

Methods: We retrospectively investigated the general charecteristics (age, gender, clinical findings at presentation and the rate of compensated or decompensated cirrhosis) of patients who had chronic HDV infection in our Hepatology Clinic between 1999-2009.

Results: We included 213 patients (M/F:149/64, median age was 43(17-76)) with chronic HDV infection. Chronic HDV infection was diagnosed in 25,6% of patients with symptoms like weakness or fatigue, 31,8% of patients for investigation of HDV in chronic hepatitis B, 9,7% of patients for high ALT levels, 4% of patients for family investigation in terms of HBV or HDV and 29% of patients complications of cirrhosis. We detected cirrhosis in 133 of 213 (62%)patients by biopsy or radiologic images. In the cirrhotic patients, 73 patients had compensated and 60 patients had decompensated cirrhosis. The reasons of decompensation were ascites in 37(27,8%), variceal bleedings in 24(%18), encephalopathy in 10 (7,5%), jaundice in 9(6,7%) patients. Median ALT level was 72U/L (5-2160). HBeAg was (+) in 34 (16%) of these patients. Median HBV DNA level was 72000IU/ml(0-7627000IU/ml)

Conclusions: Chronic HDV infection is more common in males like chronic HBV infection. 62% of patients had cirrhosis and 45% of these patients with cirrhosis had decompensated disease.Ascites was the most prominent finding of decompensation. Chronic HDV infection has insidious progress and can cause serious disease so we have to investigate the HDV infection in all chronic HBV infection patients to prevent the severe liver disease.

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HBEAG POSITIVE HEPATITIS DELTA IN GERMANY

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HBeAg can be detected in 15 to 20% of patients with chronic hepatitis D (CHD). The course of HBeAg-positive CHD is poorly defined.

Methods: We identified 38 HBeAg+ patients from a large single center cohort (Heidrich, J Viral Hepatitis 2009). Anti-HCV tested positive in nine patients. Follow up data were available for 27 patients with a median time of 51 months (range 9-193 months). 11 patients were treated with IFN-alfa, 15 had received HBV-polymerase inhibitors.

Results: HBeAg+ and HBeAg- patients did not differ in gender ratios and AST levels but HBeAg+ patients were significantly younger ($p=0.003$) , had higher values for ALT ($p< 0.05$) and higher levels of HBsAg ($p=0.0002$). 14/38 patients had HBV-DNA levels below 2000 IU/ml with 6 (16%) patients being even HBV-DNA negative despite being HBeAg positive. About two thirds remained HBeAg+ during follow up (63%). HBsAg levels showed a significant decline during follow up ($p=0.021$). Quantitative HDV-RNA levels remained rather stable with only 6 patients showing changes of more than 3 log-copies/ml (22%). Clinical endpoints (death, liver transplantation, HCC, hepatic decompensation) developed in 5/9 patients who lost HBeAg and 3/18 patients who remained HBeAg+ (56% vs. 17%; $p=0.68$). Patients who developed a clinical endpoint showed no significant differences in HBsAg, HBV-DNA and HDV-RNA levels at baseline but had a significantly higher MELD score ($p< 0.001$) and lower albumin levels ($p< 0.05$) and platelets counts ($p< 0.05$).

Conclusion: This large cohort of HBeAg+ CHD patients showed a rather severe clinical long term outcome with more than one third of patients developing liver related endpoints after a median follow up of only 4.3 years. Virological parameters were surprisingly stable in the majority of HBeAg+ patients with CHD. We suggest that HBeAg+ CHD should be considered as an independent subgroup of CHD, possibly requiring different treatment approaches.

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HEPATITIS B-DELTA VIRUS CO-INFECTION IN BELGIUM: RETROSPECTIVE AND PROSPECTIVE DATA AND COMPARISON TO HBV MONOINFECTION

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Background and aims: Recent data suggest increasing prevalence of HDV infection in Europe. Epidemiological data on this infection are lacking. A multicentric questionnaire based registry with both retrospective and prospective data on HDV infection was performed in Belgium. Prospective data was collected from March 1, 2008 till February 28, 2009 on patients with HBV-HDV co-infection seen during the screening period. These data were compared to those of a concurrent registry on HBV infection.

Methods: Prospective data from 40 patients from 14 centers with HDV-HBV co-infection were compared with 1282 HBV mono-infected patients. Active hepatitis B replication is defined as HBeAg + or HBV DNA > 2000 IU/mL HBeAg being negative. Statistical analysis of prospective data of both the BASL HDV and HBV registries was performed to measure possible differences between HDV - HBV co-infected patients and HBV mono-infected patients. Statistical analysis was performed using Mann-Whitney U test for continuous and Chi-Square test for categorical variables.

Results: A total of 61 different cases from 15 different centres have been registered, 21 of these were historic cases. Comparison with HBV mono-infected patients was performed in the remaining 40 prospective cases.

Baseline characteristics: 32/40 (80.0%) males, 19/40 (47.5%) non-Caucasian, 6/40 (15.0%) had active HBV replication, 27/40 (67.5%) had elevated ALT, with 15/40 (37.5%) ALT>2N. Metavir fibrosis grades F3 and F4 were present in 20/27 (74.1%) patients who received a liver biopsy.

Comparison of HBV mono-infected patients and HDV-HBV co-infected patients yielded the following results (Table 1):

Variable	HBV patients[a]	HBV-HDV patients[a]	Significance	
Age	41.29 (SD 13.371)	39.38 (SD 10.966)	*p=0.38*	Continuous[b]
HBV Viral load IU/ml	$4.27*10^8$ (SD $4.46*10^8$)	*6395.69* (SD 17997.04)	*p=0.00*	
Gender: male	838/1262 (66.4%)	32/40 (80.0%)	*p=0.07*	Categorical
Race: non-Caucasian	614/1245 (49.3%)	19/40 (47.5%)	*p=0.33*	
HBV active replication	480/1282 (37.4%)	6/40 (15.0%)	*p=0.00*	
Anti-HCV antibody positivity	30/1227 (2.4%)	5/40 (13.2%)	*p=0.00*	
Anti-HIV antibody positivity	33/1147 (2.9%)	0/39 (0.0%)	*p=0.28*	
ALT >2N	140/1237 (11.3%)	15/40 (37.5%)	*p=0.00*	
Fibrosis F3F4	178/517 (34.4%)	20/27 (74.1%)	*p=0.00*	

[a]Total patients differ due to missing data

[b]Means compared with Mann-Whitney-U test

[c]Means compared with cross tabulation and Chi-Square test

[d] L=df+1 with L equals the amount of levels in the categorical variable

[Table 1]

Conclusion: Based on the prospective data, three per cent (40/1322) of HBV patients in Belgium were reported to be co-infected with HDV. These patients presented with significantly more advanced liver disease, less active HBV replication, lower HBV DNA levels, and more co-infection with HCV.

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HEPATITIS DELTA VIRUS RNA LEVEL AND GENOTYPE, AND HEPATITIS B SURFACE ANTIGEN TITRE PREDICT RESPONSE TO PEG-INTERFERON THERAPY FOR CHRONIC DELTA HEPATITIS

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Background and aims: Alpha-interferon is beneficial in treating HDV infection but predictors of response are poorly defined. Therefore, we analysed factors associated with viral response to PEG-interferon-α2a (PEG-IFN) in chronic HBV/HDV.

Methods: Between 2005-2010, 14 patients with HDV (71% female; median age 32; 57% Black African, 36% Caucasian, 7% Oriental; 79% HBeAg-ve; 64% HDV genotype-1, 29% HDV genotype-5, 7% HDV genotype-6; 43% cirrhotic) were treated with PEG-IFN 180 mcg/week (median 48 weeks) and followed post-treatment for median 16.5 months. HDV RNA was measured by in-house real-time quantitative PCR assay (range $6.4x10^2$ to $6.4x10^7$ copies/mL). Genotyping was performed by direct sequencing. HBV DNA was measured using the Roche COBAS Ampliprep/TaqMan assay and HBsAg by the Abbott Architect assay.

Results: In response to PEG-IFN, 64% cleared RNA by end of treatment (EOT), 1 patient with genotype-1 relapsed, therefore 54% remain RNA negative ≥EOT+24 weeks (sustained virological response; SVR); 2 patients cleared HBsAg. Baseline HDV RNA was significantly higher in non-responders compared to those with SVR ($2.1x10^6$ vs. $1.3x10^4$ copies/mL, p=0.003) and predicted treatment response (AUROC=1.0, p=0.003). A HDV RNA >$1.96x10^5$ copies/mL predicted treatment failure (PPV 100%, sensitivity 100%; p=0.001). HDV RNA correlated strongly with HBsAg titre (r=0.82, p< 0.001). Baseline HBsAg titre was significantly higher in non-responders compared to those with SVR (10,067 vs. 5,820 IU/mL, p=0.007) and predicted treatment response (AUROC 0.95, p=0.007). HBsAg titres >9,000 IU/mL predicted treatment failure (PPV 100%, sensitivity 67%; p=0.021). All patients with HDV genotype-non-1 achieved SVR, compared to only 25% with HDV genotype-1 (p=0.02). Responders were similar to non-responders with respect to gender, age, histological scoring and pre-treatment ALT.

Conclusion: PEG-IFN was an effective treatment for chronic HDV (54% achieved SVR). Levels of HDV RNA >$1.96x10^5$ copies/mL and HBsAg titres >9,000 IU/mL predicted treatment failure, whereas HDV genotype-non-1 predicted sustained viral clearance.

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THE SERUM LEVELS OF INFLAMMATORY CYTOKINS IN LIVER CIRRHOSIS CAUSED HBV AND HDV INFECTION

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Chronic HDV infection leads to more severe liver disease than HBV monoinfection and is associated with accelerated fibrosis progression, earlier hepatic decompensation and an increased risk for the development of hepatocellular carcinoma. However the mechanism of progression of HDV infection is not clear. The critical role in the defence against the hepatotropicγ viruses as well in the fibrogenesis belongs to the immunological mechanism: activity of the mononuclears and cytokins.

The aim of the study was investigate the serum levels of the important cytokins IL-18, IL-17, INF-gamma in patients with the liver cirrhosis caused by HDV and HBV infection.

Material and methods: 33 patients with liver cirrhosis Class B (Child-Pugh) caused by HBV (group A) and 41 patients with liver cirrhosis Class B (Child-Pugh) caused by HBV and HDV infection (group B) were included in this study as well as 30 sex and age matched healthy control group. The serum concentration of IL-17, IL-18 and INFγ were estimated by ELISA (IBL)

Results: The levels of IL-17 and IL18 in group A (56, 5±8,1 pg/ml and 189,7±9,2pg/ml) are found higher than in the health group (1,27±0,06 pg/ml, P< 0,05 and 122,5±6,78pg/ml, P< 0,05, accordingly) and group B (17,1±6,7pg/ml, P< 0,05, and 134,7±5,7 pg/ml, P< 0,05, accordingly).

However the levels of INFγ were revealed significant lower in the group B (0,98±0,02 pg/ml)than in the patient with monoinfection (3,8±0,15 pg/ml, P< 0,005) and none significant compare with the healthy group (0,67±0,02, P< 0,1).

Conclusion: The low level of INFγ in the superinfection of HDV shown the low activity of Th1 lymphocyte in this group. The high levels of IL17 and IL-18 in two groups of patients have meaning for participation of autoimmune inflammatory in the progression of both monoinfection and in present HDV.

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VIRAL SUPERINFECTION RATE IN KOREA, HBV ENDEMIC AREA

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Background and aims: Recent studies from Europe reported an increased prevalence of hepatitis D virus (HDV) superinfection in chronic hepatitis B patients. However, HDV superinfection remains a rare occurrence in the far east area such as in Hong Kong and Japan. In Korea, there are no published data about the prevalence of HDV superinfection.

Methods: We examined the prevalence of anti-HDV antibodies and anti-HCV antibodies among 226 consecutive HBsAg-positive patients who underwent OLT for liver failure and HCC at Seoul National University Hospital from August 2003 to December 2009.

Results: Anti-HDV and anti-HCV antibodies were detected in only one (0.44%) and four (1.9%) of 226 HBsAg-positive patients respectively.

Conclusions: HDV and HCV superinfection remain a very rare occurrence in chronic hepatitis B patients in Korea.

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IMMUNEHISTOCHEMISTRY FOR HBSAG, HBCAG AND HDAG IN CHRONIC DELTA HEPATITIS AND EFFECT OF TREATMENT

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Introduction: Active chronic delta hepatitis is characterized by HDAg positivity in liver tissue. Recently, the effect of pegylated interferon (PegIFN)± adefovir (AD) and AD alone was assessed in a multicenter randomized controlled clinical trial (Wedemeyer et al, J Hepatol 2007).

Aim: To assess variables associated with HDAg, HBsAg and HBcAg staining in liver tissue and effect of treatment on HDAg, HBsAg and HBcAg in liver tissue.

Methods: HBsAg and HBcAg staining was performed according to the manufacturer's instructions. HDAg staining was done as previously described (Yurdaydin et al, J Hepatol 2002). HBsAg, HBcAg and HDAg staining was semiquantitatively assessed. Liver biopsies for immunochemical comparisons were available in 51 patients. Uni- and multivariate analysis and Spearman and Pearson's correlation were used where appropriate.

Results: Treatment with PegIFN based regimens decreased HDAg in liver tissue ($p< 0.0001$) without affecting HBsAg and HBcAg. AD had no effect. No difference was observed between treatment with PegIFN-AD and PegIFN monotherapy. Intensity of HBsAg staining correlated with HBcAg staining ($p=0.008$). HDAg staining did not correlate with HBsAg and HBcAg staining. By multivariate analysis, high HBV DNA(>4log) and quantitative serum HBsAg was associated with HBsAg immunostaining (HR: 8.9, $p=0.014$ and HR:4.4, $p=0.029$, respectively) whereas for HDAg in liver tissue, high serum AST and low HBV DNA were predictors (HR: 5.5, $p=0.011$ and HR:0.15, $p=0.045$, respectively). Baseline serum HBsAg correlated with HDAg in liver tissue ($p=0.032$). Baseline HDV RNA was inversely correlated ($p=0.032$) with virologic response (>2 log decline of HDV RNA) at end of treatment. Decline of HDV RNA at end of treatment correlated positively with low HDAg staining on posttreatment liver biopsy ($p=0.01$).

Conclusion: Semiquantitative evaluation of immunohistochemical staining of liver tissue pre-and posttreatment may provide important clinical and prognostic insight.

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OUTCOME OF CHRONIC DELTA HEPATITIS: EXPERIENCE GAINED FROM A LARGE SINGLE CENTER COHORT

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Aim: Aim of this study is to reveal baseline characteristics, and outcome of a large, single center cohort of CDH patients from Turkey.

Methods: 164 patients(M/F=108/56;mean age[±SD]:40.63[±10.94]) with eligible data were retrospectively analyzed from a cohort of 267 patients at Ankara University Medical School. Mean duration of follow-up with HBV and HDV diagnoses were 132.4±78.15 and 88.3±56.9 months, respectively. Treatment data was collected as nucleoside analog (NA)(>6mo), IFN±NA(1year), and extended IFN. Main outcome values were death, decompensation, hepatocellular CA(HCC), and transplantation.

Results: At baseline, 109 patients had CDH, whereas 55 were cirrhotic(6 decompansated). Number of eAg negative and positive patients were 139(84.7%) and 22(13.4%), respectively(3 unknown at baseline). HBVDNA levels of 104(63.4%) patients were undetectable. For the rest, mean HBV-DNA level was 3.98±1.65 log_{10}copies/mL. The proportion of patients treated with NA, IFN±NA and extended IFN±NA or left untreated were 24(14.6%), 64(39,1%), 39(23,7%) and 37(22,5%), respectively. Treatment response in patients receiving standard or extended IFN treatment was achieved in 29.1% and 50% of patients, respectively. By multivariate analysis, only HBeAg positivity(OR:0,203;p=0.05), was associated with poor response to therapy. Median duration for progression from CDH to cirrhosis was 85.2months(range:10-180;n=26/112[23,2%]). Progression from compensated cirrhosis to HCC occurred after 51.5months(6-130;n=14/55[25.5%]), and death or liver transplantation in 76 months(range:4.8-231;n=22;14 transplanted). Among cirrhotic patients at baseline 26.5%(13/49) decompansated at median 43(range:6-153) months. Baseline characteristics predicting progression to cirrhosis are non-IFN treatment(OR:15.1;p=0.005), low thrombocyte(OR:3.81;p=0.01). HBsAg loss was observed in 9(5.4%) patients in median 80(Range:11-128) months. Interestingly, there were 7(4.3%) extrahepatic malignancies(4 adeno Ca of GI tract and 3 leukemia), which is far higher than in the normal population.

Conclusion: Progression to cirrhosis and HCC development are the main hallmarks of burden in HDV. There may be a tendency for extra-hepatic malignancies in patients. For most patients with CDH, IFN treatment extending beyond one year is necessary**.**

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ANTIVIRAL TREATMENT FOR HEPATITIS D. A META-ANALYSIS

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Background and aims: There is no satisfactory medical treatment for patients with hepatitis D (HDV). Different doses of interferon (IFN) as well as oral antivirals have been evaluated. In this meta-analysis we evaluated the efficacy of antiviral treatment for HDV.

Methods: We searched MEDLINE using the textwords 'Hepatitis D' and 'treatment', and abstracts from major Gastrenterology/Liver meetings. We included randomized clinical trials (RCTs) comparing:

i) Group A: IFN for 12 months vs no treatment (4 RCTs, n=137 patients)

ii) Group B: IFN low dose (3 MU) vs high dose (9-18 MU) for 12 months (2 RCTs, n=60) and

iii) Group C: IFN+lamivudine vs IFN (2 RCTs, n=48).

The end-points were:

a) end of treatment complete biochemical response(EOT BR) or virologic response (EOT VR),

b) end of follow up virologic response(EOFUP VR),

c) histological improvement and

d) intrahepatic HD Ag clearance.

Results:

Group A. IFN was significantly different for: EOT BR (OR, 0.11 (95% CI,0.04-0.2)) and EOT VR (OR, 0.08 (95% CI,0.03-0.2)), but not EOFUP VR (OR, 0.49 (95% CI,0.07-3.3)). The difference was borderline not significant for histological improvement with IFN treatment (OR, 0.45 (95% CI,0.19-1.05)).

Group B. High dose IFN was significantly better: EOT BR (OR, 0.24 (95% CI,0.08-0.73)) and EOT VR (OR, 0.27 (95% CI,0.1-0.74)) but not EOFUP VR (OR, 0.52 (95% CI,0.1-2.5)), histological improvement (OR, 0.55 (95% CI,0.12-2.5)) or intrahepatic HDAg clearance (OR, 0.3 (95% CI,0.04-1.9))

Group C. There were no significant differences for combined treatment except a trend favouring histological improvement (OR, 2.9 (95% CI,0.6-13.4)).

Conclusions: Virologic efficacy of IFN (EOT) was not permanent and there was a marginal histological improvement. Higher IFN doses were better only for EOT, while there was no benefit of adding lamivudine to standard IFN. RCTs are needed to test PEGIFN and newer antivirals.

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A MATHEMATICAL AND COMPUTER MODELING OF THE LIVER'S CONTROL MECHANISMS IN DELTA HEPATITIS

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Background: Molecular-genetic aspects of viral hepatitis pathogenesis are definitively not established. It can be reached by analyzing functioning regulatory mechanisms (regulatorika) of living systems using methods for mathematical modeling and computing experiment.

Research objective is development of the quantitative methods and techniques for liver regulatorika and diagnostics of viral infection (viral hepatitis type D) stages using methods for mathematical modeling and information technology toolboxes.

Methods: For mathematical modeling the methods of the quantitative studying regulatorika of living systems have been used. The equations of mathematical models for regulatorika of liver cells and hepatitis D virus (HDV) under delta hepatitis based on the approaches generalization by B. Goodwin, M. Eigen, V. Ratner, J. Smit with taking into account cooperativity, time mutual relations and presence of the combined feedback in hepatocyte regulation system are carried out.

Results: In the course of quantitative researches the following modes of considered process have been received: clarification, symbiosis, auto-oscillations and irregular fluctuations (chaos), sharp destructive changes ("black hole" effect) which define various clinical forms of the disease (delta hepatitis).

Conclusions: The developed quantitative methods based on the mathematical modeling liver regulatorika at molecular-genetic levels, allow to predict coming chaotic, repeating changes and "black hole" effect in the liver under HDV infection. This gives the chance to diagnose coming unpredictable changes phase in liver regulatorika and beginning cirrhosis using computer calculations.

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OCCULT HDV INFECTION

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Background: By analogy with the occult over chronic HCV and HBV infections in the absence of HBV DNA, HDV RNA in the serum, chronic hepatitis D (CHD) can be regarded as an occult form of HDV infection (OHDVI).

The aim of this work was to determine the significance of serological and molecular genetic techniques in CHD and possible course of pathological process in the absence of serum HBV DNA and HDV RNA.

Methods: In 69 patients with chronic HDV infection surveyed serum bilirubin and alanine transaminase, serological and molecular-genetic markers of delta infection-anti-HDV JgM and JgG, HBsAg, quanification HBV DNA, HDV RNA, liver biopsy with definition HBV DNA, HDV RNA and ultrasound examination of the abdominal cavity.

Results: In the serum of 14 patients were not determined HBV DNA and HDV RNA and diagnosed as OHDVI. Liver biopsy and analysis of clinical and laboratory parameters of 11 patients verified as chronic hepatitis, and in 3 patients was established liver cirrhosis. In 4 patients with CHD pathological process had high activity. In all 7 samples of the liver tissue HBV DNA and HDV RNA were positive. 10 patients had low activity of the pathological process, by the lack of clinical symptoms and normal biochemical parameters, while HBV DNA, HDV RNA in the liver biopsy of 8 cases were positive. A comparison group of OHDVI with a group with the presence of HBV DNA and HDV RNA in the serum showed the identical severity of the pathological process.

Conclusions: The lack of serum markers of active replication of HBV and HDV in CHD infection does not exclude the presence of an active infectious process. In deciding whether the appointment of antiviral therapy in patients with OHDVI necessary to investigate HBV DNA and HDV RNA in the liver biopsy.

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ULTRASTRUCTURAL CHARACTERISTICS OF NEW PHENOMENON IN HEPATOLOGY: SHEDDING OF LYMPHOCYTES CELL MEMBRANE IN CHRONIC DELTA HEPATITIS LIVER

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Backround and aims: Liver sinusoids contain a heterogenous population of lymphocytes (L). In present work we investigated ultrastructural patterns of liver-associated lymphocetes in chronic delta hepatitis (CHD) liver.

Methods: Liver biopsies from 20 patients with CHD were fixed in 2,5% glutaraldehyde, 1% osmium tetroxide and embedded in Epon. Ultrathin sections were examined in a JEM-100S Electron Misroscope (JEOL, Japan).

Results: Electron microscopic study revealed cooperation of macrophage with lymphocyte in the lumen of the sinusoids and penetration of L through the sinusoidal wall between hepatocytes. These lymphocytes had similar ultrastructure of the secretory cells with well developed Golgi apparatus (Ga) and probably were cytotoxic T cells. In the liver of one patient we observed shedding of the lymphocyte cell membrane (CM). The two plasma membranes fuse, forming three-layered membrane structures. This process is most active on the surface of the L opposite to the zone of contact with target cell. Numerous sloughed fragments of the L plasmalemma are situated alongside the cells. In the process of shedding of the CM the integrity of the L plasma membrane is unimpaired. This phenomenon has not been reported elsewhere.

Discussion and conclusions: As it is described assembly of the main components of the CM occurs in the Golgi apparatus. The Golgi vesicles secrete their content into the intercellular space and their membranes fuse with the CM and the extent of the CM is substantially increased. It can be assumed that shedding of the CM of the L is a compensatory mechanism freeing it of the excess of this membrane (i.e. for releasing him from membranes unnecessary). It is important to take into account described above shedding of L cell membrane in pathogenetic therapy of CHD, including purification of the patients serum from these membranes.

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DEVELOPMENT AND ASSESSMENT OF A NOVEL REAL-TIME RT-PCR ASSAY FOR THE QUANTITATION OF HDV RNA IN PLASMA

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Background and aims: Hepatitis delta virus is a single stranded RNA virus. The aim of this study was to develop a highly sensitive and reproducible real-time RT-PCR for the quantitation of HDV RNA in plasma, which could be useful for the follow-up of infected patients under treatment.

Methods: Extraction of HDV RNA was performed from plasma samples. cDNA synthesis and amplification was done in a two-step RT-PCR. Primers well conserved among genotypes 1-4 were selected, flanking an 83-bp region in the ribozyme domain of HDV genome. A molecular beacon was designed for the amplicons detection. Serial dilutions of a synthetic 83 bp DNA derived from the same viral region was used as a standard to define the assay dynamic range. Probit analysis was performed to assess the 95% and 50% lower limits of detection (LLD). The intra- and inter-assay variability was evaluated using plasma samples of different viral load levels. The clinical sensitivity of the assay was tested in 35 HDV patients with or without treatment. The analytical specificity of the RT-PCR was determined by testing 40 anti-HDV negative blood donors.

Results: The dynamic range of the assay is $1\text{-}10^9$ copies of synthetic DNA /reaction. The 95% and 50% LLD of the assay along with the corresponding 95% confidence intervals are 43.2 (16.5-584.1) and 2.18 (0.46-4.75) copies/mL, respectively. In addition, intra-assay reproducibility as expressed by the coefficient of variation (CV) ranged from 0.55% to 11.59%, whereas the corresponding estimates for the inter assay variability ranged from 0.57% to 13.41%. The specificity of the assay is 100%. HDV RNA results in the 35 HDV patients were found to be clinically relevant. Viral load values ranged from $2.88\text{x}10^2$ to $4.67\text{x}10^9$.

Conclusions: Our real-time RT-PCR for HDV-RNA quantification combines high sensitivity and reproducibility in a high dynamic range.

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LOW RATE OF VIROLOGICAL RESPONSE TO INTERFERON IN HDV-1/HBV-D CO-INFECTED PATIENTS

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Background and aims: Co-infection with hepatitis D virus (HDV) is a major cause of cirrhosis and end stage liver disease in chronic HBsAg carriers. The only approved medicine for treatment of HDV is standard interferon alpha but little information is available on the treatment outcome of HDV-1 in HBV genotype D infected patients (common genotype among Iranian patients).

Methods: 20 HBsAg carriers with positive serology and PCR for HDV co-infection were recruited and treated for a duration of 1 year with 5 MIU interferon alpha-2b QD subcutaneously. Treatment continued 6 months after clearance of HDV viremia and sustained virological response was defined as a negative quantitative PCR 6 month after treatment cessation. Patients who were withdrawn from treatment were considered a non-responder.

Results: The patients' mean age was 40±5. 3 subjects were female and 2 patients had compensated cirrhosis. Mean baseline ALT was 72 IU/L. Over all 3 subjects (15%) achieved SVR, 9 (45%) relapsed after treatment cessation and 8 patients did not clear HDV viremia during treatment. In 7 subjects, serum HBV-DNA became negative during treatment and 6 months of untreated follow up. 6 patients normalized ALT.

Conclusions: HDV-1 co-infection with HBV-D has very low response to high dose of standard interferon alph-2b.

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HDV GENOTYPE 1 NEWLY IDENTIFIED IN POPULATION OF INJECTING DRUG USERS IN PRAGUE, CZECH REPUBLIC

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Introduction: Hepatitis D used to be an extremely rare infection in the Czech Republic (CR), only sporadic cases were occasionally identified, usually only among foreigners. CR is low prevalence country for HBV.

Mediterranean and other parts of Europe have belonged to an endemic area for HDV although the situation has improved considerably with preventative measures such as vaccination.

Changes in epidemiology of viral hepatitis related to IDU has led to introduction of HDV to formerly unaffected countries Central and Western Europe.

We were inspired by the case of our patient in whom, based on clinical signs, we confirmed HDV etiology of exacerbation of known HBV infection.

Aims of study: To assess the HDV status among all patients with known HBV infection followed in Remedis, both in the group of IDU and nonIDU patients together with demographic and epidemiological characteristics.

Patients and methods: 42 HBsAg positive patients were included and tested between 6/2008 and 4/2009. Epi data were collected by the assisted interview. ELISA was used to detect HDV-Ig antibodies, HDV DNA PCR to identify replicative status. Direct sequencing was employed to identify genotypes and assess genetic relatedness.

Results: Of 42 patients, 34 were males, average age was 35.4 years. 21 patients belonged to IDU group, where antiHD antibody was detected in 7 cases. Of them 4 had positive HDV DNA, all were genotype 1. All four isolates were relatively closely related. No HDV infection was identified in nonIDU group. Also, in IDU group, 17 patients were antiHCV positive compared to nonIDU group, where all were negative.

Conclusions: Given the low prevalence of HBV, we consider our results significant. We haven't identified neither the source of infection nor apparent transmission from abroad. It can be inferred that isolated HBV epidemic can be present for longer time among Prague IDUs.

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EPIDEMIOLOGICAL AND CLINICAL ASPECTS OF DELTA VIRUS INFECTION PATIENTS IN LATVIA

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Background: In Latvia, 2-3% of population are HBV-positive. Last 5 years showed the intense rate of 7.4 to 6.3 per 100 000 people, which is higher than the average rate in Europe. Investigations plans for Hepatitis D virus (HDV) patients have been made according to the recommendations of the European guidelines of Hepatology.

The aim of this study was to analyze the epidemiological and clinical data base for dual infection - Hepatitis B and Delta virus infection patients.

Methods: 643 blood samples were detected for HDV during years 2003 - 2010. In total, 87 patients had HDV positive serological findings. Blood samples from 29 randomly selected patients (10 females, 19 males, mean age 28 years) were clinically and laboratory diagnosed. Qualitative PCR and ELISA measurement of IgG , IgM antibodies were used.

Results: As the result, 29 positive findings were obtained, i.e., the presence of Hepatitis D was found. In 20 (69%) from the tested patients acute Hepatitis B virus and Delta infection were diagnosed, 3 patients (10%) had chronic viral hepatitis, but positive HBsAg was detected for 9 patients (31%) without the features of hepatitis. Epidemiological data showed that 6/29 were intravenous drug users, and 23/29 had marked parenteral manipulations during the last year. On the basis of obtained data the differentiation of HDV co- or superinfection, particularly in cases of chronic dual infection, was difficult. 3 from the acute Delta infection patients had severe complications due to their basic diagnosis (liver failure, coma), including one case of death.

Conclusions: In Latvia, HDV infection is predicted to be in high levels among HBV infected patients. According our data, HDV infection in intravenous drug users reaches 20% level.

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PREVALENCE OF HEPATITIS DELTA VIRUS INFECTION IN TYVA REPUBLIC, RUSSIAN FEDERATION

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Aim: The aim of this study was to determine the prevalence of HDV infection in Tyva Republic.

Methods: Serum samples from 1086 healthy individuals from age groups: < 1 year (n=97), 1-4(n=109), 5-9(n=113), 10-14(n=107), 15-19(n=105), 20-29(n=102), 30-39(n=103), 40-49(n=112), 50-59(n=115), >60(n=123) were tested for HBsAg and anti-HBc. All positives were tested for anti-HDV and HBV DNA. All anti-HDV positive samples were tested for HDV RNA by RT-PCR. Additionally 102 patients (43 male, 59 female, mean age 37,9±12,9(18-78) years) with primary diagnosis “hepatitis D” were tested for HBsAg, HBV DNA, anti-HDV, and HDV RNA.

Results: Prevalence of anti-HDV in healthy individuals was 2,5%(27/1086) with similar prevalence in men and women (2,6%(10/386) and 2,4%(17/700) respectively). The highest prevalence of anti-HDV was observed in age group 40-49(5,4% (6/112)). In other age groups anti-HDV prevalence was as follows: 1,9%(2/107) in 10-14 years, 3,8%(4/105) in15-19, 3,9%(4/102) in 20-29, 4,9%(5/103) in 30-39, 1,7%(2/115) in 50-59, and 3,3%(4/123) in >60. No anti-HDV positive cases were detected in children under 9 years old. HDV RNA was detected in 51,9%(14/27) anti-HDV positive samples. Interestingly, two HDV RNA positive samples were negative for HBsAg and HBV DNA but positive for anti-HBc, indicating the presence of escape variant of HBsAg.

Among 102 additional patients anti-HDV were detected in 92,2%(94/102), HBsAg - in 93,1%(95/102). In 94 anti-HDV positive patients 4 had HBeAg, 31,9%(30/102) were positive for HBV DNA and 33,0%(31/102) had HDV RNA. Two anti-HDV positive cases were negative for HBsAg, HDV RNA and HBV DNA suggesting resolved HDV and HBV infections.

Conclusion: Our data demonstrated high prevalence of HDV infection in Tyva Republic with highest infection burden in younger adults. Such a high burden of HDV infection indicates the need for development of special management programs for HDV-infected patients.

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HEPATITIS DELTA VIRUS TYPE I (HDV1) INFECTION IN TURKEY DOES NOT INHIBIT HBV REPLICATION AND INDICATES DIFFERENT HDV1 ORIGINS

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Background: Hepatitis delta virus (HDV) is a subviral pathogen, satellite of hepatitis B virus (HBV), which induces severe acute and chronic liver diseases. The *Deltavirus* genus consists of 8 clades, HDV1 being ubiquitous. In Turkey HDV1 infection is highly endemic among HBsAg carriers, especially in the South-East region and HBV is the most frequently identified risk factor for hepatocellular carcinoma.

Material and methods: Here, we analyzed samples from 34 HBV/HDV chronically infected patients, originating from 22 cities of rural regions in Central and Eastern parts of Turkey, to specify levels of viral replication the genetic diversity. We also used a comparison group of 38 samples from HDV1-infected untreated patients, having similar age and sex characteristics.

Results: HDV serum RNA levels ranged between 6,000 and 58,000,000 copies/mL, and HBV-DNA levels between 342 and >200,000 copies/mL. Differences in the mean HBV viral load (log copies/ml), analysed by student-t test indicated that HBV replication levels from the Turkish samples (mean log copies/ml=3.55 [2.30-5.30]) were significantly higher than that observed in the comparison panel (mean log copies/ml=2.89 [2.30-6.27]) (*p=0.0067*). This was not associated to a weaker HDV replication in Turkish patients than in comparison panel (*p=0.56*). Analyses of nucleotides 900-1280 of HDV genomes (n=34) and full-length (n=17) sequences indicated that HDV strains were affiliated to HDV1. However, a high genetic diversity (mean dissimilarity score =13%) was observed. Indeed, HDV sequences clustered either with sequences from Western Europe, Eastern Europe, Asia or Africa. All HDV1 isolates suspected to originate from Africa had a serine instead of an alanine at position 202 of the large delta protein. Contrasting to HDV-1 variability, HBV preS1 sequences all indicated HBV subgenotype D1.

Conclusion: Our results indicate that Turkey, a high endemic area for HBV-HDV dual infections, displays a wide HDV1 diversity reflecting ancient evolution and/or successive HDV1 outbreaks.

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DELTA HEPATITIS AND CIRRHOSIS IN EARLY STAGES OF LIFE - A PICTURE FROM THE AMAZON REGION

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Background and aims: The Western Amazonia region has the highest prevalence rates of hepatitis B virus and HDV virus infection in Brazil. The impact of this combination has been presented specially in young adults which increases the awareness of cirrhosis in this stage of life. This study was designed to describe the epidemiology and clinical features of HBV infected patients from Acre State.

Material and methods: A retrospective study were conducted and the medical files analysis from 682 patients with HBV infection assisted in Acre State Specialized Health Care Center were performed.

Results: Considering these 682 HBV infected patients, 23,6% (161) presented hepatic cirrhosis and 64,6% (104) were less than 40 years old. Among those young patients with cirrhosis, almost 70% were male and 88,5% related hepatitis cases in their families. See the clinical features of the cirrhotic patients in the table below

Feature (104 patients - < 40 years old and cirrhosis)	Results
HBV status	HBeAg positive : 16,3% HBeAg negative: 67,,3% Not specified : 16,3%
HDV coinfection rate	60,9%
HCV coinfection rate	2,9%

[Clinical features of the cirrhotic patients]

Discussion: These results confirm the high circulation of hepatits B virus and a high prevalence of HDV co-infection in the Amazon region. Considering the HBV markers the HBeAg negative were the most relevant status. Almost 25% of the HBV infected patients had cirrhoris and 60,9% of those were coinfected with HDV which increases the liver deterioration in early stages of life.

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DELTA HEPATITIS IMPACT IN THE STATE OF ACRE HEALTH CARE SYSTEM

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Background and aims: The Western Amazonia region has the highest prevalence rates of hepatitis B virus infection in Brazil varying from 20 to 70% with high rates of HDV coinfection and the intrafamilial transmission might be the most important considerable transmission route. This study was designed to describe the disease epidemiology and clinical features of 203 HDV infected patients from Acre State.

Material and methods: The medical files analysis from 203 patients with HDV infection assisted in Acre State Specialized Health Care Center were performed. The HBV viral load was assessed using COBAS-AMPLICOR and METAVIR score was used for evaluation of liver biopsy.

Results: Considering these 203 HDV infected patients, the median age was 30 years old, 60,1% (122) were males, 21,2% work in rural areas and 27,7% were born in high prevalence regions. Almost 75% of patients were diagnosed before the 40 years of age and the majority related some intrafamilial transmission route such as: sharing teeth brush (42,9%) and shaver (56,7%). Dental treatment with non specialists (76,4%) and a glass syringe use (34,5%) were the another issues related to HBV transmission. Only 48,9% received the completed HBV vaccine schedule. See the clinical/laboratory features in the table below

Feature	Results
HDV RNA destectable(in at least 1 sample)	34%
Liver biopsy (203 patients)	Chronic hapatitis - 49,3% and Cirrhosis - 50,7%
HBV status	HBeAg positive - 9,4%; Inactive carriers - 9,9% HBeAg negative - 29,1%
HBV DNA (available for 141 patients)	<=10.000cp/ml: 80,9%; > 10.000cp/ml:19,1%

[LABORATORY/CLINICAL HDV infection features]

Discussion: These results confirm the high circulation of hepatits B virus and a high prevalence of HDV co-infection in the Amazon region. Considering the HBV markers status, both HBeAg positive and HBeAg negative were also coinfected with HDV. A half of HDV/HBV coinfected patients presented cirrhosis which represents a considerable health care issue in this region.

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HIGH PREVALENCE OF HEPATITIS DELTA VIRUS IN ADULTS AND PREGNANT WOMEN IN MAURITANIA

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Background: In Mauritania, no data are available about the prevalence of Hepatitis B virus (HBV) and Hepatitis Delta virus (HDV).

Methods: 414 and 535 adults who visited the National Hospital of Nouakchott (CHN) and the Arafat center for routine health checks; and 1020 pregnant women who consulted in the Sabkha center were included. Individuals who had been previously diagnosed as carriers of HBV were excluded.

Subjects were screened for HBsAg, (AxSYM®-Abbott). Hepatitis Delta antibodies (Ab) (Diasorin®) were searched in subjects with detectable HBsAg. HBV DNA was measured by NucliSENS EasyQ® (BioMerieux). HDV RNA was detected using PCR. HBV genotype was determined by phylogenetic analysis of preS1.

Results: CHN and ARAFAT Center: Mean age :36.4±13.6 years (14-85). HBsAg was positive(+) in 174 (18.3%). Male (M) /female (F) ratio was 2.43/1.HBV-DNA was detected in 81/167 (48.5%) HBsAg + subjects. Mean viral load was 1.9±1.5 log IU/mL. HBV genotypes were: HBV/E =48.1%, D=40.7%, A =11.2%. 30/158 HBsAg + samples (19%) were anti-HDV Ab + (mean age: 41.5±14 years vs 35.2±12.2 in anti-HDV Ab negative subjects)($p < 0,05$). 21(70%) had detectable HDV RNA.

Pregnant women: mean age: 26.52 ± 6.3 years. HBsAg was + in 109/1020 (10.6%). HBV DNA was detected in 22/105 (21%) (mean viral load: 1.4 ± 0.5 log IU/ml). Anti HDV Ab were found + in 16/ 107 (14.9%). Of these, 11(68.7%) had detectable HDV RNA. HBV genotypes were: HBV/E = 35.7%, D= 42.8%, A =21.4%).

In the two populations, the presence of HBsAg did not differ significantly by age whereas HDVAb + patients were older. In the first population 19.7% subjects had a viral load >3log IU/mL but only 4.7% in pregnant women.

Conclusion: We confirmed a high prevalence of HBV and HDV in Mauritania. Epidemiology and molecular analysis of HDV isolates are in process in our Lab.

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IMPACT OF HEPATITIS B AND DELTA VIRUSES COINFECTION ON LIVER DISEASE IN MAURITANIA

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Background: Impact of hepatitis Delta virus (HDV) on the natural history of hepatitis B is poorly known in Africa.

Patients and methods: A transversal study including 300 consecutive HBsAg positive patients was performed at Hepato-Gastroenterology Department of the Nouakchott National Hospital, Mauritania. We compared the severity of B versus B-Delta hepatitis using non-invasive tests - FibroMeter (FM) and InflaMeter (IM) (www.biols.fr) - for the evaluation of liver fibrosis and activity. Total anti HDV antibodies were detected (Diasorin®). HBV DNA was measured by NucliSENS EasyQ®-BioMerieux. The natural history of hepatitis was evaluated using the non-linear regression of Lowess for liver lesions as a function of age. The relations among demographic and virological variables were analysed by univariate and multivariate analysis.

Results: The population characteristics were: mean age 36±12 years, 184 men/116 women (61.3%-28.7%), fibrosis stages FM Metavir: F0/1: 25.5%, F1: 16.2%, F1/2: 23.1%, F2/3: 14.8%, F3/4: 11.4%, F4: 9.0%; activity grades IM Metavir A0/1: 26.4%, A1/2: 62.0%, A2/3: 11.5%; anti HDV Ab: 33.2%. The population anti-HDV Ab negative vs. anti-HDV Ab positive characteristics were: mean age 33±11 vs. 41±12 years ($p< 10-3$), FM score F: 0.40±0.25 vs. 0.70±0.28 ($p< 10-3$), IM score: 0.38±0.18 vs. 0.57±0.22 ($p< 10-3$), severe fibrosis: 6.8% vs. 47.4% ($p< 10-3$), cirrhosis: 4.2% vs. 18.6% ($p< 10-3$). The activity and fibrosis were significantly more elevated among patients with delta Ab ($p< 10-3$) independently of age. We found that the activity increases with age only in patients co-infected B-Delta. It was independently associated with HDV positive, AST, male sex and HBV viral load. Fibrosis increased with age, and it was associated with: HDV positive, male sex, age, ALT levels and HBV viral load.

Conclusion: Hepatitis D represents a major health problem in Mauritania. It occurs in older patients, and leads to more severe liver disease than HBV monoinfection.

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HIGH PREVALENCE OF INFECTION BY THE HEPATITIS B (HBV) AND HEPATITIS DELTA (HDV) VIRUSES AMONG PREGNANT WOMEN IN CAMEROON

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Background: Since 2009, the district of Tokombéré, located in north of Cameron, far from reference laboratories, has established a program to prevent vertical transmission of HBV. HBsAg screening is performed in all pregnant women and, if positive, vaccination of the newborn is realized. The program is funded by the GEMHEP (Groupe d´étude moléculaire des hépatites).

Aim: Conduct a prevalence study of HBV infection in a cohort of pregnant women and evaluate our vaccination program for children born to positive HBsAg mothers. In a second step, assess the prevalence of HDV virus.

Patients and methods: 982 sera of pregnant women were collected in the maternal and Child Tokombéré center in 2009. HBsAg was sought by a rapid detection test (Vikia HBsAg, Biomerieux). Samples were sent to the University Hospital of Angers for confirmation and completion of further tests. Total anti-HDV antibodies (Ab) (ETI-ABDELTAK-2® Diasorin) were performed in HBsAg positive patients´ sera. IgM anti delta Ab (ETI-DELTA-IGMK-2® Diasorin) were searched in anti-HDV Ab positive sera.

Results: HBsAg were found in 191 patients (19.4%). Total anti-HDV Ab were found in 15 patients with a prevalence of 7.9%. IgM anti-HDV Ab were present in 10 of them (67%). Among the HBsAg positive mothers, the proportion of vaccinated infants with a first injection of Engerix B 10µg was 97%. Some vaccination delay was noted in rare cases, related to temporal disruption of supply of vaccine. Children should then receive three doses of vaccine.

Conclusions: Prevalence of HBsAg (19.4%) is high in the pregnant women population in Cameroon. Prevalence of HDV co-infection is also important (7.9%) with IgM in 67% of them indicating active infection. Further analysis (detection of HDV RNA, HBV and HDV genotyping, assessment of severity of liver disease by non invasive tests) are underway.

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CLONING EXPRESSION AND PURIFICATION OF RECOMBINANT ANTIGEN FOR PRODUCTION OF DELTA DIAGNOSTICS SUPPLIES

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Background and aims: The hepatitis delta virus (HDV) is a small virus, defective that requires HBV for its expression. It consists of a wrap-HBsAg, an inner portion of RNA and a protein called delta. HDV infection can be simultaneous with HBV infection, characterizing the co-infection, or may be later, causing superinfection. Required for its association with hepatitis B, widespread in extensive regions of Brazil - particularly in the Amazon region - and the great potential of clinical severity, this new type of hepatitis is of great importance in health, national. This study aims to express the delta antigen using techniques of molecular biology for production of inputs diagnoses.

Material and methods: Initially primers were designed for amplification of PCR products based on sequences stored in GenBank representing HDAg-L. The RNA extracted from the patient sample was transcribed by reverse transcriptase reaction and cDNA was amplified using PCR. DNA was cloned into vector pTZ57R (Fermentas) and sub-cloned in expression vector PRSET-A (Invitrogen, USA). The protein containing the histidine tail was purified by the method of níquel-NTA resin (Invitrogen-USA). Immunoassays were performed to verify the reactivity of the antibodies of infected patients against the recombinant protein.

Results: Our preliminary results show the PCR amplification of a fragment of 515pb. The product of expression resulted in a major band of 27 kDa. In the analysis of sera from infected patients by Western blotting was detected by reactivity against recombinant protein demonstrating the specificity of the antibodies against HDAg patient.

Conclusion: Our preliminary results show the PCR amplification of a fragment of 515pb. The product of expression resulted in a major band of 27 kDa. In the analysis of sera from infected patients by Western blotting was detected by reactivity against recombinant protein demonstrating the specificity of the antibodies against HDAg patient.

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PREVALENCE AND CLINICAL COURSE OF CHRONIC HEPATITIS D (CHD) IN GREECE DURING THE LAST 3 DECADES

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Background: Prevalence of CHD has gradually decreased in Europe since early 1980's, but recent reports have indicated a rising trend mainly due to immigration. We report relevant information from Greece, a country with >1,500,000 immigrants.

Methods: We analyzed data on CHD from the HepNet.Greece Cohort Study including retrospective-prospective information on viral hepatitis from 20 Hepatology Centers throughout Greece.

Results: Of 4672 evaluable cases with chronic hepatitis B (CHB) recorded since 1984, 2234 had been tested for anti-HDV and 111 [males 65%, median age 39.3 years] were positive. Testing for anti-HDV decreased significantly in recent years (64.6% before 1990, 54.9% 1990-1999, 44.2% after 2000; P< 0.001). Prevalence of CHD decreased from 6.8% in 1990-1999 to 4.4% in 2000-2009 (P=0.030) and it was significantly lower among native Greeks (3.5%) compared to immigrants from Balkan countries (10.5%) or those from Eastern Europe, Central Asia or Africa (9.6%) (P< 0.001). Patients with CHD compared to CHB-monoinfection were more likely to have cirrhosis at presentation (26.1% vs. 13.0%, P=0.001) at younger age (46.6 vs. 56.3, P< 0.001). Treatment was given to 66 patients (59.5%), mostly interferon-based (81.8%), while 45 patients remained untreated. Excluding patients followed-up for less than 6 months after HDV diagnosis, one or more liver-related events (liver decompensation, hepatocellular carcinoma, liver transplantation, liver-related death) were observed in 15 (17.4%) CHD and in 203 (12.0%) CHB-monoinfected patients. Although the probability of a liver-related event was higher in CHD than in CHB (14.4% vs. 5.3% at 3 years and 18.5% vs. 9.7% at 5 years, respectively), the 10-year probability of event-free survival for mono- and co-infected patients was borderline (log-rank P=0.051).

Conclusions: HDV serology in HBsAg-positive patients is being underreported in Greece. Prevalence of CHD is low in native Greeks but high in immigrants. Our data confirm that CHD is a relatively rapidly progressive disease.

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RENAL FUNCTION DURING TREATMENT WITH ADEFOVIR PLUS PEGIFN ALFA-2A VS. EITHER DRUG ALONE IN HEPATITIS DELTA

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Introduction: Long-term safety of HBV polymerase inhibitors becomes a major interest, in particular when combination therapies are explored. Adefovir-dipivoxil(ADV) therapy has previously been associated with an impairment of renal function and unexpected cases of neuropathy were observed during combination therapy of PEG-interferon with telbivudine. No study had investigated yet in detail renal function during combination therapy of adefovir and PEG-interferon.

Methods: We performed a retrospective analysis of renal function data of patients treated in the HIDIT-1-trial, a European multicenter study to investigate the efficacy of PEG-IFNα-2a+Adefovir vs. either drug alone in patients with chronic hepatitis D. A total of 90 patients had been randomised to receive PEG-IFNα-2a(180µg,qw)+ADV(10mg,qd)(group-A), PEG-IFNα-2a(180µg,qw)+placebo(group-B) or ADV-monotherapy(10mg,qd)(group-C) for 48 weeks. Creatinine levels were determined at baseline,week2,4,8,12 and every 6 weeks thereafter. Glomerular filtration rates(GFR) were calculated using the MDRD-Study equation in all patients who completed 48 weeks of treatment (PEG-IFNα-2a+ADV(n=26);PEG-IFNα-2a+placebo(n=26);ADV-monotherapy(n=28)).

Results: Baseline GFR were 95, 94, and 99ml/min in groups A, B and C, respectively. None of the patients stopped treatment because of grade 3 or 4 renal toxicity. GFR values after 48 weeks remained unchanged in PEG-IFNα-2a+ADV combination therapy(96ml/min,p=0.782), increased during treatment with PEG-IFNα-2a+placebo(102ml/min,p=0.017), but declined with ADV-monotherapy(95ml/min,p=0.076). Overall, a decline of at least 25% in GFR levels was observed at any time during treatment in 10/54 patients exposed to ADV(19%;4/26 group A;6/28 group C) but in none of the 26 patients treated with PEG-IFNα-2a alone (0%,p=0.026). At week 48, a ≥10% GFR decline was observed in 28% of patients in groups A and C vs. 12% in group B.

Conclusion: ADV but not PEG-IFNα-2a treatment was associated with a significant decrease in GFR values in about one fifths of patients with hepatitis delta.

Combination treatment of PEG-IFNα-2a+ADV in chronic hepatitis D was safe and did not lead to any further impairment of kidney function.

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ANTI-HDV-IGM TESTING IN HEPATITIS DELTA: CORRELATIONS WITH DISEASE ACTIVITY AND RESPONSE TO PEGYLATED INTERFERON ALFA-2A TREATMENT

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Introduction: Delta hepatitis is the most severe form of chronic viral hepatitis. The diagnosis is usually based on anti-HDV-IgG and HDV-RNA testing. Anti-HDV-IgM testing correlated with disease activity and treatment outcome in studies performed in the 80s and 90s. We re-examined the role of anti-HDV-IgM testing in samples obtained from the HIDIT-1-study, an international randomised multicenter trial investigating pegylated-interferon-alfa2a±adefovir vs. adefovir-monotherapy for the treatment of delta hepatitis.

Methods: 111 serum samples from 33 patients were studied (baseline,week24,week48,follow-up week24). Anti-HDV-IgM was determined using the ETI-DELTA-IGMK-2 assay (DiaSorin,Italy). OD450/620 values were determined according to the manufacturer´s instructions and correlated with different clinical parameters. Grading and staging of liver biopsy samples were performed according to the Ishak-Score by one independent pathologist.

Results: Anti-HDV-IgM tested positive in 30 patients (91%) before treatment with mean OD values of 0.63+/-0.54. Anti-HDV-IgM values did not correlate with quantitative HDV-RNA levels (Spearman r=0.127;p=0.50). Histological inflammation correlated significantly with anti-HDV-IgM ODs (r=0.51;p< 0.01) and was also higher in the group of patients with OD>0.7(p< 0.05).

Patients who cleared HDV-RNA by PegIFN/ADV treatment (5/11patients) demonstrated a continuous decline of anti-HDV-IgM during therapy, which further declined during follow-up (baseline 1.26+/-0.95, W24 0.73+/-0.63, W48 0.35+/-0.28(p=0.10), FU24 0.28+/-0.18(p< 0.05)). Patients responding to PegIFN-monotherapy(5/11) also showed a continuous decline of anti-HDV-IgM ODs during treatment which was not sustained at follow-up 24 (Baseline 0.35+/-0.30,W24 0.19+/-0.14,W48 0.09+/-0.06(p=0.08),FU24 0.41+/-0.34). Of note, no significant change of anti-HDV-IgM levels was observed in patients not responding to PegIFN+/-ADV(n=12) or receiving ADV-monotherapy(n=11). All 3 patients with a baseline anti-HDV-IgM-OD

of >1.1 cleared HDV-RNA by PegIFN/ADV combination treatment and showed a sharp decrease of HBsAg of at least $1\log_{10}$IU/ml.

Conclusions: Anti-HDV-IgM levels correlate with disease activity and may indicate stronger immune responses against HDV. Anti-HDV-IgM ODs decline during successful PegIFN-based treatment and high baseline values may be predictive for treatment response.

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SEROPREVALENCE OF HDV IN THE POPULATION OF HBSAG POSITIVE BLOOD DONORS AND PATIENTS TESTED IN CROATIAN INSTITUTE OF TRANSFUSION MEDICINE 2002-2010

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Background: Hepatitis delta infection has been rarely seen in patients in Croatia. According to the University Hospital for Infectious Diseases in Zagreb (UHID), since 2002 they have been treated 2161 patients with viral hepatitis. Table 1. Hepatitis D have had only 4/256 (1,6%) patients with chronic HBV infection. Among HDV tested HBsAg positive patients from 2002-2009 we find only 2/383(0,5%) positive. Prevalence in areas of high HDV/HBV rate as Balkan and Mediterranean countries showed decreasing trend in HDV infections. This might be a consequence of decreasing HBV infection but also as result of prevention directed to HDV specific transmission routes.

Viral hepatitis cured in UHID	N	%
Acute A	262	12,12
Acute B	259	11,99
Other Viral acute hepatitis	117	5,41
Chronic B	254	11,75
Chronic B+D	4	0,19
Chronic C	1254	58,03
Unspecified chr. Viral hepatitis	11	0,51
Total	2161	100

[Table 1]

Aim: To evaluate the HDV prevalence in the group of HBsAg positive blood donors and patients as a set point for future epidemiological studies.

Material and methods: 248 archived samples of HBsAg positive blood donors and 44 HBsAg positive random patients from 1th April-1th June 2010 were tested for HD-Ag and anti HD-IgG using Elisa test DiaSorin, Italy. All positives were tested for IgM anti HD.

Results: 4/248 (1,6%) HBsAg positive donors and 1/44 (2,2%) of HBsAg positive patients were find anti HD-IgG positive/IgM negative. HD-Ag test was negative in all tested samples.

Conclusion: In given HBsAg positive population's seroprevalence of HD was low 1,6%-2,2% compared to the surrounding countries.

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CORRELATIONS BETWEEN HBV AND HDV VIRAL LOAD, ALT AND FIBROSIS IN DELTA COINFECTED PATIENTS

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Introduction: Delta hepatitis is associated with an increase risk of severe liver disease. Monitoring the progression of the disease, the response to treatment is a challenge.

Aim: The aim of this work is to analyze if HBV and HDV viral load and transaminases (ALT) are correlated with the severity of the diseases.

Method: A retrospective study on 26 AgHBs positive, Ab anti HDV positive adult patients (pts).

We determined: HBV viral load (Unit/ml), HDV viral load (copies/ml), considering low viral load < 2000 U/ml (10000copies/ml) for both viruses, ALT and the severity of the disease (Fibrosis).

Results: There were 16 women and 10 men: 4 pts had mild Fibrosis (F0-F1), 5 had significant Fibrosis (F2), 9 had severe Fibrosis (F3), 8 had Cirrhosis (F4), and 1 has liver carcinoma. Of 3 AgHBe positive pts, all with high HBV viremia, 1 has also high HDV viremia. Severe disease (F3 and F4) was associated with older age (15/26 pts over 40 years), high ALT (5 cases slightly elevated, 11 cases with ALT more than 2 times upper limit of normal). From 8 pts with F3, only 1 pt has HDV high viremia, 1 pt has HBV high viremia; from pts with F4, 2 pts had HDV high viremia. 8 untreated pts had low viremia for both viruses (except 1 case with HDV high viremia), slightly elevated ALT and severe fibrosis (F3-4) in 4 cases.

Conclusions: Despite low viremias for both viruses, the majority of pts with co-infection delta has severe liver disease, generally with abnormal ALT. Treatment was ineffective. We cannot appreciate the risk for disease progression of co-infected pts, neither with HBV/HVD viremia, nor with ALT. Additional tests, as FibroTest/ActiTest (performed in progression), correlated with both viremias (HBV and HDV) may be useful in the future for monitoring the disease.

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VIROLOGICAL AND CLINICAL CHARACTERISTICS OF HEPATITIS DELTA VIRUS IN SOUTH EAST ASIA

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Background and aims: There is a paucity of data on impact of hepatitis D virus (HDV) in patients with hepatitis B virus (HBV) infection from South East Asia. We studied the impact of HDV co-infection on virological and clinical characteristics.

Methods: We collected data of 480 patients with HBsAg positive and HBV DNA PCR detectable who presented to ISRA University, Hyderabad and Aga Khan University, Karachi, Pakistan in last 5 years. Levels of ALT, HDV antibody, HBeAg, and HBV DNA PCR quantitative levels were checked in all patients. Patients were categorized into Asymptomatic carrier(AC), chronic active hepatitis(CAH), immuno-tolerant phase(IP), and compensated cirrhosis(CC). We divided the patients into two groups—based on HDV antibody status and compared with biochemical labs, HBeAg status, HBV DNA PCR levels, and clinical stages of hepatitis B.

Results: Anti-HDV was checked in all 480 patients and HDV co-infection was found in 169 (35.2%)s. There were 164 (34.6%) HBeAg positive and 316 (65.4%) HBeAg negative patients. Mean ALT level was 66 ±73 IU; 233(48.5%) have raised ALT. HBV DNA level was ≥10e5 in 103(21.5%) patients. Among HBeAg negative patients 71/128(55.5%) has raised ALT levels among HDV co-infection as compared to 71/188 (37.8) without HDV infection(p-value=0.002); levels of HBV DNA were equal in two groups; there were 27/128 (21%) patients with CC among HDV co-infection as compared to 23 (12%) non-HDV (p-value=0.03); there were less AC (p-value=0.009) and more CAH (p-value=0.009) in HDV co-infection patients. Among HBeAg positive the ALT, HBV DNA levels and the spectrum of HBV was similar in the two groups.

Conclusions: The levels of HBV DNA are not affected in our patients with HDV co-infection as reported in European studies. A fair proportion of HDV co-infected patients with HBeAg negative have active hepatitis B infection and even cirrhosis as compared to HBeAg positive patients.

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CLINICAL PECULIARITIES OF HDV-INFECTION IN KAZAKHSTAN

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Background and aims: HDV-infection is an important factor of liver diseases in Kazakhstan. This study was aimed to reveal the features of chronic HDV-infection in comparison with HBV-monoinfection.

Methods: 104 patients were armed into 4 groups: chronic hepatitis D (CHD, n=17), chronic hepatitis B (CHB, n=20), liver cirrhosis D (LCD, n=35), liver cirrhosis B (LCB, n=32). 8 CHD patients were given Peg-Interferon-alfa 2a, 180 mcg/week for 48 weeks. Physical examination, IFA, PCR, gemogram, coagulogram, liver function tests (LFT), AST/ALT ratio, APRI index were performed.

Results: CHD patients were 10.50 years younger (36.45±5.28) than CHÂ ones (46.9±2.81, ð=0,045). This difference was also noticed between LCD and LCB (40.68±2.33 and 49,34±2.07 respectively, ð=0,005). Amongst clinical presentations, the differences were revealed in predominance of cholestatic syndrome in LCB (OR 5.25, CI 1.01; 27.03) and high frequency of portal hypertension and hepatic encephalopathy in LCD in comparison with LCB (OR 0.21, CI 0.05; 0.85 and OR 0.27, CI 0.09; 0.87, respectively). Platelet count was low (ð=0.003) in CHD (152.4±9.1õ109/l) and LCD (114.8±10.5õ109/l) in comparison with ÑHÂ (210.6±17.6õ109/l) and LCB (169.9±11.6õ109/l) respectively. Prothrombine index was reduced (ð=0.003) in LCD (62.6±1.3%) in comparison with LCB (69.2±1.7%). LFT and AST/ALT ratio had no difference, APRI index tended to be higher in CHD and was raised (ð=0,001) in LCD (1.35±0.37) in comparison with LCB (0.40±0.10). End-of-treatment response (ETR, anti-HDV IgM and HDV-RNA negativity) was noticed in 3 of 8 patients (37.5%) and maintained in 2 patients (25.0%) 6 months after therapy.

Conclusions: HDV-superinfection causes liver disease progression in younger age; LCD is characterized by more frequent portal hypertension and hepatic encephalopathy in comparison with LCB; CHD and LCD are associated with thrombocytopenia and reduced prothrombine index; LCD is characterized by high APRI index; ETR was noticed in 37.5% and maintained in 25.0% of patients 6 months after therapy.

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QUANTITATIVE ANALYSIS OF HDV-RNA AND HBV-DNA VIRAL LOAD DURING CHRONIC DELTA HEPATITIS TREATMENT

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Aims of study: To develop a quantitative real-time PCR assay for HDV-RNA and to monitor HDV and HBV viremia fluctuations during chronic hepatitis delta therapy.

Methods: HDV-RNA, HBV-DNA and HBsAg were retrospectively quantified in serum samples of 23 chronic hepatitis delta patients, 11 treated with pegylated interferon (PEG-IFN) alpha-2b as monotherapy and 12 in combination with ribavirin (RBV) for 72 weeks.

Results: HDV-RNA real-time PCR assay showed a linearity of quantification ranging from 10^3 to 10^9 copies/ml and a sensitivity of $5x10^2$ copies/ml. At the end of therapy 7 patients were HDV-RNA negative: 4 patients treated with PEG-IFN alone and 3 with combination therapy. At baseline responder patients showed a median HDV-RNA level of $2,4x10^6$ copies/ml ($2,12x10^4$ - $1,05x10^7$ copies/ml) and HBV-DNA was < 34 IU/ml. At baseline in not responder (NR) patients median HDV-RNA level was $1,7x10^7$ copies/ml ($9,59x10^2$ - $8,13x10^7$ copies/ml) and HBV-DNA was < 34 IU/ml in 11 patients; 5 patients had higher levels of HBV viremia (70 - 27.702 IU/ml). At the end of treatment in 13/16 NR patients was observed a decrease of HDV viremia with a reduction of 5 $\log_{10}$ (1 pts), 3 $\log_{10}$ (3 pts), 2 $\log_{10}$ (4 pts) and 1 $\log_{10}$ (5pts); a reduction of HBV-DNA values was also detected. HBsAg levels at the end of treatment were always > 250 IU/ml.

Conclusions: A favourable end of treatment outcome seems to be related to lower values of HDV and HBV viremia at baseline, furthermore significant HDV-RNA decrease was also observed in the majority of NR patients. Quantitative analysis of HDV-RNA is a useful tool in the management of chronic delta hepatitis and to monitor HDV-RNA kinetics during therapy.

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AN AGGREGATED ANALYSIS OF DELTA HEPATITIS IN TURKEY AND THE QUANTIFICATION OF BURDEN OF DISEASE

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Background and aims: Chronic delta hepatitis is one of the most important health issues in Turkey. In this study we aimed to estimate age specific and region specific prevalence of anti-delta positivity referring to various literatures. Secondary aim was to estimate the burden of disease through natural history within a 20 year period using a mathematical model.

Methods: Prevalence estimates of anti-delta positivity was based on the previously published age specific HBsAg prevalence data (Toy; UHK2009-109 literature). Additional 30 studies with original data related to anti-delta positivity in HBsAg positive patients in Turkey published between 1992 - 2009 were used in order to estimate age specific, region specific and disease status specific prevalence data. A mathematical model was constructed to simulate the cohort through a finite series of health states to quantify the mortality and morbidity.

Results: According to literature anti-delta positivity in CHB patients ranges from %12 to %46 (mean %15). Age specific prevalence for age groups 0-14, 15-24, 25-34, 35-44, 45-54, 55-64 and 65+ patients are %0.61, %1.16, %1.23, %1.17, %1.01, %0.74, %0.75 respectively. Lowest prevalence rate calculated was %0.42 for western regions of the country, whereas highest prevalence (%2.53) was found to be in eastern regions. From these active disease patients, 15%(113,347) have co-infection with the delta virus, of which 36% are cirrhotic at baseline. Within a 20 year period, 66% (74,808/113,347) of the superinfection cohort will die due to liver related causes, if untreated. About 76% (55,203/72,636) will develop cirrhosis in the non-cirrhotic cohort.

Conclusions: Considering the limited data published in national and international literature delta hepatitis is an important public health problem in Turkey. Our study designates that current patients will cause a great deal of health burden in the country.

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HEPATITIS D INFECTION IN NIGERIA; IS THERE A COME BACK? (PRELIMINARY REPORT)

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Background: Hepatitis D infection is said to be on the decline due to better control measures for hepatitis B infection .However recent reports have tended to indicate otherwise. Earlier report in our locality had shown prevalence of 6.5% of antibody to hepatitis D in chronic hepatitis B liver disease in 1998 while a later study (2006) revealed an overall prevalence of 12.5% . We set out to investigate the current status of hepatitis D infection.

Aim: To determine antibody to hepatitis D prevalence in a populations of patients with asymptomatic as well as symptomatic HBsAg carriage.

Methodology: After ethical approval all consenting patients referred to the Gastroenterology/Liver unit of the Lagos state university hospital from September 2009 (still ongoing) and who met the study inclusion criteria of HBsAg carriage for more than six months were recruited. A questionnaire was used to extract basic demographics, clinical features as well as liver biochemistry and imaging findings. Ten milliliters of blood were collected from each in KEDTA bottle and plasma separated and stored at -20 c until ready for assay for hepatitis D.

Assay was by an ELISA method using HDV Ab kit from DIA.PRO Diagnostic Bioprobes srL.

Results: 150 patients who met the study criteria were recruited (M: F=123:27) within the age range of 14-70 years with a mean of 35.1. 115 were asymptomatic carriers while 35 had features of chronic liver disease (chronic hepatitis- 9, cirrhosis- 21 & PLCC- 5).Only 4 (2.7%) of the patients tested positive to anti D.

Conclusion: The prevalence rates seen in this study is lower than the 2 previous studies from our locality. This is in keeping with declining incidence as reported in other geographic areas. The higher rate noted in the second study may relate to the assay method.

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PROFILE OF HBV-INFECTION WITH DELTA HEPATITIS AMONG THE PATIENTS IN KAZAKHSTAN. "VEK CLINICS" MEDICAL CENTER, OBSTETRICS CENTER OF THE MH OF KAZAKHSTAN

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Aim: To identify specifics of chronic B hepatitis course with delta agent (HG B+D) among controlled patients from different regions of Kazakhstan.

Methods: 19 patients with HBV- infection with delta - hepatitis (m/f - 5/14, age 19-73) . Diagnosis has been determined on the basis of the clinic laboratory (BAC, EIA PCR) and instrumental (USG, CT, FGDS) test methods.

Results: HBeAg negative variant HG B has been diagnosed among all patients, among them 6 had a stage of active HBsAg positive hepatitis with delta agent, 13 with the result lither cirrhosis (LC), 3 had LC complicated with hepato- cellular carcinoma (HCC). In the case of evaluation of liver cellular deficiency under Child- Pew: class A has been determined among 2 patients, B- among 8, C - among - 4. For the first time LC has been observed among 4 pregnant women, thus 2 of the them at the age of 19 and 22 have been probably infected by hepatitis virus in perinatal period, and many parous 45 year old woman with LC had a varical bleeding from alimentary canal which brought to death. The 53 year old patient with HCC had orthotopic transplantation of the liver in Shanghai city (China). 4 patients with HG B+D completed antiviral therapy (AVT) - standard IFN - alfa2, Peg-IFN-alfa2a, Peg-IFN-alfa2b, renaissance), the rest - hepatoprotectors (essentiale, UDCA) due to absence of finance among the patients.

Conclusion: Females more often observe HG B+D (14/5), Kazakhs prevail (18/1), disease course - progressing . Late consulting and LC determination at the stage of sub and decompensation with complications indicates a necessity of early diagnostics and up-to-date antiviral treatment.

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TREATMENT OF DELTA HEPATITIS IN NON-CLINICAL TRIAL PATIENTS

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Chronic hepatitis D (CHD) is the most serious form of viral hepatitis which has no satisfactory treatment. Interferons may provide a response in almost one fifth of the patients in clinical trials.

Aim: Evaluation of the different therapeutic options in non-clinical trial patients.

The patients with CHD who were followed up for more than 6 months were retrospectively evaluated. The patients who were HDV RNA negative at baseline, and those with missed data for evaluation were excluded. Sustained response was defined as HDV RNA negativity 1 year after the completion of the treatments. At the final evaluation, 18 patients received regular interferons (IFN), 26 were treated with regular interferons+nucleos(t)ide analogs (NA), 22 with peginterferons (pegIFN), 7 with PegIFN+NA, 69 with NA, and 22 patients did not receive any treatment. Sixty-two percent were cirrhotics whose 45% had decompensated cirrhosis. Among the baseline characteristics, the rate of decompensation and HBV DNA levels were higher in NA-treated patients. The duration of the treatments, end of treatment response (ETR) and sustained response (SR) rates were shown on the table.

	n	Median duration of treatment (month)	ETR	STR
No treatment	22	13		2 (9%)
IFN	18	12	2 (11%)	2 (11%)
IFN+NA	26	12.5	6 (23%)	3 (11.5)
PegIFN	22	9.5	6 (27%)	3 (13.6%)
PegIFN+NA	7	9.5	1 (14%)	0
NA	69	14	4 (5.8%)	4 (5.8%)

[Results of the treatments]

Only regular interferons provided a decline in ALT levels (from 72 IU/L to 49 IU/L). The other treatment options did not achieve a reduction in transaminases.

Conclusions: It seems that there is not a succesful treatment of CHD. The poor response in our patients may be related to the high rate of cirrhosis.

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HBV AND HDV GENOTYPES IN HBV/HDV COINFECTIONS IN THE STATE OF ACRE (WESTERN BRAZILIAN AMAZONIA)

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Although considered a vanishing disease in Europe and US, HDV still remains a serious public health problem in Amazonia. We analyzed 101 HBsAg+/anti HDV IgG + patients, 68 males and 33 females, from Western Brasilian Amazonia Referral Centers .Patients had mean age 32,61 (+/- 12,51), median 29 yo and 34/101 (37%) were under 25 yo. 20/101 (20%) were HBeAg positive, and 36/101 (36%) had cirrhosis. No one were intravenous drug user.The mean age of HBeAg patients was 23.5 (+/-12.1) x 33.2 (+/-12.5) in HBeAg negative ones. (P=0.01).

Only 3/36 (8.1) cirhhotic patient were HBeAg positive, contrasting with non-cirrhotic cases 14/65 (21.5%) (P=0.02). Most HBeAg + cases came from Acre state.

Sera samples were tested for the HBV genotypes by partial amplification and sequencing of the PreC/C and/or the S genes. For HDV by partial amplification of the HDV genome and hybridization with HDV genotype-specific probes. 69 samples could be genotyped for the HBV and 85 for HDV. All HDV samples were genotype III. Regarding HBV; 37 (53,6%) were F (most F2); 20 (23,9%) A (13 A1 and 7 A2) ; 7(17,1%) genotype D (4 D3). In 04 (5,7%) patients we had discordance depending on Pre S or Pre C sequencing, (02 were D/F; 1 A/C; 1 C/F) and only 01 patient were genotype C. Mean age of HBV F carriers was 31.9(+/-12.6) x 33.2 (+/-13.8) among non F . (P=0.74).

Concerning HDV, in 17/85 (20%) we observed a rare mutation at the end of the small DAg gene, changing the second from last amino acid phenylalanine to tyrosine. Mean age of Mutant and non-Mutant Gen III carriers was 31.3 (+/- 12.6) and 31.7 (+/- 10.2). In 14 HDV mutants who HBV genotype could be performed, 09 were HBV non-F genotype and 05 HBV F (P=0.84). Among 17 patients with mutant HDV, 5/25 (29.9%) had cirrhosis compared to 12/57 non-cirrhotic patients (P=0.91). HBV F genotype was present in 14/37(37.8%) of cirrhotic patients x 23/50 (71.6%) non-Cirrhotic ones (P=0.06).

In conclusion:

1. We described a HDV gen III mutant in Amazonia, probably more likely to be associated with non-F HBV genotypes.

2. High frequence of HBeAg + status of the Acre patients is probably related to patient ´s age.

3. Non F HBV Genotypes, mainly Gen A is also prevalent in this population.

4. A larger clinic/molecular epidemiological study will be necessary to define the role of HBV F genotypes and HDV mutant Genotype III in the pathogenicity of liver disease.

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TRENDS IN EPIDEMIOLOGY OF HEPATITIS D VIRUS INFECTION AMONG INSTITUTIONALIZED CHILDREN IN SOUTHEAST ROMANIA

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Background: Up to 5% of the world´s population is known to be infected with HBV and at least 5% of all hepatitis B carriers are infected with HDV. Due to the better control of HBV infection achieved by HBV vaccination programs during the last 10 years, use of disposable needles, screening blood donors for HBsAg and socioeconomic improvements, HDV infection has declined significantly in many endemic areas like some parts of Southern Europe and Southeast Asia.

Aim: Our study compares the frequency of Delta hepatitis infection between two groups of patients: one group of 75 children (orphans or mentally retarded) institutionalized between 1990 and 2000, and another group of 86 children (same condition) institutionalised between 2000 and 2009.

Material and methods: We retrospectively tested sera collected from all 166 patients regarding HBV and HVD infections, using ELISA tests for HBsAg and anti-VHD. Serum HBV- DNA and HDV-RNA were determined by polymerase chain reaction (PCR) method. Results obtained in the two groups of analyzed patients were compared.

Results: HBsAg was found in 38 pts (50%) from the first group and in 31 pts (36%) from the second group (p=0.0324, 95% CI 1.674-12.772). The anti-HDV positivity was found in 13 pts (33%) among first group's chronic hepatitis B cases and in 6 pts (21%) among the second (p=0.0411, 95% CI 23.334-89.334).

Conclusions: The results of our study shows a descendant trend of HBV and HDV infection in the past ten years, pointing a decrease in the frequency of both viral infections among one of the most exposed category of people, institutionalized children.

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IS HEPATITIS B VIRUS SURFACE ANTIGEN TITER CORRELATED WITH HEPATITIS DELTA VIRUS REPLICATION LEVEL AND HISTOLOGICAL ACTIVITY IN CHRONIC HEPATITIS D?

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Background and aims: To determine the relationship of quantitative HDV RNA, HBsAg and HBV DNA levels with biochemical activity, histological activity index and fibrosis stage in chronic hepatitis D (CHD).

Methods: Of the 133 patients enrolled in this study, 46 were naive CHD and 87 naive chronic hepatitis B (33 HBeAg-positive CHB). HBsAg levels were tested by Abbott Architect kit, and HDV RNA by real time PCR.

Results: A positive correlation was detected between HBsAg and HDVRNA levels($p=0.043$). The viremia of HDV showed great variability. HDVRNA titer was not correlated with biochemical or histological activity and fibrosis stage. Comparison of viremia of HDV infection and HBsAg levels in the pre-cirrhotic and cirrhotic stages showed no difference ($p>0.05$). Our findings showed that HBV DNA positivity did not bring about any negative effects on biochemical and histological activity in patients with CHD. In CHD, serum transaminase levels and histological findings were not different between HBVDNA-negative and positive patients ($p>0.05$). Similarly, HBsAg levels showed no significant difference between HBVDNA-positive and negative groups (4.75 ± 0.2vs.4.63 ± 0.6). HBsAg levels were found to be significantly higher in HBeAg-positive patients according to the patients with CHD and HBeAg-negative CHB but it was similar between patients with CHD and HBeAg-negativity (4.89 log vs. 4.71 log and 4.50 log). In CHB patients, there was a positive correlation between serum HBVDNA and HBsAg levels ($p=0.002$). Histological activity and fibrosis stage were significantly increased in CHD than CHB patients.

Conclusions: Histological activity and fibrosis stage are not influenced by the level of HDV or HBV viremia in chronic delta hepatitis. HBsAg titers were highest in HBeAg-positive CHB followed by CHD and lowest in HBeAg-negative CHB patients. CHD is a more serious disease than CHB.

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HEPATITIS DELTA INFECTION: A RISK FACTOR FOR CIRRHOSIS AND HEPATOCELLULAR CARCINOMA

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Introduction: Romania is one of the European Countries with a high prevalence of hepatitis D virus infection (HDV). Recent studies have shown a 20% HDV positive antibody in the population with HBV infection. Chronic infection with HDV is a risk factor for cirrhosis and hepatocellular carcinoma(HCC).

Objective: To evaluate the impact of HDV infection on the occurrence of cirrhosis and hepatocellular carcinoma.

Methods: We performed a retrospective cohort study of HDV infected patients who had been monitored for at least one year in the Third Department of the „Matei Bals" Infectious Diseases National Institute. HDV infection was defined by the presence of anti-HDV antibody in hepatitis B surface antigen seropositive patients.

Results: from 2000 until now we have monitorized 72 patients with: mean age of 44 years, sex ratio M: F-1.88. The mean period of evaluation was 3.96 years (1-10 years), 37.5% being evaluated more than 5 years. All patients had the HBe antigen negative. 77.27% of patients had HDV replicative dominance. 2 patients (2.7%) developed anti HBs antibodies. 36.11%of patients developed cirrhosis, 4.16% HCC and 5.5% had liver dysplastic nodules on MRI investigation. 65.2% of patients had thrombocytopenia at the last evaluation and for 68.05% of them the platelet number had decreased compared to baseline measures. 44.4% of patients had a low level of prothrombin and for 56.25% of them the level had decreased compared to baseline. The high levels of alpha fetoprotein correlated with the development of liver dysplastic nodules and HCC ($p< 0,001$). 61.53% of patients with cirrhosis had a normal level of alphafetoprotein. The occurrence of HCC and dysplastic nodules was correlated with duration of monitoring (6.71 years vs. 3.53 years, $p< 0.01$)

Conclusions: HDV infection increases the risk for cirrhosis in HBV infected patients. The risk of HCC rises with the duration of monitoring.

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PREVALENCE OF HEPATITIS D VIRUS ANTIBODIES AMONG HEPATITIS B SURFACE ANTIGEN CARRIERS OF GENERAL AND HIGH-RISK POPULATIONS IN NORTHERN INDIA

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Background and aims: The prevalence of hepatitis delta virus (HDV) infection has been estimated as being approximately 5% among global HBsAg carriers. Hepatitis D virus (HDV) infection is present worldwide and affects all age groups. However, it does not have uniform distribution and its general pattern is parallel to that of hepatitis B virus (HBV).

Methods: A total of 521 voluntary blood donors, 76 thalassemics, 150 healthy health care workers (HCWs) and 42 drug abusers were studied to assess the current seroepidemiology of hepatitis D virus (HDV) infection in northern India. Enzyme Immuno Assay (EIA) was used for testing HBV infection markers. Radioimmunoassay was used to detect antibody against HDV (anti-HDV) among HBsAg carriers.

Results: The anti-HDV prevalence among HBsAg carriers was significantly higher in thalassemics (9.6%) and drug abusers (44.5%) than in blood donors from the general population (15.2%) and HCWs (20.7%). Males had a higher prevalence than females in blood donors, thalassemics, HCWs and drug abusers, but the difference was not statistically significant. There was no significant difference in exposure to other risk factors among these groups of patients. We found a significant relationship between the duration of HBsAg carrier status and anti-HDV positively, however, age, gender, and presence of HBeAg were not significantly associated with the development of anti-HDV positivity.

Conclusion: HDV infection remains limited to the high-risk groups and spread mainly by blood transfusion and needle sharing in India. Further, screening of delta markers in addition to hepatitis B viral markers could improve the understanding of a number of obscure cases of chronic hepatic illnesses and would help in the control of HBV and consequently HDV infection in the general population.

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LOW LEVELS OF HDV RNA REPLICATION AND HIGH LEVELS OF HBSAG EXPRESSION ARE ASSOCIATED TO LIVER DECOMPENSATION IN CHRONIC HEPATITIS D

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Background and aims: Hepatitis D is considered the most severe form of viral hepatitis in humans. Recent findings indicate that the progression of chronic hepatitis D can be related to hepatitis B virus (HBV) replication.. Aim of the study was to explore the possible associations of hepatitis B virus surface antigen (HBsAg) and hepatitis D virus RNA (HDV-RNA) levels with the outcome of chronically infected HDV patients.

Patients and methods: HDV-RNA and HBsAg were measured in base-line serum samples of 195 consecutive anti-HDV positive patients (149 males, mean age 54 yrs, 138 anti-HBe positive) followed for a mean of 256 months. HDV-RNA was quantified by quantitative real-time PCR (Roche Diagnostics), using a plasmid containing 596-bp fragment of the 5'UTR HDV-RNA as quantification standard. HBsAg was quantified by a commercially available chemoluminescent immuno assay (CMIA, Abbott Diagnostics).

Results: Liver cirrhosis was present in 122 patients (62%). The mean HDV-RNA and HBsAg levels in cirrhotic patients were $1.4x10^6$ cp/mL and 5736 IU/mL, respectively, as compared to $1.1x10^6$ cp/mL and 7502 IU/mL, respectively in non cirrhotics (p=ns). During follow-up, 58 cirrhotic patients (47%) experienced a liver related complication (29 HCC, 29 liver decompensation). The mean HDV RNA and HBsAg level in 64 cirrhotics without complication were 1.2 $x10^6$ cp/mL and 4525 IU/mL, respectively, as compared to cirrhotics who developed HCC 2.0 $x10^6$ cp/mL and 4937 IU/mL (p=ns), and cirrhotics who developed liver decompensation 6.2 $x10^5$ cp/mL and 8847 IU/mL, respectively ($p< 0.001$ for both comparisons). 28 (14%) patients died of liver related causes (14 HCC, 14 liver decompensation).

Conclusions: Low levels of HDV-RNA are associated to less progressive, event-free chronic liver disease. Liver decompensation is associated to significantly lower levels of HDV-RNA replication but significantly higher HBsAg expression.

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HEPATITIS DELTA VIRUS IN ALBANIA

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Background: HDV infection is a rare disease and always suspected in patients with chronical hepatitis B with low level of HBV DNA

The aim of the study: To appropriate the prevalence of HDV infection in patients with chronical hepatitis B in Albania (endemic country for HBV, anti HBe positive). We have evaluated the presence of HDV infection among patients with chronical HBV infection in the University Hospital Center "Mother Teresa" of Tirana.

Patients and methods: During a period of two years (September 2007 - September 2009), all patients with chronic hepatitis B (301 pts, from which 18 had compensated liver cirrhosis Child-Pugh A), admitted to the service of Hepatology and Gastroenterology and Internal Medicine have been tested for the presence of total anti- HDV (IgM+IgG). In 15 cases of them HDV RNA was performed.

Results: 31 pts were anti HDV positive (10.29%), 21 male (67,7%), 10 female (32,3%) with a mean age of 35 ± 14 years. In all these pts. anti HBe was positive and HBV DNA in very low levels or absent. The HDV RNA viral load was between 10^2 - 10^5 UI/ml (except a case with a very high level of HDV RNA of 10^7 UI/ml).

Conclusions: Albania represents a high prevalence of HDV (10,29%) among pts. with HBV infection. All cases with HDV infection were infected with mutant virus B (anti HBe positive) with a male predominance.

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SEROPOSITIVITY OF DELTA HEPATITIS IN CHRONIC HEPATITIS B PATIENTS

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Background and aims: Hepatitis B infection is a major cause of chronic liver disease in Turkey and infection with hepatitis D (HDV) increases morbidity and mortality. Although recent studies report a decline in HDV infection, the prevalence is still high in hepatitis B induced cirrhosis patients, varying from 20 % in the West of Turkey to 46% in Southeast Region.

This study was aimed to detect the seropositivity of HDV in our hepatitis B patients.

Methods: A total of 1025 patients followed for hepatitis B by our clinic for the last 10 years were evaluated retrospectively. 84 patients were excluded because of missing records; remaining 941 patients were assessed for demographic data, seropositivity for HDV and presence of cirrhosis.

Results: Among 941 patients, 857 (91%) had chronic hepatitis B and 84 (9%) were cirrhotic. There were 62% male, 38% female patients with mean age 42±13 years in the chronic hepatitis group and 77% male, 23% female with mean age 54±14 years in the cirrhotic group. HDV seropositivity was detected in 32 (3,4%) patients, but when analyzed in subgroups HDV seropositivity was found in 15 (1,8%) patients in chronic hepatitis B and in 17 (20%) in cirrhotic patients.

Conclusion: This study shows that 3,4% of our hepatitis B patients were seropositive for HDV and that seropositivity increases 11 folds in cirrhotic patients which indicate that HDV increases the severity of liver disease. We concluded that these results are similar to previous studies performed in our country and that HDV is endemic in Turkey.

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OUR CLINICAL EXPERIENCE IN PATIENTS WITH CHRONIC HEPATITIS D

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Background and aims: Treatment and follow-up of chronic hepatitis D is still controversial. Interferon (IFN) or pegylated interferon (PEG-IFN), after one to two years of administration, can lead to undetectable HDVRNA levels and normalization of ALT in approximately 20% of the patients. Although clinical data is not sufficient, it is stated that IFN/PEG-IFN treatment could impair patients with advanced fibrosis.

This study was aimed to present our clinical experience in treatment and follow-up of hepatitis D patients.

Methods: From 2001 to 2010, 20 patients followed with chronic hepatitis D were evaluated. Demographic data, liver biopsy, type and duration of treatment, response to treatment and side effects, rate of withdrawal due to side effects were investigated.

Results: In all of the 20 patients (13 male, 7 female with mean age 41,5±12,1) HDVRNA was positive and all had undergone liver biopsy, 12 of which were in a precirrhotic or cirrhotic stage. 19 patients received a therapy with mean duration of 22±10 months.

12 patients were treated with PEG-IFN; 2 patients continue treatment (9^{th} month of follow-up), in 4 patients response to therapy was achieved (undetectable HDVRNA and normalization of ALT levels), 3 patients were irresponsive and in 3 patients treatment was withdrawn due to side effects. 4 patients were given standard IFN, only one responded, the other 3 patients could not complete treatment due to side effects. 3 patients were started PEG-IFN after a standard IFN therapy, because of irresponsiveness in 1 patient and relapse in 2 patients, all three were responsive to PEG-IFN. None of the cirrhotic patients receiving treatment became decompensated.

Conclusions: Our clinical experience is in favor of administrating IFN to patients with delta hepatitis, in precirrhotic and cirrhotic phase. Continuation of treatment as long as possible with close monitoring could be an appropriate approach.

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HBSAG LOSS INCREASES WITHIN TIME AFTER SUSTAINED VIROLOGICAL RESPONSE IN CHRONIC HEPATITIS DELTA PATIENTS TREATED WITH PEGYLATED INTERFERON

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Background and aims: Conventional or pegylated interferon (PEG-IFN) is reported to be the only effective treatment of chronic hepatitis delta (CHD). We evaluated the efficacy and the long-term outcome of patients with CHD treated with PEG-IFN.

Methods: Thirty patients with CHD treated with PEG-IFN-α2a or -α2b were included. Duration of therapy was 48 weeks (20-88). Clinical, biological, histological and virological data were analyzed before, during and after the course of therapy. Early virological response (EVR) was defined as at least 2 log reduction of HDV viral load at week 12 of therapy compared with the baseline level. Sustained virological response (SVR) was defined as undetectable HDV RNA 24 weeks after the end of therapy. The median follow-up was 25 months (12-100).

Results: Baseline characteristics of the 30 patients were: 22 males, mean age 36±10 years, HBeAg negative 93%, anti-HDV IgM positive 89%, cirrhosis 27%. EVR was observed in 68% of patients. End of therapy response (EOTR) was achieved in 57%. EVR had a positive predictive value (PPV) and negative predictive value (NPV) for EOTR of 82% and 88% (p=0.002). SVR and relapse were observed in 13 (43%) and 4 (13%) patients. One patient relapsed at 48 weeks after therapy. All SVR patients achieved EVR. None of the patients without EVR attained a SVR (NPV=100%, p=0.003). At the end of follow-up period, 9 patients had undetectable HBV DNA and HDV RNA: 5 patients lost HBsAg within 0 to 80 months after the end of therapy, with HBsAg seroconversion in 3 of them. Moreover, all patients with HBsAg clearance had EVR.

Conclusion: In CHD patients treated with PEG-IFN, SVR was achieved in 43% of patients and HBsAg clearance in 38% of them. EVR is predictive of EOTR and SVR. Patients with SVR have a high probability of HBsAg loss that increases within time.

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EARLY VIROLOGICAL REPONSE IS PREDICTIVE OF SUSTAINED VIROLOGICAL RESPONSE IN CHRONIC HEPATITIS DELTA PATIENTS TREATED WITH PEGYLATED INTERFERON

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Background and aims: Pegylated interferon (PEG-IFN) is described as an efficient treatment for chronic hepatitis delta (CHD). The aims of this study were to evaluate predictive factors of response and to analyze HDV viral kinetics in patients with CHD treated with PEG-IFN.

Methods: Thirty patients with CHD were treated with PEG-IFN-α2a or -α2b for a median of 48 weeks (20-88 weeks). Clinical, biological, histological and virological data were analyzed before, during and after the course of therapy. Sustained virological response (SVR) was defined as undetectable HDV RNA 24 weeks after the end of therapy. Predictive factors were analyzed. HDV viral load kinetics was analyzed at week 12 and week 24 of treatment according to response.

Results: The 30 patients presented the following characteristics: 22 males, mean age 36±10 years, HBeAg negative 93%, anti-HDV IgM positive 89%, HDV genotype 1 87%, cirrhosis 27%. SVR was achieved in 13 (43%) patients. The factor associated with SVR was baseline HDV viral load (p=0.016). High HDV viral load was defined as > 6 $\log_{10}$cp/mL based on treatment response. At week 12, mean of HDV viral load reduction in SVR and non responders were 4.60 and 2.45 $\log_{10}$cp/mL (p=0.048), respectively. No difference between week 12 and week 24 viral kinetics was observed regarding response. Therefore, EVR was defined as at least 2 log reduction of HDV viral load at week 12 compared with the baseline level. 89% of SVR had complete EVR (undetectable HDV ARN at week 12) (p=0.004). EVR had a positive predictive value (PPV) and a negative predictive value (NPV) for SVR of 65% and 100% (p=0.003).

Conclusion: SVR was associated with baseline HDV viral load < 6 $\log_{10}$cp/mL and complete EVR. Moreover, as EVR had a strong NPV for SVR, it might be used as a stopping rule in CHD patients treated with PEG-IFN.

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NATURAL HISTORY OF DELTA HEPATITIS IN ROMANIAN BLACK SEA COAST REGION

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Background: HDV is much more common in Eastern Europe, sub-Saharan Africa, Mediterranean countries, Middle East, and northern South America than other regions of the Globe. About 20 million people may be infected with HDV. HDV infection of chronically infected HBV-carriers may lead to fulminant acute hepatitis or severe chronic active hepatitis, often progressing to cirrhosis or hepatocellular carcinoma.

Aim: The aim of our study was to evaluate the natural history in patients diagnosed with Delta hepatitis in Romanian Black Sea Coast Region.

Material and methods: We prospectively evaluate the risk of progression to cirrhosis or hepatocellular carcinoma and the rate of mortality in 44 anti-VHD positive pts. The mean following period was 8.7 yrs (range 6 to 13 years). Results were compared with a control group of 44 anti-VHD negative/HBsAg positive pts, age and sex adjusted.

Results: From the study group, 78% (34 pts) of pts with chronic hepatitis D developed cirrhosis. The median progression to cirrhosis was 6 yrs in anti-VHD positive pts, (range 2.6 to 11.3 yrs after the onset of infection) compared to 8 yrs in anti-VHD negative pts. 66% of anti-VHD positive pts (29 pts) died of hepatic failure, while hepatocellular carcinoma (HCC) occured in 29% of pts (13 pts). Kaplan-Meier five year probability of hepatocellular carcinoma (HCC) was 4% in our study group compared to 2% in controls. The risk for cirrhosis, HCC, and mortality was increased by a factor of 5.3 (1.6 to 9.0), 4.1 (1.2 to 10.9), and 2.0 (0.5 to 5.9) respectively, in anti-HDV positive related to anti-HDV negative pts.

Conclusions: Our study confirms that evolution to cirrhosis or HCC is common in Delta hepatitis, worsening the prognosis. HDV infection increases the risk for cirrhosis fivefold, HCC fourfold and mortality twofold in HBsAg positive pts from Romanian Black Sea Coast region.

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ROLE OF HDV CO- OR SUPERINFECTION IN FORMATION OF OCCULT FORMS OF HBV-INFECTION

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Objective: Traditionally hepatitis Delta is considered to be the infection possible only in association with HBsAg. However, there are also some cases of hepatitis Delta in patients without HBsAg. The aim of this study was to establish features of clinical course and diagnostic of HBsAg-negative hepatitis Delta.

Methods: A total of 834 patients with HBV-infection were studied. Among them are 423 patients with acute B hepatitis, 394 patients with chronic HBV-infection and 17 patients with HBV-pastinfection. All these three groups of patients were screened for HCV and HDV infection by ELISA and PCR.

Results: 7,8% patients has HBV-infection without HBsAg, 11,3% has hepatitis Delta. Frequency of anti-HDV-seropositive persons among patients with HBsAg was 92,4%, without HBsAg - 5,4% ($p < 0,01$). HBsAg-negative cases of hepatitis Delta among different clinical forms were divided in such a way: in coinfection - 8,6%, in chronic hepatitis B - 5,4%. HBsAg was absent in four patients with acute hepatitis B, in two of them HBV-DNA was the only marker of HBV-infection. More often HDVAb were detected in patients with manifestative course of HBsAg-positive hepatitis without HBV-DNA in PCR - 35,4%, less often - in patients with manifestative course of replicative type of chronic hepatitis B (HBV-DNA "+") - 3,2% ($p < 0,01$).

Conclusion: Estimated frequency of HBV-infection without HBsAg, and also HBV-HDV co- and superinfection without HBsAg makes us to recommend testing for hepatitis Delta as well HBsAg-negative patients. The decisive reason for HDVAb investigation is biochemical manifestation of chronic hepatitis B with HBV-DNA-clearance.

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CLINICAL FEATURES AND LONG-TERM OUTCOME OF HEPATITIS DELTA IN HEMODIALYSIS PATIENTS

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Objectives: All consensus recommendation for the most critical need in viral hepatitis research is to study the course and treatment of hepatitis in certain groups of population. The aim of this research is to study the clinical features and the long-term outcome of acute hepatitis Delta (co- or superinfection) in hemodialysis patients.

Methods: 38 patients with acute hepatitis HBV and HDV-etiology and with end stage chronic renal insufficiency who received hemodialysis were studied for 36 months. The control group - 50 patients with hepatitis of the similar etiologic structure without chronic renal failure. Activity of the pathological process, the time and intensity of immune response, duration of viremia and the incidence of hepatitis developing into a chronic form were compared.

Results: The incidence of anicteric forms of hepatitis Delta in dialysis patients and in a control group was 16,6% and 6,25% correspondingly ($p < 0,05$). Hiperbilirubinemia level in those groups was correspondingly 116,9±23,7 mcmol/l against 269,3±20,9 mcmol/l and activity of GPT - 8,5±0,8 mmol/h·l against 15,3±1,0 mmol/h·l ($p < 0,05$). HDVAb in dialysis population appeared later and their concentration was lower. Evolution of acute hepatitis Delta into a chronic hepatitis were observed in investigated group more often (29% against 12%, $p < 0,05$).

Conclusion: The clinical course of viral hepatitis Delta in patients with chronic renal failure are characterized by a high incidence of subclinical forms and a milder course of the disease with a tendency to develop into the chronic form. This can be due to a significant immune deficiency inherent to such patients, including delayed and weakened humorral response to the causative agent´s antigens.

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STANDARDIZATION OF A “IN HOUSE” MOLECULAR DIAGNOSTICS FOR HEPATITIS DELTA VIRUS (HDV) IN THE WESTERN AMAZON REGION, BRAZIL

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Background and aims: The western region of the Brazilian Amazon area considered highly endemic for HDV. Currently identified seven genotypes of HDV, being that I and III considered more virulent. The viral quantification by real time PCR, is of fundamental importance in the diagnosis and treatment monitoring viral. This study aims to elucidate the molecular characteristics of HDV in the western Brazilian Amazon and develop a diagnosis "in house" using RT-PCR for quantification of the virus.

Methods: We selected 20 patients from Rondônia and Acre with anti-HDV positive. In quantitative RT-PCR kit was used TaqMan PCR Master Mix (Applied Biosystems) with probes labeled with FAM / TAMRA primers that amplify a fragment corresponding to HDAg-L. To construct the standard curve serial dilutions were made 10^{12}-10^{1} digested and purified fragment produced "in house". For characterization of genotypes by sequencing a fragment of 403bp comprising part of the L-HDAg, was amplified 08 samples identified by RT-PCR. Amplified cDNA was purified and sequenced on an ABI PRISM ® 377 (Applied Biosystems, USA).

Results: The 20 samples were positive in the qualitative and quantitative tests, corresponding to 55 million to 55 copies / mL, which showed a linear regression curve, which correlates the number of copies/mL x Ct, coefficient of determination R2 = 0.9825. The reproducibility of the test was observed by the coefficient of variation produced by each dilution tested and the specificity of the test by not obtaining a signal in any of the negative controls added in each race. The genotype III was identified in 08 samples analyzed by sequencing.

Conclusion: A molecular approach described in this study is important and immediate impact on public health, particularly for chronic patients in the region favoring confirmation of the diagnosis as well as the orientation therapy to be instituted.

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CLEVUDINE TREATMENT OF CHRONIC DELTA HEPATITIS

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Background and aims: The only nucleos(t)ide analog with in vivo evidence of efficacy in chronic delta hepatitis (CDH) is clevudine. Clevudine, in the woodchuck hepatitis model, significantly inhibited the production of surface antigen, the only hepatitis B virus function on which hepatitis D virus (HDV) depends, in a dose-dependent manner (Peek et al, Hepatology 2001) and in a preliminary study, clevudine significantly decreased HDV RNA in woodchucks infected with HDV (Casey J et al, AAC 2005). This pilot study aimed to determine the efficacy of celvudine in patients with CDH.

Patients and methods: Six patients (3 male, 3 female, mean age: 35.3±7.4) were treated with clevudine, 30 mg, daily for a duration of 9-12 months in 5 patients. In the 6^{th} patient, treatment was discontinued after 3 months, once clevudine use in humans was linked to mitochondrial toxicity . HBV DNA was measured with Cobas TaqMan PCR (Roche Diagnostics), HDV RNA with quantitative real time PCR, HBsAg levels with the Architect assay (Abbott).

Results: All patients had compensated liver disease. Baseline liver biopsy was available in all patients and disclosed cirrhosis in 2 patients (Ishak score 5) and advanced liver disease in 3 patients (Ishak scores 3 and 4). Histologic activity score ranged from 8 to 16. 2 patients were treatment naiv and four were non-responders to interferon. Clevudine treatment had no effect on HBsAg levels (4.05 $\log_{10}$ IU/mL±0.38 vs.3.94±0.40,p=NS); none of the patients had >0.5 log decline in HBsAg levels.CLE decreased HBV DNA levels (2.51 $\log_{10}$ IU/mL± 2.08 vs. 1.15±0.93; p=not significant since 3 patients had undetectable DNA at baseline). HDV RNA levels (5.6 $\log_{10}$ copies/mL± 3.8 vs. 4.9±3.5) and ALT levels (81.5 ± 44,9 vs. 96±33.8) did not change.

Conclusion: Contrary to woodchuck data, clevudine appears to be without effect in patients with CDH.

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ELEVATED LEVELS OF D-DIMERS ARE ASSOCIATED WITH ASCITES IN HEPATITIS DELTA VIRUS RELEATED LIVER CIRRHOSIS

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Background and aims: HDV infection is endemic in populations living in rural areas of middle east. Patients infected with both HBV and HDV tend to progress more severe liver injury than those infected with HBV alone. The liver is the major production site of coagulation and fibrinolitic proteins. Due to increased fibrinolytic activity, plasma D dimer levels are elevated in patients with liver cirrhosis. Evidence of ascites represents advanced liver disease. This study was conducted to assess the correlation between D dimer levels and ascites in patients with hepatitis delta virus releated cirrhosis.

Patients and methods: In this prospective study, 19 patients with histological or clinical diagnosis of hepatitis delta virus releated cirrhosis (Male =15 Female = 4, mean age 50.5 +/- 15 years), observed from May 2009 to May 2010 were enrolled. HDV-RNA was determined by polymerasechainreaction(PCR)method. Circulating D-dimer levels were measured using a immunoturbidimetric test. Severity of liver disease was classified by Child-Pugh score.

Results: Ascites was present in 15 cases and was absent in 4 cases. In ascites positive group, mean D dimer level was 6.5 +/- 3.5 U/L and in ascites negative group mean D dimer level was 1.16 +/- 1.05 U/L. High D dimer level was associated with presence of ascites($p< 0.05$).

Conclusion: In patients with cirrhosis, presence of ascites has been demonstrated to predict outcome. As a minimally invasive procedure, analysis of D dimer levels seems to play a major role in determining the presence of ascites in patients with hepatitis delta virus linked cirrhosis. So, it could help in classifiying patients and making it possible to start diuretic theraphy.

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CLINICAL AND VIROLOGICAL CHARACTERISTICS OF HEPATITIS B AND D IN CHRONICALLY INFECTED PATIENTS WITH RESPECT TO LEVEL OF EDUCATION IN SINDH-PAKISTAN

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Background and aim: Hepatitis B virus (HBV) infection and hepatitis delta virus (HDV) present worldwide and affects all age groups. It is more prevalent in rural population. Little is known about the level of education and clinical and virological characteristics of HBV and HDV.

Method: We prospectively investigated above characteristics in 426 HBSAg positive patients at Hepatology clinic from 2006 to 2009. The participants were divided into two groups; group A less than ten years and group B more than ten years of education. Both groups were matched from mean age, ethnicity, mean weight, BMI at the first visit.

Results: Out of 426 patients, 193 (45.3%) were coinfectioned with delta virus. The sero prevalence of delta antibody and HCV antibody were significantly higher in group “A” with p-value of 0.002 and 0.04 respectively. There was no difference in mean level of HBV DNA, presence of HBeAg and mean ALT levels in both groups. There was significantly increased morbidity of liver disease (presence of cirrhosis and advanced Child's Class) associated with group “A”, independent of co-infection with HDV or HCV.

Conclusion: Lower the level of education is associated with significantly higher prevalence of delta antibody, HCV antibody and advanced liver disease in HBSAg positive patients.