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Abstract Book

1st Central and Eastern European Meeting on Viral Hepatitis and Co-infection with HIV

22 - 23 June 2015, Warsaw, Poland

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Abstracts
Oral Presentations

Abstract: 1

Treatment Issues - Hepatitis _ HIV coinfection

Does hepatitis D in HBV/ HIV co-infected patients affect liver function?

J. Kozlowska[1], J. Kubicka[2], J. Jablonska[1], T. Mikula[1], E. Siwak[2], T. Dyda[3], A. Wiercinska-Drapalo[1]

[1]Medical University of Warsaw, Hepatology and Acquired Immunodeficiencies, Warsaw, Poland; [2]Warsaw's Hospital for Infectious Diseases, Outpatient Clinic, Warsaw, Poland; [3]Warsaw's Hospital for Infectious Diseases, Molecular Diagnostics Laboratory, Warsaw, Poland

Background: According to medical literature HBV/HDV co-infection can cause severe progressive hepatitis and liver cirrhosis.
The aim of this study was to determine if hepatitis D virus (HDV, delta virus) infection in Polish patients with HBV/ HIV co-infection has any impact on the progression of liver disease.

Material & Methods: 65 patients (60 male and 5 female, aged 20-56 years, mean age 41) co-infected with HIV and HBV participated in the study. All of the patients were treated with nucleoside/nucleotide analogues active against HBV. The patients were tested for serum anti-HDV (HDV Ab) with EIA test (Dia.Pro), for serum RNA HDV with HDV Real-TM Sacace Biotech test and those with HCV infection – for quantitative RNA HCV with Roche Cobas TaqMan HCV Test. All patients were clinically evaluated for the presence of liver cirrhosis. Ultrasound examination, biochemical, serological, virological and coagulation tests were done. Immunological status of the patients was assessed.

Results: HDV antibodies were detected in 15/65 (23%) patients with HIV/HBV co-infection, 11 male and 4 female. RNA HDV was detected in 9/15 (60%) anti-HDV positive patients and in one anti-HDV negative patient - intravenous drug user. 13/16 (81%) patients with HIV/HBV/HDV co-infection were previous or current intravenous drug users. In all treated patients low or undetectable HBV viral load was detected. Almost all HIV/HBV/HDV patients (15/16) were also infected with HCV. There were 15/49 patients HCV positive among HDV-negative patients. Median HCV RNA load in HCV-positive patients (1,05 x 10^6 IU/ml) was higher in those with HDV infection than in HDV-negative patients (0,76 x 10^6 IU/ml) - p > 0,05. There was no correlation between HDV infection and HBeAg positivity nor CD4 count. ALT, AST and GGTP activity were significantly higher in HDV-positive patients (p > 0,05); hemoglobin level and platelet count were significantly lower in those with HDV infection (p > 0,05). Liver cirrhosis was diagnosed in 4/15 anti-HDV positive patients, but in 2 of them HDV RNA was not detected. There was no liver cirrhosis in HDV-negative patients.

Conclusions: HDV infection is common in Polish HIV/HBV co-infected intravenous drug users. Among HIV/HBV/HDV co-infected patients advanced liver disease is uncommon. Frequently occurring concomitant HCV infection may hinder the assessment of the impact of HDV infection on the course of liver disease in HIV/HBV co-infected patients.

No conflict of interest

Abstract: 2

Liver Steatosis

Antioxidant response in patients with chronic hepatitis B or C.

W. Wójcik-Cichy[1], P. Piekarska[1], O. Omulecka[2], J. Jablonowska[1]

[1]Clinic of Infectious Diseases and Hepatology, Department of Infectious Diseases and Hepatology Medical University of Lodz, Lodz, Poland; [2]Department od Patology, Biegansky Hospital, Lodz, Poland

Background: HBV and HCV proteins are capable of inducing reactive oxygen species (ROS) production in the liver. The balance between ROS production and antioxidant defenses determines the degree of oxidative stress. The aim of this study is to analyze the antioxidant response and its regulatory factors in chronic hepatitis B and C.

Materials and Methods: It examines the expression of the antioxidant genes GFER1(Growth factor erv1-like), HMOX-1 (hemeoxygenase (decycling) 1) and NQO-1 (NAD(P)H:quinone oxidoreductase 1) in liver biopsy specimens obtained from patients with chronic hepatitis B or C. It also investigates the importance of the regulatory genes NFE2L2(nuclear factor erythroid 2-related factor 2) and Bach1 (BTB and CNC homology 1, basic leucine zipper transcription factor 1) in the antioxidant response.The hepatic expression of these genes was determined by reverse transcription polymerase chain reaction (RT-PCR).

Results: The study group consisted of 76 patients: 42 with chronic HCV and 34 with chronic HBV infection.The hepatic expression of GFER and HMOX-1 were found to be significantly higher in patients with chronic hepatitis B compared to individuals with HCV infection ($p=0.0008$ and $p<0.0001$). Higher expression of NQO1 was also detected in patients infected with HBV but the difference was not statistically significant ($p=0.16$). The hepatic expression of the regulatory gene NFE2L2 was also significantly higher in subjects with chronic hepatitis B compared to those infected with HCV ($p=0.009$). However, the hepatic expression of Bach1 was insignificantly lower in HBV subjects than HCV individuals ($p=0.15$).

Conclusion: The hepatic expression of the antioxidant genes HMOX-1, GFER and NQO1 is higher in patients with HBV than those with HCV infection, which may be associated with a better antioxidant response in the course of this infection. Dysregulation of NFE2L2 and Bach1 in HCV patients contributes to an impaired antioxidant response.

No conflict of interest

Abstract: 3

Treatment Issues - Hepatitis _ HIV coinfection

Acute HCV infection among HIV infected individuals and disease outcome in the country of Georgia

L. Gatserelia[1], L. Sharvadze[1], A. Abutidze[1], M. Karchava[1], T. Tsertsvadze[1]

[1]Infectious Diseases Aids And Clinical Immunology Research Center, Virology, Tbilisi, Georgia

Background: HCV infection is the major cause of liver-related morbidity and mortality in patients with HIV infection. However, little is known about the clinical presentation, course of acute HCV infection (AHC) and impact of IL28b genotype as a predictor for HCV self-recovery in this population. The aim of the study was to reveal symptomatic acute HCV infection, determine the role of host genetics in disease outcome, evaluate the spontaneous HCV clearance rate among HIV/HCV co-infected patients and compare it with HCV mono-infected patients.

Material & Methods: HIV-infected individuals with negative serological markers of viral hepatitis and with a high risk for HCV infection: Men who have sex with men (MSM) and Injection Drug Users (IDUs) were prospectively investigated in time period from 2011 to 2013. Patients with symptoms of hepatitis (jaundice etc.) were tested on HCV RNA by real time PCR. Positive HCV RNA confirmed diagnosis of acute HCV infection. HCV viral load was measured monthly during the follow-up period. HCV genotype was performed by Line-probe assay based on reverse-hybridization technology and IL28b single nucleotide polymorphisms in rs 12979860 were genotyped using real-time PCR methods.

Results: A total of 171 HIV-infected MSM and 322 HIV-infected IDUs were included in the study. We revealed 26 patients with acute symptomatic HCV infection; among them 17 were MSM and 9 IDUs. HCV genotypes distribution was as the following: 10 patients had genotype 1b, 7 patients -genotype 2a/2c and 9 patients - genotype 3a. Out of 26 patients 7 (27%) cleared the virus. Among them, 2 patients had genotype 1b, 2 - genotype 2a/2c and 3 - genotype 3a. Remaining 19 patients developed chronic HCV infection. In 7 subjects who cleared the virus, five had IL28b genotype C/C and 2 C/T. While non favorable IL28b genotypes were predominant (2 C/C, 7-C/T, 10-T/T) among 19 patients, who developed chronic HCV infection.

Conclusion: Spontaneous HCV clearance rate was significantly lower in HIV/HCV co-infected patients compared to HCV mono-infected patients. Favorable IL28b genotype was associated with higher HCV spontaneous clearance rate. There was no correlation between HCV genotype and disease outcome.

No conflict of interest

Abstract: 4

Treatment Issues - Hepatitis _ HIV coinfection

Chronic Hepatitis C Treatment In Patients Coinfected With HCV/HIV

L. Moroz[1], S. Antonyak[2]

[1]Vinnitsa National Medical University named after M.I.Pirogov, Infection Diseases, Vinnitsa, Ukraine; [2]GI "Institute of Epidemiology and Infectious Diseases named after L.V.Gromashevsky at the National Academy of Medical Sciences of Ukraine", Viral Hepatitis and HIV-infection, Kyiv, Ukraine

Background: The aim of our study was to determine the major predictors of effectiveness of chronic hepatitis C antiviral treatment in patients coinfected with HCV/HIV.

Materials & Methods: 130 patients with HCV/HIV co-infection, who received treatment with pegylated interferon/ribavirin (INF/RBV) at the Clinic of GI 'Institute of Epidemiology and Infectious Diseases named after L.V.Gromashevsky', were included in our study, among which men prevailed (80/130 – 61.5%). The average age of patients was 33 years; 81% (105/130) patients had the history of intravenous drug use. Most patients were infected with genotype 1 (68/130 – 52.3%); genotypes 2 and 3 were detected in 60 patients (46.2%) and only two were infected with hepatitis C virus genotype 4 (1.5%). More than half of the patients (67/130 – 51.5%) had low viral load (<800 000 IU/mL), in 63 patients with co-infection (48.5%) it was high (>800 000 IU/ml). CD4 count was > 350 cells/ml in most patients (83.1% – 108/130), in 16.9% patients (22/130) the CD4 count was ≤ 350 cells/ml before antiviral therapy (AVT). The majority of the examined patients had stages 3 and 4 of HIV related disease (108/130 – 83.1%), according to WHO clinical staging of HIV infection in adults and adolescents (2006).

Results: According to our data 68.5% (89/130) of patients with HCV/HIV co-infection completed the full course of AVT. 31.5% of patients (41/130) did not complete treatment, of whom 23.8% (31/130) – interrupted it due to virological inefficiency and 7.7% (10/130) – due to adverse events of AVT.

The study found no dependence on the frequency of sustained virological response (SVR) of demographics and route of HIV infection. SVR in the study group was achieved in 61.5% (80/130) of patients (95% CI from 53.2% to 69.9%) with HCV/HIV co-infection. We identified the influence of HCV genotype on the effectiveness of treatment. Thus, the SVR in patients with HCV genotypes 2 and 3 was achieved in 81.7% (49/60) of the patients (95% CI from 71.2% to 91.5%), which is 1.9 times greater than in patients with HCV genotype 1 and 4 – in 44.1% (30/68) of the patients (95% CI from 32.3% to 55.9%).
Among patients with baseline CD4 count ≤ 350 cells/ml SVR was observed in 68.2% (15/22) of cases (95% CI from 48.7% to 87.6%). Among patients with an initial CD4 count > 350 cells/ml SVR was achieved CC in 60.2% (65/108) patients (95% CI 51, 0% to 69.4%). Statistically significant effect of CD4 count on virological efficacy of HCV infection treatment was not observed at the beginning of AVT.
Statistically significant interrelation between clinical stage of HIV and AVT efficiency was not established.

Conclusions: Efficacy of HCV treatment in patients coinfected with HCV/HIV does not depend on gender, age, HIV transmission route and injecting drug use history. SVR frequency was higher in patients with HCV genotypes 2 and 3, and did not depend on the baseline level of viremia. The impact of initial CD4 count, and correlation between clinical stage of HIV and AVT effectiveness for chronic hepatitis C were not established.

No conflict of interest

Abstract: 5

Treatment Issues - Hepatitis _ HIV coinfection

Toll-like receptor 4 polymorphism influence on the clinical course of chronic hepatitis C in HIV-infected patients

T. Kyrychenko[1], G. Dubynska[1], T. Koval[1]

[1]Higher Medical Educational Institution of Ukraine, Ukrainian Medical Stomatologi, Infection Disease, Poltava, Ukraine

Background: Toll-like receptors (TLRs) play an important role in the innate immune response. We investigated the impact of TLR4 polymorphism on development of chronic hepatitis C (HCV) in HIV-infected patients.

Material & Methods: The presence of TLR4 Asp299Gly single nucleotide polymorphisms (SNPs) was determined in a cohort of 45 antiretroviral treatment-naive HIV/HCV-coinfected patients and evaluated in relation to the occurrence of clinical and laboratorial features of HCV. TLR4 genotyping was performed by real-time PCR.

Results: Thirty six patients were homozygous for the wild-type genotype (AA); 9 patients (20,0%) were heterozygous for the Asp299Gly SNP (AG).
Among HIV/HCV-coinfected persons with TLR4 polymorphism more frequent observed the HCV clinical features, such as abdominal pain (56% vs. 22%), asthenovegetative syndrome (78% vs. 39%) and cytolytic syndrome (ALT, AST > 40 IU (89% vs. 52%), compared with homozygous patients. It has been shown that symptomless period of HCV becomes shorter and liver cirrhosis more rapidly when having AG genotype. A high degree of correlation was observed between AG genotype TLR4 and liver cirrhosis development in group of patients with HIV/HCV (r^2=0.58, P<0,001), compared with wild-type genotype AA.

Conclusion: TLR4 polymorphism was associated with a greater risk of more severe clinical course of chronic hepatitis C in HIV/HCV-coinfected persons.

No conflict of interest

Abstract: 6

Treatment Issues - Hepatitis _ HIV coinfection

Ledipasvir/sofosbuvir for 12 weeks in patients co-infected with HCV and HIV-1.

E. Siewaszewicz[1], S. Naggie[2], C. Cooper[3], M. Saag[4], J.C. Yang[5], L.M. Stamm[5], P.S. Pang[5], J.G. McHutchison[5], D. Dieterich[6], M. Sulkowski[7], K. Lipski[1]

[1]Gilead Sciences Poland, Medical Department, Warsaw, Poland; [2]Duke Clinical Research Institute, Department of Medicine, Durham NC, USA; [3]University of Ottawa, The Ottawa Hospital, Ottawa ON, Canada; [4]University of Alabama at Birmingham, Department of Medicine, Birmingham AL, USA; [5]Gilead Sciences Inc., Clinical Research, Foster City CA, USA; [6]Icahn School of Medicine at Mount Sinai, Department of Medicine, New York NY, USA; [7]Johns Hopkins University School of Medicine, Department of Medicine, Baltimore MD, USA

Background: Historically HIV co-infection was considered a negative predictor of HCV response to treatment with interferon/ribavirin (IFN/RBV). For sofosbuvir-based regimens, HIV/HCV patients have achieved similar sustained virologic response (SVR) rates as HCV monoinfected patients. We evaluated the safety and efficacy of the IFN-free, RBV-free, single tablet regimen of ledipasvir/sofosbuvir (LDV/SOF) in HCV genotype 1 or 4 patients co-infected with HIV-1 in the Phase 3 ION-4 study.

Materials & Methods: HCV treatment naïve and experienced HIV co-infected patients on stable, approved antiretroviral (ARV) regimens were enrolled and received LDV/SOF (90mg/400mg) once daily for 12 weeks. Patients with compensated cirrhosis were eligible. Permitted concomitant ARVs included tenofovir and emtricitabine (TDF+FTC) with raltegravir (RAL), efavirenz (EFV) or rilpivirine (RPV). Safety evaluations included adverse event (AE) and standard laboratory parameter monitoring in addition to enhanced renal toxicity monitoring, CD4 count and HIV-1 RNA levels. The primary efficacy endpoint was SVR12.

Results: 335 patients with GT1a (75%), GT1b (23%) and GT4 (2%) were enrolled; 82% were male, 61% were white, mean age was 52 (range 26-72), mean baseline HCV RNA was 6.7 $\log_{10}$ IU/mL (range 4.1-7.8), median baseline CD4 count was 662 cells/uL (Q1, Q3=469, 823), 20% had cirrhosis, 24% were *IL28B* CC genotype and 55% had not responded to prior HCV treatment. Patients were taking EFV (48%) or RAL (44%) or RPV (9%). Overall, the SVR12 rate was 96% (321/335); 2 patients had on-treatment virologic failure likely due to non-compliance and 10 had virologic relapse after discontinuing treatment. SVR12 was similar among non-cirrhotic (96%) and cirrhotic (94%) patients and also among treatment naïve (95%) and treatment experienced (97%) patients. No patient had confirmed HIV virologic rebound (HIV-1 RNA≥400 copies/mL). No patients discontinued study drug due to an AE. AEs occurring in ≥10% of patients were headache (25%), fatigue (21%) and diarrhea (11%). No significant lab abnormalities were observed.

Conclusions: The IFN-free, RBV-free, single tablet regimen of LDV/SOF administered once daily for 12 weeks is highly effective and well tolerated in treatment-naïve and experienced, genotype 1 or 4 HCV-infected patients with HIV-1 co-infection, including those with cirrhosis.

Presented at CROI 2015, Seattle, LB Oral 152LB

Abstract: 7

Liver Cancer

Mutational Analysis of Hepatitis E Virus ORF1 'X-Domain' Identifies a Putative ADPR-monophosphatase Active-Site, Critical for Virus Replication in Hepatoma Cells

M.K. Parvez[1]

[1]*King Saud University College of Pharmacy, Pharmacognosy, Riyadh, Saudi Arabia*

Background: The hepatitis E virus (HEV) has recently emerged to cause chronic hepatitis and cirrhosis in some European and American population. HEV ORF1 gene encodes the non-structural polyprotein wherein the 'X-domain' still remains poorly defined. Cellular X-domain associated ADPR-monophosphatase activities are also reported in some RNA viruses. Of these, the coronavirus, MHV liver pathology is shown to be dependent on ADPR-monophosphatase. The present study therefore, investigated the role(s) of X-domain residues in HEV replication cycle in cultured hepatoma cells.

Material & Methods: GenBank (NCBI) amino acid sequences of ORF1 X-domain of human HEV strains representing the four genotypes (1-4), including genetically-related viruses, prokaryotic and eukaryotic sequences were analyzed (ClustalW 1.83). The evolutionary conservation of X-domain residues positions (ConSurf) and the secondary structure (PROFSec) were predicted. ORF1 X-domain mutants (Asn806Ala, Asn809Ala, His812Leu, Gly815Ala, Gly816Ala and Gly817Ala), were constructed by site-directed mutagenesis in HEV-SAR55 replicon (pSK-GFP). The mutant-replicon RNA were tested in hepatoma S10-3 cells, and analyzed by fluorescence microscopy and flow cytometry (FACS).

Results: In silico analysis showed a high degree of evolutionary conservation of X-domain amino acid positions wherein the N-terminus residues 'Asn806, Asn809, His812, Gly815, Gly816 and Gly817 ' formed a potential catalytic-site homolog of coronavirus ADPR-monophosphatase. The structure prediction further revealed formation of β-3/α-2 elements by active-site residues, similar to published structures. Replication fitnes analysis showed complete abrogation of HEV replication by Gly816Ala and Gly817Ala constructs compared to Gly815Ala mutant that replicated very poorly. Furthermore, while the Asn806Ala mutant retained RNA replication, Asn809Ala and His812Leu showed non-viability. The sequential mutation analysis revealed indispensability of X-domain nucleotides on viral RNA replication. Taken together, our data strongly argue for an essential role of X-domain residues at post-translational level, indicating for its ADPR-monophosphatase activity.

Conclusions: the regulatory/catalytic role of ORF1 X-domain in HEV life cycle critically depends on the N-terminal 'Asn, Asn, His, Gly, Gly, Gly' segment/secondary-structure. Further biochemical or biophysical characterizations of HEV X-domain's ADPR-monophosphatase activity would only confirm its significance in virus biology or liver pathogenesis.

No conflict of interest

Abstract: 8

Monitoring and Diagnostic Tools

Evaluation of early cerebral alterations in the course of HIV and HCV infection using perfusion MR imaging: is the hepatitis C virus more dangerous for the brain?

J. Bladowska[1], B. Knysz[2], A. Zimny[1], A. Koltowska[1], P. Szewczyk[1], K. Malyszczak[3], J. Gasiorowski[2], M. Furdal[4], M. Sasiadek[4]

[1]Wroclaw Medical University, Department of General and Interventional Radiology and Neuroradiology, Wroclaw, Poland; [2]Wroclaw Medical University, Department of Infectious Diseases Liver Diseases and Acquired Immune Deficiency, Wroclaw, Poland; [3]Wroclaw Medical University, Department of Psychiatry, Wroclaw, Poland; [4]Wroclaw Medical University, Regional Specialistic Hospital, Wroclaw, Poland

Background: The involvement of the central nervous system (CNS) in the course of the human immunodeficiency virus (HIV) infection is already often observed in the early stage of the disease. HCV can also invade CNS. Since both viruses can infect the brain and impair CNS function, they may cause alterations in cerebral microcirculation. The aim of the study was to evaluate early disturbances in cerebral microcirculation using magnetic resonance (MR) perfusion-weighted imaging (PWI) in asymptomatic HIV-1-positive and HCV-positive patients as well as to assess the correlation between perfusion-weighted imaging (PWI) measurements and the clinical data.

Material & Methods: Fifty-six patients: 17 HIV-1-positive non-treated, 18 HIV-1-positive treated with combination antiretroviral therapy (cART), 7 HIV-1/HCV-positive non-treated, 14 HCV-positive before antiviral therapy and 18 control subjects were enrolled in the study. PWI was performed with a 1.5T MR unit using the dynamic susceptibility contrast (DSC) method. Cerebral blood volume (CBV) measurements relative to the cerebellum (rCBV) were evaluated in the posterior cingulate region (PCG), basal ganglia (BG), temporoparietal (TPC) and frontal cortices (FC), as well as in white matter of frontoparietal areas. Correlations of rCBV values with immunologic data, liver histology activity index (HAI) as well as the cognitive tests results were analysed. Analysis of variance followed by the post hoc Tukey LSD test was used for statistical evaluation (significant $p<0.05$). Additionally, we applied the Bonferroni correction (significant $p<0.0055$).

Results: Significantly lower rCBV values ($p< 0.05$) were found in the right TPC and left FC as well as in PCG in all HIV-1-positive and HCV-positive patients compared to controls. HIV-1-positive cART treated and HIV-1/HCV-positive patients demonstrated lower rCBV values in the right FC and the left TPC, while HCV-positive subjects revealed lower rCBV values in the left TPC regions. We found significantly increased rCBV values in BG in HCV-positive patients compared to controls as well as to all HIV-1-positive subjects. There were significant correlations between rCBV values in the temporoparietal and frontal cortices, basal ganglia region and the cognitive tests results. We did not observe any significant correlations between rCBV values and CD4 T cell count or HAI score. According to the Bonferroni correction only HCV subjects showed significant changes of rCBV values ($p<0.0055$).

Conclusion: PWI examination enables the assessment of HIV-related as well as HCV-related early cerebral dysfunction in asymptomatic subjects. HCV-infected patients seem to reveal the most pronounced perfusion changes. Hyperperfusion in basal ganglia may be an indicator of brain inflammation in HCV patients. In our opinion rCBV measurement could be a noninvasive neuroimaging biomarker for assessing early cerebral microcirculation impairment in HIV-1 as well as in HCV infections.

No conflict of interest

Abstract: 9

Monitoring and Diagnostic Tools

Impact of HCV coinfection on the development of subclinical atherosclerosis of carotid arteries in HIV positive patients in the Lower Silesia Region, Poland

K. Barska[1], W. Kwiatkowska[1], B. Knysz[2], J. Drelichowska[1], K. Arczynska[3], M. Zalewska[2], J. Gasiorowski[2], W. Witkiewicz[4]

[1]Regional Specialist Hospital in Wroclaw Research and Development Center, Department of Angiology, Wroclaw, Poland; [2]Wroclaw Medical University, Department of Infectious Diseases Liver Diseases and Acquired Immune Deficiencies, Wroclaw, Poland; [3]Wrovasc – Integrated Cardiovascular Center Regional Specialist Hospital in Wroclaw, Research and Development Center, Wroclaw, Poland; [4]Wrovasc-Integrated Cardiovascular Center Regional Specialist Hospital in Wroclaw Research and Development Center, Department of Angiology, Wroclaw, Poland

Background: Among HIV positive patients increased incidence of cardiovascular diseases (CVD) is observed. Reason for it are HIV infection *per se* and induction of persistent inflammation, also adverse effects of antiretroviral drugs. About 50% of HIV positive patients in Poland is HCV positive. Data regarding impact of HCV on the development of subclinical atherosclerosis in HIV(+) patients are scanty. The aim of the study was to establish impact of HCV on the development of subclinical atherosclerosis in HIV positive patients.

Material & Methods: 121 HIV positive patients living in the Lower Silesia region in Poland entered the study. Among them were 66 individuals with HCV coinfection, 55 individuals with HIV monoinfection and 42 healthy person of the control group. The following data were analysed: cardiovascular risk factors profile, cardiovascular risk (NCEP ATP III), carotid intima-media thickness (cIMT, cIMTmeanmax), occurence of atherosclerotic plaques in carotid arteries. HCV infection was confirmed by PCR (Cobas TaqMan HCV Test v.2.0). The statistical analysis was made using R and MedCalc packages. All results with a significance level $p<0.05$ were considered significant.

Results: No influence of HCV coinfection in HIV positive patients on the development of subclinical atherosclerosis (cIMT, cIMTmeanmax, occurence of atherosclerotic plaques) was observed. Progression of subclinical atherosclerosis was similar in both groups of patients: HIV monoinfected and with HCV coinfection. In these two groups the atherosclerotic changes were more advanced then in the control group. HCV coinfected patients had lower risk and different profile of cardiovascular risk factors comparing with HIV monoinfected individuals: lower levels of cholesterol: total, LDL and non-HDL, more often smoked cigarrets and less often suffered from hypertension. Age, non-HDL cholesterol, cumulative time of PIs and NRTIs and antiretroviral therapy influenced development of subclinical atherosclerosis in HCV coinfected patients. In HIV monoinfected patients age, cigarette smoking, hypertension and cumulative time of NRTIs (but not PIs) therapy strongly influenced progression of subclinical atherosclerosis.

Conclusions: HCV coinfection did not influence development of subclinical atherosclerosis and the risk of CVD was lower (lower levels of atherogenic lipids and less often hypertension). The behaviour and importance of traditional cardiovascular risk factors on the development of atherosclerosis was different in HCV coinfected patients when compared to those with a HIV monoinfection.

No conflict of interest

Abstract: 10

Monitoring and Diagnostic Tools

Endothelial dysfunction and its influence on the development of subclinical atherosclerosis in HIV/HCV positive patients

K. Barska[1], W. Kwiatkowska[1], B. Knysz[2], M. Zalewska[2], K. Arczynska[3], J. Gasiorowski[2], M. Karczewski[3], W. Witkiewicz[4]

[1]Regional Specialist Hospital in Wroclaw Research and Development Center, Department of Angiology, Wroclaw, Poland; [2]Wroclaw Medical University, Department of Infectious Diseases Liver Diseases and Acquired Immune Deficiencies, Wroclaw, Poland; [3]Wrovasc – Integrated Cardiovascular Center Regional Specialist Hospital in Wroclaw, Research and Development Center, Wroclaw, Poland; [4]Regional Specialist Hospital in Wroclaw Research and Development Center Wrovasc – Integrated Cardiovascular Center Regional Specialist Hospital Research and Development Center in Wroclaw, Department of Angiology, Wroclaw, Poland

Background: Chronic inflammation induced by HIV can lead to endothelial dysfunction and increased risk of cardiovascular diseases (CVD) including subclinical atherosclerosis.
The aim of the study was to evaluate markers of endothelial dysfunction and analysis how they depend on HIV infection, HCV coinfection, traditional risk factors and subclinical atherosclerosis.

Material & Methods: 121 HIV positive patients entered the study. Among them were 66 individuals with HCV coinfection. The following data were analysed: plasma levels of vascular cell adhesion molecule-1 (VCAM-1), von Willebrand factor (vWF), soluble thrombomodulin (sTM), also proinflammatory markers (tumor necrosis factor alfa -TNF-α, interleukin 1β - IL-1β, C-reactive protein - CRP), assessment of traditional and nontraditional risk factors for cardiovascular diseases, carotid intima-media thickness (cIMT) measurement and amount of atherosclerotic plaques in carotid arteries. HCV infection was confirmed by PCR (Cobas TaqMan HCV Test v.2.0). The analysis was made using R and MedCalc statistical packages.

Results: Levels of VCAM-1 and vWF were higher n HIV positive cohort comparing with HIV negative person (p=0,0001, p=0,004). Moreover levels of VCAM-1, vWF and sTM were significantly higher in a group of patients with HCV coinfection, comparing with a group of HCV negative patients (p=0,002, p=0,01, p=0,004). It was also established that HCV is an independent factor influencing the increased level of VCAM-1, vWF and sTM. Levels of VCAM-1 and sTM depended on TNF-α (higher in HIV/HCV positive patients). Despite more advanced subclinical changes in carotid arteries among HIV positive patients, an impact of VCAM-1 (p=0,94, p=0,41), vWF (p=0,35, p=0,52) and sTM (p=0,98, p=0,28) in regards to the cIMT and atherosclerotic plaques was not observed.

Conclusion: In HIV positive patients exacerbated endothelial dysfunction was observed, but only HCV coinfection influenced high blood levels of endothelial dysfunction markers: VCAM-1, vWF and sTM. These results can indicate HCV involvement in the development of CVD in HIV/HCV positive patients. When investigating CVD in HIV positive patients, HCV coinfection should be also considered.

No conflict of interest

Abstract: 11

Treatment Issues - Hepatitis _ HIV coinfection

Research of demographic and social predictors of depression during antiviral (combined) therapy in patients with chronic hepatitis C 1 genotype HCV in Ukraine

O.B. Vorozhbyt[1]

[1]*Lviv medical university by Danylo Galytsky, Infectious diseases department, Lviv, Ukraine*

Background: This abstract shows the results of a study of demographic and social predictors of the development of depression in patients with chronic hepatitis C (CHC) genotype 1 during antiviral (combined) therapy. Until recent times modern standards of treatment have been a combined therapy by pegilated interferons (PegIFN) α2a or α 2b in combination with ribavarin (RBV), during which the spread of depression among patients was from 6 to 70%. Widespread occurrence of CHC infection and depression in Ukraine makes it important to predict the onset of depression in patients with CHC using demographic and social risk factors before the start of the interferon therapy. Therefore, issue of a particular importance becomes prognosis of possible occurrence of depression long before therapy of patients with HHC by means of research of possible risk factors, especially demographic and social factors, proper attention to which is not often paid. In this study we elucidated the role of these factors on depression development of patients with CHC with genotype 1 during antiviral (combined) therapy.

Materials & Methods: Total of 123 patients receiving peg-IFN α2b and ribavirin treatment were analyzed (aged 18-61, 60 male, 63 female). Only patients with depression episodes occurring during 4-24 weeks of 48 weeks of treatment were included. Patients with preexisting depression and other psychiatric conditions were excluded. Zung Self-Rating Depression Scale was used to evaluate patients at 0, 4, 12 and 24 weeks of treatment. The following factors were analyzed: sex, age, marital status, educational level, level of disease knowledge, social support, existence and gravity of nosogenic reaction.

Results: Majority of depression symptoms appeared before the 12th week in therapy: during 1- 3 months of therapy: during the 4th week -16,3%, during the 8th week - 31,5%, during the 12th week - 45,5%, during the 24th week - 8,7%. Highest occurrence was in the 40-49 age cohort (39%). There was a direct correlation between female sex, a low education level (67% of patients who did not have high education), a low level of disease knowledge (72%), absence of social support (39%) and presence of nosogenic reaction with frequency and gravity of depression episodes. Maritial status did not show significant correlation with depression.

Conclusions: The treatment of patients with CHC shows an increase in frequency of development depression symptoms during the 1 – 3 months of the therapy. Most of the depressive symptoms appeared during the 12th week of the therapy - 45,5%. Before the initiation of CHV therapy, the following depression risk factors should be taken into account: age group 40-49, female sex, low education level, low knowledge about disease, absence of social support, as well as presence and gravity of nosogenic reaction.

No conflict of interest

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Abstracts
Poster Presentations

Abstract: 12

Liver Steatosis

The features of carbohydrate and lipid metabolism in patients co-infected with HIV/HCV

K. Iurko[1], V. Kozko[1], A. Adeyemi[1]

[1]Kharkov national medical university, infectious diseases, Kharkov, Ukraine

Background: Among the factors indicative of the progression of chronic hepatitis C (CHC), the leading position belongs to hepatic steatosis and insulin resistance (IR), which may be virus-induced, and metabolic. The main risk factors for the metabolic syndrome in HIV-infected individuals are high viral load, use of drugs lopinavir/ritonavir and didanosine, increased body weight and levels of Low density lipoproteins (LDL) and/or triglyceride (TG) levels, patient age, and co-infection with human immunodeficiency virus (HIV) and hepatitis C virus (HCV). Thus, HCV-infection in HIV-infected individuals is one of the major risk factors for metabolic disorders**.**

Materials & Methods: The study of insulin in the blood serum was conducted with immunofluorescence assay, the determination of glycosylated hemoglobin (HbA1C) was carried out by ion-exchange chromatography. Determination of glucose in the blood serum was carried out by a colorimetric method using a reagent kit from the company 'SpaynLab' (Spain). The HOMA IR index was determined, which was calculated by the formula: [(fasting glucose) x (fasting insulin)] mmol/l / 22.5.
The study of lipid metabolism of blood (total cholesterol (TC), TG, High-density lipoproteins (HDL), LDL) was carried out by the enzymatically-colorimetric method with diagnostic kits from the company 'SpaynLab' (Spain). The content of Very low density lipoproteins (VLDL) in blood serum was determined by the formula: VLDL=TG/5. Atherogenic coefficient (AC) was calculated by the formula: AC=(TC-HDL)/HDL. Statistical analysis was performed using the software package «Statistica for Windows», 8.0.

Results: In the investigated patients identified carbohydrate metabolism disorders as an increase in serum glucose, insulin, HbA1C, level of HOMA IR. The greatest manifestation of disorders of carbohydrate metabolism was established in patients co-infected with HIV/HCV, and the lowest - in HIV-infected individuals.
TC in patients of all groups had no significant difference with that of the control group in patients. The patients studied, compared to the control, there was a significant increase of TG, AC, LDL, VLDL and reduction HDL. Significantly higher levels of TG ($p<0.001$) was observed in patients co-infected with HIV/HCV compared to patients with chronic hepatitis C and HIV separately.

Conclusions: In HIV-infected patients with chronic hepatitis C and co-infection with HIV/HCV significant increases in serum glucose, insulin, HbA1C and HOMA IR index values were observed. This indicates a violation of carbohydrate metabolism in patients examined. The most significant manifestations of disorders of carbohydrate metabolism were observed in patients co-infected with HIV/HCV ($t=27,4$; $p<0.001$), which exceeds the specified changes in patients with CHC in 1.53 times ($t=17,9$; $p<0.001$) and HIV-infected patients ($t=12,8$; $p<0.001$) 2.14 times. The studied patients had lipid metabolism disorders, namely increases in the serum TG, AC, LDL, VLDL and HDL reduction. Significantly higher TG levels ($p<0.001$) was observed in patients co-infected with HIV/HCV compared to patients with CHC and HIV separately.

No conflict of interest

Abstract: 13

Liver transplantation

The influence of intraoperative fluid management on postoperative renal function and blood products transfusion among liver transplant recipients.

J. Pluta[1], B. Nicinska[1], B. Lagiewska[2], W. Lisik[2], T. Lazowski[1], A. Chmura[2], J. Trzebicki[1]

[1]Medical University of Warsaw, Department of Anesthesiology and Intensive Care Unit, Warsaw, Poland; [2]Medical University of Warsaw, Department of General and Transplantation Surgery, Warsaw, Poland

Background: Liver transplant recipients present rebalanced hemostasis which is a result of pro- and antihemostatic pathway changes. Intraoperative fluid replacement therapy plays an essential role in perioperative period during liver transplantation. The advantages and disadvantages of fluid restrictive (RT) and non-restrictive (N-RT) therapy are discussed. RT and low central venous pressure is advised in liver surgery to limit blood loss. However, in some studies the possible negative influence of RT on postoperative renal function was revealed. At the time of writing there was no agreement on a universal scheme of intraoperative fluid therapy in liver transplantation (LT).
The aim of the study is to evaluate the fluid restrictive (RT) or non-restrictive (N-RT) therapy's influence on postoperative renal function, based on serum creatinine level measured on the 1, 2, 3, 7, 14 and 30 day after LT.

Materials & Methods:219 patients, who underwent LT between December 2008 and December 2013, were retrospectively analyzed. Major cause of liver insufficiency (35%) was hepatitis C. Out of them, 189 patients with no history of renal dysfunction (baseline serum creatinine level 0,6-1,3mg/dl) were enrolled (42% females, aged: 20-69 (mean: 49)). Patients were divided into two groups depending on intraoperative fluid management. RT was defined as an intravenous crystalloid infusion, rate approximately 4ml/kg/hour during hepatectomy, while N-RT as 10-20ml/kg/hour.

Results: There were 97 patients included in RT group and 92 in N-RT. Median baseline serum creatinine level in RT and N-RT amounts 0,88 mg/dl and 0,9 mg/dl, respectively.
Median serum creatinine level (mg/dl) in the RT vs N-RT group were following (1,2,3,7,14 and 30 day): 1,1 vs 1,06; 1,26 vs 1,18; 1,23 vs 1,18; 1,03 vs 1,02; 1,12 vs 1,04; 1,11 vs 1,08; respectively.
The difference of serum creatinine level in the studied groups was not significant.
In RT group there were also 36 patients who underwent liver transplantation without any blood product transfusion, compared to 9 patients in N-RT group.

Conclusions: In our study the type of intraoperative fluid management has no influence on postoperative renal function, however fluid restrictive therapy seems to reduce perioperative blood products transfusion.

No conflict of interest

Abstract: 14

Drug Interactions

Clinical and immunological features of chronic viral hepatitis C with autoimmune thyroiditis

O.M. Chemych[1], A.O. Borodenko[1], M.D. Chemych[1]

[1]Sumy State University, Department of Infectious Diseases and Epidemiology, Sumy, Ukraine

Background: Features of autoimmune destruction of the thyroid gland (TG) with chronic viral hepatitis C (CVHC) were investigated.

Materials & Methods: The study involved 184 patients with CVHC treated with antiviral therapy (AVT). It was singled out patients with autoimmune thyroiditis (AIT), which debuted during the AVT (5.97%) and the group with transient increase of autoimmune antibodies without diagnosis AIT (3.8%). In these groups, duration of disease was (15.3±0.9) and (16.9±1.7) years, respectively. It was studied the level of thyroid hormones, antinuclear (ANA) and antimitochondrial antibodies (AMA), antibodies to thyroglobulin (ATTH) and thyroid peroxidase (ATPO).

Results: Among the patients with CVHC men (59.4%) were dominated, women were 1.5 times less (40.6%) ($p<0.05$). In the group with AIT women were dominated (90.90% and 9.09%) ($p<0.05$), among patients with a transient increase in antibody was a tendency to a predominance of men (57.14% and 42.86%). Among patients with Hashimoto's thyroiditis genotype 1 HVCV (81.81%) was more common, 3 - much less (18.19%). Most patients has fibrosis F3 (6 people), more rarely F2 (4) and F1 (1). In persons with a transient increase of antibodies parameters were the same statistically. All patients with Hashimoto's thyroiditis were defined with low viral load (253748.3±305.4) copies/mL against (2637059.0±394.3) copies/ml in those without it ($p<0.05$). During AVT the number of patients who have had rejection of laboratory parameters reduced. Thus, in the 1st month of treatment increased level of ATPO (312.4±42.1) IU/ml was determined in 8 cases, ATTH (206.3±60.9) IU/ml – 3, with normal ANA, AMA indices. At the 3rd month of treatment increased level of ATPO (334.5±58.6) IU / ml was found in 6 patients, ATTH (115.2±30.4) IU/ml - 3, 2 - ANA and in 1 - AMA. At the 6th month of treatment increased level of ATPO (390.2±60.8) IU / ml was detected in 3 persons, ATTH (105.1±20.3) IU/ml – 3 patients. The level of thyroid hormones (T3 and T4) remained normal during the entire observation period. Reduction of TSH was found in 3 cases, increase - 4. Among patients with a transient increase of antibodies viral load reached on the average (1421226.61±70.900) copies/ml, which is significantly more than in the group with AIT (EMF $T>T_{cr}$, $p<0.05$). Thus, the 1st month of treatment was determined by the elevated levels of ATTH in 1 patient, 3 positive results for ANA, 1 - AMA. At the 3rd month: 3 positive for ANA, one has ATTH increase. At the 6th month: 1 positive ANA and AMA, one has ATTH increase to 445.8 IU/ml, and ATPO to 122.7 IU/ml. The level of thyroid hormones T3 and T4 and TSH-free fractions also remained within normal limits.

Conclusions: AIT was diagnosed often in women with low viral load, with normal values of T3 and T4 hormones. This trend is not detected within transient increase of autoimmune thyroid antibodies. Number of patients with high titers of antibody to the thyroid was reduced during prolonged AVT, and in patients with a transient increase of autoimmune antibodies the tendency to normalization held with the conduction of the PVT, but unlike the AIT rarely ATPO indices increase, more often ANA ($p>0.05$).

No conflict of interest

Abstract: 15

Treatment Issues - Hepatitis _ HIV coinfection

The Efficiency of Antiviral Therapy of HCV in Patients With HIV infection

V. Maly[1], N.V. Shepileva[1], A.E. Cooper[2], D.B. Penkov[3], A.A. Shvaychenko[1], N.V. Bryadko[4], N.I. Fedorchuk[4], J.G. Abdou[5]

[1]Kharkov Medical Academy of Postgraduate Education, Department of Infectious diseases, Kharkov, Ukraine; [2]Kharkiv National Medical University, Department of Infectious diseases, Kharkov, Ukraine; [3]Kharkiv Regional Clinical Hospital of Infectious Diseases, Department of Infectious diseases, Kharkov, Ukraine; [4]Mykolaiv Regional Hospital of Infectious Diseases, Department of Infectious diseases, Mykolaiv, Ukraine; [5]Kharkiv Regional Clinical Hospital of Infectious Diseases, Department of Infectious diseases, Kharkiv, Ukraine

Background: At present, the epidemic situation of HIV infection in Ukraine can be characterized again by the increasing number of reported cases in most regions of Ukraine. According to the operational statistics of ' Ukrainian Center for socially dangerous diseases control of the Ministry of Health of Ukraine ' state institution on 01.01.2015, there are 139 573 HIV-infected patients registered in health institutions of Ukraine . The south-eastern regions of Ukraine remain with high HIV prevalence, the western regions- with a low level. The time and outcome

of disease in these patients are largely influenced by comorbidities, mainly with chronic viral hepatitis. The high frequency of co-infection is caused, first of all, by the same transmission mechanisms of these infections, especially among injecting drug users (IDUs). The proportion of co-infected with HCV in this category of patients, intravenous drug users, is from 70 to 90%, which causes additional problems in treating these diseases.
Interaction between viruses themselves and between antiviral drugs is very complex and not fully understood. However, the use of HAART contributes to a significant increase in life expectancy of infected and co-infection with HCV, increases the risk of liver damage (it accelerates fibrosis, and development of HCC and CPU), so mortality from these diseases in these patients at the present stage is so high that identifies the problem of HCV therapy. It is known that the presence of RVR and EVR is the most important predictor of HIV-infected patient's treatment efficacy that receive concomitant HAART and HCV treatment, and the outcome of therapy depends on the use of specific drugs from the NRTI group. The aim of the study was to determine the effectiveness of viral response during the first 12 weeks of treatment in patients with chronic hepatitis C and HIV infection.

Results: In 2014, 15 patients with HCV in HIV infection started the therapy. Of these, there were 13 men and 2 women . Genotype 1 HCV RNA recorded in 10 patients (66.7%), 3a - in 1 (6.6%), 3ab in 4 patients (26.7%). The level of fibrosis was not determined. Rapid viral response was obtained in 4 patients (26.7%), early viral response - in 6 (40%). After 24 weeks of treatment there were 9 patients (60%) with negative PCR, while HCV RNA was determined in 2 patients (13.3%), in 1 patient PCR was not studied. 10 patients (66.6%) successfully completed the treatment with a SVR, 2patients are continuing the treatment. 3 patients discontinued therapy, of whom 2 - after 12 weeks of treatment in the absence of any effect of antiviral therapy, and 1 because of identified comorbidity (active tuberculosis).

Conclusions: The majority of HIV-infected patients receiving HAART, HCV antiviral therapy during the first 12 weeks were successful, which is extremely important for the further prognosis of such patients.

No conflict of interest

Abstract: 16

Treatment Issues - Hepatitis _ HIV coinfection

Spread of HIV/hepatitis coinfection in the structure of HIV/aids mortality

L.R. Shostakovych-Koretskaya[1], O.P. Shevchenko[1], G.O. Revenko[1], K.J. Litvin[1], N.S. Suremenko[1], L.V. Timofeeva[2], V.D. Tkachenko[2], I.V. Chuhalova[3], Z.O. Chykarenko[1]

[1]Dnipropetrovsk Medical Academy, Infectious Diseases, Dnipropetrovsk, Ukraine; [2]Dnipropetrovsk municipal clinical hospital #21, Infectious Diseases, Dnipropetrovsk, Ukraine; [3]Regional center for HIV management and prophylaxis, Infectious Diseases, Dnipropetrovsk, Ukraine

Background: Common routes of transmission of viral hepatitis (B and C), increased number of injecting drug users and people having unprotected and casual sex led to a significant increase in the number of patients with co-infection of HIV / hepatitis. Therefore, the investigation of influence of HIV/viral hepatitis co-infection on the course and mortality of both viral diseases is important. So, the goal of the research was to analyze the prevalence of chronic viral hepatitis in patients with HIV infection and the impact of HIV / hepatitis co-infection on mortality rates of patients

Materials & Methods: Retrospective analysis of the structure of lethal cases of HIV / AIDS during 2011-2013 years was performed; their autopsy was conducted in Dnipropetrovsk City Hospital #21. In total 250 case histories were analyzed.

Results: In 2011, the total number of lethal outcomes among hospitalized patients with HIV-infection was 72 people. Of these 29 cases (40.3%) had co-infection and related liver disease (hepatitis B and C). In 2012, the number of lethal outcomes was similar (72 patients), of them 23 cases included co-infection (31.9%). In 2013 number of lethal outcomes among patients with HIV infection was significantly less (43 patients), nevertheless the proportion of co-infection (hepatitis B and C) increased to 41.8% (18 patients). In majority of cases autopsy was established liver injury and fibrosis of different degree; cirrhosis was established in 14% of cases. In 22% of lethal cases among HIV /

hepatitis co-infection liver damage was also caused by other reasons: 60% had history of drug using, drug toxicity or opportunistic infections. 30% of all patients were receiving ART, 65% were exposed to TB therapy.

Conclusion: Results of the performed analysis show that co-infection of HIV / AIDS with viral hepatitis B and C is presented in significant part in total mortality structure. This trend is existing currently and during recent years. The presence of co-infection complicates the course of both infections and promotes more rapid progression of liver disease. The risk of unfavorable outcome is increased by such factors as drug use or use of hepatotoxic medicine. It is necessary to pay more attention to timely diagnosis of HIV / hepatitis B co-infection with the purpose of timely treatment of the patients.

No conflict of interest

Abstract: 17

Treatment Issues - Hepatitis _ HIV coinfection

Influence of antiviral therapy of HIV infection on prevalence of markers of viral hepatitis B and C

L.R. Shostakovych-Koretskaya[1], A.V. Cherginets[1], V.V. Mavrutenkov[1], Z.O. Chykarenko[1], O.P. Shevchenko[1], I.V. Budayeva[1], V.P. Dyadik[1], A.O. Lesnichaya[2]

[1]Dnipropetrovsk Medical Academy, Infectious Diseases, Dnipropetrovsk, Ukraine; [2]Municipal center for HIV management and prophylaxis, Infectious Diseases, Dnipropetrovsk, Ukraine

Background: With appearance of antiretroviral therapy (ART), the life quality and length of HIV infected patients has significantly improved. Patients co-infected with HIV / HBV receive ART scheme including nucleoside reverse transcriptase inhibitors (NRTI), 3TC and TDF, with regard to their effect on hepatitis B virus. However NRTI are not acting on hepatitis C co-infection. So, this category of patients requires additional antiviral drugs. To plan the financial costs of the State Program 'Antihepatitis' and optimize the management of patients with HIV / viral hepatitis co-infection on ART, it is necessary to study the spread of these conditions and their structure in the cohort.

Materials & methods: We analyzed the prevalence of serological markers of HBV and HCV in a cohort of 501 patients with confirmed HIV infection in our clinic.
All patients were conducted clinical and laboratory examination, which included evaluation (CD4), HIV RNA load, biochemical tests, serological markers of opportunistic infections and viral hepatitis B (HbsAg, HbeAg, Ab HBeAg), C (Ab HCV), Ab to hepatitis D. According to WHO classification, 1st disease stage was diagnosed in 9 patients (1.8%), 2nd in 49 (9.8%), 3rd in 164 (32.7%), 4th in 279 (55.7%).

Results: Chronic liver diseases were revealed in 167 patients (33.3%): HCV markers in 53 (10.6%), of hepatitis B in 15 (2.3%), of hepatitis B + C in 48 (9.6%), of hepatitis of unknown etiology in 44 (8.8%), of liver cirrhosis in 7 (1.4%). Patients with viral hepatitis B and C were divided into 2 groups: receiving ART for at least 2 years (1st group, n = 62), without ART (2nd group, n = 41). The 1st group patients received schemes of ART which included NRTI, lamivudine and tenofovir (3TC and TDF)
Comparative analysis showed that viral markers of hepatitis B and C are found in 1st and 2nd groups with different frequency. The prevalence of chronic hepatitis B markers among 1st group is 2.9%, which is almost 9 times lower than in the 2nd group (19.1%) ($p<0.05$). Spread of HCV in both groups (36.8% and 41.2% respectively) significantly exceeded prevalence of HBV ($P<0.05$). At the same time, the frequency of HCV frequency was mainly similar between 1st and 2nd groups.

Conclusion: It was shown that co-infection of HIV / hepatitis occurs in more than 1/3 of patients. The structure of HIV / hepatitis co-infection in the total cohort shows prevalence of HCV-infection. Less frequently mixed infection (HBV + HCV) and monoinfection are seen. The prevalence of chronic hepatitis B was significantly lower in patients receiving ART, which indicates the effectiveness of ART in two directions, to restrict replication of HIV and HBV. Obtained results allow more effective management of patients with HIV / HCV and/or HBV co-infection.

No conflict of interest

Abstract: 18

Treatment Issues - Hepatitis _ HIV coinfection

Effectiveness of the medicine ribonucleic acid in patients with HIV and cirrhosis C

I. Hryzhak[1], O.Y. Pryshlyak[1], M.Y. Pereklita[1]

[1]Ivano-Frankivsk national medical university, infectious diseases and epidemiology, Ivano-Frankivsk, Ukraine

Background: Viral hepatitis C is a common co-morbidities in HIV-infected individuals. In terms immunodeficiency virus C replication increases, leading to rapid progression of liver cirrhosis [Sulkowski WS, Mehta SH, Torbenson MS, at al., 2007]. The advent of potent ART has modified the main causes of morbidity and mortality in HIV-infected persons. Non-AIDS conditions are now replacing opportunistic infections and malignancies as the majority for HIV-infected patients [Deeks SG,Phillips AN, 2009]. It showed that chronic hepatitis C is the main factor responsible for the unfavourable and fatal outcome in the patients under regular medical care [Paula Tuma, Jose Medrano, Salvador Resino et al., 2010]. The low number of CD4 + T lymphocytes, male gender, older age, alcohol abuse are aggravating factors on the course of chronic hepatitis C and accelerate its progression to liver cirrhosis and hepatocellular carcinoma [Clinical protocol for diagnosis and treatment of hepatitis C in adults with HIV, MH Ukraine, 2008, p. 3]. Objective: To investigate the effect of the drug ribonucleic acid to improve the functional state of the liver in HIV-infected persons with viral C cirrhosis.

Material & Methods: Under the supervision were 24 HIV-infected persons aged 36-54 years with chronic hepatitis C viral cirrhosis classes A - 4 patients and B - 20. Functional status of liver was determined by the parameters pigment metabolism, cholestasis and cytolysis (bilirubin, alkaline phosphatase, cholesterol, prothrombin index, albumin, ALT, AST). Digital material were worked on the program Exeel using t Student's criteria for small sample.

Results: In complex pathogenetic therapy the patients received a drugs arginine glutamate (Glutargin), silymarin (Carsil), detoxification infusion therapy, veroshpiron used if the presence of ascites. In addition 12 patients who had cirrhosis classes A - 2 persons and B-10 received drug ribonucleic acid (Nuklex, producer Ukraine) 2 capsules three times a day - 30 days. In patients who received only basic therapy (12 patients with cirrhosis: A – 2 person and B – 10) functional state of the liver improved to 25-38 days of treatment - disappear ascites, jaundice decreased symptom, patients feel slightly upgraded. Some indexes were retained at elevated level: bilirubin- 86,53 ± 11,91 mmol/L, ALT -109,2 ± 13,4 U/L, alkaline phosphatase 438,17 ± 52,82 U/L, but prothrombin index (69,90 ± 3.27%) and albumin (24,08 ± 3,18 g / l) were decreased. However, in patients were treated with ribonucleic acid the symptom of jaundice decreased at the 9-15 days of treatment, the ascites significantly reduced in the same term. After the treatment the some biochemical parameters were closer to normal than in patients with the comparison group. The level of bilirubin was 45,27 ± 11,91 mmol/L, P<0,05; ALT - 69,2±8,26 IU/L, P<0,05; alkaline phosphatase - 241,54±18,72, P<0,05; prothrombin index 76,90±2,93%; albumin - 34,08±3,31 g/L, P <0,05.

Conclusion: Use the drug ribonucleic acid as a part of pathogenetic therapy of HIV-infected patients suffering from viral C cirrhosis improves the functional state of the liver.

No conflict of interest

Abstract: 19

Treatment Issues - Hepatitis _ HIV coinfection

Faster HIV progression and development of HCV coinfection among PWID in Ukraine: retrospective cohort study

T. Koval[1], T. Andreeva[2], G. Dubynska[1], O. Danilenko[3], E. Sabinina[3], K. Michajlova[3]

[1]Higher medical educational institution of Ukraine "Ukrainian medical stomatological academy, infectious diseases, Poltava, Ukraine; [2]University of KyivMohyla Academy, School of Public Health, Kiev, Ukraine; [3]Poltava regional HIV/AIDS center, epidemiological department, Poltava, Ukraine

Background: HIVrelated mortality remains high in Ukraine with about half of deaths happening due to tuberculosis. Until recently, parenteral route of transmission accounted for the majority of new HIV cases. Additionally, population of people who infect drugs (PWID) in Ukraine has high prevalence of hepatitis C. We hypothesize that HIV among PWID is characterized with disadvantageous course with increased risk of developing tuberculosis, hepatitis C and rapid progression.

Materials & Methods: Routine clinical data of 930 HIVinfected patients aged 1565 years admitted to Poltava (Ukraine) HIV/AIDS clinic in 2003-2010 were considered as a retrospective cohort and analyzed using Cox proportional hazards regression model. All patients were observed prior to ART prescription, 44% were men, and 47% had experience of infecting drugs. Outcome measures included timetodiagnosis of tuberculosis, viral hepatitis C and fourth stage of HIV infection. Time of observation was considered starting from the first positive HIV test. Route of transmission was considered a primary predictor with control of gender, age, and experience of incarceration.

Results: All three outcomes developed earlier among patients who acquired HIV due to injection drugs use compared to those with sexual route of transmission. HCV infection was found in 507 patients (82% among PWID), HR=3.5 (95%CI 2.84.4). Tuberculosis was diagnosed among 210 patients (71% among PWID and 67% among men) with HR=1.6 (95%CI 1.22.2). Fourth stage of HIV was diagnosed among 266 patients (67% among PWID) with HR=1.5 (95%CI 1.22.0). Hazards of all three outcomes increased with age, and men were more likely to develop tuberculosis than women (HR=1.7 95%CI 1.22.3). PWID demonstrated longer term between first positive HIV test and linkage to care.

Conclusions: PWID are found to be the group of HIV patients who are characterized with increases risk of HIV progression and earlier development of HCV coinfection which can lead to increased mortality. This is assumingly caused by late linkage to care and delayed ARV treatment. Emphasized HIV care and support cascade activities aimed at PWID could be an effective means to overcome the revealed peculiarities of this highrisk group.

No conflict of interest

Abstract: 20

Treatment Issues - Hepatitis _ HIV coinfection

HIV testing in chronic hepatitis C patients treated with pegylated interferon alfa2 and ribavirin

K. Fleischer-Stepniewska[1], B. Knysz[1]

[1]Wroclaw Medical University, Infectious Diseases, Wroclaw, Poland

Background: In Poland about 60% HIV-positive patients are co-infected with HCV. However, seroprevalence of hepatitis C is lower comparing with the last decade, little is known about epidemiology of HIV in chronic hepatitis C patients. Although HIV testing is recommended in newly diagnosed with HCV, this tests are missing when initiating chronic hepatitis C (CHC) treatment with pegylated interferon alfa2 and ribavirin. We sought to determine how often HIV serostatus was defined.

Material & Methods: We retrospectively analized medical records of 400 patients treated with pegylated interferon alfa (PegIFN) and ribavirin in 2003-2007 at Department of Infectious Diseases of Medical University of Wroclaw. Data starting from the first positive anti-HCV result up to the first day of CHC treatment were taken into account as long as 38 months (±35months).

Results: The study involved 400 treatment naïve patients with median age of 46 yrs. Reporting for HIV screening tests, a total of 38 (38/400, 9,5%) patients were examined, 9 women and 29 men, above 18 years of age. Not in every case of drug addiction in medical history HIV testing was performed. Patients underwent ELISA testing and Western blot if needed, as in CDC recommendations for HIV screening and testing. Results were negative in 35 cases. Two cases of HIV infection was confirmed before start of treatment: both patients were already on ART. One patient was diagnosed with HIV infection at 6th week of CHC therapy when admitted to hospital for pneumonia with pancytopenia.

Conclusions: HIV status was not being determined as a standard in all patient with chronic hepatitis C in this cohort. HIV status must be defined for safety reasons in every case when therapy with pegylated interferon alfa2 and ribavirin is planned as the lowest accepted lymphocyte T CD4 count to start PegIFN-based therapy is above 250 cells/mm^3. HIV screening tests must be performed routinely in patients with CHC to prevent HIV resistance when initiating DAAs without antiretroviral treatment. Important therapeutic issue is to prevent drug-drug interactions ART with new DAA.

No conflict of interest

Abstract: 21

Treatment Issues - Hepatitis _ HIV coinfection

Assessment of Patients with HIV/HBV Co-Infection

A. Inci[1], M. Fincanci[2], F. Soysal[2]

[1]Kanuni Sultan Suleyman Research and Training Hospital, Department of Infectious Diseases and Clinical Microbiology, Istanbul, Turkey; [2]Istanbul Research and Training Hospital, Department of Infectious Diseases and Clinical Microbiology, Istanbul, Turkey;

Background: Presence of HIV infection has an adverse influence on the natural course of HBV infection, faster progression of hepatic fibrosis demonstrated in patients with co-infection. This study was carried out to determine the incidence of HBV infection among HIV-positive patients, and to retrospectively evaluate the demographic and laboratory characteristics of patients with HIV/HBV co-infection.

Materials & Methods: A retrospective analysis of patient files for all HIV-infected cases followed-up and treated at the department of Infectious Diseases and Clinical Microbiology, Istanbul Research and Training Hospital. Among HIV-infected cases, those with HBsAg positivity and HIV/Hepatitis B co-infection were determined. Age, gender, alcohol or substance use, use of ART, CD4 levels and treatment durations were retrospectively assessed.

Results: Of the 180 HIV-infected patients evaluated retrospectively, 8 (4.4%) had HBsAg positivity. Of these 8 cases 5 were male and 3 were female, with a mean age of 45.6 years (range: 27-73 y). No patients had a history of alcohol or substance use. The mean duration of follow up was 23 months. Five patients had negative HBV DNA at presentation, while 3 had positive HBV DNA, with normal ALT levels in all subjects. Among those four cases with negative HBV DNA who had no indication for the treatment of chronic hepatitis B, ART was initiated in 4 due to low CD4 count. In three cases, treatment was commenced since HBV DNA was elevated in conjunction with low CD4. One subject, in whom treatment was not indicated on the basis of HBV DNA and CD4 levels in conjunction with the absence of AIDS-defining clinical picture, was currently being followed-up without treatment. Of the patients receiving HAART therapy, the average CD4 count at presentation was 230 cells/mm^3 vs. 379 cells/mm^3 at the end of 12 months. In three subjects with positive HBV DNA, a decrease in HBV DNA was noted after initiation of treatment. In four patients with negative DNA who received treatment, the HBV DNA negative status was found to remain, while one patient who did not receive treatment had elevated HBV DNA and decreased CD4 levels.

Conclusion: Although our sample size is relatively small, in this group of patients with HIV/HBV co-infection HAART was found to be associated with a decrease in HBV DNA in HBV DNA positive cases, absence of transition to positivity among those with negative HBV DNA, and with increased CD4 in all subjects.

No conflict of interest

Abstract: 22

Treatment Issues - Hepatitis _ HIV coinfection

Overview of hepatitis C situation in Georgia

A. Abutidze[1], K. Nelson[2], S. Gogichaishvili[3], T. Shartava[3], M. Ezugbaia[3], N. Chkhartishvili[4], L. Sharvadze[4], N. Badridze[4], T. Tsertsvadze[5]

[1]Infectious Diseases AIDS and Clinical Immunology Research Center, Epidemiology, Tbilisi, Georgia; [2]Johns Hopkins Bloomberg School of Public Health, Epidemiology, Baltimore, USA; [3]Infectious Diseases aids and Clinical Immunology Research Center, Clinical, Tbilisi, Georgia; [4]Infectious Diseases aids and Clinical Immunology Research Center, Research, Tbilisi, Georgia; [5]Infectious Diseases AIDS and Clinical Immunology Research Center, Office of Directors, Tbilisi, Georgia

Background: Globally over 180 million people are infected with hepatitis C virus. More then 350 000 people die every year from hepatitis C related end-stage liver disease. Hepatitis C is the serious health problem in Georgia and is considered as one of the priority directions of healthcare system.

Material & Methods: We reviewed available literature including surveillance data, study reports and peer reviewed publications to describe hepatitis C situation in Georgia. One population based study was conducted from 2000 to 2002 and several surveys were conducted among most at risk populations from 1997 to 2012. Hepatitis C is a reportable disease to National CDC (NCDC).

Results: Population based survey showed that among adult general population the prevalence of hepatitis C was 6.7%. The same study identified that injection drug use was a major risk factor for hepatitis C seropositivity. Studies among most at risk populations showed, that the highest prevalence of hepatitis C was seen among injection drug users (IDUs) ranging from 62 to 90% in various time periods. HCV is common in HIV-infected patients. Analysis showed that nearly half of HIV patients in Georgia are co-infected with HCV (49%), with the highest prevalence among HIV positive IDUs – 73%. Distribution of HCV genotypes showed changing pattern over time. According to population based survey, the most common HCV genotype was genotype 1 (59%), followed by genotype 3 (27%) and genotype 2 (11%). Data from approximately 2000 HCV patients accessing care at Infectious diseases, AIDS and Clinical Immunology Research Center in 2010-2013, showed that HCV genotype 1 was found in 43% of patients, HCV genotype 3 and 2 were detected in 32% and 24% of patients respectively. There are very few cases of genotype 4 detected in the country. All modern HCV diagnostic methods and treatment approaches are implemented in Georgia. However, access is limited because of economic reasons.

Conclusion: Hepatitis C prevalence in Georgia is high, particularly among IDUs. There is need of updated data on HCV burden, including information on HCV related morbidity and mortality. Although government of Georgia made steps towards affordability of HCV treatment, additional efforts are needed to increase access to treatment including novel medications.

No conflict of interest

Abstract: 23

Treatment Issues - Hepatitis _ HIV coinfection

Loss of HBsAg in HIV/HBV Coinfected Patient with High HBV DNA Treated with Pegylated Interferon : A Case Report

A. Gunduz[1], A. Bas Oncul[1], D. Yildiz Sevgi[1], A. Hamidi[1], A. Konuklar[1], N. Uzun[1], I. Dokmetas[1]

[1]Sisli Etfal Training and Research Hospital, Department of Infectious Diseases and Clinical Microbiology, Istanbul, Turkey; [2]Gilead Sciences Turkey, Medical Affairs, Istanbul, Turkey

Background: Worldwide, approximately 4 million people are HIV/HBV coinfected. The prevalence of chronic hepatitis B (CHB) infection in individuals with HIV varies between 5 and 20% in different parts of the world. Coinfection with HBV and HIV is accompanied by an increased risk for liver related morbidity and mortality compared with monoinfection if left untreated. Most of the guidelines advocate starting highly active antiretroviral therapy (HAART) including nucleos(t)ide as part of it if the patients meet the criteria for CHB treatment even in cases with high CD4 count. Pegylated interferon alfa treatment is favored in patients with CHB infection gynotype A, low HBV DNA and high ALT levels.
We report the case of a 25-year-old homosexual man presenting with positive HIV-1 serology at first observation in March 2011. The laboratory tests showed HIV RNA 88.000 copy/ml, CD4 count 770/mm^3 , elevated liver enzymes with alanine aminotransferase (ALT) at 90 IU/ml and aspartate aminotransferase (AST) at 60 IU/ml. He was positive for HBsAg, HBeAg, anti-HBc and negative for anti-HBe, anti-HBs, anti-HDV. HBV DNA was 500.000.000 IU/ml. Anti-HAV total was positive and anti-HCV negative. The patient was followed for 96 weeks and didn't receive any HAART. The transaminases fluctuated between 1.5-2 folds of the upper normal limit.
The HBV DNA level reached 1.500.000.000 IU/ml. Liver biopsy was performed and it revealed Ishak fibrosis score:2 with histology activity index:7. HIV RNA level was 76.000 copy/ml and CD4 count 730/mm^3. Pegylated interferon alfa 2a 180 mcg weekly was initiated for 48 weeks. At week 4, 12 and 24 HBV DNA levels dropped by 0.5,1 and 3 logs respectively. At week 48 HBV DNA level was below the detectable level 20 IU/ml with HBsAg loss without any seroconversion. ALT was 23 IU/ml and AST 27 The HIV RNA was 883 copy/ml. Twelve months after stopping treatment the patient still had undetectable HBV DNA, negative HBsAg, HBeAg and normal transaminases.

Conclusions: The lower probability of spontaneous loss of HBeAg and HBsAg in HIV/HBV coinfected patients is due to impaired host innate and addaptive immunity. In this patient who had high CD4 counts a sustained virological response was achieved. These findings suggest that pegylated interferons might be a good choice especially in HIV/HBV coinfected very slow progressors, elite controllers and in patients not suitable for antiretroviral therapy

No conflict of interest

Abstract: 24

Treatment Issues - Hepatitis _ HIV coinfection

Overview of HIV Situation in Georgia

M. Tsintsadze[1], A. Abutidze[2], O. Chokoshvili[2], K. Shermadini[2], T. Tsertsvadze[3]

[1]Infectious Diseases AIDS And Clinical Immunology Research Center, Epidemiology, Tbilisi, Georgia;
[2]Infectious Diseases aids And Clinical Immunology Research Center, Epidemiology, Tbilisi, Georgia;
[3]Infectious Diseases aids And Clinical Immunology Research Center, HIV/AIDS, Tbilisi, Georgia

Background: Since the first case of HIV was detected in Georgia the number of annually detected cases has risen steadily. Overall, the country has a low HIV prevalence with 0.07% in the general population. However, HIV prevalence is higher in the capital city and the port city Batumi. High risk groups of population, such as men who have sex with men and injecting drug users show higher HIV prevalence – bio-behavioral surveillance surveys from 2012 found respectively 13% and 3%. By December 31, 2014 a total of 4695 HIV cases were registered at the Infectious Diseases, AIDS and Clinical Immunology Research Center, with an estimated total number of people infected with HIV around 6,400 (Spectrum EPP).

A total of 564 new HIV cases were reported in 2014. The majority of patients were within the age group of 25-49. Among the registered cases the majority were men (73%) and 64% were infected through unprotected sexual contact. Recent trends indicate increase in the proportion of sexually acquired infections.
In 2014, 59% of newly identified HIV infected people had a CD4 count of <350cells/mm^3, and 41% of these had a CD4 count of <200 cells/mm^3.

Conclusions: The major challenge in the HIV epidemic in Georgia is a very high proportion of late presentation for care. Scaling up testing activities is crucial in order to tackle the HIV epidemic in the country. It is crucial to strengthen provider initiated testing and support the implementation of indicator condition guided HIV testing.

No conflict of interest

Abstract: 25

Monitoring and Diagnostic Tools

Epidemiology of Viral Hepatitis C in Donetsk Region of Ukraine

I. Zaytsev[1], V. Potiy[2], V. Miroshnichenko[2], V. Kirienko[2]

[1]National Medical University, Infectious Diseases, Kyiv, Ukraine; [2]National Medical University, Infectious Diseases, Donetsk, Ukraine

Introduction: For planning of National Program for management of viral hepatitis it's extremely important to know exact data about spread of viral hepatitis, prevalence of different genotypes (g) and part of patients with advanced fibrosis and cirrhosis. There aren't such data in Ukraine. The goal of this study is to describe an epidemiology of chronic hepatitis C (CHC) and to determine features of natural history of it in Donetsk region.

Materials & Methods: 581 cases of history of patients with acute hepatitis B (AHB) or C (AHC), who were patients of Central State Hospital of Donetsk from 2005 until 2010, were analyzed. Also results of patients with CHC, who appeared to Donetsk Center of Viral Hepatitis (DCVH) first time, were analyzed: genotyping (n=667) and results of non-invasive tests for fibrosis (FibroTest, n=606). A data about possible ways of transmission were collected with help of anonymous questionnaire (167 patients with CHB and 115 patients with CHC).
Results: 1,4% cases of AHB or AHC were among patients from 16 to 45 years old (63,3% - from 16 to 30 years). It's known, that approximately 5% of AHB cases and 50-80% of AHC cases transform to chronic form of the disease after 6 months after acute hepatitis onset. So, age distribution of acute and chronic disease is very similar. Thus the most cases of viral hepatitis in Donetsk region started during young age. It's not accidentally: prevalence ways of transmission of the disease among analyzed patients were: drugs (9,6% during HBV and 11,3% during HCV), non-medical parenteral invasions (22,8% and 25,2% respectively), and sexual transmission (39,5% and 18,3% respectively).
We thought that the HCV g1 is the most spread in Ukraine, but due to our data only 51,3% of patients have this type of virus (50% subtype 1b). Further – the g3 (40,4%) and the g2 (8%). The HCV g4 have only 0,3% of patients.
Due to FibroTests F3/F4 have 11% of HBV patients and 20% of HCV patients. A part of patients with F1 (16%) and F0 (33%) are unexpectedly high. Men have advanced damage of liver more frequently (26% vs. 12% respectively).
An age of patient correlates with probability of advanced liver damage. If patient is young (16-30 years old), a probability of F3/F4 is 15%. If elder than 60, a probability of F3/F4 is 68% (22% - F3 and 46% - F4). The average age of patients of DCVH is 40,99±0,3 years (n=1957). According our data the progression of the disease from previous to next stage takes 4-6 years.

Conclusions: the most cases of viral hepatitis in Donetsk region started during age from 16 to 30 years. A part of patients with the 1 genotype is 51%, instead 70% we had thought before our study. Approximately one third of patients with advanced fibrosis or cirrhosis require immediate treatment.

No conflict of interest

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Monitoring and Diagnostic Tools

Viral hepatitis in HIV-infected in Ternopil region

O. Ivakhiv[1], M. Andreychyn[1], N. Vasylieva[1], V. Nosko[2], N. Pankiv[2], T. Burtnyak[2], I.A. Iosyk[1]

[1]Ternopil State Medical University, Department of Infectious Diseases, Ternopil, Ukraine; [2]Regional center prevention and control of AIDS in Ternopil, Regional center prevention and control of AIDS in Ternopil, Ternopil, Ukraine

Ukraine is the country worst affected by HIV/AIDS in Europe. An estimated 238,000 people aged 15-49 are living with HIV/AIDS – 0.62 per cent of the adult population as of beginning of 2013. Under medical supervision in a regional center for prevention and control of AIDS were 737 HIV-infected persons, 215 (29.2%) patients were registered viral hepatitis, including the hepatitis C 199 (92.5%), hepatitis (B+C) 12 (5.6%), hepatitis B – 4 (1.9%).
HIV infection was diagnosed on the basis of laboratory testing (HIV markers detected in ELISA), viral hepatitis HBsAg and anti-HCV (ELISA, PCR). The patients' age were from 25 to 54 on average (34,36±0,36) years. There were 148 (68.8%) male and 67 (31.2%) female. I-II clinical stage of HIV infection (Z21) diagnosed in 124 (57.7%) patients with hepatitis B, in 5 of 12 (41,7%) patients with hepatitis (B+C), in 115 of 199 (57,8%) – hepatitis C. Accordingly, III and IV clinical stage of the disease (B20) were registered in 91 (42.3%) patients, there were no patients with hepatitis B, 7 (58,3%) with hepatitis (B+C) and 84 (42 2%) patients with hepatitis C.
Study viral hepatitis and HIV transmission, among the observed patients allowed us to establish that parenteral infection (due to drug users) were considered in 151 (70.2%) patients, 1 of 4 (25.0%) patient with hepatitis B, 9 of 12 (75.0%) patient with hepatitis (B+C), 141 of 199 (70.8%) patient with hepatitis C. There were not found any indications of parenteral intervention in 64 (29.8%) patients, tattoos, so in these cases was assumed as sexual transmission. Only in one case was found homosexual contact. The 67 women were currently under medical observation in 13 (19.4%) were first diagnosed HIV during pregnancy, and 5 of them (38.5%) had problems in the family, their husband were drug users. At the same time, 6 (28.6%) of 21 pregnant belong to drug users and some of them received methadone substitution therapy. Only at one case of hepatitis (B+C) were diagnosed previous HIV infection and in 3 cases in 1,5-8 years after, others hepatitis (regardless of etiology) were discovered during a routine examination of HIV infected at the same time or even during the follow-up. 115 patients receiving HAART, with hepatitis B – all patients, half of them with hepatitis (B+C), 105 patient with hepatitis C.
Antiviral therapy of viral hepatitis has not received anyone, only 4 patients with hepatitis (B + C) + 8 of the hepatitis C were treated by pathogenetic therapy. 26 persons with AIDS died in 2014, 12 of them (46.1%) were with co-infection HIV+hepatitis, but the main cause of death in 2 patients were cirrhosis, in 4 – encephalopathy, in 6 – tuberculosis, in 2 – toxic hepatitis.Co-infection HIV/AIDS remains as actual problem, patients need purposeful treatment of hepatitis.

No conflict of interest

Abstract: 27

Monitoring and Diagnostic Tools

Decision support system for predicting of adverse effects in patients with HIV

A.I. Piddubna[1], M.D. Chemych[1]

[1]Sumy State University, Department of Infectious Diseases and Epidemiology, Sumy, Ukraine

Background: Success of many diagnostic and treatment processes are inextricably linked to the use of computerized technology on the current stage of medicine development. The aim of the present study was to create the decision support system (DSS) to predict the risk of adverse effects in persons with HIV/AIDS.

Materials & Methods: We used immunogenetic markers as prognostic criteria in patients with HIV infection in alternative serial

Wald analysis, which allows summarize the individual prognostic indexes (PI) and when it reaches a threshold value with a certain probability argues about the character of the disease progression. Training matrix classes had between 12 and 61 realizations, which consisted of 8 recognition features: serum levels of IL-10, TNF-α (pg/ml), absolute number of CD4+ T lymphocytes (cells/μL); determination of IL-10 and TNF-α genes genotype. Algorithm of functioning of the proposed DSS was based on the initial immunogenetic parameters values and the intersection of recognition classes characterizing the functional state of the disease process.

Results: In predicting of adverse outcomes in persons with HIV we determined that reliable modulators of severe CNS lesions were minor carrier genotype of IL-10 gene, heterozygous variant of TNF-α gene, high levels of IL-10 and TNF-α in case of severe immunodeficiency. Prognostic index of these parameters was -15.32, corresponding up to 95 % of implementation forecast of organic CNS lesions in people living with HIV. The most unfavorable indicators of the risk of pulmonary tuberculosis can be regarded as a combination of heterozygous variant of IL-10 gene, homozygous major allele variant of TNF-α gene, serum levels of IL-10 (≥10.0 pg/ml) and TNF-α (≥1.0 pg/ml), T-helpers count ≤200 cells/μL (PI=-15.12, CI >95 %). Prognostic significance of risk factors for extrapulmonary tuberculosis in patients with HIV infection were generally similar to modulator of pulmonary tuberculosis: carrier of C/A genotype of IL-10 gene, G/G genotype of TNF-α gene, high levels of cytokines in combination with severe immunosuppression (PI=-11.32, CI >90 %). Implementing prognosis of herpesviral infections were determined by the combination of IL-10 gene homozygous major allele variant and heterozygous TNF-α gene variant with high cytokine production and low values of CD4+ cells (PI=-10.26, CI >90 %).

Conclusions: The proposed mathematical model of the DSS may be offered for use in clinical practice to determine the risk of opportunistic infections in persons with HIV/AIDS and can better anticipate unintended consequences taking into account the individual immunogenetic features.

No conflict of interest

Abstract: 28

Monitoring and Diagnostic Tools

Epidemiological aspects of viral hepatitis incidence in the north-eastern regions Ukraine

N.G. Malysh[1]

[1]*Sumy State University, Department of Infectious Diseases and Epidemiology, Sumy, Ukraine*

Background: Viral hepatitis are widespread pathology among the population. In most cases the disease is asymptomatic and only in 3-5 % an acute clinically apparent disease develops. Treatment of hepatitis is long-lasting and costly, chronic course can last a lifetime. The aim of the research was to establish the incidence of viral hepatitis in the north-eastern Ukraine, identify areas of preventive and anti-epidemic measures.

Materials & Methods: A retrospective analysis of the viral hepatitis incidence in Sumy region in 2005-2014 years was carried out using data from branch statistical reports. Statistical processing of the obtained results was performed using conventional parametric statistical criteria.

Results: It has been found that the population incidence of acute viral hepatitis A and B in the study period fell by 11.6 and 2.8 times respectively and was within the range of 5.6-73.8 and 3.1-8.5 per 100 thousand of population. The incidence of acute hepatitis C varied from 0.9 in 2005 to 2.1 per 100 thousand of population in 2014. Change of the viral hepatitis incidence structure calls attention to itself. Thus, provided that almost 5 cases of acute viral hepatitis B and 35 cases of viral hepatitis A accounted for 1 case of acute viral hepatitis C in 2005, then in 2014 the ratio changed and amounted 1: 2.1: 3.8 respectively. Incidence of the chronic viral hepatitis in Ukraine has started to be recorded since 2008. In the period of 2008-2014 a detection frequency of chronic viral hepatitis B was within the range 9.3-22.0 per 100 thousand population, chronic viral hepatitis C – 18.9-31.3.
In epidemic foci the frequency of isolation of HBV was – 2.4 %, HCV – 4 %. In 1 and 1.6 % of contact persons respectively, of chronic

hepatitis C – 2.8 % sought medical care for acute and chronic hepatitis B.

Conclusions: Under the current conditions the incidence of viral hepatitis A is observed in Sumy region. Epidemic process of viral hepatitis B and C is characterized by decline in acute nosological forms and growth of chronic viral hepatitis. Indicators of the actively identified subclinical forms of parenteral hepatitis exceeded manifest level more than by 200 times. Given that only hepatitis B can be warned among parenteral hepatitis by carrying out vaccine prevention, reduction in the burden of the disease can be achieved by measures of nonspecific prevention.

No conflict of interest

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Monitoring and Diagnostic Tools

Cytokines serum levels influence immunodeficiency in HIV-infected persons

M.D. Chemych[1], A.I. Piddubna[1]

[1]Sumy State University, Department of Infectious Diseases and Epidemiology, Sumy, Ukraine

Background: Cytokines are involved in controlling the homeostasis of the immune system in HIV infection/AIDS patients. The measurement cytokines in plasma in people with HIV may provide additional information to complement prognostic markers and understand disease procession. We aimed to determine the IL-4, IL-10 and TNF-α profiles in Ukrainian HIV-infected individuals with different CD4 T-cell levels and hypothesize that elevated plasma cytokine levels are associated with severity of immunodeficiency and influence to pathogenesis of HIV infection.

Materials & Methods: We examined serum levels of IL-4, IL-10, TNF-α among 118 HIV-infected European Ukrainians (68 % male, 32 % female; age at diagnosis (32.61±0,87) years), and 30 healthy controls using ELISA. Patients were divided into groups depending on the levels of CD4 T lymphocytes. Group I included 52 people with T-helper cell counts ≥350 cells/μL, group II – 66 patients with T-helper cell counts ≤200 cells/μL.

Results: In the cytokine profile of HIV-infected people the increased levels of pro-inflammatory cytokine TNF-α compared to controls (group I – (0.77±0.08), group II – (2.34±0.69), healthy controls – (0.51±0.32) pg/mL, $p<0.05$) and the anti-inflammatory IL-10 (group I – (3.99±0.99), group II – (20.08± 0.44), healthy controls – (1.68±0.32) pg/mL, $p<0.001$) were demonstrated. No significant difference in IL-4 between surveyed troops and comparison group was found (group I – (0.54±0.08), group II – (0.68±0.07), healthy controls – (0.81±0.07) pg/mL, $p>0.05$). Patients with CD4 T lymphocyte levels ≤200 cells/μL showed significantly higher plasma concentration of TNF-α and IL-10 compared with the group I ($p<0.05$), which leads to the existence of deep imbalance of immune response in the later stages of the disease. Among HIV-infected from group II mean serum concentrations of TNF-α higher than that of group I in 3 times ($p<0.05$). A significant increase in the concentration of IL-10 detected in patients with severe immunodeficiency (IL-10 levels in group II was 5 times higher, $p<0.05$), which may indirectly indicate a more active involvement of IL-10 during disease progression. In favor of this assumption also indicates strength of correlation in patients of group II between the concentration of this cytokine and the index of opportunistic infections compared with TNF-α (IL-10: $r=0.23$, $p<0.05$; TNF-α: $r=0.21$, $p<0.05$); severity of the disease (IL-10: $r=0.43$, $p<0.05$; TNF-α: $r=0.25$, $p<0.05$).

Conclusions: HIV-infection is associated with an increase in serum levels of TNF-α and IL-10. Immune imbalance due to changes in concentrations of cytokines is more pronounced in HIV-infected persons with severe immunodeficiency with CD4 T lymphocyte counts ≤200 cells/μL.

No conflict of interest

Abstract: 30

Monitoring and Diagnostic Tools

Cognitive dysfunction as a complication chronic viral hepatitis

I.S. Chaika[1], O.M. Chemych[1], M.D. Chemych[1], A.I. Piddubna[1]

[1]Sumy State University, Department of Infectious Diseases and Epidemiology, Sumy, Ukraine

Background: Development of cognitive dysfunction and neuropsychiatric dynamics of patients with chronic viral hepatitis (CVH) was investigated during treatment.

Materials & Methods: It was analyzed 140 medical records and examined patients with CVH aged (47.2±3.9), the probable duration of the disease (5.8±0.9) year. There were 35 women and 105 men. Cognitive impairment was detected using neuropsychological research - test Mini-Mental State Examination (MMSE); neuropsychological tests - clock drawing test, verbal Association (TVA); general disorders scale (GDS), Hamilton Depression Scale (HDS) and Clinical Dementia Rating Scale (CDR).

Results: As a result of MMSE cognitive disorders of mild to moderate character (27.01±0.27) points (B) were found, and 15% of people had no abnormalities. The average index HDS - (10.32±0.4) B, mild depressive disorders were diagnosed in 26% of those, moderate - 3%. Using TVA it was obtained (10.43±0.28) B, that indicated a violation of semantic memory and ability to focus quickly. On a scale GDS, clear symptoms of cognitive dysfunction was observed in 24% of patients, other patients had very light disorders (65%) or normal levels (11%). According to the results of the clock drawing test it was found that 93% of patients performed the test without errors and only 7% did not fulfill it. Indicator CDR was (0.65±0.11) B, 68% of the patients received normal result or had borderline disorders, 29% - light violations, 3% - moderate violations. A direct correlation between results of MMSE scale and HDS with period of the disease ($p < 0.05$) was set. Changes of cognitive functions in people who used drugs in history ($p < 0.05$) were detected.

Conclusions: In the performance of MMSE in patients with CVH it was detected violations of mild to moderate degrees (violation of various sleep phases, poor memory and concentration) among depressive disorders prevalent. Among the identified violations of depressive disorders it was more common mild to moderate degrees (HDS). Results for GDS scale indicate light memory impairment. A direct correlation between results of MMSE scale and HDS with period of the disease ($p < 0.05$) was set. Statistically worse cognitive performance were in people who use drugs in history ($p < 0.05$). Due to the identified changes in the psycho-neurological status of patients with CVH is obvious there is need for detailed, regular and dynamic survey.

No conflict of interest

Abstract: 31

Monitoring and Diagnostic Tools

Part of aids-patients among newly detected hiv-infected

N. Zavidnyuk[1], N. Nychyk[1], O. Hrubska[1]

[1]Ternopil State Medical University, Infectious Diseases, Ternopil, Ukraine

Background: One of the most important questions of XXI century medicine is HIV infection. Every year in the world are infected about 2.7 million people. Ukraine has one of the highest rates of the epidemic in Europe.
To study the proportion of patients with newly diagnosed AIDS among HIV-positive, and determining the ratio between the period from 2000 to 2014.

Materials & methods: a comparative statistical analysis of the number of newly diagnosed HIV-positive and AIDS patients under the materials of Ukrainian Control Center for socially dangerous diseases of Ukrainian Ministry of Health (newsletters N 35-42).

Results: In 2000 it was discovered 6216 HIV-positive, of which - 648 AIDS patients (diagnosis is put the first time), accounting for 10.42% of all detected HIV-infected. The number of newly diagnosed HIV-positive increased with each passing year, and the part of patients on III-IV stage of AIDS. In 2005, the percentage of patients already was 30.61% (from 13786 new cases of HIV infection - 4220 were already sick with AIDS), which exceeded the corresponding index in 2000 almost tripled ($r \leq 0,05$).
During the following years (2006-2008) despite the increasing of virus-carriage cases in the population, the proportion of AIDS patients with newly diagnosed was declined and in 2009 was 22.38% (from 19859 newly diagnosed HIV-infected the patients were 4446). However, the positive trend is not entrenched and the following year was marked by a significant increase in both the number of new HIV infections and the proportion of patients among them. As of July 1, 2014 the number of newly diagnosed HIV-positive was 10777, including 5459 (50.65%) - the new AIDS-patients.

Conclusions: Since 2000, the annual growth of HIV-carriers (except 2012) is observed. The proportion of AIDS-patients among the newly diagnosed HIV-positive during this period increased on 40.23 %. Thus, despite improving diagnosis of HIV/AIDS, the disease manifests itself mainly in stage III-IV, which leads to the searching of new, affordable and effective screening methods of population.

No conflict of interest

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Monitoring and Diagnostic Tools

Features of mineral metabolism disorders in patients Co-infected with HIV/HCV

K. Iurko[1], V. Kozko[1]

[1]Kharkov national medical university, infectious diseases, Kharkov, Ukraine

Background: Hepatitis C virus (HCV) and human immunodeficiency virus (HIV) are characterized by their wide distribution and ability to cause health disorders of the working population, thus causing significant morbidity and mortality worldwide. Chronic hepatitis C is observed in 60-70% of HIV-infected individuals, due to the common modes of transmission of viruses. Co-infection with HIV/HCV is an important public health problem, since viruses, acting synergistically accelerate the progression of liver disease. HIV accelerates the progression of chronic hepatitis C to cirrhosis and hepatocellular carcinoma, thus increases 'liver' mortality.
Trace elements have a significant impact on the metabolic processes in the body and have a close relationship with the enzymes, hormones, vitamins and other biologically active compounds. The content of trace elements in the blood is a valuable diagnostic feature in many pathological conditions. Insufficient knowledge of their content in patients co-infected with HIV/HCV proves the feasibility of studying their role in the pathogenesis of this disease.

Materials & Methods: Study on the work carried out at the Department of Infectious Diseases of Kharkiv National Medical University, located at the Regional Clinical Hospital of Infectious Diseases of Kharkiv and Kharkiv regional center for prevention and control of AIDS.
The content of trace elements (copper (Cu), iron (Fe) and zinc (Zn)) in serum were determined by atomic absorption spectrophotometry. Features of mineral metabolism were studied in 99 patients: 32 patients with chronic hepatitis C, 34 HIV-infected patients and HIV and 33 patients co-infected with HIV/HCV. The age of patients ranged from 20 to 52 years old. The comparison group consisted of 32 healthy subjects. Blood samples were taken for the study after signing the informed consent of the patients.

Results: Patients with chronic hepatitis C when compared to the control group, showed a reduction in the content of Zn, haptoglobin, increase Cu, Fe and ceruloplasmin. In patients with HIV infection and co-infection with HIV/HCV a reduction of these trace elements (Zn, Cu, Fe) and acute phase proteins (ceruloplasmin, haptoglobin) was established.
In patients co-infected with HIV/HCV when compared with HIV infection only revealed a lower level of Zn ($p<0.001$), and lower content

of ceruloplasmin and haptoglobin. Patients co-infected with HIV/HCV, compared with a group of chronic hepatitis C have lower values for all parameters ($p<0.001$). From this it follows that HCV-infection potentiates microelement disorder manifestations in patients with HIV infection.

Conclusions: Comprehensive assessment of the degree of deviation from the control indices of the content of trace elements and activity of metal dependent acute phase proteins showed that it was typical for patients co-infected with HIV/HCV, and also higher than that of HIV-infected patients with a factor of 1.2 and 2.2 times greater than levels in chronic hepatitis C patients.

No conflict of interest

Abstract: 33

Monitoring and Diagnostic Tools

Molecular-genetic analysis of HCV and HIV in HIV/HCV co-infected patients living in Grodno region of Belarus

N. Matsiyeuskaya[1], V. Tsyrkunov[1], V. Eremin[2], E. Gasich[2]

[1]Grodno State Medical University, Department of infectious diseases, Grodno, Belarus; [2]Republic Scientific And Practical Center Of Epidemiology And Microbiology, Department of HIV infection and assosiated diseases, Minsk, Belarus

Background: Prevalence of HCV-infection among HIV-infected European patients according to WHO is 40% on the average. In Eastern and Southern Europe it is higher (47,7 and 44,9%, respectively) than in Northern Europe (24,5%) as there are more IDU in the first two regions.
In the Republic of Belarus HIV/HCV co-infection is one of the most widespread HIV associated infections, making up 40-50% in different regions of Belarus.
The aim of the research is to detect prevalence and phylogenetic relationship of various HCV genotypes and HIV subtypes in patients with HIC/HCV co-infection living in Grodno Region of Belarus.

Material & Methods: Samples of blood plasma were taken from 36 HIV/HCV co-infected patients for the analysis of phylogenetic relationship between HCV genotypes. HCV RNA was extracted from these samples using a kit «RNA-sorb» (CRI of epidemiology, Russia) in accordance with instructions. To compare genetic sequences software «Clustal W» was used. HIV subtypes with phylogenetic relations were detected in 35 patients using RT-PCR module of the commercial test-system «Corbet Research». Sequencing of the purified fragments were performed in the genetic analyzer «ABI Prism 3100 Avant» («Applied Biosystems», USA). Design and synthesis of primer pairs to HIV gag and env genes was performed using GenBank database and nucleic acid synthesizer Expedite 8900, USA. Phylogenetic analysis of nucleotide sequence was performed using software «Mega 4» (trees were constructed with neighbor-joining method).

Results: According to molecular-genetic HCV analysis in 36 HIV/HCV co-infected patients 19 (52,8%) samples belong to 3a genotype, 6 (16,6%) – to 1b, 11 (30,6%) corresponded to 1a genotype. Nucleotide p-distances inside each group made 0,06; 0,08; and 0,02 for 3a, 1b and 1a genotype, respectively. All the samples, corresponding to 1a, 1b and 3a genotypes were clustered around standard samples, obtained from GenBank, and formed several phylogenetic groups, indicating one source of their origin. According to molecular-genetic HIV analysis in 35 HIV/HCV co-infected patients all 35 samples were positive for env gene and 33 (94,3%) belonged to A subtype, prevalence of which at present is 80-85% throughout Belarus; 2 samples belonged to B subtype. Mean evolutionary p-distance inside nucleotide HIV sequences for all examined samples belonging to A subtype made 0,04 for gag gene and 0,13 – for env gene, which indicates a prolonged circulation of the same strains throughout the country.
In phylogenetic analysis of 22 gag gene positive samples it was detected that 21(95,5%) of them belong to A subtype, forming joint phylogenetic group together with reference samples from Russia and Ukraine; 1 (4,6%) sample corresponded to B subtype. Considering gag gene this sample belonged to A subtype. Ma-ul sample belonged to B subtype according gag and env gene.

Conclusion: In Grodno region among HIV/HCV co-infected patients 3a and 1a HCV genotypes and HIV A subtype prevail. Appearance of recombinant HIV AB form and HIV B subtype indicates virus introduction from other regions of the republic and certain countries; it requires constant molecular-genetic monitoring of HIV prevalence in wider patient groups.

No conflict of interest

Abstract: 34

Monitoring and Diagnostic Tools

Il-28B as a pre-treatment predictor of therapy effectiveness in children with chronic hepatitis C

M. Pluta[1], M. Aniszewska[1], B. Kowalik-Mikolajewska[1], M. Marczynska[1]

[1]Hospital for Infectious Diseases, Department of Children's Infectious Diseases Medical University of Warsaw, Warsaw, Poland

Background: Hepatitis C in children is mostly mild or asymptomatic but can lead to liver cirrhosis and hepatocellular carcinoma. Therapy consists of pegylated interferon and ribavirin. Early Viral Response (ERV) is associated with therapy effectiveness and is defined as an undetectable HCV RNA (cERV) or a greater than $2\log_{10}$ decline in HCV RNA (pERV) at week 12 of treatment. Polymorphism of IL28B (rs12979860) is thought to be a realiable pre-treatment predictor of virologic response, particularly in adults infected with genotype 1HCV. The importance of this factor in children remains unknown.
The aim of the study was to assess the relationship between the polymorphism of IL28B and ERV in HCV infected children treated with PEG-INF+RIBA.

Materials & Methods: The study included 12 children chronically infected with HCV (10 vertically infected) aged 6,5-17,3 years. Genotype (GT) 1HCV was present in 9 (75%), GT 4HCV in 2 (16.6%), GT 3HCV in 1 (8.4%). Polymorphism of IL-28B was as follows: CC, CT, TT.

Results: Polymorphism CC was detected in 9/12 (75%), CT in 2/12 (16.7%), TT in 1/12 (8.3%). High baseline viral load (>600000IU/ml) was revealed in 10/12 (83%) children. cERV was present in 7/12 (58.4%) - among them 100% were CC, pERV was attained in 3 (25%): 2 with CC, 1- CT, decline of HCV RNA $<2\log_{10}$ was in 2 (16.6%): CT and TT.
The undetectable HCV RNA at week 12 of treatment was observed only in children with favourable IL28B: CC.

Conclusion: In current standard treatment (PEG-IFN+RIBA) for children the CC genotype seems to be a good prognostic factor for virologic response.

No conflict of interest

Abstract: 35

Monitoring and Diagnostic Tools

Need for Assessing Concealed HCV Recombinant strain RF1_2k/1b in Eastern European County of Georgia

M. Karchava[1], L. Sharvadze[2], L. Gatserelia[3], N. Chkhartishvili[3], N. Dvali[3], L. Dzigua[3], T. Tsertsvadze[2]

[1]Infectious Diseases Aids And Clinical Immunology Research Center, Department of Virology, Tbilisi, Georgia; [2]Ivane Javakhishvili Tbilisi State University, Faculty of Medicine, Tbilisi, Georgia; [3]Infectious Diseases Aids And Clinical Immunology Research CenterTbilisi Georgia, Department of Virology, Tbilisi, Georgia

Background: Hepatitis C virus (HCV) infection is a major health problem globally and in Georgia as well. Hepatitis C infection is one of the most serious health challenges in the country estimating for alarmingly high prevalence of 6.7% in general adult population, 70.4% in IDUs, 49% in HIV positive persons, 22% among TB patients and 10.5% among blood donors respectively.

Materials & Methods: Efforts of the Government of Georgia over the last several years increased access to and affordability of dual therapy with pegilated interferon and ribavirin (PEG/RBV). The Government is expanding its efforts to implement national hepatitis C elimination program effective on April 21, 2015 using novel treatment options namely direct acting antiviral (DAA) Sofosbuvir. Within this initiative, hepatitis C infection will be eradicated within 5-7 year period by treating all HCV infected patients. Besides the introduction of highly effective DAAs, accurate identification of HCV genotype still remains cornerstone for defining optimal treatment duration and combination with this DAA.

Results: Preliminary studies conducted in Georgia showed high prevalence of HCV RF1_2k/1b recombinant strain among mono infected patients with genotype 2. Namely, two local scientific groups have detected high rate (68-75%) of discordant genotyping results based on HCV structural (2a/2c) and non-structural (1b) genomic regions in genotype 2 patients, which was further confirmed by sequencing and phylogenetic analyses of these discrepant samples.
More interestingly, overall SVR rate of HCV genotype 2 mono and HIV co- infected patients treated by 24 week PEG/RBV protocol, have inferior success rates (68 and 47%) than reported worldwide. Such SVR rates among easy to treat genotype 2 group can be attributed by infection of these patients by RF1_2k/1b strain. In addition, preliminary evidence on DAA treatment outcomes among HCV RF1_2k/1b patients indicates that these strains may affect response to DAAs as well, namely treating this strain as genotype 1 may be more effective.

Conclusions: Since adequate identification of the HCV genotype is still considered as the basis for DAA regimen selection, its identification based solely on one genomic region may lead to the underestimation of RF1_2k/1b recombinant strain.
Accurate identification of RF1_2k/1b recombinant strain with subsequent treatment selection will lead successful implementation of national hepatitis C elimination program in the country.

No conflict of interest

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HBV or HCV co-infected HIV Patients in Istanbul, Turkey

F. Tabak[1], R. Ozaras[1], M. Yemisen[1], B. Mete[1], F. Sargin[2], A. Gunduz[3], N. Uzun[3], B. Ceylan[4], H. Kumbasar Karaosmanoglu[5], O. Altuntas Aydin[5]

[1]Istanbul University Cerrahpasa Medical Faculty, Infectious Diseases and Clinic Microbiology, Istanbul, Turkey; [2]Goztepe Education and Research Hospital, Infectious Diseases and Clinic Microbiology, Istanbul, Turkey; [3]Sisli Etfal Research and Education Hospital, Infectious Diseases and Clinic Microbiology, Istanbul, Turkey; [4]Medipol University Faculty of Medicine, Infectious Diseases and Clinic Microbiology, Istanbul, Turkey; [5]Haseki Research and Education Hospital, Infectious Diseases and Clinic Microbiology, Istanbul, Turkey;

Background: Coinfection with HBV or HCV is frequent in HIV-infected patients due to common transmission routes. There is unsufficient data from Turkey on HIV/HBV or HCV coinfections. We aimed to determine the serological profiles of HBV or HCV among HIV-infected patients in Istanbul, Turkey which is classified as low HIV endemic region.

Materials & Methods: A multicentre observational retrospective study has been conducted by ACTHIV-IST study group, including 5 centres following-up HIV patients in Istanbul. Demographic (including age, sex, transmission routes) and laboratory data (CD4 counts, HBsAg, Anti HBs, Anti HBC IgG, Anti-HCV, HCV RNA) were collected retrospectively from the patients' files and transferred to an HIV data base system.

Results: A total of 567 HIV/AIDS patients were included in this study. Four hundred twenty nine patients for all HBV markers and 567 patients for HCV markers were tested. 8.4% had HBV infection, 9.3% had been vaccinated and 16.8 % had past infection.
the prevalence of HIV/HCV coinfection was 0.8%. Most frequent route of transmission was heterosexual intercourse (64.5%), The mean CD4 counts for HIV/HCV coinfected and HIV monoinfected patients were 43.3±48.4 and 359.9±293.6 cells/mm^3, respectively (p= 0.016). Significant difference was not detected in terms of HIV RNA level between same groups

(p=0.75). IVDU rate was 75% in patients with HIV/HCV coinfection, whereas this rate was only 0.5% in HIV monoinfected patients (p<0.001).

Conclusions: In conclusion, serological profiles of HBV must be assesed among HIV-infected patients and HBV vaccination must be offered in those without HBV markers. Determination of HBV DNA should be performed in patients with isolated anti-HBc to rule out the presence of occult infection

Conflict of interest Gilead Sciences

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The Distribution of HIV-1 Subtypes in East Black Sea Region of Turkey

A. Inci[1], M. Sayan[2], S. Kaya[3]

[1]Kanuni Sultan Suleyman Research and Training Hospital Istanbul Turkey, Department of Infectious Diseases and Clinical Microbiology, Istanbul, Turkey; [2]Medical Faculty of Kocaeli University, Central Laboratory, Istanbul, Turkey; [3]Medical Faculty of Karadeniz Technical University, Department of Infectious Diseases and Clinical Microbiology, Istanbul, Turkey;

Background: Human immune deficiency virus (HIV) has two genotypes, namely The molecular subtyping studies are of clinical significance with regard to detection of the source of circulating HIV-1 as well as for the detection of newly formed CRFs. In this study, our objective was to examine the subtype distribution of HIV-1 strains isolated from HIV/AIDS patients from the Black Sea Region of Turkey and to elucidate the circulatory dynamics of these subtypes.

Materials & Methods:A total of 12 HIV-1 positive patients followed-up at the Departments of Infectious Diseases and Clinical Microbiology, Artvin State Hospital and Karadeniz Technical University between August 2012 and February 2014 were included in this study. Plasma samples were obtained from the patients. HIV-1 RNA was detected using 'QIAsymphony SP/*Artus* HIV-1 QS-RGQ Kit' (QIAGEN GmbH, Germany), 'COBAS Ampliprep/COBAS TaqMan HIV-1 Test' (Roche Molecular Systems, USA) and 'Abbott M2000 SP/Abbott Real-Time HIV-1 Amplification Kit' (Abbott Molecular Inc. USA) isolation platforms and kits. Distribution of HIV-1 subtypes was ascertained phylogenetically using the 'neighbor-joining' methodology.

Results: The subtype distribution among our patients was as follows: CRF 01-AE %50, A1 %25, B % 8 CRF 03-AB %9, CRF 08-BC %8, with A-1, CRF 01-AE and CRF 03-AB subtypes accounting for 84% of all cases.
Conclusions:The HIV-1 subtypes determined in the Black Sea Region of Turkey are significantly different from those reported in other geographical locations in Turkey. This distribution is ascertained either as an A1 within subtype B category or as the presence of an A subtypes within a CRF combination. The HIV-1 distribution in the Black Sea region is similar to those reported in the border countries (Georgia, Russia, Ukraine, Azerbaijan, Armenia), suggesting that the route of transmission involves these reservoirs.The distribution of HIV-1 subtypes in the Black Sea Region may contribute to the efforts aiming at infection control and developing appropriate health policies.

No conflict of interest

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The non-invasive liver fibrosis assessment in patients with hereditary deficiencies of coagulation factors and HCV infection

M. Kucharska[1], A. Szymczak[1], W. Rymer[1], M. Inglot[2], M. Inglot[1]

[1]Wroclaw Medical University, Department of Infectious Diseases Hepatology and Acquired Immune Deficiencies, Wroclaw, Poland; [2]Wroclaw Medical University, Department of General and Pediatric Radiology, Wroclaw, Poland

Background: The high percentage of patients with deficiency of coagulation factors, who received blood-derived products before the year 1991, became infected with the hepatotropic viruses, particularly HCV. Approximately about 70% of patients with hemophilia are HCV-positive. With development of non-invasive methods of liver fibrosis assessment, the posibility to accurately evaluate the fibrosis stage in patients with contraindications to liver biopsy appeared. The aim of the study was to analyse liver fibrosis in patients with deficiencies of coagulation factors and presence of anti-HCV antibodies.

Material & Methods: 71 subjects, born before 1990, with hereditary deficiency of coagulation factors and HCV infection, diagnosed based on presence of anti-HCV antibodies were enrolled to the study. Among them males were 94,36% (n=67), mean age was 38,7 ± 12,8 years (range 19-71). 60 subjects (84.5%) had hemophilia A, 5 (7%) - hemophilia B, 6 (8,45%) had von Willebrand's disease or other clotting factors deficiencies. Severe hemophilia was present in 84,5% (n=60). Serological tests for blood-borne viruses (HBsAg, anti-HBc anti-HBe, anti-HCV, HIV Ag/Ab, anti-EBV, anti-CMV, anti-HTLV I/II, anti-HGV, anti-TTV) and PCR tests assesing HCV and HBV viremia in patients with anti-HBc and anti-HCV antibodies, were performed. Liver fibrosis was assessed using non-invasive methods: FibroTest and elastography SWE (Aixplorer®), using Metavir score.

Results: HCV RNA was positive in 29 subjects (40,8%), among them 7 patients underwent ineffective treatment with IFN/RBV, one subject was during therapy. In the group with undetectable HCV RNA, 50% were subjects post effective IFN/RBV treatment, the other 50% had spontaneously eliminated HCV. HCV genotype 1 was predominant (57.69%), 34.61% of subjects were infected with genotype 3 and 7.69% with genotype 4. Any markers of HBV infection were detected in 53 subjects (74,6%), in 7 subjects (9,8%) HBsAg was present. Both positive HBsAg and HCV RNA were demonstrated in 4 patients (5,6%), 2 patients (2.8%) had detectable HCV RNA and HBV DNA. Liver fibrosis assessment results using SWE elastography: F0 – F1 in 55 subjects, >F1 –<F3: 10; F3- F4: 2, with mean fibrosis stage 0.83. Liver fibrosis assessment results using FibroTest: F0 – F1 in 40 subjects, >F1 –<F3: 10; F3 - F 4: 17, with mean fibrosis stage 1.16. No clinical features of liver cirrhosis were present in subjects with advanced fibrosis. In 64 patients the fibrosis was assessed using both non-invasive methods. Concordant results, with the difference up to 1 stage, were obtained in 48 individuals (75%). The difference between the methods measurements more than 1 stage occured in 16 patients (25%), with a tendency to higher values obtained by FibroTest, among them in 7 patients the fibrosis assessment was 3 stages higher in FibroTest.

Conclusions: The high percentage of the study group has eliminated HCV spontaneously. Despite the long time of HCV infection, fibrosis in the study group was mild, probably partly because of negativity of HCV RNA. The value of FibroTest and SWE elastography in fibrosis assessment in this certain group is to be established and needs further research.

No conflict of interest

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