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Abstracts

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Door-to-door hepatitis C testing in three large cities of Georgia: A pilot study

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Background: The number of patients enrolling into the national hepatitis C treatment program in Georgia began to decline in late 2016. Lack of awareness of the program, fear of being stigmatized, or other barriers may be impacting testing rates. Outreach activities, such as door-to-door testing may be an effective strategy to increase hepatitis C detection and enrollment into the treatment program.

Methods: During March–October 2019, door-to-door testing was carried out in three high hepatitis C prevalence cities of Georgia: Tbilisi, Zugdidi and Batumi. In each city, two residential streets in low income neighborhoods were selected, where each consecutive household was approached. Those consenting to participate, were tested for HCV antibodies (anti-HCV) by rapid test in the home and result were provided during the visit. For those who stated that they had been tested previously and were anti-HCV positive, the report was validated using the hepatitis C testing and treatment program database using study participants' National ID. For those who were confirmed to be anti-HCV positive, linkage to additional follow-up (received HCV RNA testing) was confirmed. Persons testing anti-HCV positive were counseled on the result and referred to care for HCV RNA testing. Household members at any age were eligible for testing. Participants were not asked about potential risk factors for HCV infection. Outcomes of the testing strategy were described.

Results: Overall 4062 households were reached during 7 months of testing using this strategy, including 2840 households in Tbilisi, 752 - in Zugdidi and 470 - in Batumi. Of these, 1113 (27.4%) households did not open the door or no one was home. Of the 2949 (72.6%) households contacted, 682 (23.1%) refused participation. There were 6925

people residing in the 2267 (76.9%) participating households, of whom 1438 (20.7%) were not at home during the visit. Of the 5487 people available for testing, 683 (12.4%) refused participation, 401 (58.7%) of whom stated they either knew their anti-HCV positive status (138, 34.4%) or had previously tested negative for anti-HCV (263, 65.6%). Among the 4804 people tested, 48 (1.0%) tested positive for anti-HCV, including 18 (0.7%) in Tbilisi, 21 (1.7%) in Zugdidi and 9 (0.8%) in Batumi. Among the 138 previously identified anti-HCV positive people 81.4% had already received HCV RNA testing. Overall anti-HCV prevalence (newly and previously tested individuals) was 3.9% in all three cities, with the highest prevalence in Zugdidi (6.0%), followed by Batumi (3.9%), and Tbilisi (2.1%).

Conclusions: Hepatitis C door-to-door testing was feasible with high levels of household participation. A significant proportion of individuals had been previously tested, and of those who tested positive, most were linked to care. In cities and neighborhoods with low rates of testing, door to door point-of-care testing could be considered. Cost-effectiveness analysis of this intervention could inform policy makers in countries attempting hepatitis C elimination.

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The prevalence of mutations of the hepatitis C virus, associated with drug resistance to inhibitors of protein NS5A among patients of the Republic of Belarus

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Introduction: Almost all new combined treatments of hepatitis C virus (HCV) include direct-acting antiviral agents (DAA) that target domain I of the NS5A protein, which plays an important role in the replication and assembly of viruses. An important reason for the failure to achieve a sustained virologic response is the emergence of drug-resistant variants of the virus, which can be present in the long term as natural polymorphisms in patients without treatment or can form during treatment. For the 1b subtype L31V/M and Y93H, L31V/M+Y93H amino acid substitutions are the most typical and its presence can provide 28, 24, and 14,000-fold resistance, respectively. Purpose of the study is to develop a method for detecting drug resistance of 1b HCV subtype and establish the prevalence of HCV mutations associated with drug resistance to NS5A protein inhibitors.

Materials and methods: The study included 94 patients who had no treatment experience, as well as 17 patients with unsuccessful treatment or recurrence of HCV infection. Eleven NS5A nucleotide sequences of the HCV genome were isolated from serum / plasma samples of patients infected with 1b HCV subgenotype and residing in different regions of the Republic of Belarus. Amplification of the NS5A region of the virus genome was performed by the "nested" in house PCR method. Direct sequencing was conducted on an automatic sequencer 3100 Genetic Analyzer. The analysis of drug resistance mutations was performed using the available online programs.

Results: Among the 111 nucleotide sequences included in the study, amino acid substitutions L31V / M / I, Y93H, L31V / M + Y93H, L31M + R58A were found in 27 samples (24.3%). Among patients without DAA treatment experience, single mutations occurred in the L31V / M (n = 6) or Y93H (n = 3)

positions. In one case, the double mutation L31V / M + Y93H was detected. The total frequency of mutations to inhibitors of the NS5A protein reached 10.6%. In the group of patients with unsuccessful treatment, the drug-resistant variants of HCV are established in all cases. Amino acid substitution of leucine for valine / methionine (L31V / M), that determines resistance to elbasvir, ledipasvir and partially reduced sensitivity to daclatasvir and ombitasvir, was detected in three patients (2.7%). In four cases (3.6%), tyrosine was replaced with histidine in 93 (Y93H) position, which has a significant effect as a result of cross-resistance on the efficacy of all medicines of this group except pibentasvir. The most frequent of the analyzed samples were combinations: L31V/M + Y93H (9.0%). In 2 cases, double replacement of L31M/P58A (2.0%) was revealed.

Conclusion: We have developed and applied a method for detecting the drug resistance of HCV to DAA, which inhibit the NS5A proteins of the virus. The results showed a high incidence of mutations of HCV drug resistance to NS5A protein inhibitors among HCV-infected patients from Belarus. This indicates the need of screening samples obtained from patients who are planning to get prescription drugs of direct action of this group.

3

Persistence on HIV pre-exposure prophylaxis medication: A challenge in pre-exposure prophylaxis (PrEP) program in Georgia

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Background: HIV epidemic is rapidly emerging among men who have sex with men (MSM) in the country of Georgia, with HIV prevalence exceeding 20% in this population. In 2017 Georgia launched HIV Pre-exposure prophylaxis (PrEP) program for high-risk MSM and transgender women, performed by AIDS Center and non-governmental organization “Equality movement”, through the support of the Global Fund to Fight AIDS, Tuberculosis and Malaria. Main challenge of the program is retention in PrEP services. We analyzed the program data to study persistence on PrEP medication.

Materials&Methods: Enrollment in PrEP started in October 2017 based on pre-defined eligibility criteria (high risk for HIV infection, negative for anti-HIV; negative for HBsAg and creatinine clearance of ≥ 60 ml/min). Generic formulation of tenofovir/emtricitabine was used for daily PrEP. Persons attended AIDS Center for receiving PrEP services including clinical monitoring and PrEP medication pick-up, 1 month after starting PrEP and then on 3-monthly basis.

Our sample consisted of persons taking PrEP medication who were enrolled from the start of the program to March 15, 2019. We studied overall persistence on PrEP medication defined as performing at least three quarters of the scheduled visits with medication pick-up, and persistence for 3, 6, 9 and 12 months defined as amount of PrEP medication supplied for the respective period of time. Analysis was performed as of June 15, 2019.

Results: Total of 159 persons initiated PrEP from October, 2017 to March 15, 2019. Five quitted the program and 154 remained in PrEP. Of the 154 enrollees, the median age was 26 (IQR: 19-52) years, 90 (63.8%) identified themselves as gay men, 41 (29.0%) - as bisexual and there were 4 transgender women (2.8%). At baseline examination, 5 enrollees

(3.2%) were anti-HCV positive and 46 (29.8%) had evidence of syphilis on treponema pallidum hemagglutination assay (TPHA). 48.0% (74/154) of the overall sample were classified as persistent and 52.0% - non persistent on PrEP medication. Persistence significantly decreased ($p=0.008$) with the duration of follow-up: 3 month persistence was 70.8% (109 out of 154), 115 enrollees were eligible for analyzing 6 month persistence and 51.3% (59 out of 115) persisted on the medication, 9 month persistence was 39.8% (39 out of 98 eligible) and 12 month persistence – only 28.5% (16 out of 56 eligible).

Conclusions: PrEP program in Georgia faces persistence challenge: only about half of the enrollees persisted on PrEP medication. Our findings showed that at the PrEP initiation beneficiaries showed good attendance to PrEP services, but long-term persistence was poor. Further research in partnership with community based organizations would be desirable to explore reasons for non-persistence.

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Virological efficacy of first-line regimens, resistance profile and factors influencing adherence to ART in clinical practice in Ukraine

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Background: Integrase inhibitors (INI) have recently been recommended for first line therapy (FLT) in Ukraine, but non-nucleoside reverse transcriptase inhibitors (NNRTI) based regimens present a majority of FLT cases, even though testing for NNRTI mutation has not been routinely performed. Data regarding virological efficacy of ART and prevalence of drug resistance mutations in Ukraine is scarce. We evaluated the virological response, resistance profile, factors influencing adherence to treatment in patients starting a first-line regimen in clinical settings in Ukraine.

Materials and methods: We conducted a retrospective cohort study in Poltava region, Central Ukraine of 2813 newly diagnosed HIV-patients >18 years old who entered care and started ART from 2004 to 2018 and followed at least 6 months. The presence of major resistance mutation to NRTIs, NNRTIs, PIs was evaluated at virological failure (VF, defined as an HIV-RNA, VL > 1,000 copies/mL after week 24 for treatment experienced). The RNA isolation, amplification and sequencing were performed using ViroSeq HIV-1 Genotyping Kit (Celera), for the data interpretation Stanford HIV DR Database was used. Potential risk factors associated with bad adherence and treatment discontinuing have been identified by using multivariate logistic regression models.

Results: Among our cohort of 2813 HIV-patients receiving ART, heterosexual route of HIV transmission made up 62% (n = 1730). Median enrolment age was 42 years (IQR 42 - 62), 1431 (51%) were men. Late stages of HIV-infection (III, IV) were diagnosed in 66 % (n = 1849) patients. During observation period, 1617 (57.5%) patients continued initial first-line regimen ART, 891 (31.7%) had at least one switch of ART in same drug class, and 130 (4.6 %) patients developed virological failure and have been switch to second-line regimen of ART. Among

patients continued initial first-line ART during the study period, EFV-based regimens were reported in 69.2% (n = 1118), DTG – in 21.7 % (n=352), LPV/rvtv – in 5.8% (n = 95) patients. Twenty patients (15.3%) had an available genotypic resistance test at virological failure. The most frequent mutation were: NRTI class – K65R (11/20, 55%), M184V (8/20, 40%), Y115F (3/20, 15%), L74V, D67V, A62V, K219E – 2/20, 10%, NNRTI class – G190S (17/20, 85%), Y181C (15/20, 75%), K101E (13/20, 65%), PI class – M46IM (3/20, 15%), L10I (1/20, 5%). High adherence to care during ART was best predicted by social support (OR=1.4, 95%CI 1.0- 2.1), attending clinic of integrated services with access to opioid replacement therapy (ORT) (OR=1.1, 95% CI 1.0- 1.1). Bad adherence to care was significantly higher in HIV-infected patients who injected drugs and women who diagnosed during the pregnancy (OR=1.6, 95% CI 1.1- 1.8; OR=1.9, 95% CI 1.5-2.3).

Conclusion. In clinical practice, patients receiving first-line ART achieve and maintain high rates of virological suppression. NNRTI - based regimens had the most frequent rate of administration in first-line ART and high prevalence of mutation. The main factors associated with high adherence during ART were social support, good access to integrated services clinics with ORT.

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5

Epidemiology of HIV in the Baltic countries (Estonia, Latvia, Lithuania)

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Background: The HIV epidemic in the Baltic countries (Estonia –EE, Latvia –LV, Lithuania –LT) started in the MSM community, afterwards developed rapidly among PWID and has many similarities but also differences.

Methods: Countries national HIV databases overview.

Results: The first cases of HIV in the Baltics were reported in 1987 and 1988. By the end of 2018, 9901 cases have been registered in EE, 7669 in LV, and 3172 in LT. Last UNAIDS estimated N of PLWHIV in EE was 7400 (6600 - 8200), in LV – 5686 (5600 - 6600) and in LT 2800 (2500 - 3000). In 2017, the highest HIV incidence (cases per 100, 000 pop.) in EU/EEA was observed in LV (18.8), followed by EE (16.6). In LT-9.1. The highest incidence in EE was in 2001 – 105 (95% CI 32.7 – 59.3), in LV in 2001 as well - 19.9 (95% CI 32.7 – 59.3), in LT in 2002 – 10.9 (95% CI 0.2 – 12.7). HIV incidence in 2018 in LV was 16.9 and exceeded incidence in EE (14.4) for the third year in a row. LT has the lowest incidence (5.7), it has decreased after the previous three year increase in a row due to HIV transmission among PWID, especially in prison facilities. The highest increase of HIV cases in PWID was reported in LV and EE in 2001 (173% and 390% respectively as compared to 2000), in LT – in 2002 (551% increase as compared to 2001 because of an outbreak in prison). In some regions of EE more than every second drug user is HIV+. The epidemiology of HIV has changed substantially during the past decade - the heterosexual transmission has been increasing, but is more prevalent in LV compared to LT, especially since 2001 when 8% of all HIV cases in LV were attributed to heterosexual transmission, and in 2005 even 31% ($p < 0,0001$), in LT respectively 10% and 17% ($p < 0,05$). Totally 46 MTCT HIV cases were reported in EE, 75 in LV and 7 in LT.

Conclusions: HIV epidemic in the Baltic countries started about the same time. However, prevalence

of HIV in general population is different: 1. Estimated N of PLWHIV in LV and EE are higher than in LT 2.7 and 2.2 times accordingly. 2. In 2018 the highest HIV incidence was in LV. In EE 1.2 and in LT 3 times lower. 3. In all countries, the second decade of HIV epidemic was driven by PWID. The spread of HIV through bridging groups to general population in EE and LV started earlier than in LT. The least number of MTCT cases prove the recently started epidemic in LT.

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Uptake and outcomes of dolutegravir based antiretroviral therapy in Georgia

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Background: In July 2018 the World Health Organization updated antiretroviral therapy (ART) guidelines to recommend dolutegravir (DTG) as preferred first line drug. DTG was introduced in 2017 and since 2018 has been prescribed as preferred first line option. We aimed to describe uptake of DTG in Georgia and evaluate outcomes of DTG based ART.

Materials and Methods: Study included all patients initiating DTG based treatment between July 1, 2017 and June 10, 2019. Data on patient demographic, epidemiological, clinical and laboratory parameters were extracted from the national AIDS health information system. Virologic response was evaluated in patients receiving DTG-based ART at least for 6 months period. Viral suppression was defined as viral load (VL) <200 copies/ml. Missing VL data among patients on DTG based treatment for more than 12 months and discontinuation of therapy were defined as failure (VL >200 copies/ml).

Results: A total 635 patients initiated DTG-based therapy, among them the median age was 40 (IQR: 32-48) years, 459 (72.3%) were men, 326 (51.3%) were infected through heterosexual contact, 169 (26.6%) through injection drugs use and 123 (19.4%) through sex between men. The median baseline CD4 cell count was 290 (IQR: 124-452) cells/mm³ and 384 (60.5%) patients presented to care with CD4 cell count <350. Overall 487 (76.7%) patients received DTG as part of their first line regimen and 148 (23.3%) – as part of second line treatment. Per quarter uptake of DTG increased by 300% 31 persons initiating DTG-based ART in Jul-Sep 2017 to 124 persons in Apr-Jun 2019. TDF/FTC+DTG was most commonly prescribed ART (n=510, 80.3%), followed by AZT/3TC+DTG (n=55, 8.7%), ABC/3TC+DTG (n=29, 4.6%), ATV/r+DTG (n=17, 2.7%), DRV/r+DTG (n=15, 2.4%), and LPV/r+DTG (n=9, 1.4%). Patients were on DTG-based ART for the median 7.8 (IQR: 3.2-11.7) months. By the end of follow-up 605 (95.3%) patients remained on treatment, 17 (2.7%) patients

discontinued treatment and 13 (2.0%) patients died. A total 369 patients were evaluable for virologic outcomes, among them 339 (91.9%) patients had viral suppression at the last viral load measurement. Viral suppression rate was 92.9% among persons on first-line treatment and 88.8% among persons on second-line treatment (p=0.21). Analysis by treatment regimen showed the lowest response rate in patients receiving combination of DRV/r+DTG (66.7%, 6/9), the regimen used in heavily pretreated patients.

Conclusions: DTG has been successfully introduced in Georgia and the uptake has been increasing over time. Early results show effectiveness of DTG both in first- and second-line treatments. Treatment uptake, retention and viral suppression should be further monitored to inform national ART program.

7

The new tendencies in HIV and HCV epidemics in central region of Ukraine

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Background: Two severe epidemics co-exist in Ukraine – HIV-infection and hepatitis C. HIV-infected persons demonstrated high prevalence of HCV - to 44-60%. We planned to estimate the morbidity of HIV-infection and chronic hepatitis C in Poltava region in 2003-2018, create prognosis up to 2020, estimate the predictors of HCV-infection in HIV-infected patients.

Methods: Routine epidemiological data of Poltava regional center of public health and Poltava HIV/AIDS clinic about epidemics of HIV-infection and hepatitis C in 2000-2018 were analyzed and prognosis of the both epidemics in the region up to 2020 has been developed. We identify the data using epidemiological mapping method to estimate of distribution HIV-infection and hepatitis C in districts of Poltava region. Routine clinical data 4010 HIV-infected patients aged 18-65 years admitted to Poltava HIV/AIDS clinic in 2003-2018 were considered as a retrospective cohort. Binary or multinomial logistic regression models were used to identify the predictors of HCV-infection among HIV-infected patients in region.

Results: The epidemic situation of HIV-infection was characterized by the increase in morbidity from 6,8 per 100 thousand of population in 2003 to the highest level - 34,2 per 100 thousand of population in 2013 with further decrease to 28,3 per 100 thousand of population in 2018 with increasing significance of sexual transmission (from 23% in 2003 to 73,5% in 2018), predominance of male (63,0%) and individuals aged 30-49 years (45,4%). Epidemic situation of chronic hepatitis C was also characterized by the increased morbidity from 7,4 per 100 thousand of population in 2010 to 27,7 per 100 thousand of population in 2018 with predominance of male (71,4%) and individuals aged 40-49 years (46,7%). The rates of the prevalence of HIV-infection and chronic hepatitis C revealed the highest in cities and districts, located around the regional and federal highways with places

concentration of sexual workers. The resulting prognostic model shows that reduce in the incidence of HIV infection to 24.5 per 100 thousand of population and a rapid growth of chronic hepatitis C morbidity up to 46.2 per 100 thousand of population is expected in the region up to 2020.

The prevalence of HIV/HCV-coinfection in the cohort of the first diagnosed cases of HIV infection in Poltava region during the period of 2003-2007 was recorded at the level of 56.1% to 65.9% and was characterized by the predominance of male (63.4%), age group of 30-49 years (69.3%), with IV drug using (77.2%). Despite the changing of HIV-infection route of transmission to sexual from 2008, the prevalence of HCV-coinfection was recorded at the 55.4% to 61,7%. HCV-infection in HIV-infected patients after 2008 were associated with male sex (OR=1,20, p=0,045), age≥40 years (OR=1,11, p=0,038,), experience of incarceration (OR=2,13, p=0,013) and using of drugs (OR=3,242, p=0,022).

Conclusions: This study shows the prognosis of HIV and HCV-epidemics in Poltava region of Ukraine up to 2020 and suggests association between the male sex, age≥40 years, experience of incarceration and presence of HCV-infections in HIV-infected patients.

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Management of Hepatitis C in primary healthcare in the country of Georgia

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Background: In April 2015, with a partnership with Gilead Sciences and technical assistance from U.S. CDC, Georgia launched the world's first hepatitis C elimination program. By May 2019, more than 54,000 persons initiated treatment, achieving >98% cure rates. Broad access to direct acting antivirals (DAAs) resulted in rapid increase in treatment uptake in 2016, which has since declined due to barriers in diagnosis and linkage to care. To address this issue Georgia initiated service decentralization in 2018 by integrating hepatitis C virus (HCV) screening and treatment in primary healthcare centers (PHCs). We report preliminary results of an integrated model of HCV care in PHCs.

Methods: By May 2019, a total of 10 PHCs provided HCV care services throughout the country. The integrated model was based on a "one stop shop" approach, by which patients received all HCV screening, treatment and care services at the PHCs. PHCs provided care to HCV treatment-naïve patients with no or mild fibrosis (FIB-4 score<1.45) using simplified diagnostics and a treatment monitoring approach, while persons with advanced liver fibrosis/cirrhosis were referred to specialized clinics. Patients received Sofosbuvir/Ledipasvir and/or Sofosbuvir/Velpatasvir for 12 weeks. Sustained virological response (SVR) was defined as undetectable HCV RNA 12-24 weeks after end of therapy.

Results: From August 2018 through April 2019, overall 468 persons received HCV RNA or core antigen testing to determine active HCV infection in

PHCs; of those, 390 (83.3%) tested positive. Among 390 persons with active HCV infection, 318 (81.5%) were linked to care (tested for FIB-4 score). Among these, 279 (87.7%) had FIB4 score<1.45; of them, 252 (90.3%) completed HCV pretreatment evaluation and 202 (80.2%) initiated treatment. A total of 101 patients completed treatment. Of 22 patients within the 12-24 week window of SVR eligibility, 10 had been tested at the time of analysis, and all 10 achieved SVR (100% cure rate).

Conclusion: Our study reported the feasibility and effectiveness of integrating a simplified HCV diagnostic and treatment model in PHCs. Countrywide expansion of this model is warranted to bridge the gaps in the HCV care continuum and ensure high rates of treatment uptake towards achieving elimination targets.

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HCV prevalence and associated factors among people who inject drugs (PWID): Baseline results of Georgian PWID cohort study

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Background: In April 2015 in partnership with U.S. CDC and Gilead Sciences, Georgia launched the world's first national hepatitis C elimination program. The national strategic plan identifies reduction in HCV incidence among people who inject drugs (PWID) as one of the priority directions. In 2018, the Georgian PWID cohort study was established to inform the elimination program about the epidemiology of HCV in PWID. We report results of the baseline survey.

Materials and Methods: This prospective observational study started with a baseline cross-sectional survey with subsequent follow-up of anti-HCV negative persons. The study enrolled adult persons of all genders, who injected drugs within the prior 6 months, and who were able to communicate in Georgian and provide informed consent for participation. We used incentivized chain-referral sampling, with dual incentives for participation and for bringing peers. The main outcome measure was anti-HCV status determined by rapid HCV antibody test. A structured questionnaire was administered to elicit information about a) socio-demographic characteristics, b) injection practices and c) non-injection related risk factors. Factors associated with positive anti-HCV were evaluated in multivariate logistic regression analysis.

Results: A total of 1744 PWID were recruited, among them median age was 40 (IQR: 33-49) years, 1655 (94.9%) were men, 1011 (58.0%) had high school education only, 897 (51.5%) were unemployed and 1016 (58.3%) had monthly income of less than 500 Georgian Lari (180 EUR), 444 (25.5%) had history of imprisonment. The median age at the onset of injection was 19 (IQR: 16-22) years, the median duration of injection was 12 (IQR: 9-18) years. The

most commonly injected drugs within the 30 days period were so called 'sirets' (poor quality heroin) – 47.5% and homemade stimulant vint/jeff – 42.9%. Up to 73% of the study population had never been engaged in opioid substitution treatment. Overall 42.7% reported sharing syringes, 43.1% - cookers, 41.7% - cotton and 11.9% - rinse water. Anti-HCV prevalence was 32.3% (563/1744). In multivariate logistic regression analysis, factors associated with anti-HCV positivity included: history of sharing syringes (OR 12.9, 95% CI: 3.4-48.95), increasing duration of injection (20+ years OR 4.20, 95% CI: 1.70-10.36; 16-20 years OR 2.26, 95% CI: 1.02-5.02; 11-15 years OR 2.49, 95% CI: 1.16-5.35), history of imprisonment (OR 2.30, 95% CI: 1.71-3.11), and unemployment (OR 1.51, 95% CI: 1.16-1.97).

Conclusions: Anti-HCV prevalence of 32.3% was lower than in previous studies (range: 57%-68%), which might be the effect of the national elimination program. A substantial proportion of PWID engage in high risk behaviors and thus remain at risk for HCV infection. Preventing HCV transmission through engaging PWID in harm reduction services will be critical for achieving the goal of elimination.

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Diversity of HIV-1 subtypes in Russia 2009-2019

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Background: During the last 30 years HIV-1 has been spreading rapidly in the Russian Federation. The dominating sub-subtype A6, recently known as A1 variant FSU or IDU-A, was originally distributed among injecting drug users, but later began to spread through sexual contact. Subtype B viruses circulated among different risk groups in Russia with most of them found in MSM group. In the last 15 years we received the information on the circulation of recombinant forms CRF02_AG and CRF63_02A. The aim of this study was to analyze HIV-1 subtypes diversity in Russia in 2009-2019.

Methods: In this work we analyzed 3459 HIV DNA samples that were collected with informed consent in 2009-2019 in 25 cities of Russia. The collection included 51.7% IDUs, 39.9% heterosexuals, 1.25% MSMs and 5.1% cases with others or unknown route of transmission. The sequences of pol gene fragment coding protease and part of reverse transcriptase were obtained by ViroSeq HIV-1 genotyping System v. 2.0 or by in-house method. Genotyping analysis was carried out by COMET HIV-1/2v.2.3 (<https://comet.liv.lu/>). For phylogenetic analysis, we obtained GenBank reference sequences of pol gene fragment both worldwide prevalent and sequences from bordering countries such as China, Japan, Kazakhstan, Ukraine, Belarus and Estonia. Phylogenetic analysis was carried out by MEGA X (<https://www.megasoftware.net/>) and IQ-TREE (<http://www.iqtree.org/>).

Results: Our study has shown that the A6 subsubtype virus plays the main dominant role on the territory of Russia. The distribution of subtypes was as follows: sub-subtype A6 – 81.9% (48.7% IDUs and 51.3% heterosexuals), subtype B – 9.1% (42.4% IDUs, 31.3% MSM and 26.3% heterosexuals), CRF63_02A – 8.2% (49.6% heterosexuals and 46.1% IDUs), CRF02_AG – 0.48%, and other subtypes including unique recombinant forms resulted from the recombination between A6, CRF02_AG or CRF63_02A1.

In the period 2009-2014, the sub-subtype A6 virus was found in 94% of cases, the subtype B was mainly distributed in MSM and amounted to about 3%, and the number of recombinant forms such as CRF02_AG and CRF03_AB was about 4%.

In the period 2015-2019, we observed a gradual decrease in the number of infections with sub-subtype A6 (80.3%), but it still remains the main dominant HIV-1 genetic variant. At the same time, there is an increase in the number of recombinant forms (CRF63_02A1 - 10.1%, CRF02_AG - 2.8%, and CRF03_AB - 0.8%), as well as the emergence of new. This last phenomenon is becoming more and more widespread, which requires a more detailed analysis of full genome sequences.

Conclusion: The results demonstrated a wide variety of different HIV-1 subtypes in Russia. Sub-subtype A6 is still dominant in Russia but its quantity gradually decreases. At the same time, there has been a gradual increase in the number of cases of infection with HIV-1 recombinant forms, such as CRF63_02A1 and CRF02_AG, widespread in Kazakhstan, Uzbekistan and other Central Asian countries.

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Outcomes for hepatitis B vaccination among HIV-infected adults in Georgia

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Background: Vaccination for hepatitis B virus (HBV) is universally available for all non-immune HIV patients living in Georgia. The aim of our study was to assess the outcomes of hepatitis B (HBV) vaccination among HIV patients in Georgia.

Methods: A retrospective study was conducted using data extracted from the national AIDS Health Information System. Outcome of interest was development of a protective antibody (Ab) response following hepatitis B (HBV) vaccination, defined as anti-HBs >10 IU/L. Response on vaccination was considered as low immune response when anti HBs 10-100 IU/L and as high when anti-HBs >100 IU/L. Data were analyzed using R statistical package.

Results: Among 267 HIV-infected adults, who completed the three-dose vaccine series, follow-up serology testing was conducted in 228 (85.4%) persons. Among them 55 (24.1%) were women and 173 (75.9%) men, mean age was 37.1 years and 215 (94.3%) had a positive protective Ab response (anti-HBs >10 IU/L). High response was documented in 78.2% women and 75.7% men, non-response rate among women was 7.3% and 5.7% in men. The difference by gender was not statistically significant.

Among 228 patients with follow-up serology testing 38 (16.7%) were HCV Ab(+) and 190 (83.3%) - HCV Ab(-). Among HCV Ab(+) patients 32 (84.2%) developed high immune response, 5 (13.2%) - low response and 1 (2.6%) - was non-responder. Among HCV Ab(-) patients 142 (74.7%) developed high immune response, 36 (19.0%) - low response and 12 (6.3%) - was non-responder. The difference by HCV antibody status was not statistically significant.

Three strata were defined based on CD4 cell count before vaccination - the first group with CD4 <200/ μ l (n=6), second - CD4 200-500/ μ l (n=55) and third - CD4 \geq 500/ μ l (n=167). In first group 1(16.7%) patient had high response, 2 (33.3%) patients - low

response and 3 (50%) - were non-responders. In second group - 33 (60.0%) patients had high response, 20 (36.4%) patients - low response and 2 (3.6%) - were non-responders. In third group 135(80.8%) patients had high response, 21(12.6%) patients - low response and 11 (6.6%) - were non-responders. The difference by CD4 cell count strata was statistically significant ($p < 0.001$).

Patients were categorized in two groups based on HIV RNA viral load (VL) before vaccination: first group with VL <200cop/ml (n=182), second - VL \geq 200cop/ml (n=46). In first group 137(75.0%) patient had high response, 33(17.0%) patients - low response and 12 (8.0%) - were non-responders. In second group - 35(78.0%) patients had high response, 10(19.0%) patients - low response and 1 (3.0%) - was non-responder. The difference by VL group was not statistically significant.

Conclusions: We found that the CD4 T cell count at the time of vaccination to be the sole predictor of response to HBV vaccination among HIV-infected Georgian adults. Double-dose vaccination should be considered in patients with advanced immunosuppression.

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EPIDEMIOLOGY OF HEPATITIS B VIRAL INFECTION IN THE REPUBLIC OF BELARUS

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Objective: Nowadays, despite the global trend of reducing of hepatitis B virus (HBV) infection morbidity and mortality due to effective current vaccination programs, this infection still poses a problem in the European region.

Aim of the study was to assess the incidence of various forms of HBV-infection in the Republic of Belarus for the period from 1996 to 2017, as well as prevalence of viral genotypes and subtypes.

Material and methods: The absolute number of reported cases and the incidence (per 100 000 population) of acute hepatitis B (AHB), chronic hepatitis B (CHB) and the registration of "HBsAg carrier", both for the whole of the Republic of Belarus and separately by regions and age groups, were analyzed based on official statistical data.

Results: There was a trend to reduce morbidity from HBV infection from 79.5 in 1996 to 15.0 reported cases per 100 000 population in 2017, the average annual incidence rate was 31.2 cases per 100 000 population per year, the annual decline rate was - 7,4%. With a decrease in the overall incidence of HBV infection, there has been an increase in the registration of chronic forms from 5.7 (2002) to 10.0 (2017) cases per 100 000 population, with an average annual growth rate of +3.3%. The incidence rates for all forms of HBV infection in the context of administrative territories are distributed unevenly and range from 16.4 in the Gomel region to 31.5 cases per 100 000 population in the Minsk region. The greatest contribution to the structure of the incidence of all forms of HBV infection is made by age groups 21-29 years, 30-39 years (28% and 23% of the total in all age groups, respectively). Peak morbidity of AHB was in the age group of 21-29 years, of CHB – in the age group of 30-39 years.

The prevalence of HBV genotypes was analyzed in 93 of patients with chronic HBV infection living in the Gomel region. The most common was genotype D

(73 cases, 78.5%), less common – genotype A (19 cases, 20.4%), one case (1.1%) of mixed genotype A/D was found. In 34 cases additionally the viral subtypes were detected. Of these, the subtypes D1, D2 and D3 were found with a frequency of 14.7%, 26.5% and 38.2%, respectively), the subtype A2 – in 20.6%.

Conclusion: The increase of chronic hepatitis B cases cause economic burden to healthcare system and implies increased mortality from end-stage liver disease in the future. The cases of acute hepatitis B in younger age groups probably indicate insufficient vaccination coverage and therefore should be investigated.

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Implementation of the State Program on elimination of viral hepatitis C in Ukraine: achievements and challenges

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Background: According to estimated data in our country at least 5% of population is infected with HCV, that is more than 2 million of people and according to the data of Ministry of Public Health, 105,000 patients with chronic hepatitis C (CHC) are registered. In 2014 State Program on Prevention, Diagnosis and Treatment of viral hepatitis was implemented, which significantly increased access to highly effective treatment. As part of the implementation of the State Program, according to data received from the regions, 46,984 patients with chronic hepatitis C are registered. About 8,000 people with chronic hepatitis C are officially registered in the regions each year, among whom 73.3% of cases of chronic hepatitis C are diagnosed for the first time, and in 28.3% of cases the disease is diagnosed for the first time already at the stage of cirrhosis.

Materials and methods: Implementation of the State Target Social Program for the prevention, diagnosis and treatment of viral hepatitis in Ukraine was analyzed. The analysis included 7920 patients who received treatment as part of the State Program. The diagnosis of chronic hepatitis C (CHC) was established on the basis of clinical and laboratory data, verified by identifying viral RNA and the genotype of the virus by PCR. All patients were assessed for the degree of liver fibrosis.

Results: Among patients registered in the frame of State Program, 1st genotype dominates - 51.3%, on the second place - 3rd genotype with 35.0%, 3.8% of patients were infected with 2nd genotype, in 10.0% of patients genotype remains unidentified. 8920 patients were treated in the framework of National program, regional programs, support programs. In the frame of State Program both interferon-containing schemes and DAAs were available: peg-interferon + ribavirin (PEG-IFN + RB), sofosbuvir + peg-interferon + ribavirin (SOF + PEG-IFN + RB), sofosbuvir + ribavirin (SOF + RB), sofosbuvir +

ledipasvir (SOF + LED), ombitasvir / paritaprevir / ritonavir + dasabuvir (3D), however interferon-containing schemes gradually disappeared and have not already been provided for as part of government procurement for 2018. SVR achievement was analyzed in 5452 patients. Frequency of SVR depended on the treatment regimen and was the highest in DAAs regimens. SVR rate in Peg-IFN + RB combination was the lowest - 68%, using a combination of SOF + PEG-IFN + RB, increased effectiveness of therapy to 89%, SVR rate with combination SOF + LED was 95.3%, 3D - 98.9%.

Conclusions: In frame of State Program most effective were regimens using DAAs combinations of SOF + LED and 3D, SVR rate was 95.3% and 98.9%, respectively. The introduction into clinical practice DAAs has significantly increased the effectiveness of treatment, reduced duration and decreases side effects. However, in Ukraine at the moment, far from all the necessary combinations are available under the State Program. Regimens available today in Ukraine have a significant limitation of use in groups of experienced patients with cirrhosis and chronic kidney diseases. The proportion of the so-called "difficult" patients who did not reach SVR on NS5A inhibitor containing regimens is increasing.

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High level of integrase strand transfer inhibitors drug resistance mutations in INSTIs failed HIV-1 CRF06_cpx infected patients in Estonia

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Background: The use of first generation integrase strand transfer inhibitors (INSTIs), mainly raltegravir (RAL), has been on the rise during the past seven years in Eastern Europe, including in Estonia. Due to the low genetic barrier of the first generation INSTIs, patients adherence to therapy is critical for the success of RAL containing ARV therapy. However, so far in Eastern European, where significant proportion of treated population are people who inject drugs with low adherence, no such study has been conducted. Thus, we aimed to describe the distribution of INSTIs DRMs among INSTIs treatment failed patients (INSTI-s failed) and INSTIs-naive as controls.

Materials and Methods: Genotypic resistance testing was performed using plasma of 58 INSTIs-failed and 78 INSTIs-naive patients from 2013 to May 2019. Viral RNA was amplified and sequenced in HIV-1 integrase region. INSTIs (DRMs) were detected using Stanford University HIV-1 Drug Resistance Database. Subtyping was conducted using REGA HIV-1 & 2 Automated Subtyping Tool (Version 2.0).

Results: INSTIs-failed and INSTIs-naive groups consisted of 67% and 69% males with median age of 38 (IQR 33 – 42) and 35 (IQR 33 – 40), median CD4+ T cell count of 198 (IQR 114 – 312) and 248 (IQR 105 – 394) cells/mm³, and median HIV-1 viral load of 4.1 (IQR 2.9– 4.9) and 4.3 (IQR 3.4 – 4.8) log₁₀ copies/ml, at the time of DRMs testing, respectively. Nearly all INSTIs-failed patients (56/58) had received RAL and only two had received dolutegravir (DTG). Of 136 sequenced samples 71.3% were HIV-1 CRF06_cpx, 22% unique recombinant forms, 4.4% subtype A1 and 2.2% subtype B. No INSTIs DRMs were found in INSTIs-naive patients. Major INSTIs DRMs were detected in 37/58 (64%; 95% CI 50.9 – 75) INSTIs-failed patients. The most common INSTI

DRMs were Y143C/R/H (16/37) followed by N155N/H (8/37), E92Q (8/37), Q148H/K/R/N (7/37), E138K/A/T (6/37), G140GA/A (4/37), T66A/I/K (3/37), S147SG/G (2/37) and G118R (1/37). Most of the viruses had high or intermediate level resistance to elvitegravir (EVG) and/or RAL, but low, potentially low or no resistance to DTG and bictegravir (BIC). However, three viruses have high level resistance to DTG and BIC possessing the combination of DRMs E138K/G140A/Q148R, T66TA/E138K/G140GA/S147SG/Q148R, T66I/G118R/E138A/ L74I, respectively. In addition, four viruses, which have intermediate level resistance to DTG and BIC, possess mutation Q148R with other major mutations E138K, G140A, T66A and/or S147G, respectively.

Conclusions: Our results indicate a high level of INSTIs drug resistance among INSTIs-failed patients in Estonia. The accumulation of Q148H/K/R/N mutation together with other secondary mutations should encourage early discontinuation of RAL in order to preserve the activity of second generation INSTIs for rescue interventions. Therefore there is essential need for resistance testing in HIV management with INSTIs therapies. However, as no INSTIs DRMs were detected in INSTIs-naive patients there is no need for INSTIs DRMs testing prior to INSTIs initiation.

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Clinical characteristics, risk factors and response to the treatment of a series of porphyria cases in two Spanish hospitals

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Background: Delayed cutaneous porphyria (PCT) is the most common form of porphyria. It is produced by a decrease in the activity of the enzyme uroporphyrinogen decarboxylase. The prevalence of HCV in the PCT is geographically variable, from very low in New Zealand (4%) and northern Europe (17%), passing by average in the United States (56%) to a very high prevalence in southern Europe. (Italy, Spain and southern France, 70-90%) The typical patient is a middle-aged male with a history of excessive alcohol intake, liver disease and organic iron overload. The manifestations are characteristic. We describe the cases of PCT, its association with HCV and the cases not performed screening for the infection.

Materials & methods: Retrospective, observational and descriptive study of all cases from January 2008 to April 2018 in two Spanish hospitals. A statistical package SPSS V.18 was used. for the analysis of the data.

Results: In the period studied, 27 cases of PCT were diagnosed. 93% were male with a median age of 58 years (40-67). 20 patients presented, as a history, chronic enolism. Only 80% (n=21) of the patients received HCV serology, which was positive in 10 (48%). In two cases, coinfection with HIV was observed. Of the 10 cases associated with HCV, 8 were treated; of the remaining two, one refused to perform the same and subsequently died and the other patient received no treatment as he died of advanced liver disease. Eight of them were genotype 1b with advanced fibrosis degree (F3-F4). More ledipasvir and ribavirin were treated with sofosbuvir during 12 weeks, achieving a sustained viral response. There was a case of progression to hepatocarcinoma.

Conclusions: An important association between porphyrias and risk factors is shown. Despite the

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Material is strictly view only

known PCT-HCV association, there is still a significant proportion of patients who are not requested for serology for HCV. The treatments received were performed in an advanced phase of hepatic fibrosis. The new antivirals achieve an excellent sustained viral response rate. Knowing the association of HCV with other pathologies would facilitate its diagnosis in order to be able to treat cases early and avoid complications of chronic liver disease. Generating an HCV serology request alert would help to reduce the rate of undiagnosed cases since the disease is treated with direct-acting antiretrovirals with an efficacy approaching 100%

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Clinical case: Hepatitis E infection

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Hepatitis E is one of the leading causes of acute viral hepatitis worldwide. According to the World Health Organization, around 20 million cases of Hepatitis E are identified each year, 3.3 million of them are symptomatic, 56,600 deaths. Earlier, this infection was considered endemic in developing countries with poor sanitation and associated with traveling. Nowadays, hepatitis E infection is most commonly caused by genotype 3 and is transmitted by zoonotic and is common in many well-developed countries. This disease is very rare in Lithuania. Due to the low attention paid to hepatitis E infection and the lack of availability of laboratory tests in our country, hepatitis E is rarely diagnosed, so we have no data on the prevalence of infection. This presentation describes a case of acute viral hepatitis E in a young patient and provides a review of literature on this infrequently occurring infection in Lithuania.

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Non-Hodgkin's lymphoma in four cases of viral hepatitis C with advanced liver disease and four different outcomes

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Background: The association between non-Hodgkin's lymphoma (NHL) and hepatitis C virus (HCV) infection in many studies has been well documented. NHL has higher prevalence in HCV infected persons and about 15% of patients with NHL are HCV infected. HCV infection in patients with NHL may contribute to unfavorable prognosis by more advanced disease and worse survival. Patients with HCV infection and NHL are more difficult to treat. The negative HCV effect is explained by three presumptive mechanisms: chronic antigenic stimulation, CD81 engagement on B and T cells and direct B cells HCV infection. Successful anti-HCV therapy may lead to regression of low-grade HCV-associated NHL, better lymphoma therapy response, better survival and lower risk of NHL relapse. The benefit of anti-HCV therapy was documented in both interferon and directly active antivirals (DAA) era. Four patients with NHL and HCV infection were followed in Hepatology Center of Bulovka Hospital, Prague. All four patients were HCV treated and all of them had different outcome.

Materials & Methods: Since March 2009 till June 2019 four HCV-infected patients in the stage of liver cirrhosis and with NHL were followed. One out of four patients had HIV coinfection. All were HCV treated, one by combination of pegylated interferon plus ribavirin (P/R) and next three patients by DAA. In half of patients NHL was diagnosed before antiviral therapy (AVT). All four patients received chemotherapy (CHT).

Results: In 45 years old woman NHL was diagnosed three months (M) after unsuccessful therapy by P/R. She succeeded remission of NHL after CHT. Retreatment by P/R was contraindicated. DAA therapy was unfeasible that time and she died on liver failure 72 M after AVT. In 65 years old woman NHL was diagnosed 25 M before AVT. The patient had poor prognosis of life expectancy because of multiple NHL relapses after repeated CHT. AVT by

DAA was started and she succeeded sustained virological response (SVR), but after SVR has repeated relapses and undergoes next courses of CHT till recent. She survives 34 M after AVT. In 68 years old man with NHL diagnosed 72 M before AVT with remission after CHT AVT by DAA was introduced, but hepatocellular carcinoma in 6th week of AVT was diagnosed. The patient subsequently underwent liver transplantation, succeeded SVR and survives 20 months after AVT without NHL relapse. 48 years old HIV infected man on antiretroviral therapy was null responder on 1st retreatment by P/R in the past. After 2nd retreatment by DAA he succeeded SVR, but NHL was diagnosed 6 M after AVT and was treated by CHT. The patient survives 34 M after AVT without NHL relapse.

Conclusions: Two out of four HCV-infected patients with liver cirrhosis and NHL survive 20 and 34 M after SVR without NHL relapse till present. One patient survives 34 M after SVR, but with repeatedly relapsing NHL. The last patient without SVR died on liver failure. Successful AVT may contribute to enlargement of therapeutic strategies, reducing of relapses and better prognosis of patients with NHL and HCV infection.

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Effects of direct acting antiviral drugs on a fibrosis in patients with cirrhotic stage of hepatitis C

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Background: The appearance of direct acting antiviral (DAA) drugs has changed the treatment approaches for patients with chronic hepatitis C (CHC). In clinical trials, a high rate of virological response was observed in CHC patients with compensated cirrhosis. Now, even patients with decompensated stage of cirrhosis and contraindications for pegylated interferon therapy can be treated by DAA drugs. In some cases, a DAA treatment leads to a reverse liver dysfunction. In some patients, this therapy can even help to avoid a liver transplantation.

The interferon-free combination of paritaprevir/ritonavir-ombitasvir and dasabuvir (PrOD), called also the three-drug (3D) regimen, with or without ribavirin, can be indicated for the treatment of CHC in patients infected by a genotype 1 hepatitis C virus (HCV).

Materials and methods: In our case studies, three genotype 1 HCV infected patients with a cirrhosis (F4 METAVIR) were treated by a 3D regimen. All three patients (two men and one woman) were naive. The men were infected by the genotype 1b HCV, the woman was infected by the genotype 1a HCV. One man was co-infected by hepatitis B virus (HBV), with an active replication of both viruses. In case of genotype 1a HCV patient, PrOD with ribavirine was indicated for 24 weeks. In case of genotype 1b HCV patients, PrOD without ribavirine was indicated for 12 weeks. In patient with a HBV co-infection, the therapy of hepatitis B by tenofovir was indicated three months before the 3D regimen.

Results: All three patients achieved a sustained virological response. Elimination of HCV was slower in the patient with genotype 1a HCV than in the patients with genotype 1b HCV. In all patients, a significant decrease of the fibrosis level has been observed. In the patient with genotype 1a HCV, the fibrosis level decreased from F4 (26,3 kPa) in 2014 to

F3 (12,0 kPa) in 2017 and to F3 (10,1 kPa) at the end 2018. In the patients with genotype 1b HCV, the fibrosis level decreased from F4 (21,1 kPa) in 2016 to F2 (8,3 kPa) in 2017 and to F1 (6,9 kPa) in 2019. Note that despite a decreased fibrosis level, the patients still require a dynamical observation because of the hepatocellular carcinoma development risk.

Conclusion: The antiviral therapy with DAA drugs can lead to regression of fibrosis, even in patients with compensated cirrhosis.

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Impact of sustained virologic response on clinical outcomes among hepatitis C patients within the national hepatitis C elimination program in Georgia: single-center experience

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Background and aims: Georgian national hepatitis C elimination program achieved high rates of sustained virologic response (SVR) among hepatitis C patients with advanced liver fibrosis or cirrhosis approaching 98%. The aim of our study was to assess impact of SVR on long-term clinical outcomes, including occurrence of hepatocellular carcinoma (HCC).

Materials & Methods: Prospective cohort study included 113 patients with advanced liver fibrosis (n = 35) or compensated cirrhosis (n = 78) without history of HCC, who were treated with either sofosbuvir/ribavirin ± pegylated interferon or sofosbuvir/ledipasvir ± ribavirin and who achieved SVR. Patients were followed on regular basis after completing treatment until September 2018. Follow-up examinations included liver stiffness measurement by transient elastography, abdominal ultrasound and laboratory tests. HCC was documented by imaging, alpha-fetoprotein and liver biopsy.

Results: Patients were followed for the median 1.8 (IQR: 1.5-2.2) years contributing 211 person-years (PY) of follow-up. Compared to baseline pre-treatment status significant improvements were observed in: liver stiffness (median 19.9 vs. 10.4 kPa, p<0.0001), FIB-4 score (median 2.35 vs. 1.31; p<0.0001); ALT (median 83.2 vs. 22.3 U/l, p<0.0001), AST (median 64.1 vs. 22.0 U/l, p<0.0001), platelet count (median 149 vs. 176 X 10⁹/l, p<0.0001), bilirubin (median 11.9 vs. 10.0 μmol/l, p=0.03). There was no significant change in albumin level (median 44 vs. 45.6 g/l, p=0.33). Over the follow-up: 2 patients died (incidence rate: 0.9/100 PY [95% CI: 0.1-3.4]), 2 patients developed ascites (incidence

rate: 0.9/100 PY [95% CI: 0.1-3.4]) and 4 patients developed HCC (incidence rate: 1.9/100 PY [95% CI: 0.5-4.8]). The incidence of HCC among patients with cirrhosis was 2.1/100 PY (95% CI: 0.4-6.1) vs. 1.5/100 PY (95% CI: 0.1-8.4) in patients without cirrhosis, p=0.84. In multivariate analysis factors associated with HCC occurrence included increasing age, interferon-containing regimen, and baseline albumin level <35 g/l.

Conclusion: SVR is associated with regression in liver stiffness and improvement in liver function. However, patients remain at risk of HCC occurrence and portal hypertension. Continued monitoring of patients with advanced liver fibrosis and compensated cirrhosis is needed to ensure long-term health benefits of successful treatment.

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The changes of rat's behavioral reactions, S100b and GFAP level in the rat brain under chronic hepatitis C condition and effect of the 2-oxoglutarate

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The molecular mechanism by which the chronic hepatitis C causes chronic, progressive brain damage (hepatic encephalopathy) is not well known. The main goal of work was investigation of the level of glial fibrillar acid protein (GFAP) and calcium-binding protein S100b in the brain under chronic hepatitis C (CHC) and effect of the 2-oxoglutarate. The experimental CHC was developed according to patent № u2006004614. The 32 Wister rats were used for experiment according ethical rules. 2-oxoglutarate was given to rats in drinking water (0,228%). The rats were decapitated under Isofurane anesthesia according ethical rules; the brain was quickly removed and divided into different regions.

The level of S-100b was increased in all parts of the brain of rats under development of experimental CHC. The largest increase was observed in the cerebellum - 12.1 times, slightly less - 10.6 times - the number of S-100b increased in thalamus, in the sensory part and the hippocampus, the S-100b increased by 4.5 and 4.7 times respectively.

The use of 2-oxoglutarate resulted in positive changes in the calcium-binding protein S100b concentration. In all studied areas of the rat brain, there was a significant decrease in the concentration of S100b in the direction of approaching control values.

The development of CHC induced the considerable increasing of soluble GFAP concentration in the all studied brain regions: the largest changes were observed in the sensory part and in thalamus (an increase of 5.6 times). Slightly less growth occurred

in the cerebellum (4.2 times) and in the hippocampus (3.6 times). The immunohistochemical data shown that the number of astrocytes in the cerebellum changed to Alzheimer type II cells was elevated. The treatment with 2-oxoglutarate downregulated the soluble GFAP level in the brain of rats with CHC (by 72% in the cerebellum, 84% in the sensory part, and 89 in the thalamus). The level of filament GFAP under CHC condition was changed in different manner in the studied brain regions. Thus, in the hippocampus, there is a tendency to increase (by 89%), in the cerebellum and thalamus there is a tendency to decrease (by 36% and 24% respectively), while the concentration of the sensory part is almost unchanged. The treatment with 2-oxoglutarate induces normalization of GFAP level in hippocampus, however increases production of that protein in the other studied brain regions.

The obtained results show that chronic impairment of the detoxication function of the liver results in the development of intense encephalopathy with significant suppression of the locomotor and orientation/research functions of the animals and a rise in the stress sensitivity of their organisms. The treatment with 2-oxoglutarate in the case of CHC-related encephalopathy provides rather clearly manifested neuroprotective effects.

The obtained data allow suggest that changes of GFAP level can reflect the complex of the cytoskeleton modification in the different brain regions under CHC condition, the treatment with 2-oxoglutarate can partly prevent the serious brain disturbance induced by liver toxicities.

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Successful treatment of genotype 3 chronic hepatitis C in the haemodialysis patient with the combination of sofosbuvir and daclatasvir

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The treatment with direct acting antivirals for patients with chronic hepatitis C caused by genotype 3 hepatitis C virus infection comorbid with terminal renal impairment was impossible for years. All combinations of direct acting antivirals used for treatment of genotype 3 chronic hepatitis C until 2017 had NS5B polymerase inhibitor sofosbuvir. Contrary to other direct acting antivirals sofosbuvir metabolites are eliminated through kidneys. Sofosbuvir is metabolised to GS-331007, which accumulates in the body of patients with impaired kidney function and can cause adverse reactions. Therefore, chronic hepatitis C treatment for patients with chronic kidney disease with sofosbuvir based regimens should be personalized and prescribed following safety requirements. 47 year old haemodialysis patient infected with hepatitis C virus received 12 week standard dose treatment with generic sofosbuvir and daclatasvir combination, because of the lack of suitable alternatives. It is thought that chronic glomerulonephritis was as a consequence of extrahepatic manifestation of the infection. To prevent accumulation of GS-331007, the rate of haemodialysis was increased to 6 times per week. Medication had to be taken 4 hours prior haemodialysis. At week 6 early viral response was reached: virus ribonucleic acid became undetectable. During the treatment there were no major side effects or drug dose reductions noted. At the end of the treatment, at week 12 and 24 of follow up, virus ribonucleic acid was negative, sustained viral response was reached. Posttreatment patient stayed on haemodialysis, after 2 years he had a kidney transplantation. To conclude, chronic hepatitis C treatment for terminal stage renal disease patients could be sofosbuvir based therapy, when no other alternatives are possible, although the treatment must be individualized and carefully monitored.

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Hepatitis B infection and vaccination: knowledge and attitude among reproductive aged women in Georgia

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Background: Georgia is a country with high prevalence of hepatitis B. Based on a 2015 population serosurvey, the prevalence of hepatitis B surface antigen (HBsAg) is 2.9% and prevalence of anti-HBc is 25.5% in general population. Hepatitis B vaccine has been included in the national immunization schedule of Georgia only since 2002. Thus, most reproductive aged women were not vaccinated during young childhood.

Methods: Cross-sectional study was conducted in the capital of Georgia, Tbilisi. Reproductive aged women were randomly selected and then recruited from three maternity care centers during prenatal care. The self-administered questionnaire included questions on socio-demographic information, hepatitis B vaccination status and awareness of HBV infection status.

Results: A total of 2185 reproductive aged women were enrolled in the study. The mean age was 28.5 (age range 17-46) years. Most (76.4%) had a bachelor and/or master's degree. 20.0% of respondents never heard about HBV. Very few (3.3%) knew they were infected with HBV. We could not determine if women were chronically infected or were exposed and developed antibodies.

HBV knowledge was limited: 57.5% were not aware of available HBV treatment; 51.6% didn't know HBV infection could be prevented (35.8% named HBV vaccination, 29.3% named condom use). Only 10% of study participants reported being vaccinated for HBV. Awareness of HBV infection was higher among women over age 25 (72.1%) compared to women aged 25 years or less (27.9%) ($P < 0.0001$). Among women who reported having an HBV infection, 40.6% did not name vaccine as a prevention method and 38.2% did not have information about availability of HBV treatment ($P < 0.05$).

Conclusion: Based on our study results, knowledge about HBV infection and vaccination is very low among reproductive aged women in Georgia. Women's health centers can be a good place to reach reproductive aged women for counseling on HBV infection and promote vaccination against hepatitis B.

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HIV/HCV co-infected patient profile in Lithuania in 2018

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Background: HIV co-infection with hepatitis C virus (HCV) is a growing public health concern. Many studies have shown that in intravenous drug users co-infection prevalence can be as high as 90%-95%. There is increasing evidence supporting the concept that people infected with HIV have a much more rapid course of their hepatitis C infection. Patients co-infected with HIV and HCV demonstrate increased rates of hepatic fibrosis, progression to liver failure, and liver-related mortality.

Materials & Methods: Data source - the national HIV / AIDS database. Objective of the study was to describe the profile of epidemiological indicators (socio-demographic characteristics, median CD4 count, way of transmission, HIV clinical category) among HIV/HCV co-infected patients who started HAART in 2018.

Results: In 2018 HIV treatment was initiated in 403 HIV cases, of whom 217 (53.85%) were co-infected with HCV - 179 (82.5%) male and 38 (17.5 %) female; 191 (88.0 %) PWID; 22 (10.1 %) heterosexual cases; 1 (0.5 %) MSM; transmission way was unknown in 3 (1.4 %) cases. 20 (10.5%) of all PWID patients were on substitution therapy. Mean age of the HIV/HCV patients was: 37,5 years of PWID, 35,6 years of hetero/MSM/unknown way of transmission. On the time of HAART initiation: 1) median CD4 count was: 408.6/mm³- of PWID and 368.1/mm³ - hetero/MSM/unknown way of transmission, 2) A1-A2 HIV clinical categories had 70 (32.2%) patients, A3 - 5 (0.9%); B1- B3 clinical HIV categories had 112 (51.6%) patients; C1-C3 had 18 (8.3%) patients (CDC clinical category), 3) 3 patients were cured from HCV (all PWID). HIV infection via injection drug use in HIV/HCV patients was diagnosed <5 years ago in 93 cases (48.4%) and >5 years in 98 cases (51.3%). HIV/HCV/HBV co-infection was in 15 (6.9%) cases, HIV/HCV/HBV/TB co-infections was in 6 (3.1%) cases.

Conclusions: profile of HIV/HCV co-infected patient who started HAART in 2018 is: 36 years old male who has acquired HIV more than 5 years ago via injection drug use and who is a former PWID presently abstaining from drugs with diagnosed

symptomatic HIV disease (B1-B3 HIV clinical category).

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Comparison the outcomes of HIV estimation, calculated using two different methods for 2018 in Georgia.

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Background: HIV estimation is crucial to assess epidemiological situation in countries. There are two most accepted HIV estimations software's, one is SPECTRUM software provided by UNAIDS for HIV estimations and another is ECDC HIV estimation tool. Our goal was to compare HIV estimations using those two software's for 2018 in Georgia.

Methods: HIV estimations were for Georgia was calculated using SPECTRUM software and ECDC HIV estimation tool for 2018. Main indicators used for compare were estimated number of: PLHIV, PWID and MSM. To calculate the proportion of undiagnosed HIV infection in Georgia, registered number of PLHIV was divided into estimated number for each method. The difference of two proportions was tested using Chi-square test on R statistical package.

Results: SPECTRUM HIV estimation software estimated 9,400 (95% CI 8,100 – 11, 000) PLHIV in 2018 in Georgia, from them 1,430 were PWID and 2,580 were MSM. ECDC HIV estimation tool estimated 12,576 PLHIV in the same period, from the 2,923 were PWID and 1,762 were MSM. A registered number of PLHIV who know their HIV status at the end of 2018 was 5480. The proportion of undiagnosed HIV was 42% using estimated PLHIV calculated by SPECTRUM as a denominator and 56% using estimated PLHIV calculated by ECDC modeling tool. Chi-square test revealed significant statistical difference between proportions calculated using these two methods ($\chi^2 = 466$, $P < 0.001$).

Discussion: Two HIV estimation methods calculated different estimated PLHIV in 2018 in Georgia. Calculation the percent of undiagnosed HIV based on those two methods in the country showed statistically significant difference between methods. Different methods provide distinct results, but the undiagnosed fraction is still high (>40%) in both

methods, which emphasizes the importance of increase HIV testing coverage.

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HBV, HCV, HIV infection among health care workers

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Materials: 2427 serum/plasma samples from all regions of the Republic and Minsk city.

Methods: EIA, PCR, RT-PCR, sequencing. Software Sequencing Analysis Software™ (Applied Biosystems®) and Geneious® v8 (Biomatters Ltd.). Multiple alignment of nucleotide sequences was performed using the ClustalW algorithm. Phylogenetic trees were constructed using the ML (maximum likelihood) algorithm in the PHYML (Phylogenetic maximum likelihood) and GARLI (Genetic Algorithm for Rapid Likelihood Inference) programs, with the nucleotide substitution model GTR + I + G (I - the proportion of invariable sites, G - Gamma shape parameter). Optimization of tree topology - Best of NNIs and SPRs. To calculate the statistical reliability of clusters, the SH-aLRT test was used. Clusters of a phylogenetic tree were considered reliable, the root branch of which had a value of >0.9.

Results: As a result of the studies, 11.4% (n = 276) identified HBsAg, 14.7% (n = 357) - antibodies to HCV, and 1.3% (n = 32) - antibodies to HIV-1 and 72.6% (n=1762) of the samples were negative. HBV markers were more commonly detected in medical patients with specialized secondary education — 48.9% (n = 135) in the age groups 25–39 - 34.1% (n = 46) and 40–59 years old - 57.8% (n = 78). HCV markers were more often found in medical patients with specialized secondary education — 42.3% (n = 151) at the age of 25–39 years old — 31.8% and 40–59 years old - 58.3%. Antibodies to HIV were also more frequently detected by nurses 46.9% (n = 15) at the age of 25-39 years old - 33.3% (n = 5) and 40-59 years old - 53.3% (n = 8). Using synthesized primer pairs, we sequenced 102 HBV samples isolated from medical patients from different regions of the country. Studies have shown that in 58.1% (n = 55) the subgenotype D2 was detected, 16.4% (n = 14) - A2 and D3 (n = 17), in 5.5% (n = 14) - D1 and in 3.6% (n = 2) of cases, the D4 subgenotype of the virus was detected. Of the 43 sequenced HCV

samples, 35 samples (66.7%) belonged to subgenotype 1b, 6 - to 3a (23.8%) and 2- to 2a (9.5%). In general, the distribution of 1b and 3a subgenotypes among health care workers corresponds to that in the whole country, with the exception of 2a of the HCV genotype, which was detected only in patients infected with parenteral route as a result of medical intervention. Due to the low viral load, it was not possible to sequence samples that were positive for HIV markers.

Conclusion: On the basis of comparative data performed by the method of phylogenetic analysis, it can be concluded that, among medical workers, virus variants that are not interconnected mainly circulate. At the same time, genetically related virus isolates are identified, indicating the presence of a common source of infection, which requires an epidemiological investigation in each specific case in order to improve the system of epidemiological surveillance and reduce the appearance of new infections.

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Trust of the Georgia National HCV Elimination Program among reproductive aged women

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Background: Georgia is among the countries with a very high prevalence of hepatitis C virus (HCV) infection. The recent availability of highly effective, direct-acting antivirals (DAAs) capable of curing >90% of persons treated has made HCV elimination a possibility. All adult citizens infected with HCV are eligible to receive free DAAs through the Georgia National HCV Elimination Program (Program). From April 2015 to December 2018, 54,087 persons were enrolled in the Program throughout the country. However, more than 20,000 individuals are aware of their HCV antibody positive status but did not have HCV RNA testing, a necessary step to determine treatment needs. We hypothesized that a reason for hesitance to enroll in the Program may be a low level of trust of the Program.

Methods: A cross-sectional study was conducted in Tbilisi, the capital of Georgia. Reproductive aged women were randomly selected from three maternity care centers during prenatal care. The self-administered questionnaire included questions on socio-demographic information, knowledge about HCV infection and trust in the Program.

Results: A total of 2185 women of reproductive age were enrolled in the study. The mean age was 28.5 (age range: 17-46) years. The majority of the study participants (76.4%) had a university degree. The vast majority of study participants (>95%) were married and 95.1% were Georgian ethnicity. Almost 90% of the participants were aware of their HCV infection status. Most women (85.3%) had heard of HCV elimination program in Georgia; 74.6% stated that they trust the Program. However, almost 10% of surveyed women stated they would refuse to get enrolled in the Program if their anti-HCV test result is positive. Trust in the Program was higher among women aged >25 years (80.7%) compared to younger women (68.4%) ($p < 0.0001$). Level of education was also associated with trust to the program: more women with higher education level

reported that they trust the Program (78.7%) compared to women with lower education level (68.5%) ($p < 0.0001$).

Conclusion: Trust in the Georgia National HCV Elimination Program is not sufficiently high among women of reproductive age in Georgia. Effective educational campaigns are needed to improve trust to the Program for this targeted group.

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Epidemiology of HIV-HCV co-infection in the Republic of Belarus among patients treated with NS5A and NS5B inhibitors of HCV proteins

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Background: Currently, effective antiretroviral therapy has extended and improved the quality of life of people living with HIV and dramatically reduced AIDS-associated mortality. One of the leading causes of non-AIDS-related deaths is gastrointestinal diseases more commonly associated with chronic hepatitis C. Among 36.9 million people living with HIV about 4-5 million are co-infected with HCV.

Materials & Methods: to collect and analyze the data out-patient and in-patient cards of 304 patients observed in the Minsk city clinical infectious hospital were used. Statistical processing of the results was carried out using Microsoft Excel.

Aim. To give epidemiological characteristics of HIV-HCV co-infection in the Republic of Belarus in the group of patients treated with NS5A and NS5B inhibitors of HCV proteins.

Results: As of may 1, 2019, 5626 patients with HIV-HCV co-infection were registered in the Republic of Belarus. The research program included 304 patients receiving direct acting antivirals for the treatment of chronic HCV infection. Combinations of drugs and duration of treatment was administered according to international and domestic recommendations and included: sofosbuvir/daclatasvir +/- ribavirin, sofosbuvir/ledipasvir +/- ribavirin, sofosbuvir/velpatasvir of courses from 12 to 24 weeks.

The median age was 38 years. Gender distribution: men – 203(66.78%), women – 101(33.22%). Among the ways of transmission: injecting drug users – 239 (78.62%), sexual – 55(18.09%), men who have sex with men – 4 (1.32%), not installed – 6 (1.97%). All patients included in the study received ART and had an undetectable HIV load. The distribution by clinical stages of HIV was as follows: I – 181 (59.54%), II – 55

(18.09%), III – 44 (14.47%), IV – 24 (7.859%). The average number of CD4 was 546 CL/μl (minimum – 4, maximum – 3272).

1 HCV genotype was detected in 146 patients (48.03%), 2 genotype – 7 (2.30%), 3 genotype – 139 (45.72%), 4 genotype – 7 (2.30%), 5 patients were identified mixed genotypes (1.64%). In the study of the severity of liver fibrosis/cirrhosis, the following data were obtained: F0-1 - 206(67.76%), F2 - 61(20.07%), F3 - 15(4.93%), cirrhosis - 22(7.24%), among them severity class A – 10, severity class B – 7, severity class C – 5. Among the study group 7 people were previously treated for chronic HCV infection with a-interferon + ribavirin.

Conclusions:

1. Among patients with HIV-HCV co-infection the main way of transmission in the is injecting drug use.
2. HIV-HCV co-infection in Republic of Belarus is significantly more common in men: men – 203(66.78%), women – 101(33.22%).
3. Among HCV genotypes in a population of HIV-HCV co-infected patients is dominated 1 (n=146, of 48.03%) and 3 (n=139, and 45.72%) genotypes HCV.
4. Due to the early detection of HIV infection and effective ART in two thirds of patients, there is no or minimal liver fibrosis, which allows to expect a high percentage of cure HCV infection in patients of this group.

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Genetic diversity and drug resistance of the hepatitis b virus in the Republic of Belarus

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Introduction: Hepatitis B virus (HBV) is the cause of acute and chronic hepatitis, leading to the development of such severe manifestations as cirrhosis and liver cancer with a high risk of mortality. For treatment of patients, standard schemes of treatment including the use of a combination of antiviral drugs with interferons, which should suppress viral replication, are used. At the same time, an important problem of their use is the development of drug resistance due to mutations of the virus, resulting in the absence of a sustained virological response, reactivation of infection. Early detection of the drug resistance in patients who have been using the nucleos(t)ide analogs for a long time will allow them to choose patient management tactics and optimize treatment.

Aim of the study: Study of the prevalence of mutations of HBV drug resistance to nucleos(t)ide analogs in patients with a chronic form of infection.

Materials and methods: The study included 613 sequences of the HBV P gene. Viral DNA was isolated from the serum/blood plasma of patients collected from 2008 to 2018 in different regions of the Republic of Belarus. Amplification was performed by the "nested" PCR method. Direct sequencing of PCR products were performed on an automatic 3100 Genetic Analyzer sequencer (Applied Biosystems, USA). The estimation of the HBV genotypes/subtypes and the comparison with the genetically close reference sequences from the GenBank database. Mutations of drug resistance were identified using the geno2pheno (<https://www.geno2pheno.org>) and HBV-Grade programs (<http://www.hbv-grade.de>).

The results of the study: Among the samples studied, 110 (17.9%) belonged to genotype A, represented by the A2 subgenotype; 496 - to the D genotype (80.9%); 5 - to the C genotype (0.8%), represented by the C2 subtype. In two cases, recombinant forms of the virus were detected -

A/D/C and D/A (0.4%). D genotype included subtypes: D1 (20,6%); D2 (47,0%); D3 (32,3%); D4 (0.2%).

When analyzing the nucleotide sequences of the polymerase gene, clinically significant mutations were identified in 17 HBV DNA samples (2.8%) isolated from blood plasma from patients receiving and not receiving treatment with nucleos(t)ide analogues. Replacements were found in 10 cases in the rtL180M + rtM204V positions (1.6%), in 2 cases - replacements in three positions were rtV173L + rtL180M + rtM204V (0.3%); and in each case rtI181T, rtM204V, rtN236T, rtL233V, rtL80I+rtL180M+rtM204V respectively. The frequency of mutant variants of the virus varied from 1.7% to 2.7% for the A2, D2, D3 HBV subgenotypes. The detection rate of mutant forms was slightly higher for the D1 HBV subgenotype - 5.9%.

Conclusion: Obtained data show that almost 2% of patients are carriers of drug-resistant variants of the HBV. In most cases, amino acid substitutions are observed in the rtL180M and rtM204V positions associated with drug resistance to lamivudine, entecavir, and telbivudine.

The use of modern molecular genetic research methods allows for a comprehensive screening for the drug resistance in patients with acute and chronic HBV forms. This result are necessary to select a personalized treatment scheme and monitoring of the emergence of resistance during the entire treatment period.

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Genetic diversity and HIV-1 drug resistance in “naive” patients in the Republic of Belarus

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The widespread introduction of antiretroviral therapy (ART) has become a global breakthrough, helping to reduce the number of new cases and the death rate from HIV/ AIDS in recent years. Despite successes, there are proofs of an increase in the level of HIV drug resistance, that creates a threat to successful treatment and non-achievement of goals 90-90-90 by 2030. There is an increase in the level of HIV pre-treatment drug resistance (PDR), which leads to the ineffectiveness of first-line antiretroviral drugs and the further spread of these virus strains in the population.

The aim of the study is to establish the prevalence of ART resistance mutations in the PDR group.

Materials & Methods: Blood serum/ plasma obtained from 149 patients residing in the territory of the Republic of Belarus. Resistance mutations were detected by gag-pol site sequencing using the «Bel HIV-1 resistance-genotype» test systems produced by Republican Research and Development Center for Epidemiology and Microbiology (Belarus) and «AmpliSense HIV-Resist-Seq» Central Research Institute for Epidemiology (Russia) by Sanger sequencing. Multiple alignment of nucleotide sequences was performed using the ClustelW algorithm and MAFFT. The phylogenetic tree was constructed using the ML maximum likelihood algorithm in the MEGA 6.0 Phylogenetic maximum likelihood (PHML) program with the GTR + I + G nucleotide replacement model. Optimization of tree topology - Best of NNIs and SPRs. The trees were visualized in the program FigTree v.1.4.2. The PDR was assessed using the WHO drug resistance list mutation (SDRM) list 2009 and the Stanford HIVdb tool (<https://hivdb.stanford.edu/hivdb/by-sequences/>).

Results: Among the 149 patients included in the study, 73.2% (n = 109) were males and 26.8% (n = 40) were females. The dominant subtype is A, represented by the A6 sub-subtype, it was detected

in 91.9% of patients (n = 137). Subtypes B were detected in 4.0% of HIV-infected individuals and subtype G in 0.7%. In 3.4% of cases recombinant forms were detected, in particular CRF 02_AG (0,7% and CRF 03_AB (2.0%).

In 25 (16.8%) patients, drug resistance was identified due to the presence of mutations that are significant for monitoring, according to the WHO mutation list (SDRM 2009).

In 22 (14.8%) patients, drug resistance was identified due to the presence of MDRM mutations (major drug resistance mutations, 2019). The most common mutations to NNRTI are: K103N (8 patients), G190S (3 patients), V106I and Y181C (2 patients each); To NRTIs: M41L and M184V (2 patients each), in isolated cases there were identified substitutions in the positions D67N, T69N, K70R, K219Q; to protease inhibitors: M46L (1 patient). Among the additional mutations to NRTI were identified: V179T (n=4), A98G (n=2), P225H (n=1).

Conclusion: The obtained data indicate a high level (14.8%) of the prevalence of mutations in the PDR group in the Belarusian cohort. Considering the large-scale use of ART in the country, further representative studies are required, according to WHO recommendations, at the national level, and the solution of the problem of optimizing first-line ART after drug resistance studies prior to treatment is essential.

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Liver complication as a cause of death in HIV-infected patients hospitalized in 2009-2018 in main centre of infectious disease in region of Lower Silesia in Poland

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Background: This is a retrospective analysis of causes of death among HIV-infected patients hospitalized from 2009 to 2018 in two Departments of Infectious Diseases of the Regional Specialistic Hospital in Wrocław, Poland.

Methods: Data of 385 patients who deceased during hospitalization was analyzed. Among them 113 patients were HIV positive and their data was included in analysis.

Results: 20 HIV-infected patients (17.7%) died due to cirrhosis or hepatic insufficiency. Average age of the assessed groups was 42.45 years (median 39.5, range: 27-61). 16 were men (80%) and 4 (20%) were women. 100% acquired HIV and HBV and/or HCV infection through intravenous drugs use (IDU). 19 patients (95%) were anti-HCV positive of which 3 had detectable HCV RNA, 1 had negative viremia, no data about 15 patients. 6 (30%) had detectable HBs antigen (HBsAg) but only 3 (15%) had detectable HBV DNA viremia; 9 (45%) had occult HBV infection.

The mean time from admission to the hospital to death was 15.25 days (median 13 days, range: 1-44 days). The mean CD4+ T lymphocytes count at the time of death was 267 cells/mm³ (median 259 cells/mm³, range: 41-680 cells/mm³), whereas mean nadir of CD4+ T lymphocytes count was 182 cells/mm³ (median 229 cells/mm³, range: 18-349 cells/mm³). At the time of death AIDS C3 was diagnosed in 3 patients (15%) according to 1993 CDC classification. The average lifetime from HIV diagnosis to death was 9.7 years (median 10 years, range: 40 days-20 years). At the time of admission to the hospital 16 patients (80%) were on antiretroviral treatment (ART). 4 patients (20%) were without ART due to non-compliance resulting from active IDU.

The following complications of liver cirrhosis in our cohort were: ascites in 10 patients (50%),

esophageal varices in 9 (45%), encephalopathy-6 (30%), gastrointestinal tract bleeding-5 (20%), hepatorenal syndrome-5 (20%), hepatocellular carcinoma-1 (5%).

Autopsy was performed in 2 patients and complications of liver cirrhosis as the cause of death were confirmed.

A comparative analysis of data of 93 patients who died for reasons other than liver disease revealed higher prevalence of severe immunodeficiency in this group than in the group of patients who died of hepatic reasons. AIDS C3 was diagnosed in 68 patients (73.12%) vs. 3/20 (15%) in patients who died due to cirrhosis ($p < 0.05$). Mean CD4+ T lymphocytes count at the time of death was 100 cells/mm³ (median 48 cells/mm³, range: 0-1084) vs. 267 cells/mm³ in our specified group ($p < 0.05$), mean nadir was 67 cells/mm³ (median 24 cells/mm³, range: 0-426). Mean time from the diagnosis of HIV infection to death was 4.3 years (median 1 year, range: 3 days-20 years), and was shorter than in the group of patients died of hepatic complications. Smaller percentage of patients was anti-HCV positive-52.7% (49 patients), as well as smaller percentage of patients was HBsAg-positive-6.45% (6 patients) or had occult HBV infection-34.4% (32 patients).

Conclusions:

1. Liver disease is an important cause of death in HIV-infected patients without severe immunodeficiency.
2. Liver disease due to HBV or HCV infection as a cause of death in HIV-infected patients mainly affects former or active intravenous drug users without severe immunodeficiency.

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Sexual risky behavior of Needle and syringe program beneficiaries

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Background: Sexual risky behavior is one of the significant factor for spreading HIV among PWIDs in Georgia. Estimated number of PWIDs have been increasing during recent years and is considered to be 52,500. NSP program coverage of PWIDs had permanently increased during last 4 years. One of the main objective of this study is to analyze sexual risky behavior of needle and syringe program beneficiaries.

Methods: Consecutive sampling was used to recruit PWIDs during 7 months in 2017. The selection criteria were: Drug injection practice during last month; be a beneficiary of NSP program for more than 6 month; age 18/more. Sample size was 1110, totally beneficiaries of 13 NSP sites participated in the study. Structured standard questionnaire including Risk Assessment Battery (RAB) was used to assess Injecting and Sex Risk Items. SPSS 16.0 was used for data analyses.

Results: According to study results RAB score is 0.25. During the analysis for sexual practice, it is evident that the women (17.6%) in more cases have had sexual relations in exchange for drugs compared to men (1.2%). The same can be said for sexual relations done for money, mostly it is characterized for women (14.7% vs 1%, $p = 0.000$). 10% of the respondents (122) specified that for the last 6 months paid sexual relations. correlation connection between gender and RAB index ($\chi^2 (21) = 30.929$, $p = 0.075$) was unable to be proved, but difference is statistically authentic between cities ($\chi^2 (189) = 768.685$, $p = 0.000$).

the highest rate is revealed in Poti 31.3%, then comes Gori 17%, Batumi 13%, Rustavi 14% and Tbilisi 10%, in other cities relatively low rate is seen: Ozurgeti 4.3%, Kutaisi 2.8%, Samtredia 2.9% and Zugdidi 7% ($p = 0.000$).

For the last 6 months the rate for protected sexual practice is low and is differs from among the cities, which is statistically authentic $\chi^2(27) = 355.792$, $p = 0.000$

Conclusions: The study results demonstrate that With regard to RAB index according to gender is not important, but Sexual Behavior of Injecting Drug Users is still Risky at Harm Reduction Program in Georgia. Such risky behaviors are: sexual relations in exchange from drug or money and mostly unprotected sexual relations with several partners. The findings of this study will be used to address needs, modify program direction or implement new approaches to increase safe Sex behaviors of PWIDs.

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Dynamics of clinical and epidemiological manifestations among new cases of HCV-infection in the period from 1990 to 2019

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Background: At the end of 2018 in the Grodno region of Belarus about 4,900 anti-HCV-positive patients had registered.

The aim of the study was: to analyze the clinical and epidemiological data of HCV-infected patients depending on the time of diagnosis of the disease.

Materials and methods: The analysis of clinical, epidemiological and laboratory data of 150 HCV-infected patients which are living in the Grodno Regions. Depending on the time of diagnosis of HCV-infection, the patients were divided into 4 groups: group 1 - 1990-1999yrs. (15 patients / 10%), group 2 - 2000-2009yrs. (31 patient / 20%), group 3 – 2010-2015yrs. (35 patients / 23%), group 4 - 2016-2019yrs. (71 patients / 47%).

Results: The average age of patients at the time of diagnosis of HCV-infection was 23,7 years in group 1; 34,3 years in group 2; 38,7 years in group 3; and 48,5 years in group 4. In group 1 men made up 73.4% (11 cases), in group 2 – 58% (18), in group 3 – 54.5% (18), in group 4 - 41% (29) men.

For risk factors for HCV-infection surgical interventions were indicated in group 1 - in 4 (26.7%), in group 2 – in 9 (29%), in group 3 – in 6 (17.1%), in group 4 – in 13 (18.3%) patients. Transfusion of blood was in group 1 in 4 (26.7%) patients, in group 2 - in 4 (12.9%), in group 3 - in 2 (5.7%), in group 4 - in 6 (8.5%). The use of intravenous drugs - in the 2nd group indicated in 2 (6.5%), in the 3rd group in 1 (2.9%) patient. The causes are not known in group 1 – in 8 (53.3%) patients, in group 2 – in 16 (51.6%), in group 3 – in 25 (71.4%), in group 4 - in 53 (74.6%) patients.

In group 1, the 1st HCV genotype was in 12 (80%) patients, the 3rd genotype – in 3 (20%), in group 2 the 1st genotype was in 17 (55%), the 3rd - in 14 (45%), in group 3 the 1st genotype was in 12 (36%),

the 3rd – in 21 (64%) patients, in group 4 the 1st genotype was in 29 (41%), the 3rd – in 42 (59%) .

Interferon therapy in group 1 was in 7 (46.7%) patients, in group 2 - in 10 (32.3%), in 3 - in 7 (20%), in 4 - not performed. DAAs were obtained in group 1 – in 3 (20%), in group 2 - in 4 (11.7%), in 3 – in 5 (15%), in 4 – in 15 (21%) patients.

Conclusions: Over the past 3 decades, there has been an increase in the average age of patients with newly diagnosed HCV-infection from 23,7 to 48,5 years, the proportion of women – from 26.6 to 59%, the incidence of the 3rd HCV genotype – from 20 to 59%. Only 18% of patients in analyzed group received DAAs, which indicates insufficient coverage of the needy patients with modern antiviral therapy.

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Polymorphism of TNF-ALPHA (G-308A) and IL-2 (T330G) genes in HIV-infected patients depending on virus tropism

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Background: Cytokines are involved in the immunopathogenesis of HIV infection from early stages of the disease. The literature data on the effect of polymorphism of the TNF- α (G – 308A) and IL-2 (T330G) genes on the course and outcome of HIV infection are controversial.

The aim of the study was to determine the genetic polymorphism of the cytokine genes TNF- α (G-308A) and IL-2 (T330G) in HIV-infected patients, depending on the virus tropism.

Material and methods: The study group included 74 HIV-infected patients from the Grodno region of Belarus (42 (56.8%) women and 32 (43.2%) men, mean age - was 36.4 +5.8 years). TNF- α gene polymorphisms (G – 308A) were determined by real-time PCR, (Rotor-Gene 6000). Determination of the polymorphic variant T330G of the IL-2 gene was performed by the method of PCR with electrophoretic detection. Depending on the tropism of HIV, patients were divided into 2 groups: the first group - 49 (66.2%) patients infected with the R5-tropic variant of HIV, the second group - 25 (33.8%) patients infected with not R5 -tropic virus. HIV tropism was determined using the AmpliSense HIV-Resist-Seq reagent kit (Russia) (FPR = 20%). The cell immunophenotype was determined by Flow cytometry (FACS Calibur). Monoclonal antibodies produced by ExBio, Czech Republic and BD, USA were used. Statistic v.10 was used.

Results: The distribution of genotypes and alleles of cytokine genes TNF-alpha (G-308A) and IL-2 (T330G) has correlated with the Hardy-Weinberg expected equilibrium ($p > 0.05$).

In the group of patients with a non-R5-tropic type of virus, significant differences (Me, Mann – Whitney test) were observed when comparing patients with the heterozygous variant of the genotype GA TNF- α (G-308A) with the homozygous variant of the GG genotype: CD4 + T-lymphocyte helper cells (%): 24.38 (22-31) and 16.7 (6.4-25.5) ($p = 0.047$), respectively; CXCR4 + cells (cells / μ l) 157 (93-258) and 51 (14.5-166) $p = 0.034$, respectively.

It was found that patients without taking tropism into account, presence a G allele (GG and GT genotypes) of the IL-2 (T330G) gene, compared with patients with the TT genotype, associated with a higher content of CD8 + HLA-DR + activated T-cytotoxic lymphocytes (cells / μ l) (Me (IFR), Mann – Whitney test): 764 (563-698) and 412.9 (237.7-632.4) cells / μ l, respectively, $p = 0.032$, which reflects a more pronounced activation of cellular immunity.

In patients infected with a non-R5-tropic variant of HIV, the carriage of the T allele (genotypes TT and GT) had a direct reliable correlation with the FPR index of more than 10%: $R = 0.56$, $p < 0.003$.

Conclusions: No differences were found in the frequency of the genotypes and alleles distribution of the cytokine TNF-alpha (G-308A) and IL-2 (T330G) genes in HIV-infected patients, depending on the tropism of the virus.

In patients with a non-R5 tropic HIV, genetic predictors of a favorable course were: the presence of the GA TNF- α genotype (G-308A) and the carriage of the T-allele of IL-2 gene (T330G).

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The prevalence of hepatitis B and C serological markers in blood donors and pregnant women in Gomel region, Belarus

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Background: The prevalence of hepatitis B and C in the general population of the Republic of Belarus was not completely investigated. The screening programs of hepatitis B and C testing are provided in Belarus for some sub-groups of individuals (blood donors, pregnant women, healthcare workers etc.).

Materials and Methods: The cross-sectional studies were carried out in Gomel Blood Transfusion Station and in branch number 8 of the Central City Polyclinic of Gomel, Belarus. The prevalence of serological markers of viral hepatitis B (HBsAg) and C (anti-HCV) in primary blood donors (n=9514) and pregnant women (n=1998) was evaluated by enzyme immune assays.

Results: Among primary blood donors, the prevalence of HBsAg was 0.53% (95% CI 0.40–0.69), and the prevalence of anti-HCV was 1.2% (95% CI 1.0–1.44).

In pregnant women HBsAg was found in 0.65% (95% CI 0.37–1.12) and anti-HCV – in 1.7% (95% CI 1.21–2.38).

Conclusions: In these younger groups of the population selected by health status (primary blood donors) or by gender (pregnant women) the prevalence of hepatitis B (0.53–0.65%) and hepatitis C (1.2–1.7%) apparently should be lower than expected to be in general population. The knowledge of hepatitis B and C prevalence in blood donors and pregnant women will improve the prevention of parenteral viral hepatitis.

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The dynamics of the patients' population with chronic hepatitis C in Ukraine in the natural history of the disease

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Background: Ukraine is among the countries supported WHO's global strategy for elimination of viral hepatitis to 2030. The most important task for the development of this program in Ukraine is understanding of the local peculiarities of the natural course of hepatitis C.

Materials & Methods: We have developed the model of dynamics of the population of HCV-infected patients in Ukraine from 2011 to 2030.

Based on epidemiological data, we estimated the number of patients with HCV as 1.5 million at the beginning of 2011.

The distribution of the patients by sex, age and the stage of fibrosis was performed according to the investigation of a representative sample of 897 patients with chronic hepatitis C (CHC). The yearly number of new cases of CHC was considered equal to 80% of the number of the reported cases of acute hepatitis C (ACH).

The incidence of ACH after 2018 was calculated on the basis of nonlinear regression analysis of the actual incidence of ACH in Ukraine from 2003 to 2018: $Z = \exp(123.1263 - 0.0610 \cdot x)$, where Z the incidence of ACH, x – the observation year.

The total number of ACH was considered equal to the calculated incidence multiplied by 7 (the ratio of identified to undetected cases of ACH in Ukraine is 1 to 7).

Due to the absence of any data for assessing the dynamics of fibrosis in patients with HCV in Ukraine, we based our calculations on the data given in the article by H. Razavi et al.

Results: For the beginning of 2011 the total HCV-infected population was 1.5 million patients (baseline data). Estimated incidence of ACH from

2012 to 2030 are: 1.48; 1.39; 1.31; 1.23; 1.16; 1.09; 1.02; 0.96; 0.91; 0.85; 0.80; 0.75; 0.71; 0.67; 0.63; 0.59; 0.55; 0.52; 0.49 per 100 thousand population. According to our data for 2011, the number of the patients with the stage of the disease from F0 to F4 was 352844 (23.5%); 309357 (21%); 366210 (24%); 193973 (13%); 277616 patients (18.5%) of the patients respectively. The results of the modeling of the dynamics of the natural course of viral hepatitis showed that in 2030 the total population of the infected population would be 1118530 patients: F0-71054 (6%); F1 - 193143 (17%); F2-177555 (16%); F3 - 362130 (33%) and F4 - 270220 (24%). From 2011 to 2030, 302836 and 78769 people will die from decompensated cirrhosis (DC) and liver cancer, respectively.

Conclusions: By 2030, the number of HCV-infected in Ukraine will decrease by 25.4% compared with 2011 due to the prevalence of mortality over morbidity. Patients with severe fibrosis and cirrhosis will make up 57% of the population (61% - together with DC and HCC).

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Risk factors for late presentation for HIV care in 2019 in Kyiv, Ukraine

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Background: Many people living with HIV (PLHIV) are not aware of their seropositive status and are diagnosed late during the course of HIV infection in Ukraine. This study aims to assess factors associated with late presentation for HIV care among newly diagnosed PLHIV in Kyiv (Ukraine) in 2019.

Materials & Methods: We used data from records of 144 newly diagnosed HIV-positive individuals in Kyiv City HIV Centre in 2019. Descriptive analysis was performed to assess the prevalence and characteristics of late presenters. We analyzed biological and behavioral factors that might increase the risk for late presentation for HIV care: gender (and pregnancy status in women), age, mode of transmission. Multivariate analysis was used to assess the association of each factor with late diagnosis of HIV infection.

Results: 144 patients (54 women and 90 men) aged from 20 to 77 years (mean age 42.8 years) with new diagnosis of HIV-infection were included in the study. 45 (31.3%) acquired HIV by injection drug use, 79 (54.9%) by heterosexual and 20 (13.8%) by homosexual contact. 97 patients (67.4%) were late presenters with CD4 \leq 350 cells/ μ L or AIDS-defining condition regardless of the CD4 cell count at time of diagnosis. 69 patients (47.9%) presented with advanced HIV disease (AHD) having WHO clinical stage IV or CD4 count less than 200 cells/ μ L at the time of diagnosis. In this group there were 43 (62.3%) men and 26 (37.7%) women. The median CD4 cell count in group of late presenters was 45.4 (IQR 1-196) cells/ μ L. 50 patients with AHD (72.5%) sought medical care within 5 years before being diagnosed with HIV, among them 44 (88.0%) were not offered an HIV test and 6 (12.0%) refused to do it before their condition became critical. We analysed biological and behavioral factors that might increase the risk of being diagnosed late: gender (and pregnancy status in women), age, mode of transmission. Increased risk of late presentation at AHD was seen in individuals aged older than 40 years ($\chi^2=6.876$, $p<0.05$), non-pregnant women ($\chi^2=13.155$, $p<0.001$), people who acquired HIV by

injecting drug use ($\chi^2=5.367$, $p<0.05$) or heterosexual contact ($\chi^2=4.737$, $p<0.05$).

Conclusion: The following groups have been identified as groups of increased risk for HIV late presentation: individuals older than 40 years ($\chi^2 = 6.876$, $p < 0.05$), non-pregnant women ($\chi^2 = 13.155$, $p < 0.001$), people who acquired HIV by injecting drug use ($\chi^2 = 5.367$, $p < 0.05$) or heterosexual contact ($\chi^2 = 4.737$, $p < 0.05$). Active offer of HIV testing of these populations is needed to optimize early access to care and treatment. The study highlighted the need for intensification of HIV testing strategy, showing that 88.0% of patients were not offered HIV test while seeking medical care within 5 years before being diagnosed with advanced HIV disease.

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Hepatitis B immune status in healthcare workers and medical students

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Background: Hepatitis B virus (HBV) infection is a global health problem with significant morbidity and mortality. The health care workers (HCW) are at a high risk of infection with HBV through occupational exposure to blood and infectious body fluids. Vaccination is the most effective way of HBV infection prevention. The aim of the present study was to evaluate immune status against HBV among HCWs and medical students.

Materials and Methods: After informed consent, 344 individuals of both sexes (299 female and 45 male), aged 20-70 years (mean age 34.5±13.3) were examined. The study group included 222 HCWs (35 doctors, 76 nurses, 73 cleaning staff and 38 lab workers) of Gomel Regional Infectious Clinical Hospital and 122 sixth year medical students of Gomel State Medical University. The concentration of antibodies to HBV surface antigen (HBsAb) and test for the presence of antibodies to HBV core antigen (HBcorAb IgG) was done using a commercially available enzyme-linked immunosorbent assay. HBsAb level of ≥10 mIU/ml was considered as protective against HBV infection. The data was analyzed using Statistica software version 10. Comparisons were made using cross-tabulation with the Chi-square (χ^2) test, and a p-value of <0.05 was considered statistically significant.

Results: Only 55.8% (192/344) of the total subjects had HBsAb titer above 10 mIU/ml. In the age group older than 40 years, the proportion of persons with a protective level of HBsAb was significantly lower than in younger group (20-39 years) – 39.3% and 64.3%, respectively ($\chi^2=19.6$, $p<0.001$). HBsAb level was significantly higher in males (73.3%) when compared to females (53.2%) ($\chi^2=6.4$, $p=0.01$). The protective level of HBsAb was detected more common among doctors (71.4%), and among cleaning staff – only in 26% of cases ($\chi^2=35.7$, $p<0.001$). The rate of the protective immunity against HBV was significantly higher among students (66.4%) vs. HCWs (50%) ($\chi^2=8.6$, $p=0.003$). Of the

total participants, 245 (71.2%) were completely vaccinated, 18 (5.2%) were partially vaccinated, 20 (5.8%) were unvaccinated, and 61 (17.7%) had unknown history of previous vaccination. Among the completely vaccinated and partially vaccinated persons 62.4% (164/263) had protective HBsAb titers. Duration since vaccination was 1–9 years in 126 (47.9%) and ≥10 years in 137 (52.1%); in these groups, protective antibody titres were detected in 72.2% and 53.3% subjects, respectively ($\chi^2=10.0$, $p=0.002$). Of the total examined persons 9.3% had HBcorAb IgG. In the group of HCWs the detection rate of HBcorAb IgG was 11%, and in the group of students – 3.2% ($p=0.045$, Fisher's exact test). In the age group older than 40 years, the proportion of persons with the presence of HBcorAb IgG was significantly higher than in the age group 20-39 years – 15.9% and 4.8%, respectively ($\chi^2=8.8$, $p=0.003$).

Conclusions: HCWs continue to be at risk group for HBV infection. Among HCWs and medical students almost a quarter was unvaccinated or had unknown vaccination status. 44.2% of the total examined persons and 37.6% among those vaccinated had no protective immunity against HBV. Of the study participants 9.3% had signs of past or occult HBV infection.

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Material is strictly view only

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Indirect markers of liver fibrosis in patients with chronic hepatitis B

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Background: Information on the stage of liver fibrosis is essential in managing chronic hepatitis B (CHB). The aim of the present study was to evaluate the possibility using of indirect liver fibrosis markers for the estimation of fibrosis severity and timely prescribing of antiviral therapy in patients with CHB.

Materials and methods: We examined 130 patients of Gomel Regional Infectious Clinical Hospital with CHB (mean age 41.8±13.5 years, 70% of men) having known liver fibrosis stage based on fibroelastography or liver biopsy. The age of patients, 9 parameters of biochemical blood analysis (albumin, gamma-glutamyltransferase (GGT), aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), cholesterol), complete blood count (platelets (PLT)) and coagulogram (international normalized ratio (INR), prothrombin) along with 7 indices calculated on their base (AST/ALT, APRI, FIB-4, S-index, GUCI, King's score and eLIFT scale) were considered. Statistical analyses were performed using Statistica V10 and MedCalc software. Differences between groups were compared using Mann-Whitney nonparametric U test, correlation was analyzed by the Spearman's rank correlation coefficient, and a p-value of <0.05 was considered statistically significant. The diagnostic values of the indices for detecting significant fibrosis (F2-F4) were assessed by the area under the receiver operating characteristic (AUROC) curves. The sensitivity (Se), specificity (Sp), and positive (PPV) and negative predictive values (NPV) for the fibrosis indices were calculated to determine the optimal cut-off values that would predict significant fibrosis (F2-F4).

Results: According to increase of liver fibrosis stage albumin (rs -0.58), prothrombin (rs -0.56), PLT (rs -0.48), cholesterol (rs -0.37) reduce and AST (rs 0.60), INR (rs 0.58), GGT (rs 0.49), ALT (rs 0.35), ALP (rs 0.27) levels and age of patients (rs 0.38) rise (p<0.01). Among the indices, the most significant positive correlation with the liver fibrosis stage had GUCI index (rs 0.69, p<0.001), eLIFT scale (rs 0.69, p<0.001), and King's score (rs 0.68, p<0.001). All of

the laboratory parameters and indices were significantly different (p<0.01) in patients with minimal (F0-F1) and significant (F2-F4) fibrosis. The diagnostic value of the indices for predicting significant fibrosis in patients with CHB (p≤0.001): GUCI (AUROC 0.866, cut-off ≥0.7, Se 89.5, Sp 78.0, PPV 75.6, NPV 90.7); eLIFT scale (AUROC 0.856, cut-off >7, Se 73.6, Sp 85.7, PPV 78.0, NPV 82.5); King's score (AUROC 0.853, cut-off >11.38, Se 81.6, Sp 82.0, PPV 77.5, NPV 85.4); APRI (AUROC 0.831, cut-off >0.67, Se 81.1, Sp 74.0, PPV 68.3, NPV 85.1); FIB-4 (AUROC 0.817, cut-off >2.11, Se 64.2, Sp 92.2, PPV 85.0, NPV 78.9); S-index (AUROC 0.812, cut-off >0.16, Se 62.3, Sp 92.2, PPV 84.6, NPV 78.0) and AST/ALT (AUROC 0.660, cut-off >0.92, Se 50.9, Sp 80.5, PPV 64.3, NPV 70.5).

Conclusions: The assessment of indirect liver fibrosis markers in patients with CHB can be easily performed at any stage of medical care; they are quite informative and can be used for the estimation of fibrosis severity and timely prescribing antiviral therapy. Index GUCI had the best diagnostic performance (AUROC 0.866) for detecting significant fibrosis with 89.5% sensitivity and 78.0% specificity at cut-off ≥0.7.

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High hepatitis E virus seroprevalence in the absence of chronic infection in HIV-infected patients

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Background: HEV has recently been described as a new causative agent of acute and chronic hepatitis in HIV-infected patients, but chronicity rate has not been well established.

Material and methods: a retrospective study was carried out in an outpatient clinic of a Portuguese central hospital with the aim of determining the seroprevalence and chronicity rate of HEV in HIV-infected patients, randomly selected. All included individuals were tested for anti-HEV IgG/IgM (recomLine-Mikrogenm) and RT-PCR. Other laboratory data was also analyzed.

Results: Two hundred and nine HIV-infected patients were enrolled, mainly men (80,4%), with an average age of 51 years old. All except one were on ART and 82,8% had undetectable HIV RNA. In 37 patients (17,7%) anti-HEV IgG was detected and none had detectable HEV RNA. HEV viral load was also negative in the anti-HEV IgG negative group. Two separate analysis were done in IgG+/IgG-. Patients with IgG+ were older than those with IgG- ($p=.041$). No differences were found in TCD4 cell count at the time of HIV diagnosis in both groups (414 cell/mm³ vs 495 cell/mm³) ($p=.084$), as well when TCD4 cell count was stratified: < 200 ; 200-500 or > 500 cell/mm³ ($p.093$). Initial HIV RNA was not different in both groups ($p=.029$) and no statistically difference was found when looking to the prevalence of HAV (83,8% vs 79,7%) ($p=.065$), HBV (2,7% vs 4,1%) ($p=.089$), HCV (32,4% vs 34,9%) ($p=.085$) and HCV/HBV co-infection (0% vs 1,2%) ($p=.054$). There were found seven cases (4,1%) of cirrhosis in the anti-HEV IgG- group and only one case (2,7%) in the anti-HEV IgG+ group, but this one was also HCV co-infected.

Conclusions: This analysis indicates a high circulation of HEV in HIV-infected patients, but chronic hepatitis due to HEV alone was absent in this sample. Except the older age in anti-HEV IgG+ individuals, no other factors were identified as risk factors for higher prevalence of HEV in this population.

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Viral hepatitis C in patients with pulmonary tuberculosis

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Objectives: This study aimed to analyze the incidence of viral hepatitis C (HCV) in patients with pulmonary tuberculosis receiving etiotropic therapy against *Mycobacterium tuberculosis*.

Methods: Twenty two patients with pulmonary tuberculosis, receiving anti-tuberculosis therapy, and having HCV serological markers (excluding HIV-positive patients) hospitalized in regional and republican tuberculosis hospitals were chosen as research objects. Among the patients, which were aged 29–83 (average = 46.9), 19 were males (86.4%), and 3 were females (13.6%). The diagnosis of infiltrative tuberculosis was established in 16 patients (72.7%), while fibrous cavernous tuberculosis was established in 6 patients (27.3%). Patients had not previously received antiviral HCV therapy, and serological markers in most of them were detected for the first time. In addition to the standard examination, all patients were subjected to RT-PCR-based viral RNA quantitation, which was performed on a BioRad thermocycler (USA) using a test system made by Sivital (Belarus). The examination was carried out for hospitalization terms of 1 to 11 months. Eleven patients were examined twice with an interval of 5 months. Statistica 10 (USA) was used for statistical analysis.

Results: HCV markers were detected in 7.2–8.4% of patients, i.e., at an incidence rate much higher than the national average. HCV RNA was detected in 12 (54.5%) of the 22 examined patients who had HCV serological markers. The viral load ranged from 791 to 26076938 copies/mL. Viral RNA was detected in 8 out of 16 patients with infiltrative tuberculosis and in 4 out of 6 patients with fibrinous cavernous tuberculosis. Among the 10 patients in whom viral RNA was not detected before the onset of anti-TB therapy, an increase in the level of ALT (1.2–3.1 N) was observed in 5 people. No significant statistical correlation was found between the duration of anti-TB therapy, biochemical activity, and the level of viral RNA in blood. Upon the re-examination of 11 out of 22 patients, the absence of viral RNA in blood was re-confirmed for 3 of them. Among the

remaining 8 patients, 5 were tested negative for viral RNA in blood upon re-examination. The initial viral load ranged from 14839 to 7363093 copies/mL. In two cases, an increase in biochemical activity of up to 1.5–2.5 N was observed, which was attributed to a side effect of anti-TB therapy. A significant increase in the level of viral RNA in blood was observed for 3 patients. The initial viral load ranged from 791 to 26076938 copies/mL, and the load determined upon re-examination ranged from 24547 to 86696187 copies/mL. In two cases, we observed an increase in biochemical activity with an increase in the level of ALT activity to 1.5–2 N, which, however, does not exclude the progression of viral damage to liver.

Conclusions: A large fraction of patients with pulmonary tuberculosis was infected with HCV, which suggests that anti-tuberculosis therapy may be accompanied by the progression of viral hepatitis and highlights the need to decide on the appointment of antiviral therapy for this category of patients.

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Correlation between the NASH-biomarkers and HCV-genotype among the patients with chronic hepatitis C treated with direct acting antivirals

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Introduction: Obesity as well as no-alcoholic steatohepatitis (NASH) is a global public health problem and is directly related to chronic inflammation associated with metabolic syndrome and also with HCV-infection.

Background& Aims: In 2015 Georgia launched national HCV elimination program. Free of charge treatment with direct acting antivirals (DAAs) is available for all HCV infected patients. The purpose of this study was to evaluate the association between clinical and lipid profile parameters in patients with HCV chronic infection concomitant with NASH before and after treatment with DAAs within HCV elimination program in Georgia.

Method: Data from the HCV treatment program database of the HCV elimination program were analysed. Treatment regimens with sofosbuvir/ribavirin (SOF/RBV) and sofosbuvir/ledipasvir (LDV) with or without RBV were used. Association was adjusted with other potential predictive factors of SVR, including age, BMI, genotype and degree of liver fibrosis, additionally steatosis assessment. Multivariate analysis using logistic regression was conducted. 138 patients with NASH and HCV-infection were divided into 3 groups: 76 patients with HCV genotype 1 and 23 patients with genotype 2 and 39 patients with genotype 3.

Results: SVR was obtained in 132 patients. After adjustment for other factors associated with SVR, fibrosis/steatosis stage and genotype were found to be independent predictors. HCV genotype 3 was correlated with higher grades of steatosis, in 84 patients (60%). The degree of steatosis in subjects HCV genotype 3 infection was directly related also to HCV viral load, and viral eradication has been associated with an improvement in hepatic steatosis. Body mass index was most related to triglyceride levels in HCV group with genotype 3. Meanwhile,

low density lipoprotein cholesterol and apolipoprotein B were most related to total cholesterol.

Conclusion: Results demonstrate that correlation between lipid profile and clinical parameters were different in the 3 groups. It is known that the concomitant presence of NASH increases the risk of having advanced hepatic fibrosis and failure of antiviral therapy in subjects with HCV. Nevertheless the presented study showed that there was a correlation between the HCV-infection and NASH condition and additionally, after treatment with DAA-s occurred significantly improvement of NASH-biomarkers.

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Efficacy of entecavir in chronic hepatitis B patients based on previous exposure to lamivudine

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Introduction: Chronic Hepatitis B infection (CHB) is a serious health burden worldwide and is associated with complications as liver cirrhosis and HCC, hence antiviral therapy may be critical. Lamivudine (LAM) was approved as the antiviral agent of choice for CHB but recent guidelines recommended entecavir (ETV) or tenofovir (TDF) due to low risk for developing resistance.

AIM: To compare efficacy and resistance profiles of ETV between LAM-naive and LAM-exposed patients.

Materials and methods: A retrospective one-centre study was conducted in 2019. Medical histories of patients who had a clear status of LAM experience (naive/exposed) and received ETV therapy for 12 months and longer were selected for descriptive data analysis. A sample was divided into 2 groups: 1st- LAM-naive patients (n=21); 2nd- LAM-exposed patients (n=38).

Results: 59 patients met the inclusion criteria. 64% (n=38) of them were previously exposed to LAM. 87% (n=33) of LAM-exposed patients developed LAM resistance. Seroconversion occurred in 57% (n=12) vs 55% (n=21) of the patients in group 1 and 2 respectively. HBV DNA values prior to ETV therapy in group 1 and 2 were 5% vs 5% with less than 2000 IU/ml, 10% vs 18% with 2000 to 20000 IU/ml and 86% vs 76% with above 20000 IU/ml (mean $1,63 \times 10^8$ IU/ml vs $4,68 \times 10^7$ IU/ml) respectively. During follow up HBV DNA levels among LAM-naive patients dropped down more rapidly and in general were lower $>1 \log_{10}$ (with the means (IU/ml) of 38693 vs 84132 after 3 months, 38668 vs 583434 after 1 year, 27520 vs 106348 after 2 years, 163 vs 5954242 after 3 years and 23 vs 1761856 after 4 years in group 1 and 2 respectively). The prevalence of ETV resistance in the 1stgroup was 0% vs 24% (n=9) in the 2ndgroup. The mean length of ETV therapy before established ETV resistance was 38.4

months. 89% (n=9) of ETV resistant patients undergo further treatment with TDF.

Conclusions: ETV is an effective antiviral agent for CHB management but its efficacy varies depending on previous exposure to LAM. ETV is more effective in non-exposed patients as they achieved better outcomes in suppressing HBV DNA levels and none of the patients developed resistance. $\frac{1}{4}$ of the LAM-exposed patients develop resistance to ETV and the treatment occurs to be ineffective.

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Clinical features of viral diarrhea in the children of HIV

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Background: Viral diarrhea is the leading cause of uncertain etiology of acute intestinal infections. According to international statistics, 50-80% of diarrhea is viral diarrhea and children with opportunistic virus diarrhea are one of the clinical manifestations of HIV infection, resulting in rotavirus, I and II type common herpes viruses, cytomegaloviruses, picobirnaviruses, caliciviruses and adenoviruses

Methods: The study involved 30 children aged between 1 and 18 years who were treated at the Republican AIDS Center. 21 (70%) of the 30 children with diarrhea have been diagnosed with viral etiology. Children under the age of 1 year were 52.3% (11), 28.5% (6) of those aged 4-7 years, and 19.2% (4) aged 8-18 years clinical, virological, bacteriological, serologic (PCR) methods were used

Results: The study showed that viral diarrhea is more prevalent in children under the age of 3 years with HIV. 21 (70%) of the 30 children with diarrhea have been diagnosed with viral etiology. Viral diarrhea was caused in 16 children (76.2%) by rotavirus while normal diarrhea with normal Herpes type 2 (9.5%) and adenovirus diarrhea 1 (4.76%), 2 (9.5%) patients had mixed etiologic viral diarrhea. The most severe diarrhea was rotavirus diarrhea, with strong symptoms of intoxication and symptoms of multiple vomiting in children. The acute period duration was 8.7 ± 2.1 days, the maximum elevation of body temperature was 2-3 days at 38.4°C . Diarrhea syndrome lasted 11.4 ± 2.3 years, with a large number of aquatic feces without pathological complications Catarrhal signs in the rotavirus diarrhea were more susceptible to adenovirus diarrhea. The body temperature rose slowly and reached 39.1°C until 4-5 days before the onset of the disease. In the diarrhea clinic with a normal herpes virus, multiple seizures (more than 10 times) occurred suddenly on the background of sub-febrile body temperature. The return was 5.2 ± 1.8 days, the fecal matter was fluid and was observed 1-2 times a day

Conclusion: Thus, according to the results of the study, rotavirus was the leading cause of viral diarrhea in HIV-infected children. Diarrhea syndrome prevailed over vigor and vomiting

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Peculiarities of clinical manifestation of bacterial diarrhea in HIV-infected children

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Background: Diarrhea in HIV-infected children is often caused by various viruses (rotavirus, adenovirus, enterovirus) and bacterial (dysentery, salmonellosis, Klebsiella and other infections), which are caused by a weakening of the protective functions of the body. According to the WHO data, about 1.7 billion cases of acute diarrhea are registered in children every year in the world and 525 thousand children under the age of five die from that

Materials and methods: The study was conducted at the Specialized Clinic of the Republican Center for the Fight against AIDS. 50 HIV-infected children with the diarrhea syndrome of bacterial origin aged 1-5 years were included. Of the total number of children examined, 9 patients (18%) were diagnosed with Shigellosis, 4 children (8%) had salmonellosis, 6 children (12%) had Campylobacterium, 9 children had Staphylococcus (18%), enteropathogenic Escherichia coli in 10 children (20%), mixed flora in 12 children (24%). The diagnosis was based on clinical, immunological, virological, serological and bacterial studies

Results: The following clinical symptoms were observed in HIV-infected children with diarrhea syndrome diagnosed with shigellosis: high fever in all 9 children (100%), 2 children (22%) had body temperature rising to 37.5°C, 4 children (44%) - up to 38.0-39.0°C, in 3 children (33%) over 39°C. Symptoms of intoxication and dehydration of varying severity were observed in all children. Dyspeptic symptoms were also expressed to varying degrees: a sign of vomiting was noted - in 3 children (33.4%), nausea - 4 children (44%), abdominal pain and frequent loose stools mixed with blood, and tenesmus were observed in almost all children. Bacteriological examination of feces of 5 children (56%) showed Shigella flexneri, 2 children (22%) had Shigella boydii, 1 and 1 patients had Shigella dysenteries and Shigella zone (11%; 11%, respectively). In 4 HIV-infected children with

children's diarrhea syndrome, the diagnosis of "salmonellosis" is set on the basis of the bacteriological analysis of feces, where all children showed an increase in Salmonella typhimurium. Temperature reaction, which rose above 38°C, symptoms of intoxication and dehydration, pain in the epigastric region and around the navel, liquid fetid stool with mucus were observed in all patients (100%). Campylobacteriosis was accompanied in 5 HIV-infected children with children's diarrhea syndrome (83.4%) with a temperature reaction that rose to 38°C. Symptoms of intoxication and dehydration were less expressive than in children with "shigellosis" and "salmonella". Of the dyspeptic symptoms, nausea and vomiting were observed in 4 (67%). All children had frequent loose stools mixed with blood, with mucus with a fetid odor. 9 HIV-infected children diagnosed with staphylococcal infection the clinical symptoms of intoxication, diarrhea, dyspepsia, and dehydration was more expressive than in the above groups of children. In 10 HIV-infected children with Escherichia coli had normal body temperature, the symptoms of intoxication and dehydration, and frequent loose stools with mucus more than 3 times a day were less expressive(40%)

Conclusion: Thus, in HIV-infected children with diarrhea syndrome, the frequency of occurrence of bacterial agents does not differ from healthy children. The severity of clinical symptoms is more expressive

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Clinical features of gastrointestinal tract damage in HIV-infected children

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Background: The gastrointestinal tract is one of the key elements of a number of pathologic changes in HIV-infection. Gastrointestinal tract damage is one of the central stages of the pathogenesis of HIV-infection, with symptoms such as childhood backbone and adverse changes in the immune system, leading to an increase in the disease

Materials and methods: The study included 50 children aged 1 to 18 years who are being treated at the clinic of the Republican AIDS Center. The study was conducted in clinical, virological, immunological, bacteriological, PCR methods. Clinical signs of gastrointestinal disorders in HIV-positive children include 25 (50%) children with oral mucosal infection such as appetite reduction in children under 1, pain in the oral mucosa, intoxication, pain in the stomach, decreased appetite for children over 5 years, pain in oral mucosa, swallowing pain, pain in the epigastric area, appetite decrease, nausea vomiting

Results: Angular heilite 9 (36%) was characterized by redness and cracking in the corners of the mouth. Oropharyngeal candidiasis lasted more than 2 months in children over 6 months. HIV partner is experiencing the periodic stage of the oral cavity (8%), acute necrotic gingivitis (4%) and necrotic stomatitis (12%). In 3(6%) patients with HIV, oral cavity was detected. In children with HIV infection, recurrent erysleviral stomatitis (2 times per year) was detected in 17 (68%) children. Candidate esophageal cancer was recorded in 1(2%) patient. The patient was presented with signs such as pain and anguish behind the pelvis, discomfort when swallowed and difficulty swallowing, which led to anorexia. Gastritis was detected in 3(6%) patients, with nausea, abdominal pain, and vomiting in children. In 10 (20%) children with HIV VHB, 12 (24%) VHC and 4 (8%) VHB+ VHC were detected. General bilirubin in the blood and increased liver enzymes. In 8 (16%) patients cholecystitis was detected. In the infection of the biliary tract, palpation of the upper abdomen is accompanied by

cholestatic changes in pain, diarrhea and functional tests of the liver. 1 (2%) patients with HIV have been diagnosed with lymphoma of the oral cavity. In 2 (4%) patients, Kaposi's sarcoma was detected in the bowel

Conclusion: Thus, gastrointestinal tract damage is one of the leading symptoms of clinical manifestations in evaluating disease progression and prognosis in HIV-infected patients

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Evaluation of change of platelets in HIV-infected children during the treatment

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Background: The urgency of the HIV problem is not avoidable. Along with many opportunistic infections affecting the quality of life of people living with HIV, hematological disorders, including thrombocytopenia play an important role

Materials and methods: The study involved 40 children who were treated in the Republic Specialised AIDS center and under 18 years of age. The degree of immunodeficiency was determined by the level of CD4+-lymphocytes (according to WHO classification dated 2012), as well as the level of HIV RNA was detected. The median of age was 12.2±1,9

Results: Before treatment, the median platelet count was 190±2,4x10⁹/l (p<0,01). Depending on the scheme of antiretroviral therapy (ART), children were divided into 2 groups: group 1 (n=24) received 2 NRTI (Nucleoside reverse transcriptase inhibitors) plus NNRTI (Non-nucleoside reverse-transcriptase inhibitors), group 2 (n=16) received treatment according to the scheme NNRTI+NRTI+PI. As a result of treatment, after 12 weeks in group 1 of patients, the median platelet count was 170±2,4x10⁹/l (p<0,01) and in group 2 it was 185±2,1x10⁹/l (p<0,05), after 24 weeks it was 186±6,4x10⁹/l and 209±5, 1x10⁹/l (p<0,05), respectively

Conclusion: Thus, the ART schemes including the protease inhibitor were shown to have the most positive influence on the platelets count

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Assessment of the impact of alcohol abuse among young women with HIV/HCV coinfection

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Background: Alcohol use in patients with coinfection with HIV and viral hepatitis C (HCV) is an important factor that leads to additional hepatic and extrahepatic lesions, toxic and inflammatory changes, deterioration of immune status, which may require significant adjustment of medical care.

It is important to assess the nature and consequences of alcohol use in young women with HIV/HCV coinfection, which can form some socio-psychological characteristics and clinical consequences in both diseases.

Materials and methods: 167 women with HIV/HCV coinfection were examined. Among them, 77.2% of patients reported regular alcohol use (more than 2 times a week), 9.6% – daily. From the total sample, 50 women were randomly selected with laboratory-confirmed alcohol consumption (group 1). Methods for the determination of ethyl glucuronide in urine and carbohydrate-deficient transferrin in blood were used as identifiers of recent alcoholization. The comparison group included 50 women who denied a history of alcohol abuse and had negative test results (group 2). The groups were comparable in the main parameters studied. Two groups were analyzed and compared by social, psychological and clinical laboratory status with the determination of CD4 lymphocytes, HIV RNA and HCV genotype and indicators of clinical and biochemical blood tests.

Results: The age of women was 35.9±4 years. In both groups, women with secondary or secondary technical education prevailed (61%). Among the patients abusing alcohol, 78% were married, 30% of them had children. Women who denied alcohol use were married in 64% and had children in 44% of cases. Most of them were diagnosed with HIV and HCV at the same time, and the duration of infection with two diseases was more than 10 years. The parenteral transmission of HIV and HCV infection

prevailed, but among women who consumed alcohol, it was more common than sexual (96% vs 70%, $p<0.05$). The majority of women in both groups (94%) received ART, the median number of CD4-lymphocytes was 443.5 cells/ μ l, but in group 1 women the level of CD4-lymphocytes was lower than in the comparison group (423 vs 474.5 cells/ μ l, $p<0.05$). In patients who use alcohol, HCV RNA was detected more often than in women with negative results of alcohol tests (92% vs 70%, $p<0.05$). Alcohol-abusing women had higher ($p<0.05$) rates of gamma-glutamyl transpeptidase (median was 82 U/l) and total bilirubin (15 ± 8 μ mol/l), similar indicators in the comparison group were 63.2 U/l and 11 ± 4 μ mol/l.

Conclusion: There is a high incidence of problem alcohol use in young women with HIV / HCV coinfection. Due to alcohol abuse, additional immunosuppression develops, the risk of progression of inflammatory changes in the liver, activation of virus replication increases. For this category of women, it is necessary to develop programs of additional psychological and psychiatric intervention, taking into account individual and clinical psychological characteristics, as well as to identify the causes of alcoholism and their elimination, in order to optimize medical care and improve the results of antiviral therapy.

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Adherence to cART

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Background: Infection caused by human immunodeficiency virus (HIV) is one of the most serious, life threatening diseases in human history. Early use of antiretroviral treatment (ART) keeps people living with HIV (PLHIV) healthier and reduces the risk of HIV transmission.

Adherence to ART is crucial for the treatment success and is significantly associated with viral load and health related quality of life.

Objectives: To identify the level of adherence to ART and factors associated with it among PLHIV in Armenia.

Methods: The quantitative cross-sectional survey design with structured self-administered questionnaire was used for the study. The sample included 180 beneficiaries of the "Positive People Armenian Network" NGO, who were enrolled in the study by convenience sampling. The questionnaire was developed based on the questionnaires used in previous studies internationally: questions on socio-demographic data, care at the National Center for AIDS Prevention, knowledge on HIV/AIDS and ART, side effects of ART (ACTG questionnaire), adherence to ART (Morisky scale), and social support (MOS scale).

Results: The mean age of participants was 40.6. Males comprised 61.1% of the sample. About 67.8% of participants were married and 73.3% had secondary school education. Residents of Yerevan comprised 37.8% of the sample. The adherence to ART was 53.9%. In adjusted analysis marital status, residence place, gender, and knowledge on HIV/AIDS and ART score were significantly associated with the outcome variable. Adjusted odds of adherence to ART were 2.05 times higher among married people as compared to those who were not married. Odds of adherence increased 1.43 times per one unit increase in knowledge score on HIV/AIDS and ART in adjusted analysis. Females had 1.84 times higher odds of adherence to ART compared to males. People living in urban areas were 1.88 times more likely to be adherent to ART than people living in rural areas.

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Conclusion: This was the first study to explore adherence to ART among PLHIV in Armenia. The results suggest the need for educational programs to increase the knowledge on HIV/AIDS and antiretroviral treatment among PLHIV. Promotion of engagement in care and compliance to treatment should be particularly targeted towards males and residents of rural areas to enhance the adherence levels in these population groups. Further studies should be conducted to track the changes in the level of adherence to ART in Armenia and explore facilitators and barriers of

adherence in depth.

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Virologic outcomes of second-line antiretroviral therapy among patients with HIV drug resistance in Georgia

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Background: Maintaining durable suppression on second-line antiretroviral therapy (ART) is crucial for preserving health and treatment options. We evaluated virologic outcomes of second-line ART in Georgia.

Materials and Methods: Study included adult HIV patients receiving second-line ART because of HIV drugs resistance during 2014-2018, who had at least one viral load measurement at least 6 months after starting second-line regimen. Viral suppression was defined as viral load <200 copies/ml. Long-term virologic success was defined as 90% of time of follow-up spent with suppressed viral load, calculated as person-years spend with suppressed viral load divided by total person-years of follow-up. Factors associated with failure to achieve long-term treatment success was evaluated in multivariate logistic regression analysis. All statistical analyses were conducted using SAS 9.4.

Results: A total of 558 patients were included. The median age was 42 (IQR: 36-48) years, 402 (72.0%) were men, 259 (46.4%) were infected through heterosexual contact, 225 (40.3%) – through injection drug use (IDU) and 55 (9.9%) – through sex between men. Patients were known to be HIV positive for the median 5.7 (IQR: 2.7-8.5) years. Boosted lopinavir was the most commonly used protease inhibitor (PI) – 298 (53.4%) patients, followed by boosted atazanavir – 154 (27.6%), and boosted darunavir – 40 (7.2%). Fifty-one persons received integrase inhibitor based regimen – 51 (9.1%) and 15 (2.7%) were treated with combined PI and integrase inhibitor regimens. Overall 530 (95.0%) patients ever achieved viral suppression, 478 (85.7%) patients had viral suppression at the last measurement and 399 (71.5%) patients maintained viral suppression throughout the follow-up. Patients were followed for the median 1.3 (1.0-3.6) years and contributed 1179 person-years of follow-up, during

which 1015 person-years (86%) had viral suppression. Overall 451 (80.8%) maintained viral suppression 90% of time. In multivariate logistic regression factors significantly associated with failure to maintain viral suppression for at least 90% of follow-up included: age per year increase (OR: 1.03, 95% CI: 1.01-1.05, p=0.02), time since HIV diagnosis (OR: 0.92, 95% CI: 0.87-0.98, p=0.005) and time since initiating second-line ART (OR: 0.86, 95% CI: 0.75-0.99, p=0.03). No statistically significant differences were found by mode of HIV transmission and prescribed treatment regimens

Conclusions: Majority of patients achieved and maintained viral suppression on second-line treatment. Efforts are need to further increase the number of patients with durable suppression. Although lopinavir-based treatment was not associated with worse outcome, switching to atazanavir and/or daurnavir may improve adherence at least through decreasing pill burden.

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Sleep and eating disorders in a batch of HIV/AIDS patients

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Background: Sleeping and eating are probably the most important basic physiological functions that once disturbed can affect greatly the wellbeing and the quality of life. The majority of people living with HIV present sleep disturbances. Insomnia and obstructive sleep apnea syndrome are the most common disorders seen in this group of population. Also HIV infection largely impacts on the nutritional status of infected patients. Nutritional status of infected people is essential for keeping CD4 level and immune system supportive in the fight against complications. Unfortunately some patients receiving ART experience minimal drug side effects on sensory functions that alter taste and smell, decreasing appetite and so leading to unhealthy food habits and low quality diet.

Materials & Methods: This is a cross-sectional study aimed to investigate sleep disorders and carotenoid score. Insomnia is evaluated by clinical interview and STOP- BANG questionnaire. The STOP-BANG is a useful 8-item screening tool. A patented Bio Photonic Scanner was used in order to measure, at the skin surface, in a non-invasive way, the Skin Carotenoid Score (SCS)- which has been scientifically correlated to overall antioxidant status . The technology of the scanner is based on an optical method known as Resonant Raman Spectroscopy, which has been used for many years in research laboratories. Data were processed with Excel and correlations were made with Tableau Software. Significant p values were considered those under 0,05.

Results: The study included randomly 69 HIV patients in different stages. 51/69 were man. 4/69 patients were older than 50 years. Of them, almost half (33/69) declared that they are unsatisfied of their sleep. 50/69 patients feel tired/exhausted during the day and 36/69 said that the tiredness affect their daily routine. Only 12/69 accused snoring and only 5/69 patients have high blood pressure. 12/69 presented sleep apnea. 21 patients were classified as having a moderate risk of sleep apnea

and two presented a high risk of sleep apnea according to STOP-BANG questionnaire.

Regarding the SCS, the mean score was statistical significant lower ($p < 0,05$) than a control group of healthy people of the same age and sex with the study group.

Conclusions: Treatment of sleep disorders is important for improving quality of life and preventing associated health problems (especially cardiovascular disease) in people living with HIV. By SCS, we overall assumed the nutrition status and encourage HIV infected patients to make improvements to their diet and lifestyle. This measures are also helping in making an informed decision on which supplements are properly formulated to impact the patients antioxidant health.

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Adding atheromatosis to the cardiovascular risk for a 30 years old patient from Romanian HIV cohort

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Case presentation: We report the case of a 28 year-old female having HIV infection since early childhood (diagnosed in 1997, receiving ART since 2002 – considered a patient from the Romanian pediatric cohort). The patient received multiple ARV schemes including d4T, 3TC, ABC, EFV, ETR, LPV/r, DRV/r, and RAL with periods of undetectable viral load.

Starting with October 2016 the patient accused intense abdominal pain especially after meals with nausea and vomiting. Upper gastrointestinal endoscopy and abdominal ultrasound showed duodenitis and enlarge lymph nodes, finding that did not justify the symptoms. CT scan showed impressed atheromatosis of the abdominal aorta with remaining lumen of 1cm in diameter; 61% stenosis of the celiac trunk, 93% stenosis of the mesenteric artery with complete stenosis of the emergence of jejunal artery, but with re-permeability through Riolan arcade; 43% stenosis of the right renal artery.

Due to intense pain after a meal the patient stopped taking cART (DRV/r+RAL+ETR) in the last months. At admission the patient had a CD4 cell count of 104 cell/mm³ and a viral load of 11 123 copies/mL. The only mutation registered on resistance test was L10V mutation.

We started psychological counselling for restarting cART. Considering the pathophysiological of atherosclerosis we decided to initiate anticoagulant (therapeutic dose of fraxiparine) and dual antiplatelet therapy together with lipid-lowering therapy. The abdominal symptoms diminished in less than 2 weeks on anticoagulant therapy, so we decided to restart the cART with an easy to take scheme for getting the best compliance: unboosted ATV+CBV.

Conclusions: Usually in non-HIV patients, the risk of atherosclerosis and cardiovascular disease increases after 45-55 year-old, compared with HIV patient where the risk increases earlier, atherosclerosis being accelerated by the virus itself, by chronic inflammation, by cART or by immune activation after cART initiation.

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High-dose benzylpenicillin treatment induced febrile neutropenia for HIV-infected male with neurosyphilis

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Prompt therapy with high-dose intravenous benzylpenicillin for a prolonged period is critical for neurosyphilis patients to avoid irreversible sequelae. However, life-threatening neutropenia has been reported as a complication of prolonged therapy (more than 14 days) with high doses of benzylpenicillin. Here we report a 54-year-old HIV infected man who developed high-dose-benzylpenicillin induced febrile neutropenia on the 20th day of treatment. It presented as fever up to 39,8°C, severe leukopenia (WBC $<1 \times 10^9/l$), neutropenia (NE $0,2 \times 10^9/l$), slightly elevated CRP and PCT, and no clear signs of infection. A diagnosis was confirmed by excluding other possible causes of febrile neutropenia: flu, measles, sepsis, HIV-related neutropenia. 3rd generation antipseudomonal cephalosporin plus vancomycin and G-CSF were chosen as a treatment, which rapidly improved clinical and laboratory findings. This case highlights that, though rare, high-dose-benzylpenicillin induced neutropenia should be considered in neurosyphilis patients who are on long period treatment and there are no evidence of other neutropenia cause. Early detection and proper treatment are needed to prevent the condition from deteriorating further and to minimize mortality.

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Chronic viral hepatitis C therapy with direct action antiviral drugs

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Background: According to the World Health Organization there are 71 million people chronically infected with the hepatitis C virus. About 399,000 people deaths each year, mostly from cirrhosis and hepatocarcinoma. GT 1 and 3 are the most common causes of infection. Chronic HCV infection is accompanied by extrahepatic manifestations reported in up to 75% of patients, rapid development of hepatic fibrosis and accelerated time to cirrhosis and increased risk for liver failure, HCC and liver-related mortality. Treatment with direct acting antiviral drugs may result in sustained virological response (SVR) in about 95% of cases by eradicating the infection.

Material and methods: The study included 180 patients with chronic viral hepatitis C aged 21 to 77 years. The patients were divided into two groups of 90 subjects each. Patients from the first study group had been treated with Sofosbuvir 400 mg + Ledipasvir 80 mg, those from the second group - Sofosbuvir 400 mg + Daclatasvir 60 mg orally, once a day for 12 weeks. The following tests were performed: levels of viremia, genotype of the virus, level of fibrosis (Fibroscan), relevant biochemical tests and general blood test.

Results: Out of 180 patients with chronic hepatitis C, 49.5% were males and 50.5% were females. Age varied between 22 and 79 years, mean age being 50,13±1,28 years. During the whole treatment, patients from both groups had a clear positive dynamics, with substantial subsiding of cytolytic activity. Our study has shown that both regimens of treatment with Sofosbuvir / Ledipasvir and Sofosbuvir / Daclatasvir for 12 weeks in patients with chronic HCV had high efficacy. Treatment with Sofosbuvir / Ledipasvir achieved sustained virologic response in 83(92,2%) of patients and 78 (86.6%) of those who received Sofosbuvir /Daclatasvir. Treatment was effective in both naive patients and those who had been previously treated with PEG/INF and RBV without any success. During the treatment

with antiviral drugs few patients experienced side effects such as asthenia, headache, insomnia, nausea, pruritus which did not require discontinuation of treatment. From those 19 patients with therapeutic failure were mostly naive patients, female gender, with F3 fibrosis level.

Conclusions: Our study has shown that treatment with Sofosbuvir / Ledipasvir and Sofosbuvir / Daclatasvir for 12 weeks achieved a high sustained virologic response both in naïve patients with chronic HCV and those previously treated with PEG-IFN and Ribavirine. Sofosbuvir/Ledipasvir scheme was more efficient than Sofosbuvir/Daclatasvir. New antiviral drugs were well tolerated by most of the patients, minor side effects being recorded, that did not require discontinuation of treatment.

Keywords: chronic viral hepatitis C, treatment, sofosbuvir, ledipasvir, daclatasvir

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Patients with HCV RF1_2k/1b recombinant strain are highly responsive to LDV/SOF/RBV therapy

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Background and Aims: We are reporting the interim result of the 4 year prospective study, which is assessing prevalence of HCV recombination among genotype 2 and genotype 1 patients as well as efficacy of different DAA treatment options in these group.

Method: HCV infected patients receiving Sofosbuvir/Ribavirin (SOF/RBV) or Ledipasvir/Sofosbuvir/Ribavirin (LDV/SOF/RBV) within national hepatitis C elimination program were enrolled. Since 2015 541 adult patients with HCV genotype 2 and 50 HCV genotype 1 were enrolled. Genotyping was determined by 5'UTR/Core amplification and later retested in NS5B region for clarifying HCV recombinant strain. Confirmation of breakpoint positions among selected RF1_2k/1b patients was performed by whole genome sequencing.

Results: Of total 541 HCV genotype 2 patients enrolled 410 (75.7%) had RF1_2k/1b strain and 131 (24.2%) had either HCV 2a, 2k, or 2c subtypes. Of these patients, 470 (86.9%) were males with a median age of 51.2 years (IQR-42.1-62.1%), and 40.1 % had advanced liver disease. RF1_2k/1b distribution by gender was statistically significant ($p=0.003$) attesting higher prevalence of these strain between male population (77.9% versus 61.9 %). As of June, 2019, data on sustained virologic response (SVR) was available for 375 individuals. SVR rate was 96.6% (84/87) among genotype 2 and 91.3% (263/288) among RF_2k/1b patients ($p=0.16$), with an overall SVR rate of 92.5% (347/375). Highest SVR rate was observed among patients treated with LDV/SOF/RBV among both genotypes (99.2%) and lowest among SOF/RBV group (73.6%). For patients with advanced liver diseases SVR was 95.5% (42/44) among genotype 2 compared to 83.7% (121/145) among RF1_2k/1b ($p=0.046$) patients. Among non-cirrhotic patients, genotype 2 did not show statistically significant difference 97.7% (42/43)

compared to RF1_2k/1b group (SVR 99.3% (142/143)). Among patients with RF1_2k/1b treatment with LDV/SOF/RBV for 12 weeks was superior (SVR 100.0 % (197/197) to SOF/RBV for 12 weeks (SVR 68.5% (50/73)). Among HCV genotype 1 patients, no recombination events were identified and SVR rate was comparable with the overall result of the hepatitis C elimination program (99.5%).

Conclusion: RF1_2k/1b is highly prevalent in Georgia, especially in male population, and is easily treatable with LDV/SOF/RBV within Georgian national hepatitis C elimination program.

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Features and variability of high-density lipoproteins cholesterol among HIV-infected patients in Ukraine

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Background: Variability of cardiovascular risk factors influence the development of cardiovascular disease (CVD). According to the work carried out in Russia, the number of HIV-infected patients with a significant violation of lipid metabolism, high and very high cardiovascular risk increases to 2-3% of the observed patients.

Our aim was to study high-density lipoproteins HDL-cholesterol variability and its clinical significance in HIV-infected patients as a population at high risk of CVD in Ukraine.

Materials and Methods: The retrospective and prospective cohort study included 128 adult HIV-infected patients who received antiretroviral treatment. Average age patients were 47.2±7.8 years. Two studies were conducted in this group of patients. The first study was aimed at quantifying the variability of HDL-cholesterol between two consecutive patient visits to determine factors related to such changes. The second study is a retrospective cohort study to assess possible relationships between the variability of HDL-cholesterol and the occurrence cardiovascular disease. Statistical analyses were carried out using the SPSS/PC + statistical package (version 17; SPSS, Chicago, IL, USA).

Results: Males accounted for 51.2% of the surveyed cohort and mean ± standard deviation of patients' age was 47.2±7.8 years. The absolute difference in serum HDL-cholesterol between the first and second visits was 16.1±8.2 mg/dl. In 23.2% patients the absolute value of the difference between the results of serum HDL-cholesterol level was 20 mg/dl or higher. Analysis of the number of cigarettes smoked per day showed a significant negative correlation with the absolute difference serum levels of HDL-cholesterol between two visits. Overall, during the retrospective and prospective cohort portions of the study, 8.5% patients had CVD. HDL-cholesterol was

higher in those patients who did not suffered a cardiovascular event (p=0.04).

Conclusions: Variability of HDL-cholesterol among HIV-infected patients in our study was substantial. Smoking was inversely correlated with such variability among HIV-infected patients in Ukraine.

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Detection of specific antibodies to the HCV core+1 protein in “naive” chronically HCVinfected patients

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Core+1/ARFP is a product of the alternative open reading frame located within the core HCV gene. The biological role of the core+1 protein in the HCV life cycle is still unclear. Several studies demonstrated the presence of core+1 antibodies in chronically HCV-infected patients at different stages of liver fibrosis.

Anti-core+1 antibodies are present in more than 50% of patients with HCV-associated hepatocellular carcinoma. This suggests that it may be a possible factor for the liver fibrosis progression.

The aim of the present study was to evaluate the prevalence of antibodies to the HCV core+1 protein in “naive” patients chronically infected by subtype 1b and 3a HCV.

The serum samples from 86 chronically HCV-infected patients (37 men and 49 women) which have been observed in the polyclinic department of the Saint-Petersburg Botkin clinical infectious hospital in 2017 were included. The average age was 50.74 ± 2.69 . The presence of HCV anti-core+1 antibodies were detected by in-house enzyme-linked immunoassay (ELISA) using synthetic peptides the amino acid sequence of which corresponding to the antigenic determinant of core+1 protein of the HCV subtypes 1b and 3a. Samples with an S/CO of > 2.5 were considered as positive.

In total anti-core+1 antibodies were detected in 39 patients. Among them, 19 were infected by the subtype 1b, and 20 by the subtype 3a. Anti-core+1 antibodies were determined in HCV-infected patients with different stages of fibrosis as well as in HCV-infected patients with advanced cirrhosis. The potential cross-reactivity of the antibodies of patients infected by the subtypes 1b and 3a using

two synthetic peptides was also detected. Six (31.57%) of 19 anti-core+1-positive patients infected by HCV subtype 1b were found to have cross-reactivity with a synthetic peptide corresponding to the core+1 immune epitope of HCV subtype 3a, and eight (40%) of 20 anti-core+1-positive patients infected by HCV subtype 3a with a synthetic peptide corresponding to HCV subtype 1b.

The study has not indicated any statistically significant dependence between the presence of anti-core+1 and patient's gender, patient's age, disease duration, or biochemical activity of the infectious process (ALT, bilirubin).

The results indicate that it is necessary to continue the study, to increase and to expand the observations on patients with advanced cirrhosis and hepatocarcinoma. In particular, patients with different results of therapy with direct antiviral action drugs must be included in the further studies.

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Approaches to providing hepatitis C viremia testing to people who inject drugs in Georgia

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Background: In 2015, Georgia embarked on an elimination programme in line with the WHO hepatitis C virus (HCV) elimination targets. However, a large proportion of infected persons remain unaware of their infection. To expand treatment more widely to those at high risk of HCV infection, people who inject drugs (PWID) have been prioritized for test and treat strategies. Though anti-HCV screening for PWID has been implemented, access to confirmatory viremia testing remains a major gap in access to HCV care. We evaluated two novel approaches to improve access to viremia testing among PWID attending for care at harm reduction sites (HRS).

Materials & Methods: This is an ongoing cluster, non-randomized intervention study where HRS are assigned to one of three arms i) at four HRS, decentralized testing (Arm 1) where blood draw, viremia testing (using GeneXpert HCV testing) and results provision is carried out on-site on the same day, ii) at two HRS, a centralized viremia testing approach is implemented (Arm 2) with blood draw on site and confirmatory testing using centralized HCV core antigen testing. Test results are made available at HRS at a follow up visit, iii) at two HRS, testing is done as per standard of care (Arm 3) where patients are referred to a treatment centre for testing and results are provided at the treatment centre. Arm 1 and Arm 2 are using “HRS-based approaches” as participants have blood drawn and receive test results at HRS. Participants are eligible for the study if they tested anti-HCV positive on the same day and did not have prior confirmed diagnosis. The proportion of participants who completed each step in the HCV care cascade were compared across the three arms as well as the turnaround time of test results.

Results: Between May 2018- June 2019, 1646 participants were enrolled (620 in Arm 1, 465 in Arm

2; 561 in Arm 3). Participants were predominantly male (95.5%), median age 43 [19-88] years and 1266 (76.96 %) were currently injecting drugs. 1577(95.9%) participants reported ever having an HIV test and of these 12 (0.76 %) self-reported being HIV positive. To date, 1218 participants had a confirmatory test done (618 in Arm 1, 255 in Arm 2; 345 in Arm 3 and of results, 992 (81.4%) were confirmed HCV positive. 874 (88%) of HCV positive patients initiated treatment, of whom 703 (80%) completed treatment, 338 (48.1%) received SRV 12 testing, and 331 (97.9%) achieved cure. On average participants received their results in Arm 1 on the same day, Arm 2; 21.5 days and Arm 3; 18.6 days from the time of test. 100% of HIV/HCV coinfecting participants were linked to ART and HCV treatment.

Conclusions: Providing blood draw for HCV confirmatory viremia testing at HRS where PWIDs attend for care/needle provision improves access to HCV confirmatory viremia testing. The “HRS-based approaches” resulted in a larger proportion of participants receiving their confirmatory test results and the turnaround time was shortest where blood draw at HRS was combined with on-site testing.

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The expression level of miR-196a in Ukrainian patients with chronic viral hepatitis C

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Background: Regulatory mechanisms in the pathogenesis and progression of liver fibrosis in patients with chronic viral hepatitis C (HCV-infection), including genetic and epigenetic components are still not fully clarified. To date, the role of microRNA in the pathogenesis of various diseases, including liver diseases, HCC is being studied. The purpose of this study was to investigate the level of expression of miR-196a in patients with chronic HCV-infection.

Materials & Methods: The study involved 74 patients with chronic hepatitis C, G1, age (M±m): 47.5±1.4 years. Male - 38 (51.4%), female - 36 (48.6%). The average duration of the disease (Me) was 4.0 years (IQR: 2.0-8.0). Chronic HCV-infection was diagnosed according to local clinical protocols. The control group was consisted of 11 healthy individuals. We used two-stage protocol for MiRNA detection. After isolation of total RNA from plasma, Real-time quantitative PCR was performed using TaqMan® MiRNA analysis (Applied Biosystems, USA) for detection control gene U6 and expression of miR-196a. Data processing and statistical analysis was conducted using the Statistica v.6.1® software.

Results: The level of expression of the U6 gene in patients varied from 16.94 to 34.05 units, averaged 27.31±0.51 units. In the control group, U6 varied from 23.91 to 29.26, with the average level 26.95±0.47. There were no U6 expression significant differences in both groups (p=0.609) that indicates its independence from pathological conditions.

The average level of expression of miR-196a in patients with chronic viral hepatitis C was lower- 0.28 units (IQR: 0.01-1.11) in comparison with healthy individuals – 0.44 units (IQR: 0.19-2.4) p<0.4. Statistical analysis revealed a direct significant positive connotation between the level of expression of miR-196a with HCV-infection and blood parameters (Spearman's Rank Correlation

Coefficient - rs): the level of leukocytes (Le) (rs=0.384; p=0.001), platelets (Tr) (rs=0.312; p=0.007), lymphocytes (Lc) (rs=0.242; p=0.038), neutrophils (Ne) (rs=0.330; p=0.004). At the same time, a reverse correlation between the level of expression of miR-196a and the previous experience of patient treatment and failure therapy was found, namely, whether the patient is a naive patient or has had a previous failure of therapy with schemes containing interferon (non-responder or relapse of HCV-infection) (rs=-0.337; p=0.003), as well as with level of total bilirubin (rs=-0.325; p=0.005), presents of liver cirrhosis (rs=-0.328; p=0.004), splenomegaly (rs=-0.370; p=0.003).

Conclusions: the study showed that of expression of miR-196a was decreased in patients with chronic viral hepatitis C compared to healthy individuals, which may indicate his involvement in the pathogenesis of HCV-infection. The level of expression of miR-196a correlated significantly (p<0.05 to p<0.01) with CBC parameters, the presence of liver cirrhosis and splenomegaly, the previous unsuccessful treatment experience.

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New aspects of the impact of co-infection with hepatitis B virus and co-infection with human immunodeficiency virus on the probability of HCV spontaneous elimination among Ukrainian HCV-infected cohort

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Background: According to the WHO, Ukraine belongs to countries with an average prevalence of HCV-infection, where about 3% of the population (more than 1 million people) were infected. According to literary sources, spontaneous elimination of the hepatitis C virus (HCV SE) more often occurs after acute hepatitis C and can reach 3.7-53% of all HCV-infections in different parts of the world depending on the diverse life characteristics and race. Despite of the achieved progress, the natural course of HCV-infection remains a problem for specialists in this field. The purpose of this study was to determine the influence of HBV/HCV and HIV/HCV co-infection on the probability of HCV SE after acute HCV-infection among patients who live in Ukraine.

Materials and Methods: The retrospective observational study has covered 271 patients from the south-eastern and central regions of Ukraine who had HCV-infection (without antiviral therapy). Of these, chronic HCV-infection was diagnosed in 222 (81,9%) persons (1st group) and HCV SE was installed in 49 patients (18,1 %) persons (2nd group). HCV SE was defined as being HCV-RNA-negative at least 2 years after the estimated seroconversion date. Patients in both groups were tested on anti-HBcore, HbsAg, anti-HIV by enzyme-linked immunosorbent assay (ELISA), chemiluminescent immunoassay (CLIA), western blot analysis and HBV-DNA by real-time polymerase chain reaction (RT-PCR). Markers of HBV-infection and HIV-infection in both groups were compared by direct counting and Pearson's chi-square tests. SPSS version 22.0 was used for statistical analysis.

Results: Males accounted for 47.3%, females accounted for 52.7% of the cohort (average age of patients was 42.4±6.7 years). Analyzing data from both groups we have established that among patients with HCV SE markers of HBV-infection was encountered much more often than among patients with chronic HCV-infection: anti-HBcore – 27.2 % and 7.3 % (p<0.001), HBsAg – 16.3 % and 6.3 % (p=0.042), HBV-DNA - 14.3 % and 5.4 % (p=0.035) respectively among patients of the 2nd and 1st groups. Anti-HIV were determined in 9 % patients of the 1st group and only in 2 % patients of the 2nd group (p=0.030).

Conclusion: HCV SE is much less frequently found among HCV-infection persons with HIV status than in individuals without an immunodeficiency state. HBV is defined as a predictor of a favorable course of HCV-infection among HCV-infected patients in Ukraine.

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Clients' satisfaction with HIV treatment services in Bamenda, Cameroon: a cross-sectional study

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Background: Clients have explicit desires or requests for services when visiting hospitals; inadequate discovery of their needs may result in dissatisfaction. Patient satisfaction influences retention in HIV care, adherence to HAART and serves as determinant to HIV suppression. This study's objectives were to quantify clients' satisfaction with HIV services in Bamenda and determine relationship between satisfaction and clients' socio-demographic/structural characteristics.

Methods: A cross-sectional study was conducted on HIV-positive patients followed-up, on treatment and who consulted in the Bamenda Regional Hospital treatment centre between July and August 2014. Participants consent was sought and data collected on client's level of satisfaction to staff-patient-communication, staff attitudes, privacy and confidentiality and staffing and amenities situations in the hospital. Data was collected using a structured questionnaire interviewer-administered by investigator and trained health personnel. Collected data was analyzed using Epi Info version 3.5.4 and clients' satisfaction measured using frequencies and percentages.

Results: A total of 384 participants took part in this study and their median age was 37 years (IQR: 29-46). Two hundred and seventy-four (71.4%) participants were females. Overall satisfaction with HIV services was 91.2% and participants reported less satisfaction with overall staffing and amenities situation of the centre (3.6%). In the multivariate analysis, only being female, employed and perceiving high number of nurses working at the treatment centre remained significant predictors of overall satisfaction with HIV services.

Conclusion: A high proportion of participants expressed satisfaction with HIV services. However, some dissatisfaction is masked in this high satisfaction level. This dissatisfaction underscores need to improve staff attitudes, staff-patient-communication, employ more staff and build better

patient facilities. Future studies need to focus on assessing long-term progression of satisfaction levels with services and determinants of satisfaction involving larger samples in many treatment centres.

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HCV in Hemophilia patients – Treatment Results in Kyiv, Ukraine

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Background: Hemophilia increases the risk of infection with hepatitis C virus (HCV) due to contaminated or unheated blood products. And the degree of liver dysfunction mainly affects the prognosis of HCV-infected hemophilia patients. The advent of safe and potent regimens of direct antiviral agents (DAA) has revolutionized therapy of HCV in patients with hemophilia and make possible the elimination of infection in these populations. There are about 180 registered patients with hemophilia in Kyiv, and about 90-98% of them infected with HCV.

Materials and Methods: This report reviews the response to DAA therapy in patients treated at Infectious Diseases Department of O.O. Bogomolets National Medical University. We observed 11 patients with chronic hepatitis C and hemophilia A, mean age was 37,8±5,6y. All of them were positive for HCV RNA, four of them had elevated of ALT/AST levels, and two of them was diagnosed liver cirrhosis. Current HCV RNA genotypes among hemophilia patients were 1b (8 patients) and 3a (3 patients).

Results: All patients with 1b genotype (two of them was diagnosed liver cirrhosis, stage A Child-Pough) got antiviral treatment with SOF/LED (and Ribavirin for cirrhosis), and SOF/VEL– for 3a genotype during 12 weeks. During the treatment no clinically significant adverse events were not observed. Just general weakness in cirrhotic patient was present also this patient had moderate anemia, that was connected with ribavirin and its dose was reduced. Three patients had significant joints bleeding episodes during the treatment. All patients demonstrated biochemical response and eight of them had rapid virological response at 4-th week of treatment. And sustained virological response was also achieved by these patients.

Conclusions: HCV-infection is the dominant complication of substitution therapy in patients with

hemophilia and the cause of death due to end-stage liver disease. But there are not enough clinical studies of treatment of these patients. We introduced our experience, that showed good results – all 11 patients achieved sustained virological response. There are substantial clinical benefits of this treatment, such as oral administrations of DAA and no significant adverse events. But new episodes of bleeding and blood transfusions increase the risk of new infection of blood borne diseases in hemophilia patients.

So, our experience of successful treatment of HCV in patients with hemophilia show that the recommendations of treatment of non-hemophilia-related HCV can be extrapolated to the hemophilia scenario.

Micro-elimination of HCV-infection in hemophilia patients is not only decrease death level due to end-stage of liver disease in these patients, but also is one of significant part of global WHO strategy of eliminating HCV by 2030. One of key target for countries worldwide is to reduce new HCV cases by 80%.

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The Association of Depression among Patients of Hepatitis C Virus Taking Direct Antiviral Agent.

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Background: Hepatitis C virus (HCV) - induced decompensated liver cirrhosis is a life-threatening illness with an average 5-year survival rate of 50%. HCV is endemic in Pakistan and its burden is expected to increase in coming decades owing mainly to widespread use of unsafe medical procedures. A systematic review showed that HCV seroprevalence among the general adult Pakistani population is 6.8%, while active HCV infection was found in approximately 6% of the population.

Aim: To determine the association of depression among patients of hepatitis C virus taking direct antiviral agent.

Material and Methods: Study design: Cross sectional study

Setting: Unit II, Department of Medicine, Jinnah Hospital, Lahore, Pakistan

Duration: Six months from September 2017 to March 2018

Data collection procedure: Total 110 Patients fulfilling the inclusion criteria were selected from OPD of Department of Medicine, Jinnah Hospital, Lahore. Informed consent was obtained. Demographic information (name, age, gender, duration of HCV and DAA treatment) was also obtained. Then patients were evaluated for depression by a senior psychiatrist having at least 4 years' residency experience with assistance of researcher. If HADS score >11, the depression was labeled (as per operational definition). Patients with depression were managed by standard hospital protocol along with HCV treatment. All this information was recorded on proforma (attached).

Results: The mean age of the patients was 45.82±13.20 years the minimum age was 22 years and maximum was 69 years. There were 53(48.2%) males and 57(51.8%) females in our study. There

were 36(32.7%) patients who were illiterate, 41(37.3%) were middle, 33 (30%) were having education as matric or higher. There were 45(40.9%) patients with depression and 65(59.1%) without depression. There was significant association between Depression and age groups as the p-value was significant. (p-value=0.000).

Conclusion: Study findings concluded that major depression is a frequent occurrence among patients with hepatitis type C taking antiviral therapy.

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A study of Knowledge Attitude and Practices Related to HIV and AIDS among Pakistani Women

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Background: HIV has always been considered to be the Ribonucleic acid virus of the family Retroviridae this family of viruses is famous for causing the disease which is known as Acquired immunodeficiency syndrome (AIDS). If we enlist leading lethal infectious diseases AIDS is at the top of the list nearly forty million people infected throughout the world.

Material and Methods: This study was conducted upon a secondary data from demographic and health survey. This survey was conducted by national institute of population studies Islamabad.

Sample Size: The estimated sample size was 14,000 households.

Statistical Analysis: The descriptive statistics of socio demographic variables such as age of respondent, place of birth region, wealth index and education were measured. Associations between age groups, region, education, wealth Index, respondents occupation and exposure to media and ever heard of AIDS were assessed by using binary logistic regression models calculating OR with 95% CI. In our study the data was analyzed by using SPSS.

Results: In our study 2615 (19.3%) respondents were having age in the range of 14-24 years, 5161(38.1%) were having age in the range of 25-34 years, 4108(30.3%) respondents were having age in the range of 35-44 years and 1674 (12.3%) respondents were having age in the range of 45-59 years. Our study represented 6351(46.8%) respondents from urban area and 7207(53.2%) respondents were from rural area. Among 13558 women, 6557(48.5%) ever heard of sexually transmitted Infection, 5906(43.6%) women were aware about AIDS.

Conclusion: Most of the respondents in our study were aware about HIV/AIDS but the need always exists to make others aware about this lethal disease.

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Drug interactions between antiHIV and antihepatitis agents: Consequences and remedies

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Background: Both of the HIV-1 and hepatitis C virus (HCV) cause serious health problems as they affect 15.9 million people worldwide. Out which United States harbours more than 5 million individuals whereas India has about 1.5 million people containing co-infection of HIV-1 and hepatitis C virus, most of them are intravenous drug users (IDUs). Both viruses have ability to cause significant health consequences, especially when left untreated. HIV is known to attack the immune system of infected individual, specifically the CD4+ve T lymphocyte cells, which is involved in protection of the body from any pathogenic infection. On the other hand, the chronic HCV may lead to serious hepatic disorders such as liver cirrhosis or hepatic cancer. HIV and HCV possess similar transmission routes. Therefore, the HIV and HCV co-infection is very common.

Materials and Methods: The information on the subject was collected using different search engines such as google scholar, pubmed, research gate and science direct. The information was systematically reviewed, analysed and presented in this paper.

Results: According to a study, about 25% of HIV-infected patients in the USA are co-infected with HCV. Additionally, about 80% of those with HIV who inject drugs also have HCV. The HIV/HCV-co-infected patients experience more liver-related morbidity and mortality, nonhepatic organ dysfunction, and overall mortality than HCV-monoinfected patients. In recent years, however, HCV direct-acting antivirals (DAAs) have scaled some of these barriers as HCV/HIV-coinfected patients treated with newer DAA regimens have efficacy rates comparable to those of HCV-monoinfected patients. However, complex drug interactions between DAAs and antiretroviral therapy (ART) require close awareness and treatment adjustments. There is an urgent need to develop ART switches in collaboration with the HIV practitioner to allow compatibility of DAAs. Alternatively, antiHCV agents should be prescribed to take in such a way which minimizes the possibility

of their interactions with ART; for example the antiHCV regimen such as Sofosbuvir (Sovaldi), Ledipasvir / Sofosbuvir (Harvoni), Sofosbuvir / Velpatasvir (Epclusa), Ledipasvir, and Harvoni can be used with most ART (efavirenz, tenofovir, emtricitabine, rilpivirine, ritonavir-boosted darunavir, and raltegravir) as they do not exhibit drug interactions.

Conclusion: Drug interaction in case of HIV and hepatitis co-infection is a serious issue towards treatment of patients. An extensive research is, however, needed to develop a common drug of choice to interfere the progression of these twin viruses in an individual.

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