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NCDC NATIONAL CENTER FOR DISEASE CONTROL AND PUBLIC HEALTH

G E O R G I A

Prevalence and genotype distribution of hepatitis C virus in Georgia: A 2015 nationwide population-based survey

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INTRODUCTION

- Georgia is an Eastern European country with estimated high Hepatitis C (HCV) burden. However, country lacked updated, nationally representative data confirming disease burden[1].
- Georgia launched unprecedented HCV elimination program in April 2015, providing new DAAs at no cost to patients[2].
- A nationwide population-based Hepatitis C survey was conducted in 2015 to provide baseline data for the elimination program.

AIM

The survey aimed to:

- Estimate nationwide HCV prevalence
- Determine HCV genotype distribution
- Identify main risk factors for HCV infection in Georgia

METHOD

- The survey used a stratified, multi-stage cluster design (n=7,000) and included adults aged ≥18 years.
- A structured questionnaire collected data on socio-demographics, medical history, lifestyle information and HCV risk factors.
- Serum specimens were obtained and tested for anti-HCV antibody (anti-HCV). Positive samples were tested for HCV RNA and HCV genotype.
- Data were weighted using census data on sex, age, and geography. Descriptive analysis was conducted.

RESULTS

HCV Prevalence and Risk Factors

- National seroprevalence - **7.7%** (95% CI=6.7-8.9)
- Prevalence of chronic HCV infection - **5.4%** (95% CI=4.6-6.4)
- Two risk factors independently associated with anti-HCV+ status: history of injection drug use (IDU) (aOR=21.4, 95% CI=12.3-37.4), reported by 38.2% of anti-HCV positive participants, and ever receiving a blood transfusion (aOR=4.5, 95% CI=2.8-7.2), reported by 19.7% of participants;
- 46.7% of participants did not report either of these two risk factors. Among anti-HCV+ males, 50.9% reported history of IDU, 16.9% reported blood transfusion, and 38.4% reported neither risk factor.
- Among anti-HCV+ females, 2.4% reported IDU, 27.6% reported blood transfusion, and 70.0% reported neither risk factor (Figure 1).

HCV Genotypes

- The most prevalent genotype nationally was GT1b **(40.5%)** followed by GT3 **(34.7%)**, GT2 **(23.6%)** and GT1a **(0.6%)**.
- 0.7% of participants had indeterminate genotype results.
- Genotype distribution varied by sex and reported risk factors, with GT3 most common among males (39.6%) and participants reporting history of IDU (35.3%).
- GT1b was more prevalent among females (62.5%) and participants reporting history of blood transfusion (54.3%) (Figure 2).
- Among participants not reporting either IDU or blood transfusion, GT3 was the most common among males (41.9%), and GT1b was most common among females (64.9%).

Figure 1: HCV Risk Factors Reported among Anti-HCV+ Participants

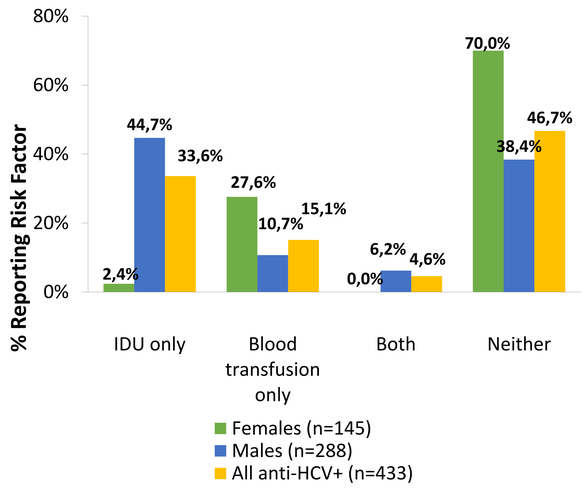
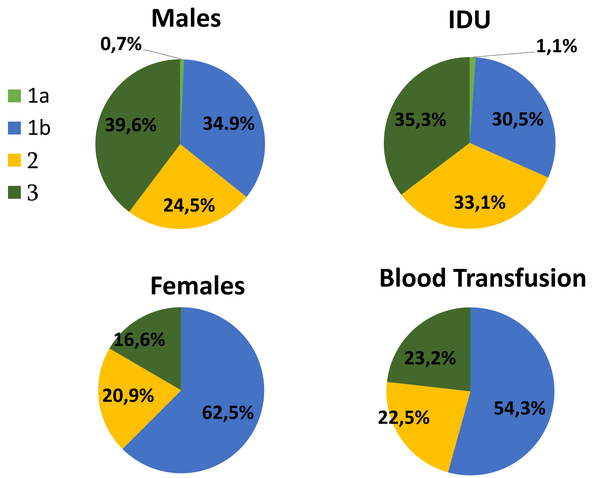


Figure 2: HCV Genotype by Sex and by Risk Factor



CONCLUSIONS

- HCV genotype distribution in Georgia varies by sex and reported risk factors.
- In the general population, genotypes 1 and 3 have similar prevalence
- Introduction of pangenotypic treatment regimens in the Georgian HCV elimination program would be beneficial.

ACKNOWLEDGEMENTS

This survey was conducted in collaboration with the U.S. Centers for Disease Control and Prevention (CDC). The authors thank survey participants, interviewers, phlebotomists, laboratorians and individuals who supported the fieldwork, as well as all respondents who agreed to participate in the survey.

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Prevalence and risk factors for hepatitis B infection in the adult population of Georgia: a nationwide survey

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INTRODUCTION

- Globally, 240 million people are chronically infected with hepatitis B and more then 686 000 people die annually due to it's complications; [1]
- Existing data were inadequate to give a complete picture of the burden of HBV infection in Georgia which shares modes of transmission and risk factors with HCV and poses additional risks of morbidity and mortality for those infected with both viruses;
- Hepatitis B vaccine has been included in the national immunization schedule since 2002, and coverage among children has reached 93.7%[2];

AIM

The primary objective of a nationally representative survey, conducted in the country of Georgia in 2015, was to estimate the prevalence of Hepatitis C and B infection in Georgia.

METHOD

- Stratified, multi-stage cluster design with random sampling;
- Sample: general population aged ≥18 years (n=7,000);
- Demographic data, medical and behavioral history, risk factors, knowledge and blood samples were collected;
- Blood specimens were tested for anti-HBc antibodies. Anti-HBc+ samples were tested for hepatitis B surface antigen (HBsAg).
- Prevalence of anti-HBc and HBsAg were estimated. bivariate associations between anti-HBc and potential exposures were examined using logistic regression.

RESULTS

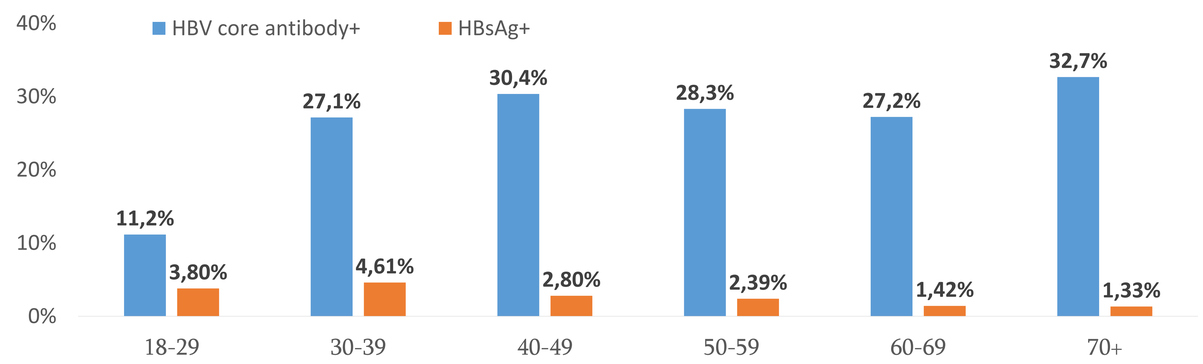
HBV Prevalence

- Hepatitis B surface antigen (HBsAg**): 2.9%** (95% CI=2.38-3.51)
- Males 3.4% (95% CI=2.48-4.34) vs. females 2.5% (95% CI=1.92-3.15)
- No statistically significant difference by urban vs. rural residence (3.1% vs. 2.8%);
- HBsAg prevalence in Tbilisi (capital) was lower (2.3%) compared to three other major cities:
  - Batumi 5.1%
  - Kutaisi 5.3%
  - Rustavi 5.2%
- Prevalence of anti-HBc was 25.5% nationally;
- Bivariate analyses revealed significant associations between anti-HBc+ status and people with history of blood transfusion, dialysis, injection drug use, at least one invasive medical procedure and incarceration (Table 1).
- Prevalence of HBsAg was highest in 30-39 age group (Table 2).

Table1. Characteristics associated with anti-HBc+ status in bivariate analyses

Characteristic	OR (95% CI)
Blood transfusion	1.9 (1.48-2.37)
Dialysis	4.0 (1.08-14.53)
Injection drug use (IDU)	2.8 (1.91-4.09)
At least one invasive medical procedure	1.2 (1.05-1.47)
Incarceration	1.9 (1.32-2.86)

Table2. Distribution of HBV core antibody+ and HBsAg+ by age groups



CONCLUSIONS

- High prevalence in other major cities indicates the need to strengthen infection control regulations and practice;
- The high prevalence of anti-HBc among persons with a history of blood transfusion, dialysis, IDU, invasive medical procedures, and incarceration could indicate that transmission occurs through these exposures;
- High anti-HBc prevalence among adults indicates that vaccination should be expanded to adults as part of Georgia's HBV prevention efforts.

ACKNOWLEDGEMENTS

This survey was conducted in collaboration with the U.S. Centers for Disease Control and Prevention (CDC). The authors thank survey participants, all interviewers, phlebotomists, laboratorians and individuals who supported the fieldwork.

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Abbott HCV Core Antigen and HCV RNA comparison study in country of Georgia

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INTRODUCTION

Hepatitis C virus (HCV) infection is endemic in many countries of the world, including Georgia. The government of Georgia launched a HCV elimination program with support from the US Center for Disease Control and Prevention. In 2015 a population-based cross-sectional household sero-survey was undertaken by the Georgian National Center for Disease Control and Public Health (NCDC) to determine the prevalence of hepatitis C (HCV) and B (HBV) virus infection in the country. These data are used to define the burden of HCV/HBV and risk factors for transmission necessary for successfully planning and execution of the HCV elimination program. Assuming an adult population of 2,800,000 with an anti-HCV prevalence of 7.7%, approximately 200,000 anti-HCV+ patients are estimated to require further testing to confirm active infection.

In light of the advances in HCV therapy, simplification of diagnosis confirmation, pre- treatment diagnostic workup and treatment monitoring is required to ensure broad access to interferon-free therapies. HCV core antigen (HCV cAg) testing is rapid, giving results in approximately 60 min, and less expensive than HCV RNA methods

AIM

To evaluate the performance of the ARCHITECT HCV core antigen test to identify patients with an active HCV infection relative to HCV RNA.

METHOD

- A total of 4,235 samples obtained from Blood Banks, Harm Reduction Networks (HRN), Provider Clinics, Screening centers and National Seroprevalence Survey (NSS) with available HCV RNA results were retrospectively tested with the ARCHITECT HCV cAg assay.
- Specimens with HCV cAg concentration <3 fmol/L are considered nonreactive, those with >3 fmol/L – reactive; specimens containing HCV cAg >3 but <10 fmol/L are considered “greyzone” (GZ) and should be re-tested in duplicate.
- A modified HCV testing algorithm that included confirmation of current infection by HCV cAg and reflex testing of HCV cAg negative samples by pooled HCV NAT (Figure 1) was compared to the use of HCV RNA alone.
- The study has the following limitations: many of the samples obtained from the HRN were lipeamic, contained fibrin, or had low volume; due to limited sample volume repeat testing of GZ samples was performed but not in duplicate.

RESULTS

- Overall agreement between HCV cAg and HCV NAT was 97.14% (1258/1294); 2.01% results (26/1294) were discordant and 0.77% (10/1294) were HCV cAg GZ unconfirmed or indeterminate.
- Of the 24 HCV RNA positive / HCV cAg negative samples:
  - From anti-HCV positive samples obtained during the screening activities 16 had viral loads <1,500IU/ml (of these 6 were <30 IU/mL) and 2 had a viral load >4,000 IU/mL, and
  - 6 samples from the HCV seroprevalence study had not quantifiable HCV RNA results, but were qualitatively positive.
- Of the 10 samples with HCV cAg GZ result 3 were HCV RNA negative and 7 were HCV RNA positive (2 had viral load 30,000 IU/mL, 4 were <1,000 IU/mL, and 1 was not quantifiable, but RNA qualitatively positive).
- The two samples which were HCV cAg positive / HCV RNA negative were low reactive <15 fmol/L.
- Estimated cost savings using a reflex algorithm for the confirmation of active infection involving HCV cAg test with sensitivity of 97% and HCV RNA are significant compared to the use of HCV RNA alone.

Abbott ARCHITECT i2000-SR

		HCV RNA		Total
		Positive	Negative	
HCV core Ag	Reactive	938	2*	940
	GZ-reactive	7**	3	10
	Nonreactive	24***	320	344
Total		969	325	1294
Percent Concordance: 97.1%				

* HCVcoreAg Low reactive <15 fmol/L
** 2 samples ~30,000 IU/ML;
4 - <1,000 IU/ML;
1 - qualitative from seroprevalence;
*** 6 samples - <30 IU/ML;
6 - <500 IU/ML;
2 - <1000 IU/ML;
2 - <1,500 IU/ML;
2 - >4,000 IU/ML;
6 - qualitative from seroprevalence;

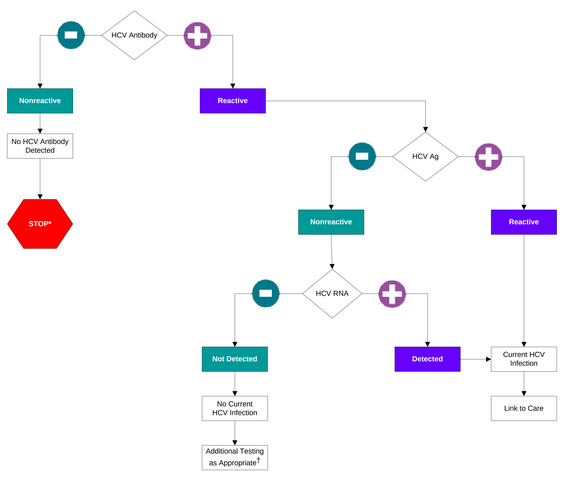

Figure 1: Algorithm for the use of HCV Antigen assay in conjunction with the HCV RNA test for the accurate identification of actively replicating HCV based on the findings of this review and previously published work.[1]

CONCLUSIONS

In this real world study HCV cAg accurately identified >97% of patients with active viremia and 100% accuracy can be achieved by reflexing all anti-HCV positive / HCV cAg negative samples for pooled HCV RNA testing with substantial cost savings. ARCHITECT HCV Core Antigen test can be used as an alternative to HCV RNA testing in a national HCV elimination program.

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- NCDC Lugar Center laboratory team- for testing and data analysis
- Abbott Diagnostics - for donating instruments, reagents, supplies and technical support
- US Centers for Disease Control and Prevention (CDC)- for TA in study design and implementation
- Ministry of Labour, Health and Social Affairs of Georgia - for general supervision and support of the study

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Treatment Outcomes of Patients with Chronic Hepatitis C Receiving Sofosbuvir-based Combination Therapy within National Hepatitis C Elimination Program in the Country of Georgia

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INTRODUCTION

- Management of HCV infection has been revolutionized after the availability of direct acting antivirals (DAAs), in particular Sofosbuvir (SOF).[1, 2]
- Georgia has one of the highest HCV prevalence rates in the world.[3]
- In partnership with the US CDC, and commitment from Gilead Sciences to donate DAAs, initially SOF, the country embarked on the world's first hepatitis C elimination program in April, 2015.[4]
- A key strategy of this program is to eliminate HCV in the country through identifying and treating all HCV infected persons.

AIM

- The aim of this study is to report the first data on SOF-based regimens in patients with chronic HCV infection in the country of Georgia.

METHODS

Study population and settings

- A retrospective cohort study was conducted among patients 18 years of age or older with HCV genotype 1-4 infection being treated with SOF-based regimens within hepatitis C elimination program between 28 April 2015 and 30 September 2016.
- Patients received treatment with SOF, Pegylated interferon (IFN) and Ribavirin (RBV) for 12 weeks or SOF and RBV for a duration of either 12, 20 or 24 weeks.
- Treatment-naive and experienced patients with cirrhosis, advanced liver fibrosis, severe extrahepatic manifestations, HCV re-infection after liver transplantation and HIV-coinfection were prioritized for enrollment in the treatment program beginning April 28, 2015.

Statistical analysis

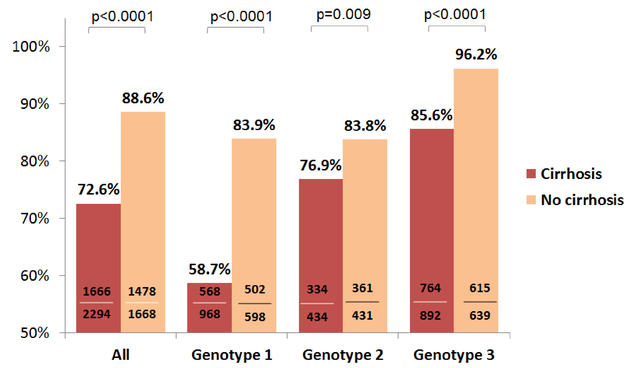
- Results for patients who completed treatment and tested for SVR through 30 September, 2016 were analyzed.
- The primary end point was Sustained virologic response (SVR), defined as undetectable HCV RNA at least 12 weeks after completion of treatment.
- Chi-square test was used to compare differences in SVR rates.

RESULTS

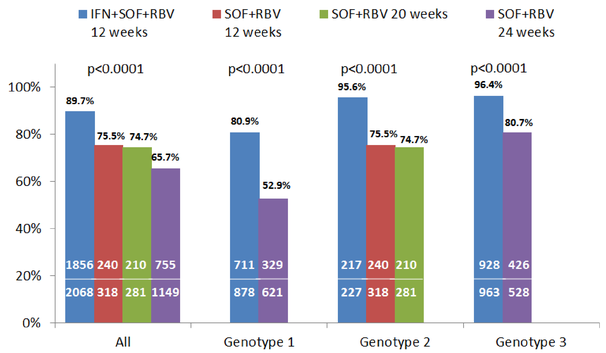
Baseline Characteristics

Characteristic	n=3966 TOTAL
Age category, n (%)	
18-30	18 (0.45)
30-45	802 (20.22)
45-60	2387 (60.19)
60+	759 (19.14)
Gender, n (%)	
Female	589 (14.85)
Male	3377 (85.15)
HCV RNA categories, n (%)	
<800,000 IU/mL	2257 (57.36)
≥800,000 IU/mL	1678 (42.64)
Cirrhosis, n (%)	
No	1671 (42.13)
Yes	2295 (57.87)
Treatment regimen, n (%)	
IFN/SOF/RBV (12 wk)	2070 (52.19)
SOF/RBV (12 wk)	346 (8.72)
SOF/RBV (20 wk)	291 (7.34)
SOF/RBV (24 wk)	1169 (29.48)
SOF/RBV (48 wk)	90 (2.27)

SVR Rates by cirrhosis status



SVR Rates by Treatment Regimen



- Overall, the treatments were highly effective. Levels of HCV RNA were undetectable in 3 147 (79.3%) of those tested, indicating a virologic cure.
- The lowest response rate was observed among genotype 1 patients (1070/1566; 68.3%), intermediate response rate was achieved in genotype 2 patients (695/865; 80.3%), while the highest response rate was among genotype 3 patients (1379/1531; 90.1%). There were only 4 patients with genotype 4 of which 3 were cured.
- SVR was significantly lower among cirrhotic patients compared with patients without cirrhosis (72.6% vs. 88.6%, P<0.0001). Difference by cirrhosis status was statistically significant in all genotypes.
- Overall, IFN/SOF/RBV regimens achieved higher response rates (90%) than SOF/RBV regimens (68%).

CONCLUSIONS

- In the present study, SOF-based regimens resulted in a high overall SVR rate, which approximates those of the clinical trials.[5]
- Lower efficacy of treatment in genotype 2 patients may have been associated with a reported high prevalence of HCV recombinant form 2k/1b, which requires different treatment regimens to achieve higher cure rate in these patients.
- With the introduction of additional DAAs, improved response rates are expected, paving the way for Georgia to achieve the goal of HCV elimination.

GEORGIA

NATIONAL HEPATITIS C ELIMINATION PROGRAM

ACKNOWLEDGEMENTS

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Real-World Effectiveness of Sofosbuvir and Ledipasvir/Sofosbuvir Based Regimens in Hepatitis C Virus Genotype 3 Infection within National Hepatitis C Elimination Program in the Country of Georgia

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INTRODUCTION

- Hepatitis C virus (HCV) has multiple genotypes, of which genotype 3 is the second most common Globally (22% of all HCV infections).[1]
- The prevalence genotype 3 is higher in Georgia, compared to global average, accounting for 34% of all HCV infections in the country.[2]
- HCV genotype 3 has traditionally been difficult to treat, especially among patients with cirrhosis.[3-5]
- In partnership with the US CDC, and commitment from Gilead Sciences to donate direct acting antivirals (DAAs) , Georgia embarked on the world's first hepatitis C elimination program in April, 2015.[6]

AIM

- The aim of this study was to evaluate the efficacy of interferon-containing and interferon free regimens for Genotype 3 patients treated within the Georgia's national hepatitis C elimination program.

METHODS

Study population and settings

- Study included 1024 Adult (age ≥18 years) patients with no prior DAA treatment receiving HCV care at 2 leading Georgian clinics – Infectious Diseases, AIDS and Clinical Immunology Research Center; Hepatology Clinic Hepa
- Persons with decompensated cirrhosis were excluded

HCV treatment regimens

- All patients received HCV treatment free of charge within hepatitis C elimination program in accordance with the national treatment protocols.
- From April 2015 through February 2016 Sofosbuvir (SOF) was the only DAA available and it was used in combination with pegylated interferon (IFN) and ribavirin (RBV) for 12 weeks or with RBV only for 24 weeks.
- From March 2016 Ledipasvir/sofosbuvir (LDV/SOF) was introduced in Georgia and combination of LDV/SOF/RBV for 12 weeks was prescribed to all genotype 3 patients

Statistical analysis

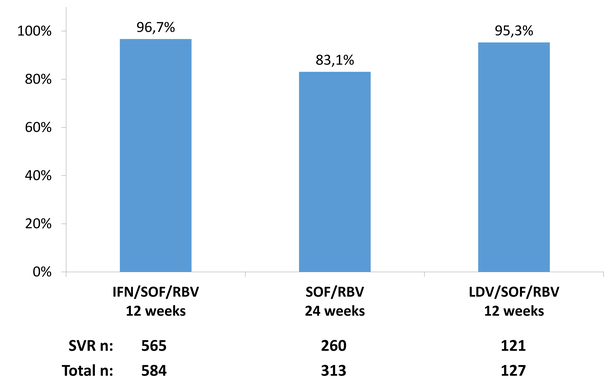
- Sustained virologic response (SVR), defined as undetectable HCV RNA at least 12 weeks after completion of treatment, was the outcome of interest
- Analysis was limited to patients who were assessed for SVR by November 15, 2016
- Differences in SVR rates were compared using Pearson's chi-square test

RESULTS

Baseline Characteristics

Characteristic	n=1024	
Age, median years (IQR)	46	(42-52)
Gender, n (%)		
Female	52	(5.1)
Male	972	(94.9)
Cirrhosis, n (%)		
Yes	509	(49.7)
No	515	(50.3)
Treatment regimen, n (%)		
IFN/SOF/RBV 12 weeks	584	(57.0)
SOF/RBV 24 weeks	313	(30.6)
LDV/SOF/RBV 12 weeks	127	(12.4)

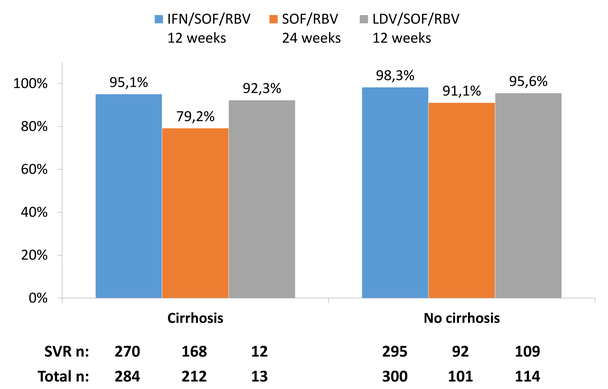
SVR Rates by Treatment Regimen



SVR Rates

- Overall SVR rate was 92.4% (946/1024), with 88.4% (450/509) of cirrhotic patients achieving SVR vs. 96.3% (496/515) in patients without cirrhosis (p<0.0001).
- In IFN/SOF/RBV arm total SVR rate was 96.7% (565/584), this regimen was more effective in non-cirrhotic patients compared to cirrhotic patients (98.3% vs. 95.1%, p=0.03).
- SOF/RBV achieved SVR in 83.1% (260/313) of patients, with significantly higher rates observed in patients without cirrhosis (91.1% vs. 79.2%, p=0.009).
- Among patients on LDV/SOF/RBV, 95.3% (121/127) of patients were cured, including 95.6% non-cirrhotic and 92.3% cirrhotic patients (p=0.48).
- IFN/SOF/RBV and LDV/SOF/RBV were more effective than SOF/RBV in (p<0.001 in all comparisons)

SVR Rates by Treatment Regimen and Cirrhosis Status



CONCLUSIONS

- We observed high cure rates in HCV genotype 3 patients.
- IFN and LDV/SOF based regimens were superior to SOF/RBV alone especially in patients with cirrhosis. LDV/SOF based regimens were equally effective in patients with or without cirrhosis.
- Combination of IFN, SOF and RBV is an effective treatment for genotype 3 but can be replaced by an IFN-free regimen with LDV/SOF and RBV with no loss of effectiveness even in difficult to treat patients with compensated cirrhosis.

GEORGIA

NATIONAL HEPATITIS C ELIMINATION PROGRAM

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High sustained viral response among hepatitis C virus genotype 3 patients with advanced liver fibrosis - real-world data of HCV elimination program in Georgia

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INTRODUCTION

Georgia has a high burden of hepatitis C virus (HCV) infection. In 2015, Ministry of health of Georgia with National Center for Disease Control and Public Health (NCDC) and US Centers for Disease Control and Prevention (CDC) conducted the study where a national probability sample of approximately 6000 adults in Georgia was tested for HCV infection, yielding a prevalence estimate of 7% for chronic HCV with an estimated 5.4% of adults currently infected. On April 28, 2015, in collaboration with CDC, Gilead Sciences and other partners, Georgia launched a comprehensive, national HCV elimination program that included free of charge treatment for all HCV infected persons. If successful, the viral reservoir will be substantially reduced and will dramatically decrease the risk of HCV transmission in the country. In the first phase of the program, patients with moderate and severe liver disease were prioritized to receive treatment. Different studies suggest that antiviral treatment outcome is associated with genotype, treatment regimen and liver fibrosis stage. HCV infected patients with genotype 3 are considered as difficult to treat with DAAs compared to genotypes 1 and 2.

AIM

- We aimed to study the real world data of treatment outcome among HCV infected patients with genotype 3 with advanced liver fibrosis stage.
- The objectives were to estimate the association of sustained viral response (SVR) at week 12 to 24 after completion of the treatment with treatment regimen, presence of liver cirrhosis, gender and age.

METHOD

The Elimination Program requires participating clinics and treatment sites to collect pre-treatment socio-demographic, clinical and laboratory data, prescribed medications, treatment adherence and monitoring data. These data are collected using standardized protocols, and entered in information management system STOP-C - Georgia's national electronic treatment database, developed for the HCV elimination program. Data collected includes HCV genotype and viral load, level of liver fibrosis, risk factors for HCV infection and treatment-related laboratory data, including SVR at week 12-24 after completion of treatment. The Elimination Program requires all patients to have a pre-treatment FIB4 score, which is computed from age, ALT, AST and platelet count. A FIB4 score is interpreted as follows: below 1.45 (low), 1.45-3.25 (equivocal), and greater than 3.25 (advanced fibrosis). For those in the equivocal range, a liver elastography is conducted and results recorded.

Data from April 28, 2015 through September 30, 2016 from STOP-C were analysed. Characteristics and outcomes of patients with genotype 3 were extracted. During the study period, the treatment for patients with genotype 3 was conducted using the combination of sofosbuvir and ribavirin (SOF/RBV) during 24 weeks or sofosbuvir, ribavirin and pegilated interferon (PEG IFN) 2a or 2b during 12 weeks, depending on IFN eligibility. Treatment outcomes were analysed by degree of liver fibrosis with patients defined as having advanced liver fibrosis (>=F3 by liver elastography or >3.25 by FIB4 score) and treatment regimen, Statistical software STATA was used for data analysis. Bivariate associations between treatment outcome with different factors, such as treatment regimen, fibrosis stage, age and gender were analysed using chi-square. Multivariate analysis with logistic regression was used to estimate adjusted prevalence ratios and define independent predictors of SVR.

RESULTS

- During the study period, 6648 patients with genotype 3 were enrolled in elimination program (34% of all genotypes). The vast majority, 6205 (93.3%) were male. By age distribution, more than half of study participants (52.47%) were aged 45-60 years, followed by the age group of 30-45 years (2,650, 39.86%). Predominating treatment regimen was 12 week course of sofosbuvir/ledipasvir/ribavirin (3,048; 45.70%), followed by triple regimen containing pegilated interferon alfa 2a or 2b with sofosbuvir and ribavirin (1,637; 24.62%). 1,146 patients (17.24%) received 24 week course of SOF/RBV.
- Sustained Virologic Response (SVR) data for patients with advanced liver fibrosis was available for 1529 individuals. Among those 1378 (90.12%) achieved SVR. Among patients with liver cirrhosis (F4 by elastography, n=892) the overall cure rate was 85.7% (n=764). Out of 637 patients with F3 or F3/F4, 614 (96.4%) achieved SVR. The SVR rate was significantly higher among those treated with interferon containing regimen compared to those ineligible for prescribing interferon based treatment. Out of 959 patients receiving PEG IFN 2a or 2b with SOF and RBV for 12 weeks, 925 (96.5%) achieved SVR compared to 80.6% cure rate among those treated with SOF and RBV for 24 weeks (424 out of 526).
- By bivariate analysis, gender was significantly associated with SVR rate. Females were more likely to be cured compared to males (74 [98.7%] vs 1304 [89.7%]). Patients at younger age (<=45) had higher chance of achieving SVR (95.7% vs 88.0%) compared to older patients.
- By multivariate analysis the independent predictors of achieving SVR were treatment regimen (Adjusted PR=1.08, 95% CI:1.04-1.13) and fibrosis stage (Adjusted PR=1.04 (95% CI:1.00-1.09).

	Total N (%)	SVR achieved N (%)	Unadjusted PR and 95% CI	Adjusted PR and 95% CI
Age group				
18-30	7 (0.46)	7 (100)	--	
31-45	413 (27.01)	395 (95.64)	1	
46-60	988 (64.62)	864 (87.45)	0.91 (0.89, 0.94)	
>60	121 (7.91)	112 (92.56)	0.97 (0.92, 1.02)	
Gender				
Male	1454 (95.09)	1304 (89.68)	1	
Female	75 (4.91)	74 (98.67)	1.10 (1.07, 1.14)	
Fibrosis stage				
F4	892 (58.34)	764 (85.65)	1	1
F3 or F3/F4	637 (41.66)	614 (96.39)	1.13 (1.09, 1.16)	1.04 (1.00, 1.09)
Treatment regimen				
SOF/RBV	566 (37.02)	449 (79.33)	1	1
IFN/SOF/RBV	959 (62.72)	925 (96.45)	1.22 (1.16, 1.27)	1.08 (1.04, 1.13)

DISCUSSION

- In this study, we examined the real world treatment experience among HCV genotype 3 infected patients with advanced liver fibrosis by sofosbuvir containing regimen with or without pegilated interferon, demonstrating overall high SVR rate (94%). Patients with liver cirrhosis in this study had higher chance of achieving SVR compared to the results reported by trials enrolling liver cirrhosis patient with HCV genotype 3.
- Several studies demonstrated SVR rates of 60% to 70 % among those receiving SOF and RBV 24 week regimen. The VALENCE trial reported overall SVR rate of 85% among genotype 3 infected patients receiving the 24 week SOF/RBV regimen. SVR 12 rates were 91% for non-cirrhotic group and 68% for the group of study participants with liver cirrhosis.
- Multivariate analysis on genotype 3-infected patients revealed that the presence of liver cirrhosis is a negative predictor of SVR 12. Our cohort including only those with advanced liver disease had similar overall SVR rate as the one including patients without cirrhosis (95% SVR rate after treatment with triple regimen treatment containing SOF/RBV/IFN).

CONCLUSIONS

The real world data of HCV treatment with SOF/RBV and SOF/RBV/INF from Georgia demonstrated high SVR rates achieved among genotype 3 patients with advanced liver fibrosis.

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Treatment outcomes of hepatitis C virus recombinant form 2k/1b with Sofosbuvir based regimens in Georgia

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INTRODUCTION

Hepatitis C virus (HCV) infection is one of the major causes of liver related morbidity and mortality.

The estimated prevalence of HCV infection in the Republic of Georgia is one of the highest in the world. From April 2015 Gilead Inc. and Georgian Government, with support of Center of Disease Control (CDC) and World Health Organization (WHO), launched National HCV Elimination Project in Republic of Georgia. The goal of the project is to reduce the morbidity, mortality and prevalence, by gradually providing accessibility to prevention, diagnostics and treatment for free with latest DAAs.

During first year of project only Sofosbuvir (SOF) based regimens were available.

It is important to know, that up to 20% of all genotypes belong to the HCV intergenotyping recombinant form RF_2k/1b, which appears to show that Georgia has the highest prevalence of this recombinant virus so far reported worldwide. RF_2k/1b were identified in only GT2 samples and appeared to be up to 70%. According to the limited data about treatment of RF_2k/1b patients with GT2 regimens, sustain virological response (SVR) rates was more similar to GT1 than GT2.

AIM

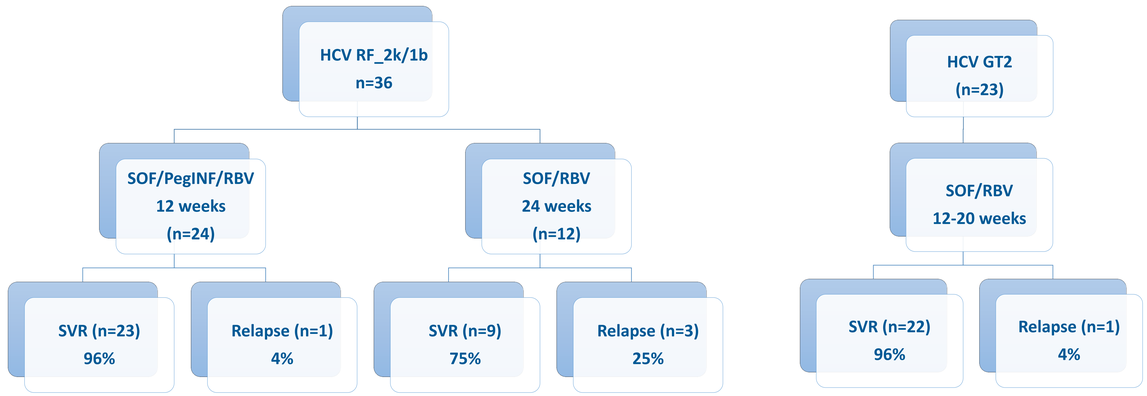
The aim of our study was to define optimal treatment regimen for RF_2k/1b within hepatitis C virus elimination project in Georgia.

METHOD

We retrospectively analyzed the data of GT2 patients identified by INNO-LiPA VERSANT HCV Genotype 2.0 in Medical Center Mrcheveli from May 2015 to May 2016. Partial genome sequencing of core and NS5B regions was performed for identification of RF_2k/1b variants before treatment. All interferon eligible recombinants were treated with Sofosbuvir (SOF) plus Pegilated Interferon (PegINF) plus Ribavirin (RBV) for 12 weeks and interferon ineligible patients with SOF/RBV 24 weeks. We compare SVR12 rates of RF_2k/1b to pure GT2 treated with SOF/RBV-12 or SOF/RBV-20 (depending on presence of cirrhosis). Also we performed regenotyping and partial sequencing of core and NS5B region in randomly selected 20 samples from 95 GT2 (by INNO-LiPA VERSANT) treatment failures from other medical centers treated with SOF/RBV 12 or SOF/RBV 20 weeks.

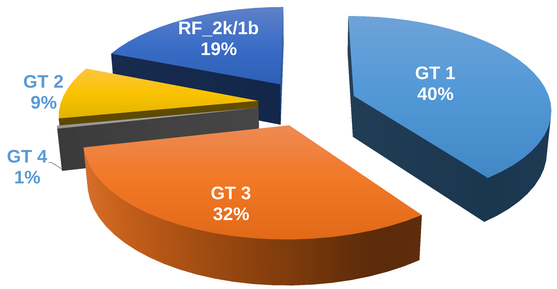
RESULTS

A total number of 67 HCV GT2 samples by INNO-LiPA were analyzed, in which 43 (64%) RF_2k/1b were identified. Antiviral therapy in 23 out of 24 GT2 patients with SOF/RBV for 12 or 20 weeks (depending on presence of cirrhosis) was initiated and SVR12 rates was achieved in 22/23 (96%) patients. 36 out of 43 RF_2k/1b patients were treated with either SOF/PegINF/RBV for 12 weeks (n=24) or with SOF/RBV for 24 weeks (n=12) depending on interferon eligibility criteria. 23/24 (96%) patients achieved SVR 12 rates in interferon-containing group and 9/12 (75%) patients in group without interferon.

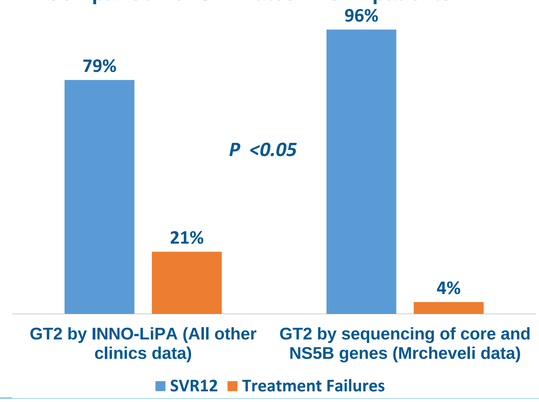


From unspecified genotype 2a/2c patients (n=446) who were treated with SOF/RBV for 12 or 20 weeks depending on presence of cirrhosis, 95/446 (21%) relapsed. Partial genome sequencing of core and NS5B regions of 20 randomly selected samples from 95 treatment failed patients was performed. All samples were consistent to RF_ 2k/1b.

Distribution of HCV Genotypes in Georgia



Comparison of SVR rates in GT2 patients



CONCLUSIONS

Despite the small number of patients our findings suggest that treatment of RF_2k/1b patients with SOF/PegINF/RBV for 12 weeks was more effective than with SOF/RBV for 24 weeks (p = 0.061).

Also we can conclude, that SVR12 rate was significantly higher in GT2 patients, confirmed by sequencing, treated with SOF/RBV 12 or 20 weeks than in unspecified GT2, who were treated with the same regimen (p <0.05).

ACKNOWLEDGEMENTS

The authors wish to express deep gratitude for the support from Ministry of Health, Labor and Social Affaires of Georgia, National Center of Disease Control of Georgia, other medical centers and patients.

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Effectiveness of DAA-based treatment of HCV in active people who inject drugs (PWID) living in middle income countries (MIC)

Results of a prospective cohort study in Tbilisi, Georgia

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BACKGROUND & OBJECTIVE

Although they carry a high HCV burden globally, PWID are often excluded from clinical research as well as national policies due to concerns about their ability to adhere to care, especially in MIC. Georgia faces high HCV rates (7.1% of antibodies in general population) with 25.6% of the cases being among PWID. An ambitious National HCV elimination Plan was launched in 2015, with initially 7000 treatments dedicated to patients with advanced liver fibrosis (≥F3).

We assessed the treatment outcomes in PWID treated in the framework of the National Plan, and receiving a peer support intervention to enhance the adherence to treatment.

MATERIAL & METHODS

We followed a prospective cohort of PWID clients of a needle and syringe exchange program and supported by peer workers during treatment. PWID were treated with sofosbuvir and ribavirin +/-pegInterferon according to the genotype, treatment experience and level of fibrosis. We collected data concerning bio-medical parameters, adherence to care, demographics, and behaviors before and during treatment. Adherence was assessed by: (1) the rate of treatment completion, (2) the attendance rate defined as the proportion of PWID who did not miss nor delay one of the bi-monthly medical appointment, and (3) the compliance rate defined as the proportion of PWID who never missed a dose of treatment.

After a descriptive analysis, we studied the factors associated with adherence to care and sustained virologic response at 12 weeks post-treatment (SVR) using adjusted logistic regressions. We additionally compared the SVR12 rate to those of patients not reporting any history of injecting drug use (non-PWID), treated at the same clinic, during the same period, adjusting for cirrhosis status, genotype, age, gender, and treatment regimen.

RESULTS

Population of PWID n=244

Profile	Mean age	46.3
	Men	99.2%
	Injected the last month	49.8%
	With OST	24.1%
HCV & coinfections	HBV HIV	4.5% 0.0%
	Cirrhosis	49.0%
	Mixed genotype Gen 1 Gen 2 Gen 3	3.7% 18.5% 25.9% 51.9%
Treatment	Past treatment	3.3%
	Sof/Rbv/pegIfn Sof/Rbv Harvoni +/- Rbv	43.4% 53.3% 3.3%
	12 weeks 20 weeks 24 weeks 48 weeks	57.4% 11.9% 30.3% 0.4%

Adherence to treatment

Completion rate	97.95%
Attendance rate	88.1%
Compiance rate	79.1%

Compliance rate was not associated with any of the covariates tested. In adjusted analysis, attendance rate was significantly associated with being unemployed (aOR 2.48; 95CI 1.01-6.10), not being under OST (aOR 3.71; 95CI 1.51-9.14), and not having injected drug during treatment (aOR 2.86; 95CI 1.16-7.03).

SVR12 & associated factors

SVR12 88.5%, associated only with cirrhosis and genotye, not with drug or alcohol use during treatment

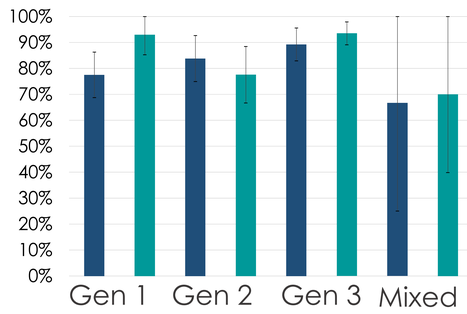
Multivariate analysis of factor associated with SVR (cofactors associated with p<0.20 at univariate analyses)

	OR	95% CI	p
Perfect intake	2.60	0.94-7.19	0.065
Cirhhosis	0.35	0.13-0.97	0.047
Genotype 1 Genotype 2 Genotype 3 Mixed genotype	Ref 0.25 1.24 0.14	- 0.06-1.14 0.29-5.22 0.02-0.98	- 0.074 0.769 0.047
Treatment with pegIFN	1.24	0.38-4.11	0.723
No side effect Non-serious side effect Serious adverse event	Ref 1.89 0.06	- 0.77-4.68 0.00-1.33	- 0.164 0.075

Comparison with non-PWID

SVR by genotype:
- *in non-PWID*
- *in PWID*

SVR12 83.2% in non-PWID, adjusted OR 1.10; 95CI 0.59-2.03 for PWID vs. non-PWID



CONCLUSION

In this real life experience, PWID were adherent to care and had SVR rates comparable to those observed in non-PWID. **Concerns about PWID ability to engage in care should not be a reason of exclusion from HCV treatment** in Georgia.

Projected impact and pathways to success of the hepatitis C virus elimination program in Georgia, 2015-2020

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Abstract

Georgia has one of the highest hepatitis C virus (HCV) prevalences in the world, with >5% of the adult population (~150,000 people) chronically infected. In April 2015 Georgia and partners launched a national program to eliminate HCV (defined as 90% reduction in HCV chronic prevalence by 2020 compared to 2015 levels) through prevention, diagnostics and curative treatment. As of December 31, 2016, 27,595 patients had initiated and 19,778 had completed treatment, with 83% cured (sustained virologic response). We project the impact of the program in terms of infections and HCV-related deaths averted and assess the feasibility of achieving the elimination goal.

We developed a model of HCV transmission incorporating changing demographics of people who inject drugs (PWID) and the general population in Georgia. The model was calibrated to HCV prevalence by age, gender and PWID status and PWID age distributions with data from a 2015 national serosurvey and PWID surveys from 1997-2015. We estimated infections and deaths averted by 2030 due to the 27,595 initiated treatments, accounting for initial targeting of treatments to patients with METAVIR scores of F3-F4. We projected whether the elimination goal will be reached if treatment initiation continues at the current rate of 2100/month or 80% of prevalent infections annually when prevalence is low, including scenarios combining treatment with increased coverage of harm-reduction measures for PWID (opiate substitution therapy (OST) and needle and syringe programs (NSP)) or prioritizing treatments for PWID.

Without HCV treatment, HCV-related mortality is projected to increase from 657 (319 - 1185) to 769 (387 - 1288) deaths/year for 2015-30 while HCV incidence decreases from 5926 (2818 - 12146) to 4013 (1668 - 9943) infections/year for 2015-30 due to changes in injecting drug use patterns since the 1990s. The initiated treatments will avert approximately 2232 (1360 - 3269) HCV-related deaths and 11635 (4817 - 24451) new infections by 2030. We project prevalence in 2020 will approach the elimination goal with 87.1% (73.4 - 93%) reduction in prevalence by the end of 2020, with increased impact (88.8% (77.1 - 93.9%) reduction) if treatment is prioritised to PWID at twice the rate of non-PWID or an additional 400 treatments are initiated per month (90.9% (82.6 - 94.4% reduction).

Georgia is on the path to achieving the HCV elimination target by shortly after 2020 if current rates of HCV treatment continue, especially if treatments for PWID are prioritized. However, to maintain the necessary treatment rate, current rates of case-finding need to be scaled up.