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CLINICAL AND EPIDEMIOLOGICAL FEATURES OF CHRONIC HEPATITIS C IN THE NORTH-WESTERN REGION OF UKRAINE

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Abstract

HCV infection had become widespread all over the world. As a result of the constant registration of a significant number of new cases with a tendency to increase, high chronicity, risk of fatal complications, lack of specific prevention and the complexity of treatment, which is expensive, the problem remains one of the most important for global health. Due to the lack of official registration of acute hepatitis C in Ukraine until 2003, and chronic hepatitis C - until 2010, the data on the incidence by region are need to be supplemented. The paper presents data on the prevalence of hepatitis C among the population of Rivne region of the North-Western region of Ukraine.

Key words: HCV; acute hepatitis C; chronic hepatitis C; HCV incidence; HCV genotype.

BACKGROUND:

In the structure of infectious pathology, viral hepatitis C occupies one of the leading places according to rates of morbidity and mortality in the world. The number of people living with the hepatitis C virus increases annually by an average for 2-3 millions of people. Today, according to various data sources, there are more than 170 millions of people in the world which are infected by hepatitis C virus. The mortality rate from liver disease associated with HCV infection is approximately 350-400 thousands of people every year. HCV infection is

the most prevalent in the Eastern Mediterranean and the European region, where 2,3% (15 million) and 1,5% (14 million) of the population are infected, respectively. Significant prevalence of hepatitis C virus is associated with limited access to diagnosis and treatment, as well as low public awareness to the problem - only 20% of people with chronic HCV in the world know about their diagnosis, of which - only 7,5% of people with chronic hepatitis C have access to treatment [2, 4, 5, 7, 9].

As of January 2020, 2,107,660 people (≈5% of the population) which were infected by HCV were registered in Ukraine and only 6,5% of them (87,269 people) were under medical supervision. However, these statistics do not reflect the real state of the problem of HCV infection in Ukraine, as official registration of acute hepatitis C in Ukraine has been conducted only since January 2003, and registration of chronic hepatitis C since January 2010. Currently in Ukraine there is unfavorable epidemic situation with regard to viral hepatitis C. Against the background of a decreasing in the number of cases of acute hepatitis C, there is an increasing in the number of chronic hepatitis C cases [10, 11, 12, 13, 14].

At the present stage, the epidemic process of viral hepatitis C is characterized by a decreasing in the incidence of acute forms, an increasing in the primary incidence of chronic hepatitis C, an increasing in the number of combined forms, changes in the age structure of patients and the structure of preferred routes of transmission. Also an increasing in the number of deaths from liver disease associated with HCV [1, 3, 6, 8].

Due to the lack of an effective system of epidemiological surveillance, insufficient level of diagnosis and treatment of patients with HCV, the question of the actual intensity of the hepatitis C epidemic process in Ukraine is extremely acute and needs further to be studied [12, 13, 14].

AIM:

Evaluate of epidemiological and genetic features of the spreading of hepatitis C virus, the main clinical manifestations of this disease in the Rivne region of the North-Western region of Ukraine in modern conditions.

MATERIALS AND METHODS:

A retrospective analysis of HCV morbidity of the population of Rivne region of the North-Western region of Ukraine for 2015-2019 was conducted on the basis of annual reporting statistical forms of the Ministry of Health of Ukraine at Rivne Regional Hepatological Diagnostic Center.

To assess the clinical and laboratory features of the course of CHC, we examined 131 patients with CHC aged from 26 years to 72 years (mean age 43,8 ± 2,4), which formed the

main group. All patients were on outpatient follow-up and inpatient treatment at the Rivne Regional Hepatological and Diagnostic Center. The diagnosis of CHC was confirmed by qualitative and quantitative determination of HCV-RNA, HCV genotyping. The control group consisted of 48 healthy individuals, representative of age and sex. All surveyed were residents of the Polissya region of Ukraine.

Indicators of the main biochemical syndromes such as cytolytic, cholestatic and hepatocellular insufficiency were evaluated. To assess the indicators of cytolytic syndrome, the activity of transaminases - alanine aminotransferase (ALT), aspartate aminotransferase (AST) was determined by unified Reitman-Frenkel method and lactate dehydrogenase (LDH) by the Sevel-Tovarek method. To assess the liver function tests, which characterize cholestatic syndrome, the content of total bilirubin was determined by the unified Endrasic-Grof-Cleghorn method, Ɣ-glutamyltransferase (GGT) by the rate of releasing of 4-nitroaniline from Ɣ-glutamylnitroanilide, and alkaline phosphatase (ALP) by the rate of releasing of p-nitrophenole, using calorimetric method. Evaluation of indicators of hepatocellular insufficiency syndrome included determination of the total protein level (microbiuret method), albumin level (unified method with bromocresol green), cholesterol level by unified method Ilka. All mentioned laboratory examinations were performed by the laboratory of Rivne Central City Hospital. Laboratory indicators were evaluated according to demographic characteristics, such as age, sex, area of residence.

All obtained data were summarized by Microsoft Excel 2018 spreadsheets and analyzed using “Statistica 10” software. Statistical probability, which were analyzed according to Student's t-test, was regarded as valid at an error of value at $p < 0,05$.

RESULTS:

A retrospective analysis of the incidence of viral hepatitis C (HCV) in Rivne region showed that for the period 2015-2019, the incidence of acute hepatitis C (AHC) in the region was consistently low and ranged from 1,21 to 0,78 per 100 thousands of population. In the city of Rivne, the incidence rates were also determined at a fairly low level, only in 2017 there was an increasing in the incidence rate to 2,04 per 100 thousands of population. The average long-term morbidity rate in the region was 0,99 per 100 thousand population, in the city of Rivne 0,81 per 100 thousands of population, which was 1,87 and 2,28 times lower than the average annual figure in Ukraine (1,85 per 100 thousands of population) (Fig. 1).

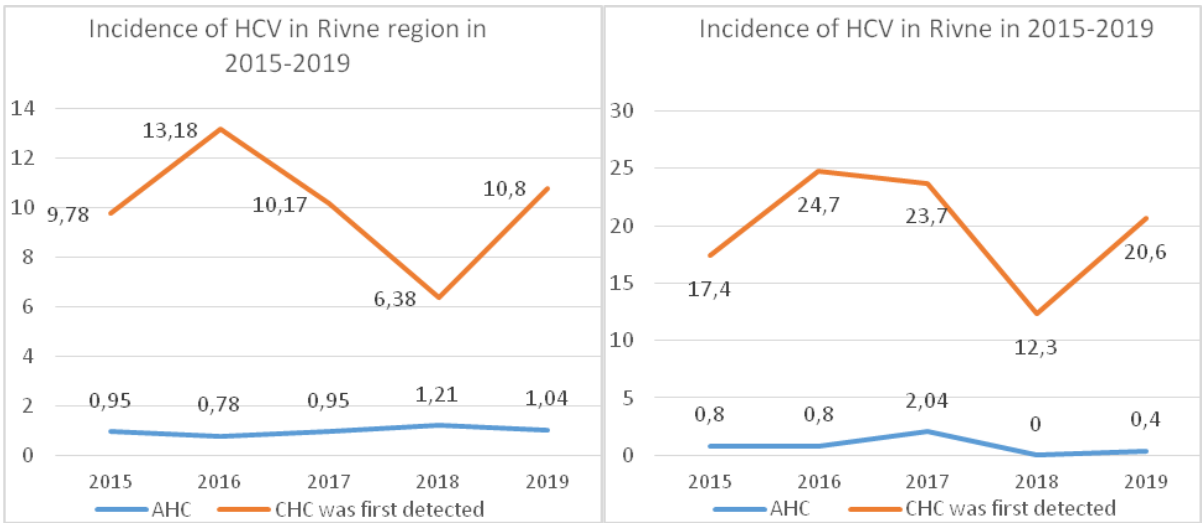

Fig. 1. Incidence of viral hepatitis C (HCV) of the population of Rivne region and Rivne for the period 2015-2019

During the observation period in the region, the incidence of first diagnosed chronic hepatitis C (CHC) ranged from 13,18 to 6,38 per 100 thousand population with a tendency to decrease during 2016-2018, but in 2019 there is an increasing in the incidence of 1,69 times compared to the previous year. The average long-term incidence rate in the region was 10,28 per 100 thousand population, which is 10,4 times higher than the incidence of AHC. The highest incidence rate of first diagnosed CHC (24,7 per 100 thousands of population) in Rivne was observed in 2016 and was 30,8 times higher than the incidence of CHC. The registered average long-term morbidity rate in Rivne was 19,74 per 100 thousands of population and 1,92 times and 1,16 times higher than in the region (10,28 per 100 thousands of population) and in Ukraine as a whole (12,25 per 100 thousands of population), respectively (Fig. 1).

According to analysis of the sex-age structure of CHC, the incidence rate among men (56,64%) is 1,3 times higher than among women (43,36%). The age structure determines the predominance of persons aged 20-39 years, which accounted for 61,6% of all registered patients with CHC in Rivne region (Fig. 2).

According to analysis of the structure of HCV genotypes in Rivne region, there is a predominance of 1b-subtype of HCV, which is detected in 59,9% of patients and 3a-subtype of HCV (29,1%), the share of other subtypes is insignificant – 1a-subtype of HCV was detected in 1,7% of patients , HCV genotype 2 in 3,8% of patients, unidentified HCV genotype in 5,5% of individuals (Fig. 3).

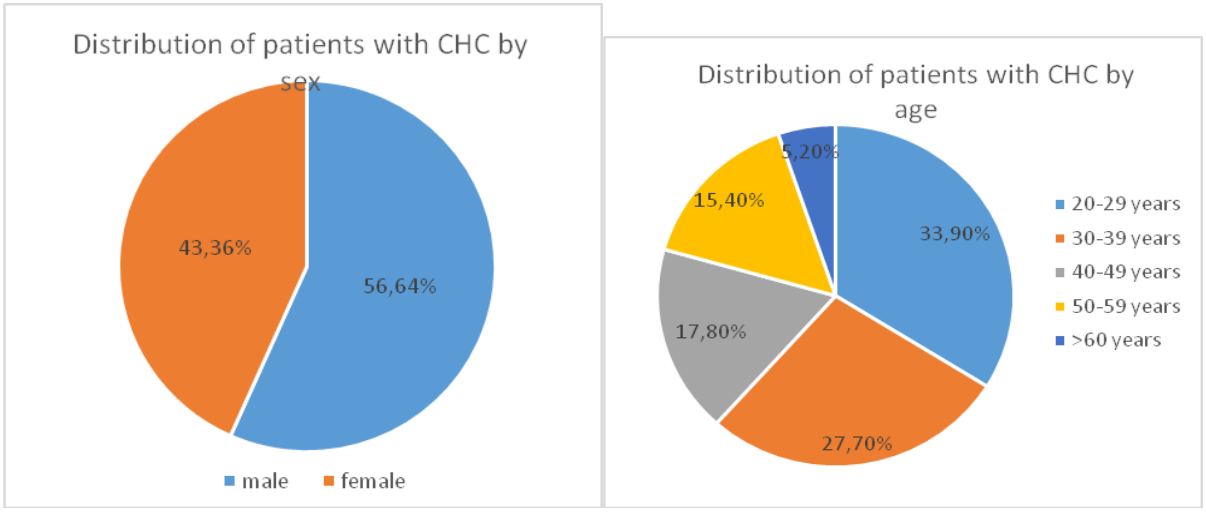

Fig. 2. Sex and age structure of the incidence of CHC in the population of Rivne region.

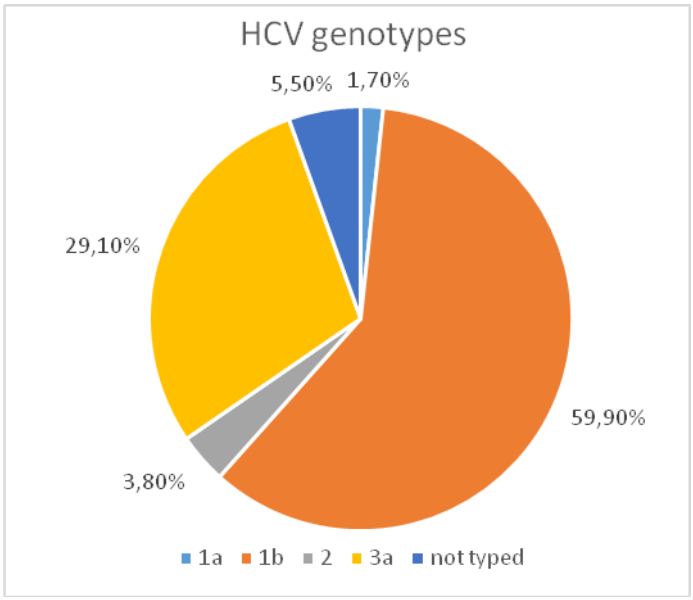

Fig. 3. Frequency of detection of HCV genotypes and subtypes among the population of Rivne region.

During the period 2015 - 2019, 1330 patients with HCV were hospitalized in the Rivne Regional Medical and Diagnostic Hepatological Center. The structure of hospitalization shows an annual increase in the number of patients with HCV-induced liver cirrhosis from 29,13% (81 patients) in 2015 to 44,05% (126 patients) in 2019 (Fig. 4).

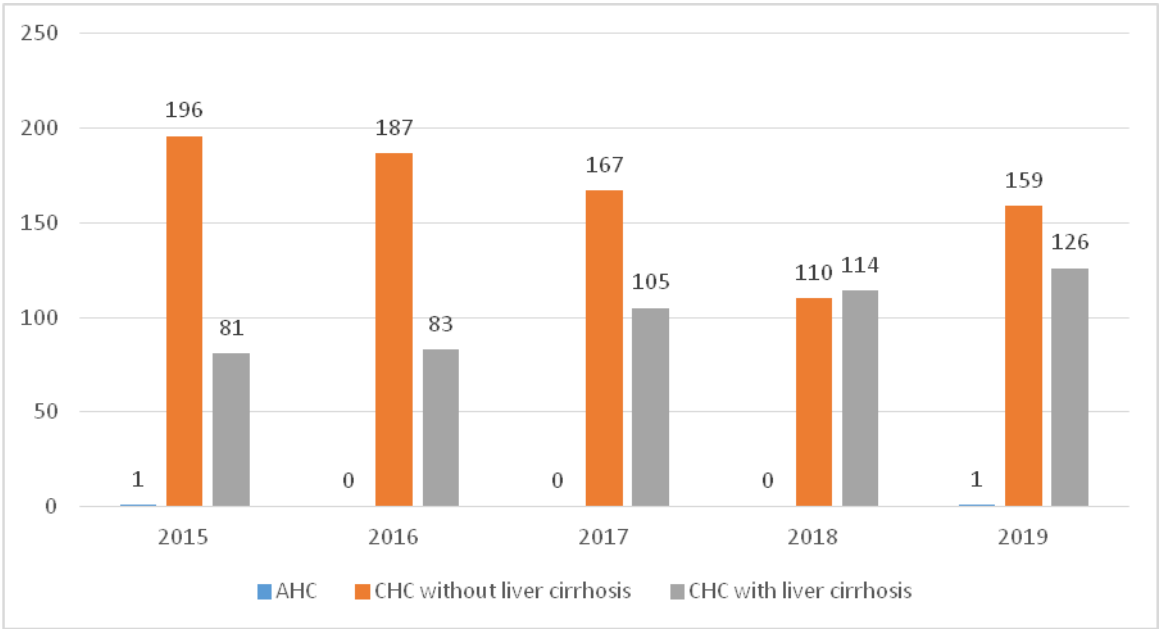

Fig. 4. The structure of hospitalization of patients with HCV to the Rivne Regional Medical and Diagnostic Hepatological Center for the period 2015-2019.

During the observation period from 2015 to 2019, 514 patients received specific antiviral therapy, of which 267 people were treated by public expense. There is a tendency to increase the level of treatment coverage, so in 2019 this figure was 3,70%, which is 1,83 times more than in 2015 (2,02%) (Fig. 5).

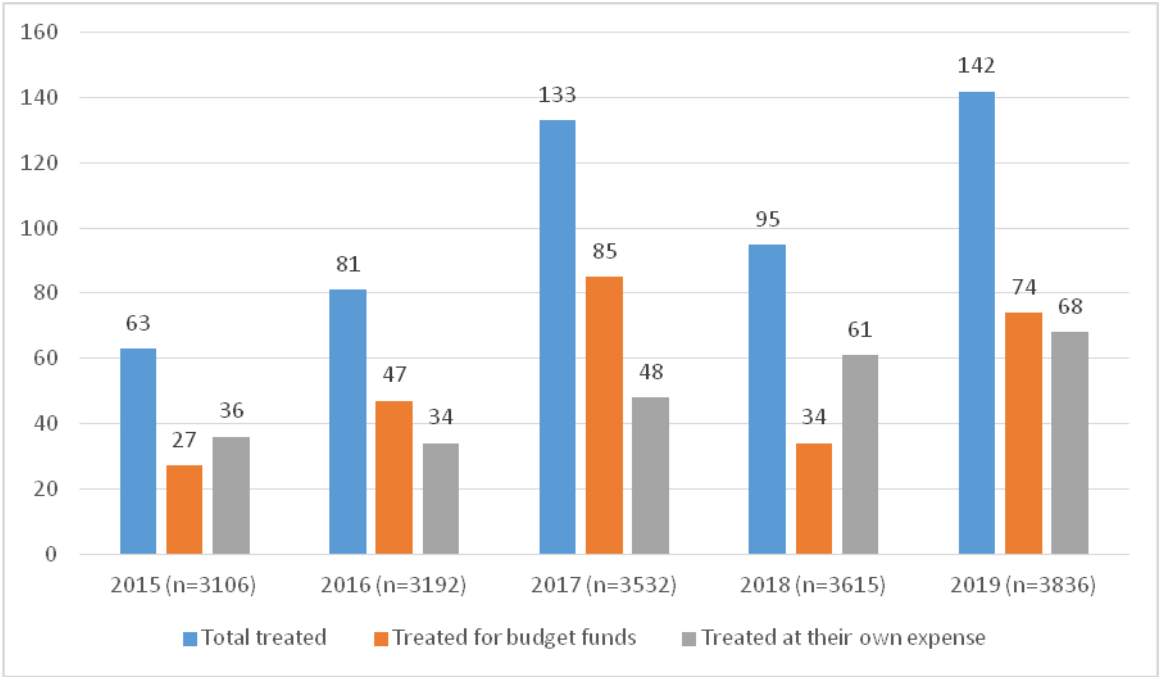

Fig. 5. The structure of treated patients with CHC in Rivne Regional Medical and Diagnostic Hepatological Center for the period 2015-2019.

For clinical and laboratory characteristic of patients with CHC, indicators of cytolytic syndrome (levels of ALT, AST, LDH), cholestatic syndrome (total bilirubin, GGT, ALP) and hepatocellular insufficiency syndrome (total protein, albumin, cholesterol) were evaluated.

We found a significant increasing in the levels of the main indicators of cytolytic syndrome in patients with CHC compared with the control group. Thus, the level of ALT in the serum of patients with CHC was 3,03 times higher, the level of AST – 2,51 times higher, the level of LDH – 1,5 times higher compared to healthy individuals (Table 1).

Table 1.

Indicators of cytolytic syndrome in healthy people and patients with CHC

Indicators	Healthy people (n=48)	Patients with CHC (n=131)
ALT (Un/l)	23,31±2,84	70,63±4,00*
AST (Un/l)	20,86±1,93	52,41±2,74*
LDH (Un/l)	164,28±3,06	247,75±4,12*

Note: * p <0,001 - the difference is significant between the groups of healthy people and patients with CHC

Aftre assessing liver function test, which characterize cholestatic syndrome, a significant increasing of the levels of all studied indicators in patients with CHC were noticed. Thus, the level of total bilirubin in the serum of patients with CHC was 1,32 times higher than in the healthy group. The level of GGT in the serum of patients in the main group was 2,62 times higher than in group of healthy respondents. The level of ALP in the serum in the group of patients with CHC was 1,4 times higher than in healthy people group (Table 2).

Patients with CHC had significantly lower levels of total protein and albumin (1,1 times) compared to healthy respondents. Cholesterol levels in patients with CHC were 1,55 times higher than in the control group (Table 3).

Table 2.

Indicators of cholestatic syndrome in healthy people and patients with CHC

Indicators	Healthy people (n=48)	Patients with CHC (n=131)	p*
Total bilirubin (μmol/l)	11,96±1,33	15,84±0,5	p<0,01
GGT (Un/l)	26,87±1,12	70,49±4,37	p<0,001
ALP (Un/l)	72,79±2,66	101,72±3,85	p<0,001

Note: * p - the difference is significant between the groups of healthy people and patients with CHC

Table 3.

Indicators of hepatocellular insufficiency syndrome in healthy people and patients with CHC

Indicators	Healthy people (n=48)	Patients with CHC (n=131)	p*
Total protein (g/l)	78,55±1,04	72,3±0,45	p<0,001
Albumin (g/l)	45,98±0,65	43,85±0,39	p<0,01
Cholesterol (μmol/l)	3,05±0,56	4,73±0,07	p<0,01

Note: * p - the difference is significant between the groups of healthy people and patients with CHC

CONCLUSIONS:

1. In the Rivne region of the North-Western region of Ukraine during the last 5 years a consistently low incidence of AHC had been registered (1,21 to 0,78 per 100 thousands of population).

2. Against the background of low incidence of CHC (0,99 per 100 thousand population) in the Rivne region there is an increase of the incidence of first diagnosed CHC (10,28 per 100 thousands of population) and liver cirrhosis (13,5 per 100 thousands people).

3. The vast majority (61,6%) of registered patients with HCV are young men under 40 years of age (56,64%).

4. There is a low level of availability of antiviral treatment with a tendency to increase (average long-term rate of 2,92%).

5. Patients with CHC have significantly higher level of biochemical markers of liver disease syndromes, such as cytolytic, cholestatic, hepatocellular insufficiency.

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