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CLINICAL AND EPIDEMIOLOGICAL FEATURES OF HEPATITIS AMONG THE RESIDENTS OF THE TRANSCARPATHIAN REGION

Summary. The clinical and epidemiological features of hepatitis A in the Transcarpathian region for years 2004–2014 were indicated. A specific cyclicism and seasonality of hepatitis A in this region of Ukraine was established. Based on the examination of 61 patients with hepatitis A a peculiarity of the clinical progression of the disease, and, also, specific microbiological changes of the quantitative and qualitative composition of the colon microflora, depending on the presence of a concomitant chronic pathology of the digestive organs, were established.

Key words: hepatitis A, dysbiosis, chronic gastroenterological diseases.

Background

The dynamics of hepatitis A (HA) incidence represents a hardly controlled infection with periodic increase and decrease rate in Ukraine. It should be stressed out that with the present economic situation in Ukraine, further increase of the incidence of HA should be expected in the next 3–5 years [1]. For the Transcarpathian region HA the problem is urgent, it is characterized by higher rates of endemicity than in the whole Ukraine.

More than 70 % of the population of Transcarpathia are farmers who use drinking water from wells. The lack of centralized sewage, flooding with groundwater, drinking raw water is one of the factors contributing to the spread of HA.

Various authorities indicate different causes of the rapid spread of the disease. One of the main factors that is contributing to this process is the pollution of the environment, which occurs with annual flooding [2, 3]. Also, a significant impact on the epidemic situation is non-observance of good personal hygiene and drinking regime by certain segments of the population.

It is known that patients with HA acquire favorable conditions in the colon for the development of dysbiotic changes, activation of opportunistic microorganisms and the manifestation of their aggressive properties. This is due

to the change of the environment of microorganisms in the large intestine, due to the dysfunction of the liver, bile, pancreas [4]. Deep microbiological and immunological investigations of HA, were mostly made in the 80s of last century [1, 2]. However, their methodological level does not fully meet the modern standards because for the last 35 years medical science, especially immunology and virology, has been enriched fundamentally with new facts [5–7].

Purpose of the study: to identify the clinical and epidemiological features of HA in residents of the Transcarpathian region and to study their microbiota species composition and population-level of the gastrointestinal tract (GIT) microflora.

Materials and Methods

In order to achieve the goal stated in the work we used data that was collected for the past 11 years by the regional sanitary epidemiological station (SES). In addition, we analyzed 621 cases of HA in patients who were treated in the

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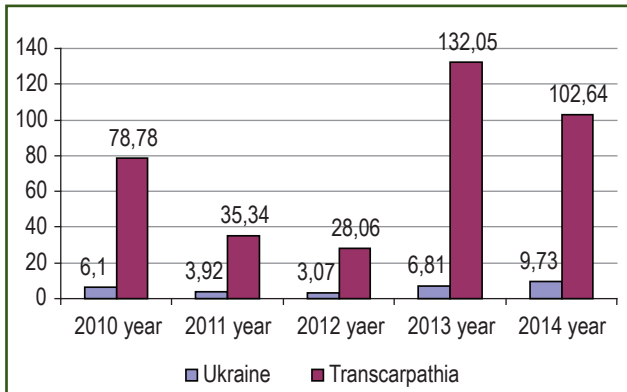


Figure 1 – The incidence of hepatitis A per 100,000 of population

Regional Clinical Infectious Diseases Hospital (RCIDH) and 61 patients with HA using a complex of clinical, laboratory and instrumental methods of microbiological examination followed by statistical analysis of the results.

Dysbiosis was studied by a quantitative method of identifying microorganisms that have grown on a nutrient medium of agar, Saburo, Endo and 5% blood agar with the disposition to 1 gram of feces, taking into account the dose of the sawn material and the degree of dilution. Also, on the dish with 5% agar we noted the presence of hemolytic forms such as intestinal and coccal microflora, their parentage comparing to the total number of colonies that have grown, the correlation between the intestinal and coccal microflora. The presence of bifidobacteria was determined by the nature of their growth on the Blaurok medium and microscopy of swabs, stained by the method of Gram. The number of bifidobacteria and lactobacillus in 1 gram of feces was determined by limiting delusion at which we observed their growth. The level of colon dysbiosis was evaluated according to the I.B. Kyvajeva and K.S. Ladodo (1991) classification.

Analysis and processing of the results of patients examination were carried out using a computer system Microsoft Excel 7.0, statistical software package Statistica 6.0.

Results of the Research and Their Discussion

Yearly there is a significant number of patients with HA in the Transcarpathian region. According to the regional SES, the incidence rate per 100,000 of population in re-

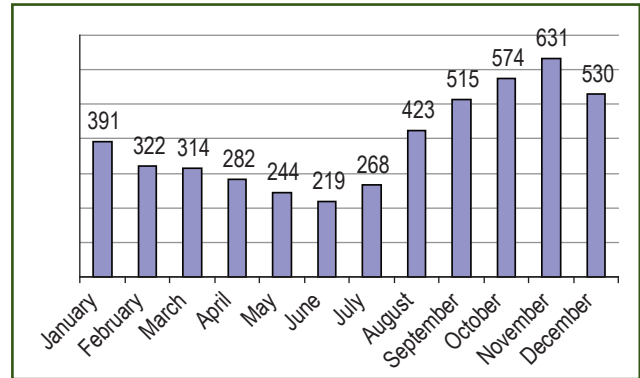


Figure 3 – The total monthly dynamics of HA morbidity in the Transcarpathian region for the past 5 years

cent years exceeds the nationwide numbers in 9–19 times (Fig. 1).

Over the past 11 years, a significant change in the number of patients with HA in the Transcarpathian region has been recorded with the highest number in 2007 and 2013 (Fig. 2).

One of the features of HA epidemic process is seasonality. The patients of the Transcarpathian region have distinct autumn and winter morbidity increase. The excess of the average rate recorded from August to January for the past five years (Fig. 3).

During the period of 2013–2014, 621 patient with HA have been treated in the RCIDH. In 2013, children slightly prevailed in number of incidence, but in 2014 — adults. Changes in the number of treated patients is shown in Fig. 4.

Among the adult patients with HA ($n = 311$) we have found no differences in the gender composition. Their age was (31.49 ± 1.02) years, and more than half of them were people under 29 years (57.9 %).

The main complaints were: icteric sclera — 93.2 %, weakness — 88.6 %, decreased appetite — 85.5 %, icteric skin — 82.9 %, nausea — 64.9 %, fever — 53.6 %, vomiting — 42.7 %, epigastric pain — 41.2 %, pain in the upper right hypochondrium — 8.4 %, discolored stool — 8.5 %, itching — 7.2 %, cough — 3.1 %.

All patients with HA were hospitalized on the (7.48 ± 0.46) day of illness, jaundice occurred on the (5.47 ± 0.38) day of illness, icteric sclera on the (5.44 ± 0.38) day, dark urine — on the (4.63 ± 0.34) day. Ultra sound size of the liver was (15.13 ± 0.47) cm, spleen — (12.11 ± 0.18) cm. The average length of the long-term healthcare was (15.74 ± 0.47) days.

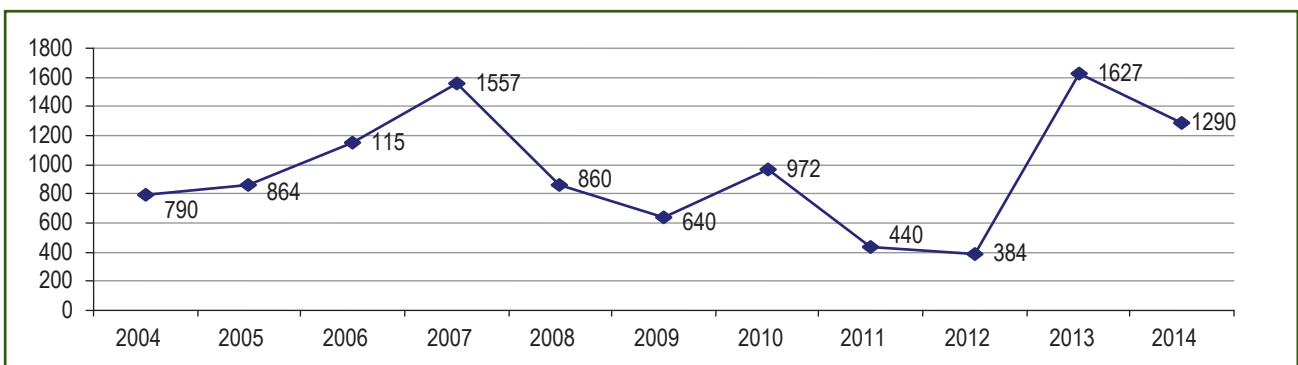


Figure 2 – Changes in the number of patients with hepatitis A in the Transcarpathian region in 2004–2014

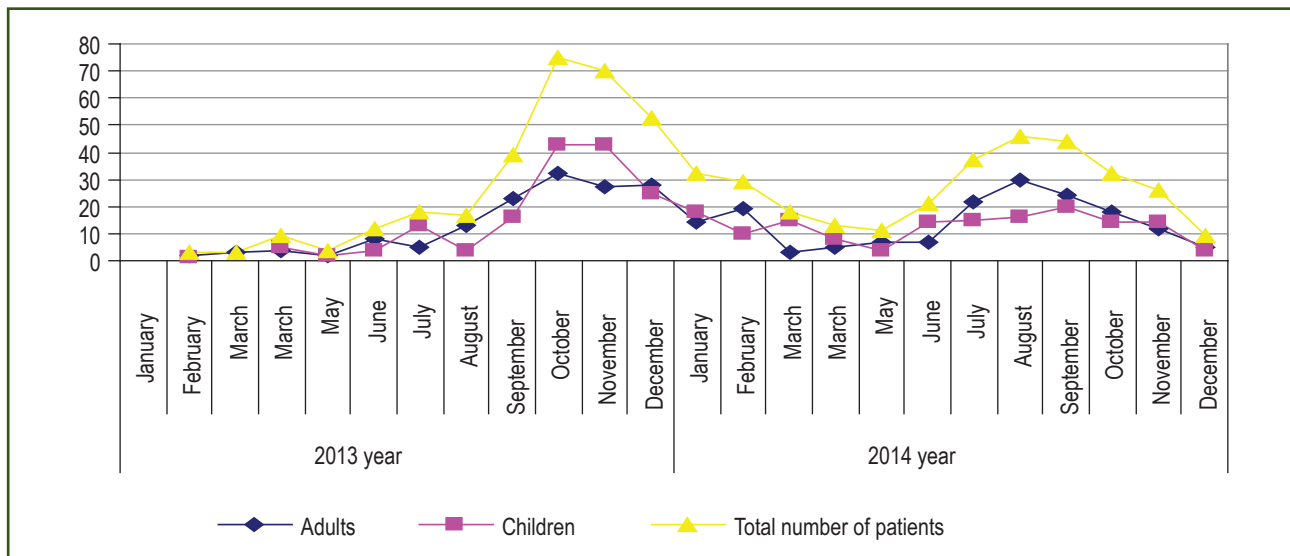


Figure 4 – The dynamics of hospitalizations of patients with hepatitis A in the RCIDH for years 2013–2014 (621 patients)

Among all of the patients, the patients with moderate severity level prevailed. The icteric form was detected in 90.0 % of cases (Fig. 5).

During September-January years 2014–2015 we clinically and microbiologically examined 61 patients with HA icteric forms, aged between 15 and 67 years. Microbiological study of the colon contents was performed in patients by determining the species composition and population of autochthonous and allochthonous number of microflora representatives in feces using conventional bacteriological methods.

As a result of the studies it has been stated, that in all patients with HA, the violation in species composition and population of microorganisms has been revealed. It was characterized by a decrease in the percentage of growing (in some cases up to a total elimination) and quantitative deficiency of indigenous bacteria: *Bifidobacterium* spp., *Enterococcus* spp., and *Lactobacterium* spp. (in lesser quantity). Inhibition of protective components of microbiota accompanied by contamination of the opportunistic *Peptostreptococcus* spp., *Citrobacter* spp., *Hafnia* spp., *Serratia* spp., *Allochthonous hemolytic* spp., enteropathogenic, enterotoxigenic, enteroinvasive *E.coli* (45.9 %), and increased population levels of anaerobic and aerobic opportunistic microorganisms as *Peptococcus* spp. (1.6 %), *Clostridium difficile* (1.6 %), *Klebsiella pneumoniae* (11.5 %), *Proteus vulgaris* (4.9 %), *Enterobacter* (4.9 %), *Staphylococcus aureus* (19.7 %), and yeast-like fungi *Candida albicans* (31.1 %) and *Candida cruzei* (9.8 %). The survey indicates severe changes in microecology of intestine, which mainly corresponds to II–III degree dysbiosis.

Based on the obtained facts about the changes of the GIT microbiocenosis by analyzing the feces bacteriogram of the patients we have identified the level of colon dysbacteriosis in each patient. According to the results of the bacteriological study, dysbacteriosis of the III level was established in 41 patient (67.2 %), dysbacteriosis of the IV level – in 6 (9.8 %) patients, and dysbacteriosis of II level – in 14 (23.0 %) patients, correspondingly. Wherein, colibacillosis etiology (serovars *E.coli* O: 111, O: 117, O: 157) of colon

dysbiosis was mainly established in 41 patients with HA. It is in these patients that the most essential feature of qualitative changes of aerobic microflora was the appearance of atypical varieties of *E.coli*, and, also, the increase of the *Klebsiella pneumoniae*, *Proteus vulgaris*, *Enterobacter* levels.

The analysis of anamnestic data of the examined patients (n = 61) with HA revealed the presence of chronic diseases of the digestive system in 43 (70.5 %) patients. 12 (19.7 %) patients that were under clinical observation, according to the place of residence, due to gastric ulcer or duodenal ulcer, disease duration was for (8.25 ± 1.12) years. 18 (29.5 %) patients had chronic non-calculous cholecystitis. The duration of the disease constituted for (8.41 ± 0.85) years. 8 (13.1 %) patients had gallstone disease (disease duration – (4.25 ± 1.12) years), 2 (3.3 %) patients had chronic pancreatitis (disease duration – (7.33 ± 0.76) years), and 3 (4.9 %) patients had non alcoholic steatohepatitis due to the metabolic syndrome (disease duration – (5.12 ± 0.45) years). In these particular patients with concomitant gastroenterological disorders HA

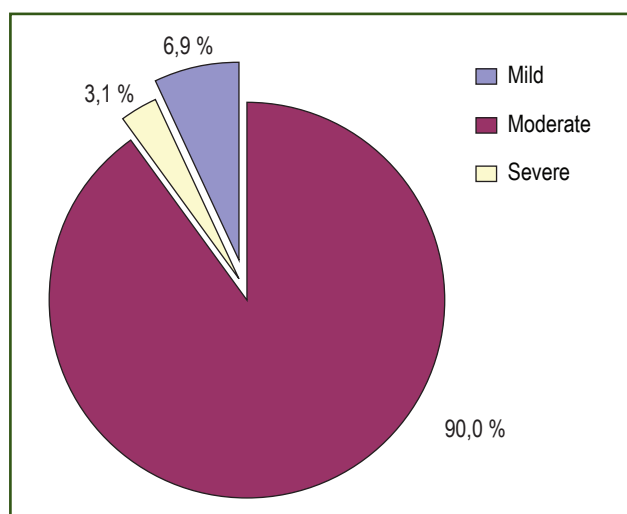


Figure 5 – Degrees of HA severity in hospitalized patients

proceeded with moderate to severe degrees of disease manifestation, and in patients with nonalcoholic steatohepatitis a severe degree of HA progression was observed.

In characterizing the results of the microbiological studies of feces in patients with HA, the findings reveal more significant changes in the quantitative and qualitative composition of the colon's microflora bacteriological composition mainly in patients with the presence of chronic digestive system diseases. Dysbacteriosis of III–IV levels in HA was established in all of the patients with gastric ulcer or duodenal ulcer, nonalcoholic steatohepatitis and chronic non-calculous cholecystitis in anamnesis.

Thus, HA on the background of chronic gastroenterological pathology in the examined patients had a more severe and prolonged disease progression, and was accompanied by significant colon dysbiotic changes, which should be considered in the treatment of such patients.

Conclusions

1. The HA disease is characterized by cyclic incidence: a significant increase in the incidence of the disease is observed every 6–7 years, and a moderate increase of the incidence is observed every 3–4 years. Epidemic process is activated in August with a peak in November.

2. The increase in the HA incidence in years 2013–2014 started in June–August 2013 and ended by March 2014 and by next the June a new increase is recorded, which has ended in December.

3. With the increase of morbidity, children (2013) are prevalent among the hospitalized, and with its attenuation — adults (2014).

4. Most often HA in adults occurs in the form of moderate severity (90 %). Only 10 % of the patients have anicteric forms of HA.

5. A qualitative and quantitative imbalance of the colon microflora with the development of dysbiosis of III–II degree was found in all of the examined patients with HA. The presence of 2 and 4 component associations of opportunistic pathogen microorganisms in the GIT was found in the majority of the examined patients.

6. In the presence of chronic lesions of the digestive system organs, in the anamnesis of the examined patients with HA, the disease has a more severe and prolonged progression, and is accompanied by significant colon microflora changes.

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КЛІНІКО-ЕПІДЕМІОЛОГІЧНІ ОСОБЛИВОСТІ ГЕПАТИТУ А У ЖИТЕЛІВ ЗАКАРПАТСЬКОЇ ОБЛАСТІ

Резюме. Наведено клініко-епідеміологічні особливості гепатиту А в Закарпатській області за 2004–2014 роки. Визначена характерна циклічність та сезонність гепатиту А в цьому регіоні України. На основі обстеження 61 пацієнта з гепатитом А встановлено особливості клінічного перебігу захворювання, а

також характерні мікробіологічні зміни кількісного та якісного складу мікрофлори товстої кишки залежно від наявності супутньої хронічної патології органів травлення.

Ключові слова: гепатит А, дисбіоз, хронічна гастроентерологічна патологія.

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КЛИНИКО-ЭПИДЕМИОЛОГИЧЕСКИЕ ОСОБЕННОСТИ ГЕПАТИТА А У ЖИТЕЛЕЙ ЗАКАРПАТСКОЙ ОБЛАСТИ

Резюме. Приведены клинико-эпидемиологические особенности гепатита А в Закарпатской области за 2004–2014 годы. Определена характерная цикличность и сезонность гепатита А в данном регионе Украины. На основе обследования 61 пациента с гепатитом А установлены особенности клинического течения заболевания, а также характерные

микробиологические изменения количественного и качественного состава микрофлоры толстого кишечника в зависимости от наличия сопутствующей хронической патологии органов пищеварения.

Ключевые слова: гепатит А, дисбиоз, хроническая гастроэнтерологическая патология.