



## Internal Diseases

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CONFERENCE ABSTRACTS  
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AZIZYAN N.G,  
SAFARYAN M.D.

Department of Phthisiology,  
YSMU

Corresponding author email:  
nazizyan@mail.ru

## TB AMONG HIV INFECTED PATIENTS UNDER THE PRESENT EPIDEMIOLOGICAL CONDITIONS

**INTRODUCTION.** Due to the data of WHO there are 42mln HIV infected people in the World. Tuberculosis (TB) is developed in 1/3 of them making the problem of TB all over the world even worse [Glynn J.R., Murray J., Bester A. et al., 2008; Meintjes G., Wilkinson R.J., Morroni C. et al., 2010; Morris A., Crothers K., Beck J.M. et al., 2011; Климов Г.В, 2016]: 2796 HIV infected patients are registered in Armenia 40% of which has developed TB.

To study the prevalence of TB/HIV coinfection, impact of clinical and social factors under the present epidemiological conditions in Armenia.

**METHODS USED.** History of disease of 209 TB/HIV coinfecting patients in the period of 2006-2013 has been studied. All the patients have undergone clinical, radiological and laboratory examinations.

**RESULTS AND DISCUSSION.** 246 (84.8%) of the above-mentioned patients are male, 44 (15.2%) - female. The majority are in 35-44 age group. The 67.6% are from urban areas, 32% are from the capital city. 37.9% are migrant workers and 22.4% are ex-prisoners. As to unhealthy habits 53.8% of the patients smoke 20-40 cigarettes a day. Alcohol and drugs were abused by 48.6%. 96.2% were consulted by doctors because of symptoms. In 38.3% cases it took 1-3 months after appearance of symptoms to be diagnosed. Lung infiltrative cases were prevailing (25.9%). In 25.5% of cases generalized TB was diagnosed and in 51% of patients the disease was revealed in the phase of dissemination and destruction. In 12.1% cases the CNS was affected. 126 (43.4%) patients had BK positive results and 50% of them had drug resistance. The main complaints were weakness (94.5%), loss of weight (61.7%), sweating (50.7%), hectic fever (41.7%). CD4+ count was low in 72.3% (less than 200). The treatment was effective for 61.7%. Treatment failed in cases of disseminated and generalized TB treatment (51%).

**CONCLUSION.** Male population of 35-44 age group get infected with TB/HIV. Severe acute start of disease is common. Infiltrative and generalized TB types on the background of immune deficiency are prevailing. In majority of cases drug resistance was present.

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### KEYWORDS:

TB,  
HIV,  
CD4+.

## CALPROTECTIN LEVEL ASSESSEMENT IN MONO- AND MIXED ACUTE INTESTINAL DISEASES

**INTRODUCTION.** Over the last decades there are numerous scientific studies about fecal biomarkers (lactoferrin, calprotectin, etc.) and their diagnostic significance in the gastrointestinal diseases. As known, fecal calprotectin is used as a useful marker to quantify mucosal inflammation, because it is stable in feces and can be determined by noninvasive methods. It is usually investigated in inflammatory bowel diseases (Crohn's disease, non-specific ulcerative colitis, etc.). In the literature there are few studies about fecal calprotectin level during acute intestinal infections among adults, it is performed mainly in the childhood and is given a comparative description during bacterial and viral intestinal infections.

Therefore, the aim of the study was to evaluate the level of fecal calprotectin among adult patients with mono- and mixed acute shigellosis.

**METHODS USED.** A total of 79 adult patients hospitalized in «Nork» infectious clinical hospital with acute intestinal infections ongoing with colitis and haemorrhagic colitis syndrome were examined. To determine the etiology of the disease, both classic culture and non culture methods were used (coloured chromathographic immunoassay, PCR, etc.). The level of fecal calprotectin was determined by enzyme-linked immunoassay method using RIDASCREEN® Calprotectin (G09036) tests of R-Biopharm AG firm according to the manufacturer's instructions (cut off value 50mg/kg). Patients were divided into two groups: mono-shigellosis and mixed shigellosis.

**RESULTS AND DISCUSSION.** In the group of surveyed patients in 40,5% Shigella's different serotypes (Shigella Sonnei, Flexneri 2a, etc.) were found, more than half of which were associated with other pathogens (Campylobacter, Salmonella, Staphylococcus Aureus, EIEC).

In the group of mono-infection (13 patients) the mean value of temperature was  $38,2 \pm 1,20$  C, the frequency of diarrhea was  $8,1 \pm 3$  times daily and the duration of the diarrhea was  $5,8 \pm 3,4$  days. The 76,9% of this group had haemorrhagic colitis with a mean duration of  $3,3 \pm 2,4$  days. The mean level of calprotectin in the feces in group of mono-infection was  $426,4 \pm 226,7$  mg/kg.

In the group of mixed infection (19 patients) the mean value of temperature was  $38,6 \pm 1,60$  C, the frequency of diarrhea was  $8,6 \pm 3,1$  times and duration -  $6,6 \pm 3,8$  days. In group of mixed infection 89,5% had a haemorrhagic colitis with duration  $3,7 \pm 2,5$  days. The mean level of fecal calprotectin was  $637,5 \pm 226,5$  mg/kg. In the blood test rate was significantly higher compared with the group of mono-infection.

**CONCLUSION.** The dynamic control of the two groups (mono- and mixed shigellosis) showed us that there was no significant difference in the clinical characteristics of the severity disease. In the group of mixed shigellosis prevailed haemorrhagic colitis and the erythrocyte sedimentation rate was significantly higher. In the same group the mean value of fecal calprotectin was higher compared with group of mono-infection, which indicates more expressed inflammatory processes.

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HARUTYUNYAN L.A.<sup>2</sup>,  
GULAZYAN N.M.<sup>1</sup>,  
ASOYAN A.V.<sup>1,2</sup>

YSMU named after M. Heratsi  
"NORK" infectious clinical  
hospital

Corresponding author email:  
harlusine@mail.ru

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Acute intestinal disease,  
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shigella,  
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mixed infection



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HAZARAPETYAN L.G.,  
GRIGORYAN S.V.,  
ADAMYAN K.G.

Department of Cardiology,  
YSMU

Corresponding author email:  
dr.hazarapetyan@mail.ru

## COAGULATION CASCADE AND MARKERS OF INFLAMMATION AND FIBROSIS IN PATIENTS WITH ATRIAL FIBRILLATION

**INTRODUCTION.** Atrial fibrillation (AF) is the most common sustained arrhythmia in clinical practice (1, 3). AF is associated with a prothrombotic or hypercoagulable state, which may be contributed to an increased risk for stroke and systemic embolism. There is plausible evidence linking inflammation and fibrosis to the initiation and progression of AF (2, 4, and 5). Various inflammation markers such as interleukin-6 (IL-6) and C-reactive protein (CRP) have been associated with AF. Transforming growth factor (TGF- $\beta$ 1) is a key cytokine involved in the pathogenesis of fibrosis in many organs, whereas IL-6 plays an important role in the regulation of inflammation. Several prothrombotic factors have been found to be elevated in AF, indicating abnormal thrombogenesis. Abnormalities of hemostasis, fibrinolysis, endothelium and platelets have all been described increasing the risk of stroke and thromboembolism. Tissue Factor (TF) is the principal initiator of the coagulation cascade. It is expressed in response to injury, as well as to a number of different extracellular stimuli, including TNF- $\alpha$ , IL-6. In this way TF is promoted blood coagulation and involved in inflammation and angiogenesis. The aim of this study is to evaluate the relationships between inflammation and fibrosis as well as the prothrombotic state in the setting of AF, including the impact of this relationship on clinical presentation and outcome of AF patients.

**METHODS USED.** 125 patients with non-valvular AF (mean age  $63.6 \pm 8.5$ ) where enrolled in this study. After the enrollment the echocardiography examination and 24-hour ambulatory Holter monitoring ECG were registered in each patient. We measured plasma indexes of inflammation (CRP, IL-6) and fibrosis (TGF- $\beta$ 1) as well as the prothrombotic state, including markers of the coagulation cascade such as tissue factor (TF) and fibrinogen (F) in all observed patients with AF and 32 healthy subjects as control group. All of blood tests in plasma were determined by ELISA on the analyzer "Stat Fax 303 Plus" using commercial kits "Bio Source". Studies were conducted on the basis of simple randomized protocols, using the universal statistical packages SPSS 13.0 and EXCEL-2007.

**RESULTS AND DISCUSSION.** The obtained results showed that compared with controls group, AF patients had higher levels of IL-6 ( $p = 0.033$ ), CRP ( $p = 0.002$ ), TGF- $\beta$ 1 ( $p = 0.001$ ), TF ( $p = 0.026$ ) and F ( $p = 0.025$ ). Plasma CRP and TGF- $\beta$ 1 levels were higher among AF patients at "high" risk of stroke ( $p = 0.004$ ). Moreover, the levels of CRP, IL-6 and especially TGF- $\beta$ 1 are markedly elevated in patients with dilated left atrium, poorly functioning left atrial appendage and longer duration of AF.

**CONCLUSION.** Sustained AF may trigger an inflammatory response leading to activation of myofibroblasts and to the release of cytokines such as TGF- $\beta$ 1 and platelet-derived TF. Increased plasma levels of IL-6, CRP and TGF- $\beta$ 1 are related to the coagulation cascade indexes and may contribute to structural remodeling of left atrium in patients with AF.

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### KEYWORDS:

AF,  
inflammation markers,  
fibrosis,  
coagulation markers.

## COMPARISON OF THE LEVELS OF CYTOKINES IN CHILDREN WITH MONO- AND MIXED ROTAVIRUS INFECTION

**INTRODUCTION.** Rotavirus is the most common cause of diarrhea among children. Mixed infections of rotaviruses and bacteria are not uncommon. Investigation of host-microbe's interaction in mixed infection can be useful for management of the patients. Of the study is comparison of the levels of Interleukin-2(IL-2), Interleukin-10(IL-10) and Tumor Necrosis Factor- $\alpha$ (TNF-  $\alpha$ ) in children with mono and mixed rotavirus infection(RI).

**METHODS USED.** Patients admitted to the "Nork" infectious clinical hospital were included in the study during the period February-June 2014. Criteria of inclusion were age under 5 years old and presence of rotavirus antigen in stool by ELISA. For detection of cytokines levels in serum by ELISA samples were collected from 93 patients on the first day of hospitalization. Mean age was  $28,7 \pm 13,3$  months, 54% were males. Patients were divided into 2 groups: mono RI (stool culture was negative) and mixed RI (stool culture was positive for pathogenic or facultative pathogenic microflora). According to the bacteriological analysis of feces, in 81,7% of cases patients had mono-rotaviral infection, while in 18,3% rotavirus was combined with pathogenic or facultative pathogenic microflora, from which Staphylococcus aureus was isolated in 56.5% of patients following Salmonella` 21,7%, Morganella` 8,7%, Proteus` 8,7%, Shigella` 4,3%.

**RESULTS.** Results of the study are presented in the table.

Cytokines	Group	Number of patients	Average level of cytokines (pg/ml)	Standard deviation	p-value
IL-2 (Norma 0 pg/ml)	Mono RI	76	0 .2	0 .89	<b>0 .039</b>
	Mixed RI	17	0 .52	1 .25	
TNF- $\alpha$ (Norma 0-0 .5 pg/ml)	Mono RI	76	0 .56	1 .33	0 .63
	Mixed RI	17	0 .68	1 .24	
IL-10 (Norma 0-5 pg/ml)	Mono RI	76	33 .77	41 .84	0 .55
	Mixed RI	17	30 .08	24 .46	

**CONCLUSION.** From the initial period of RI active stimulation of synthesis of anti-inflammatory cytokine IL-10 is observed both in mono and in mixed RI groups, while average level of pro-inflammatory cytokine IL-2 is significantly higher in case of mixed RI as compared to mono RI.



**HOVHANNISYAN A.H.,  
GYULAZYAN N.M.**

Department of Infectious Diseases, YSMU

Corresponding author email:  
alla\_hovh@yahoo.com

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mixed infection,  
cytokines



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KALIKYAN Z.G.

Department of Clinical Immunology and Allergology, YSMU

Corresponding author email:  
zkalikyan@yandex.ru

## ASSOCIATION BETWEEN ALLERGODERMATOSES AND PARASITES

**INTRODUCTION.** It is known that many parasitic infections such as *Giardia lamblia* (*G. lamblia*) and *Ascaris lumbricoides* (*A. lumbricoides*) are associated with increased prevalence of cutaneous allergies[1]. However, this association stays unclear whether parasites are cause of allergies or the dermatoses are the skin manifestations of parasites[2,3]. The aim of our study is to investigate the relationship between allergy and parasites and the role of eradication therapy on the improvement of patients with allergodermatoses.

**METHODS USED.** 95 patients (73 females and 22 males, mean age 32.7 years) with different allergodermatoses including acute and chronic urticaria, atopic dermatitis, allergic vasculitis and non-classified allergic dermatitis were studied between January 2015 and June 2017. The allergodermatoses were diagnosed according to the clinical criteria and specific allergotests. The following non-specific tests were performed to the patients: definition of total IgE level, assessment of *G. lamblia* and *A. lumbricoides* by serological tests and the analysis of stool. The ultrasound examination also was performed for clarification of some parasites (*G. lamblia*, *Echinococcus*). The appropriate eradication schemes were performed to the patients with revealed parasites. The success of eradication therapy was assessed 12 weeks after the treatment.

**RESULTS AND DISCUSSION.** The distribution of the patients by allergodermatoses was the following: 71 patients (74.7%, n=95) with urticaria, 8 (8.4%, n=95) – with atopic dermatitis, 2 (2.1%, n=95) - with allergic vasculitis and 14 (14.3%, n=95) - with non-classified allergic dermatitis. 16 patients (16.8%, n=95) were diagnosed by comorbid respiratory allergic diseases. The level of total IgE was increased (> 100 U/ml) in 60 of patients (63.2%, n=95).

Totally 36 patients (37.9%, n=95) were positive for one or more parasitic infections: 13 patients (13.7%, n=95) for *G. lamblia*, 21 (22.1%, n=95) for *A. lumbricoides*, 3 (3.2%, n=95) for *Enterobius*, and per 1 patient (1.1%, n=95) for *Taeniarhynchus saginatus* (*T. saginatus*) and *Echinococcus*. There were simultaneous infections in 4 patients (4.2%, n=95). In addition, *Helicobacter pylori* (*H. pylori*) infection was revealed in 12 patients (33.3%, n=36) with parasites.

The parasites were revealed in 23 patients with increased IgE level (38.3%, n=60). At the same time different parasites were revealed in 13 patients without increased IgE level (37.1%, n=35).

The clinical assessment of patients after an appropriate eradication therapy demonstrated improvement in 33 patients (91.7%, n=36) distributed as follows: 23 patients (95.8%, n=24) with only parasitic infection and 10 patients (83.3%, n=12) with parasites and *H. pylori* (eradication was performed also for *H. pylori*), respectively.

**CONCLUSION.** As the majority of previously published studies our investigation also showed the positive association between allergodermatoses and parasites[1-3]. On the other hand we found that parasitic infections were not associated with increased total IgE level. According to our data the eradication was highly effective for improvement of allergodermatoses especially in cases with only parasitic infection. Thus, regardless of whether the parasites are the cause for cutaneous allergic manifestations or not we can recommend to insert the tests for revealing of parasites and the eradication schemes in the allergodermatoses diagnostic and therapeutic approaches.

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### KEYWORDS:

*allergodermatosis,*  
*urticaria,*  
*Giardia lamblia,*  
*Ascaris lumbricoides,*  
*parasitic infection*

## CHANGES IN GUT MICROBIOTA AND ARGINASE INTRACELLULAR ACTIVITY IN THE LEUKOCYTES IN PATIENTS WITH TYPE 1 DIABETES

**INTRODUCTION.** Type 1 diabetes mellitus (T1DM) is one of the most frequent autoimmune disorders in childhood, adolescence and youth, developing due to autoimmune destruction of pancreatic  $\beta$ -cells, which leads to an absolute insulin deficiency. Gut microbiota (GM) is associated with the functions of the body's immune system, and immune-mediated diseases, including T1DM. However, the exact mechanisms by which GM is involved in the T1DM are still unknown. Accumulating data suggest that GM may contribute to the pathogenesis of diabetes influencing the immune response, in which arginine-metabolizing enzymes are involved, particularly arginase. Here, we examined the connection between gut microbiota and cytoplasmic and mitochondrial arginase isoforms (AI and AII respectively) in the leukocytes of patients with T1DM. The A1 activity is necessary to protect M2 macrophages from inflammation, it is constitutively expressed in human neutrophils and exhibits fungicidal activity, whereas A2 is involved in the production of reactive oxygen species implicating in the oxidative stress and inflammatory processes involved in the T1DM pathophysiology. This offers that arginases can be therapeutic targets in T1DM, and this issue is studied in the presented work.

**METHODS USED.** Children, adolescents and young adults with T1DM and healthy controls of appropriate ages were included in the study. Microbiota was examined in feces of participants in the clinical laboratory of «Nork» infectious diseases clinical hospital. Fasting venous blood was taken into 3.8% sodium citrate anticoagulant, mixed with 6 % dextran, and leukocytes were isolated by conventional procedures, then the leukocyte cytoplasmic and mitochondrial fractions were prepared by differential centrifugation. Arginase assay was based on the accumulation of L-ornithine produced by arginase in the reaction mixture during 1 hour incubation and determined by means ninhydrin. Measurement of the nitric oxide stable metabolites in protein-free samples was performed using Griess-Ilosvay reagent.

**RESULTS AND DISCUSSION.** Number of *E. coli* and *Clostridium* spp were drastically decreased with a concomitant increase in that of *Candida albicans*, and a manifestation of *Staphylococcus aureus* was also observed in T1DM, which may compete with the gut beneficial bacteria. Of note, *E. coli* and *Clostridium* spp play a protector role for GM, whereas clinical cultures of *C. albicans* has detrimental effects causing desquamation of small fragments peptidoglycan layers of cell wall and total destruction of the cytoplasm in lactobacilli.

The arginase activity was increased by 2 and 1.6 times in the cytoplasm and mitochondria of leukocytes from T1DM patients as compared respectively to control. Arginase is known contribute to decreased availability of L-Arginine in the organism, and particularly to nitric oxide synthase that may cause a subsequent reduction of NOS/NO production attributed to the pathological processes associated with diabetes. Based on this, the nitrite levels in the leukocyte cytoplasm, mitochondria and blood plasma were examined and in line with other findings it was dropped by 1.9, 2.3 and 1.6 times respectively.

**CONCLUSION.** We show remarkable changes in the gut microbiota accompanied by increased arginase activity and concomitant reduction in the nitrite levels in the leukocyte mitochondria and cytoplasm that may contribute to the alterations in the T1DM pathology that should be further investigated.

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MELKONYAN A.M.<sup>1</sup>,  
ALCHUJYAN.K.H.<sup>2</sup>,  
HOVHANNISYAN M.R.<sup>2</sup>,  
AGHAJANOVA E.M.<sup>1</sup>

<sup>1</sup>Department of Endocrinology,  
YSMU

<sup>2</sup>Department of pathological  
biochemistry and radioisotope  
methods, H. Bunyatyan Insti-  
tute of Biochemistry NAS RA

Corresponding author email:  
arthur778720@mail.ru

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MKHAYAN A.A.,  
GYULAZYAN N.M.

Department of Infectious  
Diseases, YSMU

Corresponding author email:  
anna.mkhoyan@yahoo.com

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shigella, campylobacter

## ACUTE MIXED INFECTIOUS COLITIS: ETIOLOGICAL STRUCTURE

**INTRODUCTION.** According to the literature pathogens of infectious diarrheas can complete each other's pathogenetic cycles which could lead to the effect multiplication, more expressed clinical manifestations and severe forms of the diseases. That is why mixed infections had always attracted the attention of scientists. Aforementioned infections can be presented in different combinations: bacteria-bacteria, bacteria-virus, virus-virus etc..

Differential diagnosis of acute bloody diarrheas has a paramount importance, because the treatment could be changed according to the type of causative agent. The main etiological factors of acute colitis are Shigellas, Campylobacters, EIEC and EHEC, Amoeba, Yersinias, Clostridias, Staphylococcus etc..

The aim of the study was to investigate etiological structure of acute mixed intestinal infections with colitic syndrome by using modern diagnostic methods.

**METHODS USED.** The study was conducted by inpatient treatment taking 236 adult patients with acute colitic variant intestinal infections. All patients were investigated by common and bacteriological stool examination. From specific diagnostic tests PCR was used for detection of Yersinias and diarrheagenic E. Coli. Coloured chromatographic immunoassay was used for the detection of the Campylobacter spp., EHEC O157:H7 and the toxin of *Cl. Difficile*.

**RESULTS AND DISCUSSION.** By using classical diagnostic methods out of 236 patients' stool only in 3.4% cases more than one pathogen had been found. After applying modern specific diagnostic methods from 46 more patients' stool two or more pathogens were found. Eventually, the total rate of acute mixed intestinal infections became 22,8%.

Out of 54 patients with confirmed mixed infection the mean age was  $31 \pm 16.1$ , of which more than half (57.4%) were females. The illness was higher in the autumn (74.1%), especially in September. Most of the patients (64.8%) were residents of Yerevan

The following pathogens and conditional pathogens in different combinations were detected after stool examinations: Shigella, Campylobacter spp., Salmonella spp., St. aureus, Proteus vulgaris, Clostridium difficile, EIEC, EHEC and Yersinia Enterocolitica/Pseudotuberculosis. The predominant combinations were with Shigella (72.2%).

The Shigella-Campylobacter combinations were 42,6% and 9,3% with additional third pathogen (2 cases with additional EIEC and one with Salmonella, St. Aureus and *Cl. Difficile* respectively). The number of combinations of Campylobacter with other pathogens without Shigella was almost equal to the number of Shigella combinations with other pathogens without Campylobacter (12 and 11 patients respectively). Campylobacter other mixed infections rate was 22,2% and the half of them were combined with EHEC and EIEC, 7,4%- with Salmonella and one with St.Aureus, one with *Cl. Difficile*. Other Shigella mixed infections rate was 20,4% and predominant combinations were with St.Aureus (9,3%), with EIEC and EHEC- 7,4% and two cases with combination of Proteus vulgaris.

**CONCLUSION.** By using modern diagnostic methods the rates of mixed infections increased about 4 times and among all adult patients with acute intestinal infections ongoing with colitic syndrome mixed infections were registered in one quarter cases. Shigella mixed infections were predominant more than half combined with Campylobacter spp.

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## COMPARATIVE ANALYSIS OF ANTIVIRAL THERAPY EFFICACY IN ADULTS WITH EPSTEIN-BARR VIRUS INFECTIOUS MONONUCLEOSIS

**INTRODUCTION.** One of the urgent problems of medicine is the high prevalence (>90%) of the world population with one of the opportunistic pathogens Epstein-Barr virus (EBV) [1, p. 986]. Clinical manifestations depend on the age of primary infection with EBV. In adolescence and young adults develops clinical picture of infectious mononucleosis (IM): febrile fever, tonsillitis, lymphadenopathy, hepatosplenomegaly, atypical lymphocytes in the peripheral blood. The most severe cases of EBV IM occurs in patients older than 24 years. The accumulated knowledge of the last period are also indicative of the huge role of EBV in oncological and immunological diseases [3]. However, there is still no clear pathogenetically valid treatment for patients, and existing recommendations are often contradictory [2]. Treatment of IM remains an unsolved problem of finding new approaches to therapy.

The aim of the study was to assess clinical and laboratory substantiation and to compare the effectiveness of antivirals in EBV IM.

**METHODS USED.** We carried out a dynamic observation of 15 patients (aged 17 to 40 years) with EBV IM of moderate severity within 6 months. The diagnosis was verified on the basis of ELISA (Ridascreen EBV VCA IgM (K6731) r-biopharm) and PCR real time. Patients were divided into 4 groups: I group (5 patients) received standard therapy without antivirals, II (3) - Acyclovir 800 mg 5 times a day, III (3) - Ingavirin 90 mg/day, IV (4) - Ingavirin 180 mg/day within 7 days. Patients underwent ultrasound examination, routine blood tests (with atypical lymphocytes count) and quantitative salivary PCR.

**RESULTS AND DISCUSSION.** In most cases of III and IV group at the completion of treatment levels of GPT and GOT decreased up to 12 and 17.7 times, in the II - up to 1.76 and 1.48 times respectively, in the I group - up to 3.4. In one patient from the I group GPT and GOT increased 3.45 and 2.7 times respectively. In the III and IV groups atypical lymphocytes count decreased to 39%. More pronounced decrease was noted in the group receiving Ingavirin 180 mg /day, compared with 90 mg/day. On the contrary, in the II group there was a tendency to increase by 20%. In the I group the number of atypical lymphocytes decreased to 33%. Interestingly, in the I group there was more significant decrease in size of spleen (up to 2.8 cm) compared with patients of other groups (up to 2.0 cm). As a result of analysis of the obtained data, no correlation between viral load and dynamics of laboratory parameters was found in all groups, which may be indicative of immuno-mediated damage of organs in EBV IM, which is responsible for the most severe cases of IM in adults, compared with children.

**CONCLUSION.** Thus, positive dynamics of biochemical and clinical blood tests was more pronounced in groups of Ingavirine (90 and 180 mg daily). Further investigations are needed.

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**MKRTCHYAN A.A.,  
GYULAZYAN N.M.,  
SHMAVONYAN M.V.,  
ASOYAN A.V.**

*Department of Infectious Diseases, YSMU*

*Corresponding author email:  
an.mkrt@inbox.ru*

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*EBV IM,  
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