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СОДЕРЖАНИЕ

АКЫЛБЕКОВА Д.Б., ЖУМАГАЛИЕВА Ж.С., ТОЛЫКБАЕВА Б.К., УАЗИРХАНОВА Н.Д., МАУКАЕВА С.Б. ОТНОШЕНИЕ СТУДЕНТОВ-МЕДИКОВ К ЛЮДЯМ, ЖИВУЩИМ С ВИЧ	3
АХМЕДОВА М.Д., РУЖЕНЦОВА Т.А., ИМАМОВА И.А., МИРЗАДЖАНОВА Д.Б., НАЗИРОВ Ш.А., БОБОЖОНОВ Ш.Ж. ИЗУЧЕНИЕ ПАТОГЕНЕТИЧЕСКИХ АСПЕКТОВ COVID-19	4
АХМЕДОВА М.Д., АЪЗАМОВ О.Ф., МАГЗУМОВ Х.Б., АНВАРОВ Ж.А., ГАЙБУЛЛАЕВ Ф.Х., ТАШПУЛАНОВА Ш.А. КЛИНИЧЕСКИЙ СЛУЧАЙ ЗАПОЗДАЛОГО ЛЕЧЕНИЯ ВИСЦЕРАЛЬНОГО ЛЕЙШМАНИОЗА	12
ЖУМАГАЛИЕВА Г.Д., ШАЛЕКЕНОВА С.К., БАЙГУЛИЕВА А.Б. КОКЛЮШ У ВЗРОСЛОГО ПАЦИЕНТА	16
ЖУМАГАЛИЕВА Г.Д., АБДУГАЛИЕВА Н.Ш., АСТРАХАНОВ А.Р., СИСЕНОВ А.Ж. ОСОБЕННОСТИ КЛИНИЧЕСКОГО ТЕЧЕНИЯ КОРОНАВИРУСНОЙ ИНФЕКЦИИ COVID-19 У ДЕТЕЙ ПЕРВОГО ГОДА ЖИЗНИ	17
ЖУМАГАЛИЕВА Г.Д., АСТРАХАНОВ А.Р., МАМЫРБАЕВА М.А. К ДИФФЕРЕНЦИАЛЬНОЙ ДИАГНОСТИКЕ ВРОЖДЕННОГО ЦИТОМЕГАЛОВИРУСНОГО ГЕПАТИТА У ДОНОШЕННЫХ НОВОРОЖДЕННЫХ	21
MIRKHAMIDOVA S.M., KHUDAYKULOVA G. K. THE IMPACT OF THE COVID-19 PANDEMIC ON HIV	27
ХУДАЙКУЛОВА Г.К., ЮЛДАШЕВА Ф.У. СОВЕРШЕНСТВОВАНИЕ РАБОТЫ МОБИЛЬНЫХ БРИГАД В АМБУЛАТОРНО-ПОЛИКЛИНИЧЕСКИХ УЧРЕЖДЕНИЯХ СИСТЕМЫ ЖЕЛЕЗНОДОРОЖНОГО ТРАНСПОРТА В УСЛОВИЯХ ПАНДЕМИИ COVID-19 В РЕСПУБЛИКЕ УЗБЕКИСТАН	30
ТУЙЧИЕВ Ж.Д. ВЫЯВЛЯЕМОСТЬ ПАТОГЕННОЙ КОИНФЕКЦИИ У ТЯЖЕЛЫХ БОЛЬНЫХ С COVID-19	34
ХАСАНОВА Ш.А., ТАДЖИЕВ Б.М. КАК ОЦЕНИВАТЬ РЕЗУЛЬТАТЫ ЛЕЧЕНИЯ БОЛЬНЫХ С НОВОЙ КОРОНАВИРУСНОЙ ИНФЕКЦИЕЙ (COVID-19). ШКАЛА ОЦЕНКИ КЛИНИЧЕСКОГО СОСТОЯНИЯ ПАЦИЕНТОВ	35
ТАДЖИЕВ Б.М., ИБРАГИМОВА Х.Н., ТОЙЧИЕВ А.Х., ШАМСУТДИНОВА М. И., ОСИПОВА С.О. ЭФФЕКТИВНОСТЬ АНТИПРОТОЗОЙНОЙ ТЕРАПИИ У БОЛЬНЫХ ЯЗВЕННЫМ КОЛИТОМ ЗАРАЖЕННЫХ BLASTOCYSTIS SP.	36
ТОЙЧИЕВ А.Х., ГАФНЕР Н.В., БЕЛОЦЕРКОВЕЦ В.Г., РАХМАТОВА Х.А., ОСИПОВА С.О. РОЛЬ ИНТЕРЛЕЙКИНА-1В В ДИАГНОСТИКЕ ХРОНИЧЕСКОГО АСПЕРГИЛЛЕЗА ЛЕГКИХ У БОЛЬНЫХ ХОБЛ	41
TUYSHIEV L.N., KHUDAIKULOVA G.K., SADIKOV KH.M.A. FACTORS AFFECTING ADHERENCE TO ANTIRETROVIRAL THERAPY IN CHILDREN	41
ТУЙЧИЕВ Л.Н., ХУДАЙКУЛОВА Г.К., МУМИНОВА М.Т., ЭРАЛИЕВ У.Э., МИРХОШИМОВ М.Б., ХОЛМАТОВ С.И. НОВАЯ КОРОНАВИРУСНАЯ ИНФЕКЦИЯ У ДЕТЕЙ	45
TUYSHIEV L. N., RAKHMATULLAYEVA SH.B., MUMINOVA M.T. ASSESSMENT OF THE STATE OF INTESTINAL MICROBIOTIC ECOSYSTEM IN CHILDREN WITH ACUTE INFECTIOUS DIARRHEA DEPENDING ON THE VIRAL LOAD IN HIV INFECTION	47
ТАДЖИЕВ Б.М., ДИНМУХАММАДИЕВ Н.А., ФАЙЗУЛЛАЕВА Д.Б. ВСТРЕЧАЕМОСТЬ РАЗЛИЧНЫХ ВЕНТИЛЯЦИОННЫХ НАРУШЕНИЙ ЛЕГКИХ У ДЕТЕЙ С ВИЧ ИНФЕКЦИЕЙ	50
ЗУБАЙДУЛЛАЕВА М.Т., КАРИМОВА М. Т., НИЯЗОВА Т. А. ПРОФИЛАКТИКА ОСЛОЖНЕНИЙ АНТИРЕТРОВИРУСНОЙ ТЕРАПИИ ПРИ ВИЧ ИНФЕКЦИИ	51
ЖАНАБАЕВА Г.У., АХМЕДЖАНОВА З.И., ДЖУМАГАЛИЕВА А.А. ОСОБЕННОСТИ ВЛИЯНИЯ ИНФЕКЦИИ НА ТЕЧЕНИЕ ПСОРИАЗА	54
ТАДЖИЕВ Б.М., ШАИСЛАМОВА М.С., ЗАЛЯЛИЕВА М.В., КАРИМОВА М.Т., ОСИПОВА	58

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РОЛЬ ИНТЕРЛЕЙКИНА-1В В ДИАГНОСТИКЕ ХРОНИЧЕСКОГО АСПЕРГИЛЛЕЗА ЛЕГКИХ У БОЛЬНЫХ ХОБЛ

Актуальность: хроническая обструктивная болезнь легких (ХОБЛ) является наиболее распространенным неинфекционным заболеванием легких с высоким уровнем смертности, в основном в развивающихся странах. Большинство больных ХОБЛ получают антимикробные препараты широкого спектра действия, кортикостероиды и подвержены высокому риску развития легочного аспергиллеза. Выявление хронического аспергиллеза легких (ХАЛ) как правило, значительно занижено из-за трудностей диагностики признаваемой всеми. Ранняя диагностика и контроль эффективности терапии имеют решающее значение для снижения смертности от аспергиллеза.

Цель исследования: определить роль сывороточного интерлейкина (ИЛ)-1 β как возможного биомаркера ХАЛ у больных ХОБЛ.

Материалы и методы: 102 больных ХОБЛ (III и IV стадии), систематически получавших кортикостероиды, и 61 лиц, без каких-либо жалоб со стороны здоровья (контроль) были включены в исследования. Сывороточный ИЛ-1 β , ИЛ-6, фактор некроза опухолей (ФНО)- α и *Aspergillus* IgG определяли методом ИФА. Идентификацию *Aspergillus* spp. проводили микологическим методом. Лечение ХАЛ у больных ХОБЛ проводили в соответствии с международными рекомендациями. Статистический анализ результатов проводили с помощью программы OriginLab 2018.

Результаты: уровень ИЛ-1 β у больных ХОБЛ с ХАЛ ($21,44 \pm 19,91$ пг/мл) был значительно выше, чем у больных ХОБЛ без ХАЛ ($7,58 \pm 10,32$ пг/мл; $p < 0,00001$) и лиц, входящих в контрольную группу ($2,11 \pm 1,82$ пг/мл; $p < 0,00001$). Концентрация ИЛ-6 была ниже у больных ХОБЛ с ХАЛ ($11,14 \pm 7,17$ пг/мл), чем у больных ХОБЛ без ХАЛ ($14,04 \pm 15,64$ пг/мл) ($p = 0,007$). У всех больных ХОБЛ уровень ИЛ-6 был значительно выше, чем в контроле ($2,95 \pm 2,85$ пг/мл) ($p = 0,00001$). Сывороточный уровень ФНО- α у больных ХОБЛ с ХАЛ ($8,23 \pm 6,35$ пг/мл) был значительно выше по сравнению с больными ХОБЛ без ХАЛ ($4,23 \pm 6,32$ пг/мл; $p = 0,0063$) и контролем ($1,63 \pm 1,76$ пг/мл; $p < 0,00001$). Соотношение уровней ИЛ-1 β и ФНО- α у больных ХОБЛ с ХАЛ к больным ХОБЛ без ХАЛ составило 2,8 и 1,9, соответственно. Хотя и ИЛ-1 β , и ФНО- α были значительно повышены у больных ХОБЛ с ХАЛ, первый из них имел более высокие значения. Уровни ИЛ-1 β , ИЛ-6 и ФНО- α у больных ХОБЛ с ХАЛ значительно снизились после терапии антимикотиками ($p = 0,001$).

Выводы: установлена положительная связь между уровнем ИЛ-1 β и развитием ХАЛ у больных ХОБЛ. Уровень ИЛ-1 β в сыворотке крови может быть использован в качестве дополнительного биомаркера ХАЛ у больных ХОБЛ.

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FACTORS AFFECTING ADHERENCE TO ANTIRETROVIRAL THERAPY IN CHILDREN
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Summary: Among children with low compliance, satisfactory living conditions were much less common ($p < 0.05$). At the same time, employment and housing problems were most frequently identified in this group. It is noteworthy that in half of the cases (50%) families with an HIV-infected child did not have proper information about HIV infection, which was one of the possible reasons for low adherence to ART. There was no disruption in the supply of antiretroviral drugs to the non-children we looked at. In our study, in children with low adherence, the survey revealed that in 23.7% of cases (which is significantly higher compared to other groups) there were cases of aggressive, offensive and intolerant behavior on the part of others in relation to an HIV-positive child and / or members of his family. This was the reason for the refusal of treatment or its suspension. In Groups of children with moderate and low compliance, low family income were significantly more likely to be observed ($p < 0.05$).

Key words: HIV infection, children, adherence, antiretroviral therapy, socio-demographic data, psychological characteristics.

The urgency of the problem. The advent of antiretroviral therapy (ART) has transformed HIV infection from a rapidly terminal illness into a chronic disease. ART suppresses HIV replication, reduces HIV morbidity and mortality, and improves the lives of HIV-infected children [1–5] but successful long-term treatment depends on adherence to ART regimens. Patients who do not maintain adequate adherence to ART are at greater risk of viral resistance to the available antiretroviral drugs,[6–10] of immunologic decline leading to opportunistic infections[11] and HIV disease progression,[12–14] and of transmitting resistant HIV at sexual debut.[8] Good ART adherence, typically defined as 90% or greater of doses taken as prescribed, decreases children's HIV-related morbidity and mortality.[15, 16] While children's access to ART in these settings is rapidly expanding, many patients still don't have access to second-line ART regimens and even fewer have access to third-line regimens.[17] Guidelines for pediatric HIV treatment recommend immediate ART initiation for HIV-infected infants, which should significantly reduce mortality among young children, but older children are expected to still have growing AIDS mortality.[18] Non-adherence and subsequent viral resistance could eliminate children's limited treatment options. Despite this wide range, the majority of studies from resource-limited settings report good adherence among HIV-infected children; 76% of the studies included during a systematic review of pediatric ART adherence in low- and middle-income countries reported greater than 75% ART adherence, but few had been treating children for quite 3 years.[19] Most of these studies used caregiver reports of adherence, but self-reported adherence among older children or adolescents may yield reports of more non-adherence. Purpose of the study: To assess the significance of socio-economic and socio-demographic factors in the formation of adherence to ART in children.

Materials and research methods. The research was conducted between 2017 and 2021 on the basis of clinics in Tashkent. In observational studies, 112 children aged 0-18 were diagnosed with "HIV infection". The diagnosis of "HIV infection" was established on the basis of the order of the Ministry of Health of the Republic of Uzbekistan No. 277 dated April 30, 2018.

Boys predominated among the examined children - 69 (61.6%). There were 43 girls (38.4%). Among the children included in the study, children aged 3-7 years (46.4%) and 7-14 years (25%) prevailed. The proportion of children under 3 years of age and adolescents over 14 years of age is slightly lower - 10.7% and 17.9%, respectively. The children were followed up for 6 months. At the same time, controls were performed at the start of ART, after 3 and 6 months, clinical, immunological and virological parameters were evaluated. The following research methods were used in the work: Methods of general clinical research, detecting proviral DNA. The appraisal of the state of adherence was carried out in accordance with the recommendations of WHO experts (2013) modified by Fedyaeva O.I. (2014). When assessing the significance of factors affecting the state of adherence, the following groups of factors were analyzed (Akulova M.V., 2016)

To assess the significance of various factors influencing the state of adherence to ARVT, 4 groups of possible causes were identified: 1) socio-economic and socio-demographic; 2) organizational factors related to the provision of medical and other types of assistance; 3) individual/psychological factors; 4) medical factors.

As part of this study, a survey and questioning of patients, as well as parents / guardians for small age groups, was conducted to identify: socio-demographic data not related to the underlying disease: (1) marital status, (2) education, (3) the presence of addiction factors (frequency of alcohol intake, use of psychoactive substances), the exclusion criterion was the use of psychoactive substances in the last 2 months, (4) mother's awareness of the child's HIV status; and conditions for antiretroviral therapy: (1) replacement of drugs during ART, (2) the number of pills taken per day. When modifying the treatment regime, its cause was clarified - the presence of side effects due to self-medication, the patient taking large doses of alcohol. Separately, the patient completed a questionnaire on compliance of their medication regimen with the ART requirements.

Research results. Children with low adherence were significantly less likely to have satisfactory living conditions ($p < 0.05$). At the same time, employment and housing problems were most frequently reported among this group. Attention was drawn to the fact that in half of the cases (50%) families with an HIV-infected child did not have proper information about HIV infection, which was one of the possible reasons for low adherence to ART. There was no disruption in the supply of antiretroviral drugs to the non-children we looked at. Cases were noted earlier, 5-7 years ago, but at present this sign is not considered as a factor influencing adherence. The issue of society's attitude towards HIV-positive patients deserves special attention. There are many cases described in the literature when the negative attitude of others led to a refusal to take ARV drugs. In our study, in children with low adherence, the survey revealed that in 23.7% of cases (which is significantly higher compared to other groups) there were cases of aggressive, offensive and intolerant behavior on the part of others in relation to an HIV-positive child and / or members of his family. This in some cases was the reason for refusal of treatment or its suspension. In the groups of children with moderate and low adherence, a low level of income in the family was significantly more often noted ($p < 0.05$). We explain the significance of this factor by the fact that, apparently, the level of income influenced the quality of child care (nutrition, education, etc.), which indirectly affected adherence. We did not find significant differences in the groups of children when analyzing the composition and status of the family (complete family,

divorce, etc.). It was found that in the group of children with low adherence, the lack of support from AIDS service organizations and volunteers was noted more often.

Among the organizational factors, the presence of a system of referrals between narrow specialties (phthisiatric, dermatovenereological and other services), the attitude of medical personnel towards patients and the availability and quality of medical care were highlighted. We found no significant differences between the groups for other factors.

When analyzing the characteristics of temperament, we did not reveal any significant patterns that could affect adherence to ART.

At the same time, at the time of initiation of ART, in the group of children with low adherence significantly more often ($p < 0.05$), more than half of the cases (52.6%) had a depressive state (more often in parents/guardians). It was especially pronounced in HIV-infected adolescents, with extreme forms of manifestation being suicidal moods.

In the group of patients with moderate adherence, in comparison with other groups, agitation and aggression were more often noted. The presence of internal motives in the patient, his own conviction, leads to a more stable form of commitment than motivation under the influence of external influences, such as, for example, the desire to please loved ones. According to our data, children with low adherence have the lowest motivation (76.3%) compared to other groups.

The next analyzed factor was awareness of the need for therapy and readiness for treatment (understanding the impact of therapy on the course of the disease, on long-term prospects, as well as the willingness and ability to follow certain rules in connection with taking drugs).

In our study, this factor turned out to be one of the most significant. Only in the group of children with high adherence, this indicator was high and amounted to 83.3%. In the group of children with low adherence, in more than half of the cases (65.8%), patients were not ready to start ART.

When analyzing the influence of addictions (alcohol, drugs, etc.) on the state of adherence, we did not reveal statistically significant differences, since cases of the use of psychoactive substances were isolated.

On this basis, we have not identified statistical patterns. We explain this by the fact that currently the study of the resistance of the virus to ARV drugs is not widely established and is carried out only in isolated cases. For this group of medical signs, we did not establish the influence of the severity of ARVT side effects on adherence, since, in general, side effects were either absent or were not severe. Also, the effect of the complexity of the drug regimen (frequency of administration, relationship with food intake, etc.) on the state of adherence was not revealed. This is due to the fact that in recent years the principle of ARV drug procurement has changed, which is aimed at simplified regimens to increase adherence.

Conclusions: Thus, we carried out an integral assessment of the influence of various factors on the state of adherence to ARVT. The most significant were socio-demographic and socio-economic, as well as individual/psychological factors.

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БАЛАЛАРДЫҢ АНТИРЕТРОВИРУС ТЕРАПИЯСЫН САҚТАУЫНА ӘСЕР ЕТЕТІН ФАКТОРЛАР

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Қысқаша мазмұны: ұстамдылығы төмен балаларда қанағаттанарлық өмір сүру жағдайлары айтарлықтай аз болды ($p < 0.05$). Сонымен қатар, бұл топта жұмыспен қамту және баспана мәселесі жиі байқалды. АИТВ жұқтырған балалары бар отбасылардың жартысында (50%) АИТВ-инфекциясы туралы тиісті ақпараттың жоқтығына назар аударылды, бұл АРТ-ны төмен ұстануының ықтимал себептерінің бірі болды. Біз тексерген балалардан басқалар арасында АРВ препараттарын жеткізуде үзіліс болған жоқ. Біздің зерттеуімізде ұстамдылығы төмен балаларда сауалнама 23,7% жағдайда (басқа топтармен салыстырғанда айтарлықтай жоғары) басқалар тарапынан АИТВ-ға қатысты агрессивті, қорлайтын және төзімсіз мінез-құлық жағдайлары болғанын көрсетті. оң бала және/немесе оның отбасы мүшелері. Бұл кейбір жағдайларда емдеуден бас тартуға немесе оны тоқтатуға себеп болды. Орташа және төмен ұстануы бар балалар топтарында отбасындағы табыстың төмен деңгейі айтарлықтай жиі байқалды ($p < 0.05$).

Кілт сөздер: АИТВ-инфекциясы, балалар, ұстану, антиретровирустық терапия, әлеуметтік-демографиялық деректер, психологиялық сипаттамалар.

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FACTORS AFFECTING ADHERENCE TO ANTIRETROVIRUS THERAPY IN CHILDREN

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In children with low adherence, satisfactory living conditions were significantly less common ($p < 0.05$). At the same time, problems with employment and housing were more often noted in this group. Attention was drawn to the fact that in half of the cases (50%) families with an HIV-infected child did not have proper information about HIV infection, which was one of the possible reasons for low adherence to ART. There were no interruptions in the supply of ARV drugs among the non-children we examined. In our study, in children with low adherence, the survey revealed that in 23.7% of cases (which is significantly higher compared to other groups) there were cases of aggressive, offensive and intolerant behavior on the part of others in relation to an HIV-positive child and / or members of his family. This in some cases was the reason for refusal of treatment or its suspension. In the groups of children with moderate and low adherence, a low level of income in the family was significantly more often noted ($p < 0.05$).

Key words: HIV infection, children, adherence, antiretroviral therapy, socio-demographic data, psychological characteristics.