IMPACT OF CORTICOSTEROID AND IMMUNOSUPPRESSIVE THERAPY ON THE COURSE OF CHRONIC HEPATITIS: RISKS AND PROSPECTS

Tolibov Farrux Farhodivich

tolibovf1@gmail.com

Asia International University, Bukhara, Uzbekistan.

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Abstract. *Chronic viral hepatitis is an inflammatory dystrophic-proliferative process in the liver, genetically determined by a deficiency of cellular and macrophage immunity, prolonged (more than 6 months), clinically manifested by asthenovegetative and dyspeptic syndromes, persistent hepatosplenomegaly, liver dysfunction, hyperfermentemia and dysproteinaemia.*

Keywords: *Liver encephalopathy, chronic liver disease, hypoglycaemia, Complications, cirrhosis, mucosa, coma, atrophy, pain, disorders, clinical forms, symptom, drug overdose, the portal vein system.*

ВЛИЯНИЕ КОРТИКОСТЕРОИДНОЙ И ИММУНОСУПРЕССИВНОЙ ТЕРАПИИ НА ТЕЧЕНИЕ ХРОНИЧЕСКОГО ГЕПАТИТА: РИСКИ И ПЕРСПЕКТИВЫ

Аннотация. *Хронический вирусный гепатит — воспалительный дистрофически-пролиферативный процесс в печени, генетически обусловленный дефицитом клеточного и макрофагального иммунитета, длительный (более 6 месяцев), клинически проявляющийся астеновегетативным и диспептическим синдромами, стойкой гепатоспленомегалией, нарушением функции печени, гиперферментемией и диспротеинемией.*

Ключевые слова: *Печеночная энцефалопатия, хронические заболевания печени, гипогликемия, осложнения, цирроз, слизистая, кома, атрофия, боль, расстройства, клинические формы, симптом, передозировка лекарственных средств, система воротной вены.*

Introduction: Criteria for the evaluation of chronic hepatitis are based on 4 main points - aetiology, pathogenesis, degree of activity of the process and stage of chronicisation

(degree of fibrosis).

According to the decision of the World Congress of Gastroenterologists (Los Angeles, 1994), the following variants of chronic hepatitis are distinguished:

By etiology:

-viral hepatitis (chronic viral hepatitis B, C, D, chronic viral hepatitis of unknown type);

-autoimmune hepatitis;

-chronic drug-induced hepatitis;

-alcoholic hepatitis;

-toxic hepatitis;

-cryptogenic (idiopathic) chronic hepatitis.

According to the clinical picture:

I. HBsAg carrier (ALT < 2 norms; DNA < 104cop/ml, or 2,000 IU/ml).

II. Immunoactive hepatitis B (ALT > 2 norms; DNA >

104 copies/ml, or 2,000 IU/ml; HBeAg+).

III. Immunotolerant hepatitis B.

The main cause of all chronic liver diseases is hepatotropic viruses. HCV causes 40-60 per cent of all cases and HBV 10-15 per cent of chronic hepatitis.

The current epidemic situation is particularly dangerous due to the growth of drug addiction among young people.

In this group, the risk of hepatitis infection ranges from 50 to 90 per cent, whereas in the general population the incidence does not exceed 5 per cent.

The global incidence of viral hepatitis far exceeds the incidence of many other viral infections in terms of growth rate and prevalence. In comparison, the annual global incidence of human immunodeficiency virus infections due to intravenous drug use:

- human immunodeficiency virus from 80 to 160 thousand people, - hepatitis B virus from 8 to 12 million people, - hepatitis C virus about 35 million people.

As a result of these three infections alone (HIV infection, hepatitis B and C), about 13 million people die each year.

Long-term analyses of the incidence of viral hepatitis show a decreasing trend in the proportion of acute forms of the disease in the overall structure of viral hepatitis and an increase in chronic forms.

Among hepatotropic viruses, A, HC viruses are predominantly prevalent, while B and C viruses are capable of causing a chronic process in the liver.

The clinical picture of chronic hepatitis is characterised by several symptoms and syndromes.

Hepatomegaly is a frequent and constant sign in diffuse chronic liver diseases. In CH, it is due to lymphomacrophagal infiltration, to a lesser extent hepatocyte dystrophy. Examination allows to determine the ‘tumour’ shifting during breathing in the right subcostal or subgluteal region. At percussion the left border of hepatic dullness is determined (in norm it does not go beyond the left pericardial line), increase in the size of the liver according to Kurlov (9 % 8 % 7 cm in norm).

Palpation - the liver is moderately dense, painful, its edge is pointed. However, it should be noted that the painfulness of the liver, determined palpatorily, is caused by stretching of the glisson capsule (against the background of circulatory insufficiency) or increased pressure in the biliary passages - in case of cholangitis.

Hepatalgia - in periods of activity of process at CH almost all patients have painfulness in liver area or unpleasant feeling of heaviness in liver area, which appear or intensify.

liver, which appear or intensify after physical activity.

Mesenchymal-inflammatory syndrome - its clinical signs are fever (due to impaired inactivation of pyrogens in the liver and intoxication), arthralgias and myalgias, lymphoadenopathy, hepatomegaly and splenomegaly, vasculitis (skin, lungs, kidneys). Fever is not pronounced, not accompanied by chills, body temperature does not exceed 38 °C.

Currently immunosuppressive and biological agents are used in a more extensive and earlier way in patients with inflammatory bowel disease, rheumatic or dermatologic diseases.

Although these drugs have shown a significant clinical benefit, the safety of these treatments is a challenge. Hepatitis B virus (HBV) reactivations have been reported widely, even including liver failure and death, and it represents a deep concern in these patients. Current guidelines recommend to pre-emptive therapy in patients with immunosuppressants in general, but preventive measures focused in patients with corticosteroids and inflammatory diseases are scarce. Screening for HBV infection should be done at diagnosis. The patients who test positive for hepatitis B surface antigen, but do not meet criteria for antiviral treatment must receive prophylaxis before undergoing immunosuppression, including corticosteroids at higher doses than prednisone 20 mg/d during more than two weeks. Tenofovir and entecavir are preferred than lamivudine because of their better resistance profile in long-term immunosuppressant treatments. There is not a strong evidence, to make a general recommendation on the necessity of prophylaxis therapy in patients with inflammatory diseases that are taking low doses of corticosteroids in short term basis or low systemic bioavailability corticosteroids such as budesonide or beclomethasone dipropionate. In these cases regularly HBV DNA monitoring is recommended, starting early antiviral therapy if DNA levels begin to rise. In patients with occult or resolved hepatitis the risk of reactivation is much lower, and excepting for Rituximab treatment, the prophylaxis is not necessary.

The HBV-induced liver inflammation is predominantly immune mediated: the host immune response causes a hepatocellular damage following the HBV replication, which can result in an acute or chronic liver necroinflammation. Immunosuppressants lead to an increase in DNA viral due to both a effect on the host immune response, as to a stimulatory effect of these drugs on hepatitis B virus [20].

The corticosteroids may increase the expression of HBV through a glucocorticoid-responsive element, which has been detected in viral genoma, and stimulates viral replication in patients under these treatments [21]. On the other hand, tumoral necrosis factor (TNF) α and interferon gamma (IFNγ) are important in the clearance of HBV from infected hepatocytes, so the use of anti-TNF drugs in patients with chronic HBV infections may result in an increase in viral replication [22,23]. Despite the increase in viral replication, the major damage hardly ever appears at the time of maximal immunosuppression and usually occurs once the immunosuppressive therapy is withdrawn, during the phase of immune reconstitution, when the immune system is able to destroy the hepatitis B-infected hepatocytes, producing the liver disease[5,24]. Clinically these exacerbations can vary, ranging from a subclinical or asymptomatic course to a severe acute hepatitis and even death.

Results: Eleven patients with hepatitis B e antigen (HBeAg)-positive chronic active hepatitis B were treated with an 8-wk course of prednisone followed by 28 days of adenine arabinoside 5′-monophosphate. Five individuals had a complete response (loss of HBeAg and DNA polymerase) whereas 3 had a partial response (sustained loss of DNA polymerase but persistence of HBeAg). At the present time 27 ± 3 mo has elapsed since the completion of therapy, and 4 of 5 complete responders remain negative for replicative markers while the fifth person exhibited transient reactivation of infection. Elevated DNA polymerase has reappeared in two of the three partial responders, in one 22 mo after completion of therapy. These encouraging results have led to a randomized, controlled trial using short-term prednisone followed by recombinant alpha-interferon.

Lamivudine has been the most frequent agent used agent in this scenario, having proved to reduce the reactivation risk and the associated mortality and morbidity. However, Lamivudine resistance develops in 53%-76% of patients after 3 years of treatment, therefore, this agent is only appropriate when a short course of therapy is needed. As immunosuppressants for ID usually are used for long term, nucleoside/nucleotide analogues (NAs) with a lower rate of resistance must be considered. Tenofovir and entecavir have a higher barrier to resistance, and should be used if treatments longer than 12 mo are planned [6,76,77,82,83]. In those patients with OBI with a high risk of reactivation, lamivudine may still have a role, because of its low cost, and the low or absent HBV viremia in these cases [76,78]. Alternative antiviral medications for lamivudine would be adefovir and telbivudine [20]. In all cases, but more closely if lamivudine, adefovir or telbivudine are used, serum AST/ALT levels and hepatitis B viral load must be monitored every 3 or 6 mo.

CONCLUSION: HBV reactivations are not uncommon in inactive HBV patients treated with immunosuppressive therapy for inflammatory diseases.

Current guidelines highly recommend prophylaxis in case of immunosuppressive therapy, including patients receiving steroids in monotherapy. However, steroids at low doses, treatments shorter than two weeks and low biodisponibility steroids are unlikely to need prophylaxis, although studies are lacking in this setting. These patients and those with occult or resolved HBV precise regularly HBV DNA monitoring during immunosuppressant therapy in order to detect reactivations. Entecavir or tenofovir are recommended as the optimal agents against HBV reactivation.

REFERENCES

1. Толибов, Ф. (2024). ИММУННАЯ СИСТЕМА: АНАТОМИЯ ЛИМФАТИЧЕСКОЙ СИСТЕМЫ И МЕХАНИЗМЫ ИММУННОГО ОТВЕТА. Журнал академических исследований нового Узбекистана, 1(2), 55-58.
2. Farxodivich, T. F. (2024). The Syndrome of External Secretory Function Insufficiency is a Common Complication of Chronic Pancreatitis.American Journal of Bioscience and Clinical Integrity 1 (10), 90-95
3. Farxodivich, T. F. (2024). Clinical Characteristics of Gastritis in Digestive Diseases. Research Journal of Trauma and Disability Studies, 3(3), 294-299.
4. Farxodivich, T. F. (2024). INFECTION OF COVID-19 ON COGNITIVE FUNCTIONS. SCIENTIFIC JOURNAL OF APPLIED AND MEDICAL SCIENCES, 3(4), 325-330.
5. *Tolibov F.F.* - VIOLATION OF PLATELET AGGREGATION AND IMBALANCE OF HEMOSTASIS IN PATIENTS WITH CHRONIC VIRAL HEPATITIS C//New Day in Medicine 6(68)2024 264-268 https://newdayworldmedicine.com/en/article/3758
6. *Tolibov F.F.*- CLINICAL AND MORPHOLOGICAL CORRELATIONS OF LIVER CIRRHOSIS.European Journal of Modern Medicine and Practice 4 (11), 515-520
7. TF Farhodivich.CHOLESTASIS IS A RISK FACTOR FOR THE DEVELOPMENT OF GALLSTONE DISEASE.Научный Фокус 2 (21), 317-321
8. Abdurashitovich, Z. F. (2024). APPLICATION OF MYOCARDIAL CYTOPROTECTORS IN ISCHEMIC HEART DISEASES. *ОБРАЗОВАНИЕ НАУКА И ИННОВАЦИОННЫЕ ИДЕИ В МИРЕ*, *39*(5), 152-159.
9. Abdurashitovich, Z. F. (2024). SIGNIFICANCE OF BIOMARKERS IN METABOLIC SYNDROME. *EUROPEAN JOURNAL OF MODERN MEDICINE AND PRACTICE*, *4*(9), 409-413.
10. Zikrillaev, F. A. (2024). Cardiorehabilitations from Physiotherapeutic Treatments in Cardiovascular Diseases. *American Journal of Bioscience and Clinical Integrity*, *1*(10), 96-102.

11. Abdurashitovich, Z. F. (2024). Cardiovascular System. Heart. Aorta. Carotid Artery.
12. Abdurashitovich, Z. F. (2024). MORPHO-FUNCTIONAL ASPECTS OF THE DEEP VEINS OF THE HUMAN BRAIN. *ОБРАЗОВАНИЕ НАУКА И ИННОВАЦИОННЫЕ ИДЕИ В МИРЕ*, *36*(6), 203-206.
13. Abdurashitovich, Z. F. (2024). ASTRAGAL O'SIMLIGINING TIBBIYOTDAGI MUHIM AHAMIYATLARI VA SOG'LOM TURMUSH TARZIGA TA'SIRI. *Лучшие интеллектуальные исследования*, *14*(4), 111-119.
14. Abdurashitovich, Z. F. (2024). ODAM ANATOMIYASI FANIDAN SINDESMOLOGIYA BO'LIMI HAQIDA UMUMIY MALUMOTLAR. *ОБРАЗОВАНИЕ НАУКА И ИННОВАЦИОННЫЕ ИДЕИ В МИРЕ*, *41*(4), 37-45.
15. Abdurashitovich, Z. F. (2024). THE IMPORTANCE OF THE ASTRAGAL PLANT IN MEDICINE AND ITS EFFECT ON A HEALTHY LIFESTYLE. *ОБРАЗОВАНИЕ НАУКА И ИННОВАЦИОННЫЕ ИДЕИ В МИРЕ*, *41*(4), 88-95.
16. Toxirovna, E. G. (2024). QALQONSIMON BEZ KASALLIKLARIDAN HASHIMOTO TIREODIT KASALLIGINING MORFOFUNKSIONAL O'ZIGA XOSLIGI. *Modern education and development*, *16*(7), 120-135.
17. Toxirovna, E. G. (2024). REVMATOID ARTRIT: BO'G'IMLAR YALLIG'LANISHINING SABABLARI, KLINIK BELGILARI, OQIBATLARI VA ZAMONAVIY DAVOLASH YONDASHUVLARI. *Modern education and development*, *16*(7), 136-148.
18. Эргашева, Г. Т. (2024). ОЦЕНКА КЛИНИЧЕСКОЙ ЭФФЕКТИВНОСТИ ОРЛИСТАТА У БОЛЬНЫХ ОЖИРЕНИЕМ И АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИЕЙ. *Modern education and development*, *16*(7), 92-105.
19. Ergasheva, G. T. (2024). THE SPECIFICITY OFAUTOIMMUNE THYROIDITIS IN PREGNANCY. *European Journal of Modern Medicine and Practice*, *4*(11), 448-453.
20. Эргашева, Г. Т. (2024). ИССЛЕДОВАНИЕ ФУНКЦИИ ЩИТОВИДНОЙ ЖЕЛЕЗЫ ПРИ ТИРЕОИДИТЕ ХАШИМОТО. *Modern education and development*, *16*(7), 106-119.
21. Toxirovna, E. G. (2024). GIPOFIZ ADENOMASINI NAZORAT QILISHDA KONSERVATIV JARROHLIK VA RADIATSIYA TERAPIYASINING UZOQ MUDDATLI SAMARADORLIGI. *Modern education and development*, *16*(7), 79-91.
22. ERGASHEVA, G. T. (2024). OBESITY AND OVARIAN INSUFFICIENCY. *Valeology: International Journal of Medical Anthropology and Bioethics*, *2*(09), 106-111.

23. Ergasheva, G. T. (2024). Modern Methods in the Diagnosis of Autoimmune Thyroiditis. *American Journal of Bioscience and Clinical Integrity*, *1*(10), 43-50.
24. Tokhirovna, E. G. (2024). COEXISTENCE OF CARDIOVASCULAR DISEASES IN PATIENTS WITH TYPE 2 DIABETES. *TADQIQOTLAR. UZ*, *40*(3), 55-62.
25. Toxirovna, E. G. (2024). DETERMINATION AND STUDY OF GLYCEMIA IN PATIENTS WITH TYPE 2 DIABETES MELLITUS WITH COMORBID DISEASES. *TADQIQOTLAR. UZ*, *40*(3), 71-77.
26. Toxirovna, E. G. (2024). XOMILADORLIKDA QANDLI DIABET KELTIRIB CHIQARUVCHI XAVF OMILLARINI ERTA ANIQLASH USULLARI. *TADQIQOTLAR. UZ*, *40*(3), 63-70.
27. Toxirovna, E. G. (2024). QANDLI DIABET 2-TIP VA KOMORBID KASALLIKLARI BO'LGAN BEMORLARDA GLIKEMIK NAZORAT. *TADQIQOTLAR. UZ*, *40*(3), 48-54.
28. Tokhirovna, E. G. (2024). MECHANISM OF ACTION OF METFORMIN (BIGUANIDE) IN TYPE 2 DIABETES. *JOURNAL OF HEALTHCARE AND LIFE-SCIENCE RESEARCH*, *3*(5), 210-216.
29. Tokhirovna, E. G. (2024). THE ROLE OF METFORMIN (GLIFORMIN) IN THE TREATMENT OF PATIENTS WITH TYPE 2 DIABETES MELLITUS. *EUROPEAN JOURNAL OF MODERN MEDICINE AND PRACTICE*, *4*(4), 171-177.
30. Эргашева, Г. Т. (2024). Эффект Применения Бигуанида При Сахарным Диабетом 2 Типа И Covid-19. *Research Journal of Trauma and Disability Studies*, *3*(3), 55-61.
31. Toxirovna, E. G. (2024). QANDLI DIABET 2 TUR VA YURAK QON TOMIR KASALLIKLARINING BEMOLARDA BIRGALIKDA KECHISHI. *ОБРАЗОВАНИЕ НАУКА И ИННОВАЦИОННЫЕ ИДЕИ В МИРЕ*, *38*(7), 202-209.
32. Эргашева, Г. Т. (2024). СОСУЩЕСТВОВАНИЕ ДИАБЕТА 2 ТИПА И СЕРДЕЧНО-СОСУДИСТЫХ ЗАБОЛЕВАНИЙ У ПАЦИЕНТОВ. *ОБРАЗОВАНИЕ НАУКА И ИННОВАЦИОННЫЕ ИДЕИ В МИРЕ*, *38*(7), 219-226.
33. Эргашева, Г. Т. (2024). СНИЖЕНИЕ РИСКА ОСЛОЖНЕНИЙ У БОЛЬНЫХ САХАРНЫМ ДИАБЕТОМ 2 ТИПА И СЕРДЕЧНО-СОСУДИСТЫМИ ЗАБОЛЕВАНИЯМИ. *Образование Наука И Инновационные Идеи В Мире*, *38*(7), 210-218.
34. Tokhirovna, E. G. (2024). CLINICAL AND MORPHOLOGICAL ASPECTS OF THE COURSE OF ARTERIAL HYPERTENSION. *Лучшие интеллектуальные исследования*, *12*(4), 234-243.

35. Tokhirovna, E. G. Studying the Causes of the Relationship between Type 2 Diabetes and Obesity. *Published in International Journal of Trend in Scientific Research and Development (ijtsrd), ISSN*, 2456-6470.
36. Toxirovna, E. G. (2024). ARTERIAL GIPERTENZIYA KURSINING KLINIK VA MORFOLOGIK JIHATLARI. *Лучшие интеллектуальные исследования*, *12*(4), 244-253.
37. Эргашева, Г. Т. (2024). НОВЫЕ АСПЕКТЫ ТЕЧЕНИЕ АРТЕРИАЛЬНОЙ ГИПЕРТОНИИ У ВЗРОСЛОГО НАСЕЛЕНИЕ. *Лучшие интеллектуальные исследования*, *12*(4), 224-233.
38. Эргашева, Г. Т. (2024). ФАКТОРЫ РИСКА РАЗВИТИЯ САХАРНОГО ДИАБЕТА 2 ТИПА. *ОБРАЗОВАНИЕ НАУКА И ИННОВАЦИОННЫЕ ИДЕИ В МИРЕ*, *36*(5), 70-74.
39. Эргашева, Г. Т. (2024). ОСЛОЖНЕНИЯ САХАРНОГО ДИАБЕТА 2 ТИПА ХАРАКТЕРНЫ ДЛЯ КОГНИТИВНЫХ НАРУШЕНИЙ. *TADQIQOTLAR. UZ*, *30*(3), 112-119.
40. Эргашева, Г. Т. (2023). Исследование Причин Связи Диабета 2 Типа И Ожирения. *Research Journal of Trauma and Disability Studies*, *2*(12), 305-311.
41. Tokhirovna, E. G. (2024). Risk factors for developing type 2 diabetes mellitus. *ОБРАЗОВАНИЕ НАУКА И ИННОВАЦИОННЫЕ ИДЕИ В МИРЕ*, *36*(5), 64-69.
42. Toxirovna, E. G. (2024). QANDLI DIABET 2-TUR VA O'LIMNI KELTIRIB CHIQARUVCHI SABABLAR. *Лучшие интеллектуальные исследования*, *14*(4), 86-93.
43. Tokhirovna, E. G. (2023). Study of clinical characteristics of patients with type 2 diabetes mellitus in middle and old age. *Journal of Science in Medicine and Life*, *1*(4), 16-19.
44. Toxirovna, E. G. (2024). GIPERPROLAKTINEMIYA KLINIK BELGILARI VA BEPUSHTLIKKA SABAB BO'LUVCHI OMILLAR. *Лучшие интеллектуальные исследования*, *14*(4), 168-175.
45. Toxirovna, E. G. (2023). QANDLI DIABET 2-TUR VA SEMIZLIKNING O'ZARO BOG'LIQLIK SABABLARINI O'RGANISH. *Ta'lim innovatsiyasi va integratsiyasi*, *10*(3), 168-173.
46. Saidova, L. B., & Ergashev, G. T. (2022). Improvement of rehabilitation and rehabilitation criteria for patients with type 2 diabetes.
47. Эргашева, Г. Т. (2023). Изучение Клинических Особенностей Больных Сахарным Диабетом 2 Типа Среднего И Пожилого Возраста. *Central Asian Journal of Medical and Natural Science*, *4*(6), 274-276.

48. Toxirovna, E. G. (2023). O'RTA VA KEKSA YOSHLI BEMORLARDA 2-TUR QANDLI DIABET KECHISHINING KLINIKO-MORFOLOGIK XUSUSIYATLARI. *ОБРАЗОВАНИЕ НАУКА И ИННОВАЦИОННЫЕ ИДЕИ В МИРЕ*, *33*(1), 164-166.
49. Ergasheva, G. T. (2022). QANDLI DIABET BILAN KASALLANGANLARDA REABILITATSIYA MEZONLARINI TAKOMILASHTIRISH. *TA'LIM VA RIVOJLANISH TAHLILI ONLAYN ILMIY JURNALI*, *2*(12), 335-337.
50. Ergasheva, G. (2024). METHODS TO PREVENT SIDE EFFECTS OF DIABETES MELLITUS IN SICK PATIENTS WITH TYPE 2 DIABETES. *Журнал академических исследований нового Узбекистана*, *1*(2), 12-16.
51. ГТ, Э., & Саидова, Л. Б. (2022). СОВЕРШЕНСТВОВАНИЕ РЕАБИЛИТАЦИОННО-ВОССТАНОВИТЕЛЬНЫХ КРИТЕРИЕВ БОЛЬНЫХ С СД-2 ТИПА. *TA'LIM VA RIVOJLANISH TAHLILI ONLAYN ILMIY JURNALI*, *2*(12), 206-209.
52. Шокиров, Б., & Халимова, Ю. (2021). Antibiotic-induced rat gut microbiota dysbiosis and salmonella resistance. *Общество и инновации*, *2*(4/S), 93-100.
53. Шокиров, Б. С., & Халимова, Ю. С. (2021). Пищеварительная функция кишечника после коррекции экспериментального дисбактериоза у крыс бифидобактериями. In *Актуальные вопросы современной медицинской науки и здравоохранения: Материалы VI Международной научно-практической конференции молодых учёных и студентов, посвященной году науки и технологий,(Екатеринбург, 8-9 апреля 2021): в 3-х т.*. Федеральное государственное бюджетное образовательное учреждение высшего образования «Уральский государственный медицинский университет» Министерства здравоохранения Российской Федерации.
54. Salokhiddinovna, X. Y. (2023). Anemia of Chronic Diseases. *Research Journal of Trauma and Disability Studies*, *2*(12), 364-372.
55. Salokhiddinovna, X. Y. (2023). MALLORY WEISS SYNDROME IN DIFFUSE LIVER LESIONS. *Journal of Science in Medicine and Life*, *1*(4), 11-15.
56. Salohiddinovna, X. Y. (2023). SURUNKALI KASALLIKLARDA UCHRAYDIGAN ANEMIYALAR MORFO-FUNKSIONAL XUSUSIYATLARI. *Ta'lim innovatsiyasi va integratsiyasi*, *10*(3), 180-188.
57. Халимова, Ю. С. (2024). КЛИНИКО-МОРФОЛОГИЧЕСКИЕ ОСОБЕННОСТИ ВИТАМИНА D В ФОРМИРОВАНИЕ ПРОТИВОИНФЕКЦИОННОГО ИММУНИТА. *ОБРАЗОВАНИЕ НАУКА И ИННОВАЦИОННЫЕ ИДЕИ В МИРЕ*, *36*(3), 86-94.

58. Saloxiddinovna, X. Y. (2024). CLINICAL FEATURES OF VITAMIN D EFFECTS ON BONE METABOLISM. *ОБРАЗОВАНИЕ НАУКА И ИННОВАЦИОННЫЕ ИДЕИ В МИРЕ*, *36*(5), 90-99.
59. Saloxiddinovna, X. Y. (2024). CLINICAL AND MORPHOLOGICAL ASPECTS OF AUTOIMMUNE THYROIDITIS. *ОБРАЗОВАНИЕ НАУКА И ИННОВАЦИОННЫЕ ИДЕИ В МИРЕ*, *36*(5), 100-108.
60. Saloxiddinovna, X. Y. (2024). MORPHOFUNCTIONAL FEATURES BLOOD MORPHOLOGY IN AGE-RELATED CHANGES. *Лучшие интеллектуальные исследования*, *14*(4), 146-158.
61. Saloxiddinovna, X. Y. (2024). CLINICAL MORPHOLOGICAL CRITERIA OF LEUKOCYTES. *Лучшие интеллектуальные исследования*, *14*(4), 159-167.
62. Saloxiddinovna, X. Y. (2024). Current Views of Vitamin D Metabolism in the Body. *Best Journal of Innovation in Science, Research and Development*, *3*(3), 235-243.
63. Saloxiddinovna, X. Y. (2024). MORPHOFUNCTIONAL FEATURES OF THE STRUCTURE AND DEVELOPMENT OF THE OVARIES. *EUROPEAN JOURNAL OF MODERN MEDICINE AND PRACTICE*, *4*(4), 220-227.