

БИОМЕДИЦИНА ВА АМАЛИЁТ ЖУРНАЛИ

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ETIOLOGY AND MOLECULAR GENETIC IDENTIFICATION OF CONGENITAL FEMALE GENITAL TRACT ANOMALIES.....12
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ASSISTED REPRODUCTIVE TECHNOLOGIES IN THE TREATMENT OF INFERTILITY IN WOMEN WITH PCOS.....23

ANESTHESIOLOGY AND INTENSIVE CARE MEDICINE

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MODERN APPROACHES TO ENSURING RESPIRATORY TRACT CONDUCTIVITY DURING MAXILLOFACIAL SURGERY IN CHILDREN.....31

HAEMATOLOGY

4. **Lipartia Mary Givievna, Mutalova Zumrad Sanzhar kizi.**
PROBLEMS AND PROSPECTS IN THE MANAGEMENT OF HEMOLYTIC ANEMIAS: A NARRATIVE REVIEW.....36
5. **Abdurakhmanova N. R., Kayumov A. A.**
PROGNOSTIC SIGNIFICANCE OF CD123 (IL3RA) EXPRESSION IN PATIENTS WITH ACUTE LEUKEMIAS.....45

PEDIATRIC SURGERY

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CURRENT ISSUES IN THE DIAGNOSIS AND TREATMENT OF THE RECTAL ULTRA-SHORT SEGMENT FORM OF HIRSCHSPRUNG'S DISEASE IN CHILDREN (LITERATURE REVIEW).....52
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SURGICAL METHODS FOR THE CORRECTION OF RENAL FUNCTION DISORDERS IN CHILDREN.....61

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OPTIMIZATION OF THE EDUCATIONAL CYCLE IN AN INTERNATIONAL ACADEMIC HUB: ANALYSIS OF FOREIGN EXPERIENCE AND DEVELOPMENT OF A MODEL BASED ON MICROSOFT PROJECT.....68
9. **Utepov Parkhat Duseмбаevich, Rizaev Zhasur Alimdzhанovich, Tukhtarov Bakhrom Eshnazarovich.**
A SYSTEM FOR TRAINING SPECIALISTS IN BIOLOGICAL SAFETY AND BIOLOGICAL PROTECTION IN MEDICAL ORGANIZATIONS.....72

INFECTIOUS DISEASES

10. **Seyfullaeva Bagdagul Skenderbekovna, Abduxalilova Gulnora Kudratullaevna.**
DETERMINATION OF STABILITY CHARACTERISTICS OF PSEUDOMONAS AERUGINOSA STRAINS USED IN AN EXTERNAL QUALITY ASSESSMENT PANEL.....81

11. **Nabieva Dilnoza Djurayevna.**
CLINICAL MANIFESTATIONS OF DERMATOLOGICAL DISEASES IN CHILDREN WITH HIV INFECTION.....94
12. **Oslanov Absamat Abdurakhimovich, Fayzullaev Sherzod Kobiljon ugli, Shakharov Dilshod Jura ugli, Tukhtaev Shokhzod Eshmurod ugli.**
CASES OF DRUG-INDUCED LIVER DAMAGE IN THE FIBROUS STAGE OF CHRONIC VIRAL HEPATITIS “B”.....99
13. **Samibaeva Umida Khurshidovna.**
DIAGNOSIS OF BACTERIAL COMPLICATIONS IN COVID-19-ASSOCIATED PNEUMONIA.....108
14. **Samibaeva Umida Khurshidovna.**
ETIOPATHOGENETIC ASPECTS OF THE NEW CORONAVIRUS INFECTION COVID-19 (LITERATURE REVIEW)116
15. **Shadjalilova Mukarram Salimdjanovna, Xalilova Zuhra Telmanovna.**
MODERN DYNAMICS OF SPREAD AND CLINICAL MANIFESTATIONS OF BACTERIAL INFECTIONS OF THE GASTROINTESTINAL TRACT.....125

DERMATOLOGY AND VENEREOLOGY

16. **Tashkenbaeva Umida Alisherovna, Abboskhonova Fotima Khasanovna.**
THE ROLE OF GENETIC AND BEHAVIORAL FACTORS IN FORMING THE SEVERITY OF ALOPECIA IN POSTBARIATRIC PATIENTS130
17. **Tashkenbaeva Umida Alisherovna, Abboskhonova Fotima Khasanovna.**
THE INFLUENCE OF CONCOMITANT DISEASES AND INDIVIDUAL FACTORS ON THE DEGREE OF ALOPECIA IN PATIENTS AFTER BARIATRIC INTERVENTIONS.....135

OTORHINOLARYNGOLOGY

18. **Gasymov Ayaz Veli oglu, Panahiyan Vafa Mustafa oglu, Abilova Farida Arif kyzy, Khatamov Jakhongir Abruevich.**
CONGENITAL CHOLESTEATOMA IN ADULTS.....140
19. **Khatamov Jakhongir Abruevich.**
OUR EXPERIENCE IN THE TREATMENT OF ALLERGIC RHINITIS.....146

MORPHOLOGICAL STUDIES

20. **Khamidova Farida Muinovna, Nojhigitov Azamat Musakulovich.**
THE INFLUENCE OF GSTM1 GENETIC POLYMORPHISM ON THE DEVELOPMENT OF BRONCHIECTASIS.....151
21. **Khamzaev Komiljon Amirovich, Farangiz Bahrom kizi Mamatkulova, Akhmatalieva Mayram.**
MORPHOLOGICAL FEATURES OF KIDNEY DAMAGE IN CHILDREN WITH IGA NEPHROPATHY.....163

ONCOLOGY AND RADIATION MEDICINE

22. **Tillyashaikhov Mirzagolib Nigmatovich, Khakkulov Erkin Bekmirzayevich, Alimov Jaloliddin Usmonkhon ugli.**
ANALYSIS OF URODYNAMIC PARAMETERS IN THE ASSESSMENT OF OVERACTIVE BLADDER IN PATIENTS WITH PROSTATE CANCER.....173

23. **Shakhanova Shakhnoza Shavkatona, Khoshimov Bakhodir Bakhromovich.**
MYOSTEATOSIS IN METASTATIC GYNECOLOGIC CANCER: CURRENT STATE OF THE PROBLEM.....184
24. **Yusupbekov Abrorbek Ahmedjanovich, Tuychiyeva Sabokhat Shavkatovna, Djanklich Saide Mustafayevna.**
A POPULATION-BASED APPROACH TO CERVICAL CANCER: THE CONTEMPORARY IMPORTANCE OF CANCER REGISTRIES, SCREENING, AND SURVIVAL ANALYSIS.....191
25. **Ulmasov Firdavs Gayratovich, Yarmukhamedova Nargiza Anvarovna, Raufov Farkhod Makhmudovich.**
MODERN TREATMENT METHODS OF BREAST CANCER (LITERATURE REVIEW).....199
26. **Karimova Nargiza Sunnatillayevna, Xasanboyev Saidjon G'ayratjon o'g'li.**
OPTIMIZATION OF RADIOTHERAPY PLANNING FOR HEAD AND NECK TUMORS BASED ON THE INTEGRATION OF MULTIPARAMETRIC IMAGING DATA.....206
27. **Zaredinov Damir Arifovich, Li Marina Vladimirovna, Goziev Soyibjon Orivjonovich.**
COMPARATIVE ASSESSMENT OF RADIATION EXPOSURE TO THE SKIN OF THE HANDS OF NUCLEAR MEDICAL PERSONNEL.....218
28. **Minnulin Irkin Rashidovich, Rakhimberdiev Rustam Abdunasirovich, Mirzakulov Buned Gaybullaevich, Tursunov Sherali Sirozhiddinovich, Urazov Nuriddin Elmurotovich**
UNRESOLVED ISSUES OF MEDICATION RELATED OSTEONECROSIS OF THE JAW IN BIPHOSPHONATE TREATMENT OF BONE METASTASES FROM PROSTATE CANCER.....224

OPHTHALMOLOGY

29. **Kadirova Aziza Muratovna.**
COMPLEX THERAPY OF RETROBULBAR NEURITIS OF VIRAL ORIGIN.....232
30. **Nazirova Zulfiya Rustamovna, Turakulova Dilfuza Mukhitdinovna, Abdullaeva Zulfiya Bakhodirovna.**
CLINICAL AND FUNCTIONAL CHARACTERISTICS OF VISUAL FUNCTIONS IN CHILDREN WITH PARTIAL ATROPHY OF THE VISUAL NERVE.....237
31. **Turakulova Dilfuza Mukhitdinovna, Nazirova Zulfiya Rustamovna, Karabayeva Iroda Murodjonovna.**
FEATURES OF CARRYING OUT CHILDREN WITH PRIMARY CONGENITAL GLAUCOMA ASSOCIATED WITH STERGE-WEBER SYNDROME.....242

PEDIATRIC DISEASES

32. **Makhmudova Ezoza Oybek kizi. Usmanova Munira Fayzullaevna Kardjavova Gulnoza Abilkasimovna.**
CURRENT DIRECTIONS IN RESPIRATORY THERAPY IN PRETERM INFANTS: PATHOGENESIS MECHANISMS, COMPLICATION PREVENTION MEASURES, AND EVALUATION OF THERAPEUTIC EFFECTIVENESS.....249
33. **Abdullaeva Durдона Rustamovna.**
DIGITAL VISUAL LOAD, ACCOMMODATIVE DISORDERS, AND COGNITIVE FATIGUE IN SCHOOL-AGED CHILDREN.....265
34. **Akhmedzhanova Nargiza Ismailovna.**
ASSESSMENT OF IRON LEVELS DEPENDING ON THE TYPE OF ANEMIA IN CHRONIC KIDNEY DISEASE IN CHILDREN.....273

35. **Fayzakhmatova Feruza Ozod kizi, Khamzaev Komiljon Amirovich, Mamatkulov Bahrom Bosimovich.**
USING MONOCLONAL ANTIBODIES IN THE TREATMENT OF STEROID-SENSITIVE NEPHROTIC SYNDROME IN CHILDREN.....281
36. **Khalilov Mirziyod Kholmurot ugli, Khamzaev Komiljon Amirovich, Akhmatalieva Mayram.**
GENETIC BASIS OF STEROID-RESISTANT NEPHROTIC SYNDROME IN CHILDREN AND ITS CLINICAL CORRELATIONS.....290
37. **Khamzaev Komiljon Amirovich, Bondarenko Anastasiya Romanovna, Akhmatalieva Mayram.**
EFFECT OF IMMUNOSUPPRESSIVE REGIMENS ON THE RELAPSE RATE AND CUMULATIVE CORTICOSTEROID DOSE IN CHILDREN WITH FREQUENTLY RECURRENT NEPHROTIC SYNDROME.....301

PSYCHIATRY AND NEUROLOGY

38. **Ravshanov Jakhongir, Ashurov Zarifjon.**
THE IMPACT OF SYNTHETIC CATHINONES ON SUICIDAL BEHAVIOR: A RETROSPECTIVE ANALYSIS OF PATIENTS WITH DEPENDENCE.....310
39. **Rakhmatullaeva Gulnora Kutpiddinova, Maksudova Odina Arabbaevna.**
DIAGNOSTIC VALUE OF PHENOTYPIC SIGNS AND THE BEIGHTON AND VAS SCALES IN IDENTIFYING UNDIFFERENTIATED CONNECTIVE TISSUE DYSPLASIA IN DORSOPATHY.....317
40. **Kuchimova Charos Azamatovna, Ochilov Ulugbek Usmanovich.**
CLINICAL AND DYNAMIC ASSESSMENT OF SOCIAL ACTIVITY AND QUALITY OF LIFE INDICATORS IN ELDERLY PATIENTS WITH DEPRESSIVE CONDITIONS ASSOCIATED WITH PSYCHOORGANIC SYNDROME.....326
41. **Ashurov Zarifjon, Abdulkakharova Gulnoza.**
THE GROWING CHALLENGE OF SYNTHETIC CATHINONES AND PRESCRIPTION DRUG MISUSE IN UZBEKISTAN.....333

MEDICAL REHABILITATION

42. **Kobilov Azizjon Orzikulovich, Saidov Sokhib Saidmurodovich, Yusupov Shukhrat Abdurasulovich.**
COMPLEX REHABILITATION EXPERIENCE OF CONSERVATIVE TREATMENT OF LUMBAR DISC HERNIATION.....340
43. **Isakova Gulchekhra Saitalieva**
EFFICACY OF THE MONTESSORI METHOD IN COMPLEX REHABILITATION OF SCHOOL-AGE CHILDREN WITH CEREBRAL PALSY.....346

DENTISTRY AND MAXILLOFACIAL SURGERY

44. **Khaydarov Artur Mikhaylovich, Rakhimov Akbarbek Rasulbek ugli.**
ETIOLOGY AND PATHOGENESIS OF POSTOPERATIVE COMPLICATIONS FOLLOWING DENTAL IMPLANTATION.....351
45. **Islamova Nilufar Bustanovna, Nurullayeva Guzal Abdumalikovna.**
IMPROVEMENT OF ADHESIVE TECHNOLOGIES APPLICATION FOR THE PREVENTION OF COMPLICATIONS AFTER TOOTH BLEACHING.....355
46. **Akhmedov Alisher Astanovich, Toyirov Jahongir Sobirovich.**
MODERN CONCEPTS OF TREATMENT IN ACCELERATED TOOTH TISSUE DESTRUCTION.....362

47. **Ortikova Nargiza Khayrullayevna, Khurramova Surayyo Dustmurodovna.**
OPTIMIZATION OF ORTHOPEDIC DENTAL TREATMENT METHODS IN PATIENTS WITH ARTERIAL HYPERTENSION.....369
48. **Durdiyeva Umida Berdimuradovna, Fattakhov Ravshan Abdurashidovich.**
CURRENT STATE OF THE PROBLEM OF DIAGNOSIS AND TREATMENT OF PERIODONTAL DISEASES IN PATIENTS WITH SOMATIC PATHOLOGY (RHEUMATOID ARTHRITIS): PATHOGENETIC RELATIONSHIPS AND CLINICAL APPROACHES.....376
49. **Vohidov Elbek Rahimovich, Rizaev Jasur Alimdjanovich.**
DENTAL HEALTH ASSESSMENT INDICATORS FOR MECHANICAL ENGINEERING WORKERS.....384
50. **Islamova Nilufar Bustanovna, Nabiyeva Marjona Uktamovna.**
IMPROVING THE METHODS OF TREATMENT AND PREVENTION OF COMPLICATIONS DURING THE ADAPTATION PERIOD OF PATIENTS TO REMOVABLE DENTURES.....390
51. **Norqulov Muslim Muhiddin ugli.**
MODERN STRATEGIES AND INNOVATIVE APPROACHES IN COMPREHENSIVE REHABILITATION OF PATIENTS WITH MANDIBULAR FRACTURES.....400
52. **Norqulov Muslim Muhiddin ugli.**
RISK FACTORS ANALYSIS AND MODERN APPROACHES TO THE PREVENTION OF INFECTIOUS COMPLICATIONS IN MANDIBULAR FRACTURES.....406
53. **Hayitova Mehriqul Alijon kizi, Rajabov Otabek Asrorovich.**
ERYTHEMA MULTIFORME EXUDATIVE IN THE ORAL CAVITY.....413
54. **Pulatov Oybek Abdumutolovich**
EFFICACY OF (GANOZHI PLUS) APPLICATION IN ADOLESCENTS FOLLOWING ORTHODONTIC BRACKET SYSTEM TREATMENT.....421
55. **Ismailov Saydimurad Ibragimovich, Zufarov Mirjamol Mirumarovich, Sharapov Nodir Utkirovich, Alieva Salima Bobosafarovna, Abdullaeva Mokhima Abdullaevna, Mirzaev Xondamir Alisher ugli.**
CLINICAL AND FUNCTIONAL CHARACTERISTICS OF WOMEN WITH ISCHEMIC HEART DISEASE IN THE SELECTION OF MYOCARDIAL REVASCULARIZATION METHODS.....425

PHARMACOLOGY

56. **Miskinova Fazilat Khudayorovna.**
STUDY OF THE ANALGESIC ACTIVITY OF N-BENZYL CYTISINE DERIVATIVES AND 1-PHENYLISOQUINOLINE DERIVATIVES.....438
57. **Abdurasulova Nargiza Olimovna, Ergashova Madina Muxtorovna.**
HYPOTENSIVE AND ORGANOPROTECTIVE PROPERTIES OF TELMISARTAN, A MEMBER OF THE SARTAN GROUP OF ANTIHYPERTENSIVE DRUGS.....443

INTERNAL MEDICINE

58. **Agababyan Irina Rubenovna, Rustamova Sarvinoz Botir kizi.**
THE IMPORTANCE OF EPICARDIAL ADIPOSE TISSUE IN THE PATHOGENESIS OF CARDIOVASCULAR DISEASES (LITERATURE REVIEW).....448
59. **Fattakhov Rafkat Akramovich**
METABOLIC DISORDERS AND THE RISK OF MULTIMORBIDITY IN PATIENTS WITH COPD.....455

60. **Fattakhova Yulia Edgarovna**
THE RELATIONSHIP BETWEEN VITAMIN D LEVELS AND ANXIETY-DEPRESSIVE DISORDERS AND THE SEVERITY OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE.....466

TRAUMATOLOGY AND ORTHOPEDICS

61. **Irismetov Murod Ergashevich, Khoshimov Javlon Tavakkalovich.**
POSTERIOR CRUCIATE LIGAMENT INJURY OF THE KNEE JOINT DIAGNOSIS AND ARTHROSCOPIC SURGERY.....476

UROLOGY

62. **Gafarov Rushen Refatovich, Shookla Pooja, Mansurov Umar Makhmudovich.**
THE ROLE OF TRIBULUS TERRESTRIAL PREPARATIONS IN THE TREATMENT OF SEXUAL DISORDERS IN MEN.....484

SURGERY

63. **Togayev Sherkobul Baykobulovich, Norboyev Olim Ibodullayevich, Hasanov Bobur Abduganievich.**
TOTAL COLECTOMY FOR COMPLICATED FORMS OF CROHN'S DISEASE OF THE COLON.....497

64. **Amonov Xudoyberdi Ravshanovich.**
SURGICAL TREATMENT OF CHRONIC COLOSTASIS: RISK FACTORS FOR UNFAVORABLE OUTCOMES AND STRATEGIES TO IMPROVE POSTOPERATIVE QUALITY OF LIFE.....501

65. **Ruziboev Sanjar Abdusalomovich, Amonov Xudoyberdi Ravshanovich.**
OPTIMIZATION OF THE SELECTION OF SURGICAL TREATMENT METHODS FOR CHRONIC COLOSTASIS BASED ON COMPREHENSIVE CLINICAL AND FUNCTIONAL ASSESSMENT.....519

ENDOCRINOLOGY

66. **Mamadiyarova Dilshoda Umirzokovna.**
THE SIGNIFICANCE OF THE C47T (RS4880) POLYMORPHISM IN THE SOD2 GENE IN THE DEVELOPMENT AND PERIOD OF COMPLICATIONS OF DIABETES.....529

67. **TOGAYEV Sherkobul Baykobulovich**
FOURNIER GANGRENE (CASE REPORT).....534

68. **Алимова Дурдона Дильмуратовна, Махкамов Акбаржон Мурод угли**
РОЛЬ ЭТИОЛОГИЧЕСКОГО ФАКТОРА В ВЫБОРЕ ТАКТИКИ ЛЕЧЕНИЯ ХРОНИЧЕСКОГО РИНОСИНСИТА У ДЕТЕЙ.....538


69. **UMAROVA Nazifa Abduraufovna, SATVALDIEVA Elmira Abusamatovna, SALIKHOVA Kamola Shavkatovna**
CURRENT CONCEPTS OF NECROTIZING ENTEROCOLITIS IN NEWBORNS: PATHOGENESIS, DIAGNOSIS AND NUTRITIONAL SUPPORT.....541

БИОМЕДИЦИНА ВА АМАЛИЁТ ЖУРНАЛИ
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Samarkand State Medical University, Uzbekistan**CASES OF DRUG-INDUCED LIVER DAMAGE IN THE FIBROUS STAGE OF CHRONIC VIRAL HEPATITIS “B”**

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 <http://dx.doi.org/10.5281/zenodo.19814385>**ANNOTATION**

Drug-induced liver injury (DILI) accounts for approximately 10% of all adverse reactions associated with pharmacological therapy. According to data from the World Health Organization, medications are responsible for 10–15% of cases of acute liver failure. The aim of this study was to compare the occurrence and features of DILI in patients with chronic viral hepatitis at fibrotic stages with those at non-fibrotic stages.

It has been well established that in chronic viral hepatitis, both direct and indirect viral effects contribute to endogenous intoxication and promote the development of liver fibrosis, thereby increasing hepatic vulnerability to drug-related injury. In this context, pharmacological agents represent an additional metabolic burden on the liver. The present study evaluated and compared cases of drug-induced liver injury in patients with advanced fibrotic stages of chronic viral hepatitis B and in patients without fibrosis.

Keywords: Chronic viral hepatitis B, non-fibrous and fibrous stages of the liver, drug-induced liver damage.

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СЛУЧАИ ЛЕКАРСТВЕННО-ИНДУЦИРОВАННОГО ПОРАЖЕНИЯ ПЕЧЕНИ НА ФИБРОЗНОЙ СТАДИИ ХРОНИЧЕСКОГО ВИРУСНОГО ГЕПАТИТА “В”

АННОТАЦИЯ

Лекарственное поражение печени (ЛПП) составляет около 10% всех побочных эффектов, связанных с применением фармакологических препаратов. По официальным данным ВОЗ, лекарственные препараты вызывают развитие острой печеночной недостаточности в 10-15% случаев. Целью данной статьи является сравнительное изучение лекарственно-индуцированного повреждения печени (DILI-Drug-Induced Liver Injury) в фиброзных стадиях хронических вирусных гепатитов и в стадиях без фиброза. В настоящее время научно доказано, что прямое и косвенное воздействие вирусов при хронических вирусных гепатитах приводит к эндогенной интоксикации и развитию фиброза. В таких случаях лекарственные препараты, естественно, оказывают чрезмерную нагрузку на печень. Авторы изучали случаи лекарственного поражения печени (ЛПП) у пациентов с фиброзными стадиями хронического вирусного гепатита В в сравнении с без фиброзными стадиями.

Ключевые слова: Хронический вирусный гепатит В, без фиброза и фиброзная стадии печени, лекарственное поражение печени.

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**SURUNKALI VIRUSLI GEPATIT "B" NING FIBROZ BOSQICHLARIDA JIGARNI
DORI VOSITALARDAN ZARARLANISH (DILI) HOLATLARI**

ANNOTATSIYA

Jigarni dori vositalar ta'siridan zararlanishi (DILI) farmakologik preparatlarni qo'llash bilan bog'liq barcha nojo'ya ta'sirlarining taxminan 10% ni tashkil qiladi. JSST ning rasmiy ma'lumotlariga ko'ra, o'tkir jigar yetishmovchiligi rivojlanishiga 10-15 % holatlarda dori vositalar sabab bo'ladi. Mazkur maqolani maqsadi surunkali virusli gepatitlarning fibroz bosqichlarida jigarni dori vositalar ta'siridan zararlanish (DILI- Drug-Induced Liver Injury) holatlarini fibrozsiz bosqichlari bilan qiyoslab urganishdan iborat. Hozirgi kunda surunkali virusli gepatitlarda viruslarni bevosita va bilvosita ta'siri, endogen intoksikatsiyaga va fibroz rivojlanishiga olib kelishi ilmiy jihatdan isbotlangan. Bunday holatlarda dori vositalari, jigarga ortiqcha yuk bo'lishi tabiiydir. Mualliflar surunkali virusli gepatit V ning fibroz bosqichlari rivojlangan bemorlarda, jigarni dori vositalar ta'siridan zararlanish (DILI) holatlarini fibrozsiz bosqichlari bilan qiyoslab urganishgan.

Kalit so'zlar: Surunkali virusli gepatit V, jigarning fibrozsiz va fibroz bosqichlari, jigarni dori vositalar ta'siridan zararlanishi.

Kirish. Surunkali virusli gepatitlarda virus yuklamasini o'zi organizmning endogen intoksikatsiyasiga va fibroz rivojlanishiga olib keladi. Gepatit viruslari bevosita yoki immun vositachiligida bilvosita gepatotsitlarga zararlovchi ta'sir ko'rsatadi va endogen intoksikatsiya sindromini keltirib chiqaradi. Surunkali virusli gepatitlardagi endogen intoksikatsiya sindromi klinik ko'rinishlarsiz namayon bo'lib, jigardagi o'zgarishlarning ko'lami va chuqurligini anglatadi. Virus yuklamasining miqdori, jigarda fibroz bosqichlari rivojlanishi bilan bevosita bog'liqdir.

Jigarning dori vositalar ta'siridan zararlanishi (DILI) farmakologik preparatlarni qo'llash bilan bog'liq barcha nojo'ya ta'sirlarining taxminan 10% ni tashkil qiladi. JSST ning rasmiy ma'lumotlariga ko'ra, o'tkir jigar yetishmovchiligi rivojlanishiga 10-15 % holatlarda dori vositalar sabab bo'ladi.

Butun dunyoda dorivor o'simlik preparatlarini qabul qilish va biologik faol qo'shimchalar (BFQ) qabul qilish natijasidagi jigarni dori vositalar ta'siridan zararlanishining usishi kuzatilmoqda. AQSh da har yili jigarni dori vositalar ta'siridan zararlanishi tufayli 2 mingga yaqin jigar

transplantatsiyasi amaliyoti amalga oshiriladi. Jigarni dori vositalar ta'siridan zararlanishi chastotasi yiliga 100000 aholiga 1-19 holatni tashkil qilsa, boshqa ma'lumotlarga ko'ra, dori vositalar qo'llanilgan barcha holatlarning 3-6% tashkil etadi. Dunyoda jigar patologiyasi bilan shifoxonaga yotqizilgan bemorlar ichida, dori vositalar ta'siri natijasida kelib chiqadigan sariqlik (xolestaz) 2-5% ni, dori vositalar ta'siri natijasida kelib chiqqan gepatit 10% ni tashkil qiladi.

Xorijiy mualliflarning (Björnsson E.S., Bergmann O.M., Björnsson H.K. et al.) ma'lumotlariga ko'ra, DILI (Drug-Induced Liver Injury) dori vositalar qabul qiluvchi 100000 bemorlarning 10-20 tasida kuzatiladi, kasalxonaga yotqizilgan bemorlarda 2-5% holatlarda sariqlik keltirib chiqaradi, o'tkir hepatitlarning barcha holatlarining taxminan 10 % ni tashkil etadi, o'tkir jigar yetishmovchiligiga 11 % holatlarda sabab bo'lib, yiliga 40 000 gacha o'lim DILI tufayli yuzaga keladi. Dori vositalari jigarning surunkali zararlanishiga va yaqqol fibroz/sirroz shakllanishiga sabab bo'lishi mumkin[24].

1968- yildan beri dori vositalarining nojo'ya ta'sirlarini qayd etuvchi JSST ma'lumotlar bazasining tahlillariga ko'ra, 1990- yillardan boshlab jigarni dori vositalar ta'siridan zararlanish holatlari sezilarli darajada o'sishi kuzatilgan. Ular orasida jigarni dori vositalar ta'siridan zararlanishida eng ko'p o'lim holatlari, asosan parasetamol, OIV infeksiyasini davolashda qo'llaniladigan preparatlar, epilepsiyaga qarshi preparatlar (valproy kislotasi), analgetiklar, tizimli antibakterial preparatlar va o'smaga qarshi dori vositalarini qabul qilishlar tufayli kelib chiqishi ma'lum qilingan.

Ingliz tilidagi adabiyotlarda bunday kasalliklarni ifodalash uchun DILI (Drug-induced liver injury), o'zbek tilidagi adabiyotlarda esa "jigarni dori vositalar ta'siridan zararlanishi" degan atama qo'llaniladi.

Jigarning dori vositalar ta'siridan zararlanishi bu retsept bo'yicha yoki retseptsiz beriladigan barcha turdagi dorilar (jumladan, kichik kimyoviy molekulalar, biologik agentlar, fitopreparatlar, parhez qo'shimchalari va biologik faol qushimchalar) tufayli kelib chiqadigan va qabul qilish boshlanganidan o'rtacha 5 kundan 90 kungacha bo'lgan davrda rivojlanadigan jigarning zararlanishidir.

Xalqaro tibbiyot fanlari tashkilotlari kengashi CIOMS (Council for International Organizations of Medical Sciences) tomonidan dori vositalariga nojo'ya reaksiyalarni tavsiflash uchun alohida atamalar qabul qilingan. Sarg'aygan bemorlar uchun R ko'rsatkichini aniqlash tavsiya etilgan. $R \text{ (nisbat)} = \frac{ALT \text{ (MYUCh karraligi)}}{IF \text{ (MYUCh karraligi)}}$. CIOMS tomonidan R ko'rsatkichi bo'yicha jigarni dori vositalar ta'siridan toksik zararlanishining (DILI) quyidagi tiplarga ajratish taklif etilgan.

CIOMS bo'yicha DILI tiplari.

1- jadval

Zararlanish tipi	Faollik		R
	ALT	ISh	
Gepatotsellyulyar	>2x MYuCh	< MYuCh	≥5
Xolestatik	<MYuCh	>2x MYuCh	≤2
Aralash	>2x MYuCh	>2x MYuCh	2-5

Izoh: MYuCh- me'yorning yuqori chegarasi.

Bundan tashqari, CIOMS "jigarning o'tkir shikastlanishi" atamasini kasallik davomiyligi 3 oydan kam bo'lganda, "surunkali" atamasini esa kasallik davomiyligi 3 oydan ortiq bo'lganda qo'llashni tavsiya etgan. Bu holat jigar fibrozi DILI ning hepatotsellyulyar turi boshlanganidan 3 oy o'tgach shakllanishiga asoslangan. Maddrey W.C., Boitnott J.K. lar fikricha DILI ning xolestatik turi kasallik davomiyligi 6 oy va undan ortiq bo'lganda "surunkali" atamasi qo'llaniladi. Surunkali DILI diagnozi jigarning progressiv shikastlanishini anglatmaydi[28].

DILI bo'yicha xalqaro ekspertlar ishchi guruhi tavsiyasiga ko'ra, agar dori vositasi (biologik faol qushimchalar va boshqalar) qabul qilish fonida quyida ko'rsatilgan o'zgarishlar kuzatilsa, bemorda DILI mavjud bo'lishi mumkin (tavsiyaning ishonchlilik darajasi V (dalillarning ishonchlilik darajasi 3) degan fikr yuritiladi:

- a) ALT faolligining oshishi $>2\text{MYuCh}$;
- b) yoki bog'langan bilirubin darajasining oshishi $>2\text{MYuCh}$;
- c) yoki AST, IF faolligi va umumiy bilirubin darajasi oshishining kombinatsiyasi ($\geq 2\text{MYuCh}$ ko'rsatkichlaridan biri).

Bunda jigar kasalliklarining mavjudligini hisobga olish zarur.

Agar qo'llanilayotgan dori vositasi bemor uchun hayotiy zarurat bo'lsa, u quyidagi laborator va klinik belgilar kuzatilgan holatlarda bekor qilinishi kerak bo'ladi:

- a) qon zardobida ALT yoki AST $> 8 \text{ MYuCh}$;
- b) 2 hafta va undan ortiq davrda qon zardobida ALT yoki AST $> 5 \text{ MYuCh}$;
- v) qon zardobida ALT yoki AST $> 3 \text{ MYuCh}$, bilirubin $> 2\text{MYuCh}$ yoki MNO $> 1,5$;
- g) qon zardobida ALT yoki AST $> 3 \text{ MYuCh}$, sitoliz, asta-sekin kuchayib boruvchi holsizlik, charchoq, dispepsiya simptomlari va / yoki eozinofiliya ($> 5\%$) bilan birga kelsa.

BFQ ning gepatotoksikligi odatda bemorlar va shifokorlar tomonidan yetarlicha baholanmaydi. Shu bilan birga, aholining ushbu vositalardan foydalanish chastotasi ancha yuqori. Faqat AQShda mamlakat aholisining 50-70% sog'liqni saqlash, qomat yoki turli kasalliklarni davolash uchun qo'shimcha sifatida qabul qilinishi ma'lum qilingan.

DILI ning haqiqiy tarqalganligi noma'lumligicha qolmoqda, ammo shuni ta'kidlash mumkin, klinik amaliyotda bunday diagnoz kamdan-kam hollarda asossiz ravishda qo'yiladi. Bu shartli bir nechta omillar bilan bog'liq bo'lib, ular orasida eng muhimi quyidagilardir:

- bemorlarning ba'zi dorilarni (antidepressantlar, neyroleptiklar, potensiyani oshirish uchun vositalar va boshqalar) qabul qilayotganligi to'g'risidagi ma'lumotlarni istamasliklari;
- shifokorlarning yatrogen kasalliklarni hujjatlashtirishni istamasligi; - xilma-xil simptomlarni noto'g'ri talqin qilinishi.

Surunkali virusli hepatitlarda DILI sabablariga gepatotoksik preparatlar istemol qilish, turli dori vositalarni birgalikda qabul qilishlar (bir vaqtning o'zida 2-3 xil dori vositalarni qabul qilish jigarni dori vositalar ta'siridan zararlanish xavfini oshirsa, 6 va undan ortiq turdagi dori vositalarni qabul qilish, jigarni dori vositalar ta'siridan zararlanish xavfini 80% gacha oshiradi) kiradi. Dori dozasi va istemol qilish tartibini buzish, jigar kasalliklarini (surunkali virusli hepatitlarda dori vositalarni doimiy ravishda qabul qilishni o'zi, jigarga ortiqcha yuk bo'lishi) mavjud bo'lishi, DILI xavfini yanada oshiradi.

Hozirgi vaqtda DILI da klinik diagnoz, jigar shikastlanishining klinik belgilari, bioximik tahlillardagi dinamik o'zgarishlar, dori vositalarini haqiqiy yoki idiosinkraziyali (organizmning ba'zi dorilar ta'sirini ko'tara olmasligi yoki yoqtirmasligi) gepatotoksikligini baholash (agar buni qilish imkoniyati bo'lsa), shuningdek jigar zararlanishining boshqa sabablari inkor etilgandan keyin, bemorning "dori" anamnezi har tomonlama tahlil qilingandan so'ng, istisno tariqasida quyiladi.

Jigarda fibroz va sirroz bosqichlari mavjud bo'lgan bemorlarda DILI, jigardagi fibroz va sirroz jarayonlari o'tkir yallig'lanishigaga olib kelishi ma'lum qilingan.

DILI AQSh va Yevropada o'tkir jigar yetishmovchiligining eng keng tarqalgan sabablaridan biri hisoblanadi. Fransiya va Islandiyada o'tkazilgan so'rovlarga ko'ra, DILI har 100000 aholiga taxminan 14-19 ta holatlarda uchraydi.

G. Ostapowicz va hammualliflarning tadqiqotlariga ko'ra, DILI holatlari ayollarda erkaklarga nisbatan ko'p uchrashi, parasetamol keltirib chiqaradigan reaksiyalarning 79% va dori vositalarga idiosinkraziv reaksiyalarning 73% ayollarga to'g'ri kelganligini ma'lum qilishgan[14].

Jigarni surunkali virusli kasalliklarini davolash bo'yicha keng ko'lamda ilmiy izlanishlar olib borilishi va sezilarli darajada samara berayotganligiga qaramasdan, surunkali virusli hepatitlarni kechishiga ta'sir qiluvchi boshqa turli omillarni, masalan, jigarda fibroz bosqichlari rivojlangan holatlarda DILI masalasi bo'yicha ilmiy izlanishlar to'liq olib borilgan deb bo'lmaydi. DILI bo'yicha mavjud ilmiy maqolalar, klinik tavsiyalarni tahlil qilib chiqqanimizda ushbu masala bo'yicha biror-bir tadqiqotlar olib borilganligi to'g'risida ilmiy ma'lumotlarni topa olmadik.

Masalan, Yeremina Ye.Yu "DILI" nomli maqolasida ushbu muammo bo'yicha zamonaviy ma'lumotlar va bir qator klinik kuzatuvlar, jumladan DILI diagnostikasi va davolash masalasi, DILI ning o'ziga xos xususiyatlari, uning homiladorlarda, homiladorlik muddatining uzayishi bilan

rivojlanishi, bioximik ko'rsatkichlaridagi o'zgarishlarning og'irligi bilan klinik belgilar o'rtasida qat'iy bog'liqlikning (корреляция) йўқлиги, коагулопатия хавфининг юқори бўлиши ҳақида тадқиқотлар олиб борилган [11].

Onuchina Ye.V, Rojanskiy A.A, Kazakova R.V., Poshkayte N.A. lar o'z maqolalarida DILI muammolari bo'yicha adabiyotlardagi ma'lumotlar va surunkali dori gepatiti holati uchraganligi to'g'risida ilmiy ma'lumotlar berishgan[12].

J. G. Stine va N. Chalasani ni o'zlarining tizimli sharhlarida DILI ilgari taxmin qilinganga nisbatan ko'proq uchrashi va yirik milliy reestrlari ma'lumotlariga asosan 18% gacha tarqalganligi, jigarni dori vositalar ta'siridan xolestatik zararlanishi xavfi ≤ 65 yoshlilarda yuqori bo'lishi va uzoq yashirin davri (> 365 kun) davom etishi haqida ma'lum qilishgan[13].

Avdeeva M.G., Kulbujeva M.I., Kolodko Ye.I., Chernikova N.V., Zapashnyaya O.V. o'z maqolalarida DILIni klinik ko'rinishning o'ziga xos xususiyatlari orasida kasallikning boshlanishi, o'rtacha xolestaz va ALT me'yordan 22 baravargacha, AST esa 9 baravargacha oshishi va GGTP ning oshishi xarakterlidir deb taqidlashgan[16].

Lazebnik L. B., Golovanova Ye. V., Хлынова O. V., Alekseenko S. A., Aryamkina O. L., Bakulin I. G., Bakulina N. V., Baranovskiy A. Yu., Bondarenko O. A., Varganova A. N., Volkova T. V., Vologjanina L. G., Volchegorskiy I. A., Demicheva T. P., Dolgushina A. I., Maev I. V., Minushkin O. N., Rayxelson K. L., Smirnova Ye. N., Tarasova L. V., syganova Yu. V. lar o'z maqolalarida DILI bo'yicha atamalar va tushunchalarga aniqliklar kiritishgan bo'lib, DILI etiopatogenezi, epidemiologiyasi, klassifikatsiyasi, klinik kurinishi, diagnostikasi, davolash hamda homilador ayollarda DILI kechishi, profilaktikasi masalalarini atroflicha bayon etishgan[3].

V.M. Chernova jigarni toksik zaharlanishi nomli o'z maqolasida yiliga dunyo bo'yicha 1 mln kishi dori vositalarni nojuya ta'siridan jabrlanishi, 180000 o'lim holati qayd etilayotganligi, bevosita gepatotoksiklik deganda moddaning o'zi, bilvosita gepatotoksiklik deganda esa uning metabolitlari zaharliligi tushunilishi, DILI bo'yicha zamonaviy qarashlar va yondashuvlarni bergan[18].

S.F. Galimova o'zining DILI nomli maqolasida DILI mexanizmlari, tasnifi, diagnostikasi va davolash to'g'risidagi zamonaviy g'oyalar yoritilgan bo'lib, jigarning barcha ma'lum bo'lgan o'tkir va surunkali kasalliklari niqobi ostida kechishi, dori vositalari dunyoning ko'plab mamlakatlarida fulminant jigar yetishmovchiligi rivojlanishining yetakchi sabablaridan biri hisoblanishi, diagnostikasini asosida dori anamnezini sinchkovlik bilan yig'ish, boshqa mumkin bo'lgan sabablarni istisno qilish, jigar shikastlanishlari va diagnostik shkalalarni (CIOMS/RUCAM) qo'llash haqida fikrlar yuritgan[4].

Pisarev A. A. o'z maqolasida DILI jigardagi morfologik, funksional buzilishlar bilan tavsiflanishi, ular farmakologik preparatlarning keng ro'yxati tufayli yuzaga kelishi mumkinligi, DILI hozirgi vaqtda kech tashxislanadigan holat ekanligi, bu noxush kechishga olib kelishi, jigar shikastlanishining og'ir shakllarini rivojlanishiga yordam berishi va davolash samaradorligiga ta'sir qilishi, muayyan dori vositasi yoki ularning kombinatsiyalarining ta'sirlari keltirilgan bo'lib, uni diagnostikasi, davolashga yondashuvlar, antidot va gepatoprotektorlar bilan davolash va ushbu muammolarni hal qilishning dolzarb yo'nalishlarini atroflicha yoritib bergan[5].

Molostvova A.F., Xabirova G.I., Xarisova Yu.I., Salimova L.M lar o'z maqolalarida DILI bioximik ko'rsatkichlarning yengil og'ishidan tortib, o'tkir jigar yetishmovchiligigacha bo'lgan keng ko'lamli klinik holatlarni o'z ichiga olishi, jigarning aksariyat nojo'ya reaksiyalari induktor preparatlar oxirgi marta qabul qilingandan so'ng 5-90 kun oralig'ida boshlanishi, shifokorlarda DILI ni to'g'ri diagnostika qilish va davolash bilan bog'liq ko'plab hal etilmagan masalalar mavjudligi, unga birinchi navbatda, farmatsevtik preparatlarni nazoratsiz tayinlash va qabul qilish, biologik faol qo'shimchalar, oxir-oqibat polipragmaziyaning rivojlanishi va shunga mos ravishda preparatlarning gepatotoksikligini kuchaytirishi haqida ma'lumotlar berishgan[2].

Rossiya terapevtlar ilmiy tibbiyot jamiyati va Rossiya gastroenterologlar ilmiy jamiyati tomonidan ishlab chiqilgan, hamda Rossiya Federatsiyasi Sog'liqni saqlash vazirligi ilmiy kengashi tomonidan 2022-yilda tasdiqlangan katta yoshdagi kishilarda jigarni dori vositalar ta'siridan zararlanishi (DILI) bo'yicha klinik tavsiyanomada, DILI dagi tushunchalarga, atamalarga aniqliklar

kiritilgan bo'lib, DILI etiopatogenezi, epidemiologiyasi, tasnifi, klinik kurinishlari, diagnostikasi, diagnoz mezonlari, davolash va profilaktikasi masalalariga batafsil tuxtalishgan[19].

Ivashkin V.T., Baranovskiy A.Yu., Rayxelson K.L., Palgova L.K., Maevskaya M.V., Kondrashina E.A., Marchenko N.V., Nekrasova T.P., Nikitin I.G. lar DILI bo'yicha klinik tavsiyanomalarida epidemiologik ma'lumotlar, qo'llaniladigan atamalar, diagnostik tamoyillar, tasnifi, prognozi va DILI bilan og'rikan bemorlarni olib borish, keltirib chiqaradigan, jumladan o'limga olib kelishi mumkin bo'lgan farmakologik vositalar, dozaga bog'liq va bashorat qilinadigan, hamda dozaga bog'liq bo'lmagan va bashorat qilinmaydigan (idiosinkraziv) DILI lar, eng ishonchli diagnostik va prognostik shkalalar va indekslar, DILI patogenezi va xavf omillari, DILI ning klinik-morfologik shakllarini atroflicha bayon etishgan[6].

Drapkina O.M., Maev I.V., Axmedov V.A., Vologjanina L.G., Dolgushina A.I., Igumnova O.A., Kozlova I.V., Lazebnik L.B., Okovityy S.V., Pirogova I.Yu., Saenko A.A., Tarasova L.V., Tixonova T.A., Turkina S.V., Хлынов I.B., Хлынова O.V., сыганова Yu.V. lar tomonidan ishlab chiqilgan DILI nomli klinik tavsiyanomada, uni ta'rifi, etiopatogenezi, epidemiologiyasi, tasnifi, klinikasi, diagnostikasi, diagnostik kriteriyalari, davolash va profilaktika masalalari atroflicha bayon etilgan [1].

Xitoylik mualliflar Deng Y, Wang C, Fu Y, Li D, Ji D. 2022- yil noyabr oyidagi chop etishgan maqolalarida, jigarni dori vositalardan surunkali zararlanishida jigarda fibroz bosqichlari ortib borishi haqida ilmiy ma'lumotlar berib borishgan[7].

Dorota M. Kozielwicz, Piotr Stalke 2025yilda chor etilgan DILI nomli maqolalarida boshqa ksenobiotiklar bilan o'zaro ta'siri to'liq o'rganilmagan dori vositalari va biologik faol qo'shimchalarni iste'mol qilishning ko'payishi DILI ning ko'payishiga olib kelganligi, dori-darmonlarni o'zaro ta'siri bilan bog'liq nojo'ya ta'sirlar tobora muhim ahamiyat kasb etayotganligi, bemorlarning fikriga ko'ra, o'simlik dori vositalari zararli bo'lishi mumkin emasligi va ular shifokorlarga ularni iste'mol qilish haqida xabar berishmasliklari, nojo'ya ta'sirlarning klinik manzarasi polimorfligi, ba'zi hollarda jigarning o'zgaruvchan intensivlikdagi shikastlanishi kuzatilishi, ba'zan ko'p yillardan keyin jigar sirrozi va gepatotsellyulyar karsinomasiga olib kelishi haqida ma'lumotlar berishgan.

Khoury T. et al: lar o'zlarining DILI nomli o'z maqolalarida DILI kam uchraydigan, ammo hayot uchun xavfli ekanligi, DILI o'tkir yoki surunkali jigar kasalligining har qanday morfologik xususiyatlariga ta'sir qilishi va uning gistopatologik xususiyatlari o'tkir virusli gepatit kabi jigar shikastlanishining boshqa sabablaridan farq qilmasligi, DILI ning klinik xususiyatlari, patogenezi, tashxis usullari va natijalar haqida ma'lumotlar berishgan[8].

Marwan Ghabril o'zining DILI nomli maqolsida DILI global muammo ekanligi, diagnostikasi klinik jihatdan murakkab ekanligi, jigar shikastlanishini og'ir kechishi, jigar yetishmovchiligi, o'lim yoki jigar transplantatsiyasiga olib kelishi mumkinligi, surunkali jigar kasalliklari bo'lgan bemorlarda DILI yuqori xavfli bo'lishi haqida ma'lumotlar bergan.

Paul H. Hayashi, MD, MPH and Einar S. Bjornsson, MD, PhD o'zlarining "DILI dan keyingi uzoq muddatli natijalar" nomli maqolalarida DILI ning spektri, ular yengil surunkali zararlanishdan to'kechki jigar yetishmovchiligi va o'limgacha bo'lishi mumkinligi, DILI holatlarining kichik, ammo muhim qismi tuzalmasligi, natijada surunkali shikastlanish va hatto jigar yetishmovchiligi rivojlanishi, ushbu holatlarni aniqlash va tan olish qiyinligi, jigarni dori vositalar ta'siridan zararlanishi holatlarining kamdan-kam uchrashi va surunkali shikastlanishlar undan ham kam uchrashi haqida ma'lum qilishgan [9].

Paul H. Hayashi, MD, MPH Robert J. Fontana, MD o'zlarining DILI nomli maqolalarida idiosinkratik DILI bilan og'rikan bemorlar gastroenterolog uchun diagnostik, prognostik va terapevtik muammolarni keltirib chiqarishi, DILI ning namoyon bo'lishi jigar fermentlarining asimptomatik ko'tarilishidan tortib to o'tkir jigar yetishmovchiligigacha o'zgarishi mumkinligi, dori to'xtatilgandan so'ng aksariyati o'tib ketishi, bemorlarning 20% da DILI surunkali kechishi, bu esa shifokorning diagnostika va boshqaruv ko'nikmalarini yanada qiyinlashtirishi, ba'zi dori-darmonlar fibroz, ensefalopatiyaga olib kelishi mumkinligi, DILI ni aniq tashxislash uchun ob'ektiv testlar yo'qligi, sababiy bog'liqlikni baholash vositalari mavjud bo'lsada, ularning hech biri keng tarqalgan

yoki qo‘llaniladigan klinik amaliyot emasligi, klinik diagnoz to‘liq va aniq anamnez yig‘ishga, kasallikni klinik kechishini kuzatishga va jigar shikastlanishining keng tarqalgan sabablarini istisno qilishga qaratilganligi haqida ilmiy fikrlarni bildirishgan[9].

Harshad C. Devarbhavi, Cyriac Abby Philips o‘zlarining DILI nomli maqolalarida DILI dastlab jigarni bioximik taxlillari asosida jigar fermentlarining ko‘tarilishi, sirroz rivojlangan bosqichlarida bilirubin miqdorining oshishi yoki uzoq muddatli xalqaro me‘yorlashtirilgan nisbat yoki MELD (Model For End-Stage Liver Disease- jigar kasalligining yakuniy bosqichi uchun model) kabi global jigar funktsiya buzilishining birinchi belgisi bo‘lishi mumkinligi, jigarni asosiy kasalliklari (jigarni yog‘ kasalligi, steatogepatit, surunkali xolestatik kasalliklar va jigar sirrozi) bo‘lgan bemorlarda jigarni dori vositalar ta‘siridan zararlanishini aniqlash, baholash va boshqarish bo‘yicha konsensus ko‘rsaarini ishlab chiqishga harakat qilinganligi, dori vositalarni sitoxrom P450 fermentlarga ta‘sir qilishi, bu esa gepatotsitlar ichida dori ta‘sirining kuchayishiga olib kelishi, dori vositalarining nojo‘ya ta‘sirini oshirishi haqida ilmiy ma‘lumotlar berishgan[10].

Xitoylik boshqa bir guruh tadqiqotchilar Xitoydagi klinik sharoitlardan kelib chiqqan holda, o‘z qo‘llanmalarida, shuningdek, surunkali jigar kasalliklarida DILI uning qayta faollashuviga olib kelishiga alohida e‘tibor qaratishgan.

Yuqorida bayon etilgan tadqiqotchilar o‘z ilmiy maqolalarida DILI bo‘yicha atroflicha ilmiy ma‘lumotlar, diagnostik mezonlar, davolash buyicha tavsiyalar berishgan bo‘lsalarda, biroq surunkali virusli gepatitlarning (virus yuklamasini o‘zi jigarga ortiqcha yuk bo‘lishi, jigarda fibroz rivojlanishiga olib kelishi) fibrozsiz va fibroz bosqichlarida DILI holatlarini qiyoslab urganish masalasida aniq bir tadqiqotlar olib borilganligini topa olmadik.

Tadqiqotni maqsadi: Surunkali virusli gepatit V ning fibrozsiz va fibroz bosqichlarida DILI holatlarini qiyoslab urganish.

Tadqiqotni vazifalari:

1. Surunkali virusli gepatit V ning fibrozsiz bosqichlarida jigarni dori vositalar ta‘siridan toksik zararlanish holatlarini aniqlash.

2. Surunkali virusli gepatit V ning fibroz bosqichlarida DILI holatlarini qiyoslab aniqlash.

Tadqiqot materiallari va usullari. 2025- yilda Samarqand viloyatining turli tumanlarida surunkali virusli gepatit V ning fibrozsiz va fibroz bosqichlari bilan “D” nazoratida turgan bemorlarda DILI holatlari qiyoslanib o‘rganildi. Jigardagi fibroz bosqichlari FibroScan 430 (Fransiya) apparati orqali aniqlandi. Surunkali virusli gepatit S IFA va PSR usulida aniqlandi. Jigarni dori vositalar ta‘siridan zararlanishi xalqaro tibbiyot fanlari tashkilotlari kengashi CIOMS (Council for International Organizations of Medical Sciences) tomonidan tavsiya etilgan R (nisbat) = ALT (MYuCh karraligi) / IF (MYuCh karraligi) bo‘yicha va sinchikovlik bilan yig‘ilgan dori anamnezi orqali aniqlandi.

O‘rganilayotgan bemorlar yoshi 20 yoshdan 75 yoshgacha bo‘lgan 388 nafar bemorlar bo‘lib, bemorlarni o‘rtacha yoshi ($Mv=(x1+x2+...+xn)/n$) 47,5+₁₀ yoshni tashkil qiladi.

SVGV ga chalingan 388 nafar (shundan 40 yoshgacha bo‘lganlar 202 nafarni, 40 yoshdan kattalar 186 nafarni tashkil qiladi) bemorlarni 226 nafarida jigarda fibroz bosqichlari rivojlanmaganligi, 162 nafarida fibroz bosqichlari rivojlanganligi aniqlandi. SVGV ga chalingan 388 nafar bemorlarni 199 nafarni erkaklar, 189 nafarni ayollar tashkil qiladi.

Surunkali virusli gepatit V da jigarni dori vositalar ta‘siridan zararlanish holatlari urganilganda quyidagilar aniqlandi (2-jadval).

2-jadval

№	Fibroz bosqichlari	Kuzatilgan bemorlar soni	DILI bemorlar soni	DILI ayollar soni
SVGV ga chalingan bemorlar soni 388 nafar				
1	F -O	226	10 (4,42%)	2 (20%)
	Fibrozsiz bosqichlari	226	10 (4,42%)	2 (20%)
1	F- 0-2	128	11 (8,59%)	3
2	F-2-3	8	0 (0%)	

3	F- 3-4	13	3 (23,07%)	
4	F-4 dan yuqori	13	3 (23,07%)	
	Fibroz bosqichlari	162	17 (10,49%)	
	Jami	388	27 (6.95)	5 (18,51%)

Xulosalar.

1. Surunkali virusli gepatit V ning fibroz bosqichlari rivojlanmagan bemorlarda jigarni dori vositalar ta'siridan zararlanish holatlari 4,42% ni tashkil qilganligi aniqlandi.

2. Surunkali virusli gepatit V ning fibroz bosqichlari rivojlangan bemorlarda jigarni dori vositalar ta'siridan zararlanish holatlari 10,49% ni tashkil qilganligi aniqlandi.

Tavsiyalar.

1. Surunkali virusli gepatit V ning fibroz bosqichlari rivojlangan bemorlarga hayotiy zarurat bo'lmagan holatlarda patogenetik dori vositalarni qo'llashni cheklash.

2. Surunkali virusli gepatit V da dalillarga asoslanganlik darajasi yuqori bo'lgan dori vositalarni qo'llash.

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