

# БИОМЕДИЦИНА ВА АМАЛИЁТ ЖУРНАЛИ

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EFFECTIVENESS OF POSTOPERATIVE INTENSIVE THERAPY IN PREGNANT WOMEN WITH VARICOSE VEINS.....12

## NEUROLOGY, PSYCHIATRY

2. **Mansurova Nargiza Asrorovna**  
DIAGNOSTIC VALUE OF INFLAMMATORY PROCESSES IN DIFFERENTIATING PARKINSONISM SUBTYPES.....18
3. **Tulyaganova Nodirakhon Malikovna.**  
EPIDEMIOLOGICAL ASPECTS OF DEVELOPMENTAL DISORDERS IN CHILDREN BORN FROM CONSANGUINEOUS MARRIAGES.....26
4. **Ochilov Ulug'bek Usmanovich, Turaev Bobir Temirpulotovich, Sultanov Shoxrux Khabibullaevich**  
CORRECTION OF DEPRESSIVE DISORDERS AND EVALUATION OF THE EFFECTIVENESS OF COMPREHENSIVE REHABILITATION IN PATIENTS WITH CHEMICAL ADDICTIVE DISORDERS.....34
5. **Turaev Bobir Temirpulotovich, Sultanov Shoxrux Khabibullaevich**  
FACTORS INFLUENCING THE EFFECTIVENESS OF MEDICAL AND SOCIAL REHABILITATION IN PATIENTS WITH CHEMICAL ADDICTIVE DISORDERS (LITERATURE REVIEW).....41
6. **Khakimova Sakhiba Ziyadulloyevna, Gaffarova Parvina Abdurafikovna**  
ETIOPATHOGENETIC SIGNIFICANCE OF MAO-B INHIBITORS IN PARKINSON'S DISEASE AND THEIR ROLE IN REDUCING MOTOR SYMPTOMS.....48
7. **Mirzhuraev Elbek Mirshavkatovich, Adambaev Zufar Ibragimovich, Mamatkhanova Charos Bahodirovna**  
STRATIFICATION OF MANAGEMENT FOR PATIENTS WITH COMBINED VERTEBROGENIC PATHOLOGY AND PELVIC ORGAN DYSFUNCTION: A MULTIDISCIPLINARY APPROACH.....55
8. **Rogov Alexey Vladimirovich, Lipartiya Mary Givievna**  
CHARACTERISTICS OF THE SEVERITY OF PARANOID SCHIZOPHRENIA IN PATIENTS WITH AUTOAGGRESSIVE MANIFESTATIONS IN THE EARLY PERIOD OF THE DISEASE.....63

## MORPHOLOGY

9. **Kiyomov Ikhtiyor Ergashevich, Islamov Shavkat Erjigitovich**  
MORPHOLOGICAL CHANGES IN THE THYMUS DURING ACUTE EXPOSURE TO A DEFOLIANT.....69

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10. **Abdikarimov Azizbek Khurshidjon ugli, Yusupbekov Abrorbek Akhmedjanovich, Usmonov Begzod Boymatovich, Xasanov Akbar Ibroximovich**  
HUMAN PAPILLOMAVIRUS AND OROPHARYNGEAL CANCER: CURRENT CLINICAL-EPIDEMIOLOGICAL AND PROGNOSTIC ASPECTS (REVIEW).....77

11. **Iskandarova Shakhnoza Tulkinovna, Khakimova Laylo Nuraliyevna, Yusupov Anvar Sobirovich**  
STUDY OF THE DYNAMICS OF PROLACTIN AND GLUCOSE LEVELS IN PATIENTS WITH GASTRIC CANCER DURING THE PERIOPERATIVE PERIOD UNDER COMBINED EPIDURAL ANESTHESIA.....89
12. **Rakhmatov Dilshod Bakhridinovich**  
EVALUATION OF RADIATION DOSE LOAD TO ORGANS AT RISK WHEN SWITCHING TO A HYPOFRACTIONATED REGIMEN OF POSTOPERATIVE RADIOTHERAPY FOR LEFT BREAST CANCER.....95
13. **Shernazarov Otamurod Narmuratovich**  
ACOUSTIC ANALYSIS OF VOICE FUNCTION IN PATIENTS WITH BENIGN LARYNGEAL LESIONS.....101
14. **Ten Vladimir Denisovich, Alimov Ijod Rustamovich, Umarov Rustam Dilshodovich.**  
OUR EXPERIENCE OF PERCUTANEOUS BIOPSY IN METASTATIC LESIONS OF THE LUMBAR SPINE.....105
15. **Umarov Rustam Dilshodovich, Alimov Ijod Rustamovich, Ten Vladimir Denisovich.**  
ISOLATED LATERAL SURGICAL APPROACH FOR VERTEBRAL BODY TUMORS WITH EXTRADURAL INTRACANAL INVASION AT TH11–L2.....109
16. **Ismailov Avaz Alisherovich, Umarov Rustam Dilshodovich, Alimov Ijod Rustamovich,**  
POSTERIOR DECOMPRESSIVE AND STABILIZING APPROACH FOR THORACIC AND LUMBAR VERTEBRAL BODY TUMORS WITH INTRACANAL EXTENSION.116
17. **Umarov Rustam Dilshodovich, Alimov Ijod Rustamovich, Ten Vladimir Denisovich**  
ISOLATED LATERAL SURGICAL APPROACH FOR VERTEBRAL BODY TUMORS WITH EXTRADURAL INTRACANAL INVASION AT TH11–L2 LEVELS.....121
18. **Sharopov Sadullo Shukurillovich**  
CORRELATION BETWEEN ELECTROENCEPHALOGRAPHIC CHANGES AND MRI CHARACTERISTICS IN PATIENTS WITH BRAIN TUMORS.....129

#### **MEDICAL REHABILITATION**

19. **Raimkulova Dilnoza Farkhaddinovna**  
PROGNOSTIC CRITERIA AND ANALYSIS OF PHYSICAL PERFORMANCE IN ADOLESCENTS ENGAGED IN DIFFERENT TYPES OF SPORTS.....135
20. **Mamatkhanova Charos Bahodirovna**  
STRATIFICATION OF SURGICAL AND REHABILITATION TREATMENT FOR POST-TRAUMATIC MYELOPATHIES AT THE CERVICAL AND THORACIC SPINE LEVELS.....142
21. **Mamatkhanova Charos Bahodirovna**  
ANALYSIS OF PATIENTS WITH SPINAL PATHOLOGY AND SPINAL CORD DISEASES AT THE REPUBLICAN CENTER FOR REHABILITATION OF DISABLED PERSONS.....149
22. **Tukhtaev Firdavs Mukhitdinovich, Kadirov Jonibek Fayzullayevich**  
THE IMPACT OF MINERAL AND ACID–BASE METABOLIC CORRECTION ON POSTOPERATIVE REHABILITATION IN CHILDREN WITH UROLITHIASIS.....155

#### **DENTISTRY AND MAXILLOFACIAL SURGERY**

23. **Boymurodov Shukhrat Abdujalilovich, Kurbanov Yoqubjon Khamdamovich, Yusupov Shokhrukh Shuhratovich, Djurayev Jamolbek Abdukakharovich, Soatov Ilyosjon Olimovich**  
SIGNIFICANCE OF IL10 RS1800872, SERPINE1 RS1799768, NOS3 RS2070744, AND IL1B RS1143627 GENE POLYMORPHISMS IN PURULENT-NECROTIC PROCESSES OF THE MAXILLOFACIAL REGION.....160

24. **Alyavi Mufassal Nasirkhanovna, Khaydarov Artur Mikhaylovich, Alieva Muattar Abdulkhayevna**  
COMPLEX TREATMENT OF CHRONIC GENERALIZED PERIODONTITIS IN PATIENTS WITH STABLE ANGINA PECTORIS.....171
25. **Ismoilov Mirkamol Xusan o'g'li Nigmatova Iroda Maratovna**  
THE ROLE OF VITAMIN D IN THE CONDITION OF PERIODONTAL TISSUES DURING ORTHODONTIC TREATMENT IN PREGNANT WOMEN.....180
26. **Irgashev Shokhrukh Khasanovich**  
ANALYSIS OF THE HYGIENIC INDICATORS OF THE ORAL MUCOSA OF PERSONS WHO HAVE UNDERGONE ORTHOPEDIC STOMATOLOGICAL TREATMENT.....190
27. **Ibragimova Malika Khudaiberganovna, Abduvahobova Dilnoza Anvarovna**  
CLINICAL AND DIAGNOSTIC ASPECTS OF RED FLAT AND DEPRESSED ORAL MUCOSA.....196
28. **Rizaev Jasur Alimjanovich, Akhmedova Sayyora Mukhamadovna, Absalamova Nigora Fakhriddinovna**  
IMPROVEMENT OF TREATMENT STRATEGIES FOR ORAL MUCOSAL LEUKOPLAKIA BASED ON IMMUNOHISTOCHEMICAL RESULTS.....204
29. **Otkhonova Mohinog Ganiyon qizi, Khramova Natalya Vladimirovna, Gafurov Zafar Atkhamovich**  
JUSTIFICATION OF MAXILLARY RECONSTRUCTION USING A TIBIAL BONE AUTOGRAFT.....212
30. **Madazimov Madamin Muminovich, Turaev Feruz Fakhtullaevich, Yusufovna Mohamed Khava, Pustovetova Maria Gennadievna, Akramova Nozima Akramovna**  
CELL-ASSISTED LIPOTRANSFER IN THE CORRECTION OF AESTHETIC AND POST-TRAUMATIC DEFORMITIES OF FACIAL SOFT TISSUES.....219

#### TRAUMATOLOGY

31. **Axtamov A'zam, Axtamov Azim**  
STUDYING THE RESULTS OF RECONSTRUCTIVE SURGICAL TREATMENT OF COMBINED MENISCLE WOUNDS.....228
32. **Axtamov Azim, Axtamov A'zam**  
DIAGNOSIS AND MODERN METHODS OF TREATMENT OF ACETABULUM INJURIES (LITERATURE REVIEW).....233
33. **Axtamov A'zam, Axtamov Azim**  
EXPERIENCE IN TREATING INTRA-ARTICULAR FRACTURES OF THE DISTAL PART OF THE HUMERUS IN CHILDREN.....241
34. **Davirov Sharof Majidovich, Urinbaev Payzilla Urinbaevich, Mansurov Djalolidin Shamsidinovich**  
OSTEOPLASTIC RECONSTRUCTION OF EXTENSIVE DIAPHYSEAL LONG BONE DEFECTS USING EXTERNAL FIXATION DEVICES.....246

#### PEDIATRICS

35. **Choliev Matyoqub Sulaymanovich, Khotamov Khusniddin Narzullayevich, Tilavov O'ktam Khamrayevich**  
SOFT TISSUE NECROSIS IN CHILDREN: CLINICAL FEATURES, DIAGNOSIS AND PRINCIPLES OF TREATMENT.....256
36. **Umarova Saodat Sulaymonovna**  
VITAMIN D DEFICIENCY AS A PREDICTOR OF INFLAMMATORY ACTIVITY IN CHILDREN WITH ACUTE RHEUMATIC FEVER.....264

37. **Rakhmatullaev Akmal Abadbekovich, Ergashev Mukhammadjon Tursunovich**  
EFFECTIVENESS OF ENDOSCOPIC CORRECTION METHODS IN CHILDREN WITH  
PRIMARY HIGH-GRADE VESICoureTERAL REFLUX.....275
38. **Akhmedzhanova Nargiza Ismailovna, Ganieva Marifat Shokirovna, Majidova Nilufar  
Mansuralievna.** INNOVATIV METHODS OF EARLY DIAGNOSIS OF  
TUBULOINTERSTISIAL LESIONS IN ACUTE PYELONEPHRITIS IN CHILD.....281
39. **Terebayev Bilim Aldamuratovich, Barnakulov Umrzok Khasanovich**  
PROBLEMS OF DIAGNOSIS AND TREATMENT OF DOLICHOSIGMA ASSOCIATED  
WITH CHRONIC CONSTIPATION IN CHILDREN.....288
40. **Tilavov Uktam Khamraevich, Chuliev Matyokub Sulaimonovich, Khotamov Khusniddin  
Narzullaevich, Abduqodirov Oybek Ahmadjonovich**  
DIAGNOSIS AND TREATMENT OF CYSTIC ADENOMATOID MALFORMATION OF  
THE LUNGS IN CHILDREN.....299
41. **Tukhtaev Firdavs Mukhitdinovich, Kadirov Jonibek Fayzullayevich**  
PERSONALIZED METABOLIC APPROACHES IN CHILDREN'S MEDICAL  
REHABILITATION.....307
42. **Ibragimova Sapura Zakhidovna, Almedova Nargiza Nigmatjonovna, Botirov Mirzokhid  
Mansurzhon Ugli, Shadibekova Oksana Borisovna, Aripova Nazokat Bahodirovna,  
Erimbetova Indira Oralbaevna**  
RESULTS OF THE USE OF EMICIZUMAB IN PATIENTS WITH HEMOPHILIA A – A  
PILOT SINGLE-CENTER STUDY.....312
43. **Khaidarov Khusan Anvarovich**  
THE ROLE OF VITAMIN D STATE IN DETERMINING THE SEVERITY AND  
EFFECTIVENESS OF INPATIENT TREATMENT OF RECURRENT RESPIRATORY  
TRACT INFECTIONS IN YOUNG CHILDREN.....319

## SURGERY

44. **Abdurahmonov Ma'mur Mustafaevich, Umedov Xushvaqt Alisherovich,**  
ASSESSMENT OF THE IMMUNE SYSTEM STATUS IN ACUTE DESTRUCTIVE  
PANCREATITIS.....325
45. **Kurbanov Aslbek Sadullaevich, Arziev Ismoil Alievich, Arzieva Gulnora Borievna**  
DIAGNOSTIC AND THERAPEUTIC POTENTIAL OF LAPAROSCOPY IN PATIENTS  
WITH BLUNT ABDOMINAL TRAUMA.....331
46. **Yuldashov Parda Arzikulovich, Rakhmanov Kosim Erdanovich, Sayinaev Farrukh  
Karamatovich**  
OPTIMIZATION OF SURGICAL TREATMENT OF POSTOPERATIVE VENTRAL  
HERNIAS BASED ON LAPAROSCOPIC PROSTHETIC METHODS.....336
47. **Kurbanova Sanobar Yuldashevna, Kamalov Zainitdin Saifutdinovich, Azizova Zukhra  
Shukhratovna**  
CLINICAL, IMMUNOLOGICAL, AND IMMUNOGENETIC FEATURES OF DISEASE  
DEVELOPMENT IN ADULT PATIENTS WITH PYELONEPHRITIS (A LITERATURE  
REVIEW).....346
48. **Umedov Xushvaqt Alisherovich, Abdurahmonov Ma'mur Mustafaevich**  
CONTEMPORARY CLINICO-MORPHOLOGICAL CLASSIFICATION OF ACUTE  
PANCREATITIS AND ITS COMPLICATIONS.....355
49. **Ollabergenov Odilbek Tozhiddinovich, Terebaev Bilim Aldamuratovich, Parpiev  
Mirziyod Mirsaitovich**  
CURRENT TRENDS IN THE DIAGNOSIS AND SURGICAL TREATMENT OF LIVER  
ECHINOCOCCOSIS IN CHILDREN.....362

50. **Askarov Pulat Azadovich, Bazarov Bahrom Boymamatovich, Kurbaniyazov Zafar Babadjanovich**  
THE IMPACT OF CONCOMITANT SURGICAL PATHOLOGY ON THE OUTCOMES OF SIMULTANEOUS OPERATIONS IN PATIENTS WITH VENTRAL HERNIAS AND MORBID OBESITY.....369
51. **Egamberdiev Abdukahhor Abduqodirovich, Arzieva Gulnora Borievna**  
ASSESSMENT OF CLINICAL OUTCOMES AND TECHNICAL FEATURES OF ENDOVIDEOSURGICAL TREATMENT OF HIATAL HERNIA.....377
52. **Madazimov Madamin Muminovich, Turaev Feruz Fakhtullayevich, Kiziun Yana Viktorovna, Pustovetova Maria Gennadievna, Akramova Nozima Akramovna, Kiyamov Azizbek Utkirovich**  
STUDY OF BREAST BLOOD SUPPLY USING DUPLEX ULTRASOUND IN REDUCTION MAMMOPLASTY.....385

### INFECTIOUS DISEASE

53. **Imamov Otabek Sunnatovich, Mahmudov Sherzod Xasanovich, Djumaev Normurod Davlatovich, Bakhodirova Shahlo Bahoriddinovna, Tokhtayev Gairatillo Shukhratillo ugli.**  
THE IMPORTANCE OF TEMPERATURE IN THE ETIOLOGY AND MODERN LABORATORY DIAGNOSTICS OF DERMATOMYCOSIS.....394
54. **Imamov Otabek Sunnatovich, Mahmudov Sherzod Xasanovich, Djumaev Normurod Davlatovich, Ernazarova Feruzabonu Ravshanbekovna, Tokhtayev Gairatillo Shukhratillo ugli**  
MODERN ETIOLOGICAL SPECTRUM OF DERMATOMYCOSIS PATHOGENS IN THE TASHKENT REGION.....403
55. **Yusupov Mashrab Ismatillovich**  
GUT MICROBIOTA: CORRELATION OF PHYSICAL LOAD, DIET, AND HEAT EXCHANGE.....409
56. **Faizullaev Sherzod Kobiljon ugli, Shakharov Dilshod Zhura ugli, Tukhtaev Shohzod Eshmurod ugli, Khuzhamberdiev Sodikjon Uchkun ugli, Samibaeva Umida Khurshidovna**  
FEATURES OF THE CLINICAL PICTURE OF THE NEW CORONAVIRUS INFECTION (COVID-19).....420
57. **Samibaeva Umida Khurshidovna, Faizullaev Sherzod Kobiljon ugli, Shakharov Dilshod Zhura ugli, Tukhtaev Shohzod Eshmurod ugli, Khuzhamberdiev Sodikjon Uchkun ugli**  
EVALUATION OF THE CLINICAL EFFICACY OF GLYCYRRHIZIC ACID IN PATIENTS WITH COVID-19.....435
58. **Samibaeva Umida Khurshidovna, Faizullaev Sherzod Kobiljon ugli, Shakharov Dilshod Zhura ugli, Tukhtaev Shohzod Eshmurod ugli, Khuzhamberdiev Sodikjon Uchkun ugli**  
EVALUATION OF THE CLINICAL EFFICACY OF GLYCYRRHIZIC ACID IN PATIENTS WITH COVID-19.....447
59. **Rashidov Zafar Rakhmatullaevich**  
CLINICAL SIGNIFICANCE OF DOPLEROGRAPHY IN THE DETECTION AND MONITORING OF RENAL TUBERCULOSIS.....453

### OPHTHALMOLOGY

60. **Nazirova Zulfiya Rustamovna, Turakulova Dilfuza Mukhitdinovna, Khamrayev Shakhruh Ilkhom ugli.**  
SURGICAL TREATMENT OF CONGENITAL AND ACQUIRED CATARACTA IN CHILDREN: ANALYSIS OF MODERN METHODS AND STAGES.....460

61. **Turakulova Dilfuza Mukhitdinovna, Nazirova Zulfiya Rustamovna, Axrorova Malika Nosir qizi.**  
ANALYSIS OF SURGICAL TREATMENT OF INTRAOCULAR LENS SUBLUCATION IN CHILDREN.....470
62. **Iskandarova Shakhnoza Tulkinovna, Miralimova Malika Mukhammadovna, Yangiyeva Nodira Rakhimovna**  
ASSESSMENT OF THE INFORMATIVE VALUE OF PARENTAL QUESTIONNAIRES IN THE EARLY DETECTION OF REFRACTIVE DISORDERS IN PRESCHOOL CHILDREN.....477

## NEUROSURGERY

63. **Asadov Khamidulla Fatkhullaevich, Okhunov Alisher Oripovich, Asadov Khumoyun Hamidullaevich.**  
A NERVE-SPARING ENDOSCOPIC TUNNEL TECHNIQUE FOR THE SURGICAL TREATMENT OF CHRONIC OCCIPITAL MIGRAINE.....485
64. **Okhunov Alisher Oripovich, Asadov Khamidulla Fatkhullaevich, Asadov Khumoyun Hamidullaevich.**  
STRATEGY FOR SELECTING THE EXTENT AND STAGING OF SURGICAL TREATMENT IN COMBINED FORMS OF CHRONIC MIGRAINE.....492



Rasim-5. O'ng qo'l: II-III-IV-Y panja barmoqlarining nekrozi.

Xirurgik davodan keyingi 4 kun uyiga javob berildi va yashash joyida davomuolajalarini davom qildirish, choklarini 10-11 kunlari olish tavsiya qilindi.

Chok ornidagi-yaqinidagi to'qimalar nekrozi. Birinchi koruvdagi - tikilgan jaroxat o'rnidagi o'zgarishi natijalari: chap soning ichgi yuqoro 3/1 qicmida (10-14 sm xajmidagi) koagulyatsion nekroz sohasi kuzatiladi. Qobiq ostidan ajralish yo'q. Nekrotik to'qima atrofida aniq demarkatsiya chizig'i hosil bo'lgan (1-rasm). Klinik ko'rinishga asoslanib, 2024-yil (xirurgik infeksiya bo'limida, kasalxonaga yotqizilganining to'rtinchi kuni) jarrohlik davolash amalga oshirildi: tikilgan choklar olindi va nekrektomiya amaliyoti (nekrotik to'qimalarni teri osti yog' qatlamigacha tozalandi) amaliyoti bajarildi. Jaroxat chetlaridagi terining bir qismiga ikkilamchi choklar qo'yildi va qolgan (5,5 x 3,5 cm. maydonga teri ko'chirib o'tqazilli (6-rasm).



Rasim-6. Chap son yuqori 3/1 qismi, ichki yuzasi chok o'rni va atrof to'qumalarining nekrozi. a) oldingi ko'rinishit, b) nekreytamiyadan keyingi ko'rinishi.

Teri transplantatsiyasidan keyingi 7 chi kuni jaroxat o'rniterining yaxlit-ligi to'liq tiklandi.

Kuyishlardan keyingi nekroz; Bu kuyishdan keyin (termik, kimyoviy, elektr, nurlanishdan) shikastlanish agentining ta'siri tufayli yuzaga keladigan to'qimalarning (teri, mushak, suyak) o'limi. Bu chuqur kuyish chandiqlari, deformatsiyalar va funktsional buzilishlarni o'z ichiga olgan murakkab davolashni talab qiladi. Nekroz dermadan suyak to'qimasigacha turli chuqurliklarda paydo bo'lishi mumkin va uning darajasi kuyishning og'irligi va davomiyligiga bog'liq. Chuqur kuyishlardan keyin, funktsional buzilishlar: Bo'g'imlarning harakatlanishining cheklani, kosmetik nuqson-lar, deformatsiyalar bilan bog'liq muammolardan biri. Gipertrofik va keloid kuyish chandiqlari shifokorlar va bemorlar uchun katta muammo keltrib chiqaradi. Manbalardagi ma'lumotlarga ko'ra bu bolalarda 41% tashkil qiladi. Bolalardagi kuyishlardan keyingi yana bir muamm, bu bola tana hajmi o'sishi bilan ortadi, ammo chandiqlik hajmi o'smaydi va jarayon yanada kuchayadi. Bu jiddiy muammo murakkab rekonstruktiv jarrohlik jarayonini talab qiladi. Bizga murojat qilib kelgan bemorda shunga o'xshash xolar qayt etildi. Yashash joyida davo muolajalarini uzoq vaqt olgan va chap qo'l tirsak bo'g'umidan, panja ucti va barmoqlarigacha chuqur kuyish chandiqlari, deformatsiya va funktsional buzilishlar bilan murojat qilib keldi (rasim-7).



Rasim-7. Chap qo'l bilak, panja barmoqlarning kuyushdan keyingi nekrozi. 2-ki bosqichli nekrektomiyadan keyingi ko'rinishi.

Beborning umumiy ahvoli qoniqarli, keyingi davo muolajalarini davom qildirish uchun, plastik jarrohlik bo'limiga otkazildi.

Davolash. Barcha bemorlarni davolash yuqumli kasalliklar bo'yicha mutaxassis, reanimatsiya bo'yicha mutaxassis va jarrohlar tomonidan birgalikda amalga oshirilishi shart. Bu shoshilinch bo'lishi va to'rtta tamoyilga asoslangan bo'lishi mumkin:

1. Yiringli fokusni radikal jarrohlik yo'li bilan tozalash.
2. Antibakterial terapiya.
3. Mahalliy terapiya, dori vositalari va fizio terapiya.

4. Intensiv terapiya, hayotni qo'llab-quvvatlash choralari va ekstrakorpo-ral detoksifikatsiyani ta'minlash.

Xulosa. Yumshoq to'qimalar nekrozi (infektsiyasi) keng tarqalgan, bu juda og'ir holat bo'lib, o'lim darajasi 10% gacha. Ushbu maqolada bolalar yoshida tananing turli sohalarida bo'ladigan turli xildagi nekrozlar va ularni muvaffaqiyatli davolash holati keltirilgan. Jarayonining rivojlanishi, kelib chish sabablari, tasnifi, bakteriologik, rentgenografik va ultratovush tekshiruvlari, klinikasi va davolash tamoyillari berilgan. Bemorlarni davolashda: Kasallikning klinik ko'rinishiga, qo'shimcha diagnostik vosi-talarga, laborator taxlillariga asoslangan xolda, konservativ, operativ 1-2 bosqichli nekrekreytomiya va operatsiyadan keyingi jaroxatlarni mahalliy to'qima bilan tiklashga qaratilgan bir nechta jarrohlik amaliyotlari baja-rildi. Jarrohlik davodan tashqari, bemorga antibakterial terapiya, turli maxamlar va immuno stimulyatsiya qiluvchi terapiyalar berildi. Bizda davolangan, katta maydonda nekrektamiya qilingan bemorlarning ba'zi-lari, keyingi davo muolajalarini davom etirish maqsadida plastik jarrixlik bo'limiga o'tkazildi. Bir so'z bilan aytganda yumshoq to'qimalarning nekrozlovchi infeksiyasini, fasisitni davolash yaxshi natijaga erishildi.

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# БИОМЕДИЦИНА ВА АМАЛИЁТ ЖУРНАЛИ

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## VITAMIN D DEFICIENCY AS A PREDICTOR OF INFLAMMATORY ACTIVITY IN CHILDREN WITH ACUTE RHEUMATIC FEVER

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### ANNOTATION

**Background:** Acute rheumatic fever (ARF) remains a significant pediatric health concern in developing countries. Recent studies suggest that vitamin D plays an important immunomodulatory role in inflammatory diseases.

**Objective:** To investigate the relationship between vitamin D deficiency and inflammatory cytokines (IL-1 $\beta$ , IL-6, IL-8, IFN- $\gamma$ ) in children with acute rheumatic fever.

**Methods:** The study included 60 children aged 5–15 years diagnosed with ARF. As part of this study, the concentration of 25(OH)D in children with acute rheumatic fever (ARF) was evaluated and compared with data from healthy children of the same age group. Serum levels of 25(OH)D and proinflammatory cytokines were measured before and after treatment. Vitamin D levels were assessed by ELISA, and cytokines were determined using Vector-Best immunoassays.

**Results:** A significant inverse correlation was observed between serum vitamin D levels and IL-6 concentrations ( $r = -0.42$ ,  $p < 0.05$ ). The majority of children with severe carditis presented with pronounced vitamin D deficiency and elevated IL-6 and IFN- $\gamma$  levels. After treatment, cytokine levels decreased while vitamin D status modestly improved.

**Conclusion:** Vitamin D deficiency may serve as a predictor of inflammatory activity in ARF and correlates with elevated proinflammatory cytokines, particularly IL-6. Assessing vitamin D status may help in the early detection of immune-mediated activity in children with ARF and guide preventive and therapeutic strategies.

**Keywords:** acute rheumatic fever, vitamin D deficiency, IL-6, cytokines, children, inflammation, immune response.

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ДЕФИЦИТ ВИТАМИНА D КАК ПРЕДИКТОР ВОСПАЛИТЕЛЬНОЙ АКТИВНОСТИ У ДЕТЕЙ С ОСТРОЙ РЕВМАТИЧЕСКОЙ ЛИХОРАДКОЙ

**АННОТАЦИЯ**

**Введение:** Острый ревматический лихорадочный синдром (ОРЛ) остается серьезной проблемой детского здравоохранения в развивающихся странах. Недавние исследования показывают, что витамин D играет важную иммуномодулирующую роль при воспалительных заболеваниях.

**Цель:** Исследовать взаимосвязь между дефицитом витамина D и воспалительными цитокинами (ИЛ-1 $\beta$ , ИЛ-6, ИЛ-8, ИФН- $\gamma$ ) у детей с острым ревматическим лихорадочным заболеванием.

**Методы:** В исследование были включены 60 детей в возрасте 5–15 лет с диагнозом острая ревматическая лихорадка (ОРЛ). В рамках исследования оценивалась концентрация 25(OH)D у детей с острой ревматической лихорадкой (ОРЛ) и сравнивалась с данными здоровых детей той же возрастной группы. Уровни 25(OH)D и провоспалительных цитокинов в сыворотке крови измерялись до и после лечения. Уровни витамина D оценивались методом ИФА, а цитокины определялись с помощью иммуноферментного анализа Vector-Best.

**Результаты:** Была обнаружена значительная обратная корреляция между уровнями витамина D в сыворотке крови и концентрациями ИЛ-6 ( $r = -0,42$ ,  $p < 0,05$ ). У большинства детей с тяжелым кардитом наблюдался выраженный дефицит витамина D и повышенные уровни ИЛ-6 и ИФН- $\gamma$ . После лечения уровни цитокинов снизились, а уровень витамина D незначительно улучшился.

**Заключение:** Дефицит витамина D может служить предиктором воспалительной активности при ОРЛ и коррелирует с повышенными уровнями провоспалительных цитокинов, особенно ИЛ-6. Оценка уровня витамина D может помочь в раннем выявлении иммуноопосредованной активности у детей с острой ревматической лихорадкой и определить стратегии профилактики и лечения.

**Ключевые слова:** острая ревматическая лихорадка, дефицит витамина D, ИЛ-6, цитокины, дети, воспаление, иммунный ответ.

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**O'TKIR REVMATIK ISITMA BO'LGAN BOLALARDA YALLIG'LANISH  
FAOLIYATINING PREDIKTORI SIFATIDA D VITAMINI YETISHMAYDIGANLIGINI  
BAHOLASH**

**IZOHNOMA**

O'tkir revmatik isitma rivojlanayotgan mamlakatlarda bolalar salomatligining muhim muammosi bo'lib qolmoqda. So'nggi tadqiqotlar shuni ko'rsatadiki, D vitamini yallig'lanish kasalliklarida muhim immunomodulyator rol o'ynaydi.

**Maqsad:** O'tkir revmatik isitma bilan og'rigan bolalarda D vitamini yetishmasligi va yallig'lanish sitokinlari (IL-1 $\beta$ , IL-6, IL-8, IFN- $\gamma$ ) o'rtasidagi bog'liqlikni o'rganish.

**Usullar:** Tadqiqotda ARF tashxisi qo'yilgan 5-15 yoshli 60 bola ishtirok etdi. Ushbu tadqiqotning bir qismi sifatida, o'tkir revmatik isitma bilan og'rigan bolalarda 25(OH)D konsentratsiyasi baholandi va shu yoshdagi sog'lom bolalarning ma'lumotlari bilan taqqoslandi. Davolashdan oldin va keyin 25(OH)D va yallig'lanishga qarshi sitokinlarning zardobdagi darajasi o'lchandi. D vitamini darajasi ELISA yordamida baholandi va sitokinlar Vector-Best immunoassaylari yordamida aniqlandi.

**Natijalar:** Zardobdagi D vitamini darajasi va IL-6 konsentratsiyasi o'rtasida sezilarli teskari korrelyatsiya kuzatildi ( $r = -0.42$ ,  $p < 0.05$ ). Og'ir kardit bilan og'rigan bolalarning aksariyati D vitamini yetishmovchiligi va IL-6 va IFN- $\gamma$  darajasining oshishi bilan og'rigan. Davolashdan so'ng, sitokin darajasi pasaygan, D vitamini holati esa biroz yaxshilangan.

**Xulosa:** D vitamini yetishmovchiligi yallig'lanish faolligini bashorat qiluvchi omil bo'lib xizmat qilishi mumkin va yallig'lanishga qarshi sitokinlarning, ayniqsa IL-6 ning oshishi bilan

bog'liq. D vitamini holatini baholash RI bilan og'rigan bolalarda immunitet vositasida faollikni erta aniqlashga yordam beradi va profilaktika va terapevtik strategiyalarni boshqaradi.

**Kalit so'zlar:** o'tkir revmatik isitma, D vitamini yetishmovchiligi, IL-6, sitokinlar, bolalar, yallig'lanish, immun javob.

**Acute rheumatic fever (ARF)** develops as a result of a complex interaction of various factors. The acute inflammatory process affects the joints, brain, cardiac muscle, and/or skin, and is caused by an atypical immune response. While the clinical manifestations of the disease may resolve completely, cardiac involvement (carditis) can lead to **chronic rheumatic heart disease (RHD)**, which is associated with serious complications and can be potentially fatal [1,3].

It has been established that **vitamin D exerts selective effects** on various groups of innate immune cells, modulating their development, metabolic activity, antigen-presenting capabilities, and the production of signaling molecules such as cytokines and chemokines [7,9,11].

**Vitamin D deficiency** is a widespread problem affecting public health globally, particularly among children [4,5,12]. Studies indicate that vitamin D may influence the immune system and reduce inflammation in various infectious and autoimmune diseases. In a small number of studies involving pediatric patients, decreased serum concentrations of 25(OH)D were observed in children with autoimmune disorders.

The incidence of upper respiratory tract infections peaks during the winter and spring months, when 25(OH)D levels are expected to be at their lowest due to reduced sun exposure. Additionally, children aged 5 to 15 years undergo active growth, increasing their need for vitamin D [10].

**Cytokines** are key immune mediators that play a crucial role in the pathogenesis of autoimmune diseases<sup>7</sup>. In recent years, a growing body of evidence has demonstrated the involvement of proinflammatory cytokines in the development of ARF and RHD [7,8]. Among the most studied mediators whose levels are significantly elevated in the systemic circulation of patients with ARF and RHD are **interleukin-6 (IL-6)**, **interleukin-8/CXCL8**, and **tumor necrosis factor-alpha (TNF- $\alpha$ )**.

Adequate serum concentrations of 25(OH)D are associated with increased levels of anti-inflammatory cytokines, such as **interleukin-4 (IL-4)** and **interleukin-10 (IL-10)**, and with decreased levels of proinflammatory cytokines like **IL-1** and **IL-6** [3].

**Objective:** The aim of this study was to investigate the relationship between vitamin D deficiency and pro-inflammatory cytokines in children with acute rheumatic fever (ARF).

**Study Design:** This cross-sectional study involved 96 children aged 5 to 18 years, who were divided into two main groups. Group 1 included 60 children diagnosed with acute rheumatic fever based on the modified Jones criteria; Group 2 consisted of 36 healthy children matched by age and sex. The study was conducted at the multidisciplinary clinic of the Samarkand State Medical University (SamSMU), in the pediatric department, from 2024 to April 2025.

**Methods:** Vitamin D levels were determined by enzyme-linked immunosorbent assay (ELISA) using the EUROIMMUN 25-OH Vitamin D ELISA kit (E150519BY) manufactured by EUROIMMUN AG. The reproducibility of the test meets international standards, and its correlation with reference methods (high-performance liquid chromatography and IDS ELISA) is recognized as very high. The ELISA kit was used semi-manually, and results were evaluated using a calibration curve.

Cytokine levels were assessed by immunoassay (ELISA) using a standard commercial reagent kit from HEMA (Russia). The vitamin D tests were conducted in the biochemical laboratory of the multidisciplinary clinic at SamSMU.

**Results:** The study included children with acute rheumatic fever (ARF) aged 5 to 18 years. The majority were children aged 5 to 9 years, accounting for 24.7% (n=37); children aged 10 to 14 years comprised 10.7% (n=16), and those aged 15 to 17 years made up 4.63%. Among the age group 10–14 years, girls predominated, whereas boys were more numerous in the 5–9 year age group.

Given the existing data on the pathogenetic relationship between vitamin D deficiency and ARF, it was deemed appropriate to analyze the seasonal variations of the disease in children. A

prospective analysis of ARF incidence revealed that the peak prevalence occurred during the winter-spring months (Fig. 1).

Gender analysis showed a slight predominance of girls (51.7%) compared to boys (48.3%) among the examined patients (Fig. 2).

In the group of 60 children with ARF under our observation, serum vitamin D levels were analyzed using liquid chromatography (see Table 1).

**Table 1.**  
**Distribution of Vitamin D Levels in Children with ARF and Healthy Children**  
(ng/mL)

Vitamin D Level (ng/mL)	Children with ARF (n = 60)	%	Healthy Children (n = 36)	%
0–20 (Severe deficiency)	13	21.7%	3	8.4%
20–30 (Deficiency)	34	56.7%	7	19.4%
30–100 (Adequate level)	13	21.7%	26	72.2%

Based on serum vitamin D levels, children were divided into three groups. The first group (Group I) included children with severe deficiency — 13 children (21.7%), with a mean vitamin D level of  $17.38 \pm 0.93$  ng/mL. The second group (Group II) consisted of 34 children (56.7%) with vitamin D deficiency, with a mean level of  $23.90 \pm 0.44$  ng/mL. The third group (Group III) included 13 children (21.7%) with adequate vitamin D levels, with a mean concentration of  $45.10 \pm 4.80$  ng/mL. Thus, 78.4% of children with ARF had either a deficiency or a severe deficiency of vitamin D.

**Table 2.**  
**Results of Correlation Analysis Between Vitamin D Levels and Interleukin Levels in Children with ARF**

Parameters	Spearman's $\rho$	Strength of Correlation (Cheddock Scale)	p-value
Vitamin D – IL-1 $\beta$	-0.282	Weak	< 0.001*
Vitamin D – IL-6	-0.701	Strong	< 0.001*
Vitamin D – IL-8	-0.147	Weak	0.072
Vitamin D – IFN- $\gamma$	-0.154	Weak	0.061

\* Differences are statistically significant ( $p < 0.05$ ).

**Statistical Analysis:** Statistical analysis was performed using the software StatTech v. 4.6.3. Quantitative variables were tested for normality using the Kolmogorov–Smirnov test. The direction and strength of correlations between two quantitative variables were assessed using Spearman's rank correlation coefficient (for non-normally distributed data). A predictive model characterizing the dependence of a quantitative variable on influencing factors was developed using linear regression analysis. Differences were considered statistically significant at  $p < 0.05$ . A weak inverse correlation was found between IL-1 $\beta$  and vitamin D. An increase of 1 ng/mL in vitamin D was associated with a decrease of 0.036 pg/mL in IL-1 $\beta$ . The resulting model explained 5.4% of the observed variance in IL-1 $\beta$ . A strong inverse correlation was found between IL-6 and vitamin D. An increase of 1 ng/mL in vitamin D was associated with a decrease of 0.069 pg/mL in IL-6. The model explained 25.7% of the observed variance in IL-6. A weak inverse correlation was observed between IL-8 and vitamin D. An increase of 1 ng/mL in vitamin D was associated with a decrease of 0.038 pg/mL in IL-8. The model explained 3.5% of the observed variance in IL-8.

A very weak inverse correlation was found between IFN- $\gamma$  and vitamin D. An increase of 1 ng/mL in vitamin D was associated with a decrease of 0.004 pg/mL in IFN- $\gamma$ . The model explained 0.0% of the observed variance in IFN- $\gamma$ .

**Discussion.** In the studied cohort of patients with acute rheumatic fever (ARF), the majority were children of primary school age (5–9 years), accounting for 24.7% ( $n = 37$ ) of the total sample. The proportion of patients aged 10–14 years was 10.7% ( $n = 16$ ), while adolescents aged 15–17 years represented the smallest group at 4.63% ( $n = 7$ ). These findings are consistent with literature data indicating that ARF most commonly manifests between the ages of 5 and 15, with peak incidence occurring in the younger age groups<sup>12</sup>.

Of particular interest is the gender distribution across different age categories. Among children aged 5–9 years, boys predominated, whereas among those aged 10–14 years, girls were more frequently affected. These differences may reflect variations in immune responses, hormonal status, and the influence of environmental or lifestyle factors on the risk of developing ARF at different stages of childhood.

Analysis of the overall gender structure among patients with ARF revealed a slight predominance of girls — 51.7% ( $n = 31$ ) compared to 48.3% ( $n = 29$ ) boys, yielding a female-to-male ratio of 1.06:1. Other studies have shown that the initial incidence of ARF does not demonstrate significant sex-related differences; however, the progression rate of rheumatic heart disease is reportedly higher among females<sup>13</sup>.

Both the ARF and control groups demonstrated a high prevalence of vitamin D deficiency and insufficiency. Children with ARF had significantly lower mean serum concentrations of 25(OH)D compared to the healthy controls.

It has been established that within inflammatory processes, the interaction between vitamin D and the cytokine profile plays a key role in promoting a pro-inflammatory state via several molecular mechanisms. In our study, an inverse correlation was found between serum 25(OH)D levels and the concentration of the pro-inflammatory cytokine IL-6 in children with ARF. We also observed weak inverse correlations with IL-1 $\beta$ , IL-8, and IFN- $\gamma$ . These findings suggest that vitamin D may suppress IL-6 secretion by monocytes and macrophages through inhibition of the p38 MAPK signaling pathway via the induction of MKP1. It is known that the MAPK pathway is activated by various stress stimuli and initiates the production of pro-inflammatory cytokines not only in immune cells but also in cardiomyocytes.

**Conclusion.** The results of this study suggest the possible involvement of inflammatory and/or immune-mediated mechanisms associated with vitamin D deficiency in the pathogenesis of acute rheumatic fever (ARF). A significant correlation was found between reduced vitamin D levels and elevated concentrations of interleukin-6 (IL-6), which plays a key role in the inflammatory response in ARF.

Among the risk factors for vitamin D deficiency in the pediatric population, the winter season stands out. The overlap between seasonal peaks in vitamin D deficiency and ARF incidence may further support the hypothesis that vitamin D insufficiency serves as a predisposing factor for the development of the disease.

Thus, vitamin D deficiency, accompanied by reduced immunomodulatory activity, may contribute to the activation of immune responses and the initiation of autoimmune processes in ARF. To gain a deeper understanding of the role of vitamin D deficiency in the pathogenesis of rheumatic fever and its impact on the clinical and immunological phenotype of the disease, large-scale prospective studies involving broader patient cohorts are required.

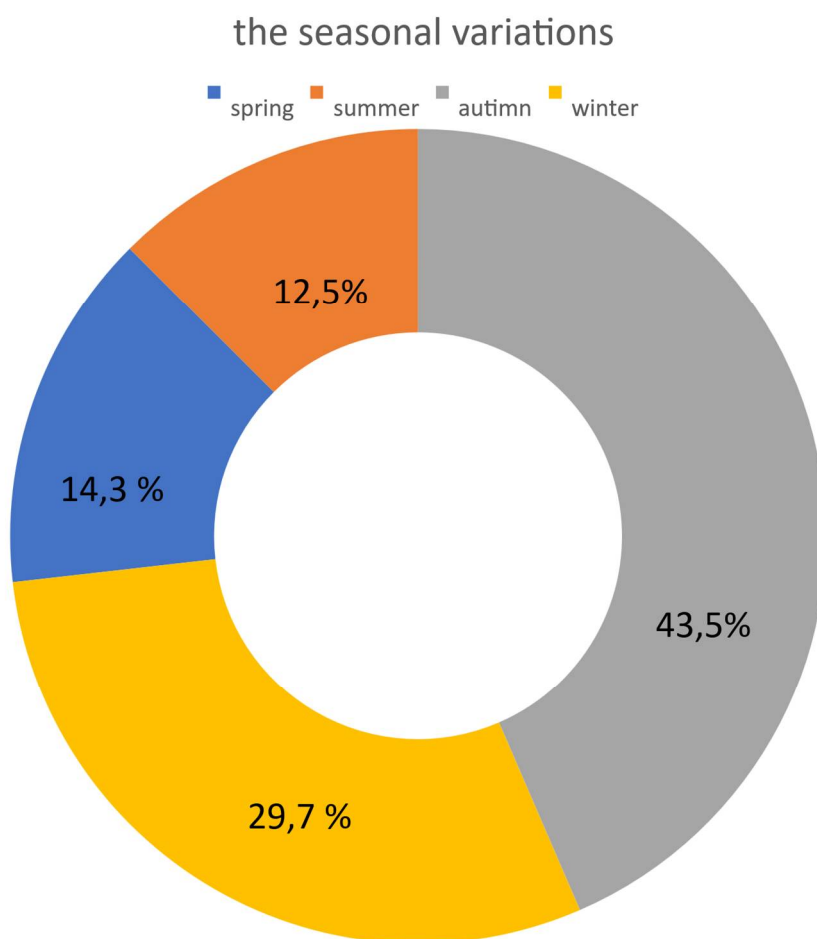


Fig.1. the seasonal variations

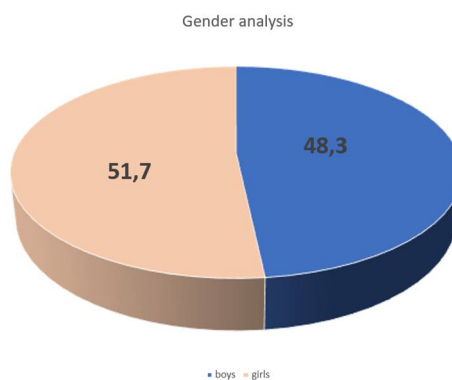


Fig.2. Gender analysis

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