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ЖУРНАЛ БИОМЕДИЦИНЫ И ПРАКТИКИ
JOURNAL OF BIOMEDICINE AND PRACTICE

ДАВРИЙЛИГИ: 2016-2026

ЖИЛД 11
СОН 3

2026



ЧОП
ЭТИЛГАН САНА:
20.06.2026

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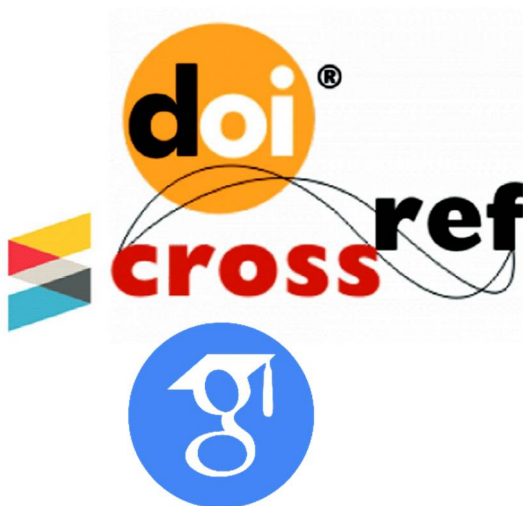
11 ЖИЛД, 3 СОН

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ТОМ 11, НОМЕР 3

JOURNAL OF BIOMEDICINE AND PRACTICE

VOLUME 11, ISSUE 3



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COMPARATIVE EVALUATION OF THE EFFECTIVENESS OF VARIOUS TREATMENT METHODS USED IN THE MANAGEMENT OF POSTPARTUM ENDOMETRITIS.....12

ANESTHESIOLOGY AND INTENSIVE CARE MEDICINE

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PATHOPHYSIOLOGICAL RATIONALE AND PERSONALIZATION OF MULTIMODAL ANALGESIA WITH ESP BLOCK IN PURULENT-SEPTIC DISEASES OF THE THORACIC CAVITY.....19

MATERNAL AND CHILD HEALTH

3. **Nuritdinova Gavhar Taipovna, Atajanova Shoira Khalilovna, Arzibekova Umida Abdukodirovna, Sanjarova Gozaloy Nizamiddin kizi.**
STUDY OF CHANGES IN THE COMPOSITION OF FOOD INGREDIENTS AND CALORIC CONTENT OF BREAST MILK IN WOMEN WITH ANEMIA.....25

PUBLIC HEALTH AND HEALTH CARE SYSTEM

4. **Xamrayev Rustam Istamovich, Axmedov Murod Erkinovich.**
CLINICAL-ORGANIZATIONAL ASPECTS OF ARTERIAL HYPERTENSION PREVENTION IN THE PRIMARY OUTPATIENT CARE SYSTEM.....32
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HYGIENIC ASSESSMENT OF THE ACADEMIC LOAD OF STUDENTS IN MODERN STATE AND PRIVATE SCHOOLS.....38

PEDIATRIC SURGERY

6. **Akhmedov Islomjon Yusufjonovich, Rizaev Jasur Alimjanovich, Yatsyk Sergey Pavlovich, Akhmedov Yusufjon Makhmudovich.**
OPTIMIZATION OF A REGIONAL MODEL OF PERINATAL MONITORING AND MANAGEMENT TACTICS FOR CHILDREN WITH CONGENITAL OBSTRUCTIVE UROPATHY.....47

LABORATORY MEDICINE

7. **Daminov Feruz Asadullayevich, Xanturayev Shahriyor Komilovich.**
LITERATURE REVIEW OF HELICOBACTER PYLORI GENOME DIVERSITY AND GEOGRAPHICAL DISTRIBUTION.....53
8. **Xaydarova Feruza Alimovna, Oyxudjayeva Kamila Farruxovna, Ismiddinov Alijon Olimjon O'g'li, Begmatova Xafiza Ashirmetovna, Dushamova Mexribon Shavkatovna**
FEATURES OF METABOLIC AND INFLAMMATORY MARKERS IN DIFFERENT CLINICAL AND LABORATORY PHENOTYPES OF CHRONIC KIDNEY DISEASE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS.....58

OTORHINOLARYNGOLOGY

9. **Lutfullayev Gairat Umrilloevich, Kobilova Shakhodat Shokirovna, Mayusupova Bibifotima Muxamadsobirzoda.**
SENSORINEURAL HEARING LOSS IN TODAY'S OTORHINOLARYNGOLOGY: TRENDS AND LITERATURE INSIGHTS.....65
10. **Fayzullayev Ali Ibadulloevich, Lutfullayev Gairat Umrilloevich.**
FIBROLARYNGOSCOPIC MONITORING OF REACTIVE CHANGES IN THE POSTOPERATIVE AREA IN PATIENTS WITH BENIGN LARYNGEAL NEOPLASMS..72
11. **Makhkamova Nigora Ergashevna, Nabiyeva Djamila Malikovna, Nasritdinova Maxzuna Taxsinovna.**
IMPROVING DENTAL CARE IN UZBEKISTAN USING A CONCEPTUAL APPROACH TO IMPROVE ITS QUALITY.....80
12. **Khushvakova Nilyufar Jurakulovna, Khamrakulova Nargiza Orzuevna, Makhmudova Saodat Kurbonbekovna.**
IMPROVEMENT OF DIAGNOSTIC APPROACHES AND CONSERVATIVE TREATMENT OF CHRONIC RHINOSINUSITIS IN CHILDREN WITH CYSTIC FIBROSIS.....87
13. **Nasretdinova Makhzuna Takhsinovna, Khayitov Alisher Adkhamovich.**
COMPREHENSIVE DIAGNOSIS, TREATMENT AND PREVENTION OF CYSTIC MAXILLARY SINUSITIS.....98
14. **Nasretdinova Makhzuna Takhsinovna, Dustboboev Dilshod Sadullaevich.**
OPTIMIZATION OF CONSERVATIVE TREATMENT FOR EXUDATIVE OTITIS MEDIA IN CHILDREN: THE SYNERGISTIC EFFECT OF LOW-INTENSITY LASER THERAPY, TOPICAL IMMUNOCORRECTION, AND PLAY AUTOINSUFFLATION.....112
15. **Nasretdinova Makhzuna Takhsinovna, Dustboboev Dilshod Sadullaevich.**
STAGE-BY-STAGE DIAGNOSIS OF EXUDATIVE OTITIS MEDIA IN CHILDREN BASED ON TRANSFERRIN AND CERULOPLASMIN LEVELS IN ORAL FLUID.....126
16. **Nasretdinova Makhzuna Takhsinovna, Khayitov Alisher Adkhamovich, Uktamov Diyorbek Shukhratovich.**
APPROACH TO TREATING CHILDREN WITH OTOMYCOSIS COMPLICATED BY CHRONIC SUPPURATIVE OTITIS MEDIA.....133
17. **Khasanov Ulugbek Saidakramovich, Khudoyberganov Umidbek Ruziboevich.**
ASSESSMENT OF THE CYTOLOGICAL STATUS OF ADENOID VEGETATIONS AFTER VARIOUS TREATMENTS.....143
18. **Khasanov Ulugbek Saidakramovich, Abdurakhimova Shakhnoza Saidasilovna.**
COMPARATIVE ANALYSIS OF METHODS OF TREATING HYPERTROPHIC RHINITIS.....152

MORPHOLOGY

18. **Nurmatov Siroj Tajibaevich.**
CORRECTION OF MORPHOLOGICAL CHANGES IN THE ADRENAL GLANDS UNDER THE INFLUENCE OF CARBON MONOXIDE USING THE PLANT ASPARAGUS OFFICINALIS.....159

NEUROSURGERY

19. **Ravshanov Davron Mavlonovich.**
TRENDS IN THE MANAGEMENT OF INTRACRANIAL MENINGIOMA.....165

20. **Ravshanov Davron Mavlonovich.**
CLINICAL AND FUNCTIONAL CHARACTERISTICS AND THE EFFECTIVENESS OF SPECIALIZED NEUROREHABILITATION AFTER SURGICAL TREATMENT OF SPINAL MENINGIOMAS.....172
21. **Kilichev Farrukh Akhmadovich, Yarmukhamedova Nargiza Anvarovna, Aliev Mansur Abdukholikovich.**
OPTIMIZATION OF ENDOVASCULAR STRATEGY IN ACUTE ISCHEMIC STROKE CONSIDERING ANGIOARCHITECTURE AND COLLATERAL CIRCULATION.....182

ONCOLOGY

22. **Yusupbekov Abrorbek Ahmedjanovich, Tuychiyeva Saboxat Shavkatovna, Djanklich Saide Mustafayevna.**
A POPULATION-BASED APPROACH TO CERVICAL CANCER: THE CONTEMPORARY IMPORTANCE OF CANCER REGISTRIES, SCREENING, AND SURVIVAL ANALYSIS.....191
23. **Zakhirova Nargiza Negmatovna, Saydaxmedova Viloyat Amirdinovna.**
THE IMPORTANCE OF ARTIFICIAL INTELLIGENCE TECHNOLOGIES IN THE EARLY DETECTION OF CERVICAL CANCER: INTERNATIONAL EXPERIENCE AND OPPORTUNITIES FOR THE NATIONAL HEALTHCARE SYSTEM.....199
24. **Shomansurova Nodira Saidarifovna, Nigmanova Nigora Anvarovna.**
CLINICAL AND ECONOMIC EFFECTIVENESS OF THE SENTIMAG MAGNETIC NAVIGATION SYSTEM IN SENTINEL LYMPH NODE DETECTION IN BREAST CANCER.....215
25. **Reymnazarova Gulsara Djamalovna.**
MORPHOMETRIC FEATURES OF THE CERVIX WITH BENIGN LESIONS AND EROSION IN THE PREMENOPAUSAL PERIOD.....225
26. **Tuychiev Otabek Dilshod ugli, Djumanazarov Temirbek Matchanovich, Madiyorov Bakhtiyor Toshpulatovich, Usmanov Bekzod Baymatovich, Ismailova Djadida Akhmedjanovna.**
EPIDEMIOLOGY OF ESOPHAGEAL CANCER IN THE REPUBLIC OF UZBEKISTAN AND THE DEGREE OF HELICOBACTER PYLORI CONTAMINATION IN ESOPHAGEAL CANCER PATIENTS.....230
27. **Sharipov Khurshed Saidjonovich, Rizaev Jasur Alimdjanovich, Ashurov Gayur Gafurovich.**
DYNAMICS OF CHANGES IN THE CONCENTRATION OF BONE TISSUE DESTRUCTION MARKERS AND PH LEVEL IN THE ORAL FLUID OF PATIENTS WITH ONCOPATHOLOGY DURING CHEMORADIO THERAPY.....240
28. **Nishonov Doniyor Anarboyevich, Babakulov Sharaf Xamrakulovich, Navruzova Visola Sarimbekovna, Sulaymanova Nodira Jumayevna, Babakulova Shahlo Xamidullayevna.**
PATHOGENETIC FOUNDATIONS AND EVALUATION OF CLINICAL EFFICACY OF PROBIOTIC THERAPY IN THE COMPLEX TREATMENT OF SUPERFICIAL BLADDER CANCER.....247
29. **Lipartia Meri Givievna, Fazliyev Mekhrojiddin Shamsiddinovich, Turakulov Adash Farmonovich, Rahimov Nodir Maxammatkulovich, Shakhanova Shakhnoza Shavkatovna**
RELATIONSHIP BETWEEN BONE MARROW MYELOGRAM PARAMETERS AND PERIPHERAL BLOOD INDICES IN CHEMOTHERAPY-INDUCED LEUKOPENIA....253

OPHTHALMOLOGY

30. **Kadirova Aziza Muratovna, Khakimova Mavluda Shavkatjonovna.**
CLINICAL AND IMMUNOHISTOCHEMICAL CHANGES IN THE UPPER EYELID IN BLEPHAROCHALASIS IN WOMEN OF DIFFERENT AGE AND HORMONAL GROUPS.....266
31. **Sayfiddinov Fayzullo Azamjon o'g'li, Azizova Shohidaxon Adhamjon qizi.**
EARLY DIAGNOSIS OF OPEN-ANGLE GLAUCOMA USING THE ICARE TONOMETER AND THE MAKLAKOV TONOMETER.....272

PEDIATRICS

32. **Usmanova Munira Fayzullaevna, Urunova Manzura Allamurodovna, Kardjavova Gulnoza Abilkasimovna.**
CARDIAC-SPECIFIC MARKERS OF MYOCARDIAL INJURY IN CHILDREN WITH COMMUNITY-ACQUIRED PNEUMONIA.....278
33. **Makhmudova Dilorom Salakhitdinovna, Shadibekova Oksana Bronislavovna, Almedova Nargiza Nigmatdaganovna, Dekhkanov Sattor Kakhramonovich, Mustafaev Arseniy Ruslanovich.**
RETROSPECTIVE ANALYSIS OF THE INHIBITOR FORM OF HEMOPHILIA A IN CHILDREN.....285
34. **Yunusaliyeva Umida Rakhidin kizi, Dustmukhamedova Dinora Khamidovna, Umarnazarova Zulkhumor Ernazarovna, Kamilova Altinoy Tursubaevna.**
SHORT BOWEL SYNDROME: CURRENT CONCEPTS OF PATHOGENESIS, DIAGNOSIS AND TREATMENT.....291
35. **Inakova Barno Baxodirovna, Nuritdinova Gavxar Taipovna, Solieva Mavlyuda Odiljanovna, G'ulomjanova Yulduz.**
NEUROPSYCHOLOGICAL DEVELOPMENT OF CHILDREN BORN TO MOTHERS WITH TORCH INFECTION.....301

PSYCHONEUROLOGY, PSYCHIATRY

36. **Turaev Bobir Temirpulotovich, Ochilov Ulug'bek Usmanovich, Sultanov Shoxrux Khabibullaevich.**
ASSESSMENT OF THE RELATIONSHIP BETWEEN BLOOD BIOCHEMICAL PARAMETERS, COGNITIVE AND PSYCHOEMOTIONAL IMPAIRMENTS, AND REHABILITATION EFFECTIVENESS IN PATIENTS WITH CHEMICAL ADDICTIONS.....309
37. **Khudaynazarova Salomat Ruzibaevna, Kuryazova Sharofat Masharipovna.**
ASSESSMENT OF PHYSICAL DEVELOPMENT BY THE "WHO ANTHROPLUS" METHOD IN PRIMARY SCHOOL-AGED CHILDREN.....315
38. **Usmanov Saidolim Akhralovich.**
CLINICAL AND NEUROPSYCHOLOGICAL EFFECTIVENESS OF TRANSCRANIAL MICROPOLARIZATION IN THE THERAPY OF CHILDREN WITH DELAYED PSYCHO-SPEECH DEVELOPMENT.....321
39. **Mansurova Nargiza Asrorovna**
IMMUNOLOGICAL AND NEUROSPECIFIC BIOMARKERS IN THE DIFFERENTIAL DIAGNOSIS OF PARKINSON'S DISEASE AND VASCULAR PARKINSONISM.....326
40. **Mamatkhanova Charos Bohadirovna**
MODERN STRATEGY OF CONSERVATIVE THERAPY OF DEGENERATIVE CERVICAL MYELOPATHY: NEURORECOVERY, NEUROREGENERATION AND NEUROMODULATION (LITERATURE REVIEW).....333

RADIOLOGY

41. **Adambayev Zufar Ibragimovich, Samiyev Asliddin Saitovich.**
THE VALUE OF QUANTITATIVE MRI METHODS (DIFFUSION TENSOR IMAGING)
IN THE EARLY DIAGNOSIS OF THE PRECLINICAL STAGE OF BINSWANGER'S
DISEASE.....345

REHABILITATION

42. **Rizaev Jasur Alimdjanovich, Usmonov Otabek Abdirazakovich.**
A DIFFERENTIATED ALGORITHM FOR PRESCRIBING A REHABILITATION
PROGRAM WITH FIVE BASIC PROTOCOLS DEPENDING ON THE TYPE OF ANKLE
SURGERY.....352

DENTISTRY

43. **Akhrorqulov Akhtamboy Akmaljonovich, Akhmadov Inomjon Nizomitdinovich.**
MODERN TRANSFORMATION OF THE BIOLOGICALLY ORIENTED PREPARATION
TECHNIQUE (BOPT): HYBRID ANALOG-DIGITAL APPROACH AND CLINICAL-
BIOLOGICAL FOUNDATIONS OF THE FULLY DIGITAL EASYBOPT
PROTOCOL.....360
44. **Ismoilov Akhrorjon Anvarjon, Sanakulov Jamshed Obloberdiyevich.**
ENHANCING THE EFFICIENCY OF MULTIMODAL REGISTRATION OF CBCT AND
INTRAORAL SCANS BASED ON ARTIFICIAL INTELLIGENCE.....365
45. **Akhmedov Alisher Astanovich, Mukhiddinov Shokhrux Gafurjon ugli.**
IMPROVING THE QUALITY OF RESTORATION OF TEETH WITH CROWN DEFECTS
USING MODERN POST-CORE CONSTRUCTIONS.....374
46. **Rizaev Jasur Alimdjanovich, Zaynutdinov Muradilla Omonullaevich, Normuradov Nodirjon Alisherovich.**
APPLICATION OF L-PRF TECHNOLOGY IN THE COMPREHENSIVE SURGICAL
TREATMENT OF MEDICATION-RELATED OSTEONECROSIS OF THE JAWS.....381
47. **Iskhakova Zukhra Sharifkulovna, Normuradov Nodir Alisherovich.**
OPTIMIZATION OF TREATMENT OF FOCAL PERIODONTAL LESIONS USING
TOOTH-PRESERVING SURGERIES.....389
48. **Iskhakova Zukhra Sharifkulovna, Normuradov Nodir Alisherovich.**
MODERN APPROACHES TO SURGICAL TREATMENT OF FOCAL PERIODONTAL
LESIONS WITH TOOTH-PRESERVING OPERATIONS (LITERATURE
REVIEW).....396
49. **Shukurov Akobir Furkatovich, Inoyatov Amrillo Shodiyevich, Shukurova Nodira Tillayevna**
INFORMED CONSENT IN DENTAL SCIENCE: LEGAL ESSENCE AND PRACTICAL
ISSUES.....404

TRAUMATOLOGY AND ORTHOPEDICS

50. **Rakhmonov Shokhimordon Sherkul ugli.**
MODERN METHODS OF APPLYING REHABILITATION AFTER ARTHROSCOPIC
REPAIR OF THE ANTERIOR CRUCIATE LIGAMENT OF THE KNEE JOINT
(LITERATURE ANALYSIS).....409

51. Davirov Sharof Majidovich, Urinbaev Payzilla Urinbaevich, Mansurov Djalolidin Shamsidinovich, Abdurakhmanov Sheramat Begaliyevich, Hamiraev Siroj Pirnazarovich. FIBULA AUTOGRAFTING AND EXTERNAL FIXATION FOR POST-OSTEOMYELITIC FEMORAL DEFECTS.....416

UROLOGY

51. Allazov Saloh Allazovich. CYSTIC NEOPLASMS OF THE SCROTUM ORGANS AND MALE REPRODUCTIVENESS.....429
52. Allazov Saloh Allazovich. RARE TWO CASES FROM UROGYNECOLOGICAL PRACTICE.....436
53. Allazov Saloh Allazovich, Allazov Iskandar Salakh ogli. THE IMPORTANCE OF ORCHIDOMETRY IN ASSESSING MEN'S HEALTH.....442
54. Rahimov Nodir Maxammatkulovich, Shaxanova Shaxnoza Shavkatovna, Xafizov Qodirjon Olimovich. CLINICAL AND MORPHOLOGICAL PREDICTORS OF PERSISTENT URINARY INCONTINENCE AFTER RADICAL PROSTATECTOMY.....450

SURGERY

55. Abdullayev Sayfullo Abdullaevich. TACTICS OF TREATMENT FOR POSTOPERATIVE VENTRAL HERNIAS.....458
56. Dvoryankin Dmitriy Vladimirovich, Kurbaniyazov Zafar Babadjanovich, Rafikov Behbujon Rustamovich, Kochetkov Aleksandr Vladimirovich, Askarov Pulat Azadovich. FACTORS OF COMPLICATED POSTOPERATIVE COURSE IN ONE-STAGE SURGICAL TREATMENT OF PATIENTS WITH POSTOPERATIVE VENTRAL HERNIAS AND OBESITY.....466
57. Klimenko Grigoriy Alekseevich, Kapralov Sergey Vladimirovich, Mayorov Rodion Vladimirovich, Zhirkova Anastasiya Gennadyevna, Ziyadullaev Shukhrat Khudayberdievich. PREDICTION OF RISK FACTORS FOR PARASTOMAL COMPLICATIONS IN THE EARLY POSTOPERATIVE PERIOD472

ENDOCRINOLOGY

58. Mamadiyarova Dilshoda Umirzokovna, Azimova Sevara Bakhodirovna. THE SIGNIFICANCE OF THE C718T (RS713041) POLYMORPHISM IN THE GPX4 GENE IN TYPE 2 DIABETES MELLITUS COMPLICATED BY ANGIOPATHY.....479
59. Narimova Gulchekhra Jumaniyazovna, Makhmudova Farangiz Batirovna, Kayumova Durdona Tuygunovna. ASSESSMENT OF THE EFFECT OF MELATONIN ON SLEEP QUALITY AND CARBOHYDRATE METABOLISM IN REPRODUCTIVE-AGED PATIENTS WITH TYPE 2 DIABETES MELLITUS.....484
60. Xaydarova Feruza Alimovna, Begmatova Xafiza Ashirmetovna, Dushamova Mexribon Shavkatovna, Oyxudjayeva Kamila Farruxovna, Ismiddinov Alijon Olimjon O'g'li, Issayeva Saodat Saydullayevna. ASSOCIATION OF BMP-7 WITH C-PEPTIDE LEVELS: A MARKER OF β -CELL RESERVE IN TYPE 2 DIABETES MELLITUS.....490

БИОМЕДИЦИНА ВА АМАЛИЁТ ЖУРНАЛИ

ЖУРНАЛ БИОМЕДИЦИНЫ И ПРАКТИКИ | JOURNAL OF BIOMEDICINE AND PRACTICE

УДК 616.33-002:616-022.7:579.835.12

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LITERATURE REVIEW OF HELICOBACTER PYLORI GENOME DIVERSITY AND GEOGRAPHICAL DISTRIBUTION

For citation: Daminov Feruz Asadullayevich, Xanturayev Shahriyor Komilovich. Literature review of Helicobacter pylori genome diversity and heographical distribution// Journal of Biomedicine and practice.

<http://dx.doi.org/10.5281/zenodo.21313034>

ANNOTATION

The genomic diversity and geographical distribution of the bacterium Helicobacter pylori, considered to be the oldest companion of humanity, is analyzed. H. pylori has a high level of genetic polymorphism and recombination, which ensures its adaptation to the gastric environment of different populations. The study examines the phylogeographic grouping of bacterial strains into hpEurope, hpAfrica, hpEastAsia and their relationship to human migration

Keywords: helicobacter pylori, genome diversity, geographical distribution, population, genetics, virulence factors, evolution

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ОБЗОР ЛИТЕРАТУРЫ ПО ГЕНОМНОМУ РАЗНООБРАЗИЮ И ГЕОГРАФИЧЕСКОМУ РАСПРОСТРАНЕНИЮ HELICOBACTER PYLORI

АННОТАЦИЯ

В статье анализируется геномное разнообразие и географическое распространение бактерии Helicobacter pylori, считающейся древнейшей спутницей человечества. H. pylori обладает высоким уровнем генетического полиморфизма и рекомбинации, что обеспечивает её адаптацию к желудочной среде различных популяций. Исследование рассматривает филогеографическую группировку бактериальных штаммов в группы hpEurope, hpAfrica, hpEastAsia и их связь с миграцией населения.

Ключевые слова: helicobacter pylori, геномное разнообразие, географическое распространение, популяция, генетика, факторы вирулентности, эволюция.

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HELICOBACTER PYLORI GENOM XILMA-XILLIGI VA GEOGRAFIK TAQSIMOTI ADABIYOTLAR SHAHRI

ANNOTATSIYA

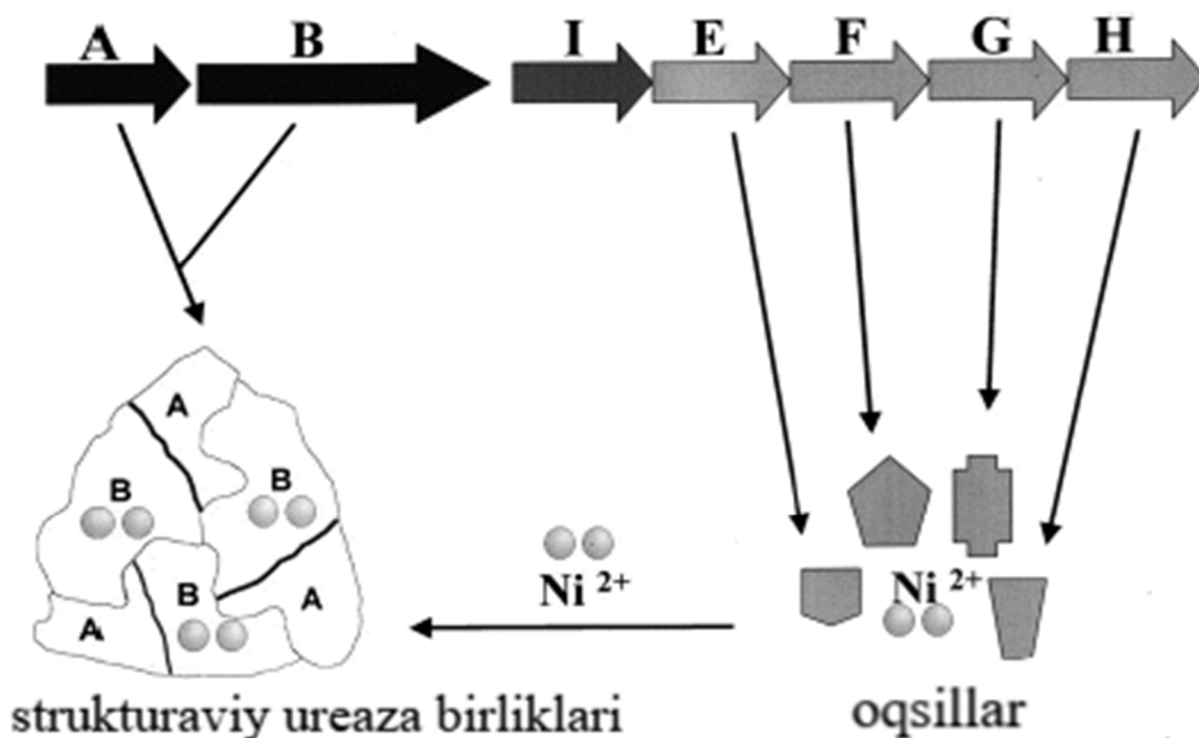
Insoniyatning eng qadimiy hamrohi hisoblangan *Helicobacter pylori* bakteriyasining genom xilma-xilligi va uning dunyo bo'ylab geografik taqsimoti tahlil qilinadi. *H.pylori* yuqori darajadagi genetik polimorfizm va rekombinatsiya xususiyatiga ega bo'lib, bu uning turli populyatsiyalar oshqozon muhitiga moslashishini ta'minlaydi. Tadqiqotda bakteriya shtammlarining filogeografik guruhlanishi hpEurope, hpAfrica, hpEastAsia va ularning insoniyat migratsiyasi bilan bog'liqligi ko'rib chiqiladi. **Kalit so'zlar:** helicobacter pylori, genom xilma-xilligi, geografik taqsimot, populyatsiya, genetikasi, virulentlik omillari, evolyutsiya.

Kirish: *Helicobacter pylori* bakteriyasi insoniyat bilan 100 000 yildan ortiq vaqt davomida birga yashab kelmoqda. U oshqozon yarasi va saratoni kabi oshqozon kasalliklari bilan bog'liq asosiy etiologik agent hisoblanadi. Shunga qaramay, dunyo aholisining yarmidan ko'pi *H.pylori* bilan zararlangan bo'lsa-da, ularning 2% dan kamrog'ida esa oshqozon saratoni rivojlanadi [1,2] Inson organizmi bilan yaqin simbiotik aloqalar, asosan vertikal yo'l bilan yuqishi bilan bir qatorda, *H.pylori* ning bir necha turli geografik populyatsiyalarga bo'linib evolyutsiya qilishiga olib keldi. Tadqiqotlar shuni ko'rsatadiki, nomutanosiblik yuz berganda oshqozon saratoni xavfi yuqori bo'ladi, bunda kelib chiqishi afrikalik bo'lgan inson bakteriyaning yevropa shtammi bilan zararlansa. Bunday holatda immun tizimi va bakteriya bir-birini tanimaydi, bu esa kuchliroq yallig'lanishga sabab bo'ladi hamda *H.pylori* infeksiyasi keltirib chiqaradigan kasalliklarning rivojlanish xavfi geografik mintaqaga qarab sezilarli darajada farq qiladi [3,4,5] *Helicobacter pylori* (*H.pylori*) – me'da shilliq qavatida koloniya hosil qiluvchi, grammanfiy spora hosil qilmaydigan, uchi yumaloq, S-simon yoki spiralsimon egilgan tayoqcha shaklidagi mikroaerofil bakteriya hisoblanadi. Kam hollarda U-simon va V-simon shakllari ham uchraydi. Oxirgi ikki shaklli bakteriyalarning spiralsimon va kokk shakllari o'rtasidagi oraliq bo'g'in hisoblanadi [5,6]. Tashqi muhitning noqulay omillari harorat yoki pH o'zgarishi ta'sirida, *H.pylori* kokk shakllarini hosil qilish qobiliyatiga ega, bu esa uning omon qolishiga yordam beradi hamda bakteriyalarning epidemiologiyasi va tarqalishida muhim omil bo'lib xizmat qiladi [7] Kokk holatida fermentativ faollikni va ko'payish qobiliyatini yo'qotadi hamda tashqi ta'sirlarga, shu jumladan antibakterial preparatlarga chidamlidir bu vaqtda ularda moddalar almashinuvi sekinlashadi, bu esa bakteriyalarning ichakda yoki tashqi muhitda tirik saqlanib qolishi uchun qulay sharoit yaratadi va shu holatda odamga fekal-oral yo'li bilan yuqishi mumkin. Qulay sharoitga tushgach *Helicobacter pylori* bunday shakllari yana me'da shilliq qavatida koloniya hosil qilish xususiyatiga ega bo'lgan vegetativ shakllarga aylanishi mumkin. Kokksimon hujayralar hujayra devori tuzilishining o'ziga xos jihatlari bilan ajralib turadi, bu esa organizmni immun tizimi orqali bakteriyani tanib olish jarayonining buzilishiga bakterial mimikriya olib keladi [6]. *H.pylori* patogenlik faoliyati uchun ko'p faktorlarga ega, ularning aksariyati ushbu mikroorganizmning oshqozon shilliq qavatida parazitlik qilish uchun yaxshi moslashgan, uning oshqozon kislotali muhitida omon qolishini va shilliq qavatda koloniya hosil qilishini ta'minlaydi [8,9] *Helicobacter pylori* yana bir himoya mexanizmiga ega, ko'p miqdorda superoksiddismutaza va katalaza ishlab chiqaradi. Bular esa fagotsitozga to'sqinlik qiladi. *H.pylori* ajratadigan proteazalar yordamida oshqozon shilliq osti qavatiga kirib boradi va uyerdagi pH muhitni kislotalidan neytral muhitga

o'tkazish bilan uziga qulay muhit yaratadi. Hamda ularning spirallasimon shakli va bir uchida xivchinlar borligi ularga shilliq qatlamiga tezda o'tib olish imkonini beradi.[10,11]

H. pylori genomi nisbatan kichik (1.6-1.7 Mbp) bo'lishiga qaramay, u bakterial dunyodagi eng yuqori genetik xilma-xillik darajasiga ega. Bu xilma-xillik yuqori mutatsiya chastotasi, rekombinatsiya va gorizontaal gen almashinuvining kombinatsiyasi natijasida yuzaga keladi. *H. pylori* genomi odatda ikki qismga bo'linadi: "core genome" – barcha shtamlarda mavjud bo'lgan va asosan metabolizm va hujayra tuzilishi uchun mas'ul bo'lgan genlar to'plami va "plasticity regions" – shtamlar o'rtasida katta farq qiladigan, ko'pincha virulentlik, antigenlik xususiyatlar yoki atrof-muhitga moslashish bilan bog'liq bo'lgan genlar va genomlar tuplami. *H. pylori* genomida mikrororganizmning yuqori patogenligi bilan bog'liq bo'lgan *vacA*, *cagA*, *iceA*, *babA*, *dupA* kabi genlar mavjud.

*H. pylori*ning ureaza gen klasterida yettita gen aniqlangan: *ureA*, *ureB* — ureazaning tarkibiy qismlarini kodlaydi; *ureE*, *ureF*, *ureG*, *ureH* — ureazaning yig'ilishi va unga Ni^{2+} ionlarining birikishi uchun zarur bo'lgan qo'shimcha oqsillarni kodlaydi; *ureI* — vodorod ionlari (H^+) uchun kanalni kodlaydi va asosan mochevinaning bakteriya sitoplazmasiga o'tishini ta'minlovchi transport tizimi hisoblanadi.(12)



*H. pylori*da katalitik faol ureazaning sintez modelida. Yetti xromosoma bilan kodlangan genlardan tashkil topgan ureaza geni klasteri xromosomasida bitta nusxa sifatida mavjud. *ureA* va *ureB* genlari mos ravishda 26,5 kDa va 60,3 kDa og'irlikdagi birliklarni kodlaydi. Har bir birlikning oltita nusxasi o'z-o'zidan, katalitik faol bo'lmagan apoferment hosil qiladi. Rasmda ureaza oqsili har bir birlikning uchta nusxasini ko'rsatadi va *Klebsiella aerogenes* ureazaning kristall tuzilishiga moslashgan (13). *H. pylori* ureazaning ma'lum molekulyar hajmi (550 kDa) tasvirlangan rasmda oqsil tuzilmalari ikkitasi bog'langan bo'lishini talab qiladi (14). Bu joylashuv hali to'liq o'rganilmagan. *ureE*, *ureF*, *ureG* va *ureH* yordamchi genlari *UreE*, *UreF*, *UreG* va *UreH* yordamchi oqsillarini kodlaydi, ular boshqa turlarning gomologlariga o'xshab, energiya sarflaydigan reaksiyalarda (15) apoenzimga nikel ionlarini (Ni^{2+}) kiritishga xizmat qiladi. *UreE* nikel bilan bog'lovchi dimerdir.

Inson va *H. pylori* o'rtasidagi 100 ming yildan ko'p bo'lgan koevolyutsion munosabatlar davomida, adaptiv mutatsiyalar va rekombinatsiya hodisalarining yuqori tezligi *H. pylori* turining noodatiy yuqori darajada genom polimorfizmiga olib keldi. Shunga qaramay, *H. pylori* shtamlari ularning geografik kelib chiqishiga qarab turli xil populyatsiyalar va subpopulyatsiyalarga bo'lindi.

Xozigi kunda yettita zamonaviy populyatsiya shtamallari aniqlangan *H.pylori*: hpAfrica1, hpAfrica2, hpEastAsia, hpEurope, hpAsia2, hpNEAfrica va hspSahul.(17,18,19) Bular o'z navbatida bundan oldingi oltita avlod populyatsiyalardan kelib chiqqan ancestral European-1, ancestral European-2, ancestral EastAsia, ancestral Africa1, ancestral Africa2, ancestral Sahul. Ko'p tadqiqotlar shuni ko'rsatadiki *H.pylori*ning kelip chiqish joyi Afrika qitasiga to'g'ri keladi. (17) Alohida hududlardagi *H.pylori* yettita populyatsiyaning «hp» har birini subpopulyatsiyalarga «hsp» bo'lingan, ular birbiridan genetik jihatdan farq qiladi, lekin populyatsiyalarga qaraganda kamroq differentsiatsiyalashgan.(20) O'z navbatida *H.pylori*ning Afrika populyatsiyasi 3 ta populyatsiyaga bo'lingan hpAfrica1, hpAfrica2 va hpNEAfrica. Bakteriyani o'rganish davomida global filogenetik tahlillarga ko'ra ikkita super-liniyani aniqlandi. Ulardan biri hpAfrica2 populyatsiyasi ikkinchisi esa qolgan barcha populyatsiyalarni yagona monofiletik birlashmasi.

Bu tadqiqotlarga assoslanib hpAfrica2 populyatsiyasi eng qadimiy populyatsiya hisoblanadi. Qolgan ikki populyatsiya hpNEAfrica, hpAfrica1 populyatsiyalari insoniyat migratsiyasi davomida migratsiya bo'lib evolyutsion rivojlanib boruvorgan.(21)

Xulosa: *Helicobacter pylori* – genetik jihatdan eng xilma-xil va dinamik bakteriyalardan biri bo'lib, uning genomining o'ziga xos tuzilishi va yuqori o'zgaruvchanligi uning uzoq muddatli kolonizatsiyasi va patogenligini ta'minlaydi. Uning populyatsiyalari odamlar migratsiyasi tarixini aniq aks ettiradi, shuning uchun u antropologik tadqiqotlar uchun “molekulyar soat” sifatida ishlatilishi mumkin. Virulentlik genlaridagi geografik xilma-xillik turli mintaqalarda infeksiyaning turli klinik natijalarining sabablarini tushunishda muhim ahamiyatga ega. Kelajakdagi tadqiqotlar butun genom ketma-ketligi va transkriptomika usullaridan foydalangan holda *H. pylori* genotipi, genetikasi va atrof-muhit omillari o'rtasidagi murakkab o'zaro ta'sirni ochib beradi. Bu esa individual tashxis va davolash strategiyalarini ishlab chiqishga imkon beradi.

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