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INDIVIDUALIZATION OF ART PROTOCOLS IN PATIENTS WITH DIFFERENT OVARIAN RESERVE

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ABSTRACT

Infertility remains one of the most important challenges in modern reproductive medicine and requires an individualized approach to improve the effectiveness of assisted reproductive technologies (ART). The aim of this study was to evaluate ART outcomes in patients with different ovarian reserve levels and to determine the role of personalized treatment protocols. This prospective study included 60 infertile women treated at the “Beshik” Reproductive Medicine Clinic (Samarkand, Uzbekistan) during 2025–2026. The participants were divided into two groups according to ovarian reserve: normal ovarian reserve (n=30) and diminished ovarian reserve (n=30). Ovarian reserve was assessed using anti-Müllerian hormone levels and antral follicle count, and all patients were additionally stratified according to the POSEIDON concept. Although patients with diminished ovarian reserve demonstrated lower numbers of retrieved oocytes and less favorable embryological outcomes, individualized ovarian stimulation protocols allowed satisfactory rates of oocyte maturation, fertilization, and blastocyst formation to be achieved. The findings indicate that personalization of ART protocols based on ovarian reserve assessment and POSEIDON stratification contributes to improved reproductive outcomes.

Keywords: infertility, assisted reproductive technologies, IVF, ICSI, ovarian reserve, AMH, POSEIDON, personalization

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ИНДИВИДУАЛИЗАЦИЯ ПРОТОКОЛОВ ВРТ У ПАЦИЕНТОК С РАЗЛИЧНЫМ ОВАРИАЛЬНЫМ РЕЗЕРВОМ

АННОТАЦИЯ

Бесплодие является одной из наиболее актуальных проблем современной репродуктивной медицины и требует индивидуализированного подхода для повышения эффективности вспомогательных репродуктивных технологий (ВРТ). Целью исследования явилась оценка результатов ВРТ у пациенток с различным овариальным резервом и определение значения

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GENETIC ASPECTS OF UROGENITAL REACTIVE ARTHRITIS

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ABSTRACT

Urogenital reactive arthritis is an immune-inflammatory disease belonging to the group of seronegative spondyloarthropathies, in which infectious and genetic factors play an important role. The aim of the study was to evaluate the diagnostic and prognostic significance of genetic markers associated with IL-17A and the TLR system in urogenital reactive arthritis. The study was conducted at the multidisciplinary clinic of Samarkand State Medical University. The main group included 40 patients with urogenital reactive arthritis, while the control group consisted of 30 apparently healthy individuals. Clinical, laboratory, molecular-genetic, and immunological investigations were performed. The results demonstrated that the A allele and GA/AA genotypes of the IL-17A G-197A polymorphism were significantly more frequent among patients with reactive arthritis. In addition, the Gly allele and Gly/Gly genotype of the TLR4 Asp299Gly polymorphism may be associated with susceptibility to the development of reactive arthritis. The findings indicate the important role of immunogenetic markers in the early diagnosis and prediction of chronic progression of reactive arthritis.

Keywords: reactive arthritis, urogenital infection, IL-17A, TLR4, genetic polymorphism, immunogenetics, diagnostics

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ГЕНЕТИЧЕСКИЕ АСПЕКТЫ УРОГЕНИТАЛЬНОГО РЕАКТИВНОГО АРТРИТА

АННОТАЦИЯ

Реактивный артрит урогенитической этиологии относится к группе серонегативных спондилоартритов, в развитии которого важную роль играют инфекционные и генетические факторы. Целью исследования явилась оценка диагностического и прогностического значения генетических маркеров, связанных с IL-17A и системой TLR, при урогенитальном реактивном артрите. Исследование проведено на базе многопрофильной клиники Самаркандского государственного медицинского университета. Основную группу составили 40 пациентов с урогенитальным реактивным артритом, контрольную группу — 30 практически здоровых лиц. В ходе исследования проведены клинико-лабораторные, молекулярно-генетические и иммунологические методы обследования. Установлено, что аллель A и генотипы GA и AA полиморфизма IL-17A G-197A достоверно чаще встречались у пациентов основной группы. Кроме того, выявлено, что аллель Gly и генотип Gly/Gly полиморфизма TLR4 Asp299Gly могут быть связаны с предрасположенностью к развитию реактивного артрита. Полученные результаты свидетельствуют о важной роли иммуногенетических маркеров в ранней диагностике и прогнозировании хронического течения реактивного артрита.

Ключевые слова: реактивный артрит, урогенитальная инфекция, IL-17A, TLR4, генетический полиморфизм, иммуногенетика, диагностика

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UROGENITAL REAKTIV ARTRITNING GENETIK JIHATLARI

ANNOTATSIYA

Urogenital etiologiyali reaktiv artrit seronegativ spondiloartritlar guruhiga kiruvchi immun-yallig'lanish kasalligi bo'lib, uning rivojlanishida infeksion va genetik omillar muhim ahamiyat kasb etadi. Tadqiqotning maqsadi urogenital reaktiv artritda IL-17A va TLR tizimi bilan bog'liq genetik markerlarning diagnostik va prognostik ahamiyatini baholashdan iborat bo'ldi. Tadqiqot Samarqand davlat tibbiyot universiteti ko'p tarmoqli klinikasi bazasida olib borildi. Asosiy guruhni urogenital etiologiyali reaktiv artrit bilan kasallangan 40 nafar bemor, nazorat guruhini esa 30 nafar deyarli sog'lom shaxs tashkil etdi. Tadqiqot davomida klinik-laborator, molekulyar-genetik va immunologik tekshiruvlar o'tkazildi. Natijalarga ko'ra, IL-17A G-197A polimorfizmining A alleli hamda GA va AA genotiplari asosiy guruhda sezilarli yuqori uchrashi aniqlandi. Shuningdek, TLR4 Asp299Gly polimorfizmining Gly alleli va Gly/Gly genotipi reaktiv artrit rivojlanishiga moyillik bilan bog'liq bo'lishi mumkin. Olingan natijalar immunogenetik markerlar reaktiv artritni erta tashxislash va surunkalashish xavfini prognoz qilishda muhim ahamiyatga ega ekanligini ko'rsatdi.

Kalit so'zlar: reaktiv artrit, urogenital infeksiya, IL-17A, TLR4, genetik polimorfizm, immunogenetika, diagnostika

---

Dolzarbligi. Reaktiv artrit (ReA) seronegativ spondiloartritlar guruhiga kiruvchi, organizmda kechgan infeksion jarayondan keyin rivojlanadigan autoimmun-yallig'lanish kasalligi hisoblanadi [1,5]. Kasallik ko'pincha urogenital yoki enterogen infeksiyalardan so'ng kuzatiladi hamda asosan bo'g'imlar, ko'z, teri va shilliq qavatlarning yallig'lanishi bilan namoyon bo'ladi [6,7]. Urogenital etiologiyali ReA rivojlanishida eng muhim trigger omil sifatida Chlamydia trachomatis e'tirof etiladi, shuningdek Ureaplasma urealyticum, Neisseria gonorrhoeae va boshqa jinsiy yo'l bilan yuqadigan infeksiyalar ham kasallik patogenezida muhim o'rin tutadi [2,3]. Jahon sog'liqni saqlash tashkiloti ma'lumotlariga ko'ra, har yili dunyo bo'yicha 127 milliondan ortiq yangi xlamidial infeksiya holatlari

qayd etiladi va bu reproduktiv yoshdagi aholida eng keng tarqalgan urogenital infeksiyalardan biri hisoblanadi [7].

So‘nggi yillarda ReA ning klinik va immunogenetik jihatlariga bo‘lgan qiziqish ortib bormoqda. Tadqiqotlar shuni ko‘rsatadiki, reaktiv artrit urogenital infeksiyaga chalingan bemorlarning taxminan 1–4 % da rivojlanadi [6,10]. Kasallik ko‘pincha 20–40 yoshdagi erkaklarda uchraydi, bu esa aynan ushbu yosh guruhida jinsiy yo‘l bilan yuqadigan infeksiyalar yuqori uchrashi bilan bog‘liq [7,10]. ReA ning dolzarbligi nafaqat uning tarqalishi, balki surunkali kechish, bo‘g‘im destruksiyasi, funksional cheklanish va mehnatga layoqatning pasayishiga olib keluvchi asoratlari bilan ham izohlanadi [1,13]. Ayrim hollarda kasallik uzoq davom etuvchi sakroileit, spondiloartrit yoki surunkali autoimmun yallig‘lanish shakliga o‘tishi mumkin [14].

Reaktiv artrit diagnostikasi hozirgi kungacha murakkab muammolardan biri bo‘lib qolmoqda, chunki kasallik klinik jihatdan boshqa yallig‘lanishli artritlarni taqlid qilishi mumkin [5,11]. An’anaviy laborator ko‘rsatkichlar, jumladan SOE va C-reaktiv oqsil yallig‘lanish faolligini aks ettirsada, kasallikning immunopatogenetik xususiyatlarini to‘liq baholash imkonini bermaydi [8]. Shu sababli zamonaviy tadqiqotlarda immunogenetik markerlarga alohida e’tibor qaratilmoqda. Xususan, IL-17A sitokini va TLR-4 retseptorining yallig‘lanish jarayonidagi roli faol o‘rganilmoqda [14–16]. IL-17A Th17-hujayraviy javobning asosiy mediatorlaridan biri bo‘lib, surunkali yallig‘lanish va bo‘g‘im destruksiyasida muhim ahamiyatga ega [14,16]. TLR-4 esa tug‘ma immunitet tizimi retseptori sifatida bakterial antigenlarni tanib olish va yallig‘lanish kaskadini faollashtirishda ishtirok etadi [15].

Hozirgi kunda ReA ning genetik va immunologik markerlarini aniqlash kasallikni erta tashxislash, surunkalashish xavfini baholash hamda individual diagnostik algoritmlarni ishlab chiqishda istiqbolli yo‘nalishlardan biri hisoblanadi [4,9,18]. Shu bois urogenital reaktiv artritning genetik jihatlarini o‘rganish kasallikning patogenezini chuqurroq anglash va diagnostik imkoniyatlarni optimallashtirishda muhim ilmiy-amaliy ahamiyat kasb etadi.

Tadqiqot maqsadi. Urogenital etiologiyaning reaktiv artritining genetik jihatlarini xususiyatlarini o’rganish.

Tadqiqotning materiallari va metodlari. Tadqiqot Samarqand davlat tibbiyot universitetining ko‘p tarmoqli klinikasi bazasida olib borildi. Tadqiqotga kiritish va chiqarish mezonlari asosida urogenital etiologiyali reaktiv artrit tashxisi tasdiqlangan 40 nafar bemor jalb qilindi. Nazorat guruhini yoshi va jinsi bo‘yicha taqqoslanadigan 30 nafar deyarli sog‘lom shaxs tashkil etdi. Barcha ishtirokchilar O‘zbekiston Respublikasi Sog‘liqni saqlash vazirligining amaldagi klinik tavsiyalari va diagnostik protokollariga muvofiq kompleks klinik-laborator hamda instrumental tekshiruvlardan o‘tkazildi. Diagnostik algoritm anamnestik ma’lumotlarni tahlil qilish, klinik simptomlarni baholash, umumiy va biokimyoviy laborator ko‘rsatkichlarni aniqlash, shuningdek urogenital infeksiyalarni polimeraza zanjir reaksiyasi (PZR) usuli yordamida verifikatsiya qilishni o‘z ichiga oldi.

Yuqumli omil va bo‘g‘im sindromi rivojlanishi o‘rtasidagi patogenetik bog‘liqlikni aniqlash maqsadida immunologik va molekulyar-genetik tekshiruvlar ham amalga oshirildi. Xususan, IL-17A G-197A (rs2275913) va TLR4 Asp299Gly (rs4986790) gen polimorfizmlari molekulyar-genetik usullar yordamida O’zbekiston Respublikasi fanlar akamediyasi negizidagi immunologiya va inson genomikasi institutida shartnoma asosida o‘rganildi. Genom DNK periferik venoz qon namunalaridan standart usul yordamida ajratib olindi. IL-17A G-197A (rs2275913) va TLR4 Asp299Gly (rs4986790) polimorfizmlarini genotiplash allel-spetsifik primerlardan foydalangan holda real vaqt rejimidagi polimeraza zanjir reaksiyasi (Real-Time PCR) usuli yordamida amalga oshirildi. Amplifikatsiya test-tizim ishlab chiqaruvchisining tavsiyalariga muvofiq bajarildi. Olingan natijalar fluoressensiya egri chiziqlarini avtomatik tahlil qilish asosida baholandi.

Statistik tahlil olingan natijalarning ishonchliligini baholash maqsadida zamonaviy biostatistik usullar asosida amalga oshirildi. Ma’lumotlarga ishlov berish Microsoft Excel va Statistica 8.0 dasturlari yordamida bajarildi. Miqdoriy ko‘rsatkichlar o‘rtacha arifmetik qiymat va standart og‘ish ko‘rinishida (M±SD) ifodalandi. Guruhlar o‘rtasidagi farqlarni baholashda ma’lumotlarning taqsimlanish xarakteridan kelib chiqib parametrik va noparametrik usullardan

foydalanildi. Ikki guruh o‘rtasidagi miqdoriy ko‘rsatkichlarni taqqoslash uchun Student t-testi hamda Mann–Whitney U-testi qo‘llanildi. Sifat ko‘rsatkichlari χ^2 (Xi-kvadrat) testi yordamida baholandi.

Immunologik markerlar (IL-17A va TLR-4) bilan klinik-laborator ko‘rsatkichlar o‘rtasidagi bog‘liqlik Spearman korrelyatsion tahlili yordamida aniqlandi. Statistik jihatdan ishonchli farq mezoni sifatida $p<0,05$ qabul qilindi. Tadqiqot Jahon tibbiyot assotsiatsiyasining Xelsinki deklaratsiyasi (2013) tamoyillari hamda O‘zbekiston Respublikasining biotibbiy tadqiqotlarni o‘tkazish bo‘yicha amaldagi qonunchilik talablariga muvofiq amalga oshirildi. Tadqiqotda ishtirok etgan barcha shaxslardan tadqiqotda qatnashish va shaxsiy ma’lumotlarini qayta ishlash uchun yozma ravishda xabardor qilingan ixtiyoriy rozilik olindi.

Tadqiqot natijalari. Tadqiqot natijalariga ko‘ra, urogenital etiologiyali reaktiv artrit bilan kasallangan bemorlarda klinik va laborator ko‘rsatkichlarning sezilarli o‘zgarishlari aniqlandi. Tekshirilgan bemorlarning aksariyatida bo‘g‘im sindromi yetakchi klinik belgi sifatida namoyon bo‘ldi. Eng ko‘p tizza bo‘g‘imlari shikastlanishi kuzatilib, u 56,7% holatda qayd etildi, boldir-tovon bo‘g‘imlari zararlanishi esa 46,7% bemorda aniqlandi. Bo‘g‘imlarda og‘riq, shish va giperemiya bilan kechuvchi yallig‘lanish belgilarining mavjudligi 70% bemorda kuzatildi. Ertalabki karaxtlik va harakat cheklanishi 50% holatda qayd etildi.

Klinik faollikni baholash davomida DAS28 indeksining o‘rtacha ko‘rsatkichi 5,1±0,8 ni tashkil etib, bemorlarning ko‘pchiligida o‘rta va yuqori faollikdagi yallig‘lanish jarayoni mavjudligini ko‘rsatdi. Laborator tekshiruvlarda C-reaktiv oqsil va SOE ko‘rsatkichlarining nazorat guruhiga nisbatan ishonchli yuqoriligi aniqlandi ($p<0,05$). C-reaktiv oqsilning o‘rtacha qiymati 18,2±3,6 mg/l ni, SOE esa 28,6±4,3 mm/soatni tashkil etdi. Leykotsitoz 63,3% bemorda kuzatildi.

PZR diagnostikasi natijalariga ko‘ra, barcha bemorlarda urogenital infeksiya verifikatsiya qilinib, asosiy etiologik omil sifatida Chlamydia trachomatis hamda ayrim hollarda Ureaplasma urealyticum aniqlanildi. Kasallikning surunkali yoki qaytalanuvchi kechishi 40% bemorda kuzatilib, ularda bo‘g‘im sindromining uzoq davom etishi va yallig‘lanish markerlarining yuqori darajada saqlanib qolishi qayd etildi.

Tollga o'xshash retseptorlar (TLR) infektsiyalarga qarshi immunitet reaktsiyasida asosiy rol o'ynaydi va tug'ma immunitetning muhim tarkibiy qismidir. TLRlar lipopolisaxaridlar, nuklein kislotalar va boshqa bakterial komponentlar kabi patogen molekulalarni aniqlaydi. Urogenital kasalliklar (masalan, Chlamydia trachomatis) bilan bog'liq patogenlar bilan infektsiyalanganida, TLRlar faollashadi va yallig'lanish bilan bog'liq genlarning transkripsiyasini boshlaydi. TLR faollashuvi interleykin-1 (IL-1), interleykin-6 (IL-6) va o'sma nekrozi omili (TNF-a) kabi turli xil sitokinlar va kimyokinlarning ishlab chiqarilishiga olib keladi. Bu molekulalar yallig'lanish reaksiyasining rivojlanishida muhim rol o'ynaydi, bu esa o'z navbatida reaktiv artritning rivojlanishiga yordam beradi.

Reaktiv artritli bemorlarda bo'g'im to'qimalarda TLR faollashuvining kuchayishi bo'g'imlarning keyingi yallig'lanishga sezgir bo'lishiga olib keladi. Surunkali yallig'lanish bo'g'imlarda tizimli o'zgarishlarga olib kelishi va ularga zarar yetkazishi, artrit belgilarini yomonlashishi mumkin. Shunday qilib, TLRlar urogenital infektsiyalar bilan bog'liq reaktiv artrit patogenezida muhim molekulalardir, chunki ular patogenni aniqlash, yallig'lanish reaktsiyasini faollashtirish va immun tizimi bilan o'zaro ta'sir qilishda ishtirok etadi.

Jadval 1.

TLR4 Asp299Gly polimorfizmi allellari va genotiplari taqsimlanishining bemorlar va nazorat guruhidagi chastotasi

Guruh	Asp alleli n / %	Gly alleli n / %	Asp/Asp n / %	Asp/Gly n / %	Gly/Gly n / %
Asosiy guruh (n=40)	67 (83,75%)	13 (16,25%)	30 (75,00%)	7 (17,50%)	3 (7,50%)
Nazorat guruhi (n=30)	54 (90,00%)	6 (10,00%)	24 (80,00%)	5 (16,67%)	1 (3,33%)

Jadval natijalariga ko‘ra, asosiy guruhda Gly allelining uchrash chastotasi nazorat guruhiga nisbatan yuqoriroq ekanligi aniqlandi. Shuningdek, Gly/Gly genotipi reaktiv artrit bilan kasallangan bemorlarda nazorat guruhiga qaraganda ko‘proq uchradi. Olingan ma’lumotlar TLR4 Asp299Gly polimorfizmi yallig‘lanish jarayonining rivojlanishi va immun javob faollashuvida muhim ahamiyatga ega bo‘lishi mumkinligini ko‘rsatadi.

Jadval 2.

TLR4 Asp299Gly polimorfizmining reaktiv artrit bilan assotsiatsiyasi

Faktor	Guruhlar	SE	SP	AUC	OR	95% CI	p
Asp	Asosiy guruh // Nazorat guruhi	0,84	0,10	0,47	0,60	0,24–1,48	0,214
Gly	Asosiy guruh // Nazorat guruhi	0,16	0,90	0,53	1,67	0,67–4,13	0,214
Asp/Asp	Asosiy guruh // Nazorat guruhi	0,75	0,20	0,48	0,75	0,28–1,99	0,563
Asp/Gly	Asosiy guruh // Nazorat guruhi	0,18	0,83	0,50	1,06	0,31–3,57	0,921
Gly/Gly	Asosiy guruh // Nazorat guruhi	0,08	0,97	0,52	2,42	0,24–24,12	0,432

Jadval ma’lumotlariga ko‘ra, TLR4 Asp299Gly polimorfizmining Gly alleli va Gly/Gly genotipi asosiy guruhda nazorat guruhiga nisbatan ko‘proq uchrashi kuzatildi. Gly alleli uchun odds ratio (OR) 1,67 ni tashkil etib, ushbu allel reaktiv artrit rivojlanishi xavfi oshishi bilan bog‘liq bo‘lishi mumkinligini ko‘rsatdi. Gly/Gly genotipi uchun OR ko‘rsatkichi 2,42 ga teng bo‘lib, bu genotip kasallikning surunkali va faol kechishiga moyillik bilan bog‘liq bo‘lish ehtimolini aks ettirdi. Shu bilan birga, statistik jihatdan ishonchli farq aniqlanmadi (p>0,05), bu esa tanlov hajmining cheklanganligi bilan izohlanishi mumkin. Olingan natijalar TLR4 Asp299Gly polimorfizmining urogenital reaktiv artrit patogenezidagi ehtimoliy prognostik ahamiyatini ko‘rsatadi.

Jadval 3.

IL-17A G-197A polimorfizmi allellari va genotiplari taqsimlanishining bemorlar va nazorat guruhidagi chastotasi

Guruh	G alleli n / %	A alleli n / %	GG n / %	GA n / %	AA n / %
Asosiy guruh (n=40)	49 (61,25%)	31 (38,75%)	15 (37,50%)	19 (47,50%)	6 (15,00%)
Nazorat guruhi (n=30)	52 (86,67%)	8 (13,33%)	23 (76,67%)	6 (20,00%)	1 (3,33%)

3-jadval natijalariga ko‘ra, asosiy guruhda IL-17A G-197A polimorfizmining A alleli va AA genotipi nazorat guruhiga nisbatan yuqoriroq uchrashi aniqlandi. Ayniqsa, GA va AA genotiplarining reaktiv artrit bilan kasallangan bemorlarda ko‘proq qayd etilishi IL-17A genining yallig‘lanish jarayonlari va immun javob shakllanishidagi ehtimoliy rolini ko‘rsatadi. Olingan natijalar IL-17A polimorfizmi kasallikning immunopatogenezida ehtimoliy prognostik marker bo‘lishi mumkinligini tasdiqlaydi.

Jadval 4.

IL-17A G-197A polimorfizmining reaktiv artrit bilan assotsiatsiyasi

Faktor	Guruhlar	SE	SP	AUC	OR	95% CI	p
G	Asosiy guruh // Nazorat guruhi	0,61	0,13	0,37	0,25	0,11–0,53	<0,001
A	Asosiy guruh // Nazorat guruhi	0,39	0,87	0,63	4,02	1,88–8,61	<0,001
GG	Asosiy guruh // Nazorat guruhi	0,38	0,23	0,31	0,20	0,07–0,50	<0,001
GA	Asosiy guruh // Nazorat guruhi	0,48	0,80	0,64	3,62	1,32–9,90	0,002
AA	Asosiy guruh // Nazorat guruhi	0,15	0,97	0,56	5,12	0,56–46,70	0,041

4-jadval ma’lumotlariga ko‘ra, IL-17A G-197A polimorfizmining A alleli reaktiv artrit rivojlanishi xavfi bilan ishonchli bog‘liq ekanligi aniqlandi. A alleli uchun odds ratio (OR) 4,02 ni tashkil etdi (p<0,001), bu esa ushbu allelning kasallikka moyillikni oshiruvchi omil bo‘lishi mumkinligini ko‘rsatadi. Shuningdek, GA va AA genotiplari asosiy guruhda nazorat guruhiga qaraganda sezilarli yuqori uchradi. Ayniqsa, AA genotipi uchun OR 5,12 ni tashkil etib, ushbu

genotip surunkali yallig‘lanish va kasallikning og‘irroq kechishi bilan bog‘liq bo‘lish ehtimolini ko‘rsatdi. Olingan natijalar IL-17A G-197A polimorfizmining urogenital reaktiv artrit patogenezida muhim immunogenetik marker ekanligini tasdiqlaydi.

Jadval 5.

IL-17A G-197A polimorfizmi bo‘yicha Hardy–Vaynberg muvozanati

Genotip	Kuzatilgan (n)	Kutilgan (n)
GG	23	22,53
GA	6	7,93
AA	1	0,53

Nazorat guruhida IL-17A G-197A va TLR4 Asp299Gly polimorfizmlari bo‘yicha genotiplar taqsimlanishining Hardy–Vaynberg muvozanatiga mosligi tekshirildi. Tahlil natijalariga ko‘ra, IL-17A G-197A polimorfizmi uchun χ^2=0,54; p=0,46 (5-jadval), TLR4 Asp299Gly polimorfizmi uchun esa χ^2=1,10; p=0,29 ni (6-jadval) tashkil etdi. Har ikkala holatda ham genotiplar taqsimlanishida statistik jihatdan ishonchli og‘ish aniqlanmadi (p>0,05), bu nazorat guruhi tanlovining reprezentativligi hamda genotiplash natijalarining ishonchliligini tasdiqlaydi.

Jadval 6.

TLR4 Asp299Gly polimorfizmi bo‘yicha Hardy–Vaynberg muvozanati

Genotip	Kuzatilgan (n)	Kutilgan (n)
Asp/Asp	24	24,30
Asp/Gly	5	5,40
Gly/Gly	1	0,30

Muhokama. O‘tkazilgan tadqiqot natijalari urogenital etiologiyali reaktiv artrit rivojlanishida immunogenetik omillarning muhim ahamiyatga ega ekanligini ko‘rsatdi. Tadqiqotda IL-17A G-197A polimorfizmining A alleli hamda GA va AA genotiplari reaktiv artrit bilan kasallangan bemorlarda nazorat guruhiga nisbatan sezilarli darajada yuqori uchrashi aniqlandi. Ushbu natijalar IL-17A sitokinining surunkali yallig‘lanish, Th17-hujayraviy immun javob va bo‘g‘im to‘qimalarining shikastlanishidagi muhim rolini ko‘rsatgan tadqiqotlar bilan mos keladi [14,16]. Ma’lumki, IL-17A yallig‘lanish mediatorlari sintezini kuchaytirib, sinovial qavatda yallig‘lanish reaksiyalarining davomiyligini ta’minlaydi hamda bo‘g‘im destruksiyasiga olib keluvchi immun mexanizmlarni faollashtiradi [14].

Bizning natijalarimizga ko‘ra, IL-17A G-197A polimorfizmining A alleli reaktiv artrit rivojlanish xavfi bilan ishonchli bog‘liq bo‘lib, odds ratio ko‘rsatkichi 4,02 ni tashkil etdi (p<0,001). Shuningdek, AA genotipi uchun OR 5,12 ga teng bo‘ldi, bu esa ushbu genotip kasallikka moyillikni oshiruvchi genetik omillardan biri bo‘lishi mumkinligini ko‘rsatadi. Olingan ma’lumotlar IL-17A genining immunopatogenezdagi ahamiyatini tasdiqlab, ushbu markerning diagnostik va prognostik qiymatga ega ekanligini ko‘rsatadi [14,16].

TLR4 Asp299Gly polimorfizmi bo‘yicha olingan natijalarda Gly alleli va Gly/Gly genotipi asosiy guruhda nazorat guruhiga nisbatan ko‘proq uchrashi kuzatildi. Biroq ushbu farqlar statistik jihatdan ishonchli darajaga yetmadi (p>0,05). Shunga qaramasdan, Gly alleli uchun OR=1,67 va Gly/Gly genotipi uchun OR=2,42 ko‘rsatkichlari TLR4 signal yo‘lining reaktiv artrit rivojlanishida ma’lum darajada ishtirok etishi mumkinligini ko‘rsatadi. Bu natijalar tug‘ma immunitet tizimi retseptorlari, xususan TLR oilasining bakterial antigenlarni tanib olish va yallig‘lanish kaskadini faollashtirishdagi roli haqidagi ma’lumotlar bilan mos keladi [15]. Chlamydia trachomatis va boshqa urogenital patogenlar bilan bog‘liq infeksion jarayonlarda TLR retseptorlarining faollashuvi yallig‘lanish reaksiyasini kuchaytirishi va kasallikning surunkalashishiga zamin yaratishi mumkin [9,15].

Tadqiqot davomida barcha bemorlarda urogenital infeksiya mavjudligi PZR usuli yordamida tasdiqlandi. Bu holat reaktiv artritning infeksion triggerlari haqidagi zamonaviy qarashlarni yana bir bor tasdiqlaydi [6,7]. Adabiyotlarda qayd etilishicha, Chlamydia trachomatis urogenital reaktiv

artritning eng muhim etiologik omillaridan biri hisoblanadi va uning organizmda persistensiyasi immun javobning uzoq muddat saqlanishiga olib keladi [2,3,9].

Klinik natijalar ham adabiyot ma’lumotlari bilan mos keldi. Bemorlarda asosan tizza va boldir-tovon bo‘g‘imlarining zararlanishi, bo‘g‘imlarda og‘riq va shish, ertalabki karaxtlik hamda yallig‘lanish markerlarining oshishi kuzatildi. Bu belgilar reaktiv artritning klassik klinik ko‘rinishlari sifatida boshqa tadqiqotlarda ham qayd etilgan [6,7,10,11]. Bundan tashqari, kasallikning surunkali yoki qaytalanuvchi kechishi kuzatilgan bemorlarda yallig‘lanish markerlarining yuqori darajada saqlanib qolishi immunogenetik omillarning klinik faollik bilan bog‘liqligini ko‘rsatadi.

Shunday qilib, olingan natijalar IL-17A G-197A polimorfizmi urogenital reaktiv artrit rivojlanishida muhim immunogenetik marker ekanligini, TLR4 Asp299Gly polimorfizmi esa kasallikka moyillikni belgilovchi qo‘shimcha omillardan biri bo‘lishi mumkinligini ko‘rsatdi. Immunogenetik markerlarni amaliyotga joriy etish kasallikni erta tashxislash, yuqori xavf guruhlarini aniqlash hamda individual davolash strategiyalarini ishlab chiqish imkoniyatlarini kengaytiradi [13,18].

Tadqiqotning ayrim cheklovlari mavjud. Xususan, tanlov hajmining nisbatan kichikligi va tadqiqotning bir markazda o‘tkazilgani natijalarni umumlashtirish imkoniyatlarini ma’lum darajada cheklaydi. Kelgusida ko‘proq bemorlarni qamrab olgan ko‘p markazli tadqiqotlar o‘tkazish maqsadga muvofiq hisoblanadi.

Xulosa. O‘tkazilgan tadqiqot natijalari urogenital etiologiyali reaktiv artrit rivojlanishida immunogenetik omillarning muhim o‘rin tutishini ko‘rsatdi. Kasallik bilan og‘rigan bemorlarda IL-17A G-197A polimorfizmining A alleli hamda GA va AA genotiplari nazorat guruhiga nisbatan sezilarli yuqori uchrashi aniqlandi. Shuningdek, TLR4 Asp299Gly polimorfizmining Gly alleli va Gly/Gly genotipi reaktiv artrit bilan bog‘liq immun-yallig‘lanish jarayonlarida ehtimoliy assotsiatsiyaga moyillik kuzatildi. Klinik-laborator tekshiruvlar natijasida bemorlarda yallig‘lanish faolligining yuqoriligi, bo‘g‘im sindromining ustunligi hamda IL-17A va TLR4 gen polimorfizmlarining reaktiv artrit rivojlanishi bilan bog‘liqligi kuzatildi. Ushbu markerlarning kasallikning klinik faolligi va surunkalashish xavfi bilan bog‘liqligi aniqlandi.

Olingan natijalar IL-17A va TLR tizimi bilan bog‘liq genetik polimorfizmlar urogenital reaktiv artritning immunopatogenezida muhim rol o‘ynashini tasdiqlaydi. Immunogenetik markerlarni kompleks diagnostik algoritmlarga kiritish kasallikni erta tashxislash, surunkali kechish xavfini prognoz qilish va individual terapevtik yondashuvni tanlash imkoniyatlarini kengaytiradi.

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