

# IMMUNOPATOGENETIC FEATURE OF THE DEVELOPMENT OF CHRONIC KIDNEY DISEASE IN CHILDREN

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Received: 08 March 2023

Revised: 14 March 2023

Accepted: 24 March 2023

Published: 31 March 2023

## Funding source for publication:

Andijan state medical institute and I-EDU GROUP LLC.

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**Abstract.** Objective. To determine the significance of cytokine profile management in normal and pathological conditions in children, in particular, in the immunopathogenetic development of chronic kidney disease. Conclusion: various properties of cytokine mediators serve to protect the body from infectious agents and repair tissues. First of all, cytokines regulate the development of local protective processes, cause the formation of an inflammatory reaction. Therefore, the composition and ratio of pro-inflammatory and anti-inflammatory cytokines can be considered as the most objective indicators of the inflammatory process and the growth of fibrosis. The prediction of an imbalance in the cytokine system can be used as a biomarker for chronic kidney disease, disease progression, and treatment efficacy. An analysis of the literature data revealed the scientific and practical significance of studying the cytokine status in chronic kidney disease.

**Key words.** children, cytokines, chronic kidney disease, glomerulonephritis.

**Kirish.** Ma'lumki, so'nggi 10-15 yil davomida bolalarda buyrak va peshob tizimi kasalliklarining sezilarli darajada ortishi kuzatilmoqda va surunkali buyrak kasalligi muammosi eng dolzarb muammolardan biri bo'lib qolmoqda. Bu o'rinda patologik jarayonning rivojlanish mexanizmi, progressiyasi, surunkali buyrak yetishmovchiligi va boshqa asoratlarni kelib chiqishini erta prognozlashda sitokinnarning tutgan o'rni, hamda kasallik rivojlanishida ishtirok etish mexanizmlarining xilma-xilligi to'g'risida adabiyot manbalarida ma'lumotlar keltirilgan.

So'nggi yillarda olib borilgan tadqiqotlarda siydikdagi interleykinlar darajasini o'rganish bilan mahalliy yallig'lanish mexanizmlarini o'rganishga alohida e'tibor qaratilmoqda. Sitokinnar nospetsifik himoya reaksiyalari va o'ziga xos immunitet o'rtasidagi munosabatni amalga oshiradi. Yallig'lanish markazida sintez qilingan sitokinnar yallig'lanishda ishtirok etadigan deyarli barcha hujayralarga ta'sir qiladi. Mahalliy himoya reaksiyalari ishlamay qolganda, sitokinnar qon aylanishiga kiradi va ularning ta'siri tizimli darajada bo'ladi, bu esa organizmda o'tkir fazali javobning rivojlanishiga olib keladi.

Ma'lumki, bugungi kunda surunkali buyrak kasalligini (SBK) tashxislash va davolashning ko'plab usullari mavjudligiga qaramay, kasallikning faollik darajasini baholashga, klinik va laboratoriya remissiyaning davom etishi va terapiyani optimallashtirishga qaratilgan yangi uslubiy usullarning imkoniyatlari hali ham o'rganilmoqda. Shu nuqtai nazardan, SBK bo'lgan bolalarda mahalliy yallig'lanish va mahalliy himoya ko'rsatkichlarini baholashda interleykinlar ishlab chiqarilishini o'rganish katta ahamiyatga molikdir [2, 3].

Surunkali buyrak kasalligi bu - laboratoriya va instrumental tadqiqotlar natijalariga ko'ra, buyraklar filtrlash funksiyasining pasayishi bilan 3 oy yoki undan ko'proq davom etadigan buyrak shikastlanishi belgilari bilan barcha klinik-laborator o'zgarishlarni birlashtirgan supranozologik tushunchadir. Ma'lumki, bolalik davrida namoyon bo'ladigan ko'plab buyrak kasalliklari o'smirlar va kattalarda rivojlanishda davom etadi.

Klinik nuqtai nazardan, «surunkali buyrak kasalligi» tushunchasi patologik jarayonning muqarrar ravishda keyingi rivojlanishini nazarda tutadi. Bu K/DOQI (Kidney Disease Outcomes Quality Initiative) tavsiyasiga binoan turli xil nefrologik kasalliklarni surunkali buyrak kasalliklari guruhiga birlashtirishga olib keldi. «Surunkali buyrak kasalligi» atamasi terapevtik amaliyotdan olingan bo'lib, pediatriyada birinchi marta Hogg R.J. tomonidan qo'llanilgan bo'lib, proliferativ jarayonlar, differentsiatsiya, o'sish va hujayra faoliyatini tartibga solishda aynan sitokinnar ishtirok etishi aniqlangan [1, 2, 3].

Interleykinlar (IL) immunitet reaksiyasi va yallig'lanishning turi va davomiyligini tartibga solishga imkon beradi. Sitokinnarning miqdoriy tarkibi va ularning nisbati patologik jarayonning dinamikasini aks ettiradi, kasallikning faoliyati bilan bog'liq, bu esa terapiya samaradorligini baholash va kasallikning natijasini taxmin qilish imkonini beradi [2, 3, 4]. Tabiiy immunitet regulyatorlari- yallig'lanish sitokinnar: IL-1 va IL-6, o'sma nekrozi omili (TNF- $\alpha$ ); xemokin (IL-8), monotsitar xemotaksik oqsil (MXO-1), organizmni bakterial

va virusli infeksiyalardan nospetsifik himoya qilishda, ya'ni fagotsit hujayralari bo'lgan makrofaglar va granulotsitlarni faollashtirishda ishtirok etadi. IL-6 V-limfotsitlarning antitanachalar ishlab chiqaruvchi hujayralarga differenziatsiyasini keltirib chiqaradi. Bundan tashqari, ushbu sitokin mezangial hujayralarning ko'payishini stimullaydi va glomerulopatiyaning rivojlanishida asosiy rol o'ynaydi [5]. IL-8 xemokin subturlariga tegishli bo'lib, asosan neytrofil xemoattractant xisoblanadi. Shuningdek, bugungi kunda ushbu xemokinning glomerulalar o'tkazuvchanligiga ta'sir qilishini tasdiqlovchi klinik va eksperimental ma'lumotlar mavjud [6].

TNF- $\alpha$  yallig'lanishga qarshi sitokin bo'lib, uning sintezi angiotenzin II tomonidan stimullanadi. TNF- $\alpha$  miofibroblastlarni differenziatsiyalashda ishtirok etadi va yallig'lanish va immunitet reaksiyalarida ishtirok etadigan genlarni boshqarishda asosiy rol o'ynovchi transkripsiya faktorini (NF-KB) faollashtiradi. O'roqli glomerulopatiyaning eksperimental modelida, genetik jihatdan aniqlangan TNF- $\alpha$  yetishmovchiligi va bu sitokinning farmakologik ingibitsiyasi glomerulyar shikastlanishlarning rivojlanishini kamaytiradi [6, 7].

Maxsus immun javobni tartibga soluvchi sitokinlar-IL-2 va IL-4, o'sishni o'zgartirish omili (TNF- $\beta$ ) oqsillari yetuk limfotsitlarni faollashtirish, o'sish va differenziatsiyasida ishtirok etadi. Maxsus immun jarayonda paydo bo'ladigan yallig'lanish reaksiyalarini boshqaruvchi sitokinlar tug'ma va moslashgan immunitetda rol o'ynaydigan interferon- $\gamma$ , limfotoksin, IL-5, IL-10dir. Ularning asosiy vazifasi nospetsifik effektor hujayralari bo'lgan sitotoksik makrofaglar va tabiiy killerlarni faollashtirishdan iborat [8].

IL - 10 antigen stimullovchi hujayralarni faollashuvi va differenziatsiyasini, shuningdek, asosiy kompleksning II sinf gistomosligini ifodasini pasaytiradi va TNF- $\alpha$  kabi yallig'lanish sitokinlarining IL-12, IL-1 va IL-10 ishlab chiqarilishini kamaytiradi. Bundan tashqari, tabiiy killer - NK- hujayralari (CD8), sitotoksik T-limfotsitlar va T-xelper hujayralar, semiz hujayralar, keratinotsitlar, endotelial va mezangial hujayralar o'sishi va differenziatsiyasini tartibga soladi. Buyraklarda IL-10 asosan mezangial va endotelial hujayralar tomonidan ajralib chiqadi va buyrakning normal faoliyatini tartibga solish va saqlashda, oddiy va patologik sharoitlarda shu jumladan surunkali buyrak yetishmovchiligi rivojlanishida ishtirok etadi, [9].

Shuni ta'kidlash joizki, yallig'lanishga qarshi sitokinlarning himoya roli quyidagicha namoyon bo'ladi, ya'ni mediatorlar yallig'lanish markazida mahalliy ishlaydi, biroq, yallig'lanish sitokinlarini ortiqcha va umumlashtirilgan tartibda ishlab chiqarilishi organlar disfunktsiyasiga olib keladi. Tanadagi yallig'lanish jarayonining haddan tashqari namoyon bo'lishini oldini olish uchun sitokinlar va yallig'lanishga qarshi sitokinlarning ishlab chiqarilishi vositachiligida salbiy nazorat mexanizmlari faollashadi [10]. Sitokinlar immun javobni induksiya qilish va amalga oshirish, gemopoezni tartibga solish, yallig'lanish va reparativ jarayonlar uchun zarur bo'lgan hujayralararo aloqalarni ta'minlovchi multifaktorial, ko'p funksiyali mexanizm sifatida ishlaydi [11]. Sitokin ishlab chiqarilishida muvozanat katta fiziologik ahamiyatga ega bo'lib sitokin muvozanatidagi buzilishlar patologik jarayon rivojlanishiga katta hissa qo'shadi.

Bugungi kunda bolalardagi surunkali buyrak kasalliklarida interleykinlar va sitokin potensialini tahlil qilishning dolzarbligi bir qator mualliflarning ilmiy-tadqiqot ishlarida o'z aksini topgan. Masalan, buyraklar tubulointerstitsial shikastlangan bolalar tekshirilganda, jarayonning rivojlanishi yallig'lanish sitokinlarini (IL-1, IL-6, IL-8, yallig'lanish TNF- $\alpha$ , sklerozni qo'llovchi TNF- $\beta$ ) siydik bilan chiqarilishining bosqichma-bosqich o'sib borishi ta'riflangan. Shu bilan birga, yallig'lanishga qarshi IL-10 siydik bilan chiqarilishining bir vaqtning o'zida asta-sekin pasayishi aniqlangan bo'lib, bu esa tubulointerstitsial nefrit rivojlanishida buyrakdagi shikastlanish tarqoq fibrogenez jarayonidan iboratligini tasdiqlaydi [12, 13].

Sitokin profilidagi o'zgarishlar natijasida kelib chiqadigan reaksiyalar kaskadi turlicha bo'ladi. Sitokinlar kamdan-kam hollarda yolg'iz harakat qilishadi. Javob, qoida tariqasida, bir nechta sitokinlarning birgalikdagi ta'sirini aks ettiradi, ularning har biri hujayralarning boshqa omillar sezgirligiga ta'sir qiladi [13]. Paunova S.S.ga [14] ko'ra, sitokinlar kundalik siydik ajratish aniqlash (IL-1, IL-6, IL-8, IL-10) va o'sish omillari (TNF- $\alpha$ , TNF- $\beta$ ) vezikulyar-ureterial reflyuks bilan bog'liq bolalarda tubulointerstitsial buyrak kasalligini bashorat qilish uchun ma'lumot beradi [15, 16].

Yallig'lanish omillari ta'siri ostida (TNF- $\alpha$ , TNF- $\beta$ , IL-1, IL-6 va boshqalar) faollashtirilgan fibroblastlar, miotsitlar va endoteliotsitlar sitokinlar va o'sish faktorlarini ishlab chiqaradi va ular yallig'lanish reaksiyasini uzaytirishda kuchli kimyoviy ta'sir ko'rsatadi [17]. Sitokinlar va o'zgaruvchan o'sish omilining siydik bilan chiqarilishining

ilmiy taxlil natijasi bolalarda buyrak kasalligi shakllanishi va rivojlanishida yallig'lanish jarayoniga nisbatan fibrogenez jarayonining ustunligini isbotlaydi. Shu o'rinda ham ta'kidlash joizki, to'qima yoki organning umumiy tuzilishi va faoliyatini qayta tiklash uchun yallig'lanishga va yallig'lanishga qarshi sitokinlarning muvozanati muxim xisoblanadi, ya'ni ular o'z vaqtida va o'zaro tasir etib, yallig'lanish jarayonini reparatsiyaga yo'naltirib yakunlash qobiliyatiga egadir [16, 18].

Surunkali pielonefritda tubulointerstitsial to'qimalarning progressiv shikastlanishi, mikrobl yallig'lanish, urodinamik buzilish, dismetabolik jarayonlar buzilishi natijasida kelib chiqadi va yallig'lanishni kuchaytiradigan va yallig'lanishga qarshi sitokinlarning muvozanati buzilishi bilan kechadi [19,20,21]. Koren'kov D.G., Pavlova A.L.fikricha, yallig'lanishni kuchaytiradigan IL-8 ni siydikdagi darajasi, zararlangan buyrakdan naychalar orqali chiqqan siydikda surunkali pielonefrit faol bosqichi og'irlik darajasining asosiy markeri sifatida xizmat qilishi mumkin [22].

Shu bilan birga, qon plazmasidagi yallig'lanish sitokinlari (IL-6, IL-8, TNF- $\alpha$ ) darajasi surunkali pielonefritning o'tkir davrida me'yordan 5-7 baravar oshadi, va urosepsis rivojlanish ehtimolini ko'rsatadi. Ortega va A. Fornoni [23] fikri bo'yicha, qon plazmasidagi sitokin darajasini aniqlash o'tkir va surunkali buyrak kasalliklarining keyingi klinik ko'rinishlarini rivojlanishida prognostik ahamiyatga ega bo'lishi mumkin. Siydikdagi IL-6 va IL-8 darajasini aniqlash siydik yo'llarining obstruksiyasi va buyrak chandiqlari rivojlanishini bashorat qiluvchi omil sifatida xizmat qilishi mumkin [24].

Shuni ta'kidlash kerakki, buyrak kasalligining turli bosqichlarida sitokinlarning diagnostik roli katta ahamiyatga yega. Masalan, birlamchi surunkali pielonefrit bilan og'rigan bemorlarning siydigida IL-8 ning yuqori konsentratsiyasi yashirin yallig'lanish va nefroskleroz xavfini ko'rsatadi va remissiya bosqichida IL-8 ning yuqori darajasi an'anaviy diagnostika usullari yordamida aniqlanmagan, lekin buyrakda kechayotgan yashirin yallig'lanish jarayoni mavjudligini tasdiqlaydi.

Merkodanova Yu.A ga binoan, surunkali pielonefrit davomiyligi ortishi bilan siydikda IL-8 darajasining ortishi keyingi yallig'lanish nefroskleroz bilan rivojlanishini isbotlaydi. Bundan tashqari, kasallik davomiyligi ortishi bilan buyrakdagi profibrotik jarayonlar ham kuchayib boradi. Ushbu xol ko'pincha buyrak ssintigrafiyasi yordamida aniqlanuvchi va IL-8 darajasini surunkali pielonefritning barcha variantlarida ortishini va uning sklerotik o'zgarishlar bilan bevosita bog'liqligini isbotlaydi [24, 25].

Bychkovskih V.A fikriga ko'ra, turli nefrourologik patologiyalarda, ayniqsa buyrak operatsiyasidan keyingi erta davrda rivojlanuvchi yagona buyrakning surunkali o'tkir pielonefritida, yallig'lanishni qo'llaydigan va yallig'lanishga qarshi sitokinlar (IL-1, IL-2, IL-4, IL-8, interferon - $\gamma$ ) muvozanatining buzilishi kuzatiladi. Bunda qon zardobida yallig'lanishni qo'llaydigan sitokinlar ko'rsatkichi ortadi va yallig'lanishga qarshi sitokinlar ko'rsatkichi esa kamayadi. Sitokin profilining kuzatilgan buzilishi bakterial infeksiyaning faollashuvini va bunday bemorlarda tananing himoya immuniteti pasayishini aks ettiradi [26, 27,28].

Zaharova N.B. va boshk. fikriga ko'ra, siydikdagi yallig'lanishni qo'llaydigan sitokinlarning asosiy guruhi tarkibining ko'payishini koralloidli nefrolitiaz va pielonefrit bilan og'rigan bemorlarda buyrak parenximasi shikastlanishining eng muhim ko'rsatkichlaridan biri deb aytish mumkin. Kalkulez pielonefritning kuchayish davrida yallig'lanishni qo'llovchi sitokinlar ko'rsatkichlari ortadi va bu buyrak parenximasida infiltratlar ko'payishi va siydik kanalchalarining epiteliya qoplamasining shikastlanish darajasi bilan birga keladi. Siydikdagi yallig'lanishni qo'llovchi sitokinlar darajasining ortishi ularni tubulyar epiteliy tomonidan ishlab chiqarilishining ortishi natijasi deb hisoblanishi mumkin.

Siydik yo'llariga patogen mikroorganizmlarning kirishi siydik yo'llari epiteliy qoplamasi darajasida immun javob reaksiyasini rivojlanishiga olib keladi. Immun reaksiya namoyon bo'lishi IL-1, IL-6 va IL-8 kabi yallig'lanish sitokinlarining faol ishlab chiqarilishida kuzatiladi. Sitokinlar to'qima tuzilmalari infiltratsiyasini keltirib chiqaradi, siydik yo'llari yallig'lanish reaksiyasi makrofaglar va leykotsitlar tomonidan o'rab olinishi natijasida sitokinlar tubulointerstitsial yallig'lanishni faollashtiruvchi omillardan biriga aylanadi [29, 30].

Bulatova A.V. va boshq., o'z ilmiy izlanishlari natijasida bolalarda surunkali pielonefritning qo'zish davrida yallig'lanishni kuchaytiruvchi sitokinlar (TNF- $\alpha$  va IL-8) konsentratsiyasi xam parallel ravishda ortishini aniqladilar. Bundan tashqari, obstruktiv pielonefritning og'ir shakllari rivojlanishi ham yallig'lanishni qo'llovchi sitokinlarning yuqori darajasi bilan bogliq tarzda kechadi. Pielonefrit kechishining turli xil variantlarida sitokin arxitektonikasidagi bu siljishlar nafaqat sitokin tarkibidagi nomutanosiblikni, balki mavjud

surunkali pielonefrit kuchayishini yoki kasallikning yangi turi rivojlanish xavfini tasdiqlaydi [30].

Slobodyan E.I. va boshq. fikriga ko'ra, yallig'lanishni kuchaytiruvchi sitokinlar IL-4, IL-10, IL-12 va IL-17 konsentratsiyasining ortishi va yallig'lanishga qarshi sitokinlar konsentratsiyasining kamayishi, surunkali pielonefritning remissiya davrida an'anaviy tekshirish usullari bilan aniqlanmaganda ham latent yallig'lanish jarayonining saqlanib qolishini tasdiqlaydi va faol fibrogenez jarayoni saqlangan xolda keyingi bosqichlarda buyrak disfunktsiyasi rivojlanishi uchun asos bo'ladi [31].

So'nggi yillarda o'tkazilgan turli tadqiqotlar natijalariga ko'ra, buyrak kasalliklarida sitokinlar profili va interleykinlarni buyrak to'qimalari shikastlanishining biomarkeri sifatida qo'llash mumkin. Masalan, IL-8 pielonefritning o'tkir epizodidan keyin paydo bo'lgan buyrak chandiqlarining prognostik biomarkeri bo'lib xizmat qilishi mumkin. IL-6ni gemolitik-uremik sindromning o'tkir bosqichidan keyin rivojlanadigan surunkali buyrak shikastlanishining biomarkeri sifatida qo'llash mumkin [32, 33].

O'z navbatida ta'kidlash joiz, Karzakova L.M., va boshq., surunkali glomerulonefritning patomorfologik varianti bo'yicha sitokin holatini o'rganishlari natijasida qon zardobidagi sitokinnarning eng yuqori disbalansi membranoproliferativ glomerulonefrit bilan og'riqan bemorlarga xosdir degan xulosaga keldilar. Mualliflar olingan ma'lumotlar natijasida surunkali glomerulonefritning turli xil variantlarida o'ziga xos bo'lgan immunpatogenetik xususiyatlar mavjudligini va bu kasallikni davolashning yangicha, adekvat usullarini izlash uchun asos bo'lishini takidlashdi [34].

Beglyarov R.O. malumotlariga ko'ra, mahalliy himoya reaksiyalarini tartibga solish asosan siydikning sitokin profilining holatiga bog'liq. Surunkali glomerulonefritning turli xil klinik variantlarini tekshiruvda qon zardobida yallig'lanishni qo'llaydigan sitokinnarning ustunligi aniqlandi [35]. Shu bilan birga, adabiyot manbalardagi malumotlarga mos ravishda IL-1 va TNF- $\alpha$  tarkibida kasallikning nafaqat o'tkir, balki remissiya bosqichida xam eng muhim farqlar aniqlandi [36]. Xususan, surunkali glomerulonefritning turli xil klinik variantlarida qon zardobidagi sitokinlar ko'rsatkichining nomutanosibli va yallig'lanishni qo'llovchi sitokinlar ishlab chiqarilishining ustunligi aniqlandi. Eng muhim farqlar IL-1 va TNF- $\alpha$  tarkibida topilgan bo'lib, organizmda faol yallig'lanish jarayoni mavjudligini tasdiqlaydi [37].

Anders H. J. fikriga ko'ra buyrak yallig'lanishida asosiy ko'rsatkich sifatida IL-1 $\alpha$  va IL-1 $\beta$  asosiy rol o'ynaydi: bu interleykinlar deyarli barcha buyrak hujayralarida uchraydi va sitokinlar va xemokinnarning chiqarilishini yanada kuchaytiradi [38]. Koryakova N.N. surunkali glomerulonefritda qon zardobidagi interleykinlar miqdorini tekshirganda, kasallikning nafaqat patogenetik rivojlanish bosqichlarida sitokinnarning o'zaro muhim o'rin tutishini, balki turli klinik va morfologik variantlarida xam sitokin profili o'zaro farqlarini aniqladi. Eng yuqori sitokinlar disbalansi membranoproliferativ glomerulonefritga xosligi ma'lum bo'ldi [39]. Muallifning fikricha, ushbu ilmiy izlanish natijalari asosida olingan ma'lumotlar, surunkali glomerulonefritning turli xil variantlarida immunpatogenetik xususiyatlar mavjudligini tasdiqlaydi hamda bemorlarni davolashda yangicha, adekvat usullarni asoslash va qo'llashni zarurligini tasdiqlaydi.

Kolesnyk M. va boshq. fikriga ko'ra, surunkali glomerulonefrit kechishi jarayonida yallig'lanishga qarshi sitokinnarga nisbatan yallig'lanishni qo'llovchi sitokinnarning ustunlik qilishini asoslovchi ko'rsatkichlar kasallikda immunsupressiv terapiya natijalarini prognoz qilishda muxim ahamiyatga ega [40]. Latifova N.F va boshq. fikriga ko'ra, surunkali buyrak kasalligida, asosiy immunitet mexanizmidan qat'i nazar, glomerulyar apparatlarga zarar yetkazilishi leykotsitlar, makrofaglar va o'zlarining glomerulyar hujayralarini faollashtiradigan sitokinlar, xemokinnlar va antimikrob peptidlar kabi yallig'lanish mediatorlarini ishlab chiqarish bilan tavsiflanadi [41].

Ma'lumki, sitokinlar va antimikrob peptidlar sintezining ko'payishi, limfotsitlar va makrofaglar tomonidan yallig'lanish reaksiyasining kuchayishiga olib keladi. Shu bilan birga, interleykinlarni sintez qilishga qodir fibroblastlarning o'zgarishini o'zgartiradigan mezangial hujayralar faollashadi. Surunkali buyrak yetishmovchiligida bemorlar nazorat guruh bilan taqqoslaganda etiologiyasidan qat'iy nazar, qondagi yallig'lanishni qo'llovchi sitokinlar konsentratsiyasini ortishi kuzatiladi. Shu jumladan, surunkali glomerulonefrit bilan og'riqan bemorlardagi yallig'lanish jarayonida IL-8 faol ishlab chiqariladi va eng yuqori ko'rsatkichi kuzatiladi. Olingan ilmiy-tadqiqot natijalariga asoslanib, olimlar surunkali buyrak kasalliklaridagi yallig'lanish patogeneza sitokinlar va antimikrob peptidlarning muhim roli va ularni surunkali buyrak shikastlanishining dastlabki belgisi

sifatida qo'llashning asosligi haqida xulosa qilishgan [40, 41].

Yuqorida aytganimizdek, sitokinlar ishlab chiqarilishining nomutanosibligi surunkali buyrak kasalligi progressiyasi va asoratlari rivojlanishiga olib keladi. [42]. Shu jumladan, Murkamilov I.T. va boshq., o'z ilmiy izlanishlari natijasida surunkali buyrak kasalligi bo'lgan bemor bolalarda glomerulyar filtratsiya tezligi (GFT) 60 ml/min pastroq bo'lganida IL-6 mikdorining ko'payishini asoslab berganlar [43]. Surunkali buyrak kasalligida, qondagi IL-6 ko'rsatkichi glomerulyar filtratsiya tezligi va diastolik qon bosimi ko'rsatkichi bilan chambarchas bog'liqdir. Shu bilan birga, tadqiqotchilar yallig'lanishni qo'llovchi sitokinlar, xususan IL-6 ishtirokida surunkali buyrak kasalligi rivojlanishining patofiziologik mexanizmlari juda xilma-xilligi, murakkabligini va o'z navbatida ushbu soxa mutaxassislari tomonidan keyingi bosqichlarda chuqur o'rganish hamda ilmiy-izlanishlar olib borish zarurligini takidladilar.

Surunkali buyrak yetishmovchiligida yallig'lanishni qo'llovchi sitokinlarning yallig'lanishga qarshi sitokindan ustunligi surunkali buyrak kasalliklaridagi yallig'lanish patogenezida sitokinlar o'rtasidagi o'zaro ta'sirning muhim rolini tasdiqlashga imkon beradi [44]. Shu bilan birga, sitokin profillaridagi farqlar surunkali buyrak kasalligi etiologiyasi va kasallikda uchraydigan boshqa o'zgarishlar bilan bog'liq bo'lishi ham mumkin [45,46].

**Xulosa.** Shunday qilib, bolalardagi me'yoriy va patologik jarenlarda, xususan surunkali buyrak kasalligi immunpatogenetik rivojlanishida sitokin profili boshqaruvi katta ahamiyatga ega va muxim o'rin tutadi. Sitokin mediatorlarining turli xil xususiyatlari organizmni yuqumli agentlardan himoya qilish va to'qimalarni tiklashga xizmat qiladi. Birinchi navbatda, sitokinlar mahalliy himoya jarayonlarining rivojlanishini tartibga soladi, yallig'lanish reaksiyasining shakllanishini sodir etadi. Shuning uchun ham yallig'lanishni qo'llovchi va yallig'lanishga qarshi sitokinlarning tarkibi va ularning nisbatini yallig'lanish jarayoni va fibrozning kuchayishini eng ob'ektiv ko'rsatkichlari deb hisoblash mumkin. Sitokin tizimidagi nomutanosiblikni bashorat qilish, surunkali kasallikning biomarkeri sifatida, kasallikni kechishi va davolash samaradorligini baholashda qo'llanilishi mumkin. Adabiyot ma'lumotlarini tahlil qilish surunkali buyrak kasalliklarida sitokin holatini o'rganishning ilmiy va amaliy ahamiyatini yoritib berdi.

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