УДК: 616.61-001:611.018.74:616.98:578.834.1-07

COVID-19 BILAN KASALLANGAN BOLALARDA INFEKSIYA SHTAMMLARIGA KO'RA SARS-COV.2 MARKER PROFILINING XUSUSIYATLARI

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Respublika ixtisoslashtirilgan pediatriya ilmiy-amaliy tibbiyot markazi, Toshkent

РЕЗЮМЕ

В данной статье обследованы дети узбекской популяции, больные COVID-19, в возрасте от 3 месяцев до 18 лет. В ходе исследования установлена частота циркуляции штаммов SARS-CoV.2 возрастная восприимчивость к их инфицированию. В течении COVID-19 у детей различают не менее 4-х вариантов серологического профиля, проявления которых варьировали от вида штаммов (мутаций) SARS-CoV.2 и фазы болезни. Высота инфекционного индекса и высокая контагиозность больных детей соотносилась с инфицированием delta- и особенно с gamma-штаммами вируса. В условиях активной репликациии SARS-CoV.2 ранний гуморальный ответ ассоциировался с британским (alpha) и китайским (wuhan) штаммами; поздний – с delta штаммом и ареактивность иммунной системы – с бразильским (gamma) штаммом, что отчасти может свидетельствовать не только о врожденной иммунологической реактивности детей, но и об антигенных свойствах SARS-CoV.2 и дозы вирусной нагрузки в условиях мутации вируса.

Ключевые слова: *Covid-19, популяция штаммов SARS-CoV.2, серологические маркеры SARS-CoV.2, дети.*

SUMMARY

In this study, children from the Uzbek population aged 3 months to 18 years with COVID-19 were examined. The research determined the circulation frequency of SARS-CoV-2 strains and the age-related susceptibility to infection. In the course of COVID-19 in children, at least four variants of the serological profile were identified, with manifestations varying depending on the SARS-CoV-2 strains (mutations) and the phase of the disease. A high infectious index and significant contagiousness among sick children were associated with infection by the delta and especially the gamma variants of the virus. Under conditions of active SARS-CoV-2 replication, an early humoral response was associated with the British (alpha) and Chinese (Wuhan) strains; a delayed response was linked to the delta strain, while immune system non-reactivity was associated with the Brazilian (gamma) strain. This may partially reflect not only the innate immunological reactivity of children, but also the antigenic properties of SARS-CoV-2 and the viral load dose under conditions of viral mutation.

Keywords: *COVID-19, SARS-CoV-2 strain population, SARS-CoV-2 serological markers, children.*

2019-yilda butun dunyoni qamrab olgan SARS-Cov-2 keltirib chiqargan COVID-19 bilan bog'liq pandemiya bugungi kunda ham tarqalishda davom etmoqda, bu esa infeksiya avj olishining o'ziga xos hududiy mavsumiyligini belgilaydi [30,31,10,12,16 va boshq.]. COVID-19 uzoq davom etuvchi tibbiy-ijtimoiy va iqtisodiy salbiy oqibatlar ("koronakrizis") bilan tavsiflanadi. SARS-Cov-2 tarqalishining tez sur'ati yuqori mutagenlik bilan bog'liq bo'lib, ular orasida virusning yuqish tezligi, virusning immun javobdan qochishi, tizimli vaskulitlar rivojlanishi bilan qon tomir endoteliysiga virulentlik va troplik kabi xususiyatlarini oldindan belgilaydigan differensiatsiyalangan genetik liniyalarga ega 6 ta shtamm (alpha, betta, gamma, delta, yota, lambda) barqaror ekanligi aniqlandi [2, 5, 6, 13 va boshq.]. Kasallikning og'irligini shakllantiruvchi makroorganizmning immun javobi ham muhim ahamiyatga ega [26,27,28]. Immunitet disbalansi fonida SARS-Cov-2 ning yaqqol ifodalangan replikatsiyasida kasallik og'ir kechib, interstitsial pnevmoniya, limfopeniya rivojlanishi va tug'ma va orttirilgan immun hujayralari tomonidan sitokinlarning boshqarib bo'lmaydigan "sitokin bo'roni" shaklida kechadi, bu esa 8-19% hollarda O'RDS, nafas yetishmovchiligi, ichki a'zolar patologiyasi va 6% gacha o'limga olib keladi [9,18,19,32,33]. SARS-CoV-2 va makroorganizmning o'zaro ta'sir mexanizmlari, virus antigenlari bilan uchrashganda postinfeksion immunitetning shakllanishi ilmiy va tibbiy hamjamiyatlarda munozarali mavzu bo'lib qolmoqda. Ushbu munozaraning sababi, bir tomondan, mavjud infeksiyani tashxislash uchun o'ziga xos antitanachalarning yordamchi ahamiyati, boshqa tomondan - o'tkazilgan infeksiyaga immun javobni baholash va emlash monitoringi uchun asosiy parametr sifatida, uchinchi tomondan - kasallik bosqichida fikr yuritish/ajratish imkoniyati va to'rtinchi tomondan - immunokimyoviy xususiyatlari bo'yicha boshqa koronaviruslarning o'ziga xos antitanachalari va IgM revmatoid omiliga o'xshash "kesishgan" antitanachalarning mavjudligi, test tizimlarining past sezgirligi yoki kasallikning seronegativ bosqichida biomaterial olish yoki immuniteti past bo'lgan

bemorlarni tekshirish natijasida noto‘g‘ri ijobiy va/yoki noto‘g‘ri salbiy javoblar natijasida diagnostika tizimlarining nomukammalligi bilan bog‘liq. Shu sababli, ushbu muammoni hal qilish uchun COVID-19 sharoitida koronavirus serologik markerlarining o‘zaro bog‘liqligini o‘rganish dolzarb masala bo‘lib qolmoqda.

TADQIQOTNING MAQSADI bolalarda COVID-19ni yuqtirish shtammlariga ko’ra SARS-Cov.2 marker profilining xususiyatlarini aniqlashdan iborat edi.

TADQIQOT MATERIALI VA USULLARI

2021-yil iyun-dekabr oylarida pandemiya davrida COVID-19 bilan kasallangan 2 oylikdan 18 yoshgacha bo‘lgan 108 nafar bola, o‘g‘il bolalar 44,4%, qiz bolalar 55,6%, kuzatuv ostida bo‘lgan. COVID-19 tashhisi “Clinical management of severe acute respiratory infection when novel coronavirus (2019-nCoV) infection is suspected: interim guidance, WHO-2020” tavsiyalari asosida qo‘yildi [20]. Bemorlarni tanlash burun/og‘iz-halqumdan olingan surtmalarni SARS-CoV-2 RNKga tekshirishning ijobiy natijasi asosida amalga oshirildi. Surtma namunalaridan “M-Sorb-OOM” reagentlar to‘plamidan foydalangan holda nukleosorbtsiya usuli bilan RNK ajratib olindi. Ajratib olingan RNK konsentratsiyasi va tozaligi BioSpec-nano (Shimadzu Biotech, Japan) spektrofotometri yordamida o‘lchandi. SARS-CoV.2 RNK deteksiyasi “Biotest- SARS-CoV-2” to‘plamidan foydalangan holda real vaqt rejimida teskari transkripsiyali PZR usuli bilan DTprime - (DNK Texnologiya, Rossiya) amplifikatorida amalga oshirildi. IFA usuli yordamida qon zardobida “Mindray MR-96A” apparatida “DIA.PRO” (Italiya) firmasining to‘plamlaridan foydalangan holda IgM va IgG ning ikki sinfidagi SARS-CoV.2 ga qarshi antitanalar aniqlandi.

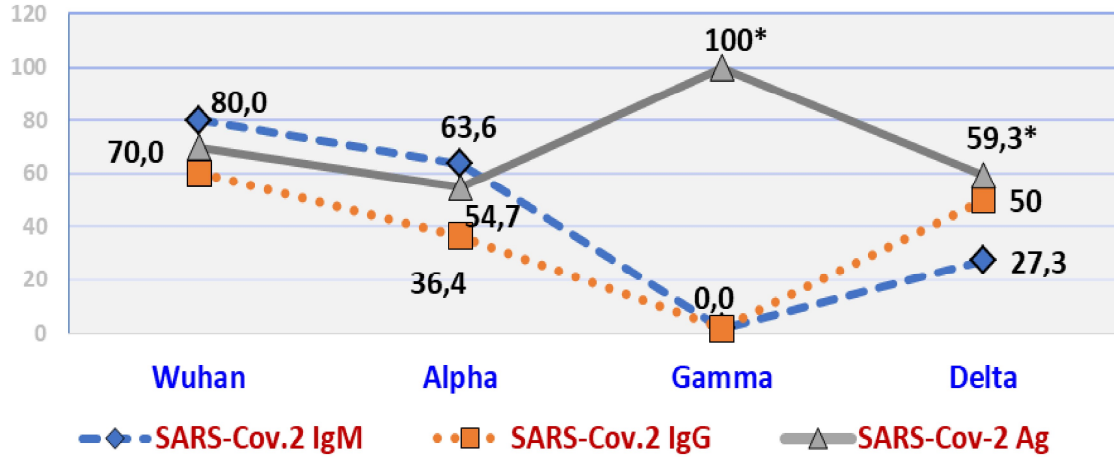
Olingan barcha natijalar Statistic 6 maxsus dasturi yordamida parametrik Styudent t-statistikasi usulida matematik qayta ishlandi, tavsifiy statistika va qiymatlarning dispersion tengligini hisobga olgan holda mustaqil guruhlarning qiyosiy tahlili o‘tkazildi.

NATIJALAR VA ULARNING MUHOKAMASI

Tekshirilgan bemorlarda turli mutatsiyalarni aniqlash uchun SARS-Cov.2 genotiplash tahlili virusning to‘rtta genetik kichik turini (shtammlarini) aniqladi, bu yerda bolalar asosan hind delta shtammi bilan kasallangan (77,8%). Bir xil chastotada Xitoyning wuhan-shtammi (9,2%) va Britaniyaning alpha-shtammi (10,2%) va nisbatan kam hollarda Braziliya gamma-shtammi (2,8%) qayd etilgan. Shu bilan birga, bolalarning SARS-Cov.2 ga sezuvchanligining yoshga bog‘liq xususiyatlariga e’tibor qaratildi, bu yerda eng past o‘rtacha yosh Braziliya shtammi bilan kasallangan bolalar orasida 0,76±0,26 yoshni tashkil etdi, aksincha, kattaroq yoshdagi bolalar hind (8,1±0,3 yosh) va Britaniya (6,1±0,5 yosh) shtammlariga sezgirliklari aniqlandi ($r<0,001$). Ushbu fakt, bir tomondan, makroogranizmning virus kirishiga tug‘ma immun javobining bir xil bo‘lmagan ishtiroki, boshqa tomondan, virusning yuqumliligi, immun javobdan qochishi va virulentligining yangi xususiyatlarini keltirib chiqaradigan genom SARS-Cov.2 tuzilishidagi muhim o‘zgarishlarni ko‘rsatdi. Shunga ko‘ra, antigen tasir mexanizmlari ilmiy tibbiyot hamjamiyatlarida munozarali masala bo‘lib qolmoqda [1,9,14,15,22].

Tekshirilgan bolalarda SARS-Cov.2 marker profilini o‘rganish shuni ko‘rsatdiki, 100% tasdiqlangan RT-PCR tahlili fonida umumiy immunoglobulinlar va o‘ziga xos antigenning ijobiy deteksiyasi mos ravishda 48,7% va 65,9% hollarda qayd etildi. Shu bilan birga, IgM va IgG sinfidagi immunoglobulinlar 29,1% va 48,7% hollarda aniqlangan, immunitet shakllanishining turli kinetikasi bilan - IgM IgG dan oldin, keyin va birgalikda aniqlandi.

Infeksiya shtammiga ko‘ra serologik markerlarning o‘zaro bog‘liqlik tendensiyalarini tahlil qilish shuni ko‘rsatdiki (1-rasm), SARS-CoV.2 ning RNK aniqlanishi fonida Braziliya gamma-shtammi bilan kasallanish sharoitida spetsifik antigen 100% hollarda aniqlandi. Bu esa bemorlarning infeksion indeksi va kontagiozligining yuqoriligidan dalolat berdi. Delta-shtamm holatlarida spetsifik Ag va IgM aniqlanish chastotasi nisbati 32% ga farq qilib, antigen ustunlik qildi ($p<0,001$).

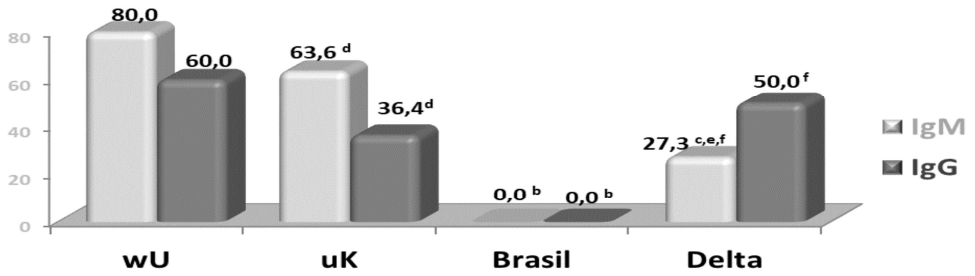


1-rasm. Tekshirilgan bolalarda SARS-CoV-2 biomarkerlari, %
Farqlar ishonchliligi: * - Ag va IgM o‘rtasida ($p<0,05$-$0,001$).

Wuhan va alpha-shtammlar bilan kasallangan bolalarda ko‘rib chiqilayotgan parametrlarning o‘zaro bog‘liqligiga kelsak, ularning qiymatlari IgM ning mos ravishda 10% va 8,9% ga ustunlik qilish tendensiyasiga ega bo‘ldi (p>0,05).

IgG parametrlarining spetsifik antigenga nisbatan tahlili gamma-shtamm bilan kasallangan bemorlardan tashqari hech qanday farqni aniqlamadi, ular uchun himoya antitanachalarining to‘liq yo‘qligida 100% Ag aniqlanishi xos bo‘ldi (p<0,001).

SARS-CoV-2 antitanachalarining aniqlanishi ham infeksiya shtammiga ko‘ra farq qildi (2-rasm), bu yerda IgM ning eng yuqori chastotasi wuhan-shtamm (80%) va alpha-shtamm (63,6%, p<0,001) bilan kasallangan bolalar orasida aniqlandi. 27,3% holatda antitanachalar delta-shtamm bilan zararlanganda va COVID-19 ning Braziliya gamma-shtammi bilan kasallangan bolalarda immun tizimining gumoral javobining to‘liq yo‘qligi aniqlandi. IgG ga nisbatan shunga o‘xshash ko‘rinish ko‘rib chiqildi, delta-shtamm bilan kasallangan bemorlar bundan mustasno, bu yerda chastota IgM qiymatidan 1,8 baravar yuqori bo‘ldi (p<0,001).



2-rasm. COVID-19 bilan kasallangan bolalarda SARS-CoV-2 ga turli sinf Ig ning tarqalish chastotasi, %
Farqlar ishonchliligi: a - I-II; b - I-III; c - I-IY; d - II-III; e - II-IY; f - III-IY (p<0,05-0,001).

SARS-Cov.2 shtammlarining turiga ko‘ra turli sinflardagi antitanalarning vaqti va miqdoriy kinetikasi ham farq qildi (1-jadval), bu yerda IgM ning eng past o‘rtacha darajasi Wuhan shtammi bo‘lgan bemorlarda (3,07±0,91 birlik/ml) qayd etilgan, bu delta va gamma shtammlari bo‘lgan bolalar guruhidan statistik jihatdan sezilarli darajada farq qildi (p<0,05-0,001). Alpha-infitsirlangan bolalar guruhida IgM Xitoy shtammiga chalingan bemorlar ko‘rsatkichlaridan yuqori bo‘lsa-da, ishonchli farq qilmadi. Spetsifik IgG dinamikasiga kelsak, umuman olganda, barcha tekshirilgan bolalar orasida ularning qondagi mavjudligi o‘rtacha 7,94±0,7 kun ichida o‘rganilayotgan guruhlar ichida antitanachalarning turli miqdoriy darajalari bilan aniqlandi. Wuhan-shtamm bilan kasallangan bemorlarda IgG sinfiga mansub nisbatan “kechki” antitanachalar 13,5±1,1 kunda 3,74±0,70 yed/ml titrda aniqlandi (p<0,01-0,001). Kasallikning deyarli bir xil davrida (4-6 kun) alpha- va delta-shtammlar bilan kasallangan bemorlar orasida IgG mos ravishda 5,35±0,51 birlik/ml va 4,40±0,30 birlik/ml miqdorda qayd etilgan.

1-jadval

COVID-19 bilan kasallangan bolalarda SARS-CoV.2 ga turli sinflardagi Ig shakllanishi dinamikasi

Biomarker	SARS-CoV-2 ning turli shtammlari bilan kasallangan bolalar			
	Wuhan	alpha	gamma	delta
SARS-Cov.2 IgM umumiy birlik/ml	3,07±0,91 7,50±1,7	3,75±1,07 d 4,67±0,7	0,0±0,0 b 3,45±0,1 b	5,45±0,36 s, f 4,96±0,3 s
SARS-Cov.2 IgG umumiy birlik/ml	3,74±0,70 a 13,5±1,1 a	5,35±0,51 d 4,67±0,7	0,0±0,0 b 3,45±0,1 b	4,40±0,30 f 5,64±0,8 s, f

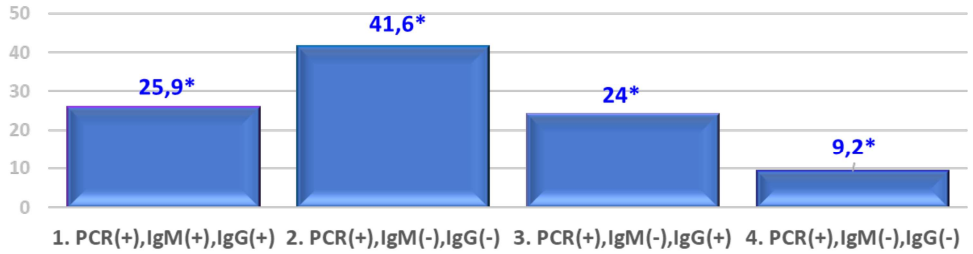
Farqlar ishonchliligi: a - I-II; b - I-III; c - I-IY; d - II-III; e - II-IY; f - III-IY (p<0,05-0,001).
Surat - o‘rtacha miqdoriy daraja, maxraj - kasallik kuni.

Shu bilan birga, bolalarda COVID-19 ning simptomatik davrining dastlabki 5 kunida immunoglobulinlar dinamikasining boshqa tahlili Britaniya, keyin Xitoy va Hindiston shtammlari bo‘lgan bemorlarda IgM ning eng erta ishlab chiqarilishini ko‘rsatdi. Ushbu davrda IgG (+) kasalliklari faqat Britaniya shtammi bilan kasallangan bemorlarga xos bo‘ldi (p<0,001).

Demak, SARS-CoV.2 ning Britaniya va Xitoy shtammlari nisbatan “erta” antigen imprintingiga ega bo‘lgan, bu immunologik xotiraning faolligi va koronavirus infeksiyalarining oldingi variantlari (MERS/SARS-CoV) bilan yaqin qarindoshligining ehtimoliy dalili bo‘lib xizmat qilgan, virus mutatsiyasining yangi varianti bilan to‘qnashish sharoitida antigenlarga qarshi ishlab chiqarilgan antitanalar va T-hujayralarning “muzltilgan” repertuaridan foydalanish imkoniyati bilan [4, 8, 11, 19, 20, 21, 25.]. Bundan farqli o‘laroq, SARS-CoV-2 ning delta shtammi himoya antitanalarining nisbatan “kech” shakllanishi bilan ajralib turdi. Infeksiyaning Braziliya gamma-shtammi sharoitida immun tizimi mutlaq

areaktivligi bilan ajralib turdi. Koronavirus infeksiyasini o‘rganish bo‘yicha jahon tadqiqotchilarining natijalarini hisobga olgan holda, katta yoshli aholi orasida SARS-CoV.2 serologik biomarkerlari dinamikasining o‘rtacha ko‘rinishi IgM uchun 5,2-17,5 kun va IgG uchun 9,2-23,2 kun oralig‘ida ekanligini hisobga olsak [3, 7, 16, 17, 23, 24, 28, 29], shuni ta’kidlash mumkinki, o‘zbek populyatsiyasining COVID-19 bilan kasallangan bolalari uchun G sinfidagi himoya antitanachalarining nisbatan erta paydo bo‘lishi xos bo‘lib, bu bola organizmining immun javobining genetik determinatsiyasi bilan ham oldindan belgilanishi mumkin.

SARS-CoV.2 ning turli xil serologik profillarining qiyosiy tahlili PZRning ijobiy natijasi bilan birlashtirilgan antitanalarning ijobiy va salbiy natijalari kombinatsiyasining kamida 4 ta variantini aniqlashga imkon berdi (3-rasm), bu faqat ijobiy PZR surtmasi (PCR+/IgM-/IgG-) bilan tavsiflangan bemor bolalarning 41,6% da kasallikning erta bosqichini (ehtimol, kech inkubatsion) talqin qilishga imkon berdi (p<0,02).



3-rasm. Tekshirilgan bolalarda COVID-19 marker profili variantlari, %
* - guruhlar o‘rtasidagi farqlarning ishonchliligi (p<0,05-0,001)

Kasallikning boshlang‘ich bosqichi (PCR+/IgM+/IgG-) bemorlarning 9,2% da kuzatildi, bu IgM ishlab chiqarilishi bilan organizmning immun javobining boshlang‘ich rivojlanishini aniqladi (p<0,001). Barcha ko‘rsatkichlar (PCR+/IgM+/IgG+) verifikatsiyasi bilan ajralib turadigan yangi COVID-19 ning faol bosqichi bemor bolalarning to‘rtdan bir qismida (25,9%) qayd etildi. 3-variant (24% - PCR+/IgM-/IgG+) alohida e’tiborga loyiq bo‘lib, qonuniyatga zid ravishda virusning molekulyar tasdiqlanishi qonda IgG ishtirokida maxsus IgM ning yo‘qligi bilan kechdi. Bemorlar ma’lumotlari tahlil qilinganda, ushbu bolalarning aksariyati anamnezida turli og‘irlikdagi COVID-19 o‘tkazganligi aniqlandi, bu esa ijobiy yuqori avid IgG-antitanachalar va SARS-CoV-2 bilan qayta kasallanish mavjudligini taxmin qilish imkonini berdi.

Keyinchalik, SARS-CoV.2 ning 4 ta serologik variantlarining infeksiya shtammlari turiga ko‘ra tarqalish xususiyatlarini o‘rganish shuni ko‘rsatdiki (2-jadval), birinchi variant RNA+/IgM+/IgG+ ko‘rinishida nisbatan tez-tez va deyarli bir xil chastota bilan COVID-19 bilan kasallangan bemorlar orasida wuhan- va alpha-shtammlari bilan mos ravishda 40% va 54,4% hollarda (boshqa shtammlarga nisbatan r<0,02) uchragan.

2-jadval

Tekshirilgan bemor bolalarda turli shtammlar bilan zararlanishiga qarab SARS.Cov.2 serologik profili

Marker profili SARS.Cov.2	NIK bilan kasallangan bolalar, SARS Cov.2 ning turli shtammlari bilan kasallanganlar							
	Wuhan (I)		Alpha (II)		Gamma (III)		Delta (IY)	
	%	Ag (+)	%	Ag (+)	%	Ag (+)	%	Ag (+)
IgM (+)/IgG (+)	40,0±15,4	20,0±12,6	54,5±15,0 d	36,6±14,5	0,0±0,0 b	0,0±0,0	21,4±4,4	15,4±3,9
IgM (-) /IgG (-)	0,0±0,0 a	0,0±0,0	45,5±15,0 d	18,1±11,6 d	100±0,0 b	100±0,0 b	44,0±5,4 c, f	21,4±4,4 c, f
IgM (-) /IgG (+)	20,0±12,6	20,0±12,6	0,0±0,0	0,0±0,0	0,0±0,0	0,0±0,0	28,6±4,9 e, f	20,2±4,3
IgM (+)/IgG (-)	40,0±15,4 a	30,0±14,4	0,0±0,0	0,0±0,0	0,0±0,0 b	0,0±0,0	5,95±2,5 c, e, f	2,3±1,6
Kasallik kuni	10,6±1,6 a		3,84±0,4		3,5±0,3 b		4,6±0,6 s	

Farqlar ishonchliligi: a - I-II; b - I-III; c- I-IY; d- II-III; e-II-IY; f-III-IY (p<0,05-0,00).

Musbat spetsifik antigen bilan nisbat teng darajada bo‘ldi (wuhan-, alpha- va delta-shtammlari bo‘lgan bemorlarda mos ravishda 20, 36,6% va 21,4%, p>0,05). Ikkinchi variant (RNK+/IgM-/IgG-) musbat antigen bilan birgalikda Braziliya gamma-shtammi bilan kasallangan yangi COVID-19 bilan kasallangan bemor bolalar orasida xarakterli bo‘lgan (100% hollarda, boshqa bolalar guruhlariga nisbatan p<0,001). Ushbu variant

45,5% va 44% hollarda alpha- va delta-shtammlari bo‘lgan yangi COVID-19 bilan kasallangan bemorlarda aniqlangan, bunda deyarli bir xil chastotada Ag (+) mos ravishda 18,1% va 21,4% bolalarda aniqlangan (Xitoy va Braziliya shtammlari bilan kasallangan bemorlarga nisbatan p<0,01).

Marker profilining uchinchi varianti (RNK+/IgM-/IgG+) faqat wuhan (20%) va delta (28,6%) shtammlari bilan kasallangan bemor bolalar orasida uchradi, shu bilan birga 20% hollarda antigenning aniqlanishi qayd etildi. Oxirgi variantga (RNK+/IgM+/IgG-) kelsak, profilning umumiy ko‘rinishi oldingi variantni takrorlaydi, ammo wuhan-shtammli bolalar orasida uning qayd etilishi ustunlik qiladi (delta-shtammli bemorlarning 5,95% ga nisbatan 40%), 30% hollarda spetsifik antigen nisbiy aniqlanadi (delta-shtammli bemorlarning 2,3% ga nisbatan, p<0,001).

XULOSA

2021-yil iyul-dekabr oylarida COVID-19 pandemiyasi sharoitida o‘zbek populyatsiyasidagi bolalar orasida SARS-CoV.2 shtammlari sirkulyatsiyasida Hindistonning delta shtammi ustunlik qildi. Kamroq darajada Britaniya (alpha), Xitoy (wuhan) va Braziliya (gamma) shtammlar qayd etildi. Shu bilan birga, infeksiyaga yoshga bog‘liq sezuvchanlik aniqlandi, bu SARS-CoV.2ga tug‘ma immun javobning bir xil bo‘lmagan ishtiroki va antigen impritingining mumkin bo‘lgan mexanizmlarini ko‘rsatdi. Delta-shtamm bilan zararlanishga yuqori sezuvchanlik katta yoshdagi bolalarda, kichik yoshdagi bemorlarda esa wuhan- va alpha-shtammlari bilan zararlanishga yuqori sezuvchanlik kuzatildi. Noyob Braziliya gamma shtammi faqat chaqaloq bolalarning sezuvchanligi bilan ajralib turdi. Shu bilan birga, COVID-19 sharoitida bolalarda SARS-CoV.2 marker profilini o‘rganish shuni ko‘rsatdiki, bemorlarning aksariyati kasallikning simptomatik davrining erta va faol bosqichlarida bo‘lgan (65,9%). Bolalarda COVID-19 kechishida serologik profilning 4 ta varianti farqlanadi, ularning namoyon bo‘lishi infeksiya turiga (mutatsiyalariga) va kasallik bosqichiga qarab o‘zgardi. Infeksion indeksning yuqoriligi va bemor bolalarning yuqori kontagiozligi SARS-CoV-2 ning delta-, va, ayniqsa, Gamma-shtammlari bilan kasallanish bilan bog‘liq bo‘ldi. Koronavirusning faol replikatsiyasi sharoitida (SARS-CoV-2 RNA+/Ag+) erta gumoral javob Britaniya (alpha) va Xitoy (wuhan) shtammlari bilan bog‘liq bo‘ldi; kech - delta shtammi va immunitet tizimining areaktivligi - Brazils (gamma) shtammi bilan bog‘liq bo‘lib, bu qisman nafaqat bolalarning tug‘ma immunologik reaktivligini, balki SARS-CoV-2 ning antigen xususiyatlarini va virus mutatsiyasi sharoitida virus yuklamasining dozasini ham ko‘rsatishi mumkin.

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