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QANDLI DIABET 2-TURI BILAN KASALLANGAN BEMORLARNING ICHAK MIKROBIOTASI HOLATI

Vafoyev Sh.F., Shagazatova B.X.
Toshkent davlat tibbiyot universiteti

Annotatsiya

Tadqiqotning maqsadi qandli diabet 2-turi (QD) bilan kasallangan, hali gipoglikemik davo boshlanmagan bemorlarda ichak mikrobiotasining tarkibiy o'zgarishlarini, hamda ushbu o'zgarishlarning tana vazni indeksi (TVI), bel aylanasi va glikirlangan gemoglobin (HbA1c) darajalari bilan bog'liqligini baholash. Natijalar. Bemorlarning aksariyatida ortiqcha vazn va semizlik kuzatildi (TVI o'rtacha 32,14±3,74 kg/m^2). TVI darajasi ortishi bilan Akkermansia muciniphila miqdori pasaydi (ortiqcha vaznda 6,87 lg, 3-darajada 4,67 lg). Faecalibacterium prausnitzii va Bifidobacterium spp. ko'rsatkichlari ham TVI ortishi bilan kamaydi. Davolanishdan oldingi qandli diabet 2-turi bemorlarida ichak disbioz holati shakllangan bo'lib, u semizlik darajasi va metabolik nazoratning yomonlashuvi (HbA1c ≥8,5%) bilan kuchayadi. Foydali, qisqa zanjirli yog' kislotalarini ishlab chiqaruvchi va shilliq qavatni himoyalovchi bakteriyalar kamayishi hamda shartli-patogen flora ortishi qandli diabetda metabolik buzilishlarning mumkin bo'lgan mexanizmlaridan biri sifatida qaralishi mumkin.

Kalit so'zlar: qandli diabet 2-turi, ichak mikrobiotasi, disbioz, tana vazni indeksi, bel aylanasi, glikozillangan gemoglobin, semizlik, metformin.

STATUS OF THE GUT MICROBIOTIA OF PATIENTS WITH TYPE 2 DIABETES

Vafoyev Sh.F., Shagazatova B.Kh.
Tashkent State Medical University

Abstract

The aim of the study was to assess the structural changes in the gut microbiota in patients with type 2 diabetes mellitus (T2DM) who had not yet started hypoglycemic treatment, and the relationship of these changes to body mass index (BMI), waist circumference, and glycated hemoglobin (HbA1c) levels. Results. The majority of patients were overweight and obese (mean BMI 32.14±3.74 kg/m^2). With increasing BMI levels, the amount of Akkermansia muciniphila decreased (6.87 lg in overweight, 4.67 lg in type 3). Faecalibacterium prausnitzii and Bifidobacterium spp. also decreased with increasing TVI. In patients with type 2 diabetes mellitus before treatment, a state of intestinal dysbiosis was formed, which was aggravated by the degree of obesity and worsening metabolic control (HbA1c ≥8.5%). A decrease in beneficial, short-chain fatty acid-producing and mucosal-protective bacteria and an increase in opportunistic flora can be considered as one of the possible mechanisms of metabolic disorders in diabetes mellitus.

Keywords: type 2 diabetes mellitus, intestinal microbiota, dysbiosis, body mass index, waist circumference, glycosylated hemoglobin, obesity, metformin.

СОСТОЯНИЕ МИКРОБИОТЫ КИШЕЧНИКА У ПАЦИЕНТОВ С САХАРНЫМ ДИАБЕТОМ 2 ТИПА

Вафоев Ш.Ф., Шагазатова Б.Х.
Ташкентский государственный медицинский университет

Аннотация

Целью исследования было оценить структурные изменения кишечной микробиоты у пациентов с сахарным диабетом 2 типа (СД2), которые еще не начали гипогликемическое лечение, а также взаимосвязь этих изменений с индексом массы тела (ИМТ), окружностью талии и уровнем гликированного гемоглобина (HbA1c). Результаты. Большинство пациентов имели избыточный вес и ожирение (средний ИМТ 32,14±3,74 кг/м^2). С увеличением ИМТ количество Akkermansia muciniphila уменьшалось (6,87 мкг у пациентов с

избыточным весом, 4,67 мкг у пациентов с СД3). Количество Faecalibacterium prausnitzii и Bifidobacterium spp. также уменьшалось с увеличением общего индекса массы тела (TVI). У пациентов с сахарным диабетом 2 типа до начала лечения формировалось состояние кишечного дисбиоза, которое усугублялось степенью ожирения и ухудшением метаболического контроля (HbA1c ≥8,5%). Снижение количества полезных бактерий, продуцирующих короткоцепочечные жирные кислоты и защищающих слизистую оболочку, и увеличение количества условно-патогенной флоры можно рассматривать как один из возможных механизмов метаболических нарушений при сахарном диабете.

Ключевые слова: сахарный диабет 2 типа, кишечная микробиота, дисбиоз, индекс массы тела, окружность талии, гликозилированный гемоглобин, ожирение, метформин.

Kirish. Qandli diabet 2-turi (QD) dunyo bo'yicha eng tez tarqalayotgan surunkali metabolik kasalliklardan biri bo'lib, uning rivojlanishida genetik moyillik, ortiqcha tana vazni, ovqatlanish tarzi va past jismoniy faollik bilan bir qatorda so'nggi yillarda ichak mikrobiotasining roli alohida e'tiborga olinmoqda. Ichak mikrobiotasi organizm metabolizmiga faol ta'sir ko'rsatuvchi o'ziga xos "metabolik organ" sifatida qaralib, glyukoza va lipid almashinuvi hamda insulinga sezuvchanlikni boshqarishda ishtirok etadi [1, 2].

So'nggi yillarda o'tkazilgan kuzatuv va tadqiqotlar qandli diabet 2-turi bilan ichak disbiozi o'rtasida mustahkam bog'liqlikni ko'rsatdi: kasallikda ichak mikrobiotasi jamoasining tarkibi va xilma-xilligi sog'lom shaxslardagidan farq qiladi. Tizimli izlanishlarda Escherichia–Shigella, Enterococcus va Fusobacteria kabi taksonlarning ko'payishi QD bilan ijobiy, Akkermansia [5], Bifidobacterium, Bacteroides, Roseburia, Faecalibacterium va Prevotella ning kamayishi esa salbiy bog'langanligi qayd etilgan; ayniqsa Escherichia–Shigella izchil ravishda QD bilan, Faecalibacterium prausnitzii esa himoyaviy ta'sir bilan bog'langan [3, 4].

Disbioz sharoitida ichak baryerining buzilishi hisobiga bakterial translokatsiya va surunkali yallig'lanish kuchayadi; qisqa zanjirli yog' kislotalari (atsetat, propionat, butirat), tarmoqlangan zanjirli aminokislotalar va bakterial lipopolisaxarid singari mikrob metabolitlari orqali xo'jayin to'qimalariga uzatiladi, bu esa glyukoza gomeostazi va insulin sezuvchanligini o'zgartiradi. Shu bilan birga, semizlik mustaqil ravishda mikrobiota tarkibini o'zgartiruvchi omil bo'lib, tana vazni indeksi ortishi bilan mikrobiota xilma-xilligi pasayishi qator tadqiqotlarda ko'rsatilgan [7, 8].

Mikrobiotaning qandli diabetdagi o'rni haqidagi ma'lumotlarni talqin qilishda muhim metodologik masala—qabul qilinayotgan dori vositalari, ayniqsa metformin, mikrobiota tarkibini sezilarli o'zgartirishidir. Metformin Escherichia spp. va Akkermansia muciniphila ulushini oshirib, Intestinibacter bartlettii ni kamaytirishi va butirat hamda propionat ishlab chiqarilishini kuchaytirishi qayd etilgan. Shu sababli kasallikning "tabiiy" mikrobiologik manzarasini baholash uchun davolanishdan oldingi (davolash boshlanmagan) bemorlarni o'rganish katta ahamiyatga ega [6,9].

Mazkur ishning maqsadi — davolanishdan oldingi qandli diabet bemorlarida (metformin guruhiga rejalashtirilgan, ammo hali dori qabul qilmagan) ichak mikrobiotasining miqdoriy tarkibini baholash hamda uning tana vazni indeksi, bel aylanasi va glikirlangan gemoglobin darajalari bilan bog'liqligini aniqlashdan iborat.

Tadqiqot materiallari va usullari. Ushbu tadqiqotga qandli diabet 2-turi tashxisi qo'yilgan, gipoglikemik davo hali boshlanmagan 52 nafar bemor kiritildi. Bemorlarning 30 nafari (57,7%) ayollar, 22 nafari (42,3%) erkaklarni tashkil etdi. Barcha ko'rsatkichlar davolanishdan oldingi (boshlang'ich) bosqichda qayd etildi.

Har bir bemorda tana vazni, bo'y, tana vazni indeksi (TVI, kg/m^2) va bel aylanasi (sm) o'lchandi. Bemorlar TVI bo'yicha to'rt guruhga taqsimlandi: ortiqcha vazn (25–29,9 kg/m^2), 1-daraja semizlik (30–34,9 kg/m^2), 2-daraja (35–39,9 kg/m^2) va 3-daraja (≥40 kg/m^2). Bel aylanasi jins jihatidan tahlil qilindi: ayollarda 88 sm, erkaklarda 102 sm chegara qiymat sifatida olindi. Bio-

kimyoviy tahlilda umumiy xolesterin, trigliseridlar, past zichlikdagi lipoproteidlar (ZPLP) va yuqori zichlikdagi lipoproteidlar (ZYLP) hamda glikirlangan gemoglobin (HbA1c) aniqlandi. HbA1c bo'yicha bemorlar <8,5% va ≥8,5% guruhlariga ajratildi.

Ichak mikrobiotasining miqdoriy tarkibi Kolonoflor-16 (Alfalab, Rossiya) real vaqtli polimeraza zanjir reaksiyasi (RT-PZR) usulida o'rganildi. Umumiy bakterial massa va 22 ta indikator takson (ya'ni Lactobacillus spp., Bifidobacterium spp., Bacteroides spp., Faecalibacterium prausnitzii, Akkermansia muciniphila, Escherichia coli va shartli-patogen va patogen mikroorganizmlar) baholandi. Tahlil natijalari log10 birliklarida (lg nusxa/ml) ifodalandi. Fusobacterium nucleatum, Parvimonas micra, Salmonella spp. va Shigella spp. barcha namunalarda aniqlash chegarasidan past bo'lgani uchun jadvallarga kiritilmadi.

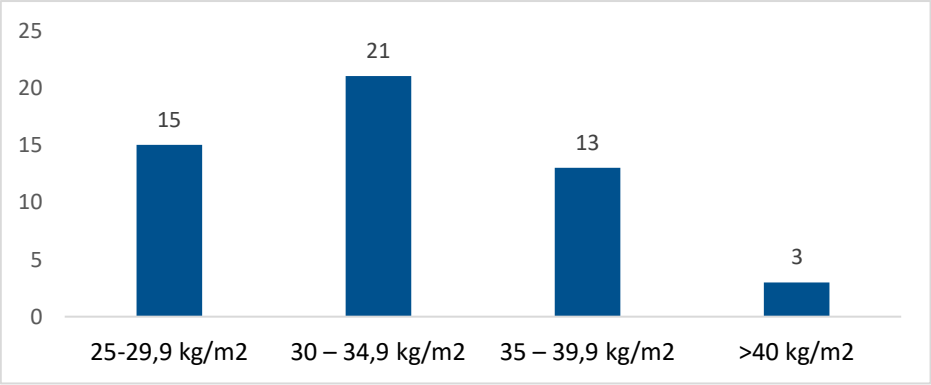
Ko'rsatkichlar o'rtacha qiymat va standart og'ish (M±SD) ko'rinishida berildi. Mikrobiota tarkibiy miqdori tana vazni indeksi, bel aylanasi va glikirlangan gemoglobinlar kesimida o'rtacha qiymatlar bo'yicha taqqoslandi. Mazkur ishda boshlang'ich (davolanishdan oldingi) holat tavsifiy tahlil qilingan.

Natijalar va muhokama. Bemorlarning umumiy tavsifi. Qandli diabet guruhida bemorlarning katta qismi ortiqcha vazn yoki semizlikka ega bo'ldi. Tana vazni indeksi bo'yicha taqsimot 1-jadvalda keltirilgan: eng katta ulush (40%) 1-daraja semizlikka to'g'ri keldi.

Jadval 1

Qandli diabet 2-turi guruhida bemorlarning tana vazni indeksi (TVI) bo'yicha taqsimoti.

TVI, kg/m²	Soni	Foizi
25–29,9 (ortiqcha vazn)	15	29%
30–34,9 (1-daraja)	21	40%
35–39,9 (2-daraja)	13	25%
≥40 (3-daraja)	3	6%
Jami	**52**	**100%**



Rasm 1. TVI bo'yicha bemorlar soni.

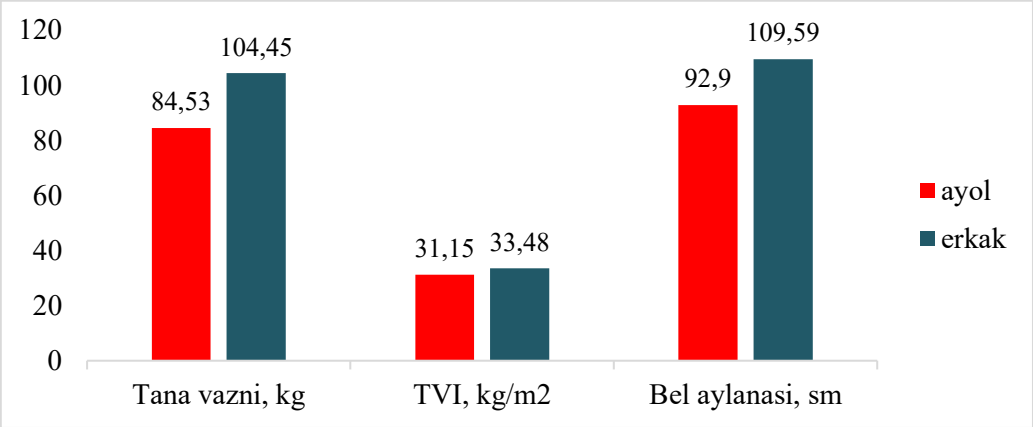
Jadval 2

Qandli diabet 2-turi guruhida antropometrik ko'rsatkichlar.

Ko'rsatkich	Ayol (n=30)	Erkak (n=22)	Umumiy (n=52)
Tana vazni, kg	84,53±8,97	104,45±13,79	92,96±14,93
TVI, kg/m²	31,15±3,45	33,48±3,77	32,14±3,74
Bel aylanasi, sm	92,9±8,51	109,59±9,33	99,96±12,1

Antropometrik ko'rsatkichlar jins bo'yicha 2-jadvalda berilgan. Erkaklarda tana vazni, TVI

va bel aylanasi ayollardagidan yuqori bo'ldi. Umumiy jinsda TVI o'rtacha 32,14±3,74 kg/m² (eng kichik 26,22; eng katta 40,29 kg/m²) ni tashkil etdi.



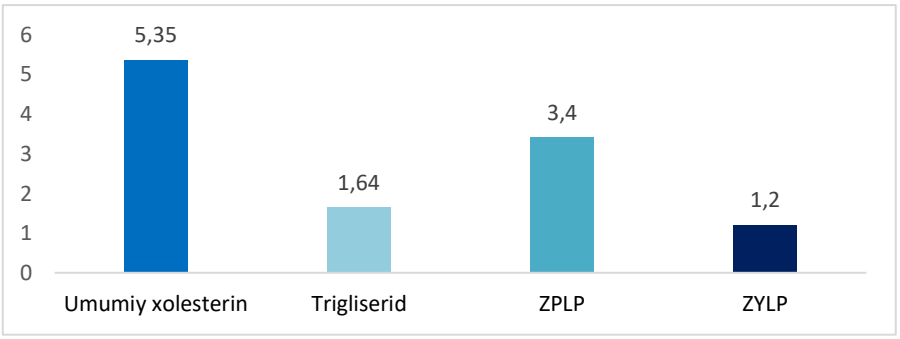
Rasm 2. Qandli diabet guruhida tana vazni, tana vazni indeksi, bel aylanasi bo'yicha taqsimlanishi.

Lipid profili bo'yicha guruh o'rtacha ko'rsatkichlari 3-jadvalda keltirilgan; umumiy xolesterin va trigliseridlarning chegaraviy yuqori darajalari kuzatildi.

Jadval 3

Qandli diabet 2-turi guruhining lipid profili.

Ko'rsatkich	Umumiy xolesterin	Trigliserid	ZPLP (LDL)	ZYLP (HDL)
O'rtacha	5,35±0,48	1,64±0,16	3,4±0,48	1,2±0,08



Rasm 3. Qandli diabet 2-turi guruhining lipid profili.

Ichak mikrobiotasining tana vazni indeksi bo'yicha o'zgarishi. Umumiy jinsda (n=52) mikrobiota tarkibining TVI darajalari bo'yicha o'zgarishi 4-jadvalda keltirilgan. Eng sezilarli o'zgarish — Akkermansia muciniphila miqdorining TVI ortishi bilan kamayishi: ortiqcha vaznda 6,87 lg dan 3-daraja semizlikda 4,67 lg gacha. Bifidobacterium spp. (8,87 → 7,33) va Faecalibacterium prausnitzii (8,0 → 7,0) ham yuqori TVI darajalarida kamaydi. Aksincha, Enterococcus spp. (6,6 → 8,31), Citrobacter spp. (4,4 → 6,31), Klebsiella pneumoniae (4,87 → 5,92), Candida spp. (5,4 → 7,0) va Staphylococcus aureus (4,67 → 6,15) ko'rsatkichlari, ayniqsa 2-daraja semizlikda, yuqori bo'ldi.

Jins bo'yicha alohida tahlilda ham o'xshash o'zgarishlar saqlanib qoldi. Ayollarda (5-jadval) Akkermansia muciniphila ortiqcha vaznda 6,83 lg dan 3-darajada 3,0 lg gacha pasaydi; Enterococcus spp., Klebsiella pneumoniae, Candida spp. va Staphylococcus aureus 2-daraja semizlikda eng yuqori qiymatlarga yetdi (mos ravishda 8,75; 6,75; 6,75 va 6,75 lg).

Erkaklarda (6-jadval) Akkermansia muciniphila ortiqcha vaznda 7,0 lg dan 2-darajada 5,0 lg gacha kamaydi, Citrobacter spp. (4,67 → 6,33), Candida spp. (5,33 → 7,11) va Staphylococcus aureus (4,67 → 5,89) esa semizlik darajasi ortishi bilan ko'paydi.

Jadval 4

Qandli diabet guruhida ichak mikrobiotasi tarkibining TVI bo'yicha o'zgarishi. Umumiy jins (n=52), lg nusxa/ml.

	Ortiqcha vazn (n=15)	1-daraja (n=21)	2-daraja (n=13)	3-daraja (n=3)
Umumiy bakterial massa	10.47	10.48	10.31	8
Lactobacillus spp.	7.2	7.38	6.85	7.67
Bifidobacterium spp.	8.87	8.57	7.92	7.33
Escherichia coli	8.07	8	8.38	8.67
Bacteroides spp.	9.07	9.33	9	9.33
Faecalibacterium prausnitzii	8	8.29	7.38	7
Bacteroides thetaiotaomicron	6.93	7	6.92	6
Akkermansia muciniphila	6.87	5.43	5.15	4.67
Enterococcus spp.	6.6	6.76	8.31	7
Escherichia coli enteropathogenic	4.53	4.48	5	5
Klebsiella pneumoniae	4.87	4.76	5.92	5.33
Klebsiella oxytoca	4.13	3.95	3.46	3.67
Candida spp.	5.4	5.71	7	5.67
Staphylococcus aureus	4.67	4.86	6.15	5.67
Clostridium difficile	1.06	1.14	1.23	0.66
Clostridium perfringens	1.13	1	1.15	0.33
Proteus vulgaris/mirabilis	4.4	4.24	4.31	3.33
Citrobacter spp.	4.4	4.52	6.31	6.33
Enterobacter spp.	4.8	5.05	5.77	4

Izoh: Fusobacterium nucleatum, Parvimonas micra, Salmonella spp. va Shigella spp. barcha guruhlarda aniqlanmadi.

Jadval 5

Ichak mikrobiotasi tarkibining TVI bo'yicha o'zgarishi. Ayollar (n=30), lg nusxa/ml.

	Ortiqcha vazn (n=12)	1-daraja (n=13)	2-daraja (n=4)	3-daraja (n=1)
Umumiy bakterial massa	10.5	10.38	11	7
Lactobacillus spp.	7.17	7.38	7.25	8
Bifidobacterium spp.	8.75	8.38	7.5	6
Escherichia coli	8	8.15	8	8
Bacteroides spp.	9.08	9.15	9.25	12
Faecalibacterium prausnitzii	8	8.23	7.25	8
Bacteroides thetaiotaomicron	7.42	7.08	7.75	3
Akkermansia muciniphila	6.83	5.31	5.5	3
Enterococcus spp.	6.42	6.69	8.75	3
Escherichia coli enteropathogenic	4.5	4.69	5.25	4
Klebsiella pneumoniae	4.83	4.69	6.75	4

	Ortiqcha vazn (n=12)	1-daraja (n=13)	2-daraja (n=4)	3-daraja (n=1)
Klebsiella oxytoca	4.08	3.85	3.75	4
Candida spp.	5.42	5.77	6.75	4
Staphylococcus aureus	4.67	5.08	6.75	4
Clostridium difficile	0.92	1.23	1.25	1
Clostridium perfringens	1	1.15	0.75	1
Proteus vulgaris/mirabilis	4.42	4.62	3.5	4
Citrobacter spp.	4.33	4.77	6.25	5
Enterobacter spp.	4.75	5.31	6.25	2

Jadval 6

Ichak mikrobiotasi tarkibining TVI bo'yicha o'zgarishi. Erkaklar (n=22), lg nusxa/ml.

	Ortiqcha vazn (n=3)	1-daraja (n=8)	2-daraja (n=9)	3-daraja (n=2)
Umumiy bakterial massa	10.33	10.63	10	8.5
Lactobacillus spp.	7.33	7.38	6.67	7.5
Bifidobacterium spp.	9.33	8.88	8.11	8
Escherichia coli	8.33	7.75	8.56	9
Bacteroides spp.	9	9.63	8.89	8
Faecalibacterium prausnitzii	8	8.38	7.44	6.5
Bacteroides thetaiotaomicron	5	6.88	6.56	7.5
Akkermansia muciniphila	7	5.63	5	5.5
Enterococcus spp.	7.33	6.88	8.11	9
Escherichia coli enteropathogenic	4.67	4.13	4.89	5.5
Klebsiella pneumoniae	5	4.88	5.56	6
Klebsiella oxytoca	4.33	4.13	3.33	3.5
Candida spp.	5.33	5.63	7.11	6.5
Staphylococcus aureus	4.67	4.5	5.89	6.5
Clostridium difficile	1.67	1	1.22	0.5
Clostridium perfringens	1.67	0.75	1.33	–
Proteus vulgaris/mirabilis	4.33	3.63	4.67	3
Citrobacter spp.	4.67	4.13	6.33	7
Enterobacter spp.	5	4.63	5.56	5

Ichak mikrobiotasining bel aylanasi bo'yicha o'zgarishi. Bel aylanasi normadan katta bo'lgan bemorlarda shartli-patogen flora ko'proq namoyon bo'ldi. Ayollarda (7-jadval) bel aylanasi >88 sm bo'lganda Akkermansia muciniphila pasaydi (6,5 → 5,55), Candida spp. (5,4 → 5,85), Staphylococcus aureus (4,7 → 5,3) va Citrobacter spp. (4,4 → 5,0) esa ortganli aniqlandi.

Erkaklarda (8-jadval) bel aylanasi >102 sm bo'lganda Escherichia coli (7,57 → 8,6), Candida spp. (5,14 → 6,8), Citrobacter spp. (4,0 → 6,0), Staphylococcus aureus (4,43 → 5,67) va Entero-

bacter spp. (4,14 → 5,53) ko'rsatkichlari yuqori bo'lib, Akkermansia muciniphila (6,14 → 5,27) va Bacteroides spp. (9,86 → 8,73) pasaydi.

Jadval 7

Ichak mikrobiotasi tarkibining bel aylanasi bo'yicha o'zgarishi. Ayollar (n=30), lg nusxa/ml.

	<88 sm (n=10)	>88 sm (n=20)
Umumiy bakterial massa	10.3	10.45
Lactobacillus spp.	7.2	7.35
Bifidobacterium spp.	8.6	8.2
Escherichia coli	8.2	8
Bacteroides spp.	9.1	9.3
Faecalibacterium prausnitzii	7.9	8.05
Bacteroides thetaiotaomicron	7.2	7.15
Akkermansia muciniphila	6.5	5.55
Enterococcus spp.	6.7	6.75
Escherichia coli enteropathogenic	4.5	4.75
Klebsiella pneumoniae	4.9	5.05
Klebsiella oxytoca	4	3.9
Candida spp.	5.4	5.85
Staphylococcus aureus	4.7	5.3
Clostridium difficile	0.9	1.2
Clostridium perfringens	1	1.05
Proteus vulgaris/mirabilis	4.5	4.3
Citrobacter spp.	4.4	5
Enterobacter spp.	4.9	5.2

Ichak mikrobiotasining glikozillangan gemoglobin bo'yicha o'zgarishi. Metabolik nazorat yomonlashgan (HbA1c ≥8,5%) bemorlarda shartli-patogen taksonlar yuqoriroqligi aniqlandi (9-jadval): Candida spp. (5,31 → 6,22), Staphylococcus aureus (4,38 → 5,53), Enterobacter spp. (4,5 → 5,36), Escherichia coli enteropathogenic (4,25 → 4,83), Klebsiella pneumoniae (4,75 → 5,28) va Citrobacter spp. (4,69 → 5,19). Akkermansia muciniphila esa HbA1c ≥8,5% guruhida esa bir oz pastroq bo'ldi (6,0 → 5,61).

Mazkur tadqiqot davolanishdan oldingi qandli diabet bemorlarida ichak mikrobiotasining tabiiy manzarasini, ya'ni metformin yoki boshqa dori vositalarining ta'sirisiz holatni aks ettiradi. Bu jihat muhim, chunki metformin Escherichia spp. va Akkermansia muciniphila ulushini oshirib, qisqa zanjirli yog' kislotalari ishlab chiqarilishini kuchaytirishi va mikrobiota tarkibini sezilarli o'zgartirishi ma'lum; shu sababli davolangan bemorlardagi natijalarni kasallikning o'ziga bog'lash qiyin.

Tadqiqotimizning asosiy o'zgarishlaridan biri bu Akkermansia muciniphila miqdorining tana vazni indeksi va bel aylanasi ortishi bilan, shuningdek metabolik nazorat yomonlashuvi (HbA1c ≥8,5%) bilan izchil pasayishidir. Bu adabiyot ma'lumotlariga to'la mos keladi: Akkermansia muciniphila QD va semizlik bilan salbiy bog'langan bo'lib, uning kamayishi insulin sekretsiyasi va glyukoza gomeostazining buzilishiga olib keladigan omil sifatida ko'rsatilgan. Bu ichak shilliq qavatini(mutsin) parchalovchi, ammo ichak baryerini mustahkamlovchi mikroorganizmning pro-

biotik sifatidagi xususiyatlarini tasdiqlovchi meta-tahlillar va klinik sinovlar bilanmosligi aniqlandi.

Jadval 8

Ichak mikrobiotasi tarkibining bel aylanasi bo'yicha o'zgarishi. Erkaklar (n=22), lg nusxa/ml.

	<102 sm (n=7)	>102 sm (n=15)
Umumiy bakterial massa	10.43	10
Lactobacillus spp.	7.43	6.93
Bifidobacterium spp.	8.57	8.53
Escherichia coli	7.57	8.6
Bacteroides spp.	9.86	8.73
Faecalibacterium prausnitzii	8.14	7.6
Bacteroides thetaiotaomicron	6.29	6.67
Akkermansia muciniphila	6.14	5.27
Enterococcus spp.	7.14	7.87
Escherichia coli enteropathogenic	4.14	4.87
Klebsiella pneumoniae	4.71	5.53
Klebsiella oxytoca	4.14	3.6
Candida spp.	5.14	6.8
Staphylococcus aureus	4.43	5.67
Clostridium difficile	1.43	1
Clostridium perfringens	1.28	0.93
Proteus vulgaris/mirabilis	4.29	4
Citrobacter spp.	4	6
Enterobacter spp.	4.14	5.53

Faecalibacterium prausnitzii va Bifidobacterium spp. ning yuqori TVI darajalarida kamayishi ham himoyaviy, qisqa zanjirli yog' kislotalarini (xususan butirat) ishlab chiqaruvchi flora kamayishini ko'rsatadi. F. prausnitzii izlanishlarda QD ga qarshi himoyaviy ta'siri borligi aniqlangan; uning kamayishi yallig'lanishga qarshi himoya zaiflashuvi va ichak baryeri o'tkazuvchanligi ortishi bilan kechishi aniqlangan.

Aksincha, shartli-patogen va proteobakterial taksonlar — Enterococcus spp., Klebsiella pneumoniae, Citrobacter spp., Enterobacter spp., Candida spp. va Staphylococcus aureus — semizlik darajasi, bel aylanasi va HbA1c ortishi bilan ularning miqdori ko'paydi. Bu qandli diabetda Enterobacteriaceae oilasi va boshqa fakultativ-patogen mikroorganizmlar miqdorining ortishi haqidagi ma'lumotlarga mos bo'lib, bakterial translokatsiya, endotoksemiya va surunkali yallig'lanish mexanizmlari orqali insulinga rezistentlikni kuchaytiradi. Erkaklarda bel aylanasi katta bo'lganda Escherichia coli ning ortishi visseral semizlik bilan disbioz o'rtasidagi bog'liqlikni qo'shimcha tasdiqlaydi.

HbA1c ≥8,5% bo'lgan bemorlarda shartli-patogen flora va Candida spp. ning yuqoriligi metabolik nazorat darajasi mikrobiota holati bilan o'zaro bog'liq ekanini ko'rsatadi. Giperglikemiya sharoitida shilliq qavat muhitining o'zgarishi shartli-patogen mikroorganizmlar ko'payishiga qulay sharoit yaratilishi bilan bog'liq. Patogen taksonlar (Salmonella, Shigella, Fusobacterium nucleatum,

Parvimonas micra) ning aniqlanmagani esa kuzatilgan o'zgarishlar o'tkir infeksiya emas, balki dasturiy disbioz tabiatiga ega ekanini ko'rsatadi.

Jadval 9

Ichak mikrobiotasi tarkibining HbA1c darajasi bo'yicha o'zgarishi (n=52), lg nusxa/ml.

	HbA1c <8,5% (n=16)	HbA1c ≥8,5% (n=36)
Umumiy bakterial massa	10.25	10.31
Lactobacillus spp.	7.13	7.25
Bifidobacterium spp.	8.5	8.39
Escherichia coli	8.25	8.11
Bacteroides spp.	9.31	9.11
Faecalibacterium prausnitzii	7.69	8
Bacteroides thetaiotaomicron	6.38	7.14
Akkermansia muciniphila	6	5.61
Enterococcus spp.	7.06	7.14
Escherichia coli enteropathogenic	4.25	4.83
Klebsiella pneumoniae	4.75	5.28
Klebsiella oxytoca	3.88	3.86
Candida spp.	5.31	6.22
Staphylococcus aureus	4.38	5.53
Clostridium difficile	1.06	1.14
Clostridium perfringens	1.06	1.03
Proteus vulgaris/mirabilis	4.63	4.08
Citrobacter spp.	4.69	5.19
Enterobacter spp.	4.5	5.36

Xulosa. Davolanishdan oldingi qandli diabet 2-turi bemorlarida ichak disbiozi shakllangan bo'lib, u quyidagi yo'nalishda namoyon bo'ladi: foydali, shilliq qavatni himoyalovchi va qisqa zanjirli yog' kislotalarini ishlab chiqaruvchi bakteriyalar (Akkermansia muciniphila, Faecalibacterium prausnitzii, Bifidobacterium spp.) miqdorining kamayishi hamda shartli-patogen flora (Enterococcus spp., Klebsiella pneumoniae, Citrobacter spp., Candida spp., Staphylococcus aureus) ning ko'payishi. Ushbu o'zgarishlar tana vazni indeksi va bel aylanasi ortishi, shuningdek metabolik nazoratning yomonlashuvi (HbA1c ≥8,5%) bilan yana ham kuchayadi. Olingan natijalar qandli diabet 2-turida ichak mikrobiotasini metabolik buzilishlarning mumkin bo'lgan ishtirokchisi sifatida ko'rib chiqish va kelgusida mikrobiotaga yo'naltirilgan (probiotik, prebiotik, diyetologik) yondashuvlarni o'rganish zarurligini asoslaydi.

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