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Microbial contamination in intra-abdominal infection with underlying diabetes mellitus: An experimental study

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Abstract
Materials and Methods: 4 groups of 15 white rats: 1st - intact, 2nd - model of diabetes mellitus, 3rd - model of intra-abdominal infection, 4th - model of diabetes and intra-abdominal infection. Intra-abdominal infection was simulated by intraabdominal injection of autofaeces mixture. Diabetes was simulated by injection of aloxane solution. Intra-abdominal infection was simulated 3 months after diabetes simulation. The small and large intestines, peritoneal exudate microflora was studied. The material for examination was taken before simulation of intra-abdominal infection, 6, 12, 24, 48 h after.
Results: Dysbacteriosis was detected in the 2nd group. In the 3rd group, in 6 h, dysbacteriosis was detected, in the 4th group-dysbacteriosis progression. In the 4th group, in 12 h, dysbiosis (candidiasis) was detected, which further progressed. During the development of intra-abdominal infection, permanent changes in the intestinal microbiocenosis and peritoneal exudate microflora were detected. In the 4th group, the changes were more severe. In the 3rd group, in 48 h, microflora's changes in both intestines, in peritoneal exudate indicate slightly regression of pathological processes. In the 4th group, in 48 h, progression of pathological processes was detected.
Conclusion
1. Intestinal dysbacteriosis was detected in rats 3 months after diabetes mellitus modeling.
2. Modeling of intra-abdominal infection in intact rats causes intestinal dysbacteriosis, a syndrome of excess bacterial colonization of small intestines.
3. Modeling of intra-abdominal infection in rats with diabetes mellitus models increases intestinal dysbacteriosis, causes the syndrome of excess bacterial colonization of small intestines, dysbiosis in large intestines.
4. In intact rats, 48 h after intra-abdominal infection modeling, signs of dysbacteriosis regression and a decrease in the number of microorganisms in peritoneal exudate were detected, instead in rats with diabetes mellitus models, signs of dysbacteriosis and dysbiosis progression and an increase in the number of microorganisms in peritoneal exudate were detected.

Keywords: Diabetes mellitus; intra-abdominal infection; gut microflora; peritoneal microflora

Introduction
Prevalence of diabetes mellitus (DM) is growing worldwide [1, 2]. DM is one of the main causes of morbidity and mortality [2, 3]. Studies show a negative correlation between DM and health status [4]. DM adversely affects the functional state of all organs and systems [1-4]. Patients with diabetes are often multimorbidity [5].
At the same time, the prevalence of intra-abdominal infection (IAI) is constant [6-8]. Therefore, the number of patients with acute IAI associated with DM is constantly growing [9]. In general, infectious diseases are more frequent and serious in patients with DM, which potentially increases their morbimortality [10, 11]. The greater frequency of infections in DM patients is caused by the hyperglycemic environment that favors immune dysfunction, angiopathies, neuropathy, gastrointestinal dysmotility, etc.
The number of postoperative complications increases in patients with diabetes mellitus [7, 8, 12]. DM is an independent risk factor for mortality in IAI [13-15].

The consequences of IAI significantly depend on the functioning of immune mechanisms [15, 16]. At the same time, diabetes significantly changes the state of the immune system [17, 18]. The association of DM and IAI changes the pathogenesis of inflammation [15, 20, 21]. But all the mechanisms of the such comorbidity development have not yet been clarified [21]. Studies show that with the comorbidity of DM and IAI, the microflora (MF) that is the cause of IAI changes [22, 23]. But changes in MF have not yet been studied comprehensively [10, 11].

The importance of such studies is determined by the main role of endogenous intestinal MF in the IAI development and progression [6]. At the same time, it is well known about the gut microbiocenosis disorders in DM [23]. These disorders are important for the occurrence and progression of the negative consequences of DM and its complications [24-26].

So, the complex study of MF changes in IAI that develops with underlying DM seems to be quite relevant. Such studies in patients are problematic, since patients differ greatly in age, causes of IAI, state of health, etc. Therefore, for the standardization of data, experimental studies are needed.

Materials and Methods

150 white non pedigree female rats. All rats were sexually mature (age 6 months). The rats' mass was from 180 to 200 g. The rats were in a vivarium before the start of the experiment. The conditions of stay and food were the same for all rats. After the start of the experiment, the rats were in the same conditions and had the same drink.

The rats were divided into 4 groups: 1st - intact (15), 2nd - DM model (15), 3rd - IAI model (60), 4th - DM model and IAI model (60).

IAI was simulated by intraabdominal injection of 10% autofaeces mixture in the dose of 10 ml per 100 g of mass. DM was simulated by subcutaneous introduction of 1.6% aloxane solution on distilled water in the dose of 16 mg per 100 g of mass.

The main criterion of simulated DM was the blood plasma glucose presence within the range of 5.39±0.25 mmol/l. In intact animals, the blood plasma glucose was presence within the range of 3.21±0.53 mmol/l (p<0.01). IAI was simulated in 3 months after DM had been simulated. The small (SI) and large intestines (LI), peritoneal exudate (PE) microflora was studied. Before modeling of IAI, as well as in 6, 12, 24, 48 h from the moment of its inducement, laparotomy was performed and material was taken for examination. 5 g of the intestinal contents for microbiological examination were taken in the middle part of SI and in the middle part of LI. 5 ml of the exudate was taken from the area of greatest accumulation. 5 ml of sterile 0.9% NaCl solution was poured into the abdominal cavity, in animals of the 1st and 2nd groups after laparotomy, and in 10 min the solution was taken for microbiological examination.

All manipulations were performed under the sevorane anesthesia. The animals were taken out of the experiment by overdose of sevorane.

Microbiological examination included the study of the quantitative and species composition of the peritoneal exudate MF, small and large intestines MF. Microbiological research was carried out by bacteriological and mycological methods with the isolation and identification of pure cultures of the pathogen to the genus and species. Selective nutrient media were used to isolate microorganisms (MO). The number of aerobic MO was counted after 1-2 days. The number of anaerobic MO was counted after 5-7 days of cultivation on nutrient media in an anaerostat. The concentration of MO was expressed in logarithms (lg) of colony-forming units (CFU) in 1 g or 1 ml of the collected material - lg CFU/g or lg CFU/ml.

The isolated microorganisms' groups and types frequency of occurrence (FO) was determined by the formula:

$$FO = \frac{Ni \times 100\%}{Nt},$$

Where: FO is the frequency of occurrence; Ni is the number of objects in which the corresponding microorganism was isolated; Nt is the number of objects taken for examination.

After identification of microorganisms' strains, the dominance coefficient (DC) was determined by the formula:

$$DC = \frac{Nn}{Nt},$$

Where: DC is the dominance coefficient; Nn is the number of this species (genus) microorganisms' isolated strains; Nt is the total number of isolated microorganisms' strains.

While carrying out the study the researchers kept to the basic guideline of Vancouver Conventions (1979, 1994) concerning biomedical experiments, the Council of Europe Convention on the Protection of Vertebrate Animals Used in Experiments and for Other Scientific Purposes (1986).

The hypothesis of normal data distribution (Gaussian distribution) was tested in samples by Shapiro-Wilk criterion. Verification of the hypothesis of average data equality was carried out by Wilcoxon and Mann-Whitney-Wilcoxon criterion. To discover the strength of a link between sets of data the Spearman's Rank Correlation Coefficient was used. The significance level (alpha) 0.05 was set in the study. The results of the study were statistically processed by the Microsoft® Office Excel (Build 11.5612.5703) tables. We have set the level of significance 0.05.

While performing the work, the norms of conducting research in the field of biology and medicine were observed: the Vancouver Conventions on Biomedical Research (1979, 1994), the Council of Europe Convention on the Protection of Vertebrate Animals Used in Experiments and for Other Scientific Purposes (1986).

Results

In the 1st group, *E. coli* (FO=100%) and *B. fragilis* (FO=100%), which are saprophytic MO, were found in SI (Table 1). Anaerobic MF dominated slightly. DC of anaerobic bacteria was 0.54. In the 2nd group *Proteus* spp. (FO=100%) and *P. niger* (FO=80%) were found, in addition to those MO. Anaerobic MF dominated slightly. DC of anaerobic bacteria was 0.53. The total number of MO, the number of aerobic and anaerobic MO in the 2nd group was significantly higher.

Table 1: Microflora of the rat's small intestine

Microorganisms	1st group	2nd group
E. coli	2.651±0.022	2.540±0.028
Proteus spp.	-	2.263±0.026
B. fragilis	3.088±0.273	3.772±0.033
P. niger	-	1.651±0.738
All aerobic	2.651±0.022	4.803±0.002 $p<0.01$
All anaerobic	3.088±0.273	5.423±0.705 $p<0.05$
Total number	5.676±0.224	10.225±0.707 $p<0.01$

In the 1st group, *E. coli* (FO=100%), *Proteus* spp. (FO=100%), *B. fragile* (FO=100%), *P. niger* (FO=100%), gram-positive diplococci (GPD) (FO=100%) were found in LI (Table 2). Aerobic MF dominated (DC was 0.64). In the 2nd group, LI microflora was depleted. The number of *E. coli* (FO=100%), *Proteus* spp. (FO=100%), and *P. niger* (FO=100%) was lower. The number of *B. fragilis* (FO=100%) was higher. GPA were not found. Aerobic MF slightly dominated (DC was 0.57). The total number of aerobic MO and total number of MO was significantly lower than in the 1st group.

Table 2: Microflora of the rat's large intestine (lg КУО/мл)

Microorganisms	1st group	2nd group
E. coli	7.161±0.141	6.801±0.046
Proteus spp.	2.424±0.098	2.263±0.026
GPD	3.151±1.409	-
B. fragile	4.500±0.089	4.690±0.095
P. niger	2.540±0.028	2.239±1.001
All aerobic	12.735±1.649	9.064±0.019 $p<0.05$
All anaerobic	7.040±0.117	6.929±0.906
Total number	19.775±1.765	15.993±0.925 $p<0.05$

Abdominal lavages were sterile in all rats.

In 6 h after IAI simulation in the 3rd group, the number of *E. coli* (FO=100%) and *B. fragilis* (FO=100%) in the SI significantly increased (Table 3). At the same time, *Proteus* spp. (FO=80%) and *P. niger* (FO=46.67%) were found. The number of aerobes and the total number of MO increased significantly. Aerobes dominated (DC was 0.64). In the 4th group, the number of *E. coli* (FO=100%), *B. fragilis* (FO=100%), and *P. niger* (FO=100%) in SI significantly increased. At the same time, lactose-negative enterobacteria (LNE), which is a gram-negative conditionally pathogenic MF, were found. FO of LNE was 80%. The number of aerobes, anaerobes and the total number of MO increased significantly. But aerobes dominated (DC was 0.54). The number of aerobes, anaerobes and the total number of MO in the 4th group was significantly higher.

Table 3: Microflora of the rat's small intestine in 6 h after IAI modelling

Microorganisms	3rd group	4th group
E. coli	4.778±0.079 **	3.772±0.033 $p<0.05$,*
Proteus spp.	2.643±0.021	2.322±0.201
LNE	-	3.389±0.039
B. fragilis	3.724±0.169*	4.661±0.082 $p<0.05$,*
P. niger	0.423±0.189	3.301±0.009 $p<0.01$,**
All aerobic	7.422±0.079 **	9.483±0.007 $p<0.01$,**
All anaerobic	3.746±0.358	7.962±0.082 $p<0.01$,*
Total number	11.168±0.279 **	17.445±0.089 $p<0.01$,**

Note: *- validity coefficient between the output data < 0,05, ** - < 0,01 (only statistically significant differences are given).

In the 3rd group, the number of *Proteus* spp. (FO=100%) and *B. fragilis* (FO=100%) in LI significantly increased (Table 4). At the same time, gram-positive spore-forming anaerobes (GPSFA) were found (FO=53.33%). The number of aerobes, anaerobes and the total number of MO did not change significantly. DC of aerobes decreased to 0.56. In the 4th group, the number of *E. coli* (FO=80%) significantly decreased, the number of *B. fragilis* (FO=100%) and *P. niger* (FO=100%) significantly increased. At the same time, LNE (FO=80%) were found. The number of aerobes, anaerobes and the total number of MO increased significantly. Aerobic MF slightly dominated (DC was 0.57). The number of anaerobes in the 4th group was significantly higher. The total number of MO in the 4th group was higher.

Table 4: Microflora of the rat's large intestine in 6 h after IAI modelling

Microorganisms	3rd group	4th group
E. coli	7.929±0.011	4.900±0.024 $p<0.01$,*
Proteus spp.	3.246±0.185 *	2.643±0.052 $p<0.05$
LNE	-	4.389±0.039 *
B. fragilis	5.040±0.117 *	5.588±0.050 $p<0.05$,*
P. niger	2.651±0.022	4.588±0.050 $p<0.05$, *
GPSFA	1.151±0.515	-
All aerobic	11.174±0.173	11.932±0.015 *
All anaerobic	8.841±0.653	10.176±0.009 $p<0.05$, *
Total number	20.015±0.826	22.108±0.015 **

Note: *- validity coefficient between the output data < 0,05, ** - < 0,01 (only statistically significant differences are given).

In the 3rd group, *E. coli* (FO=100%) and *B. fragilis* (FO=80%) were found in PE (Table 5). Anaerobic MF slightly dominated (DC was 0.54). In the 4th group, *E. coli* (FO=100%), *B. fragilis* (FO=86.67%), LNE (FO=60%) were found in PE. Anaerobic MF dominated (DC was 0.59). The number of *B. fragilis* in the 4th group was significantly higher. The total number of MO and the number of aerobic MO in the 4th group was significantly higher.

Table 5: Microflora of peritoneal exudate in 6 h after IAI modelling

Microorganisms	3rd group	4th group
E. coli	0.452±0.028	0.423±0.189
LNE	-	0.699±0.125
B. fragilis	0.540±0.107	0.772±0.033 $p<0.05$
All aerobic	0.452±0.067	1.122±0.189 $p<0.05$
All anaerobic	0.540±0.107	0.772±0.033
Total number	0.991±0.039	1.894±0.156 $p<0.01$

The total number of MO in PE in the 3rd group was directly and closely correlated with the total number of MO in both the small and large intestines (Table 6). In the 4th group, the correlation coefficient with the number of large intestines MO was insignificant. The number of aerobic MO in PE in the 3rd group was directly correlated with the number of MO in both the small and large intestines (Table 7). In the 4th group, the correlation coefficient with the number of large intestines MO was insignificant. The number of anaerobic MO in PE in both groups was directly correlated with the number of MO in both the small and large intestines (Table 8). But the correlation coefficient with large intestines MO was significantly higher.

Table 6: Correlations between the total number of peritoneal exudate microflora and gut microflora in 6 h after IAI modelling

Group	r	p	Localization
3rd	0.94	<0.05	Small intestine
4th	0.71	<0.01	
3rd	0.90	<0.05	Large intestine
4th	0.03	<0.05	

Table 7: Correlations between the number of peritoneal exudate aerobic microflora and gut aerobic microflora in 6 h after IAI modelling

Group	r	p	Localization
3rd	0.77	<0.05	Small intestine
4th	0.65	<0.05	
3rd	0.65	<0.05	Large intestine
4th	0.03	<0.05	

Table 8: Correlations between the number of peritoneal exudate anaerobic microflora and gut anaerobic microflora in 6 h after IAI modelling

Group	r	p	Localization
3rd	0.94	<0.05	Small intestine
4th	0.65	<0.01	
3rd	0.93	<0.05	Large intestine
4th	0.97	<0.01	

In 12 h after IAI simulation, in the 3rd group, the number of *E. coli* in the SI significantly increased, and the number of *B. fragilis* significantly decreased (Table 9). The number of aerobes, anaerobes and the total number of MO has hardly changed. Aerobes dominated (DC=0.67). In the 4th group, the number of all MO increased. The number of *P. niger* increased significantly. The number of aerobes and anaerobes was almost the same (DC of aerobes was 0.51). The total number of MO and the number of anaerobic MO was significantly higher.

Table 9: Microflora of the rat's small intestine in 12 h after IAI modelling

Microorganisms	3rd group	4th group
E. coli	6.301±0.178 **	3.812±0.015 $p<0.01$
Proteus spp.	2.263±0.026	2.377±0.024
LNE	-	3.602±0.135
B. fragilis	2.772±0.033 *	4.772±0.033 $p<0.01$
P. niger	0.540±0.107	4.540±0.028 $p<0.01$,*
All aerobic	8.564±0.204	9.790±0.144
All anaerobic	3.312±0.074	9.312±0.005 $p<0.01$,*
Total number	11.876±0.130	19.102±0.149 $p<0.01$,*

Note: *- validity coefficient between the previous term of observation < 0, 05, ** - < 0,01 (only statistically significant differences are given).

In the 3rd group, the number of *E. coli* in LI almost did not change (Table 10). Hemolytic strains of *E. coli* were found (FO=40%). The number of *B. fragilis* and *Proteus* spp. significantly decreased. The number of *P. niger* has increased significantly. At the same time, LNE (FO=80%) and *Staphylococcus* spp. were found. (FO=60%). The number of aerobic MO increased significantly and aerobes dominated (DC=0.61). The total number of MO has slightly increased. In the 4rd group, the number of *E. coli* and *B. fragilis* significantly increased. At the same time, GPD (FO=100%), GPSFA (FO=80%) were found. The number of aerobes, anaerobes and the total number of bacteria increased significantly. Aerobic MO dominated, but DC (0.59) was smaller than in the 3rd group. The total number of bacteria, the number of aerobes and anaerobes was significantly higher. In addition, Candida fungi were found (FO=60%).

Table 10: Microflora of the rat's large intestine in 12 h after IAI modelling

Microorganisms	3rd group	4th group
E. coli including hemolytic strains	7.866±0.039	7.841±0.028 **
	0.151±0.067	-
Proteus spp.	2.738±0.042 *	2.643±0.125
LNE	2.151±0.962	4.739±0.018 $p<0.01$
GPD	-	6.588±0.050
Staphylococcus spp.	1.239±0.554	3.389±0.039 $p<0.01$
B. fragilis	4.327±0.167 *	6.661±0.082 $p<0.01$, *
P. niger	3.239±0.206 *	4.540±0.107 $p<0.05$
GPSFA	1.239±0.554	5.874±0.013 $p<0.01$
All aerobic	13.993±0.362 *	25.200±0.035 $p<0.01$, **
All anaerobic	8.804±0.515	17.075±0.202 $p<0.05$, *
Total number	22.797±0.188	42.275±0.237 $p<0.01$, **
Candida fungi	-	2.151±0.962

Note: *- validity coefficient between the previous term of observation < 0,05, ** - < 0,01 (only statistically significant differences are given).

In the 3rd group, the number of *E. coli* and *B. fragilis* significantly increased in PE (Table 11). In addition, *Proteus* spp. were detected. (FO=100%) and *P. niger*. (FO=60%). Microbial contamination of PE has increased significantly. Aerobes dominated (DC=0.79). In the 4th group, the number of *E. coli*, LNE, and *B. fragilis* significantly increased. GPSFAs were found. The total number of MO was almost no different from the 3rd group. The number of aerobes was significantly lower, at the same time the number of anaerobes was significantly higher. Anaerobic MO dominated (DC=0.56).

Table 11: Microflora of peritoneal exudate in 12 h after IAI modelling

Microorganisms	3rd group	4th group
E. coli	2.588±0.050 **	1.349±0.604 $p<0.05$,**
Proteus spp.	2.204±0.048	1.102±0.493
LNE	-	1.661±0.365 **
B. fragilis	0.841±0.028 *	2.588±0.050 $p<0.01$,**
P. niger	0.423±0.189	-
GPSFA	-	0.903±0.021
All aerobic	4.903±0.000 **	2.763±0.858 $p<0.05$,*
All anaerobic	1.263±0.217 **	3.491±0.050 $p<0.01$,**
Total number	6.166±0.217 **	6.254±0.808 **

Note: *- validity coefficient between the previous term of observation < 0, 05, ** - < 0, 01 (Only statistically significant differences are given).

The number of MO in the PE did not correlate with the number of MO in SI in both groups. There was a direct close correlation with the number of MO in LI in both groups (Table 12). In the 3rd group, the number of aerobic MO in PE was directly correlated with the number of MO in SI and LI (Table 13). In the 4th group, the number of aerobic MO in PE was inversely correlated with the number of MO in the SI, while it was directly correlated with the number of MO in LI. The number of anaerobic MO in PE in the 3rd group was directly correlated with the number of MO in SI and LI (Table 14). At the same time, in the 4th

group, there was a direct correlation with the number of MO in SI, and an inverse correlation was with the number of MO in LI.

Table 12: Correlations between the total number of peritoneal exudate microflora and large intestine microflora in 12 h after IAI modelling

Group	r	p
3rd	0.94	<0.05
4th	0.83	<0.05

Table 13: Correlations between the number of peritoneal exudate aerobic microflora and gut aerobic microflora in 12 h after IAI modelling

Group	r	p	Localization
3rd	0.66	<0.05	Small intestine
4th	-0.66	<0.05	
3rd	0.66	<0.05	Large intestine
4th	0.83	<0.05	

Table 14: Correlations between the number of peritoneal exudate anaerobic microflora and gut anaerobic microflora in 12 h after IAI modelling

Group	r	p	Localization
3rd	0.94	<0.05	Small intestine
4th	0.90	<0.05	
3rd	0.98	<0.05	Large intestine
4th	-0.66	<0.05	

In 24 h after IAI simulation, in the 3rd group, the number of all MO in SI significantly increased (Table 15). But the number of anaerobes increased more significantly. DC of aerobes decreased to 0.62. In the 4th group, the number of *E. coli* and *Proteus* spp. significantly increased. At the same time, GPSFA were found (FO=80%). The number of aerobes, anaerobes and the total number of MO increased significantly. There were slightly more aerobes than anaerobes. But the DC of aerobes (0.52) was insignificant. The total number of MO, the number of aerobes and anaerobes was significantly higher.

Table 15: Microflora of the rat's small intestine in 24 h after IAI modelling

Microorganisms	3rd group	4th group
E. coli	6.874±0.013 *	4.500±0.089 $p<0.01$,*
Proteus spp.	2.734±0.052 *	2.838±0.044 *
B. fragilis	4.190±0.263 **	4.778±0.144
P. niger	1.588±0.398 *	4.389±0.039 $p<0.01$
GPSFA	-	4.500±0.089 $p<0.01$
All aerobic	9.612±0.055	14.627±0.305 $p<0.05$,*
All anaerobic	5.778±0.135 *	13.667±0.050 $p<0.01$,*
Total number	15.390±0.190 *	28.294±0.256 $p<0.01$,*

Note: *- validity coefficient between the previous term of observation < 0,05, ** - < 0,01 (only statistically significant differences are given).

In the 3rd group, the number of MO in LI increased significantly, with the exception of *Staphylococcus* spp. (Table 16). DC of aerobes decreased to 0.57. Instead, in the 4th group there were both quantitative and qualitative changes of MO. Hemolytic *E. coli* strains were found (FO=60%), GPD and LNE were not found. The total number of bacteria decreased. DC of aerobes also decreased to 0.57. The total number of MO, the number of aerobes and anaerobes did not differ significantly. At the same time, the number of Candida increased significantly (FO=100%).

Table 16: Microflora of the rat's large intestine in 24 h after IAI modelling

Microorganisms	3rd group	4th group
E. coli including hemolytic strains	9.724±0.054 *	6.272±0.191 $p<0.01$
	0.239±0.107 *	0.452±0.067 $p<0.05$
Proteus spp.	3.246±0.185 *	10.852±0.408 $p<0.05$, **
LNE	4.239±1.896 **	-
Staphylococcus spp.	1.239±0.554	4.452±0.067 $p<0.01$
B. fragilis	7.073±0.102 *	5.278±0.224 $p<0.05$, *
P. niger	5.040±0.196 *	4.588±0.050 $p<0.5$
GPSFA	1.349±0.604	5.161±0.141 $p<0.05$
All aerobic	17.913±2.818 *	20.325±0.632 *
All anaerobic	13.462±0.306 **	15.027±0.415 *
Total number	31.375±3.124 **	35.352±1.047 *
Candida fungi	-	4.588±0.050 *

Note: *- validity coefficient between the previous term of observation < 0, 05, ** - < 0, 01 (only statistically significant differences are given).

In the 3rd group, the number of *E. coli*, *B. fragilis*, and *P. niger* significantly increased in PE (Table 17). In addition, *Staphylococcus* spp. (FO=80%) and hemolytic strains of *E. coli* (FO=33.33%) were founded. The total number of MO, the number of aerobes and anaerobes increased significantly. DC of aerobes decreased to 0.66. In the 4th group, the number of *Proteus* spp. significantly increased. *Staphylococcus* spp. were found (FO=60%). *E. coli* and LNE were not found. The total number of MO and the number of aerobes increased significantly. DC of aerobes increased to 0.82. The total number of MO and the number of aerobes was significantly higher.

Table 17: Microflora of peritoneal exudate in 24 h after IAI modelling

Microorganisms	3rd group	4th group
E. coli including hemolytic strains	4.040±0.117 **	-
	0.151±0.067	-
Proteus spp.	2.204±0.125	10.830±0.042 $p<0.01$, **
Staphylococcus spp.	1.151±0.515	0.772±0.033 $p<0.01$
B. fragilis	2.500±0.089 **	1.628±0.380 $p<0.01$, *
P. niger	1.423±0.636 **	-
GPSFA	-	0.874±0.874
All aerobic	7.627±0.324 *	11.510±0.075 $p<0.05$, **
All anaerobic	3.923±0.547 *	2.502±0.393
Total number	11.549±0.224 **	14.012±0.318 $p<0.05$, **

Note: *- validity coefficient between the previous term of observation < 0, 05, ** - < 0, 01 (only statistically significant differences are given).

In the 3rd group, the total number of MO in the PE was directly correlated with the number of MO in SI and LI (Table 18). At the same time, in the 4th group, there was a correlation only with the number of MO in SI. In the 3rd group, the number of aerobic MO in PE was directly correlated with the number of MO in SI and inversely correlated with the number of MO in LI (Table 19). In the 4th group, the number of aerobic MO in PE correlated only with the number of MO in SI. In the 3rd group, the number of anaerobic MO in PE was directly correlated with the number of MO in the SI and LI (Table 20). In the 4th group,

the number of anaerobic MO in PE directly and closely correlated with the number of MO in LI.

Table 18: Correlations between the total number of peritoneal exudate microflora and gut microflora in 24 h after IAI modelling

Group	r	p	Localization
3rd	0.94	<0.05	Small intestine
4th	0.89	<0.01	
3rd	0.94	<0.05	Large intestine
4th	0.20	<0.05	

Table 19: Correlations between the number of peritoneal exudate aerobic microflora and gut aerobic microflora in 24 h after IAI modelling

Group	r	p	Localization
3rd	0.60	<0.01	Small intestine
4th	0.94	<0.05	
3rd	-0.60	<0.05	Large intestine
4th	0.20	>0.05	

Table 20: Correlations between the number of peritoneal exudate anaerobic microflora and gut anaerobic microflora in 24 h after IAI modelling

Group	r	p	Localization
3rd	0.66	<0.05	Small intestine
4th	-0.14	>0.05	
3rd	0.66	<0.01	Large intestine

In 48 h after IAI simulation, in the 3rd group, the number of *E. coli*, *Proteus* spp., *B. fragilis* in SI significantly decreased (Table 21). *P. niger* was not found. GPD were found (FO=80%). The number of aerobes, anaerobes and the total number of MO significantly decreased. DC of aerobes almost did not change (0.65). In the 4th group, the number of *E. coli*, *Proteus* spp., *B. fragilis*, *P. niger* in SI decreased. The number of GPSFA increased. A large number of LNE was found (FO=100%). The number of aerobes, anaerobes and the total number of MO significantly decreased. Anaerobes dominated (DC=0.57). The number of aerobes, anaerobes and the total number of MO was significantly higher.

Table 21: Microflora of the rat's small intestine in 48 h after IAI modelling

Microorganisms	3rd group	4th group
E. coli	2.812±0.015 **	3.628±0.067
Proteus spp.	2.424±0.098	2.424±0.098
GPD	1.151±0.515	-
LNE	-	3.452±0.067
B. fragilis	3.452±0.067 *	3.000±0.313 *
P. niger	-	3.724±0.054 *
GPSFA	-	4.739±0.018
All aerobic	6.386±0.598 *	9.503±0.233 $p<0.05$, *
All anaerobic	3.452±0.067 *	11.462±0.385 $p<0.05$, *
Total number	9.837±0.530 *	20.965±0.152 $p<0.01$, *

Note: *- validity coefficient between the previous term of observation < 0, 05, ** - < 0, 01 (only statistically significant differences are given).

In the 3rd group, the number of LNE, *Staphylococcus* spp., and *E. coli* in LI significantly decreased (Table 22). GPD were found (FO=100%). The total number of MO, the number of aerobes and anaerobes decreased significantly. DC of aerobes did not change (0.57). In the 4th group, the number of *E. coli* and *Proteus* spp. significantly increased. LNEs were found (FO=100%). The number of *P. niger* and GPSFA increased significantly. The total number of MO, the number of aerobes and anaerobes increased significantly. Aerobes dominated (DC=0.64). The number of Candida fungi slightly increased. The number of aerobes, anaerobes and the total number of MO was significantly higher.

Table 22: Microflora of the rat's large intestine in 48 h after IAI modelling

Microorganisms	3rd group	4th group
E. coli including hemolytic strains	6.801±0.046 **	7.540±0.107 *
	-	0.651±0.022 *
Proteus spp.	2.204±0.105 *	11.746±0.185 *
LNE	-	6.040±0.117
GPD	3.239±1.448	-
Staphylococcus spp.	-	4.739±0.118
B. fragilis	4.661±0.082 **	4.889±0.184
P. niger	4.301±0.037 *	7.540±0.107 $p<0.01$, **
GPSFA	0.349±0.156 **	6.588±0.050 $p<0.01$*
All aerobic	12.244±1.403 *	30.063±0.436 $p<0.01$,**
All anaerobic	9.312±0.074 *	19.017±0.028 $p<0.01$, *
Total number	21.555±1.477 **	49.080±0.464 $p<0.01$, *
Candida fungi	-	4.628±0.067

Note: *- validity coefficient between the previous term of observation < 0, 05, ** - < 0,01 (only statistically significant differences are given).

In the 3rd group, the number of all MO in PE significantly decreased (Table 23). *Staphylococcus* spp. and *P. niger* were not found. DC of aerobes increased to 0.78. At the same time, in the 4th group, the total number of MO increased significantly. *E. coli* was found (FO=60), including hemolytic strains (FO=40%). LNE (FO=60%) and *P. niger* (FO=40%) were found. The number of GPSFA increased significantly. DC of aerobes decreased to 0.7. The number of aerobes, anaerobes and the total number of MO was significantly higher. In addition, a small number of Candida was found (FO=26.67%).

Table 23: Microflora of peritoneal exudate in 48 h after IAI modelling

Microorganisms	3rd group	4th group
E. coli including hemolytic strains	0.690±0.039 **	0.812±0.015
	-	0.301±0.041
Proteus spp.	2.225±0.180	9.350±0.227 $p<0.05$
LNE	-	0.588±0.050
Staphylococcus spp.	-	0.540±0.107
B. fragilis	0.801±0.046 **	2.540±0.028 $p<0.01$, *
P. niger	-	0.349±0.156
GPSFA	-	2.389±0.039 **
All aerobic	2.894±0.039 **	12.590±0.379 $p<0.01$
All anaerobic	0.801±0.046 **	5.278±0.224 $p<0.01$, *
Total number	3.695±0.085 **	17.869±0.602 $p<0.01$, *
Candida fungi	-	0.195±0.032

Note: *- validity coefficient between the previous term of observation < 0, 05, ** - < 0, 01 (only statistically significant differences are given).

In the 3rd group, the total number of MO in PE was inversely correlated with the number of MO in SI, directly correlated with the number of MO in LI (Table 18). At the same time, in the 4th group, the number of MO in PE was directly correlated with the number of MO in SI and LI. In the 3rd group, the number of aerobic MO in PE was inversely

correlated with the number of MO in SI and directly correlated with the number of MO in LI (Table 19). In the 4th group, the number of aerobic MO in PE was inversely correlated only with the number of MO in LI. In the 3rd group, the number of anaerobic MO in PE was inversely correlated with the number of MO in SI and directly correlated with the number of MO in LI (Table 20). The 4th group had the same changes, but the correlation coefficient with the number of MO in LI was significantly higher.

Table 24: Correlations between the total number of peritoneal exudate microflora and gut microflora in 48 h after IAI modelling

Group	r	p	Localization
3rd	-0.77	<0.05	Small intestine
4th	0.54	<0.05	
3rd	0.83	<0.01	Large intestine
4th	0.67	<0.01	

Table 25: Correlations between the number of peritoneal exudate aerobic microflora and gut aerobic microflora in 48 h after IAI modelling

Group	r	p	Localization
3rd	-0.77	<0.05	Small intestine
4th	0.09	>0.05	
3rd	0.71	<0.05	Large intestine
4th	-0.63	<0.05	

Table 26: Correlations between the number of peritoneal exudate anaerobic microflora and gut anaerobic microflora in 48 h after IAI modelling

Group	r	p	Localization
3rd	-0.66	<0.05	Small intestine
4th	-0.66	<0.05	
3rd	0.54	<0.05	Large intestine

Discussion

The above shows that there are dysbacteriotic changes in 2nd group, which confirms known data [23]. In SI, anaerobic MO were found, which in intact animals were found only in LI. In LI of the 2nd group animals, the number of *E. coli* was reduced, there was no GPD, which was in intact animals. Among the reasons for such changes, we can mention immune disorders characteristic of DM [17-20], a decrease of the intestinal mucosa colonization resistance, which is one of the important mechanisms of the immune dysfunction development [16, 27, 28].

In 6 hours after IAI modeling, signs of dysbacteriosis were detected in the 3rd group. It was the appearance of *Proteus* spp. and *P. niger* in SI, appearance of GPSFA in LI. At the same time, the total number of MO increased against the background of some saprophytic MO disappearance. In the 4th group, intestinal microbiocenosis disorders progressed, in particular, LNE were detected in both the small and large intestines. This indicates more significant violations of the colonization resistance of the intestinal mucosa. Dysbacteriosis is a well-known phenomenon that occurs with IAI [29]. At the same time, in the 4th group, the signs of dysbacteriosis are more severe. The basis of these changes is apparently dysbacteriosis caused by DM. The values of the correlation coefficients indicate that in this period the microbial promoters of IAI are the MF of different intestine parts. But in the 4th group, the main source of MF is LI.

In 12 h after IAI modeling, in the 3rd group, the composition of the microbiocenosis did not change significantly in SI. The ratio between MO changed. In the 4th group, the microbiocenosis also changed only quantitatively. But a large number of MO indicates the development of the syndrome of excess bacterial colonization of SI and high contamination with anaerobic MF. In LI in both groups, changes in the microbiocenosis are significantly greater. At the same time, dysbiosis (Candidiasis) was detected in the 4th group. In both groups, PE is contaminated with microbial associations that differ in their characteristics. In the 3rd group there is more aerobic MF. In the 4th group there is more anaerobic MF. It is important that there were GPSFA in PE. GPSFA produce exotoxins that have a severe proteolytic and hemolytic effect [15, 27, 29]. The result of such action is the destruction of the tissues. This burdens the development of IAI. The values of the correlation coefficients indicate that MF of LI is more important for the progression of IAI during this period. But in the 4th group, the aerobic MO in PE are more influenced by the MO of SI.

In 24 h after IAI modeling, in the 3rd group, the microbial biotope of SI was transformed only quantitatively. At the same time, GPSFA was detected in the 4th group, which indicates severe dysbacteriosis. In the 3rd group, the microbial biotope of LI was transformed, mostly quantitatively, although GPD disappeared. In the 4th group, changes in the microbial biotope were more severe. GPD and LNE are gone. A significant increase the number of Candida indicates the progression of dysbiosis. It is possible that the decrease in the amount of bacterial MF was a consequence of the antagonistic effect of Candida fungi on bacteria [30, 31]. The quantitative and species composition of MO in PE in both groups changed. Aerobes dominated in both groups. But in the 4th group in PE there were GPSFA, which are very aggressive MO. The values of the correlation coefficients indicate that in the 3rd group, changes in the MO in PE are associated with changes in the MO in SI and LI. In the 4th group, changes of aerobic MO in PE are more influenced by MO of SI, and changes of anaerobic MO are more influenced by MO of LI.

In 48 h after IAI modeling, changes in intestinal microbiocenosis continued in both groups. During this period, species changes of MF in SI were first detected in the 3rd group. At the same time, dysbacteriosis in SI persisted in the 4th group. The number of MF in LI significantly increased, the number of anaerobic MO increased, the number of Candida increased. In the 3rd group, the number of MO in PE decreased, some strains of MO disappeared. It is possible that this was a consequence of the activation of immune defense mechanisms, which is also indicated by changes in the intestinal MF [15, 16, 20, 29]. At the same time, in the 4th group, negative changes of MF in PE progressed. New MO were detected in PE, the number of highly aggressive GPSFA increased. Candida fungi were detected, indicating severe immune disorders [32]. The values of the correlation coefficients indicate that in the 3rd group, the changes of MO in PE are more related to the changes of MO in SI and LI. In the 4th group, the changes of MO in PE are more related to changes of MO in LI.

Therefore, it can be summarized that the simulation of DM causes dysbacteriosis in SI and LI. After modeling of IAI, dysbacteriosis occurs in intact rats, dysbacteriosis progresses in rats with DM models. Dysbiosis occurs 12 h after IAI modeling in rats with DM models. During the development of IAI, permanent changes in the intestinal microbiocenosis and microbial associations in PE are

observed. Changes are more substantial in rats with DM models.

Changes of MF in SI, LI and PE in intact rats 48 h after IAI simulation indicate the activation of protective immune mechanisms. Instead, changes of MF in SI, LI and PE in rats with DM models indicate the progression of pathological processes. At later times, experiments were not carried out, because all rats with models of DM and IAI died.

The presented study has a number of limitations. The study used small samples (15 rats each). It is necessary to conduct additional experiments on a larger number of animals to confirm the data. Female rats were used in the previous study. Therefore, male rats should be used to confirm the data in future studies. Material for microbiological examination were taken in the middle part of SI and in the middle part of LI. It is advisable to study other parts of the intestines for better results. The previous study used rats. To confirm the data, it is advisable to conduct experiments with other species of animals. Specific data from other studies regarding the types of microorganisms, their number, etc., may differ. Such data are affected by various factors: the type of animals, feeding characteristics, living conditions, characteristics of applied simulating ways, etc. But, taking into account the known physiological and pathological regularities common to all warm-blooded mammals, these limitations will not have a significant affect the generalizability of the findings. It can be expected that the basic regularities will be confirmed, but some indicators may change slightly.

Conclusion

1. Intestinal dysbacteriosis was detected in rats 3 months after diabetes mellitus modeling.
2. Modeling of intra-abdominal infection in intact rats causes intestinal dysbacteriosis, a syndrome of excess bacterial colonization of small intestines.
3. Modeling of intra-abdominal infection in rats with diabetes mellitus models increases intestinal dysbacteriosis, causes the syndrome of excess bacterial colonization of small intestines, dysbiosis in large intestines.
4. In intact rats, 48 h after intra-abdominal infection modeling, signs of dysbacteriosis regression and a decrease in the number of microorganisms in peritoneal exudate were detected, instead in rats with diabetes mellitus models, signs of dysbacteriosis and dysbiosis progression and an increase in the number of microorganisms in peritoneal exudate were detected.

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Conflict of Interest

Not available

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References

1. Popejoy MW, Long J, Huntington JA. Analysis of patients with diabetes and complicated intra-abdominal infection or complicated urinary tract infection in phase 3 trials of ceftolozane/tazobactam. BMC Infect Dis. 2017;17(1):316. DOI: 10.1186/s12879-017-2414-9
2. Jaghutriz BA, Wagner R, Kullmann S, Fritsche L, Eckstein SS, Dannecker C, *et al*. The TUDID Study - Background and Design of a Prospective Cohort. Exp Clin Endocrinol Diabetes. 2022;130(1):43-48. DOI: 10.1055/a-1221-9618
3. Saeedi P, Salpea P, Karuranga S, Petersohn I, Malanda B, Gregg EW, *et al*. Mortality attributable to diabetes in 20-79 years old adults, 2019 estimates: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. Diabetes Res Clin Pract. 2020;162:108086. DOI: 10.1016/j.diabres.2020.108086
4. Al-Ibrahimy AS, Rabea IS. Evaluation of General Health Status in Diabetic Patients Using Short Form Health Survey (SF-36). Curr Diabetes Rev. 2023;19(9):e081420184858. DOI: 10.2174/1573399816666200814133535
5. Van Den Boom L, Buchal G, Kaiser M, Kostev K. J Multimorbidity Among Adult Outpatients With Type 1 Diabetes in Germany. Diabetes Sci Technol. 2022;16(1):152-160. DOI: 10.1177/1932296820965261
6. Napolitano LM. Intra-abdominal Infections. Semin Respir Crit Care Med. 2022;43(1):10-27. DOI: 10.1055/s-0041-1741053
7. Sartelli M, Chichom-Mefire A, Labricciosa FM, Hardcastle T, Abu-Zidan FM, Adesunkanmi AK, *et al*. The management of intra-abdominal infections from a global perspective: 2017 WSES guidelines for management of intra-abdominal infections. World J Emerg Surg. 2017;12:29. DOI: 10.1186/s13017-017-0141-6
8. Coccolini F, Sartelli M, Sawyer R, Rasa K, Viaggi B, Abu-Zidan F, *et al*. Source control in emergency general surgery: WSES, GAIS, SIS-E, SIS-A guidelines. World J Emerg Surg. 2023;18(1):41. DOI: 10.1186/s13017-023-00509-4
9. Kim EJ, Ha KH, Kim DJ, Choi YH. Diabetes and the Risk of Infection: A National Cohort Study. Diabetes Metab J. 2019;43(6):804-814. DOI: 10.4093/dmj.2019.0071
10. Casqueiro J, Casqueiro J, Alves C. Infections in patients with diabetes mellistus. A review of pathogenesis. Indian J Endocrinol Metab. 2012 Mar;16(1):27-36. DOI: 10.4103/2230-8210.94253
11. Wang JL, Hsu CR, Wu CY, Lin HH. Diabetes and obesity and risk of pyogenic liver abscess. Sci Rep. 2023;13(1):7922. DOI: 10.1038/s41598-023-34889-z
12. Tan DJH, Yaow CYL, Mok HT, Ng CH, Tai CH, Tham HY, *et al*. The influence of diabetes on postoperative complications following colorectal surgery. Tech Coloproctol. 2021;25(3):267-278. DOI: 10.1007/s10151-020-02373-9
13. Luo X, Li L, Ou S, Zeng Z, Chen Z. Risk Factors for Mortality in Abdominal Infection Patients in ICU: A Retrospective Study From 2011 to 2018. Front Med (Lausanne). 2022;9:839284.

DOI: 10.3389/fmed.2022.839284.
14. Arvaniti K, Dimopoulos G, Antonelli M, Blot K, Creagh-Brown B, Deschepper M, *et al*. Epidemiology and age-related mortality in critically ill patients with intra-abdominal infection or sepsis: an international cohort study. Int J Antimicrob Agents. 2022;60(1):106591. DOI: 10.1016/j.ijantimicag.2022.106591
15. Yan Y, Ye Q, Liu L. Characteristics of pathogenic bacteria in intra-abdominal infection and risk factors for septic shock in patients with liver cirrhosis. Am J Transl Res. 2022;14(3):1742-1749.
16. Abbas AK, Lichtman AH, Pillai Sh. Cellular and molecular immunology. 7th ed. International edition. Philadelphia: Elsevier/ Saunders; c2012. p. 545.
17. Berbudi A, Rahmadika N, Tjahjadi AI, Ruslami R. Type 2 Diabetes and its Impact on the Immune System. Curr Diabetes Rev. 2020;16(5):442-449. DOI: 10.2174/1573399815666191024085838
18. Girard D, Vandiedonck C. How dysregulation of the immune system promotes diabetes mellitus and cardiovascular risk complications. Front Cardiovasc Med. 2022 Sep 29;9:991716. DOI: 10.3389/fcvm.2022.991716
19. Boyko VV, Riga AS. Type 2 diabetes mellitus - IL-8 and IL-10 profile in patients with intraabdominal postoperative abscesses. Wiad Lek. 2020;73(2):220-223. DOI: 10.36740/WLek202002102
20. Grynchuk FV, Polianskiy IY, Grynchuk AF, Sheremet M, Maksymyuk VV, Tarabanchuk VV, *et al*. Characteristics of cytokine status in intra-abdominal infection with underlying diabetes mellitus: An experimental study. RJDNMD [Internet]. 31Oct.2021 [cited 27Nov.2023];28(3):255-60. Available from: https://www.rjdnmd.org/index.php/RJDNMD/article/view/1054
21. Núñez SA, Lacal V, Núñez J, Serruto G, Zárate MS, Verón MT. Antibiotic Resistance in Community-Acquired Intra-Abdominal Infections: Diabetes Mellitus as a Risk Factor. Surg Infect (Larchmt). 2020 Feb;21(1):62-8. DOI: 10.1089/sur.2019.032
22. Carrillo-Larco RM, Anza-Ramírez C, Saal-Zapata G, Villarreal-Zegarra D, Zafra-Tanaka JH, Ugarte-Gil C, *et al*. Type 2 diabetes mellitus and antibiotic-resistant infections: a systematic review and meta-analysis. J Epidemiol Community Health. 2022 Jan;76(1):75-84. DOI: 10.1136/jech-2020-216029
23. Moreira LAA, Da Paz Lima L, De Oliveira Falcão MA, Rosado EL. Profile of Gut Microbiota of Adults with Diabetes Mellitus Type 1: A Systematic Review. Curr Diabetes Rev. 2023;19(4):e280322202706. DOI: 10.2174/1573399818666220328150044
24. Woldeamlak B, Yirdaw K, Biadgo B. Role of Gut Microbiota in Type 2 Diabetes Mellitus and Its Complications: Novel Insights and Potential Intervention Strategies. Korean J Gastroenterol. 2019;74(6):314-320. DOI: 10.4166/kjg.2019.74.6.314
25. Tanase DM, Gosav EM, Neculae E, Costea CF, Ciocoiu M, Hurjui LL, *et al*. Role of Gut Microbiota on Onset and Progression of Microvascular Complications of Type 2 Diabetes (T2DM). Nutrients. 2020;12(12):3719. DOI: 10.3390/nu12123719.
26. Iatcu CO, Steen A, Covasa M. Gut Microbiota and Complications of Type-2 Diabetes. Nutrients. 2021;14(1):166. DOI: 10.3390/nu14010166
27. Kim S, Covington A, Pamer EG. The intestinal microbiota: Antibiotics, colonization resistance, and enteric pathogens. Immunol Rev. 2017 Sep;279(1):90-105. DOI: 10.1111/imr.12563
28. Lawley TD, Walker AW. Intestinal colonization resistance. Immunology. 2013;138(1):1-11. DOI: 10.1111/j.1365-2567.2012.03616.x
29. Lobo LA, Benjamim CF, Oliveira AC. The interplay between microbiota and inflammation: lessons from peritonitis and sepsis. Clin Transl Immunology. 2016 Jul 15;5(7):e90. DOI: 10.1038/cti.2016.32
30. Allison DL, Willems HME, Jayatilake JAMS, Bruno VM, Peters BM, Shirtliff ME. Candida-Bacteria Interactions: Their Impact on Human Disease. Microbiol Spectr; c2016 Jun, 4(3). DOI: 10.1128/microbiolspec.VMBF-0030-2016
31. Kapitan M, Niemiec MJ, Steimle A, Frick JS, Jacobsen ID. Fungi as Part of the Microbiota and Interactions with Intestinal Bacteria. Curr Top Microbiol Immunol. 2019;422:265-301. DOI: 10.1007/82_2018_117
32. Arce Miranda JE, Baronetti JL, Sotomayor CE, Paraje MG. Oxidative and nitrosative stress responses during macrophage-Candida albicans biofilm interaction. Med Mycol. 2019 Jan 1;57(1):101-113. DOI: 10.1093/mmy/myx143

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