

ORIGINAL ARTICLE  
PRACA ORYGINALNA

## TYPE 2 DIABETES MELLITUS – IL-8 AND IL-10 PROFILE IN PATIENTS WITH INTRAABDOMINAL POSTOPERATIVE ABSCESES

DOI: 10.36740/WLek202002102

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### ABSTRACT

**The aim:** To assess of pro-inflammatory IL-8 and anti-inflammatory IL-10 serum concentration in patients with T2DM with intraabdominal postoperative abscesses in perioperative period.

**Materials and methods:** The 48 participants, aged 40 – 75 years, among them 24 males and 24 females. All patients were divided into groups: group 1 – 12 patients with T2DM and intra-abdominal postoperative abscesses, group 2 – 12 patients without T2DM but with intra-abdominal postoperative abscesses and 24 healthy individuals. The level of IL-8 and IL-10 serum was determined on the day before surgery, on the 2-3rd and 5-7th day after surgery in patients with type 2 diabetes and intra-abdominal postoperative abscesses.

**Results and conclusions:** The trajectories of the level of interleukins in patients with type 2 Diabetes mellitus were different from the trajectories of their level in patients without diabetes, which indicates a special immune response to nosocomial infection and surgical trauma. The mechanism of changes in serum levels of IL-8 and IL-10 in patients with type 2 Diabetes mellitus and postoperative intra-abdominal abscesses should be further studied in future studies on the specific causative agent of nosocomial infection and the cytokine response to it.

**KEY WORDS:** type 2 Diabetes mellitus, postoperative intra-abdominal abscesses, interleukin-8, interleukin-10

Wiad Lek. 2020;73(2):220-223

### INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a global epidemic costly condition [1, 2]. Individuals with T2DM sustain reduction in quality of life, and high prevalence of morbidity and mortality [3].

The pathophysiology of T2DM has enough been studied [4]. The infections are more in patients with T2DM with the course of them is more complicated. One of the possible causes of this increased prevalence of infections is defects in immunity. It depends on hyperglycemia, decreased immune cellular responses [5].

Many clinical conditions generally require expensive and time-consuming investigations for their diagnosis. The very important problem in surgery is a diagnosis and management of postoperative abscesses, especially in patients with T2DM. There is therefore a general need for exploring non-invasive markers in clinical medicine. Interleukin-8 (IL-8) and interleukin-10 (IL-10) is currently being applied in various subspecialties of medicine either for the purpose of rapid diagnosis or as a predictor of prognosis [6].

### THE AIM

To assess of pro-inflammatory IL-8 and anti-inflammatory IL-10 serum concentration in patients with T2DM with intraabdominal postoperative abscesses in perioperative period. Hypothesis: There is a difference in serum IL-8 and IL-10 between diabetics and non-diabetic

patients with intra-abdominal postoperative abscesses in perioperative period.

### MATERIALS AND METHODS

A case-control study is designed to compare of clinical course of perioperative period and cytokines (IL-8 and IL-10) at the day before surgical intervention, at the 2<sup>nd</sup>-3<sup>rd</sup> day and 5<sup>th</sup>-7<sup>th</sup> day after surgical intervention in patients with T2DM and intra-abdominal postoperative abscesses due to intra-abdominal infections.

The 48 participants were recruiting from the Hospital of State Enterprise “Institute of General and Emergency Surgery named after V.T.Zaytsev” NAMS of Ukraine” in 2016-2018 aged 40 – 75 years, among them 24 males and 24 females. All patients were divided into groups: group 1 – 12 patients with T2DM and intra-abdominal postoperative abscesses, group 2 – 12 patients without T2DM but with intra-abdominal postoperative abscesses and 24 healthy individuals.

**Inclusion criteria.** 1. Having intra-abdominal postoperative abscesses and T2DM. 2. Willingness to participate. 3. Age: 40-75 years old.

**Exclusion criteria.** Patients who do not presented intra-abdominal postoperative abscesses with T2DM and those who do not agreed to participate of this study.

**Blood samples.** For immunological analysis, it was obtained of 5 ml blood from 24 healthy volunteers and each

patient (group 1 and 2) by vacuum sterile disposable tubes (Vacutainer) at the day before surgical intervention, on 2<sup>nd</sup>-3<sup>rd</sup> day and on 5<sup>th</sup>-7<sup>th</sup> day after surgical intervention. Serum was centrifuged at 800 g for 10 min at 4°C and has stored at -20°C. Extracellular IL-8 and IL-10 in the serum was assessed with VectorBESTUkraine test system cytokines kit, according to manufacturer's instructions in immune enzyme analyzer "LabLine-90" (Austria).

**Ethical Considerations.** This study was approved by the Ethics Committee of the Kharkiv National Medical University (Report No 6 from 05.10.2016). Informed consent was obtained for every patient.

**Statistical analyses.** Normality of data distribution is evaluated using Kolmogorov-Smirnov test. Comparison of data between two groups is done by Mann-Whitney U (not normal distribution). Comparison of percentages was performed using the Fisher criterion. Statistical descriptive analysis was performed with the MedCalc Software (Acaciaaan 22 B-8400 Ostend, Belgium), for all statistical methods,  $p < 0.05$  was considered statistically significance.

## RESULTS

There were previous surgical interventions due to intra-abdominal infections among patients of 1<sup>st</sup> and 2<sup>nd</sup> group. All patients took antibacterial therapy according hospital local protocol. Among patients with T2DM all were medication-treated, 10 have had diabetic complications: polyneuropathy (4/12), retinopathy (4/10), urine albumin excretion (2/12). The average glycated hemoglobin (A1C) level was 9.6%.

The common comorbidities, surgical approaches, and demographic data of patients are present in Table 1.

The manifestation of postoperative abscesses, complains, characteristics, surgical approaches and demographic data of patients with and without T2DM have not significant difference as well as characteristics of origin of intra-abdominal infections and localization of postoperative abscesses. Difference was in variation of days of hospitalization in patients both group. The median, minimal and maximal value of serum IL-8 in 24 healthy individuals were 72,08 (16,68; 96,36) pg/ml, serum IL-10 – 4,87 (2,35; 8,94) pg/ml.

We obtained statistically significant differences of serum concentrations of IL-8 and IL-10 in 1<sup>st</sup> and 2<sup>nd</sup> group's patients at the day before surgery, at 2<sup>nd</sup> -3<sup>rd</sup> day and 5<sup>th</sup> -7<sup>th</sup> day after surgery compared with the values of healthy individuals. So we obtained statistically significant differences of serum concentrations of IL-8 and IL-10 comparing 1<sup>st</sup> and 2<sup>nd</sup> group's patients (Table 2).

The distribution of cytokines levels by day in the perioperative period shows that both IL-8 and IL-10 are significantly lower in patients with T2DM: pro-inflammatory IL-8 is reduced by 5<sup>th</sup> -7<sup>th</sup> days, and anti-inflammatory IL-10 is reduced by 2<sup>nd</sup> -3<sup>rd</sup> days of the postoperative period in serum and saved so by 5<sup>th</sup>-7<sup>th</sup> days. The level of serum IL-8 was increasing in patients with postoperative intra-abdominal abscesses and

without T2DM by the 5<sup>th</sup> -7<sup>th</sup> day of the postoperative period. The level of anti-inflammatory IL-10 was significant higher in patients without T2DM. It suggest about mature immune reaction to nosocomial infection and surgical trauma.

## DISCUSSION

According to numerous publications, T2DM is a risk factor for the development of intra-abdominal infections [7, 8]. Chronic hyperglycemia contributes to increase the risk of gastrointestinal infectious processes [5].

The most studies show decreased functions of diabetic polymorph nuclear cells and diabetic monocytes/macrophages compared to cells of healthy persons [9]. But the data on the level of cytokines are contradictory. So, study of Cimini F.A. et al, demonstrates that serum IL-8 is increased in diabetic patients [10]. Similarly contradictory information regarding the concentration of serum IL-10: mononuclear cells and monocytes of persons with T2DM secrete less cytokines in response to stimulation by lipopolysaccharides [5]. However, other studies reported that the increased glycation could inhibit the production of IL-10 by myeloid cells, impairing cell immunity [11]. Some investigators claim that the differences in the risk factors for infection between diabetic and non-diabetic patients result either from non-controlled studies or biased studies. However, most researchers conclude that there is clinical evidence pointing to the higher prevalence of infectious diseases among individuals with T2DM [7, 12].

Of course, the immune response of the cytokine profile varies in patients with bacterial infection of the intra-abdominal cavity. But no final result has been achieved with respect to the determination of the levels of interleukins. Some study shows increasing serum IL-8 and IL-10, as well as their decreasing in the perioperative period in other studies [13, 14].

Our study showed that both pro-inflammatory and anti-inflammatory interleukins IL-8 and IL-10 in formation of postoperative intra-abdominal abscesses have low values compared with the values of healthy individuals, and the lowest values in patients with T2DM. The combination of T2DM and postoperative intra-abdominal abscesses is accompanied by a complex relationship between the immune response of the macroorganism and nosocomial flora.

A low level of serum pro- and anti-inflammatory response to infection in T2DM explains the longer hospitalization of patients with postoperative intra-abdominal abscesses.

Assessing the risk of formation of postoperative intra-abdominal abscesses in patients with T2DM is important for infection's agents' control, and antimicrobial therapy, and control of diabetes. In a matched cohort study using a Canadian electronic medical record-based surveillance system, the odds of any infection were higher among 1779 patients with diabetes (22 percent on insulin) compared with 11,066 matched controls, after controlling for potential confounders (adjusted odds ratio 1.21, 95% CI 1.07-1.37) [15].

In another retrospective cohort study using a large primary care database in England, the incidence rate ratio (IRR) for any infec-

**Table 1.** Clinical characteristics, surgical approaches and demographic data of patients

Data	Group 1, n=12	Group 2, n=12	p
Age, years (Median, (min; max))*	63 (53; 70)	61 (50; 69)	0.5641
Men, n (%)	5 (42)	7 (58)	0.4415
Systemic arterial hypertension, n (%)	8 (67)	6 (50)	0.4071
Obesity (increase than 20 % of an individual's ideal body weight), n (%)	4 (33)	2 (17)	0.3752
Body temperature > 38.0°C, n (%)	5 (42)	8 (67)	0.2318
Critical state at hospital admission, n (%)	3 (25)	5 (42)	0.3842
Chronic cholecystitis/pancreatitis, n (%)	5 (42)	3 (25)	0.3842
Duration in hospital, days (Median, (min; max))*	13 (8; 98)	17 (7; 34)	0.0489
Minimally invasive surgical intervention (abscess puncture), n (%)	10 (83)	12 (100)	0.1847
Hepatic abscess, n (%)	7 (58)	5 (42)	0.4415
Subhepatic abscess, n (%)	1 (8)	2 (17)	0.5120
Subphrenic abscess, n (%)	1 (8)	4 (33)	0.1435
Mixed abscess localization, n (%)	3 (25)	1 (8)	0.2740

\*Mann-Whitney test

**Table 2.** Distribution of IL-8 and IL-10 serum level in patients in perioperative period

Perioperative period	Group 1 n=12	Group 2 n=12	p
IL-8, pg/ml, median, (min; max)			
Day before surgical intervention	27,11 (18,09; 48,42)	38,44 (20,11; 59,55)	0.1955
2 <sup>nd</sup> -3 <sup>rd</sup> day after surgical intervention	23,99 (17,31; 40,7)	38,39 (16,99; 64,4)	0.0683
5 <sup>th</sup> -7 <sup>th</sup> day after surgical intervention	20,08 (12,13; 30,81)	43 (19,78; 56,5)	0.0358
IL-10, pg/ml, median, (min; max)			
Day before surgical intervention	12,08 (7,62; 18,16)	17,86 (9,06; 28,1)	0.0683
2 <sup>nd</sup> -3 <sup>rd</sup> day after surgical intervention	7,26 (4,87; 14,93)	12,89 (6,06; 22,91)	0.0449
5 <sup>th</sup> -7 <sup>th</sup> day after surgical intervention	7,5 (4,39; 15,17)	12,68 (4,03; 21,03)	0.0349

tion was higher among 5863 patients with type 1 diabetes mellitus (IRR 1.66, 95% CI 1.59-1.74) and 96,930 with T2DM (1.47, 95% CI 1.46-1.49) compared with age, sex, and practice-matched controls (n = 11,696 for type 1 and n = 191,822 for type 2) [16].

Our data decrease serum IL-8 level in perioperative period both patients with or without T2DM are corresponding data of Zhengwen Xiao et al. [13] and João Fernando Gonçalves Ferreira et al. [17] which proved that the greatest concentration of IL-8 is contained in the inflammatory focus compared with serum.

Our data corresponding data about cell-mediated immunity are all depressed in diabetics with hyperglycemia that were published in 1997 and 2000 [18, 19]. Our result supports that correct choice of antibiotic therapy early during infection is important to prevent not only bacterial over growth, but also uncontrolled inflammation and uncontrolled

T2DM. Accordingly, Barnett et al. also observed that nosocomial-acquired infections are more severe, requiring longer hospitalization and showing higher death rates in risk-group patients. [20].

## CONCLUSIONS

The mechanism of value serum IL-8 and IL-10 in patients with T2DM and postoperative intra-abdominal abscesses should be explored with future studies targeting a specific causative agent of nosocomial infection and cytokine response.

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#### Conflicts of interest:

Authors declare no conflict of interest.

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**Received:** 11.05.2019

**Accepted:** 20.12.2019

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**A** – Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis, **D** – Writing the article, **E** – Critical review, **F** – Final approval of the article