J Renal Inj Prev. 2022; 11(3): e31976.

http://journalrip.com doi: 10.34172/jrip.2022.31976

Journal of Renal Injury Prevention

IL-17 gene polymorphism (rs763780) in kidney recipients with post-transplant diabetes

Sepideh Zununi Vahed[1], Jalal Etemadi[1], Taraneh Majidi[1], Seyyedeh Mina Hejazian[1,2], Paria Ronaghi[1,2], Mohammadreza Ardalan[1*]

[1]Kidney Research Center, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran
[2]Student Research Committee, Tabriz University of Medical Sciences, Tabriz, Iran

ARTICLE INFO

Article Type:
Original

Article History:
Received: 27 October 2021
Accepted: 11 December 2021
Published online: 24 April 2022

Keywords:
Post-transplant diabetes mellitus
NODAT
Interleukin-17
IL-17F gene polymorphism
Kidney transplantation

ABSTRACT

Introduction: New-onset diabetes mellitus after transplantation (NODAT) is a common complication of organ transplantation, leading to allograft dysfunction. Genetic alterations of inflammatory cytokines have been reported to be associated with glucose homeostasis and diabetes.

Objectives: This study evaluated the rs763780 polymorphism of IL-17F gene in transplant recipients with and without NODAT.

Patients and Methods: The present retrospective study was conducted on ninety-one patients who have had a kidney transplant for at least three months. Patients were divided into two subgroups; recipients with NODAT (n = 32) and kidney recipients without NODAT (n = 59). After DNA extraction from patients' blood samples, amplification and evaluation of specific polymorphism of the gene were performed using amplification refractory mutation system-polymerase chain reaction (ARMS-PCR). Clinical and demographic data of patients were collected.

Results: The NODAT was detected in 81.3% (n = 26) of TT genotype carriers, 12.5% of TC genotype carriers and 6.3% of CC genotype carriers. No statistically significant differences between the studied groups in the frequency of C and T alleles and the distribution of the abovementioned genotypes were detected ($P \geq 0.721$). In the NODAT group, graft rejection and age of patients were higher significantly ($P \leq 0.017$).

Conclusion: No significant correlation between the incidence of diabetes and rs763780 polymorphism of IL-17F gene was observed.

Implication for health policy/practice/research/medical education:
Dysfunction of pancreatic β-cells, insulin resistance, oxidative stress and low-grade chronic inflammation play important roles in the development of new-onset diabetes mellitus after transplantation (NODAT) among kidney transplant recipients. IL-17 polymorphisms impact on the pathogenesis of NODAT and variations in IL-17R is connected with type 1 diabetes (T1D) that are reported to be associated with the pathogenesis of NODAT.

Please cite this paper as: Zununi Vahed S, Etemadi J, Majidi T, Hejazian SM, Ronaghi P, Ardalan M. IL-17 gene polymorphism (rs763780) in kidney recipients with post-transplant diabetes. J Renal Inj Prev. 2022; 11(3): e31976. doi: 10.34172/jrip.2022.31976.

Introduction

New-onset diabetes mellitus after transplantation (NODAT) is a severe complication that occurs after kidney transplantation, affecting 2% to 53% of allograft recipients (1,2). The NODAT is linked with an elevated risk of allograft rejection, infection and cardiovascular disease. Moreover, it is correlated with an increase in three-year mortality and a decline in the survival of allografts and transplant recipients (3).

The result of a meta-analysis on 7140 kidney recipients indicates that acute rejection, tacrolimus administration, history of hypertension, viral infection (hepatitis B and C viruses), polycystic kidney disease, body mass index (BMI) (4), older age and family history of diabetes are risk factors for the development of NODAT (5). It has also been recently reported that high serum uric acid is connected with an increased risk of NODAT developing, independent of proven risk factors (6). Predisposing genetic factors as risk factors are also participated in the development of NODAT (7-9). Unfortunately, the results between

***Corresponding author**: Prof. Mohammadreza Ardalan, Email: ardalan34@yahoo.com, ardalanm@tbzmed.ac.ir

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different populations are inconclusive and the clinic needs to identify the carriers of pharmacogenetics variants and the genetic risk factors involved in the development of NODAT. Early detection, management and treatment of NODAT may improve transplant outcome.

Numerous experimental and clinical studies have reported that inflammatory cytokines can be related to diabetes. IL-17F promotes several pro-inflammatory chemokines and cytokines and is considered as an inflammatory cytokine (10). Evidence supports definite role of IL-17 in the pathogenesis of type 2 (T2D) and type 1 (T1D) diabetes. Through activating NF-κB (nuclear factor-kappa B) pathway, IL-17 triggers production of pro-inflammatory cytokines involved in the stimulation of insulin resistance, resulting in T2D development (11). Similar to T2D, dysfunction of pancreatic β-cells, insulin resistance, oxidative stress and low-grade chronic inflammation play significant roles in the NODAT development in kidney transplantation (12,13).

Objectives

There is an overlap of risk factors for T2D and NODAT. However, the pathophysiology and clinical courses are different. Although β-cell destruction can be the main cause for the NODAT, rarely have there been reports on the impact of IL-17 polymorphisms on the pathogenesis of NODAT. Variations of IL-17RB, IL-17R, IL-17E and IL-7R that is connected with T1D are reported to be associated with the pathogenesis of NODAT (14). Here, the association between IL-17 gene polymorphism rs763780 and NODAT was examined in a group of Iranian renal transplant patients with and without NODAT.

Patients and Methods

Patients

This retrospective study recruited renal kidney transplants from the transplantation ward of Imam-Reza hospital (Tabriz, Iran) between July 2012-2017. Patients with pre-transplant fasting blood sugar of ≤99 mg/dL, ≥18 years old, patients who received allograft at least three months before this study and treated with the same protocol were included. Patients with pre-transplant diabetes and active viral infection (cytomegalovirus and BK virus) were excluded from the study. All clinical and demographic data of patients were collected. Genomic DNA was obtained from whole blood samples (2 mL) by ZiAViZ DNA extraction kit (Iran). In this method, magnetic nanoparticles were employed for higher efficiency. Amplification refractory mutation system-polymerase chain reaction (ARMS-PCR) method was used to examine the polymorphism of the gene using forward; 5-AGACAGGACTTGTTGCAGAGCACTG 3, reverse wild type; 5-CGTCACCCCTGTCATCCAACG-3, and reverse mutant 5-CGTCACCCCTGTCATCCAACA-3 primers.

Statistical analysis

Data analysis was conducted using SPSS software version 23.0. In descriptive statistical methods, normality was determined by Shapiro-Wilk test. The correlation between the gene polymorphism and each clinical parameters was reported as frequency (percentage) using chi-square or Fisher's exact tests to compare the two groups. Ninety-five percent confidence interval (CI) were utilized; additionally *P* value less than 0.05 was considered statistically significant.

Results

In this retrospective study, the records of 369 transplant patients who had received kidney transplants in the transplant ward of Imam-Reza hospital in Tabriz between 2012 and 2017 were reviewed. Of those, 30 patients died and 248 patients were excluded from the study for various reasons such as age <18 years, foreigners, pre-transplant diabetes, post-transplant cancer and dissatisfaction with participation in the study. Ninety-one patients including thirty-two kidney recipients with NODAT and 59 patients with no-diabetes met our criteria to be studied.

Patients' characteristics

There was a statistically significant difference between NODAT and non-diabetic groups regarding the age of participants; the mean age of NODAT cases was higher than the non-diabetic patients ($P < 0.001$). In the study of cholesterol ($P = 0.246$) and BMI ($P = 0.501$), no significant differences were observed between the two groups. Moreover, the mean level of triglyceride in the NODAT group was higher than the non-diabetic group, however, this difference was not statistically significant ($P = 0.069$). The duration of dialysis was significantly different between the two groups; median of 25.5 (18-35.75) months in NODAT group compared to 16 (7-28) months in non-diabetic group ($P = 0.003$). The initial ($P = 0.063$) and three months after transplantation ($P = 0.538$) serum creatinine levels between the two groups were not statistically significant; however, six months post-transplantation, it became statistically significant ($P = 0.023$).

Among patients in the NODAT group, the incidence of diabetes was the same in both men and women ($P = 0.229$). Intragroup changes in serum creatinine levels of diabetic patients in different measurements (at discharge, three months and six months post-transplantation) were statistically significant ($P = 0.013$). Thus, the amount of creatinine shows a significant increase over time. No significant difference was observed between the groups regarding serum creatinine levels in repeated measurements ($P = 0.077$; Table 1).

There was no significant association between family history of diabetes and NODAT ($P = 0.608$). Among people with a family history of diabetes in the NODAT

Table 1. Demographic and basic characteristics of the participants

Variables	Non-NODAT recipients	NODAT recipients	*P* value*
Number	59	32	
Gender (F/M)	28/31	11/21	0.22
Age (years)	40.44 ± 10.63	51.59 ± 11.14	**<0.001**
BMI (kg/m^2)	30.08 ± 30.89	26.6 ± 3.88	0.501
Cholesterol (mg/dL)	166.19 ± 38.42	176.66 ± 45.02	0.246
TG (mg/dL)	159.76 ± 81.69	213.34 ± 139.03	0.069
Creatinine (mg/dL)	1.23 ± 0.3	1.38 ± 0.36	0.063
Creatinine after 3 month (mg/dL)	1.33 ± 0.38	1.4 ± 0.44	0.538
Creatinine after 6 month (mg/dL)	1.3 ± 0.35	1.49 ± 041	**0.023**
Dialysis length	16 (7-28)	25.5 (18-35.75)	**0.001**[a]

TG: triglyceride, BMI: body mass index, F: female, M: male, NODAT: new-onset diabetes mellitus after transplantation.The quantitative data are expressed as mean ± SD.

[a] Median (interquartile range) is presented. * *P* value is based on Mann-Whitney U test and *P* value ≤ 0.05 was considered as statistically significant outcome.

group, 8 (40%) developed diabetes and this rate was twenty-four (33.8%) in patients without a history of diabetes. No significant association was observed between living donor or deceased donor and NODAT ($P = 0.9$). However, all three patients who received transplant rejection (100%) were reported to be diabetic. We also found a significant connection between transplant rejection and presents diabetes ($P = 0.017$).

The frequency of IL-17 rs763780 gene polymorphism among studied groups

It was revealed that 82.4% (n=75) of transplant patients were carriers of TT genotype, 12.1% (n=11) were carriers of TC genotype and 5.5% (n=5) were carriers of CC genotype. The distribution of TT, TC and CC genotypes of rs763780 genotype and its comparison between case and control groups is shown in Table 2. We observed that 81.3% (n=26) of NODAT patients were TT genotype carriers, 12.5% were TC genotype carriers and 6.3% were CC genotype carriers. Moreover, no statistically significant difference between the groups in the distribution of the genotypes was detected ($P = 0.721$).

Associations of IL-17 gene polymorphism and NODAT

The correlation between the studied polymorphism and clinical parameters and the incidence of diabetes in transplant patients was investigated. In the NODAT group, fast blood sugar (FBS) six months after transplantation was higher in C allele carriers compared to T allele; however this difference was not significant ($P = 0.856$). According to Table 3, no significant correlation was seen between the distribution of TT, TC and CC genotypes of rs763780 genotype and any of the clinical parameters in transplant patients ($P > 0.05$). Moreover no significant difference between the genotypic distribution of rs763780 genotype and serum creatinine concentration in the first, third and sixth months after transplantation was seen. The correlation coefficient between this polymorphism and the incidence of diabetes was (Phi=0.027) since this correlation coefficient was not significant ($P = 0.249$).

Discussion

In the present study, no significant association was detected between the allele frequency and distribution of TT, TC and CC genotypes of rs763780 IL-17F gene and the incidence of NODAT in kidney transplant patients.

In NODAT, both insulin secretion and peripheral insulin function appear to be impaired, where inflammatory cytokines and chemokines also play roles in this process (15). Numerous studies have been shown that inflammatory cytokines can promote beta cell damage and apoptosis in diabetes. Genetic variants of interleukins are linked with an elevated NODAT risk. Th17 and Treg cells are essential factors in the development of diabetes.

Table 2. The results of the studied polymorphism in kidney transplants

	Cases No. (%)	Controls No. (%)	Chi-square	OR (95% CI)	*P* value*
Genotypes					
TT	24 (80%)	50 (84.7%)	0.005	0.878 (0.0278-2.771)	0.941
TC	4 (12.5%)	6 (10.2%)	0.030	1.128 (0.291-4.373)	0.861
CC	2 (6.3)	3 (5.1%)	0.128	1.119 (0.176-7.112)	0.721
Alleles					
T	52 (86.7%)	106 (89.83%)	0.001	0.886 (0.34-2.31)	0.998
C	8 (13.3%)	12 (10.17%)	0.001	1.128 (0.433-2.941)	0.998

Note: Obtained results were based on https://wpcalc.com/en/equilibrium-hardy-weinberg, OR: odds ratio, CI: confidence interval. *P value ≤0.05 was considered as statistically significant outcome.

Table 3. Frequency of IL-17 rs763780 genotype regarding clinical variables

Parameters	Genotypes	Mean	Std. Deviation	95% CI for mean		*P* value*
				Lower Bound	Upper Bound	
Age (years)	TT	43.69	11.826	40.97	46.41	0.216
	TC	44.82	13.029	36.06	53.57	
	CC	53.40	11.104	39.61	67.19	
BMI (kg/m^2)	TT	29.707	27.4086	23.401	36.013	0.777
	TC	25.545	3.8459	22.962	28.129	
	CC	23.460	1.6592	21.400	25.520	
On dialysis time (month)	TT	24.44	20.055	19.83	29.05	0.848
	TC	21.27	12.618	12.80	29.75	
	CC	26.60	25.432	-4.98	58.18	
FBS (mg/dL)	TT	83.81	10.151	81.48	86.15	0.314
	TC	88.55	10.348	81.59	95.50	
	CC	81.60	13.885	64.36	98.84	
FBS after 3 months (mg/dL)	TT	122.39	92.430	101.12	143.65	0.911
	TC	111.55	30.878	90.80	132.29	
	CC	113.80	40.598	63.39	164.21	
FBS after 6 months (mg/dL)	TT	105.69	38.620	96.81	114.58	0.809
	TC	102.82	32.854	80.75	124.89	
	CC	116.40	62.540	38.75	194.05	
Cholesterol (mg/dL)	TT	170.17	41.996	160.51	179.84	0.944
	TC	170.55	39.868	143.76	197.33	
	CC	163.80	32.268	123.73	203.87	
TG (mg/dL)	TT	180.23	112.432	154.36	206.09	0.952
	TC	172.18	79.351	118.87	225.49	
	CC	168.40	107.614	34.78	302.02	
Creatinine (mg/dL)	TT	1.3067	0.35220	1.2256	1.3877	0.355
	TC	1.1927	0.13719	1.1006	1.2849	
	CC	1.1440	0.22678	0.8624	1.4256	
Creatinine after 3 months (mg/dL)	TT	1.3864	0.43098	1.2872	1.4856	0.300
	TC	1.2500	0.23550	1.0918	1.4082	
	CC	1.1520	0.19018	0.9159	1.3881	
Creatinine after 6 months (mg/dL)	TT	1.3576	0.36883	1.2727	1.4425	0.556
	TC	1.4936	0.50680	1.1532	1.8341	
	CC	1.3540	0.43276	0.8167	1.8913	

BMI: body mass index, FBS: fast blood sugar, F: female, M: male, TG: triglyceride, NODAT: new-onset diabetes mellitus after transplantation. *P* value ≤ 0.05 was considered as statistically significant outcome.

Although beta-cell dysfunction is a major cause of NODAT, studies of cytokines associated with beta-cell dysfunction in patients with NODAT have rarely been conducted.

Studies on solid organ transplantation including bone marrow transplantation have highlighted the importance of polymorphisms of the IL-17F and IL-17A genes in the pathogenesis of allograft rejection (16). The association between IL-17A (17) and IL-17F gene polymorphisms with acute rejection (16) and the use of IL-17 serum levels as the primary marker of acute rejection (18,19) have been reported in kidney transplantation. IL-17F gene SNP 7489A/G is linked with graft failure (20). Moreover, the association of IL-17A rs2275913 gene polymorphism with histopathological changes of kidney allograft (21) and its association (rs2275913 GG) with an increased risk of delayed graft function and higher serum creatinine have been reported (22). The GA genotype of the IL-17F gene polymorphism (rs11465553) might be associated with a high risk of transplanted renal function and return to dialysis after kidney transplantation (22).

The IL-17F T/C (rs763780) variant can lead to a substitution of histidine with arginine at amino acid position 161, inhibiting the function of IL-17F in regulating IL-17 synthesis (23). Romanowski et al reported that this variant is significantly associated with NODAT (22). In the present study, NODAT was detected in 81.3% (n=26) of TT genotype carriers, 12.5% of TC and 6.3% of CC genotypes carriers. There was no statistically significant variance between the groups regarding the frequency of distribution of the above genotypes. The frequency of TT genotype in our patients was higher than the study by Romanowski et al (22). In their study, NODAT was observed in 10.97% of TT carriers and 42.86% of individuals with TC genotype. Diabetes was significantly associated with IL-17F T/C polymorphism (rs763780)

(22), since in the present study, no significant association between NODAT and CC and TC genotypes was seen. In previous studies, the C17 allele of the IL-17F rs76378 gene polymorphism was associated with high concentrations of long-term creatinine and high severity of tubular atrophy and interstitial fibrosis were reported (21). However, in the present study, no significant difference was observed between the distribution of genotypes of the IL-17F T/C (rs763780) and the amount of creatinine and FBS three months and six months after transplantation.

In this study, we found that the age of recipients was statistically different between the studied groups and the NODAT were older than controls. This result was consistent with the results of a cohort of young transplant recipients with a lower risk of NODAT, which may be due to active immunity and general body physiology (24). Likewise, the results showed that gender does not have an important role in the incidence of diabetes, but in a previous study, male gender dominance was a prominent feature (24). In addition, no statistically significant difference between the two groups in BMI was seen. In contrast, most results from previous studies reported a significant relationship between the incidence of diabetes and BMI (5).

Conclusion

No significant link was detected between the IL-17F rs763780 polymorphism and NODAT in kidney recipients of northwest of Iran. Further investigation is required to confirm our results. Moreover, a significant association between NODAT and acute rejection was observed. Identification of the predisposing genetic factors are needed to identify the recipients with a higher risk to develop diabetes after transplantation.

Limitations of the study

Small sample size was one of the limitations of the study. Results requires further investigation with a larger sample size. Given that a network of genes may be involved in the pathogenesis of NODAT in transplant patients, it is suggested that in future studies, instead of one or more genes, a set of genes be examined to select candidate genes with diagnostic role. Genetic biomarkers associated with NODAT will be effective in selecting appropriate immunosuppressive therapy and patient management.

Authors' contribution

Conceptualization: MRA. Validation: MRA. Formal Analysis: SZV. Investigation: JE. Resources: SMH. Data Curation: SZV. Writing—Original Draft Preparation: SMH. Writing—Review and Editing: SZV. Visualization: MRA. Supervision: MRA and JE. Project Administration: MRA. Funding Acquisition: JS.

Conflicts of interest

The authors declared no conflicts of interest.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. This study was approved by the Tabriz university of medical sciences, Tabriz, Iran (Ethics committee code: IR.TBZMED.REC.1399.566). Written informed consent forms were signed by all participants. This study was extracted from residency thesis of Paria Ronaghi at the Kidney Research Center at this university (Thesis# 63315). Additionally, the authors completely have observed the ethical issues including data fabrication, falsification, plagiarism, double publication misconduct or submission and redundancy.

Funding/Support

This work was financially supported by the kidney research center of Tabriz university of medical sciences, Tabriz, Iran (Grant #63315).

References

1. Pham PT, Pham PM, Pham SV, Pham PA, Pham PC. New onset diabetes after transplantation (NODAT): an overview. Diabetes Metab Syndr Obes. 2011;4:175-86. doi: 10.2147/DMSO.S19027.
2. First MR, Dhadda S, Croy R, Holman J, Fitzsimmons WE. New-onset diabetes after transplantation (NODAT): an evaluation of definitions in clinical trials. Transplantation. 2013;96:58-64. doi: 10.1097/TP.0b013e318293fcf8.
3. Sarno G, Muscogiuri G, De Rosa P. New-onset diabetes after kidney transplantation: prevalence, risk factors, and management. Transplantation. 2012;93:1189-95. doi: 10.1097/TP.0b013e31824db97d.
4. Bzoma B, Konopa J, Chamienia A, Łukiański M, Kobiela J, Śledziński Z, et al. New-onset Diabetes Mellitus After Kidney Transplantation-A Paired Kidney Analysis. Transplant Proc. 2018;50:1781-5. doi: 10.1016/j.transproceed.2018.02.119.
5. Xia M, Yang H, Tong X, Xie H, Cui F, Shuang W. Risk factors for new-onset diabetes mellitus after kidney transplantation: A systematic review and meta-analysis. J Diabetes Investig. 2021;12:109-22. doi: 10.1111/jdi.13317.
6. Sotomayor CG, Oskooei SS, Bustos NI, Nolte IM, Gomes-Neto AW, Erazo M, et al. Serum uric acid is associated with increased risk of posttransplantation diabetes in kidney transplant recipients: a prospective cohort study. Metabolism. 2021;116:154465. doi: 10.1016/j.metabol.2020.154465.
7. Guad RM, Taylor-Robinson AW, Wu YS, Gan SH, Zaharan NL, Basu RC, et al. Clinical and genetic risk factors for new-onset diabetes mellitus after transplantation (NODAT) in major transplant centres in Malaysia. BMC Nephrol. 2020;21:388. doi: 10.1186/s12882-020-02052-9.
8. McCaughan JA, McKnight AJ, Maxwell AP. Genetics of new-onset diabetes after transplantation. J Am Soc Nephrol. 2014;25:1037-49. doi: 10.1681/asn.2013040383.
9. Ong S, Kang SW, Kim YH, Kim TH, Jeong KH, Kim SK, et al. Matrix Metalloproteinase Gene Polymorphisms and New-Onset Diabetes After Kidney Transplantation in Korean Renal Transplant Subjects. Transplant Proc. 2016;48:858-63. doi: 10.1016/j.transproceed.2015.11.036.

10. Chang SH, Dong C. IL-17F: regulation, signaling and function in inflammation. Cytokine. 2009;46:7-11. doi: 10.1016/j.cyto.2008.12.024.
11. Abdel-Moneim A, Bakery HH, Allam G. The potential pathogenic role of IL-17/Th17 cells in both type 1 and type 2 diabetes mellitus. Biomed Pharmacother. 2018;101:287-92. doi: 10.1016/j.biopha.2018.02.103.
12. Heldal TF, Ueland T, Jenssen T, Hartmann A, Reisaeter AV, Aukrust P, et al. Inflammatory and related biomarkers are associated with post-transplant diabetes mellitus in kidney recipients: a retrospective study. Transpl Int. 2018;31:510-9. doi: 10.1111/tri.13116.
13. Zelle DM, Corpeleijn E, Deinum J, Stolk RP, Gans RO, Navis G, et al. Pancreatic β-cell dysfunction and risk of new-onset diabetes after kidney transplantation. Diabetes Care. 2013;36:1926-32. doi: 10.2337/dc12-1894.
14. Kim YG, Ihm CG, Lee TW, Lee SH, Jeong KH, Moon JY, et al. Association of genetic polymorphisms of interleukins with new-onset diabetes after transplantation in renal transplantation. Transplantation. 2012;93:900-7. doi: 10.1097/TP.0b013e3182497534.
15. Ahmed SH, Biddle K, Augustine T, Azmi S. Post-Transplantation Diabetes Mellitus. Diabetes Ther. 2020;11:779-801. doi: 10.1007/s13300-020-00790-5.
16. Haouami Y, Sfar I, Dhaouadi T, Gargah T, Bacha M, Bardi R, et al. Impact of Interleukin-17F Gene Polymorphisms in Outcome of Kidney Transplantation in Tunisian Recipients. Transplant Proc. 2018;50:110-4. doi: 10.1016/j.transproceed.2017.11.029.
17. Yapici Ü, Kers J, Bemelman FJ, Roelofs JJ, Groothoff JW, van der Loos CM, et al. Interleukin-17 positive cells accumulate in renal allografts during acute rejection and are independent predictors of worse graft outcome. Transpl Int. 2011;24:1008-17. doi: 10.1111/j.1432-2277.2011.01302.x.
18. Millán O, Rafael-Valdivia L, San Segundo D, Boix F, Castro-Panete MJ, López-Hoyos M, et al. Should IFN-γ, IL-17 and IL-2 be considered predictive biomarkers of acute rejection in liver and kidney transplant? Results of a multicentric study. Clin Immunol. 2014;154:141-54. doi: 10.1016/j.clim.2014.07.007.
19. Haouami Y, Dhaouadi T, Sfar I, Bacha M, Gargah T, Bardi R, et al. The role of IL-23/IL-17 axis in human kidney allograft rejection. J Leukoc Biol. 2018;104:1229-39. doi: 10.1002/jlb.5ab0318-148r.
20. Park H, Shin S, Park MH, Kim YS, Ahn C, Ha J, et al. Association of IL-17F gene polymorphisms with renal transplantation outcome. Transplant Proc. 2014;46:121-3. doi: 10.1016/j.transproceed.2013.05.015.
21. Domanski L, Kłoda K, Patrzyk M, Wisniewska M, Safranow K, Sienko J, et al. IL17A and IL17F genes polymorphisms are associated with histopathological changes in transplanted kidney. BMC Nephrol. 2019;20:124. doi: 10.1186/s12882-019-1308-z.
22. Romanowski M, Kłoda K, Osękowska B, Domański L, Pawlik A, Safranow K, et al. Influence of the IL1 7 A and IL1 7 F gene polymorphisms on the long-term kidney allograft function and return to dialysis after kidney transplantation. Clin Transplant. 2015;29:1187-94.
23. Kawaguchi M, Adachi M, Oda N, Kokubu F, Huang SK. IL-17 cytokine family. J Allergy Clin Immunol. 2004;114:1265-73; quiz 74. doi: 10.1016/j.jaci.2004.10.019.
24. Jahromi M, Al-Otaibi T, Othman N, Gheith O, Mahmoud T, Nair P, et al. Immunogenetics of new onset diabetes after transplantation in Kuwait. Diabetes Metab Syndr Obes. 2019;12:731-42. doi: 10.2147/dmso.s195859.