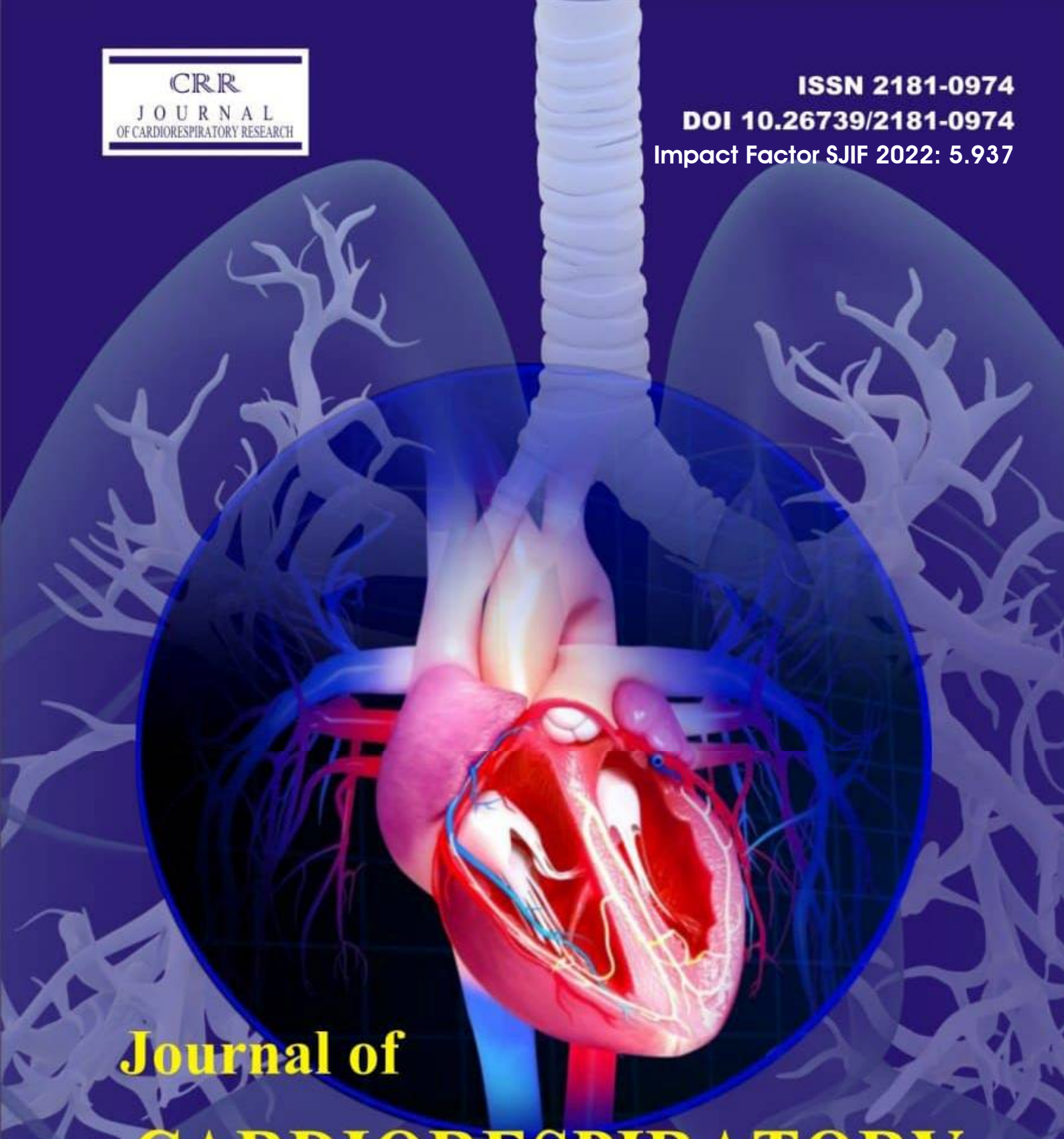
CRR
JOURNAL
OF CARDIORESPIRATORY RESEARCH

ISSN 2181-0974
DOI 10.26739/2181-0974
Impact Factor SJIF 2022: 5.937



Journal of CARDIORESPIRATORY RESEARCH

Volume 6, Issue 3
2025

МИНИСТЕРСТВО ЗДРАВООХРАНЕНИЯ
РЕСПУБЛИКИ УЗБЕКИСТАН

Журнал кардиореспираторных исследований

JOURNAL OF CARDIORESPIRATORY RESEARCH

Главный редактор: Э.Н.ТАШКЕНБАЕВА

Учредитель:

Самаркандский государственный медицинский университет

Tadqiqot.uz

Ежеквартальный научно-практический журнал

ISSN: 2181-0974
DOI: 10.26739/2181-0974

№ 3
2025

ЖУРНАЛ КАРДИОРЕСПИРАТОРНЫХ ИССЛЕДОВАНИЙ

№3 (2025) DOI http://dx.doi.org/10.26739/2181-0974-2025-3

KARDIORESPIRATOR TADQIQOTLAR JURNALI
№3 (2025) DOI http://dx.doi.org/10.26739/2181-0974-2025-3

JOURNAL OF CARDIORESPIRATORY RESEARCH
№3 (2025) DOI http://dx.doi.org/10.26739/2181-0974-2025-3

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ISSN: 2181-0974
www.tadqiqot.uz
JOURNAL OF CARDIORESPIRATORY RESEARCH
ЖУРНАЛ КАРДИОРЕСПИРАТОРНЫХ ИССЛЕДОВАНИЙ

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ГЕНЕТИЧЕСКАЯ ПРЕДРАСПОЛОЖЕННОСТЬ К ОЖИРЕНИЮ ПРИ ХРОНИЧЕСКОЙ БОЛЕЗНИ ПОЧЕК: РОЛЬ ПОЛИМОРФИЗМОВ FTO (RS9939609) И TNF (RS1800629)

For citation: Mirzayev R.Z., Nasirova Z.A. GENETIC SUSCEPTIBILITY TO OBESITY IN CHRONIC KIDNEY DISEASE: THE ROLE OF FTO (RS9939609) AND TNF (RS1800629) POLYMORPHISMS. Journal of cardiorespiratory research. 2025, vol. 6, issue 3.

http://dx.doi.org/10.26739/2181-0974/2025/6/3/1

АННОТАЦИЯ

Целью настоящего исследования было изучение ассоциации между полиморфизмами FTO A23525T (rs9939609) и TNF G308A (rs1800629) и развитием ожирения у пациентов с хронической болезнью почек (ХБП). Было проанализировано 98 образцов ДНК пациентов с ХБП (58 с ожирением и 40 без ожирения), а также образцы здоровых лиц. Установлено, что аллель T и гомозиготный генотип TT FTO A23525T достоверно ассоциированы с ожирением у больных ХБП, тогда как аллель A и генотип AA имеют протективный эффект. Для полиморфизма TNF G308A (rs1800629) выявлена связь аллеля G и генотипа GG с ХБП в целом, однако различий между подгруппами по наличию ожирения не обнаружено. Полученные результаты подчеркивают значимость генетического тестирования в персонализированном подходе к ведению пациентов с ХБП и ожирением.

Ключевые слова: FTO rs9939609, TNF rs1800629, хроническая болезнь почек, ожирение, генетический полиморфизм, персонализированная медицина

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GENETIC SUSCEPTIBILITY TO OBESITY IN CHRONIC KIDNEY DISEASE: THE ROLE OF FTO (RS9939609) AND TNF (RS1800629) POLYMORPHISMS

ANNOTATION

The aim of this study was to investigate the association between FTO A23525T (rs9939609) and TNF G308A (rs1800629) polymorphisms and the development of obesity in patients with chronic kidney disease (CKD). DNA samples from 98 CKD patients (58 with obesity and 40 without obesity), as well as samples from healthy individuals, were analyzed. It was established that the T allele and the homozygous TT genotype of FTO A23525T are significantly associated with obesity in CKD patients, while the A allele and AA genotype have a protective effect. For the TNF G308A (rs1800629) polymorphism, an association between the G allele and GG genotype with CKD overall was revealed; however, no differences were found between subgroups regarding the presence of obesity. The obtained results emphasize the importance of genetic testing in a personalized approach to managing patients with CKD and obesity.

Keywords: FTO rs9939609, TNF rs1800629, chronic kidney disease, obesity, genetic polymorphism, personalized medicine

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SURUNKALI BUYRAK KASALLIGIDA SEMIZLIKKA GENETIK MOYILLIK: FTO (RS9939609) VA TNF (RS1800629) POLIMORFIZMLARINING ROLI

ANNOTATSIYA

Ushbu tadqiqotning maqsadi surunkali buyrak kasalligi (SBK) bo‘lgan bemorlarda FTO A23525T (rs9939609) va TNF G308A (rs1800629) polimorfizmlari bilan semizlikning rivojlanishi o‘rtasidagi bog‘liqlikni o‘rganish edi. 98 nafar SBK bilan kasallangan bemorlarning (58 nafari semiz va 40 nafari semiz bo‘lmagan) hamda sog‘lom shaxslarning DNK namunalari tahlil qilindi. FTO A23525T polimorfizmining T alleli va gomozigot TT genotipi SBK bo‘lgan bemorlarda semizlik bilan sezilarli darajada bog‘liqligi, A alleli va AA genotipi esa himoya ta’siriga ega ekanligi aniqlandi. TNF G308A (rs1800629) polimorfizmiga kelsak, G alleli va GG genotipi umumiy SBK bilan bog‘liqligi aniqlandi, biroq semizlik mavjudligi bo‘yicha kichik guruhlar o‘rtasida farqlar topilmadi. Olingan natijalar SBK va semizligi bor bemorlarni davolashda shaxsiy yondashuvda genetik tekshiruvning muhimligini ta’kidlaydi.

Kalit so‘zlar: FTO rs9939609, TNF rs1800629, surunkali buyrak kasalligi, semizlik, genetik polimorfizm, shaxsiylashtirilgan tibbiyot.

Obesity is one of the leading problems of modern healthcare, characterized by a steady increase in its prevalence worldwide. According to the World Health Organization (WHO), by 2025, the number of people with excess body weight could exceed 2.7 billion, with a significant portion suffering from complicated metabolic diseases. One such complication is chronic kidney disease (CKD), which is closely related to metabolic homeostasis disorders, systemic inflammation, insulin resistance, and renin-angiotensin-aldosterone system activation[8,10,24,27].The relationship between obesity and CKD is confirmed by numerous epidemiological and clinical studies: the presence of excess body weight increases the risk of developing CKD, and in patients with already existing renal failure, obesity worsens the prognosis, accelerates the progression of nephropathy, and increases mortality. However, the clinical course and severity of CKD in patients with the same body weight levels can differ significantly, indicating the possible involvement of genetic factors in the modulation of metabolic disorders[3,5,7,14].

One of the most studied genes associated with obesity is the FTO gene (Fat mass and obesity-associated gene). The greatest attention is paid to the mononucleotide polymorphism rs9939609 (A23525T), in which the A allele is associated with an increase in fat mass, hyperphagia, and reduced sensitivity to leptin[6,9,10,16]. The FTO gene is primarily expressed in the hypothalamus, and its protein product - α-ketoglutarate-dependent dioxygenase - participates in the regulation of metabolism, gene expression, energy metabolism, and apoptosis. A high level of FTO expression contributes to the activation of the hunger center and, consequently, increased calorie intake. Carriage of the A allele rs9939609 is significantly associated with an increase in body mass index and the development of obesity in various populations, including in Asia and Europe[1,12,24].

Another important genetic factor potentially influencing the development of complicated obesity is the polymorphism of G308A (rs1800629) in the promoter region of the TNF gene (tumor necrosis factor-alpha). This variant is associated with changes in the expression level of the pro-inflammatory cytokine TNF-α, which plays a key role in the pathogenesis of chronic inflammation, insulin resistance, and tissue remodeling. TNF-α participates in the development of glomerulosclerosis and tubulointerstitial fibrosis in CKD, and is also capable of influencing lipid and carbohydrate metabolism. Elevated expression of TNF-α in the presence of the A allele can exacerbate metabolic dysfunction and impair kidney function[2,8,13,21].

While the effect of the FTO rs9939609 polymorphism on obesity has been well studied in the general population, its significance in the context of chronic kidney disease remains poorly understood. Similarly, the role of TNF G308A in the development of obesity in CKD requires further study, taking into account the inflammatory component of this condition[3,7,11,22].

Thus, the relevance of this study is due to the need to identify genetic markers capable of predicting the development of obesity in patients with CKD, which can contribute to a more accurate risk stratification, personalization of therapy, and prevention of complications[17,23,25].

Purpose of the research:

To assess the distribution of alleles and genotypes of FTO rs9939609 (A23525T) and TNF rs1800629 (G308A) polymorphisms in patients with and without obesity, as well as to establish possible associations with the risk of obesity in chronic kidney disease.

Materials and methods:

Study design

This study is observational, analytical, and cross-sectional (case-control) in nature, aimed at assessing the distribution of genetic variants FTO rs9939609 and TNF rs1800629 in patients with chronic kidney disease (CKD) who are obese and non-obese, compared to a healthy control group.

Study population

The study included 98 patients with CKD under observation in nephrology and internal medicine inpatient units. Of these, 58 patients had clinically confirmed obesity, defined as body mass index (BMI) ≥30 kg/m2 according to WHO criteria, while 40 patients had normal or overweight without obesity (BMI <30 kg/m2).

The control group consisted of 54 apparently healthy volunteers of comparable age and sex, with no history of CKD, obesity, metabolic syndrome, or acute/chronic inflammatory diseases at the time of inclusion in the study.

Inclusion criteria:

age 18 to 70 years;

confirmed diagnosis of CKD stages I-V according to the KDIGO classification;

written informed consent for participation.

Exclusion criteria:

history of acute inflammatory diseases in the past 3 months;

presence of oncological, autoimmune, or systemic connective tissue diseases;

pregnancy, use of immunosuppressants or glucocorticoids.

Anthropometric and clinical data

Demographic and clinical parameters were recorded for all patients: age, sex, BMI, CKD stage, comorbidities (hypertension, type 2 diabetes mellitus), as well as laboratory parameters (GFR, creatinine levels, glucose, lipid profile, etc.).

Genotyping methods

Genetic analysis was conducted in a molecular biology laboratory. DNA was isolated from whole venous blood collected in EDTA tubes using standard reagent kits and protocols (Qiagen, Germany).

Polymorphisms of the FTO A23525T (rs9939609) and TNF G308A (rs1800629) genes were determined by PCR with subsequent restriction fragment length polymorphism analysis (PCR-RFLP). Specially designed primers were used for amplification (sequences available upon request). Results were visualized on 2% agarose gel with subsequent analysis under UV light.

Quality control included: positive and negative controls for each reaction; repeat typing of 10% randomly selected samples (100% concordance of results).

Statistical analysis

Data analysis was performed using SPSS v.26.0 and GraphPad Prism 9.0. Allele and genotype frequencies were calculated by direct counting. Conformity of genotype distribution to Hardy-Weinberg equilibrium was assessed using the $\chi 2$ test. Frequency comparisons between groups were conducted using: Pearson's $\chi 2$ test or Fisher's exact test (for small samples); calculation of odds ratios (OR) with 95% confidence intervals (CI); statistical significance was set at $p < 0.05$. Additionally, logistic regression and stratified analysis were employed to evaluate the relationship between genotypes and phenotypic traits, including BMI and CKD stage.

Ethical considerations

The study was approved by the local ethics committee at [Institution Name], complies with the provisions of the Helsinki Declaration (2013) and national standards for biomedical research. All participants provided written informed consent.

Results

1. Distribution of FTO rs9939609 alleles and genotypes in the overall group of CKD patients

Initially, a comparative analysis of allele and genotype frequencies for the FTO rs9939609 (A>T) polymorphism was conducted in the overall sample of CKD patients (n = 98) compared to the healthy control group (n = 54). The distribution showed no statistically significant differences between the groups.

Table 1. Distribution of FTO rs9939609 alleles and genotypes in the overall group of CKD patients and in the control group

Genotype / Allele	CKD (n = 98)	%	Control (n = 54)	%	OR	95% DI	χ^2	p-value
Allele A	124	63,27	76	70,37	0,725	0,4377 – 1,201	1,562	0,1059
Allele T	72	36,73	32	29,63	1,379	0,8324 – 2,285	–	–
AA	39	39,80	26	48,15	0,712	0,3644 – 1,391	0,992	0,1596
AT	46	46,94	24	44,44	1,106	0,5673 – 2,155	0,087	0,3839
TT	13	13,27	4	7,41	1,912	0,5911 – 6,183	1,203	0,1370

Table 1 presents the distribution of alleles and genotypes of the FTO rs9939609 (A>T) polymorphism in patients with chronic kidney disease (CKD) compared to the group of conditionally healthy individuals. Allele and genotype frequencies were compared with the calculation of odds ratio (OR), 95% confidence intervals (CI), $\chi 2$-value, and statistical significance level (p-value).

Analysis showed that the frequency of A and T alleles, as well as AA, AT, and TT genotypes in patients with CKD, did not statistically differ from the control group. The A allele was more common in both patients (63.27%) and controls (70.37%), however, the difference did not reach the level of statistical significance ($p = 0.1059$). The AA genotype was found somewhat less frequently among patients (39.8% versus 48.15%), while heterozygous AT and homozygous TT genotypes did not exhibit a reliable association with the presence of CKD.

Thus, in the general cohort of patients with CKD, the FTO rs9939609 polymorphism did not show a statistically significant association with the disease, which may indicate the absence of a direct influence of this genetic variant on the risk of developing CKD in the studied population.

2. Analysis of the FTO rs9939609 genotypes in patients with obesity.

In the second part of the study, a subgroup of patients with CKD and obesity (n=58) was analyzed. It has been established that the T allele and homozygous TT genotype are associated with an increased risk of obesity in patients with CKD. At the same time, the A allele and AA genotype proved to be protective.

Table 2. Frequency of FTO rs9939609 alleles and genotypes in patients with CKD with obesity

Genotype / Allele	CKD with obesity (n=58)	%	Control (n = 54)	%	OR	95% DI	χ^2	p-value
Allele A	62	53,45	76	70,37	0,485	0,2774 – 0,8404	6,771	0,0046
Allele T	54	46,55	32	29,63	2,062	1,190 – 3,605	–	–
AA	16	27,59	26	48,15	0,414	0,1852 – 0,906	5,045	0,0123
AT	30	51,72	24	44,44	1,336	0,6322 – 2,838	0,594	0,2205
TT	12	20,69	4	7,41	3,261	0,9819 – 10,83	4,029	0,0223

Table 2 presents data on the distribution of alleles and genotypes of the FTO rs9939609 (A>T) polymorphism among patients with chronic kidney disease (CKD) with obesity compared to the conditionally healthy control group. The analysis was performed to identify a possible genetic predisposition to obesity in this category of patients.

The obtained results demonstrate statistically significant differences between the groups. The frequency of the T allele in patients with CKD and obesity was significantly higher (46.55%), compared to the control group (29.63%), while its carriage was associated with an increased risk of obesity (OR = 2.062; 95% CI: 1.190-3.605). At the same time, the A allele and homozygous AA genotype occurred significantly less frequently in patients with obesity, demonstrating, on the contrary, a protective effect ($p = 0.0046$ and $p = 0.0123$, respectively).

The TT genotype, associated with a nearly threefold increase in the risk of obesity in patients with chronic kidney disease (OR = 3.261; $p = 0.0223$), deserves special attention, which confirms its possible role as

a genetic marker of a high predisposition to obesity in the context of chronic kidney disease.

Thus, the table results confirm the presence of a reliable association between the T-allele and the risk of obesity in patients with CKD, which can have clinical significance in risk stratification and the formation of individual cardiometabolic rehabilitation programs.

3. Genetic profile of FTO rs9939609 in patients with CKD without obesity

In the subgroup of patients with chronic kidney disease without obesity (n=40), no significant differences were found in the distribution of alleles and genotypes compared to the control.

Table 3. Frequency of FTO rs9939609 alleles and genotypes in patients with obesity-free CKD

Genotype / Allele	CKD without obesity (n = 40)	%	Control (n = 54)	%	OR	95% DI	χ^2	p-value
Allele A	62	77,50	76	70,37	1,450	0,7438 – 2,828	1,197	0,1376
Allele T	18	22,50	32	29,63	0,689	0,3536 – 1,344	–	–
AA	23	57,50	26	48,15	1,457	0,6396 – 3,319	0,805	0,1848
AT	16	40,00	24	44,44	0,833	0,3635 – 1,910	0,186	0,3333
TT	1	2,50	4	7,41	0,321	0,0344 – 2,983	1,099	0,1481

Table 3 presents data on the distribution of alleles and genotypes of the FTO rs9939609 (A>T) polymorphism in patients with chronic kidney disease (CKD) without obesity, compared to the control group.

Analysis showed that no significant differences were found in the frequency of A and T alleles, as well as AA, AT, and TT genotypes between the groups. The A allele prevailed both in the group of patients with chronic kidney disease without obesity (77.5%) and in the control group (70.37%) ($p = 0.1376$). The AA genotype was more common in patients without obesity (57.5%) compared to the control group (48.15%), however, the difference was statistically insignificant ($p = 0.1848$).

The heterozygous AT genotype and the rare TT genotype also did not exhibit a significant association with the absence of obesity in CKD. Thus, the TT genotype was extremely rare - only in one patient (2.5%), and although its frequency was lower than in the control group (7.41%), this difference also did not reach the level of statistical significance ($p = 0.1481$).

Thus, the obtained data do not confirm the presence of a relationship between FTO rs9939609 polymorphism and the absence of obesity in patients with chronic kidney disease, which may indicate a limited influence of this genetic variant on the development of obesity outside the context of other risk factors.

4. Frequency of TNF rs1800629 alleles and genotypes in the general group of CKD

Analysis of the TNF G308A (rs1800629) polymorphism showed a significant decrease in the frequency of the G allele and the homozygous GG genotype in patients with CKD, which may indicate its protective role. GA heterozygotes were significantly more frequent in patients.

Table 4. Frequency of TNF rs1800629 alleles and genotypes in the general group of patients with CKD

Genotype / Allele	CKD (n = 98)	%	Control (n = 54)	%	OR	95% DI	χ^2	p-value
Allele G	168	85,71	359	90,66	0,618	0,3662 – 1,044	3,276	0,0351
Allele A	28	14,29	37	9,34	1,617	0,9576 – 2,731	–	–
GG	70	71,43	161	81,31	0,575	0,3264 – 1,011	3,737	0,0266
GA	28	28,57	37	18,69	1,741	0,9888 – 3,064	3,737	0,0266
AA	0	0,00	0	0,00	–	–	–	–

Table 4 presents the results of the analysis of the distribution of alleles and genotypes of the TNF rs1800629 (G>A) polymorphism in the general group of patients with chronic kidney disease (CKD) compared to conditionally healthy individuals in the control group.

Analysis revealed a statistically significant decrease in the frequency of the G-allele in patients with CKD (85.71%) compared to the control group (90.66%) ($p = 0.0351$), which may indicate a potential protective role of the G-allele in relation to the development of CKD. Accordingly, the frequency of the A-allele was higher in patients (14.29%) versus 9.34% in the control group.

It was established that the homozygous GG genotype was significantly less common in patients (71.43%) compared to the control group (81.31%) ($p = 0.0266$; OR = 0.575), which confirms its possible protective association. At the same time, the heterozygous GA genotype was statistically more frequent in patients (28.57%) versus 18.69% in the controls ($p = 0.0266$; OR = 1.741), which may indicate an increased risk of CKD in the presence of the A-allele in a heterozygous state.

Homozygotes for the A allele (AA-genotype) were not detected in any of the groups, which corresponds to the low population frequency of this genotype.

Thus, the obtained data indicate an association between carrying the A-allele and an increased risk of developing CKD, while the GG genotype can have a protective effect, making the TNF rs1800629 polymorphism a potential marker of genetic predisposition to chronic kidney disease.

5. TNF rs1800629 in patients with and without obesity

In both subgroups (CFT with and without obesity), no significant differences were found compared to the control group. This indicates the absence of an independent relationship between this polymorphism and obesity in CKD.

Table 5. TNF rs1800629 in patients with CKD with obesity

Genotype / Allele	CKD with obesity (n=58)	%	Control (n = 54)	%	OR	95% DI	χ^2	p-value
Allele G	100	86,21	359	90,66	0,644	0,3441 – 1,206	1,914	0,0833
Allele A	16	13,79	37	9,34	1,552	0,8294 – 2,906	–	–
GG	42	72,41	161	81,31	0,603	0,3063 – 1,188	2,164	0,0707
GA	16	27,59	37	18,69	1,658	0,8418 – 3,264	2,164	0,0707

Table 5 presents a comparative analysis of the frequency of alleles and genotypes of the TNF rs1800629 (G>A) polymorphism in patients with chronic kidney disease (CKD) suffering from obesity, compared to the control group. The results showed that differences in the distribution of alleles and genotypes between groups did not reach statistical significance. The G allele maintained a high frequency in both patients with CKD and obesity (86.21%), and in the control group (90.66%) ($p = 0.0833$). The frequency of the A allele was, respectively, higher in patients (13.79%) compared to the control group (9.34%), however, this difference was also insignificant ($p > 0.05$). The GG genotype was

found in 72.41% of patients with obesity and in 81.31% of individuals in the control group (OR = 0.603; p = 0.0707), indicating a tendency towards a decrease in the frequency of GG among patients, but without statistical significance. Similarly, the GA genotype was more common in patients (27.59%) compared to the control group (18.69%), with a moderate increase in relative risk (OR = 1.658), but also without significant differences (p = 0.0707). Thus, the obtained data do not confirm the presence of an independent association between TNF rs1800629 polymorphism and obesity in patients with CKD. This indicates that this genetic variant is likely not a key factor predisposing to obesity in the context of chronic renal pathology, despite the previously identified connection with the very fact of the presence of CKD (see Table 4).

Table 6. TNF rs1800629 in patients with CKD without obesity

Genotype / Allele	CKD without obesity (n = 40)	%	Control (n = 54)	%	OR	95% DI	χ^2	p-value
Allele G	68	85,00	359	90,66	0,584	0,2898 – 1,177	2,306	0,0645
Allele A	12	15,00	37	9,34	1,712	0,8496 – 3,451	–	–
GG	28	70,00	161	81,31	0,536	0,2496 – 1,152	2,605	0,0533
GA	12	30,00	37	18,69	1,865	0,868 – 4,007	2,605	0,0533

Table 6 presents the distribution of alleles and genotypes of TNF rs1800629 (G>A) polymorphism in patients with chronic kidney disease (CKD) without obesity, compared to the control group.

The frequency of the G allele in patients was 85.00%, while in the control group it was 90.66%; however, this difference was not statistically significant (p = 0.0645). The A allele was detected in 15.00% of patients and in 9.34% of controls, while the tendency towards an increased frequency of the A allele in patients with CKD without obesity did not reach statistical significance (OR = 1.712; 95% CI: 0.8496-3.451). Among the genotypes, the GG genotype was somewhat less common in patients (70.00%) compared to the control group (81.31%), with a reduced relative risk (OR = 0.536), but the difference was not statistically significant (p = 0.0533). The frequency of the heterozygous GA genotype in patients was 30.00%, which was higher than in the control group (18.69%) and was accompanied by a moderate increase in risk (OR = 1.865), but without statistical significance (p = 0.0533).

Thus, the obtained results do not confirm a significant association between TNF rs1800629 and the absence of obesity in patients with CKD, despite the observed tendency towards a higher frequency of the A allele and GA genotype. These data are consistent with the results of the obesity subgroup analysis (see Table 5) and collectively indicate the absence of an independent association between this polymorphism and obesity in CKD, although the possible involvement of TNF rs1800629 in the pathogenesis of CKD itself is not excluded (see Table 4).

Discussion of the research results:

Our data confirm that carrying the T allele and especially the homozygous TT genotype of the FTO rs9939609 polymorphism is associated with an increased risk of obesity in patients with CKD (OR ≈ 3.26; p = 0.022). This is consistent with previously published meta-analyses demonstrating a significant relationship between this polymorphism and obesity in adolescents and adults; the A allele (designated as T in your notation) was associated with a higher BMI and an increased risk of obesity. Mechanistic studies have shown that the A allele increases food intake by influencing the neural regulation of hunger and satiety.

Since obesity is a known risk factor for the progression and complications of CKD, identifying this genetic marker is of interest for identifying patients with increased metabolic risk and for developing personalized prevention strategies.

In the general group of patients (Table 1) and among individuals without obesity (Table 3), we did not find statistically significant differences in the prevalence of FTO alleles and genotypes compared to the control group. This indicates that the effect of the polymorphism is not due to the presence of CKD itself, but rather to the presence of obesity, supporting the hypothesis about the specific role of FTO in the metabolic component of the disease. 3) we did not reveal statistically significant differences in the prevalence of FTO alleles and genotypes compared to the control.

We found a statistically significant decrease in the frequency of the G allele and GG genotype in patients with CKD (Table 4), which suggests a protective effect of the G allele against disease development. Conversely, carrying the A allele is associated with an increased risk of CKD (OR ~1.74; p = 0.0266).

Previously, a similar relationship was observed in acute kidney injury (AKI), where the A allele was associated with increased severity of nephron damage, as well as in patients with renal failure, where the role of the A allele was noted as a risk factor for the progression to kidney disease. This is reflected in mechanisms associated with increased production of TNF-α, a pro-inflammatory cytokine that contributes to endothelial dysfunction and the progression of chronic kidney diseases.

Neither in the group with obesity (Table 5) nor without it (Table 6) did we find a significant association of TNF polymorphism with obesity, despite a tendency towards an increased frequency of the A allele. This indicates that the influence of TNF rs1800629 is directed at the inflammatory components of the diseases rather than directly at metabolic disorders. 6) we did not reveal a reliable association of TNF-polymorphism with obesity, despite a tendency towards an increase in the frequency of the A-allele.

Analyses in other contexts confirm that the A allele enhances the inflammatory response and is associated with metabolic disorders such as metabolic syndrome and coronary heart disease; however, its association with obesity is less pronounced and often depends on the context (e.g., diet, inflammation level).

Analyses of meta-studies on TNF rs1800629 indicate that the effect of polymorphism can vary depending on ethnicity (for example, significant effects were observed in autosomal cardiomyopathy in Asian populations). Our research likely reflects the specificity of the population (presumably European or mixed type), which requires confirmation in larger and more diverse cohorts.

Conclusions

The FTO rs9939609 (A>T) gene polymorphism in the general population of patients with chronic kidney disease (CKD) did not demonstrate a significant association with the presence of CKD itself, which allows us to rule out its role as a universal marker of predisposition to renal pathology in the studied sample.

A significant association was established between the T allele and TT genotype of the FTO rs9939609 gene and obesity in patients with CKD. The homozygous TT genotype was associated with a nearly threefold increase in the risk of obesity, while the A allele and AA genotype had a protective effect. This indicates the involvement of FTO rs9939609 in the development of obesity in the context of CKD.

In the subgroup of CKD patients without obesity, differences in the distribution of FTO rs9939609 alleles and genotypes compared to the control group did not reach statistical significance, which confirms the selective nature of the association specifically with obesity, rather than with CKD itself.

The TNF rs1800629 (G>A) polymorphism in the general group of CKD patients showed a statistically significant decrease in the frequency of the G allele and GG genotype, which may indicate a potentially protective role of the G allele against the development of CKD. Simultaneously, an increased frequency of the GA genotype in patients may reflect the inflammatory component of the pathogenesis.

In subgroups of CKD patients with and without obesity, the TNF rs1800629 polymorphism did not demonstrate a significant association with obesity, which allows us to conclude that it has no independent influence on metabolic disorders in CKD.

The obtained results emphasize the different roles of the studied genetic markers in the pathogenesis of chronic kidney disease and obesity. Specifically, FTO rs9939609 can be considered a genetic risk factor for obesity in patients with CKD, while TNF rs1800629 is a possible immuno-inflammatory marker associated with the presence of renal pathology itself.

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