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The Relationship between Methylenetetrahydrofolate Reductase C677T Gene Polymorphism and Diabetic Nephropathy in Croatian Type 2 Diabetic Patients

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ABSTRACT

Methylenetetrahydrofolate reductase (MTHFR) polymorphism has been shown to be associated with the development of diabetic nephropathy in many ethnic groups. In this study, we examined the correlation between MTHFR C677T polymorphism and microalbuminuria in patients with diabetes mellitus type 2 in Croatian patients. 85 patients with diabetes mellitus type 2 were recruited. Patients were classified into two groups – with and without diabetic nephropathy according to urinary albumin excretion rate in urine collected during 24 hours. The C677T genotype was determined by real-time PCR analysis. The genotype frequencies were CC 36,5%, CT 42,3% and TT 21,2% in diabetic patients without nephropathy versus CC 39,4%, CT 45,4% and TT 15,2% in those with nephropathy. There was no statistically significant difference in allele distribution between patients with nephropathy and those without (p=0,788). Our study did not show a correlation between mutations in the MTHFR gene and diabetic nephropathy in Croatian patients. Diabetic nephropathy is influenced by multiple risk factors which can modify the importance of MTHFR polymorphism in its development.

***Key words**: allele distribution, methylenetetrahydrofolate reductase mutations, type 2 diabetes mellitus, diabetic nephropathy, genetic polymorphism, Croatia*

Introduction

Diabetes mellitus is the most frequent chronic metabolic disease characterised by complications on blood vessels, nerves and basal membranes of different tissues[1]. The number of people with diabetes is constantly increasing because of many reasons: aging of the population, population growth, urbanization which includes sedentary lifestyle and lack of physical activity and significant increase of prevalence of obesity[2]. It is assumed that the number of the diseased will increase from about 285 million adults in 2010 to 439 million adults in 2030[3]. The number of people with diabetes in Croatia is also increasing, and diabetes is one of the leading causes of death in Croatia[4,5].

Diabetic nephropathy is a serious complication of diabetes mellitus and the leading cause of chronic renal disease and end stage renal failure[6,7]. The etiology of diabetic nephropathy is multifactorial and involves not only chronic hyperglycaemia and arterial hypertension, but also environmental factors and genetic susceptibility.

5,10-methylenetetrahydrofolate reductase (MTHFR) is one of the key enzymes in the metabolism of homo-

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cysteine, where it catalyses homocysteine remethylation to methionine. The thermolabile form of this enzyme was discovered two decades ago[8]. The autosomal recessive point mutation C677T in the MTHFR gene leads to a valine-to-alanine substitution at amino acid 226. The result of this mutation is decreased activity and increased thermolability of this enzyme[9]. There are three possible genotypes in the case of the MTHFR C677T polymorphism. The CC genotype is refered to as »wild type«, the CT genotype is described as »heterozygous« and the TT genotype as the »homozygous variant«. Many studies showed that patients who are homozygous for C677T MTHFR mutation are predisposed to elevated homocysteine levels in plasma compared with heterozygous or wild type[10].

The »homocysteine hypothesis of arteriosclerosis« was first proposed in 1969 by McCully[11]. Since then, in addition to established risk factors, epidemiologic data and many studies showed that elevated plasma homocysteine concentration is an independent risk factor for vascular disease[12–20]. Recent in vitro studies indicate that homocysteine enhances the expression of VEGF (vascular endothelial growth factor), which is a pro-angiogenic factor with a known role in the pathogenesis of diabetic nephropathy[21,22]. Based on this evidence, it can be considered that the polymorphism of C677T gene for MTHFR as basis for hyperhomocystinaemia could be involved in the development of diabetic nephropathy.

Many authors came to the conclusion that genetic polymorphism of the MTHFR gene can have different influence on homocysteine metabolism and on the risk of diabetic nephropathy in different ethnic groups. It was assumed that homocysteine metabolism could be modified by genetic factors which can vary among different populations[7,21,24–26]. On the other hand, some studies did not prove such connection[23,27].

The aim of this study is to determine the correlation between MTHFR C677T polymorphism and microalbuminuria as an early sign of diabetic nephropathy in patients with diabetes mellitus type 2 in Croatian patients.

Subjects and Methods

Subjects

The subjects included in the study were men and women who were ≥18 years old and hospitalized in the Medical Department during 2009. All included patients were diagnosed with diabetes mellitus type 2 based on 1999 WHO and EASD & ESC classification and guidelines[28,29]. All of the patients on haemodialysis were excluded from the study in order to exclude the influence of renal failure on homocysteine metabolism. The Hospital Ethics Committee approved the study, and the informed consent was obtained from all included participants. The general data about all included subjects were recorded, including age, gender, body weight, blood pressure. The venous blood samples were collected for measurement of glycosylated haemoglobin (HbA1c) and plasma venous glucose level, and additional blood samples for MTHFR C677T genotype analysis and analysis of total homocysteine level were taken. Patients were classified into two groups- with diabetic nephropathy or without it according to urinary albumin excretion rate in urine collected during 24 hours. Diabetic nephropathy was defined as micro- or macroalbuminuria (≥30 mg/24 h), whereas normal albumin excretion rate was defined as <30 mg/24 h[30,31].

Determination of MTHFR genotype

The blood samples were taken from fasting subjects and placed into vacutainer tubes containing EDTA. Leukocyte DNA was isolated from whole-blood samples (QIAamp DNA Blood Mini Kit). The C677T mutation in the MTHFR gene was analyzed by polymerase chain reaction (real-time PCR) of genomic DNA using the following primer pairs: MTHFR-F: 5'-CCT CAA AGA AAA GCT GCG TGA-3'and MTHFR-R: 5'-AAG CAC TTG AAG GAG AAG GTG TC-3'. The analysis was conducted on »Taqman 7300 Real Time PCR System«, Applied Biosystems. According to the increase of the signal of the defined essay, the SDS 1.3.1. Software 7300 Real Time PCR System defined whether the samples were homozygous for the wild type (C/C), heterozygous (C/T) or homozygous for the mutation (T/T).

Homocysteine level measurement

The blood samples were taken into vacutainer tubes containing EDTA during standard procedure. The homocysteine level was determined by fluorescence polarization immunoassay technology (FPIA) on AxSYM homocysteine machine, using AxSYM Homocysteine Reagent Pack according to manufacturer's instructions (Abbot). According to the manufacturer's package insert, hyperhomocysteinaemia was defined as the homocysteine level higher than 16.00 μmol/L for men, and higher than 20.44 μmol/L for women[32].

Statistical analysis

The qualitative parameters are presented as absolute numbers and percentages. The quantitative data are presented as median and range. The differences between qualitative parameters were tested by χ^2 test, using Yates correction in 2x2 tables. The differences in quantitative data between two groups were tested by non-parametric Mann-Whitney U test.

The statistical analysis was performed using Statistica 6.0 software. In all tests, statistical significance was taken at nominal $p<0.05$ for all comparisons.

Results

Eighty-five patients participated in the study, thereof 38 men (44.7%) and 47 women (55.3%). Out of 85 studied patients, 33 (38.8 %) had evidence of microalbuminuria (Table 1). The differences between qualitative parameters were tested by χ^2 test, using Yates correction in 2x2 tables. The differences in quantitative data between two groups were tested by non-parametric Mann-Whitney U test. There were no differences between patients with and without diabetic nephropathy in terms of gender, body weight, systolic blood pressure, plasma glucose level and glycosylated haemoglobin. Differences between those with and without nephropathy were noted for age and homocysteine level.

In the analyzed group, 32 patients (37.65%) had the C/C allele, whereas 37 (43.53%) were heterozygous (C/T) and 16 (18.82%) were homozygous for the C677T mutation (T/T). There was no statistically significant difference in allele distribution between patients with nephropathy and those without (Table 2). Because of the dependency of homocysteine level on the patient's gender, the statistical analysis of the correlation between the MTHFR C677T mutation and the homocysteine level was performed separately for males and for females[32–36].

There was no statistically significant difference in the homocysteine level considering the MTHFR genotype (Table 3). In the group of males it is only noted that the homocysteine level was somewhat higher in the group of homozygotes (T/T), and the lowest in the group »wild type« (C/C). This difference is notable, but not statistically significant.

Discussion and Conclusion

In this study, we analyzed the correlation of MTHFR C677T gene polymorphism with diabetic nephropathy in the population. MTHFR genotype and allele frequencies

TABLE 1
CLINICAL CHARACTERISTICS OF PATIENTS CLASSIFIED INTO TWO GROUPS – WITH DIABETIC NEPHROPATHY AND WITHOUT IT

	AER		p value
	<30 mg/24h, N=52	≥30 mg/24h, N=33	
Gender			
– male	22 (42.3%)	16 (48.5%)	0.738
– female	30 (57.7%)	17 (51.5%)	
Age (years)	65 (41–88)	71 (39–88)	0.022
Body weight (kg)	80 (52–157)	80 (65–150)	0.533
Blood pressure-systolic (mm Hg)	135 (90–220)	140 (110–170)	0.239
tlparHomocysteine (μmol/L)	12.5 (6.4–25.3)	15.2 (4.4–27.7)	0.023
Glucose level (mmol/L)	8.8 (4.3–19.8)	9.6 (3.8–24.3)	0.334
Glycosylated haemoglobin (%)	8.0 (6.1–12.2)	7.9 (6.1–14.7)	0.821

AER – albumin excretion rate

TABLE 2
METHYLENETETRAHYDROFOLATE REDUCTASE (MTHFR) C677T GENOTYPES (NUMBER OF SUBJECTS AND PERCENTAGES) IN PATIENTS WITH AND WITHOUT DIABETIC NEPHROPATHY

MTHFR C677T genotype	Albumin excretion rate		p value
	<30 mg/24h, N=52	≥30 mg/24h, N=33	
Homozygous (T/T)	11 (21.2%)	5 (15.2%)	0.788
Heterozygous (C/T)	22 (42.3%)	15 (45.4%)	0.788
»Wild type« (C/C)	19 (36.5%)	13 (39.4%)	0.788

MTHFR – methylenetetrahydrofolate reductase

TABLE 3
THE CORRELATION BETWEEN METHYLENETETRAHYDROFOLATE REDUCTASE (MTHFR) C677T MUTATIONS AND THE HOMOCYSTEINE LEVEL

Homocysteine level (μmol/L) in:	MTHFR			Mann-Whitney U test	
	T/T	C/T	C/C	T/T vs. C/C	C/T vs. C/C
All patients	13.7 (7.9–25.3)	13.1 (6.4–25.1)	13.4 (4.4–27.7)	p=0.6777	p=0.937
Male	14.9 (9.5–25.3)	13.1 (6.4–25.1)	10.1 (4.4–27.7)	p=0.0829	p=0.137
Female	13.1 (7.9–17.3)	13.4 (7.4–23.0)	15.2 (8.0–21.6)	p=0.3798	p=0.535

MTHFR – methylenetetrahydrofolate reductase were not different between type 2 diabetic patients with and without nephropathy. This finding concurs with that of Eroglu et al. who reported that the MTHFR gene polymorphism is not associated with the development of diabetic nephropathy in Turkish type 2 diabetic patients[37]. Similar results were obtained in Japanese population[23,38].

Unlike the above examples, many published research papers pointed to the relationship between the MTHFR gene polymorphism and the development of diabetic nephropathy. The results of the research on Tunisian population clearly showed that homozygosity for C677T and hyperhomocysteinemia were associated with diabetic nephropathy[7]. These findings are in agreement with observations in the Chinese population according to the research of Sun and associates from 2004 and 2006 and based on which authors concluded that MTHFR C677T polymorphism could represent a genetic risk factor for diabetic nephropathy in Chinese type 2 patients[24]. Another research in the Chinese Han population showed similar results[39]. The confirmation of these results was also obtained in Lebanese and Polish patients, but the results of another research on the Polish population speak in favor of relationship between MTHFR polymorphism and diabetic nephropathy only in male patients[40–42]. Finally, a meta-analysis of 15 available studies that analized the association between diabetic nephropathy and MTHFR C677T showed heterogeneity between studies and a marginal correlation between development of diabetic nephropathy and genetic polymorphism[21].

It is evident that all above mentioned studies and reports were conducted on different populations. Since genetic factors can vary among different human groups, ethnic variations of the genetic polymorphism of the MTHFR gene could explain the variety of results in different populations.

From the results of our study it is obvious that patients in the group with diabetic nephropathy were statistically significantly older than in the normoalbuminuric group. This result is not unexpected, since older age is associated with reduced kidney function and creatinine clearance, as well as with higher probability of longer duration of diabetes and its chronic complications. The present study also shows that individuals with microalbuminuria had higher plasma homocysteine compared with patients with normoalbuminuria. There is no statistically significant difference in the homocysteine level considering MTHFR polymorphism, in the whole study population, or in separate groups of men and women. Observing separately the group of men, a somewhat higher medium homocysteine level (14.9 μmol/L) is evident in the group of homozygotes (T/T), and the lowest in the group of »wild types« (10.1 μmol/L). This difference is probably not statistically confirmed due to a relatively small number of patients. In the female part of the population such a trend is not evident.

Some studies state that hyperhomocysteinaemia is positively correlated with diabetic nephropathy. The study conducted by Chico et al showed the results similar to ours – patients with both types of diabetes and nephropathy had higher plasma homocysteine levels than the patients without nephropathy[25]. One Australian research showed that patients with microalbuminuria had higher levels of homocysteine than those with normoalbuminuria[43]. Another study suggests significant correlation of plasma homocysteine level with microalbuminuria, but only in patients with diabetic nephropathy who had C677T polymorphism[44]. In contrast, the findings published by Soares et al did not find meaningful difference between the subjects when homocysteine levels were assessed according to the MTHFR genotype[45]. The differences between these results could be a consequence of the diversity of laboratory methods, different analyzed sample sizes, different nutritional status or could be genetically determined.

In conclusion, our study did not show a correlation between MTHFR polymorphism and diabetic nephropathy in Croatian patients. However, the possibility that MTHFR polymorphism could be a risk factor for nephropathy cannot be completely excluded because diabetic nephropathy is influenced by multiple risk factors which can modify the importance of MTHFR polymorphism in its development. To detect that correlation it would be necessary to conduct larger additional studies in patients with diabetic nephropathy.

REFERENCES

1. AMERICAN DIABETES ASSOCIATION, Diabetes Care, 28 (2005) 1:S37. — 2. WILD S, ROGLIC G, GREEN A, SICREE R, KING H, Diabetes Care, 27 (2004) 1047. DOI: 10.2337/diacare.27.5.1047. — 3. SHAW JE, SICREE RA, ZIMMET PZ, Diabetes Res Clin Pract, 87 (2010) 4. DOI: 10.1016/j.diabres.2009.10.007. — 4. METELKO Z, PAVLIC-RENAR I, POLJICANIN T, SZIROVITZA L, TUREK S, Diabetes Res Clin Pract, 81 (2008) 263. DOI: 10.1016/j.diabres.2008.04.016. — 5. POLJICANIN T, METELKO Z, Medix, 80/81 (2009) 82. — 6. GROSS JL, DE AZEVEDO MJ, SILVEIRO SP, CANANI LH, CARAMORI ML, ZELMANOVITZ T, Diabetes Care, 28 (2005) 164. DOI: 10.2337/diacare.28.1.164. — 7. MTIRAOUI N, EZZIDI I, CHAIEB M, MARMOUCHE H, AOUNI Z, CHAIEB A, MAHJOUB T, VAXILLARE M, ALMAWI WY, Diabetes Res Clin Pract, 75 (2007) 99. DOI: 10.1016/j.diabres.2006.05.018. — 8. KANG SS, WONG PWK, SUSMANO A, SORA J, NORUSIS M, RUGGIE N, Am J Hum Genet, 48 (1991) 536. — 9. LOVRICEVIC I, BJORN DF, TOMICIC M, VRKIC N, DE SYO D, HUDOROVIC N, SONICKI Z, LONCAR R, Coll Antropol, 28 (2004) 647. — 10. SCHPICHINETSKY V, RAZ I, FRIEDLANDER Y, GOLDSCHMIDT N, WEXLER ID, BEN-JEHUDA A, FRIEDMAN G, J Nutr, 130 (2000) 2493. — 11. MCCULLY KS, Am J Pathol, 56 (1969) 111. — 12. ZUNTAR I, TOPIC E, ANTOLJAK N, Biochem Med, 1–2 (2003) 1. — 13. BOUSHNEY CJ, BERESFORD SA, OMENN GS, MOTULSKY AG, JAMA, 274 (1995) 1049. — 14. GRAHAM IM, DALY LE, REFSUM HM, ROBINSON K, BRATTSTRÖM LE, UELAND PM, PALMA-REIS RJ, BOERS GH, SHEAHAN RG, ISRAELSSON B, UITERWAAL CS, MELEADY R, MCMASTER D, VERHOEF P, WITTEMAN J, RUBBA P, BELLET H, WAUTRECHT JC, DE VALK HW, SALES LÚIS AC, PARROT-ROULAND FM, TAN KS, HIGGINS I, GARCON D, ANDRIA G, JAMA 277 (1997) 1775. — 15. POLLEX RL, MAMAKEESICK M, ZINMAN B, HARRIS SB, HANLEY AJG, HEGELE RA, Cardiovasc Diabetol, 4 (2005) 17. DOI: 10.1186/1475-2840-4-17. — 16.

ALAM MA, HUSAIN SA, NARANG R, CHAUHAN SS, KABRA M, VASISHT S, Mol Cell Biochem, 310 (2008) 111. DOI: 10.1007/s11010-007-9671-7. — 17. FROSST P, BLOM HJ, MILOS R, GOYETTE P, SHEPPARD CA, MATTHEWS R, BOERS GJ, DEN HEIJER M, KLUIJTMANS LA, VAN DEN HEUVEL LP, ROZEN R, Nat Genet, 10 (1995) 111. DOI: 10.1038/ng0595-111 — 18. SCHMELEVA VM, KAPUSTIN SI, PAPAYAN LP, SOBCZYNSKA-MALEFORA A, HARRINGTON DJ, SAVIDGE GF, Thromb Res, 111 (2003) 351. DOI: 10.1016/j.thromres.2003.10.004 — 19. MCCULLY KS, Nat Med, 2 (1996) 386. DOI: 10.1038/nm0496-386 — 20. CIACCIO M, BIVONA G, BELLIA C, Ther Clin Risk Manag 4 (2008) 219. — 21. ZINZTARAS E, UHLIG K, KOUKOULIS GN, PAPATHANASIOU AA, STEFANIDIS I, J Hum Genet, 52 (2007) 881. DOI: 10.1007/s10038-007-0189-3 — 22. KHAMAISI M, SCHRIJVERS BF, DE VRIESE AS, RAZ I, FLYVBJERG A, Nephrol Dial Transplant, 18 (2003) 1427. DOI: 10.1093/ndt/gfg242 — 23. MAEDA M, YAMAMOTO I, FUKUDA M, MOTOMURA T, NISHIDA M, NONEN S, KASAYAMA S, FUJIO Y, AZUMA J, J Diabetes Complicat, 22 (2008) 119. DOI: 10.1016/j.jdiacomp.2006.12.002 — 24. SUN J, XU Y, ZHU Y, LU H, Diabetes Res Clin Pract, 64 (2004) 185. DOI: 10.1016/j.diabres.2003.10.022 — 25. CHICO A, PEREZ A, CORDOBA A, ARCELUS A, CARRERAS G, DE LEIVA A, GONZALEZ-SASTRE F, BLANCO-VACA F, Diabetologia, 41 (1998) 684. — 26. SUN J, XU Y, ZHU Y, LU H, J Endocrinol Invest, 29 (2006) 814. — 27. SCAGLIONE L, GAMBINO R, GAY M, CASSADER M, PAGANO G, CAVALLO-PERRIN P, Diabetologia, 42 (1999) A329. — 28. REPORT OF A WHO CONSULTATION. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus. Report No 99.2., 1999. Geneva: World Health Organization, accessed 09.11.2012. Available from http://www.who.int/diabetes/currentpublications/en/. — 29. RYDEN L, STANDL E, BARTNIK M, VAN DEN BERGHE G, BETTERIDGE J, DE BOER MJ, COSENTINO F, JÖNSSON B, LAAKSO M, MALMBERG K, PRIORI S, ÖSTERGREN J, TUOMILEHTO J, THRAINSDOTTIR I, Eur Heart J, 28 (2007) 88. / No DOI found/ — 30. FORSBLOM CM, GROOP PH, EKSTRAND A, TÖTTERMAN KJ, SANE T, SALORANTA C, GROOP L, Diabetes Care, 21 (1998) 1932. — 31. ZELMANOVITZ T, GERCHMAN F, BALTHAZAR APS, THOMAZELLI FCS, MATOS JD, CANANI LH, Diabetol Metab Syndr 1 (2009)10. — 32. Package insert Abbott AxSYM homocysteine system: 1–8, accessed 09.11.2012. Available from: www. promtest.am/tests/.../Homocysteine.pdf. — 33. RASMUSSEN K, MOLLER J, LYNGBAK M, HOLM PEDERSEN AM, DYBKJAER L, Clin Chem, 42 (1996) 630. — 34. REIS RP, AZINHEIRA J, REIS HP, PINA JE, CORREIA JM, LUIS AS, Rev Port Cardiol, 18 (1999) 155. — 35. VERHOEF P, MELEADY R, DALY LE, GRAHAM IM, ROBINSON K, BOERS GHJ AND THE EUROPEAN COMAC GROUP, Eur Heart J, 20 (1999) 1234. /No DOI found/ — 36. MAYER O JR, SIMON J, ROSOLOVA H, Cas Lek Cesk, 138 (1999) 525. — 37. EROGLU Z, ERDOGAN M, TETIK A, KARADENIZ M, CETINALP S, KOSOVA B, GUNDUZ C, OZGEN AG, YILMAZ C, Diabetes Metab Res Rev, 23 (2007) 621. DOI: 10.1002/dmrr.735 — 38. FUJITA H, NARITA T, MEGURO H, ISHII T, HANYO O, SUZUKI K, KAMOI K, ITO S, J Diabetes Complications, 13 (1999) 284. — 39. WANG L, WANG J, XUE Y, CHEN Y, ZOU H, Zhonghua Yi Xue Yi Chuan Xue Za Zhi, 18 (2001) 276. — 40. NEMR R, SALMAN RA, JAWAD LH, JUMA EA, KELESHIAN SH, ALMAWI WY, Clin Chem Lab Med, 48 (2010) 1091. — 41. KSIAZEK P, BEDNAREK-SKUBLEWSKA A, BURACZYNSKA M, Med Sci Monit, 10 (2004) 47. — 42. MOCZULSKI D, FOJCIK H, ZUKOWSKA-SZCZECHOWSKA E, SZYDLOWSKA I, GRZESZCZAK W, Nephrol Dial Transpl, 18 (2003) 1535. DOI: 10.1093/ndt/gfg211 — 43. DAVIES L, WILMHURST EG, MCELDUFF A, GUNTON J, CLIFTON-BLIGH P, FULCHER GR, Diabetes Care, 24 (2001) 1805. DOI: 10.2337/diacare.24.10.1805 — 44. UKINC K, ERSOZ HO, KARAHAN C, EREM C, EMINAGAOGLU S, HACIHASANOGLU AB, YILMAZ M, KOCAK M, Endocrine, 36 (2009) 255. DOI: 10.1007/s12020-009-9218-7 — 45. SOARES AL, FERNANDES AP, CARDOSO JE, SOUSA MO, LASMAR MC, NOVELLI BA, LAGES GF, DUSSE LM, VIEIRA LM, LWALEED BA, CARVALHO MG, Pathophysiol Haemost Thromb, 36 (2008) 275.

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POVEZANOST POLIMORFIZMA C677T GENA ZA METILENTETRAHIDROFOLAT REDUKTAZU I DIJABETIČKE NEFROPATIJE U BOLESNIKA SA ŠEĆERNOM BOLESTI TIP 2 U HRVATSKOJ

SAŽETAK

Polimorfizam gena za metilentetrahidrofolat reduktazu (MTHFR) je povezan s razvojem dijabetičke nefropatije u mnogim etničkim skupinama.U ovoj studiji istraživali smo povezanost između polimorfizma C677T gena za MTHFR i mikroalbuminurije u bolesnika sa šećernom bolesti tip 2 u hrvatskih bolesnika. Osamdeset pet bolesnika sa šećernom bolesti je obrađivano i svrstano u dvije skupine – sa dijabetičkom nefropatijom i bez nje, ovisno o vrijednostima izlučenog albumina u 24-satnom urinu. Mutacija C677T gena za MTHFR određena je metodom izolacije DNA i alel specifične lančane reakcije polimeraze (PCR). Raspodjela genotipova u skupini bolesnika s normoalbuminurijom bila je: CC 36,5%, CT 42,3% i TT 21,2%, dok je u skupini bolesnika sa mikroalbuminurijom bila: CC 39,4%, CT 45,4% i TT 15,2%. Nije bilo statistički značajne razlike među grupama u distribuciji C677T genotipova ($p=0,788$). Naše istraživanje nije pokazalo povezanost između mutacije gena za metilentetrahidrofolat reduktazu i dijabetičke nefropatije u hrvatskih bolesnika. Mnogostruki čimbenici mogu modificirati značajnost utjecaja polimorfizma MTHFR na nastanak dijabetičke nefropatije.