RISK FACTOR ANALYSIS FOR GOUT IN THE LATVIAN POPULATION

Erika Nagle^{1,#}, Nellija Luksa², Georgijs Moisejevs^{2,3}, and Linda Gailīte²

¹ Department of Biology and Microbiology, Rīga Stradiņš University, 16 Dzirciema Str., Rīga, LV-1007, LATVIA

² Scientific Laboratory of Molecular Genetics, Rīga Stradiņš University, 16 Dzirciema Str., Rīga, LV-1007, LATVIA

³ Department of Nephrology and Renal Replacement Therapy, Rīga East Clinical University Hospital,
2 Hipokrāta Str., Rīga, Latvia, LV-1038

Corresponding author, erika.nagle@rsu.lv

Communicated by Aivars Lejnieks

Gout (Gr. podagra) is a multifactorial pathology, which means that both genetic and environmental factors play a role in the aetiology of the disease. For these reasons, revealing risk factors could be of very high importance in prevention and treatment of gout. In the present study, we found that a major role in gout predisposition is played by specific alleles in the ABCG2 gene. The study used survey data for 43 gout patients and 99 healthy control individuals who were genotyped for rs2231142. It was found that allelic variant rs2231142 in the ABCG2 gene had the strongest association with gout. Among other co-factors studied, sex, and increased body mass index were associated with gout.

Key words: podagra, ABCG2 gene, Q141K, rs2231142.

INTRODUCTION

Gout is a common metabolic disease. In Western developed countries, the contemporary prevalence of gout is 3–6% in men and 1–3% in women (Kuo *et al.*, 2015; Dalbeth *et al.*, 2016). Patients with gout can be characterised by monosodium urate crystal-induced, extremely painful inflammatory arthritis, which can lead to joint destruction and disability if untreated (Cleophas *et al.*, 2017). For the population of Latvia, gout is a severe health problem that affects both males and females, but there are no data about gout incidence or prevalence in Latvia. In each year between 2014 and 2017, there were about 10 000 visits with the primary diagnosis of gout (M10), according to data from the Centre of Disease Prevention and Control of Latvia. Analysis of genetic factors and their co-variants in gout is of great importance, due to the possibility of identifying aetiological factors involved in the pathogenesis of this disease, which could improve prophylaxis and treatment.

It is believed that gout is a disorder with high heritability (Lv *et al.*, 2014). Gout is a disease with multifactorial aetiology involving both genetic and environmental factors (Yu *et al.*, 2017). In genetic studies there are reported associations with genetic variants in multiple genes encoding renal

and gut uric acid transporter proteins, such as SLC2A9/GLUT9, ABCG2, SLC22A11/OAT4, SLC22A12/URAT1, and SLC17A1/NPT1 proteins encoding genes (Dalbeth *et al.*, 2018), but most evidence is reported concerning the ABCG2 gene (OMIM 603756) (Matsuo *et al.*, 2011; Dalbeth and Stamp, 2016). Protein ABCG2 is a high-capacity urate transporter (Nakayama *et al.*, 2011). Genetic variants of the ABCG2 gene influence expression of ABCG2, which results in reduction of the urate transport rate, and consequently, increased serum urate levels lead to gout (Matsuo *et al.*, 2011). Patients with severe ABCG2 dysfunction were found to have earlier symptom onset, more severe manifestation of gout, and even a modified risk factor effect, on the development of gout (Macfarlane and Kim, 2014). All this suggests the clinical relevance of ABCG2 gene variants and the need for more detailed studies. The most significant evidence for the association between the genetic variants of this gene and gout is known for rs2231142 (traditional name: Q141K). More precisely, the presence of the T allele results in loss of functions of this transport protein and leads to hyperuricemia and gout, especially in persons of European ancestry (Zhang *et al.*, 2013).

The role of genetic factors in the aetiology of gout is well documented, but along with genetic studies, demographic

analysis has shown that education level, body mass index (BMI), and arterial blood pressure are important risk factors for gout development. In addition, sex plays a crucial role in gout aetiology. Males are affected more commonly, more severely, and at younger age than females (Macfarlane and Kim, 2014). It is obvious that study of the role of genetic factors and their co-variants in the aetiology of gout could open the door for the prophylaxis of this metabolic disorder.

We performed a case-control study with the aim of assessing the association of gout development with rs2231142, adjusted for other potential risk factors in patients from Latvia.

MATERIALS AND METHODS

Sampling. A study group and a control group were involved in the retrospective study, using data available from the Genome Database of the Latvian Population (LGDB), a government-funded biobank. The LGDB is the national biobank of health and genetic information collected from adult residents of Latvia. The available data were collected by medical personnel as described previously (Rovite *et al.*, 2018). The age of an individual represented the age at which they were enrolled in the study, not the age when a diagnosis was confirmed. Data of anthropometric measurements (including weight and height) were obtained by direct measurement. Information about education level, smoking habits, alcohol usage were obtained via questionnaire-based interview. All recorded data related to health status were affirmed by experienced physicians using the World Health Organisation's International Classification of Diseases (ICD-10) codes.

The study group included individuals with an established diagnosis of gout — all individuals with ICD-10 code M 10.0. For gout patients, no detailed information about the uric acid level and clinical symptoms was available. The control group included healthy individuals without any recorded diseases. A total of 142 individuals were selected from LGDB records. There were 43 individuals (38 men and 5 women) in the study group and 99 control group individuals (70 men and 29 women). Education was classified into three levels: basic (graduated primary school), secondary (graduated secondary school) and tertiary level (graduated university). Information with respect to smoking habit was classified as: never smoked, former smokers and daily smokers. By alcohol usage the individuals were divided into categories based on the frequency of alcohol usage: never, occasional use (using alcohol in exceptional cases) and frequent use (combining the groups that consumed alcohol 1–2 times per week, at least three times per week, and every day).

Written confirmed consent had been acquired from all LGDB participants (Rovite *et al.*, 2018). The study protocol was approved by the Central Medical Ethics Committee of Latvia (protocol No. 18.01.2017.).

Genotyping. We used study groups to determine genotypes of the individuals with respect to *ABCG2* gene variant rs2231142. Genotyping was performed using TaqMan probes (probe C_15854163_70, detecting alleles G and T) according to the manufacturer's protocol (Thermo Fisher Scientifics, USA) including positive and negative control samples in every run using 5xHotFirePol Universal qPCR mix (Solis Biodyne, Estonia) and alleles detected by Rotor-Gene 2000 (Qiagen, Germany) equipment. For the analysis, duplicates were included and ten samples were sequenced using the Big Dye Terminator kit v.1.1. according to manufacturer protocol (Thermo Fisher Scientifics, USA). In 100% duplicated cases genotypes were identical.

Statistical analysis. Available continuous variables for both study groups were expressed as median and interquartile range (IQR). The strength of association between disease and co-variants was assessed by calculating the odds ratio (OR) and 95% confidence interval (CI 95%) via binary regression analysis. Independent factors that were significantly associated with gout risk in unifactorial analysis were adjusted by inclusion in the multifactorial binary regression model. Analysis was done using SPSS 20.0 (SPSS Inc., Chicago, IL, USA) and PLINK software.

RESULTS

Survey data. From available survey data, known co-factors for gout manifestations like sex, education level and life style habits (e.g. smoking and alcohol usage) were considered. The obtained results are shown in Table 1. The strongest association with gout was observed with respect to sex.

Table 1. Description of categorised variables among the study and control groups

Variables	Study group	Control group	OR	CI95%
Sex				
women	5	29	1	-
men	38	70	3.15	1.13-8.80
Education				
basic	4	6	1	-
secondary	28	41	1.02	0.27-3.97
tertiary	11	51	0.32	0.08-1.34
ND	0	1		
Alcohol consumption*				
no	8	11	1	-
sometimes	26	45	0.79	0.28-2.23
regular	8	40	0.28	0.08-0.90
ND	1	3		
Smoking habits*				
no	20	42	1	-
smoking history	18	32	1.18	0.54-2.59
active smoker	5	25	0.42	0.14-1.26

OR: odds ratio; CI95%: 95% confidence interval; ND no data available

*for the study group, information was collected following diagnosis confirmation

Table 2. Description of continuous variables between the study group and controls

Variables	Study group			Controls				
	Number of individuals	Median	IQR	Number of individuals	Median	IQR	OR	CI95%
Age, years	43	61.0	58.0-72.0	99	48.0	43.0-65.0	1.078	1.04-1.11
BMI, kg/m ²	43	28.3	24.7-33.0	99	24.2	22.8-30.6	1.133	1.05-1.22
Waist circumference, cm	38	98.0	87.0-109.0	71	89.0	82.0-98.0	1.041	1.01-1.07
Systolic arterial blood pressure, mmHg	39	138.0	125.0-146.0	73	123.0	116.0-140.0	1.029	1.00-1.06
Diastolic arterial blood pressure, mmHg	39	80.0	75.0-90.0	73	80.0	76.0-90.0	1.004	0.97-1.05
Mean arterial blood pressure, mmHg	39	96.7	93.3-106.7	73	94.7	89.5-105.8	1.024	0.99-1.06

IQR: interquartile range; OR: odds ratio; CI95%: confidence interval 95%; BMI: body mass index

Men tend to develop gout at least three times more often than women (OR = 3.15, $p = 0.029$). Regular alcohol usage was significantly lower (OR = 0.32, $p = 0.033$) among gout patients 8/42 in comparison with controls — 40/96. The level of education and smoking habits showed no significant differences among study groups.

In Table 2, the effects of age, BMI, and arterial blood pressure on gout manifestation is shown by comparison of the study and control groups. Older age, increased BMI, increased waist circumference and elevated systolic blood pressure, but not diastolic blood pressure and mean arterial blood pressure, were significantly associated with gout. The strongest association was observed for BMI (OR = 1.33, $p = 0.001$, CI95% 1.05–1.22): patients with gout had elevated BMI (28.3 kg/m²) in comparison to controls, who had normal BMI (24.2 kg/m²).

Genotyping data. Statistically significant differences in T allele frequency were detected between the groups (in the study group 0.221 and in controls 0.071), confirming T as a risk allele for gout development — OR = 3.73, CI 95% = 1.77–7.85, $p = 0.0003$. Genotype distribution in the groups is shown in Table 3. As the controls did not include any individual who was homozygous with T alleles, the risk of gout manifestation in the case of at least one T allele in the genotype was calculated using the dominant model of inheritance (genotypes GT and TT were considered versus GG) — OR = 3.60, CI95% = 1.56–8.32, $p = 0.0003$.

Multifactorial analysis. To clarify the strength of genotype association with gout, genotype was adjusted for other significant non-modifiable potential risk factors (age and sex). Table 4 shows results of multifactorial analysis of non-modifiable potential risk factors. All factors were significantly associated with gout development. T allele presence showed a stronger association to gout phenotype (OR = 6.43, $p = 0.001$) than for male gender (OR = 5.48, $p = 0.006$).

DISCUSSION

In the present study, we studied the association of potential risk factors with gout development in a group of the population of Latvia. Data presented in Table 1 indicate that

Table 3. Genotyping results of *ABCG2* gene allelic variant rs2231142 in the study group and in controls

Genotypes	Study group (n=43)	%	Control group (n=99)	%
GG	27	63	85	86
GT	13	30	14	14
TT	3	7	0	0
T allele (minor allele) frequency	0.221		0.071	

Table 4. Multifactorial analysis of non-modifiable potential risk factors of gout

Parameter	Gout vs controls		p -value
	OR	CI95%	
Gender			
female	1	-	
male	5.483	1.627-18.474	0.006
Genotype			
GG	1	-	
GT or TT	6.433	2.297-18.013	0.001

among categorical variables analysed, the strongest association with gout was for sex (OR for male 3.15), as observed previously (Zhang *et al.*, 2013; Harrold *et al.*, 2017). Patient education should highlight knowledge of the disease and treatment (Li *et al.*, 2013). While the degree of education was not significantly associated with gout development, patients with tertiary level of education displayed a lower tendency to develop gout (OR = 0.32). Possibly, individuals with a lower level of education are less aware of risk factors for diseases and have a poorer understanding about the importance of preventive measures against gout (Treharne *et al.*, 2018). Education preferences in gout patients were identified in some New Zealand populations (Treharne *et al.*, 2018). In the literature, a well-known co-factor of gout is alcohol usage (Lieber, 1965; Teng *et al.*, 2013; Seki *et al.*, 2016), corresponding to increased serum uric acid concentration. In our study group, we found conflicting results — regular alcohol consumption was negatively associated with gout (OR = 0.28). This might be because patients changed their habits after diagnosis, decreasing their alcohol usage. Despite the general view of smoking habit as a risk factor for gout, we had unexpected results: for patients with a

smoking history, the OR is higher (OR = 1.18) in comparison with active smokers (OR = 0.42), but this finding was not statistically significant. The explanation here could be similar to that for alcohol usage — it is possible that after diagnosis, patients quit smoking. However, there are studies that have demonstrated similar results to our observation regarding active smoking (Gee Teng *et al.*, 2016). In analyses of male cohorts, ex-smoking was found to be associated with higher concentrations of serum urate and higher prevalence of hyperuricemia compared to current smoking (Fanning *et al.*, 2018). Active smoking has also been associated with lower risk of gout in men in an Asian cohort (Gee Teng *et al.*, 2016).

Among continuous variables described in Table 2, gout is more common in patients with increased BMI (OR = 1.133). High BMI indicates the absolute importance of dietary counselling in gout and proves why this counselling may influence the long-term well-being of a patient with gout (Beyl Hughes and Morgan, 2016). Increased systolic arterial blood pressure also is associated with gout (OR = 1.029). Therefore, patients with gout show phenotype similarity with metabolic syndrome. A study in the sub-Saharan African population showed that roughly one in every two gout patients also had metabolic syndrome. Gout patients with metabolic syndrome had a significantly higher BMI, and had significantly higher levels of serum uric acid levels (Doualla-Bija *et al.*, 2018).

Genotyping data (Table 3) showed that allele T in *ABCG2* gene variant rs2231142 was associated with gout development in a sample population of Latvia residents (OR = 3.60). To clarify the strength of genotype association with gout, genotype was adjusted for other significant non-modifiable potential risk factors (age and gender). In multi-factorial analysis, allele T in *ABCG2* gene variant rs2231142 showed the strongest association with gout (OR = 6.43). The significance of our results strengthens information about T allele frequencies in other related populations. In the control group in Latvia, the frequency of allele T was 0.071, compared to 0.091 and 0.080 in Finland and Russia, respectively (Auton *et al.*, 2015), and 0.081 in Estonia (Rajeevan *et al.*, 2012). Furthermore, the reported geographical and ethnical variation in T allele frequency (e.g. East Asian 0.291, South Asian 0.097, African 0.013, American 0.141, and European 0.094) (Auton *et al.*, 2015) reflects genetic differences between populations. There previously were no reports on T allele frequency in rs2231142 in Latvia. There is a need for regional data to be able to evaluate T allele as a risk allele for gout. Our results are supported by the observation that individuals having allele T (141K allele) have reduced excretion of uric acid through the gut, which adds to the urate circulation, overloading the kidney excretion system and resulting in increased uric acid levels (Ichida *et al.*, 2012) that lead to gout. The significance of *ABCG2* gene allelic variants in the aetiology of gout is reinforced by the fact that these variants not only increase urate levels, but also may influence crystal formation and inflam-

matory responses to deposited crystals (Merriman *et al.*, 2016).

The key question in studying pathogenic variants of the *ABCG2* gene is how knowledge of the risk allele predisposition to gout can impact management of patients. There are several possibilities. Firstly, as dysfunctional *ABCG2* variants increase the risk of gout, knowing the high-risk alleles allows to develop preventive measures against development of gout (Matsuo *et al.*, 2011). Secondly, information about risk alleles could help to predict the adverse effects of drugs. For instance, researchers found that the Q141K allele (rs2231142 allele T) conferred a significantly increased risk of poor response to allopurinol (Petru *et al.*, 2016, ZhangSun and Shi, 2018). Thirdly, *ABCG2* variants have also been associated with tophaceous disease in people with gout. In a Taiwanese study of people with gout, the 141K allele was associated with tophi in both Han and Aboriginal Taiwanese populations (Cleophas *et al.*, 2017). The polymorphism rs2231142 in the *ABCG2* gene, which causes a Glu141Lys amino acid substitution, accounted for 0.57% of the variation in serum urate, and a functional study of rs2231142 showed that it causes a 53% reduction in the rate of *ABCG2*-mediated urate transport compared with wild-type *ABCG2* (Chen *et al.*, 2018).

Weak points of the study included: the study population was formed based on convenience sampling, so study results might not extrapolate to all gout patients in Latvia. The study was based on retrospective data and no laboratory data, with only a small amount of clinical information available. A further, larger prospective study with a representative population and precise clinical data should be conducted to clarify the association between allele T in *ABCG2* gene variant rs2231142, along with the degree of joint damage, serum blood concentration of uric acid, response to therapy, and other important clinical factors.

CONCLUSIONS

Association between gout and several factors were studied in order to find associations with gout risk. The genotype of variant rs2231142 in the *ABCG2* gene revealed its crucial role in gout development. It is recommended that genotyping be conducted in clinical practice.

ACKNOWLEDGEMENTS

We acknowledge the Genome Database of the Latvian Population, and the Latvian Biomedical Research and Study Centre, for providing data and DNA samples.

REFERENCES

- Auton, A., Brooks, L. D., Durbin, R. M., Garrison, E. P., Kang, H. M., Korbel, J. O., Marchini, J. L., McCarthy, S., McVean, G. A., Abecasis, G. R. (2015). A global reference for human genetic variation. *Nature*, **526**, 68–74.
- Beyl, R. N., Jr., Hughes, L., Morgan, S. (2016). Update on importance of diet in gout. *Amer. J. Med.*, **129** (11), 1153–1158.

- Chen, C. J., Tseng, C. C., Yen, J. H., Chang, J. G., Chou, W. C., Chu, H. W., Chang, S. J., Liao, W. T. (2018). *ABCG2* contributes to the development of gout and hyperuricemia in a genome-wide association study. *Sci. Rep.*, **8** (1), 3137.
- Cleophas, M. C., Joosten, L. A., Stamp, L. K., Dalbeth, N., Woodward, O. M., Merriman, T. R. (2017). *ABCG2* polymorphisms in gout: Insights into disease susceptibility and treatment approaches. *Pharmacogenomics Pers. Med.*, **10**, 129–142.
- Dalbeth, N., Merriman, T. R., Stamp, L. K. (2016). Gout. *The Lancet*, **388**, 2039–2052.
- Dalbeth, N., Stamp L. K., Merriman T. R. (2017). The genetics of gout: Towards personalized medicine? *BMC Med.*, **15** (1), 108.
- Doualla-Bija, M., Lobe Batchama, Y., Moutchia-Suh, J., Ama Moor, V. J., Kamdem, F., Lekpa, F. K., Luma Namme, H. (2018). Prevalence and characteristics of metabolic syndrome in gout patients in a hospital setting in sub-Saharan Africa. *Diabetes Metab. Syndr.*, **12** (6), 1007–1011.
- Fanning, N., Merriman, T. R., Dalbeth, N., Stamp, L. K. (2018). An association of smoking with serum urate and gout: A health paradox. *Semin. Arthritis Rheum.*, **47** (6), 825–842.
- Gee Teng, G., Pan, A., Yuan, J. M., Koh, W. P. (2016). Cigarette smoking and the risk of incident gout in a prospective cohort study. *Arthritis Care Res. (Hoboken)*, **68** (8), 1135–1142.
- Harrold, L. R., Etzel, C. J., Gibofsky, A., Kremer, J. M., Pillinger, M. H., Saag, K. G., Schlesinger, N., Terkeltaub, R., Cox, V., Greenberg, J. D. (2017). Sex differences in gout characteristics: Tailoring care for women and men. *BMC Musculoskelet. Disord.*, **18** (1), 108.
- Ichida, K., Matsuo, H., Takada, T., Nakayama, A., Murakami, K., Shimizu, T., Yamanashi, Y., Kasuga, H., Nakashima, H., Nakamura, T., Takada, Y., Kawamura, Y., Inoue, H., Okada, C., Utsumi, Y., Ikebuchi, Y., Ito, K., Nakamura, M., Shinohara, Y., Hosoyamada, M., Sakurai, Y., Shinomiya, N., Hosoya, T., Suzuki, H. (2012). Decreased extra-renal urate excretion is a common cause of hyperuricemia. *Nat. Commun.*, **3**, 764.
- Kuo, C. F., Grainge, M. J., Zhang, W., Doherty, M. (2015). Global epidemiology of gout: Prevalence, incidence and risk factors. *Nat. Rev. Rheumatol.*, **11** (11), 649–662.
- Li, Q. H., Dai, L., Li, Z. X., Liu, H. J., Zou, C. J., Ou-Yang, X., Lu, M., Li, T., Li, Y. H., Mo, Y. Q., Schumacher, H. R. (2013). Questionnaire survey evaluating disease-related knowledge for 149 primary gout patients and 184 doctors in South China. *Clin. Rheumatol.*, **32** (11), 1633–1640.
- Lieber, C. S. (1965). Hyperuricemia induced by alcohol. *Arthritis Rheum.*, **8** (4), 786–798.
- Lv, X., Zhang, Y., Zeng, F., Yin, A., Ye, N., Ouyang, H., Feng, D., Li, D., Ling, W., Zhang, X. (2014). The association between the polymorphism rs2231142 in the *ABCG2* gene and gout risk: A meta-analysis. *Clin. Rheumatol.*, **33** (12), 1801–1805.
- Macfarlane, L. A., Kim, S. C. (2014). Gout: A review of nonmodifiable and modifiable risk factors. *Rheum. Dis. Clin. North Amer.*, **40** (4), 581–604.
- Matsuo, H., Takada, T., Ichida, K., Nakamura, T., Nakayama, A., Suzuki, H., Hosoya, T., Shinomiya, N. (2011). *ABCG2/BCRP* dysfunction as a major cause of gout. *Nucleosides Nucleotides Nucleic Acids*, **30** (12), 1117–1128.
- Merriman, T. R., Phipps-Green, A., Boockvar, J., Riches, P., Tausche, A. K., Radstake, T., Janssen M., Joosten, L. A. B., Jansen, T. L., So A., Hindmarsh, J. H., Stamp, L. K., Dalbeth, N., Wrigley, R. (2016). Pleiotropic effect of *ABCG2* in gout. *Arthritis Rheumatol.*, **68** (suppl 10). Available at: <https://acrabstracts.org/abstract/pleiotropic-effect-of-abcg2-in-gout/> (accessed 19 December 2018).
- Nakayama, A., Matsuo, H., Takada, T., Ichida, K., Nakamura, T., Ikebuchi, Y., Ito, K., Hosoya, T., Kanai, Y., Suzuki, H., Shinomiya, N. (2011). *ABCG2* is a high-capacity urate transporter and its genetic impairment increases serum uric acid levels in humans. *Nucleosides Nucleotides Nucleic Acids*, **30** (12), 1091–1097.
- Petru, L., Pavelcova, K., Sebesta, I., Stiburkova, B. (2016). Genetic background of uric acid metabolism in a patient with severe chronic tophaceous gout. *Clin. Chim. Acta.*, **460**, 46–49.
- Rajeevan, H., Soundararajan, U., Kidd, J. R., Pakstis, A. J., Kidd, K. K. (2012). ALFRED: an allele frequency resource for research and teaching. *Nucleic Acids Res.*, **40** (Database issue), D1010–1015.
- Rovite, V., Wolff-Sagi, Y., Zaharenko, L., Nikitina-Zake, L., Grens, E., Klovins, J. (2018). Genome Database of the Latvian Population (LGDB): Design, goals, and primary results. *J. Epidemiol.*, **28** (8), 353–360.
- Seki, S., Oki, Y., Tsunoda, S., Takemoto, T., Koyama, T., Yoshimura, M. (2016). Impact of alcohol intake on the relationships of uric acid with blood pressure and cardiac hypertrophy in essential hypertension. *J. Cardiol.*, **68** (5), 447–454.
- Teng, G. G., Tan, C. S., Santosa, A., Saag, K. G., Yuan, J. M., Koh, W. P. (2013). Serum urate levels and consumption of common beverages and alcohol among Chinese in Singapore. *Arthritis Care Res. (Hoboken)*, **65** (9), 1432–1440.
- Trehanar, G. J., Richardson, A. C., Neha, T., Fanning, N., Janes, R., Hudson, B., Judd, A., Pitama, S., Stamp, L. K. (2018). Education preferences of people with gout: Exploring differences between indigenous and nonindigenous peoples from rural and urban locations. *Arthritis Care Res. (Hoboken)*, **70** (2), 260–267.
- Yu, K. H., Chang, P. Y., Chang, S. C., Wu-Chou, Y. H., Wu, L. A., Chen, D. P., Lo, F. S. and Lu, J. J. (2017). A comprehensive analysis of the association of common variants of *ABCG2* with gout. *Sci. Rep.*, **7** (1), 9988.
- Zhang, L., Spencer, K. L., Voruganti, V. S., Jorgensen, N. W., Fornage, M., Best, L. G., Brown-Gentry, K. D., Cole, S. A., Crawford, D. C., Deelman, E., Franceschini, N., Gaffo, A. L., Glenn, K. R., Heiss, G., Jenny, N. S., Kottgen, A., Li, Q., Liu, K., Matise, T. C., North, K. E., Umans, J. G., Kao, W. H. (2013). Association of functional polymorphism rs2231142 (Q141K) in the *ABCG2* gene with serum uric acid and gout in 4 US populations: the PAGE Study. *Amer. J. Epidemiol.*, **177** (9), 923–932.
- Zhang, W., Sun, S. and Shi, Z. 2018. Polymorphisms of *ABCG2* and its impact on clinical relevance. *Biochem Biophys Res Commun.*, **503** (2), 408–413.

Received 19 December 2018

Accepted in the final form January 2020

PODAGRAS RISKĀ FAKTORU ANALĪZE LATVIJAS IEDZĪVOTĀJU GRUPĀ

Podagra (*gr. podagra*) ir metabolisma slimība, kas skar lielu sabiedrības daļu. Podagras pacienti cieš no ļoti stipru sāpju epizodēm locītavu iekaisuma dēļ. Iekaisuma dēļ locītavas var tikt stipri bojātas. Podagra ir multifaktoriāla patoloģija, tās etioloģijā liela nozīme ir gan ģenētiskajiem, gan vides faktoriem. Minēto iemeslu dēļ riska faktoru atklāšana varētu dot nozīmīgu ieguldījumu patoloģijas profilaksē un ārstēšanas stratēģijas izstrādē. Šajā pētījumā tika noskaidrots, ka galvenā loma predispozīcijā pret podagru pieder *ABCG2* gēna specifiskām alēlēm. Šie rezultāti var būt noderīgi klīniskajā praksē, lai paredzētu predispozīciju podagrai. Savukārt izvairīšanās no podagru veicinošiem vides faktoriem var palīdzēt ierobežot podagras attīstību. Tā kā *ABCG2* gēna patogēniskie varianti samazina urātu transportu, *ABCG2* disfunkcija ir par cēloni agrīnākai un smagākai simptomu izpausmei. Tādējādi ir acīmredzams, ka riska faktoru, kas veicina podagras attīstību, analīze nevar tikt pārvērtēta.