Different types of glomerulopathies, generally membranous glomerulonephritis, have been associated with solid tumors. However, paraneoplastic IgA-N has been reported rarely.

Primarily, IgA-N associations with cancer of the buccal cavity, the nasopharynx and the respiratory tract have been described. Mesangial IgA deposits have been found at autopsy in patients who died of a gastro-intestinal neoplasm without prior clinical evidence of nephropathy. Despite intensive investigation, the mechanism underlying glomerular IgA deposition in IgA nephropathy has not been clarified. There are two isotype subclasses of IgA: IgA1 and IgA2. Gastrointestinal and respiratory tracts plasma cells produce both IgA1 and IgA2; however plasma cells in the spleen, lymph nodes and bone marrow produce predominantly IgA1. Invasion of the intestinal mucosa by malignancy increases the circulating IgA level and therefore leads to the formation of mesangial deposits.

In conclusion, paraneoplastic IgA nephropathy with nephrotic syndrome could be a clinical problem in patients with malignancies, besides the treatment chart has not been well-documented yet. To the best of our knowledge, we report the first case of paraneoplastic IgA-N associated with recurrence of gastric adenocarcinoma. IgA-N should take into account in patients with malignancy and nephrotic syndrome even if primary disease was on remission and it could be a harbinger for the relapse of disease.

Conflicts of interest
The authors declare that they have no conflicts of interest related to the contents of this article.


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Dear Editor,
Results of large-scale studies and meta-analyses\textsuperscript{1-4} strongly indicate that K23 allele is associated with higher prevalence and incidence of type 2 diabetes in adult Caucasians. Some studies\textsuperscript{1-5} have shown that the K allele may have a diabetogenic effect by impairing glucose-induced insulin release.

The aim of our study was to investigate an association between E23K \textit{KCNJ11} gene polymorphism and anthropometric, biochemical, beta-cell secretion and insulin sensitivity parameters among adult ADPKD patients with normal kidney function and no diagnosis of diabetes. The comparison of geno-type-phenotype associations between ADPKD and non-ADPKD subjects could reveal a hypothetical mechanism of genetic determination of diabetes specific for ADPKD patients.

METHODS
The study group included 49 adult individuals with diagnosed ADPKD (19 males, 30 females) while the control group comprised 50 gender- and age-matched healthy individuals (22 males, 28 females).

The oral glucose tolerance test (OGTT) was performed according to WHO guidelines (with 75 g of glucose). Venous blood was collected to measure fasting glucose, insulin, total cholesterol, LDL, HDL and triglyceride levels. Glucose concentration was measured by an enzymatic-amperometric method (Super GL; Dr Müller Gerätebau GmbH, Freital, Germany). Insulin concentration
was measured by microparticle enzyme immunoassay (AxSYM MEIA; Abbott Laboratories, Abbot Park, USA. For serum creatinine and lipid levels a Cobas Integra 800 bioanalyser was used.

The beta-cell function indexes were used in our study: ratios of insulin-to-glucose concentrations for each OGTT time point (INS/GLU 0, 30, 60, 90, 120), ratio of the area under curve of insulin to glucose (AUC Insulin) and glucose (AUC Glucose)) concentrations (SECR AUC), and glucose (AUC Glucose) concentrations for each OGTT used in our study: ratios of insulin-to-glucose (INS/GLU 0, 30, 60, 90, 120), glucose concentrations for each OGTT (Table 2).

The genotypes of G67A (E23K) KCNJ11 polymorphism (rs5219) were determined using a by PCR-RFLP technique, as described previously.\(^8\)

Mann-Whitney test was used for quantitative variables, while the Fisher exact test was implemented for qualitative variables.

**RESULTS**

Differences in E23K KCNJ11 genotype distribution among ADPKD patients (33% EE, 51% EK, 16% KK) and controls (46% EE, 42% EK, 12% KK) proved insignificant (\(p=.39\)). Both distributions were consistent with Hardy-Weinberg equilibrium (\(p>.7\)).

**ADPKD group**

KK homozygotes were significantly younger than allele E carriers. Other anthropometric parameters were not associated with genotype (Table 1).

There was a trend to lower serum total cholesterol concentration among KK homozygotes if compared to E allele carriers, but HDL-cholesterol was significantly lower among K allele carriers in comparison to EE homozygotes (Table 1). Glucose levels during OGTT did not differ significantly between the genotypes, but we have found trend to lower insulin levels among K allele carriers than in EE homozygotes in the 30\(^{th}\) minute of OGTT (Table 2). Similarly, in the 60\(^{th}\) minute of the test, there was a trend to lower insulin levels among KK homozygotes than in E allele carriers. INS/GLU 30 min ratio and values of the SECR1P 30 min, SECR2P 30 min and INSGENIN indexes were significantly lower among K allele carriers than in EE homozygotes. No significant associations between KCNJ11 E23K genotype and other carbohydrate metabolism parameters were observed (Table 2).

**Table 1.** Association between the G67A (rs5219 E23K) variant of the KCNJ11 gene and anthropometric and biochemical parameters among ADPKD and control groups

<table>
<thead>
<tr>
<th>Parameter</th>
<th>ADPKD group (n=49)</th>
<th>Control group (n=50)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EE (n=16)</td>
<td>EK (n=25)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(n=21)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>38.6±7.97</td>
<td>36.6±12.4</td>
</tr>
<tr>
<td>BMI (kg/m(^2))</td>
<td>25.6±5.25</td>
<td>25.1±4.98</td>
</tr>
<tr>
<td>WHR</td>
<td>0.8±0.40</td>
<td>0.8±0.09</td>
</tr>
<tr>
<td>Serum total cholesterol (mg/dL)</td>
<td>199±44</td>
<td>198±36</td>
</tr>
<tr>
<td>LDL-cholesterol (mg/dL)</td>
<td>125±40</td>
<td>131±36</td>
</tr>
<tr>
<td>HDL-cholesterol (mg/dL)</td>
<td>61.8±9.33</td>
<td>54.4±15.2</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>97.8±45.8</td>
<td>108±70</td>
</tr>
<tr>
<td>Glucose 0 min (mg/dL)</td>
<td>93.7±31.9</td>
<td>90.5±12.3</td>
</tr>
<tr>
<td>Glucose 30 min (mg/dL)</td>
<td>131±26</td>
<td>140±29</td>
</tr>
<tr>
<td>Glucose 60 min (mg/dL)</td>
<td>119±28</td>
<td>132±43</td>
</tr>
<tr>
<td>Glucose 90 min (mg/dL)</td>
<td>103±19</td>
<td>109±33</td>
</tr>
<tr>
<td>Glucose 120 min (mg/dL)</td>
<td>87.6±15.5</td>
<td>91.1±25.2</td>
</tr>
<tr>
<td>Insulin 0 min (µU/mL)</td>
<td>9.14±5.28</td>
<td>8.94±4.78</td>
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<tr>
<td>Insulin 30 min (µU/mL)</td>
<td>65.5±24.7</td>
<td>55.1±42.4</td>
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<tr>
<td>Insulin 60 min (µU/mL)</td>
<td>84.3±35.0</td>
<td>73.3±48.1</td>
</tr>
<tr>
<td>Insulin 90 min (µU/mL)</td>
<td>54.3±26.4</td>
<td>65.9±56.9</td>
</tr>
<tr>
<td>Insulin 120 min (µU/mL)</td>
<td>29.6±14.3</td>
<td>49.5±64.4</td>
</tr>
</tbody>
</table>

**BMI:** body mass index; **HDL:** high-density lipoprotein; **LDL:** low-density lipoprotein; **WHR:** waist-to-hip ratio.

\(^{a}\) - EE vs. EK + KK; Mann-Whitney test.

\(^{b}\) - EE + EK vs. KK; Mann-Whitney test.

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Reference:

1. The genotypes of G67A (E23K) KCNJ11 polymorphism (rs5219) were determined using a PCR-RFLP technique, as described previously.\(^8\)

2. Mann-Whitney test was used for quantitative variables, while the Fisher exact test was implemented for qualitative variables.

3. Differences in E23K KCNJ11 genotype distribution among ADPKD patients (33% EE, 51% EK, 16% KK) and controls (46% EE, 42% EK, 12% KK) proved insignificant (\(p=.39\)). Both distributions were consistent with Hardy-Weinberg equilibrium (\(p>.7\)).

4. KK homozygotes were significantly younger than allele E carriers. Other anthropometric parameters were not associated with genotype (Table 1).

5. There was a trend to lower serum total cholesterol concentration among KK homozygotes if compared to E allele carriers, but HDL-cholesterol was significantly lower among K allele carriers in comparison to EE homozygotes (Table 1). Glucose levels during OGTT did not differ significantly between the genotypes, but we have found trend to lower insulin levels among K allele carriers than in EE homozygotes in the 30\(^{th}\) minute of OGTT (Table 2). Similarly, in the 60\(^{th}\) minute of the test, there was a trend to lower insulin levels among KK homozygotes than in E allele carriers. INS/GLU 30 min ratio and values of the SECR1P 30 min, SECR2P 30 min and INSGENIN indexes were significantly lower among K allele carriers than in EE homozygotes. No significant associations between KCNJ11 E23K genotype and other carbohydrate metabolism parameters were observed (Table 2).
Control group
Among KK homozygotes, in comparison to E allele carriers, significantly lower glucose levels in the 60th minute of OGTT as well as lower insulin levels in the 60th and 120th minute of OGTT were observed – a similar trend was observed for insulin in the 90th minute. Moreover, lower values of INS/GLU 60 min and INS/GLU 120 min ratios as well as area under curve (AUC) for insulin were observed among KK homozygous subjects. A trend to lower insulin were observed among KK homozygous subjects. A trend to lower insulinogenic index and anthropometric parameters (Table 1) did not significantly differ between the genotype groups.

DISCUSSION

Our report is the first evaluation of the association between E23K polymorphism of the KCNJ11 gene and anthropometry, lipid and glucose metabolism parameters in a homogenous group of patients with ADPKD.

The results obtained in this study reveal an association between the KCNJ11 E23K variant and lower insulin secretion during OGTT among non-diabetic patients with ADPKD and non-ADPKD controls. In patients with ADPKD such an influence was observed for carriers of one or two K alleles, while among controls it was significant only among KK homozygotes. Results of clinical studies on the E23K polymorphism indicated that among non-diabetic subjects9 IGT diagnosed individuals10 or patients with diabetes type 211 the K23 variant is significantly associated with lower insulin secretion during OGTT. Our study confirmed this association for ADPKD patients, but it is possible that the model of genotype-phenotype association in ADPKD and non-ADPKD subjects is different (eg. dominant vs. recessive). Such results support the necessity for further study on the influence of this variant on the risk of pre- and post-transplant diabetes development among ADPKD patients. It is possible that contrasting research results on the frequency of post-transplant diabetes in this group of patients will be clarified in the future by genetic studies.

Conflicts of interest
The authors declare that they have no conflicts of interest related to the contents of this article.


**Effect of allopurinol on smoking**

**To the Editor:**

Allopurinol is a xanthine oxidase inhibitor. Xanthine oxidase is an enzyme that has hypoxanthine and oxygen as substrates and uric acid and free radicals as products. The beneficial effects of allopurinol are not only due to the decrease in uric acid, but also the reduction in oxidative stress and the increase in hypoxanthine and tissue oxygen (Figure 1). As such, there are data that support the conclusion that allopurinol improves endothelial dysfunction, decreases vascular oxidative stress, improves myocardial ischaemia and decreases left ventricular hypertrophy.1 Furthermore, several studies have shown that allopurinol reduces total mortality,2,3 and in studies on a small number of patients it has been suggested that it reduces the number of cardiovascular events.4,5

In a previous study on 112 patients with stage 3 chronic renal failure, all without a history of cardiovascular events, we observed that none of the 30 patients who took allopurinol were smokers (0% smokers who received allopurinol compared with 20.73% smokers amongst those who did not receive it; p=0.29). As the pa-