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Diabetic Nephropathy in Children with Type 1 Diabetes: Clinical and Molecular Triggers of Development

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Abstract: *diabetic nephropathy is one of the severe microvascular complications of Diabetes Mellitus, Type 1, which can begin in childhood and significantly affect the further prognosis of patients. Despite significant progress in diagnosis and treatment, the incidence of this complication remains high, which necessitates the early detection and control of risk factors. The presented review analyzes studies that used both pediatric and adult registries to assess the impact of various risk factors on the development of Diabetic Nephropathy. Among the established risk factors, the most significant is the duration of diabetes. Family history of Type 1 and Type 2 diabetes and Diabetic Nephropathy significantly increases the risk of its development: in brothers and sisters of such patients, it is three times higher than in relatives of diabetic patients without nephropathy. Diabetic nephropathy is more prevalent among African American, Asian, and Native American populations compared to individuals of European descent. Genetic predisposition, sex, and puberty determine individual vulnerability to renal complications and can affect the rate of their progression. Among the modifiable prognostic factors, it is important to list Hypertension, Increased Body Mass Index, Dyslipidemia, and Microalbuminuria. In the ranking of risk factors, Hyperglycemia is considered the strongest factor. The presence of a pre-existing microvascular complication may contribute to the development of another complication in patients with Type 1 Diabetes.*

Keywords: Diabetes Mellitus Type 1; Diabetic Nephropathies; Risk Factors; Hyperglycemia; Albuminuria.

Introduction

Diabetes mellitus (DM) is one of the important problems of clinical medicine due to its wide distribution, diverse clinical manifestations and severity of complications. There is a significant increase in the incidence of diabetes mellitus worldwide. According to World Health Orgainization (WHO), 422 million people in the world suffer from this disease, and 1.5 million deaths are directly related to it every year. Over the past decades, the number of cases and prevalence of DM has been increasing [1]. Among children under 14 years of age, about 110 thousand new cases of type 1 diabetes are registered annually. By the age of 20, this number increases to 130 thousand cases of the disease for the first time, which indicates a significant prevalence among the young population, who may face the development of chronic diabetic complications and a deterioration in the quality of life. According to the International Diabetes Federation (IDF) Atlas, in Ukraine in 2022, 32,093 new cases of type 1 diabetes mellitus were registered under the age of 20. According

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to scientists, more than 1.1 million children and adolescents in the world suffer from type 1 diabetes, with more than half of them (54%) under the age of 15. Diabetic nephropathy (DN) is one of the most severe microvascular complications of type 1 diabetes, which can lead to early disability of patients [2]. The incidence of diabetic nephropathy is 5-6% for people under 10 years of age and 25-40% for people under 20 years of age. Usually, DN develops 4-5 years after the diagnosis of diabetes.

If something can be predicted, it can be controlled. It is impossible to assess the risk of the onset and progression of a complication without understanding its predictors. The problem of kidney damage in patients with type 1 diabetes remains one of the key problems in modern medicine and an important topic of research. Prevention of the development of DN through early diagnosis and correction of risk factors remains the basis of patient management. The number of risk factors for the development and progression of DN is significant and constantly growing. Researching these factors, carefully monitoring them, and managing them is key to early prevention, personalized treatment, predicting the course of the disease, and reducing its complications [1,2].

Aim

Conducting an analysis of literature data on the role of major clinical prognostic factors and prognostic markers of diabetic nephropathy in children and adolescents.

Materials and methods

The literature analysis used peer-reviewed articles, reviews, and descriptions of experimental studies from 2021–2024. The study describes stable and modifiable prognostic factors for diabetic nephropathy, their identification, prevalence, and relationship in patients with type 1 diabetes. Relevant literature published during 2021-2025 was retrieved from the PubMed database.

Review and discussion

Permanent risk factors. Age

In general, age itself is not a modifiable risk factor, but it indirectly affects the development of DN through the duration of diabetes, hormonal changes, and the cumulative effect of other concomitant factors. The progression of DN may differ depending on the age at the time of the onset of type 1 diabetes. The complex interaction between age at diagnosis, disease duration, onset, development, and progression of DN can be called. Thus, in population cohort studies in Sweden and Finland, patients with prepubescent (0 to 9 years) onset of type 1 diabetes had a lower risk of developing end-stage renal disease compared to those who were older at the onset of the disease [3]. At the same time, there is a study that registered progressive glomerular lesions in patients aged 14 to 15 years with type 1 diabetes, regardless of the age of onset. The study included 11,681 patients with type 1 diabetes with a disease duration of more than 13 years. The median follow-up period was 20 years. During the follow-up period, 127 patients developed ESRD due to DN. In both sexes, the onset of type 1 diabetes before the age of 10 years was associated with a reduced risk of DN. The inconsistent, not fully understood age-dependent effect is consistent with previous studies. Importantly, the incidence of DN progression in men and women was 4.1% and 2.5%, respectively. The highest risk of ESRD due to DN was found in men diagnosed with type 1 diabetes at the age of 20–34 years. In women diagnosed at the age of 20–34 years, the risk was as low as in patients diagnosed before the age of 10 years [3,4].

Previous animal studies have shown a close relationship between the progression of DN and sex hormones: estrogens have been identified as a factor slowing the progression of DN, in contrast to testosterone, which increases the development of the complication. Puberty is considered an ambiguous but significant risk factor for DN. Studies show that albuminuria, impaired renal function, progresses more rapidly during puberty. Patients in whom type 1 diabetes began during puberty have a higher risk of nephropathy than those in whom it began earlier. Another group of patients with type 1 diabetes in Korea demonstrated a higher prevalence of DN, a more pronounced degree of decline in GFR in patients with diabetes diagnosed in childhood or adolescence compared with patients of older age groups [5]. At the same time, a study of

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type 1 diabetes in Hong Kong showed a faster progression of DN in patients over 40 years of age compared with those who developed the disease in childhood or adolescence. Such discrepancies can be interpreted as incorrect age distribution relative to puberty, different genetic background of ethnic variability, and also a possible combination of characteristics of type 1 and type 2 diabetes. The Taiwan Diabetes Registry Research Group showed that compared with prepubescent patients, the risk of DN increased 1.6 times in patients aged from puberty to 30 years ($p = 0.012$) after taking into account the duration of diabetes [4,5].

Gender

Age has been shown to influence the relationship between gender and DN, with men and women of different age groups having different course and outcomes of DN. Numerous studies have shown that with the same baseline glomelular filtration rate (GFR), hypertension, treatment of diabetes and its complications, initial albuminuria was lower in adult women. Adolescent girls are at increased risk of microalbuminuria. Adolescent girls have been reported to have higher Hb1Ac levels, which helps to explain why female patients excrete albumin faster than male patients. The prevalence of microalbuminuria in girls is higher than in boys, in whom the prevalence of microalbuminuria increases rapidly over 10–25 years of diabetes [6].

Diabetes duration

A retrospective observational longitudinal cohort study of 224 patients with type 1 diabetes mellitus for 10 years or more (mean duration 12.6 years) in Taiwan reported that 19.6% of patients developed DN with a mean age of onset of symptoms of 7.9 years. In the Oxford Regional Prospective Study, a large population-based cohort study in the United Kingdom that included 527 patients with a mean age of onset of 8.8 years, the cumulative prevalence of microalbuminuria was 18% after 10 years of diabetes [1] The relationship between microalbuminuria and duration of diabetes is clear. The incidence of microalbuminuria greater than 15% with diabetes duration of up to 10 years has been reported in another study. It has been reported that children and adolescents with diabetes duration of more than 5 years were more likely to have an elevated albumin-to-creatinine ratio (ACR), which predicts progression of DN [1,7].

There are studies that reveal structural changes and their correlation with functional indicators of kidney function. Biopsies performed in children and adults with type 1 diabetes confirm that the first detected sign is thickening of the basement membranes of the glomeruli and tubules of the kidneys 1.5-2.5 years after the onset of diabetes. And 5-7 years after the onset of diabetes, further expansion is observed first of the mesangial matrix, later the interstitium due to the accumulation of the cellular component, and later of fibrillar collagen as DN progresses [8]. The rate of progression of various lesions in different patients with type 1 diabetes depends on many components. The duration of prepubertal diabetes as a factor in the development of microalbuminuria remains a debatable issue. However, the overall period of the disease, rather than the separation of the duration before or after puberty, probably determines the combined risk of microalbuminuria and structural changes of the kidneys in DN. A study by Weerasooriya L. examined kidney biopsy specimens from 17 children with type 1 diabetes and found DN in 4 cases and DN-IgA nephropathy complications in 3 cases. The age of the identified patients with DN ranged from 10 to 15 years, and the duration of diabetes ranged from 36 to 179 months. This is further confirmation of the individual patterns of DN development in childhood [7,8].

Family history of diabetic complications. Genetics.

The development of DN is more common in relatives. Seaquist et al. first reported this phenomenon (familial clustering of DN), finding that patients with diabetes who had close relatives (e.g., parents or siblings) with DN had a significantly higher risk of developing this complication. Observation of family groups with DN and the study of potential genes associated with the development of nephropathy confirmed the existence of a genetic or familial predisposition to DN. The study confirmed that, compared with diabetics whose siblings did not have nephropathy, the probability that

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the diabetic siblings of a diabetic proband with nephropathy would also have nephropathy was 250-300% higher. Similar conclusions were obtained as a result of a large-scale clinical trial DCCT/EDIC [2,9]. When examining the glomerular structure of siblings with type 1 diabetes, a very pronounced correspondence was found in the severity and nature of the damage. Another study documented the evidence of a family history of hypertension as a factor in the increased susceptibility to the development of microalbuminuria in subgroups of insulin-dependent diabetic patients. Earle et al. found that parents of patients with DM complicated by DN had an excess of cardiovascular disease compared with parents of diabetic patients who did not develop DN [3,9].

A population-based case-control study based on data from the Abruzzo type 1 diabetes registry assessed the role of family history as a determinant of T1D. A detailed questionnaire was administered to parents for type 1 diabetes and type 2 diabetes. The risks of T1D associated with first- and second-degree relatives were calculated using regression analysis. The risks of type 1 diabetes for children whose parents or siblings had diabetes and its complications were 11 and 20 times higher, respectively, compared to children without a family history. A family history of type 2 diabetes was not associated with such risks [10].

A Swedish population-based study comparing the prevalence of paternal diabetes in children with and without type 1 diabetes is noteworthy. In the BDD (Better Diabetes Diagnosis) cohort of 3,603 children, 40.5% had a first- or second-generation family history. Children with type 1 diabetes were more likely to have a father or grandfather with type 1 or type 2 diabetes than mothers or grandmothers with either form of diabetes [4]. Among children aged 11-13 years in the BDD cohort (n=801), 8.4% had parents with type 1 diabetes and 3.5% with type 2 diabetes. In the control group (n=11,050), these figures were 2.1% and 1.9%, respectively. These results emphasize the importance of considering family history of diabetes to better understand the clinical variability of childhood type 1 diabetes. At the end, it was reported that 35% of the risk of developing DN is due to genetic heredity, the remaining 65% is the influence of external factors (duration and severity of diabetes, arterial hypertension, lifestyle, etc.) [4,11].

There are a number of studies investigating the association between DN and genetic variations associated with the presence (I insertion) or absence (D-deletion) (I/D) of a specific DNA sequence in the angiotensin-converting enzyme gene. There is mixed evidence regarding the effect of the DD genotype on the risk of nephropathy. Studies show that carriers of the DD genotype have a higher probability of developing and rapidly progressing DN, especially with poor blood pressure and glycemic control. In addition, the I/D polymorphism may affect the effectiveness of ACE inhibitor therapy. In general, the I/D polymorphism is a genetic marker that can help predict the risk of DN and select personalized therapy for a patient with diabetes [8,11]. Other genome-wide scanning studies are associated with the search for chromosomal regions that contain genes that determine the risk of developing diabetic nephropathy. Recent results from a Finnish study have confirmed the existence of a link in families of European descent in favor of the existence of a gene or genes on chromosome 3q that are demonstrably involved in the predisposition to diabetic nephropathy [4,8,11].

The study by the Faculty of Medicine, Cairo University, on the role of circulating microRNAs in the early development of DN is highlighted. In this study, a statistically significant higher level of expression of miRNA-93 in patients with DN is found, and miRNA-93 is a significant independent variable for the development of albuminuria. The importance of miRNA-377, miRNA-93, miRNA-216 miRNA-21, related to the pathogenesis of DN, as diagnostic biomarkers, as well as therapeutic targets in DN, is documented. The possible renoprotective role of miRNA-25 is noted [7,8,11].

Racial identity and ethnicity.

According to a study from Taif, Saudi Arabia (a country ranking fourth globally in type 1 diabetes population), researchers examined the prevalence and risk factors of diabetic nephropathy in patients with type 1 diabetes.

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Based on the results of the study, the prevalence of DN was 23.7% in the presented study group (collective prevalence in the country is 20.59%). This is considered a high prevalence, but it is lower than in other populations reported in other studies. For example, in Oman among the Middle East countries is 50.46%, in Yemen is 33%, the collective average prevalence in the Middle East countries is 28.96%, in China is 27%, in the Republic of Ireland is 25%, in Hail Saudi Arabia is 69%, and in Tanzania is 84% [1,12]. Among racial differences, African Americans, Native Americans, and Asians with type 1 diabetes are more susceptible to developing DN with progression. Caucasians are less prone to DN. It is also known that belonging to the Mongoloid race increases the risk of developing DN, which is further evidence of certain genetic or ethnic factors that influence the susceptibility to this complication. Regarding the regions with the highest rates of type 1 diabetes among children, Northern Europe, North America, and North Africa are listed. East and South Asia have the lowest rates, which may be due to differences in genetic factors, lifestyle, or diagnostic approaches. In Ukraine, according to the registry, in 2020, 10,598 children with diabetes mellitus who received insulin therapy were registered. In 2022, 32,093 patients under 20 years of age with type 1 diabetes were registered in Ukraine [2,13].

Modifiable prognostic factors

Poor glycemic control, hyperglycemia

In the ranking of risk factors for DN, both for any albuminuria and for macroalbuminuria, poor glycemic control is the strongest proven risk factor. In the Oxford Regional Prospective Study, the overall risk of microalbuminuria increased by 36% for every 1% increase in HbA1c. A Spanish study of 716 patients with type 1 diabetes demonstrated that a 1% increase in HbA1c increased the risk of DN by 13% at 5 years and by 68% at 10 years after the onset of diabetes. The largest Asia-Pacific multicenter study of 898 patients with type 1 diabetes confirmed this finding. There are two types of glycemic variability: short-term (variability within a single day and between days) and long-term (in changes in glycated hemoglobin levels) [14]. In childhood, there was a strong correlation between HbA1c variability and the rate of development of microalbuminuria, suggesting that high long-term variability is associated with an increased risk of diabetic

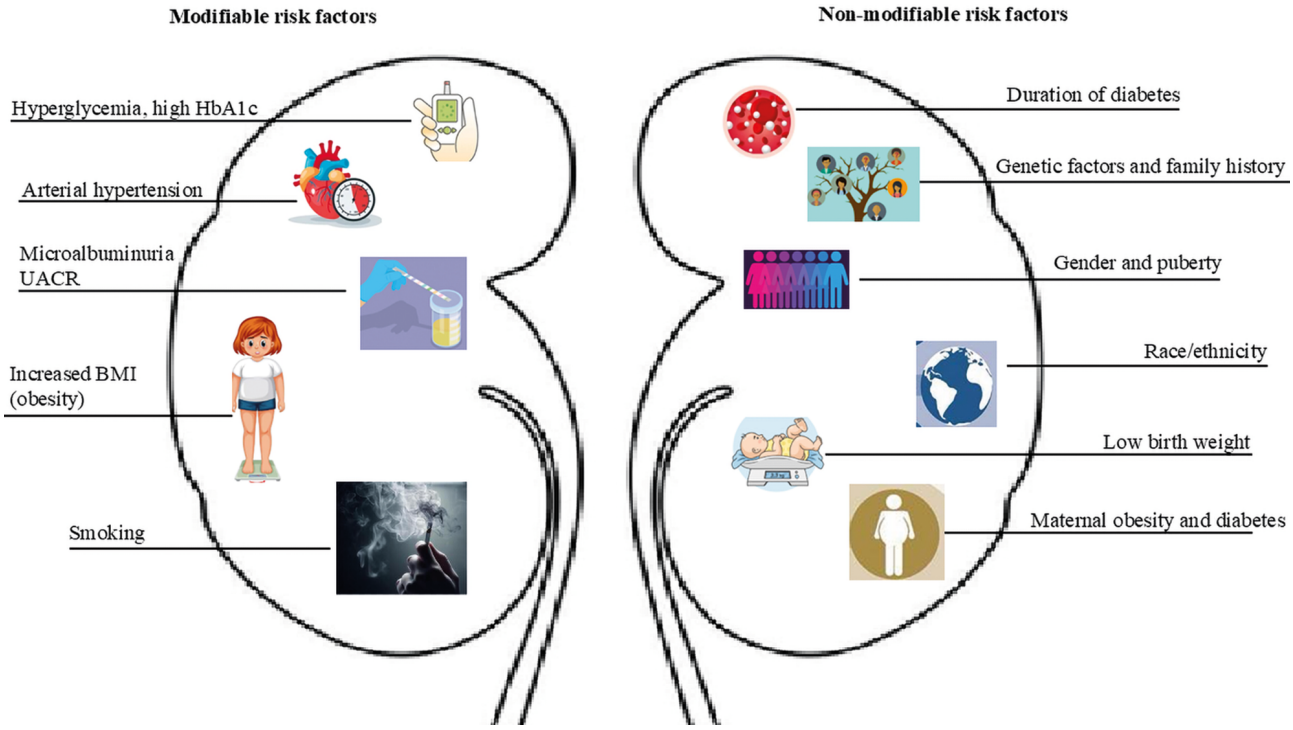

Figure 1. Factors that predispose to the development of diabetic nephropathy [1,7,8].

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complications, including cardiovascular and nephropathy. Regardless of the mean HbA1c level, variability in this parameter in the Diabetic Control and Complications Trial (DCCT) was strongly associated with the time to onset of microalbuminuria and nephropathy. Several large observational studies have demonstrated that the glycemic threshold with the lowest risk of complications is possible at HbA1c values of 5.0–5.5% [2,14]. Reducing glycated hemoglobin to 7% reduced complications, but according to an intervention study, it did not improve clinical outcomes by reducing HbA1c below 7%. The optimal glycemic target for patients with diabetes is not fixed, but depends on the balance between the risks and benefits of a particular therapy. Thus, chronic hyperglycemia, as measured by mean blood glucose or HbA1c, and fluctuations in these parameters, is associated with the development and progression of microvascular complications. Another cross-sectional analysis found that glycemic control was also an important mediator of lipid abnormalities in young people with diabetes [9,15].

Arterial hypertension

Blood pressure is of fundamental importance for the development and progression of diabetic kidney disease. The DCCT study demonstrated that diabetes treatment reduced the risk of developing microalbuminuria and macroalbuminuria by 39% and 54%, respectively, in the entire study cohort and that the risk of developing microalbuminuria was reduced by 55% in participants who were 13 to 18 years old at the time of the study. The same study demonstrated that blood pressure control and regulation with ACE inhibitors/ARBs slows the progression of microalbuminuria to macroalbuminuria [16]. Reports of studies that systolic and diastolic blood pressure are independently associated with microalbuminuria have been presented to the scientific community. It has previously been reported that moderate elevations in blood pressure in patients with type 1 diabetes are associated with preclinical DN up to 5 years before the onset of microalbuminuria [3,16]. It has been hypothesized that the association of biomarkers of endothelial dysfunction, early renal damage (in particular, NGAL) and increased systolic blood pressure may reflect the early asymptomatic stages of progression of DN in patients with type 1 diabetes and help to understand the main early kidney damage. In a study focused on a young population in two different age groups with type 1 diabetes of different duration of the disease, markers of structural damage to kidney cells were positively correlated with increased blood pressure, even if the latter remained within the prehypertensive or normal range. Elevated diastolic blood pressure threatens the progression of chronic kidney disease in children [4,17]. The conclusion of another study: in young people with moderately elevated albuminuria, changes in blood pressure are insignificant, perhaps manifesting only in the form of a decrease in nocturnal diastolic blood pressure. Variability of systolic and diastolic blood pressure independently indicates the development of albuminuria in DN. Numerous studies have demonstrated that arterial hypertension aggravates DN. Doubts have also been expressed as to whether microalbuminuria precedes arterial hypertension or is its consequence [7,17]. Analyzing in detail the results of a large number of studies, it can be concluded that increased blood pressure both contributes to and aggravates early diabetic nephropathy. Important conclusions are presented by a large European cohort study involving 2105 children with type 1 diabetes from 15 to 18 years: age, duration of diabetes, sex, body mass index, glycated hemoglobin values, and insulin dose are associated with variations in blood pressure. In particular, significantly higher nocturnal blood pressure parameters were recorded in adolescents with diabetic nephropathy: systolic BP +0.50, diastolic BP +0.58, mean BP +0.80, which mostly caused microalbuminuria. In addition, there is a relationship between BMI and arterial hypertension, with a 6% increased risk for each one-unit increase in BMI for hypertension [8,18].

High BMI

The association of this risk factor with the development of DN is also illustrated in the aforementioned Swedish study. Among patients in the BDD cohort, a total of 10.4% were overweight or obese. Among children with a family history of type 1 diabetes, this figure

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was 12.7%. A family history of type 2 diabetes may increase the risk of developing type 1 diabetes and overweight, indicating the possible influence of shared genetic or environmental factors [1,7,19]. Previous studies also confirm the association between overweight, obesity and an increased risk of type 1 diabetes. Similar findings are relevant for DN, since obesity and insulin resistance can contribute to the progression of renal complications in type 1 diabetes, and genetic predisposition to metabolic disorders may play a role in the development of DN in children with type 1 diabetes. A family history of type 2 diabetes may indicate common mechanisms of renal damage related to impaired glycemic control, hypertension, or dyslipidemia. Overweight, like type 1 diabetes, is an emerging problem in the population. Li et al. demonstrated that patients with increased BMI had an increase in HbA1c along with weight gain. Obesity can be considered as a factor predicting the progression of type 1 diabetes and the development of its vascular complications. In a retrospective cohort study of 9248 German and Austrian children with type 1 diabetes, BMI was inversely associated with the age of onset of diabetes. The higher BMI at the onset of type 1 diabetes, as well as the observation that prediabetic children have a higher body weight and higher insulin resistance compared with their peers, may indicate a convergence of the phenotypes of type 1 and type 2 diabetes. Obesity and insulin resistance are predictors of persistent microalbuminuria in adolescents in Australia. However, lower BMI is a risk factor for microalbuminuria in the US Type 1 Diabetes Research Network registry [19,20].

Dyslipidemia

Redondo et al. in their study showed that children with type 1 diabetes and overweight were 1.4 times more likely to have dyslipidemia than children with type 1 diabetes who were normal weight. However, blood pressure values between these groups did not differ significantly [10,14]. Dyslipidemia is often detected in patients with type 1 diabetes. According to numerous clinical and experimental studies, serum cholesterol may be a driving mediator in the occurrence and progression of DN. The DCCT/EDIC study showed that elevated total cholesterol and LDL cholesterol, as well as elevated glycerides, contribute to the development of microalbuminuria. Low levels of both cholesterol and triglycerides were independent predictors of regression of microalbuminuria in its short duration [7,8,21]. According to the results of a Swedish study, the risk of albuminuria increased at the following blood lipid levels: triglycerides above 1.0 mmol/l, total cholesterol above 5.0 mmol/l, LDL below 4.0 mmol/l and HDL below 1.0 mmol/l. Of the blood lipids, triglycerides had the strongest influence on the risk of albuminuria after HbA1c and diastolic blood pressure. Recently, the Oxford Regional Prospective Study found that 15.3% of patients had a total cholesterol level above 5.2 mmol/l, and 17.9% had a triglyceride level above 1.7 mmol/l. Similar trends were observed in the Nephropathy Family Study, where among 895 adolescents aged 10-16 years with type 1 diabetes, a significant proportion had persistent lipid abnormalities [4,14,21].

Microalbuminuria, urine albumin to creatinine ratio (UACR)

Microalbuminuria has been established as a marker of early and progressive diabetic nephropathy. DN is defined as a persistent UACR of more than 30 mg/g. Microalbuminuria-UACR 30-300 mg/g in at least 2 consecutive samples with a 3-month interval. In the presented study, 156 patients were still children or adolescents at the last assessment, with a mean follow-up of 7.1 years. 6.4% of them had microalbuminuria. Only 8% of patients with microalbuminuria had a decrease in GFR. The same prevalence of DN among children and adolescents from Australia, the USA and the UK is 4-9.7% [18,21]. This indicator among children and adolescents with type 1 diabetes in Poland is 22%. Regression of microalbuminuria in type 1 diabetes occurs from 36-64% according to statistical data. Most cases of decreased GFR are preceded by albuminuria, in a significant minority (24%) the decrease in GFR is observed in the complete absence of microalbuminuria, which is a difficult obstacle to determining albuminuria as the main predictor of DN. At the same time, a temporary decrease in albuminuria as a result of treatment indicates a

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slowdown in the progression of renal pathology [17,22]. The higher the level of albuminuria, the faster the progression of renal dysfunction. This confirms that albuminuria is not only a marker, but also a factor that directly affects the course of the disease. Hyperfiltration (GFR 120-150 ml/min/1.73m2) is reported at a frequency of 25-40% in young people with diabetes, is considered a strong prognostic factor for further loss of GFR and progression of DN. Data on the relationship between hyperfiltration and albuminuria are ambiguous, further experimental studies are needed [17,18,22].

Smoking

Among adolescents with diabetes, smoking has been reported in 7–48% of cases. The rate of progression of nephropathy is 11%, 53%, and 33% lower in nonsmokers compared with smokers and patients who have quit smoking, respectively. In a large observational study of 943 patients, the rate of microalbuminuria was higher among smokers than nonsmokers, with 7.9 versus 2.2 cases per 100 person-years [22]. Furthermore, smoking exacerbated the negative effects of hyperglycemia, increasing the risks associated with inadequate glycemic control. Smoking is more common among children with borderline albuminuria and is associated with an increased rate of urinary albumin excretion, independent of age or other factors. In addition, smokers with higher baseline GFR had a more pronounced decline compared to nonsmokers, indicating that smoking is an independent risk factor for worsening kidney function. All structural lesions in the kidneys of smokers showed more pronounced negative changes compared to the kidneys of nonsmokers [22,23].

Biomarkers that can be considered as predictors

There is a group of studies assessing the prognostic value of other early markers of kidney damage: NGAL, Cystatin C, b2-microglobulin, KIM-1, xanthine oxidase, TGF-b, uric acid, which in different age groups of patients with type 1 diabetes mellitus showed similar results. For example, a study from the University of Athens with 57 children, whose average age is 13.9 years and the average duration of diabetes is 5.4 years [23,24]. Serum NGAL showed a significant positive correlation with increased systolic blood pressure, even if the latter remained within the prehypertensive or normal range for children with diabetes, which, according to the conclusions of scientists, reflects the early asymptomatic stages of progression of diabetic nephropathy. Also indicative is a cohort

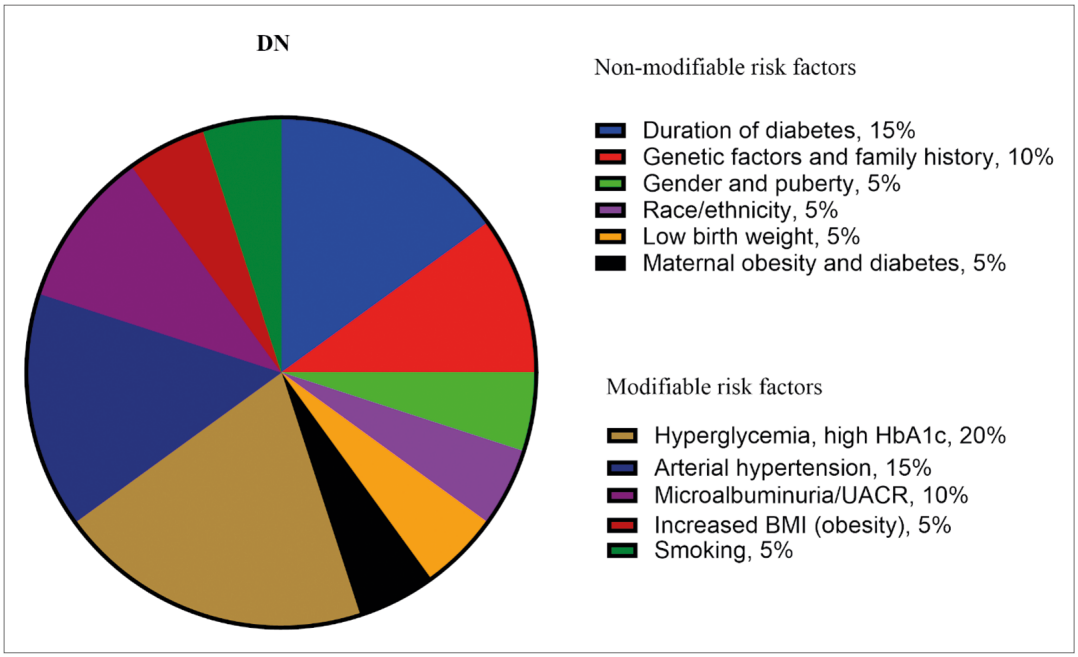

Figure 2. Approximate assessment of the degree of aggressiveness of the main risk factors for DN [5-8, 19-23].

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study that included 277 patients with the debut of type 1 diabetes with a mean follow-up period of 18.1 years, in which DN was diagnosed. Uric acid was measured at baseline and again 3 years after the onset of diabetes, but before the onset of microalbuminuria. During the follow-up period, 23 patients developed macroalbuminuria. The study showed that early elevation of uric acid levels in patients with type 1 diabetes is an independent predictor of future DN [25,26].

Conclusions

1. Early assessment of the risk of diabetic nephropathy in children and adolescents with type 1 diabetes is key to determining the level of threat and optimizing disease control. Since DN can begin in the early stages of diabetes, this period is crucial for preventing further progression of the disease, and possibly the reverse development of microalbuminuria.
2. Two groups of risk factors for diabetic nephropathy have been identified in children with type 1 diabetes: stable and modifiable prognostic factors. Both a single factor and their combination can contribute to the destruction of renal tissue, which significantly increases the risk of complications. Regular monitoring and correction of modifiable risk factors in childhood can significantly reduce the likelihood of developing severe complications in the future.
3. The algorithm for predicting and early detection of diabetic nephropathy is important for the practical activities of pediatricians, but it is not yet final. Further research into new possible risk factors is needed to improve early diagnosis methods and develop effective strategies for implementation in future screening programs.

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Conflict of interest

There is no conflict of interest in the presented work.

Consent to publication

All authors have read and approved the final version of the manuscript to publish this manuscript.

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A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation, D – Writing the article, E – Critical revision of the article, F– Final approval of article.

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Діабетична нефропатія у дітей із цукровим діабетом 1 типу: клінічні та молекулярні тригери розвитку

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Анотація: *діабетична нефропатія є одним із найсерйозніших мікросудинних ускладнень цукрового діабету 1 типу, яке може розпочатися в дитячому віці та суттєво впливати на подальший прогноз пацієнтів. Незважаючи на значний прогрес у діагностиці та лікуванні, частота цього ускладнення залишається високою, що зумовлює необхідність раннього виявлення та контролю факторів ризику. У представленому огляді проаналізовано дослідження, що використовували як педіатричні, так і дорослі реєстри для оцінки впливу різних факторів ризику на розвиток діабетичної нефропатії. Серед встановлених факторів ризику найзначущішим є тривалість діабету. Сімейний анамнез цукрового діабету 1 та 2 типу і діабетичної нефропатії значно підвищує ризик її розвитку: у братів і сестер таких пацієнтів він у три рази вищий, ніж у родичів діабетиків без нефропатії. Афроамериканці, азіати та корінні американці страждають на діабетичну нефропатію частіше, ніж представники європеоїдної раси та європейці. Генетична схильність, стать та пубертатний період визначають індивідуальну вразливість до ураження нирок та можуть впливати на швидкість їх прогресування. Серед модифікованих прогностичних факторів важливо виділити гіпертонію, підвищений індекс маси тіла, дисліпідемію та мікроальбумінурію. У рейтингу факторів ризику гіперглікемія вважається найсильнішим фактором. Наявність вже існуючого мікросудинного ускладнення може сприяти розвитку іншого ускладнення у пацієнтів із цукровим діабетом 1 типу.*

Ключові слова: цукровий діабет 1 типу; діабетична нефропатія; фактори ризику; гіперглікемія; мікроальбумінурія.