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DYNAMICS OF CLINICAL, BIOCHEMICAL AND THERAPEUTIC INDICATORS IN THE COURSE OF DIABETIC NEPHROPATHY IN A CHILD: CASE REPORT

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Summary

Introduction. Diabetic nephropathy (DN) is a chronic microvascular complication of type 1 diabetes mellitus (T1DM). DN incidence has been gradually increased worldwide. Prevalence of the DN varies between age groups, patients' cohorts, countries, and continents. Factors such as smoking, hypertension, hyperglycemia, hyperfiltration and late nephroprotective treatment are the major risk factors in the DN progression. Numerous diverse causes are associated with kidney function impairment in children with DN. The latter are uncompensated kidney failure and hypertensive nephrosclerosis, leading to the complications, i.e. hypertension, proteinuria, and progressive reduction in the kidney function. DN remains incompletely understood in pediatric practice, particularly requiring an understanding of the individual course, mechanisms of pathogenesis and progression of its early stages in children.
Case presentation. We describe a 17-year-old female patient diagnosed type 1 diabetes followed by Diabetic nephropathy development. We conducted an analysis of the dynamics of clinical, biochemical and therapeutic indicators in the course of type 1 diabetes mellitus with the development of diabetic nephropathy in a child during 4 years.
Conclusions. Diabetic nephropathy is a life-threatening progressive complication of type 1 diabetes. Course of the DN is accompanied by a range of biochemical and clinical deviations and disorders. In this study we show that diabetic nephropathy is accompanied by a wide range of biochemical and clinical disorders, i.e. hyperglycemia-related disorders, hypercholesterolemia, pro-inflammatory status, functional changes in ECG, compensatory hypertrophy of the kidneys, glomerular hyperfiltration and disorders of Vitamin D system. Monitoring of patients with diabetic nephropathy requires constant and timely assessment of both standard indicators of the course of type 1 diabetes (blood glucose, Hb1Ac, albuminuria, GFR, serum cholesterol, albumin/globulin ratio) and additional ones – vitamin D. Nephroprotective therapy should be started as soon as possible in diabetic nephropathy to guarantee that kidney damage markers return to normal. A crucial component of the treatment of diabetic nephropathy is correcting vitamin D insufficiency.

Keywords: **type 1 diabetes, diabetic nephropathy, children, progression, nephroprotection, treatment**

INTRODUCTION

Diabetic nephropathy (DN) is a chronic microvascular complication of type 1 diabetes mellitus (T1DM). According to statistics, the global prevalence of DN ranges from 1.5 to 3-4 % to 8-10 % of the total population. Diabetic nephropathy is a major cause of early mortality and disability among patients. In Ukraine, the incidence rates of T1DM are increasing annually [1]. DN remains incompletely understood in pediatric practice, particularly requiring an understanding of the mechanisms of pathogenesis and progression of its early stages in children. According to the World Health Organization (WHO), the number of children and adolescents with diabetes has increased from 493,000 in 2000 to approximately 1.1 million in 2019, almost doubling [2, 3].

This significant rise in the prevalence of diabetes among children emphasizes the need for a deeper understanding of the mechanisms of the disease progression and its complications, particularly diabetic nephropathy.

Children facing this condition are at an elevated risk of developing chronic kidney failure, which can seriously deteriorate their quality of life and lead to death [4].

Scientific research conducted within epidemiological studies indicates that children with diabetes have a higher risk of developing nephropathy compared to the general population. For instance, findings from a study by the International Diabetes Federation reveal that over 30 % of children with diabetes show signs of nephropathy before reaching the age of 25 [5].

Considering these conclusions, it is crucial to focus on the development and improvement of strategies for the management and monitoring of diabetic nephropathy in pediatric medicine. Modern diagnostic and therapeutic methods, including the use of advanced technologies and medications, can significantly enhance the prognosis and quality of life for children with diabetes facing diabetic nephropathy. It is also important to develop individualized approaches to treatment, taking into account the unique characteristics of each patient.

AIM

The aim of the study was to conduct an analysis of the dynamics of clinical, biochemical and therapeutic indicators in the course of type 1 diabetes mellitus with the development of diabetic nephropathy in a child.

CASE PRESENTATION

Patient A, 17 years old. From the medical history, it is known that she has been diagnosed with type 1 diabetes for 9 years. She is undergoing insulin therapy in a basal-bolus regimen. Throughout the observation period from 2020 to 2023, the glycemic profile showed deviations throughout the day within the range of 4.24-17.16 mmol/L (Figure 1).

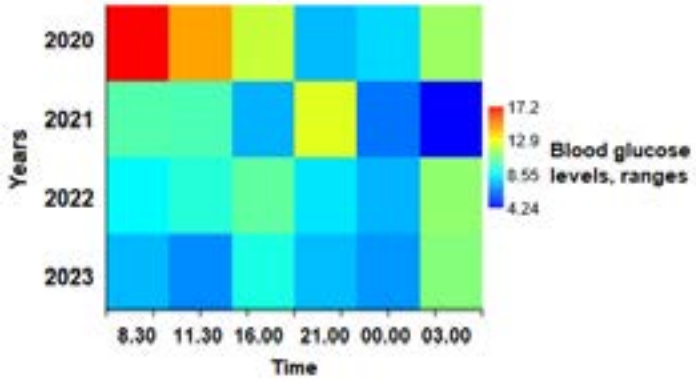

Figure 1. Matrix diagram of the glycemic control of the examined patient.

It is noted in the medical history that the child frequently violates the diet and the insulin therapy regimen. HbA1c levels ranged from 9.3 % to 11.2 % during the observation period which is higher than recommended Hb1Ac values necessary for a good T1D management (Figure 2).

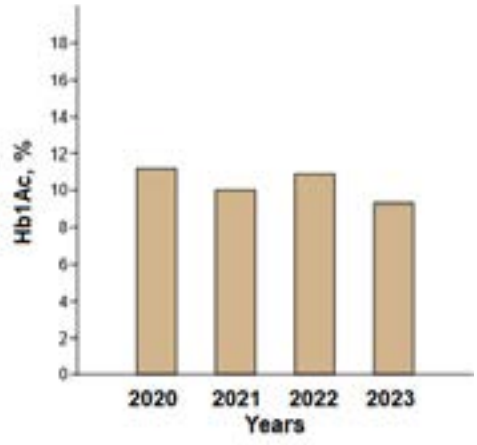

Figure 2. Dynamics of Hb1Ac levels in examined patient.

The dynamics of microalbuminuria (MAU) was 91.3 mg/day in 2020, 53.9 mg/day in 2021, 11.3 mg/day in 2022, and 67 mg/day in 2023, corresponding to stage III diabetic nephropathy according to Mogensen's classification, except for normal range value in 2022, when the patient received nephroprotective therapy (enalapril) (Figure 3).

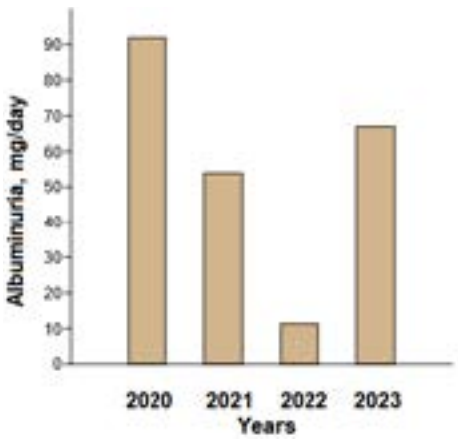

Figure 3. Dynamics of albuminuria levels in examined patient.

Glomerular filtration rate (GFR) was used to assess kidney function. Schwartz formula for children and adolescents 1 to 17 years old was used:

eGFR=0.413x(height/Scr) if height is expressed in centimeters OR 41.3 x (height/Scr) if height is expressed in meters (eGFR (estimated glomerular filtration rate) = mL/ min/1.73 m^2; Scr (standardized serum creatinine) = mg/dL.

Our results show that GFR value exceeded normal at each of four follow-ups during 2020-2023. The highest GFR value documented in 2023-141,74 mL/min/1.73 m^2 (Figure 4).

Biochemical deviations detected in patient include vitamin D deficiency (14.98 ng/mL in 2020, 13.96 ng/mL in 2021, 19.31 ng/mL in 2022 and 24.05 ng/mL in 2023), hypercholesterolemia up to 5,4 mmol/L (Figure 5A) and reduced albumin/globulin ratio down to 0,87 mml/L in 2022 (Figure 5B).

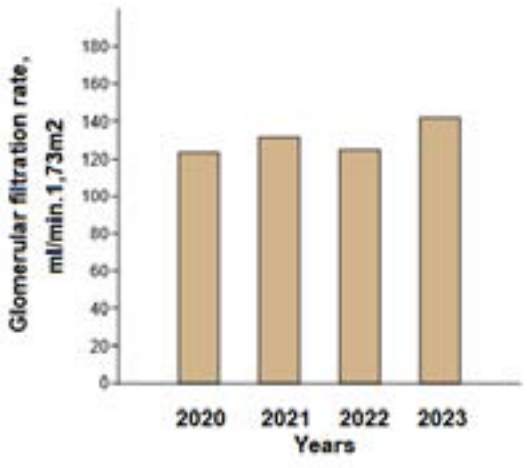

Figure 4. Dynamics of GFR levels in examined patient.

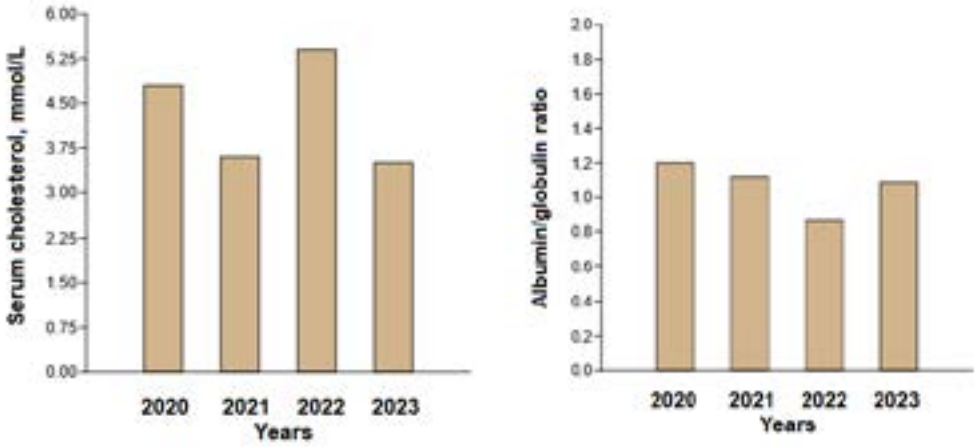

Figure 5. Dynamics of serum cholesterol (A) levels and albumin/globulin ratio (B) in examined patient.

Dynamics of the key biochemical and functional parameters (Hb1Ac, albuminuria, GFR, serum cholesterol, albumin/globulin ratio, serum vitamin D) during the period of observation (2020-2023) given in mosaic diagram (Figure 6).

Kidney ultrasound shown an increased kidney size by 5,6% (right kidney) and 4,9% (left kidney) in 2022 as compared to the corresponding age values. In 2020, 2021 and 2023 the kidney size documented within the normal value for the appropriate age group.

Among the registered comorbidities, there were functional 'minor changes on the ECG' throughout the entire observation period. Diabetic cataract has been treated surgically in 2015. The treatment regimen during the observation period included insulin therapy, alpha-lipoic acid, multivitamins (group B), hepatoprotectors (during 2020-2023), enalapril (in 2020, 2022, 2023), and vitamin D (in 2023).

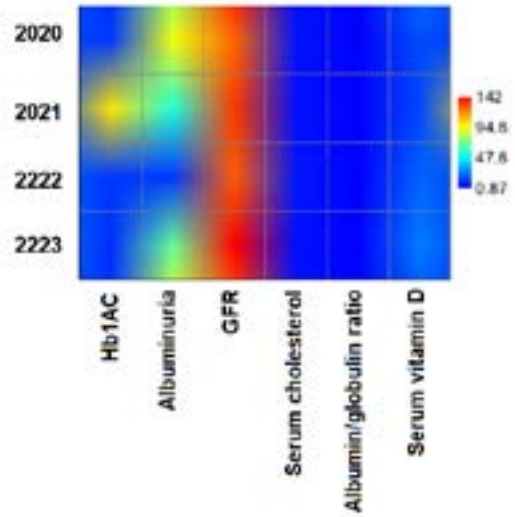

Figure 6. Dynamics of the key biochemical and functional parameters during the period of observation (2020-2023).

DISCUSSION

About 40 % of people with diabetes have diabetic nephropathy (DN), a dangerous microvascular consequence. DN, which affects 700 million people globally and is disproportionately associated with social poverty, is currently the major cause of end-stage renal disease (ESRD) [1-3]. The main cause of end-stage renal disease, diabetic nephropathy, is a consequence of diabetes mellitus. Damage to the kidneys' blood arteries and glomeruli is the condition's hallmark, and it causes proteinuria, hypertension, and renal failure. With the development of numerous pharmaceutical and non-pharmacological therapies to manage the disease, tremendous progress has been made in the prevention and treatment of DN. The expanding knowledge of the underlying biological causes of the illness, such as the function of inflammation and oxidative stress, and epigenetic modifications improved understanding and management of DN [3, 5].

Diabetic nephropathy is a serious progressive complication of type 1 diabetes, the course of which is accompanied by a range of biochemical and clinical deviations and disorders. Inadequate compensation of type 1 diabetes and the untimeliness of therapy play a crucial role in the progression of damage in diabetic nephropathy [6]. Progression of DN is a serious multifactorial complication of type 1 diabetes, the course of which is accompanied by a number of biochemical and clinical abnormalities and disorders. Insufficient compensation of type 1 diabetes and untimely therapy play an important role in the progression of damage in diabetic nephropathy [7].

Here we show on described case that diabetic nephropathy is accompanied by a wide range of biochemical and clinical lesions of organs and systems – hyperglycemia-related disorders, hypercholesterolemia, pro-inflammatory status, functional changes in ECG, compensatory hypertrophy of the kidneys, glomerular hyperfiltration and disorders of Vitamin D system.

Many physiological processes depend on vitamin D, and deficiencies in this vitamin have been linked to a wide range of acute and chronic conditions, such as problems with calcium metabolism, autoimmune diseases, certain cancers, types 1 and 2 diabetes mellitus, cardiovascular disease, and infectious diseases [8].

Significant progress has been achieved in the prevention and treatment of diabetic kidney disease (DN), a consequence of diabetes that damages the kidneys, in recent years [6]. New therapy approaches, enhanced diagnostic instruments, and a deeper comprehension of the disease's fundamental causes have all contributed to this advancement. The chance of developing diabetic neuropathy has been reduced by preventive interventions such strict blood pressure, cholesterol, and glucose control. Modifying one's lifestyle to include regular exercise and a healthy diet can also help stop the disease from starting and spreading [6, 7, 9].

Our previous findings have shown that vitamin D administration, when combined with traditional treatment, has demonstrated to have a significant impact on alterations in BcL-xL levels, a crucial molecule within the Bcl family in apoptosis controlling, in children diagnosed with early DN. When toddlers received early DN treatment with vitamin D in addition to a typical regimen that included antioxidants like vitamin E and angiotensin-converting enzyme inhibitors (ACEi), the antiapoptotic benefits were more pronounced. It's interesting to note that more kids in the DN group treated with the concentration scheme experience macroalbuminuria episodes during the course of three years [9, 10].

CONCLUSIONS

Unsatisfactory compensation of type I diabetes (Hb1Ac levels) in the examined patient is one of the decisive moments in the formation of chronic complications of type I diabetes, including the formation of diabetic nephropathy. Timely appointment of nephroprotective therapy in diabetic nephropathy ensures the normalization of indicators of kidney damage. Interruptions in this direction of therapy lead to deterioration of indicators. Correction of vitamin D deficiency is an important point in the therapy of diabetic nephropathy, which will provide both nephroprotection and prevention of the occurrence and progression of disorders. Monitoring of patients with diabetic nephropathy requires constant and timely assessment of both standard indicators of the course of type 1 diabetes (blood glucose, Hb1Ac, albuminuria, GFR, serum cholesterol, albumin/globulin ratio) and additional ones – vitamin D.

Study limitations and future perspectives. Study limitations are dealing with absence of other than Vitamin D and albuminuria novel markers of the kidney damages analysis. Perspectives of the study are connected to the further complex management of such patients.

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COMPLIANCE WITH ETHICAL REQUIREMENTS

Written parental consent for publication obtained and will be provided if requested. Informed consent was obtained by the patient, both in the form of verbal and written consent. This includes both patient information and images to be published for the educational purposes of this case report.

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Резюме

ДИНАМІКА КЛІНІКО-БІОХІМІЧНИХ ТА ТЕРАПЕВТИЧНИХ ПОКАЗНИКІВ У ПЕРЕБІГУ ДІАБЕТИЧНОЇ НЕФРОПАТІЇ У ДИТИНИ: КЛІНІЧНИЙ ВИПАДОК

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Вступ. Діабетична нефропатія (ДН) є хронічним мікросудинним ускладненням цукрового діабету 1 типу (ЦД I типу). Захворюваність на ДН поступово зростає у всьому світі. Поширеність ДН варіюється в залежності від вікової групи, когорти пацієнтів, країни і континенту. Такі фактори, як паління, гіпертонія, гіперглікемія, гіперфільтрація та пізнє нефропротекторне лікування, є основними факторами ризику прогресування ДН. Численні різноманітні причини пов'язані з порушенням функції нирок у дітей з ДН. До останніх відносяться некомпенсована ниркова недостатність і гіпертонічний нефросклероз, що призводить до ускладнень – артеріальної гіпертензії, протеїнурії та прогресуючого зниження функції нирок. ДН залишається не до кінця вивченим у педіатричній практиці, особливо потребує розуміння індивідуального перебігу, механізмів патогенезу та прогресування його ранніх стадій у дітей.

Презентація кейсу. Описано клінічний випадок дитини, 17 років, у якої діагностовано цукровий діабет I типу з подальшим розвитком діабетичної нефропатії. Проведено аналіз динаміки клініко-біохімічних та терапевтичних показників при перебігу цукрового діабету 1 типу з розвитком діабетичної нефропатії у дитини протягом 4 років.

Висновки. Діабетична нефропатія є небезпечним для життя прогресуючим ускладненням цукрового діабету I типу. Перебіг ДН супроводжується низкою біохімічних і клінічних відхилень і порушень. У цьому дослідженні ми показуємо, що діабетична нефропатія супроводжується широким спектром біохімічних і клінічних розладів, тобто розладів, пов'язаних з гіперглікемією, гіперхолестеринемією, прозапальним статусом, функціональними змінами на ЕКГ, компенсаторною гіпертрофією нирок, клубочковою гіперфільтрацією та розладами в системі вітаміну Д. Моніторинг хворих на діабетичну нефропатію потребує постійної та своєчасної оцінки як стандартних показників перебігу ЦД 1 типу (глюкоза крові, Hb1Ac, альбумінурія, ШКФ, холестерин сироватки крові, співвідношення альбумін/глобулін), так і додаткових – вітаміну D. Нефропротекторна терапія повинна починатись якнайшвидше при діабетичній нефропатії, щоб гарантувати нормалізацію маркерів ураження нирок. Важливим компонентом лікування діабетичної нефропатії є корекція недостатності вітаміну D.

Ключові слова: **цукровий діабет 1 типу, діабетична нефропатія, діти, прогресування, нефропротекція, лікування**