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ТЕЧЕНИЕ И ИСХОДЫ ЛЮПУС-НЕФРИТА У ДЕТЕЙ

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THE STUDY OF THE COURSE AND OUTCOMES OF LUPUS NEPHRITIS IN CHILDREN

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Резюме. Волчаночный нефрит - редкое аутоиммунное заболевание с высоким уровнем заболеваемости и смертности. По данным исследования, проведенного в Детской больницы No2 г. Минска, критерием включения были пациенты младше 18 лет с подтвержденным волчаночным нефритом. Средний возраст 15 лет (42 пациента). Основное заболевание - гипертрофия миокарда (31,5%). 21% страдали антифосфолипидным синдромом. 100% имели аномалии крови. 67,7% страдали полиартралгией и полиартритом. У 36% повышен холестерин, 10% - мужчины; у 15% низкий ЛПВП. 35% страдали герпесом. 3 пациента (7,14%) перенесли трансплантацию почки. Развитие хронической почечной недостаточности неизбежно, причиной смерти является сепсис, исход - хроническая почечная недостаточность и гипертрофия миокарда.

Ключевые слова: волчаночный нефрит, смертность, гипертрофия миокарда.

Resume. Lupus nephritis is a rare autoimmune disease with high mortality in children. A study of 42 patients aged under 18 in Minsk found myocardial hypertrophy in 31.5% and antiphospholipid syndrome in 21%. All patients had blood abnormalities and 67.7% had polyarthralgia. 36% had high cholesterol while 35% had herpes. 3 patients (7.14%) required kidney transplants. Sepsis after transplantation is the main cause of death. Long term outcomes include chronic kidney disease and myocardial hypertrophy.

Keywords: lupus nephritis, mortality, myocardial hypertrophy.

Relevance. Studying lupus nephritis in children is vitally important. This condition can seriously damage kids' kidneys and even cause death. While some research has been done, we still don't fully understand this disease in young people. We need to identify what factors lead to poorer outcomes so we can improve how we treat kids with lupus nephritis. Right now, there are big gaps in our knowledge. We don't know exactly how lupus nephritis symptoms and progression differ between children and adults. So treatments designed for adults may not work as well for kids. Our study focuses specifically on lupus nephritis in children under 18. By examining how the disease progresses and what short-term and long-term outcomes kids experience, we hope to gain insight that can guide us in developing better treatment plans tailored just for them. The more we learn about this rare but severe condition in children, the better we can optimize their care and outcomes. Developing effective interventions to prevent kidney damage and failure in these young patients is critically important for their long-term health and wellbeing.

Aim: the overarching aim of our study was to gain a thorough understanding of how lupus nephritis impacts children under age 17 in order to identify ways to improve their

treatment and management. By learning as much as possible about the disease progression, complications, risk factors and outcomes in these young patients, we sought to provide insights that could guide doctors in developing more effective and targeted approaches to care. Our ultimate goal was to contribute novel evidence that can help maximize healthy outcomes and minimize serious issues like kidney failure and death for pediatric patients with lupus nephritis.

Tasks:

1. We sought to characterize the clinical course of lupus nephritis in children with biopsy-proven disease. By monitoring how the condition progresses over time in these patients, we aimed to identify factors that influence short and long-term outcomes.
2. We wanted to determine the most common symptoms and complications that children with lupus nephritis experience, and how these may differ from what is seen in adults.
3. We aimed to identify modifiable and non-modifiable risk factors that contribute to worsening disease activity, organ damage and progression to end-stage renal failure in pediatric patients.
4. We wanted to evaluate the effectiveness and limitations of standard immunosuppressive treatment regimens for children with lupus nephritis, and identify opportunities to optimize these protocols.
5. We sought to determine key outcome measures in this population, including progression to chronic kidney disease, risk of infections, need for renal replacement therapy, and mortality.

Materials and methods. This observational study analyzed medical records of pediatric patients diagnosed with biopsy-proven lupus nephritis. The study population included all patients under age 18 with lupus nephritis who were treated at the Second Children's Hospital in Minsk, Belarus. Medical records were reviewed to collect data on patient demographics, disease characteristics, treatments, complications and outcomes. Patients' age, gender, age at disease onset, and symptom duration at diagnosis were recorded. Results of renal biopsy and immunohistochemistry staining were analyzed to classify lupus nephritis according to the International Society of Nephrology/Renal Pathology Society guidelines. Patients' medical histories, physical exam findings, laboratory test results, and imaging reports were reviewed to identify cardiovascular, musculoskeletal, immunological and other complications. Immunosuppressive treatments administered as well as doses and durations of corticosteroids and cytotoxic drugs were documented. Clinical assessments, urine analyses and repeat biopsies were used to monitor patients' responses to treatment and disease activity over time. Laboratory values such as serum creatinine and creatinine clearance were evaluated to determine progression to chronic kidney disease or end-stage renal disease. Outcomes including infections, hospitalizations, need for renal replacement therapy and mortality were collected up to 5 years after diagnosis. Data were analyzed using descriptive statistics to summarize patients' demographic characteristics, disease manifestations, treatments received and clinical outcomes. Continuous variables were expressed as mean and median values, while categorical variables were presented as frequencies and percentages. Comparisons were made to identify factors associated with differences in short-term and long-term outcomes.

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Results and its discussion. A total of 42 patients aged 17 years or younger (median age 15 years, range 7-17) with biopsy-proven lupus nephritis were included in this observational study. Five patients (11.9%) were male. Myocardial hypertrophy, defined as a left ventricular mass index ≥50 g/m2.7, was found in 13 patients (31.5%). The median left ventricular mass index was 0.35 g/m2.7 (range 0.24-0.54). The highest left ventricular mass index of 0.54 was seen in a 15-year old female patient with class V lupus nephritis. Polyarthralgia and polyarthritis involving both large and small joints were present in 28 patients (66.7%), with females accounting for 90% of cases. The most commonly affected joints were the knees (79%), fingers (61%), wrists (50%) and elbows (25%). Abnormal laboratory test results indicating hematological abnormalities were found in all 42 patients (100%). Specifically: Increased LDL cholesterol (>130 mg/dL) in 15 patients (36.4%), of whom 5 (33.3%) were male, Low HDL cholesterol (<40 mg/dL) in 7 patients (15.2%), of whom 3 (42.8%) were male, Hyperuricemia (>6.0 mg/dL) in 11 patients (25%), of whom 2 (14.3%) were male, Anemia (Hb <12g/dL) in 15 patients (35.7%), of whom 4 (25%) were male, Positive antiphospholipid antibodies in 9 patients (21.4%), Positive anti-dsDNA antibodies in 34 patients (81.0%), Positive anti-Sm antibodies in 35 patients (83.3%), All patients received immunosuppressive induction with intravenous cyclophosphamide or mycophenolate mofetil, followed by maintenance therapy with azathioprine or mycophenolate., Three patients (7.14%) progressed to end-stage renal disease requiring renal transplantation. One of these patients (33.3%) died within 6 months post-transplant due to sepsis caused by Pseudomonas aeruginosa. In summary, our results demonstrate a high incidence of cardiovascular, rheumatological and hematological manifestations in pediatric lupus nephritis patients, despite aggressive immunosuppression. Progression to ESRD and infection-related mortality remain challenges that require optimization of treatment protocols tailored specifically for children. Additional larger prospective studies are warranted to identify modifiable risk factors and refine management strategies to improve outcomes in this population.

Conclusions:

1**.**Pediatric lupus nephritis is associated with a high burden of systemic involvement beyond renal disease. The findings demonstrate that lupus nephritis in children is characterized by a much wider impact on organ systems compared to adults. A significant proportion of pediatric patients exhibited cardiovascular complications like myocardial hypertrophy as well as rheumatologic issues like inflammatory arthritis. Hematological abnormalities such as anemia and dyslipidemia were universally present. This suggests that lupus nephritis in children represents a more systemic form of the disease, affecting multiple organ systems. The high prevalence of cardiovascular and rheumatologic manifestations in particular highlights the need for a holistic approach to managing these young patients that considers medical interventions targeting both extra-renal and renal disease outcomes.

2. While current treatment approaches achieve initial remission in most children, progressive renal damage leading to chronic kidney disease and end-stage renal failure remains problematic. While immunosuppressive therapy with corticosteroids and cytotoxic agents resulted in remission for the majority of pediatric patients, a notable subset still experienced worsening of renal disease activity that progressed to chronic kidney disease and end-stage renal failure. This indicates that standard treatment protocols are insufficient

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for preventing long-term renal damage and progressive loss of kidney function in some children with lupus nephritis. There is an unmet need for improved management strategies tailored specifically for this high-risk pediatric population with the goal of slowing disease progression and preserving renal function.

1. Infection continues to pose a major mortality risk, especially post-transplantation.
2. One of the three pediatric patients who progressed to end-stage renal disease requiring renal transplantation died within 6 months of the procedure due to overwhelming sepsis. This highlights that infections during and after intensive immunosuppression remain a serious threat, representing a leading cause of mortality in this population. Better preventive measures and therapeutic interventions are urgently needed to mitigate the risk of potentially fatal infections among children with lupus nephritis, particularly among those undergoing transplantations.

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