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Original scientific paper

MANIFESTATION OF LUPUS ERYTHEMATOSUS IN PATIENTS WITH CHRONIC KIDNEY DISASESS

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ABSTRACT

Systemic Lupus Erythematosus (SLE) is a chronic multifactorial autoimmune disease characterized by the involvement of many organs mediated by changes and disorders of the immune complex. One of the organs affected by SLE is the kidneys and the appearance of Lupus Nephritis, which is characterized by progressive glomerulonephritis as a result of the deposition of immune complexes in the glomeruli, causing a chronic inflammatory reaction and damage to the renal parenchyma and, over time, gradual progressive damage to renal function.In addition to the numerous complications of Chronic Kidney Disease (CKD), lupus erythematosus is one of the conditions that can lead to end-stage CKD requiring treatment with chronic hemodialysis or kidney transplantation. Recent studies have confirmed that 10-30% of patients with SLE develop LN after several years (3-6 years) and after end-stage chronic kidney disease (CKD), requiring treatment with chronic intermittent hemodialysis (HD) [1,2,3].The most common form of Lupus Nephritis (LN) is chronic glomeru-lonephritis, chronic pyelonephritis and renal fibrosis. The clinical picture of LN is manifested by: proteinuria, hematuria, albuminuria, edema of the face and lower extremities, malar rash, redness of the face in the form of a “butterfly”. hypertension, periorbital edema and edema of the legs, fever, The diagnosis of LN is confirmed by the appearance of proteinuria >100 mg/mmol, hematuria, arterial hypertension, renal biopsy, damage to the glomerular basement membrane, reduction of the glomerular filtration rate (GFR)< 59mL/min/1.73 m2, increase in urea, creatinine, uric acid in serum, hypocalcemia, hyperkalemia and other.The purpose of the paper: was the assessment of renal damage asa result of LN using the results obtained from the examined parameters in patients with chronic kidney disease (CKD).**Matherials and Methods:** In this prospective cohort research (,, cross-section “) study are included 100 patients with CKD (55 were men with an average age of 58.00±7.60 years old with chronic renal disease and 45 were female with an average age of 56.40 ±10.00 years old), with basic kidney disease.All patients (men+women) were in the third degree a and b according to the degree of glomerular filtration within the limits of values: 30-50 mL/min/1.73 m^2, table number 3) with the onset of the disease 6-8 years ago. All patients were monitored in the period,Maj- 2022-Maj-2024. From the total number of patients (100) with chronic renal insufficiency, 18 of them manifested symptoms of LN (women-13 while men-5) and all fulfilled the clinical

and laboratory criteria for LN according to the International Society of Nephrology(ISN)/Renal Pathology Society and the Renal Pathology Society (RPS) 2003/2004.**Statistical analysis of the examined material:** The obtained results from the examined patients with CKD and the control group were statistically processed with arithmetic mean value, standard deviation X ± SD, with studentov, "t" test, Mann-Whitney and Wilcoxon test. The results were processed with the appropriate state of the art statistical program SPSS V26. Results: the results obtained at the beginning of the study (for all patients with LN and CKD: women and men) as well as after 24 months of treatment are presented in tables and graphs number:

4 and 8.**Conclusion:** from the obtained results we can conclude that LES apparently affects the appearance of renal damage, therefore early detection and treatment of the initial stages of LN seem to affect the reduction of its activity. Therefore, we prefer that timely treatment (with nonsteroidal anti-inflammatory,corticosteroid ther apy,antimalarial,immunosuppressive therapy, antihistamine, ACE inhibitors or Angio-tensin Receptor Blockers (ARBs and antilipemic in patients with pre-uremia should be the main goals and objectives of nephrologists and rheumatologists in order to prevent the progression of the disease towards failure chronic end-stage renal disease.

Key words:skin manifestation,LES,renal diseases.

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INTRODUCTION

Systemic Lupus Erythematosus (SLE) is an autoimmune inflammatory chronic systemic disease in which the body's immune system attacks its own cells and organs. SLE is a disease of unknown etiology. SLE mainly affects women during their reproductive years and is characterized by joint, kidney, and serous membrane involvement and the presence of antinuclear antibodies (ANA). African,Americans, Hispanics/Latinos, and Asians are more likely to have SLE than Caucasians. Lupus nephritis (LN) is more common in men than in women [4]. Between 10% and 30% of people with LN develop (if untreated) end-stage renal disease [5]. In the United States, 1 in 250 African American women develop LN.Kidney damage occurs within the first 2 to 5 years. Symptoms are classified according to histopathological findings of the International Society of (ISN)/Renal Pathology Society (RPS) and renal disease [6-9]. LN manifests with VI classes (of "butterfly"),lack of appetite, etc. [10-15]. Over time, LN can worsen and as a chronic consequence of endocapillary glomerular proliferation, lead to end-stage chronic renal failure when hemodialysis treatment is imposed for chronic renal failure. LN is characterized by the deposition of immune complexes due to the malfunction of normal homeostatic mechanisms, renal fibrosis and disease progression to the terminal stage of CKD. [16,17].The consequ-ences of LN are manifested by: modifications of chromatin structures that induce plasmacytoid dendritic cells with thyroid acid production, DNA demethylation that is responsible for regulating the production of C3 and histone interferon--, which is a potent promoter of the immune system, and acetylation that regulates the production of

profibrotic autoimmunity derived from platelets.This leads to the produ-ction of autoantibodies. Other growth factor genes (PDGF), extracellular matrix fibrosis, endothelial autoantibodies, including anti-ds DNA antibodies, develop through cellular activation, infiltration and activation of immune cells in the process of disease progression through mitochondrial dysfunction and tubular damage. Assessment of the occurrence of renal scarring is very important because early detec-tion and treatment of renal involvement can greatly affects the outcome and course of renal disease [18,19].

AIM THE PURPOSE OF THE PAPER: was the assessment of renal damage as a result of LN using the results obtained from the examined parameters in patients with chronic kidney disease (CKD).

MATHERIALS AND METHODS

In this prospective cohort research (,, cross-section ") study are included 100 patients with CKD (55 were men with an average age of 58.00±7.60 yearsyears old with CKD(chronic kidney disease), while 45 were female with an average age of 56.40±10.00 years old), (tabl.no.3).All patients were monitored in the period,Maj-2022-Maj-2024. From the total number of patients (100) with CKD,18 of them manifested symp-toms of LN (women-13 while men- 5) and all fulfilled the clinical and laboratory criteria for LN according to the International Society of Nephro-logy (ISN)/Renal Pathology Soci-ety (RPS), 2003/2004.

Table 1: Presentation of patients with CKD according to gender and average age

Total number of patients with CKD-100,Females-45	withCKD=100 D.M AHT GMN
(45%) Males-55 (55%)	chr APCKD Undefinied
Mean age±SD 56.40±10.00	Males-55 23 11 12 4 5
years 58.00±7.60 years	Female-45 13 10 12 5 5

Table nr.2:Presentation of patients with CKD in the third stage, GFR of 30-59 mL/min/1.73 m2 according to MDRD, according to gender, underlying disease.

Table nr.3: Presentation of patients with LN according to classes according to International Society of Nefrology (ISN) /Renal Patology Society and the Renal Pathology Society (RPS) 2003/2004,16 (females-11 and males-5

Total nr. of pat.	

Total number (M+F) with CRD and LN= 18 Males -5 Females -13

Class I-Minimal mesangial LN 3 9

Class II-mesangial proliferative LN 1 2

Class III-Focal LN (<50% of glomerulus) 1 2

STATISTICAL ANALYSIS

The obtained results from the examined patients with CKD and the control group were statistically processed with arithmetic mean value, standard deviation

X ± SD, with Student's "t" test, Mann-Whitney and Wilcoxon test. The results were processed with the appropriate state of the art statistical program SPSS V26.

RESULTS

Obtained at the beginning of the study (for all patients with LN and ESRD: women and men) as well as after 24 months of treatment are presented in tables number 4,5,6,7.

Table 4: Results obtained from the examined parameters of patients with LN at the beginning of the study

Examined parameters Females with LN=11 Males with LN=5		
Sediment.(SE) mm/30 min(r.v.=4-10)	110±14.50	112±15.00
Hemoglobin (Hb) mmol/l(RV=7.76-10.6)	5.30±0.40	6.20±0.90
Erythrocytes(RBC) 1012/L(RV=4.2-5.5)	3.10±0.60	3.50±0.80
Hematocrit (Htc, RV =0,37-0,40)	0.25±0.30	0.36±0.20
Platelets (Plt) 109/L(RV=140-340)	90,40±6.50	95.60±3.80
Leucocytes(WBC) 109/L(RV=4-9)	15,00±2.00	17.00±1.00
Neutrophils %(RV=0.58-0.66)	0.40±0.30	0.45±0.36
C-Reactive Protein(CRP mg/l, RV=0-50)	42.00±8.60	60±0.40
Glycemia (Gl mmol/l, RV=3.5-5.5)	5.30±1.00	5.20±0,80
serum iron(sFe µmol/l(RV=7.3-28)	6.00±1.00	6.50±1.50
C3 (RV=80-128 mg/dl)	C3<43	C3<44
C4 (RV=12-42 mg/dl)	C4<13	C4<15
ANAs(Antinuclear antibodies RV=≤1:60-)	>182 (positive)	>178 (positive)

Table5: The results obtained from the examined parameters of nitrogen degradation products in patients with LN at the beginning of the study

Examined parameters Females with	

LN=13 Males with LN=5

Urea(serum,mmol/l), RV=2.0-8.3 16,40±10,40 16.80±9.00

Creatinine(serum, µmol/l),

RV=F=53-88, M=71-115) 170.50±18.00 180.60±15.60

Uric acid-µmol/l(RV=F=155-

357,M=208-428) 380.00±10.60 430±8,50µmol/l

Proteinuria g/24 ore (RV=<150

mg/24/ 15 g/mmol) >3,6 g/24 orë >3,9 g/24 orë

BUN-Blood Urea Nitrogen (RV=2.4-

6.4 mmol/L) >9,4 >11,5

GFR(Glomerular Filtration Rate

(National Kidney Foundation,

normal results range from 90-120

mL/min/1.73 m2)

48 mL/

min/1.73 m2

66 mL/min/1.73

m2

From the table of results obtained at the beginning of the study, a disorder of all the examined parameters of the patients (F+M) with LES and LN during diagnosis and manifestations of the disease is observed.

Table 6: Results obtained after 12 months of LN treatment

Examined parameters Females with

LN=11 Males with LN=5

SE mm/30 min(RV=4-10) 40.00±5.00 48.00±2.00

Hb mmol/l(RV=7.76-10.6) 6.70±1.50 7.20±1.30

RBC 1012/L(RF=4.2-5.5) 4.10±0.80 4.80±1.00

Htc (RV=0,37-0,40) 0.35±040 0.42±0.60

Plt 109/L(RV=140-340) 126.00±14.00 175±14.00

Le 109/L (RV=4-9) 12.00±1.30 13.60±1.00

Neutrophil %(RV=0.58-0.66) 0.54±0.80 0.60±0.30

CRP mg/l (RV=0-50 10.00±1.50 14.00±6.00

Gl mmol/l(RV=3.5-5.5) 5.80±1.00 5.20±0,80

sFe µmol/l(RV=7.3-28) 9.60±4.90 12.00±14.50

C3 (RV=80-128 mg/dl 92.00 94.00

C4 (RV=12-42 mg/dl) 28 30

ANA(Antinuclear antibodies-

ANAs (RV=≤1:60) >170 >176

Table 7: The results obtained from the examined parameters of nitrogen degradation products in patients with LN after 24 months of treatment

Examined parameters Females with
LN=11
Males with
LN=5
Urea(serum,mmol/l), RV=2.0-8.3 24.40±6.50 27.30±3.00
Creatinine(serum,µmol/l),RV=F=53-
88,M=71-115) 280.00±23.00 290.00±204.00
Uric acid-µmol/l(RV=F=155-
357,M=208-428) 346±9.50 430±6.00µmol/l
Proteinuria g/24 ore (RV=<150 mg/24/
15 g/mmol) >3,0 g/24 h >3,2 g/24 h,
BUN-Blood Urea Nitrogen (RV=2.4-6.4
mmol/L) 7.8 8.2
GFR(Glomerular Filtration Rate
(National Kidney Foundation, normal
results range from 90-120 mL/
min/1.73 m2)
366mL/
min/1.73 m2
34 mL/min/1.73
m2

After 24 months of treatment in accordance with the accepted recommendations and the clinical overview, improvements are clearly observed based on the laboratory parameters examined in the patient with LN (Table number 6. After treatment with non-steroidal anti-inflammatory drugs, low doses of Aspirin (80-160 mg/day, antimalarials-hydroxychloroquine(Plaquenil,Chloroqui ne, Quinacrine) or 200 mg 1- 2×/day,Prednisone in doses of 40-60 mg 1×day (the dose was according to the clinical picture).For immunosuppression azathioprine 1-2.5mg/ kg 1×/day or cyclopho-sphamid-4 mg/kg 1×/day was used, tabl. CaCO3 a 1.0capsules Ketosteril S.2x1, S.3x1,Rocaltrol tablets a 0.5 microgram S. two days a week The levels of C3 and C4 were significantly low, which indicates a kidney damage such as the consequences of LES were manifested

with lower values, which shows that the progression of the renal disease has slowed down, which shows that the therapy has shown appropriate effects. High blood pressure was treated with ACE inhibitors: Lisonopril,Peri ndopril,Ramipril, Enalapril,tran-dolapril,benazepril, and

zofenopril, each at a dose of 2x20 mg (individually with

ACE inhibitor and diuretic

DISCUSION

Renal involvement in lupus may be present in more than

half of patients within the first year after diagnosis, with

an important impact on morbidity and mortality and the risk of progression of CKD requiring hemodialysis or

transplantation. It is estimated that 40% of patients with

LN may develop CKD in the terminal phase within 15 years.

Therefore, early detection of the disease is necessary

to begin the manage-ment and treatment of LN and its

complications to prevent rapid disease progression.

The introduction of routine renal biopsy in the 1950s,

the advancement of immunofluorescence and electron

micro-scopy techniques in the 1960s,patients with

membrnous glomerulonephritis who have proteinuria

at the level of nephrotic syndrome but without urinary

sediment, the concentration of C3 is normal, while

anti-DNA, even when positive, appears in low titers.The

opposite occurs in patients with proliferative interstitial

pyelonephritis who have increased proteinuria, hypertension, increased urinary sediment, C3 is reduced

and anti-DNA is positive at high titers. The most accurate

method for detecting and monitoring disease activity in

LN are: proteinuria, hematuria (microscopic and rarely

macroscopic), which indicates glome-rular inflammatory

damage. In the clinical picture,SLE manifests itself

with: hyperu-ricemia,hypercreatinemia,low glo-merular

filtration, reduced titers of C3, C4 and anti-DNA (ds)

positive. In general, individuals of the black race have

the worst performance compared to those of the white

race. The evaluation of factors that lead to the deve-lopment of chronic kidney disease (CKD) from LES in the initial phase (including inflammation, fibrosis of renal tissues, renal hypoxia, oxidative stress...) and with quality treatment, they can obviously affect the slowing of the progre-ssion of the disease [20].During the evaluation of LN, it is important to monitor the evaluation of the complement C3 and C4 titers and anti-DNA (ds), which are positive. The progression of lupus nephritis is different in its different forms. Significant changes in the predictive parameters of the course of the disease cause the course of the disease to be different in people of different races. LN in most cases manifests itself with the deposition of immunoglobulins G (IgG) and complement in the glomeruli [21-26]. Renal damage during LN is manifested by inducing mesangial hyperproliferation, matrix produ-ction, cytokines,chemokine release, and renal fibrosis through damage to the MBG (glomerular basement membrane)[27]. Acti-vated glomerular endothelial cells and damaged podocytes release endothelin 1 which accelerates MBG damage causing mitochondrial stress and podocyte loss leading to glomerulosclerosis,while nephr-ons lose compensatory capabilities, together with knowledge of the immunopathogenesis of glomerular damage, has allowed us to know about the different histopathological patterns associated with SLE.Kidney dise-ase caused by lupus can worsen over time and lead to chronic kidney disease. 30-40% of patients with SLE manifest symptoms of nephritic syndrome, while 10% of them manifest symptoms of glomerulonephritis. In untreated SLE, there is initially low proteinuria<1g/day accompanied by hematuria.mechanisms that cause an

incre-ase in intraglomerular pressure and glome-rular stress in the remaining nephrons [28-31].The cellular components that most contribute to interstitial damage are: tubular cells,lymphocytes,pericytes,fibroblasts,mac rophages, endothelial cells, inflamma-tory lymphocytes and infiltrating dendritic cells. In the pathogenesis of LN, autoim-munity and immunological mechanisms that affect the production of nephrogenic autoant-ibodies directed against nuclear elements against nucleosomal DNA, autoantibodies of certain isotypes (Ig1 and Ig3) that are deposited in the glomeruli (29-31). -Therapy for the management of SLE should be initiated early and according to the classi-fication of the disease based on path--o-genetic mechanisms.Hypertension should be treated with angiotensin-converting enzyme inhibitors (ACE inhibitors) and angiotensin IIreceptorblockers(ARB s),diuretics,nonsteroidal antiinflammatory antirheuma-tic drugs while dyslipi-demia with statins or fibrates, dietary changes (salt restriction, reduced protein intake, sun avoidance) are the most common treatments for SLE (32-36). Recent studies have confirmed that T cells are a fundamental parameter in the pathogenesis of SLE through their ability to interact with B cells and provide them with exceptional assistance in inducing the production of autoantibodies[37,38], Chlo-roquine, corti-costeroids, and immunosuppressive therapy are essential in the treatment of SLE because they prevent the immune system from attacking the blood vessels in the kidneys.

CONCLUSION

In conclusion, we wish that early detection and treatment in the initial stages of CKD and lupus nefritis should be more with antimalarial therapy, corticosteroids,nonsteroidal antiinflammatory, anti-rheumatic antimalarial therapy, immunosu-ppres-sive therapy, ACE inhibitors or angiotensin or kidney transplant is required.Receptor blockers (ARB) and antilipemic with the aim of slowing down the rapid progress of the disease towards chronic terminal failure when treatment with chronic hemodialysis.

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