Bilirubin as an additional biomarker of active lupus?

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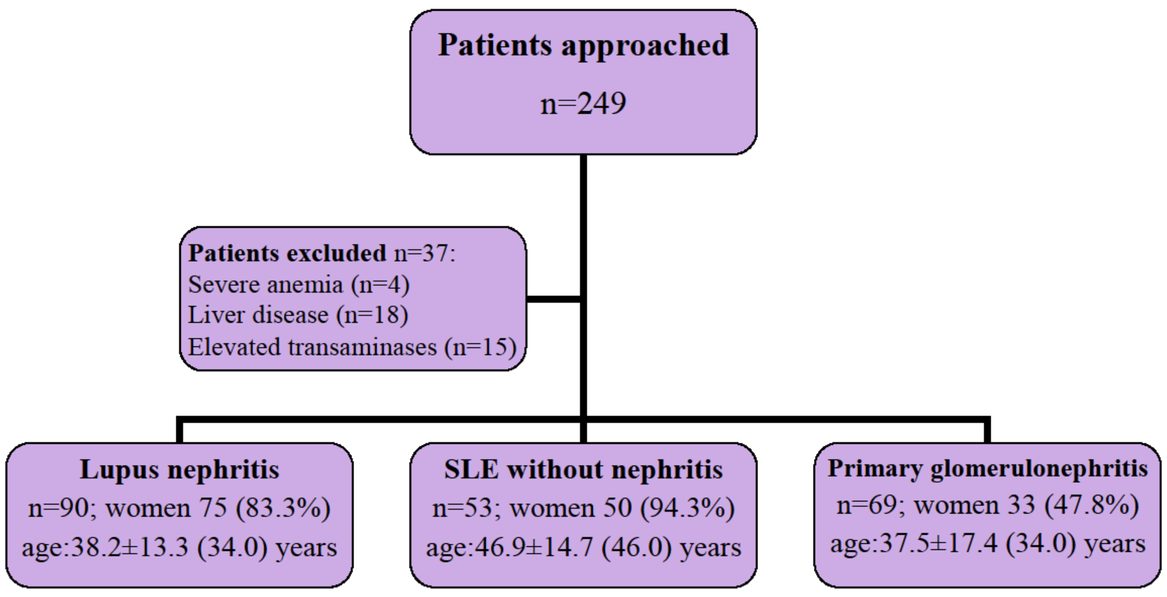
INTRODUCTION AND AIM

Oxidative stress may trigger autoimmunity by initiating damage to deoxyribonucleic acid and modification of self-antigens, which contribute to the production of autoantibodies. Therefore, oxidative stress plays an important role in the development and progression of autoimmune diseases including systemic lupus erythematosus (SLE). Bilirubin - the breakdown product of heme catabolism - has an important antioxidant properties, which provide defense against increased oxidative stress [1].

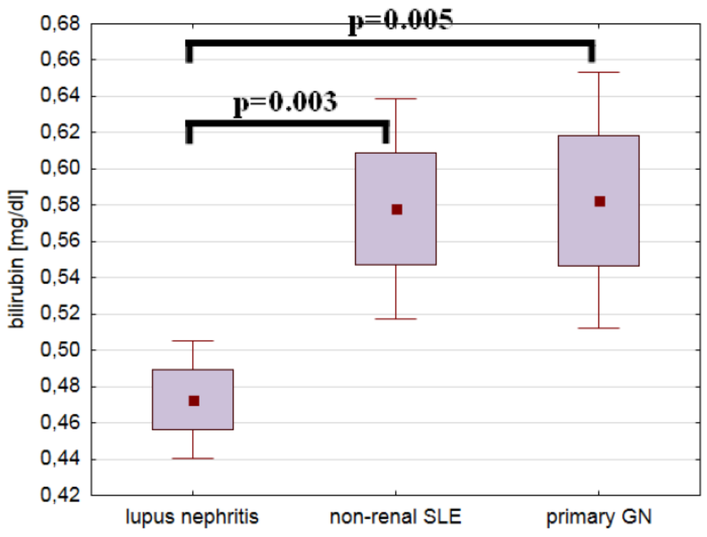
In recent studies, low bilirubin concentrations in patients with SLE and the relationship between bilirubin levels and disease activity were shown [2, 3, 4]. The aim of the study was to verify the association between bilirubin levels and the clinical activity of SLE, as well as lupus nephritis (LN) in our cohort of patients.

METHODS



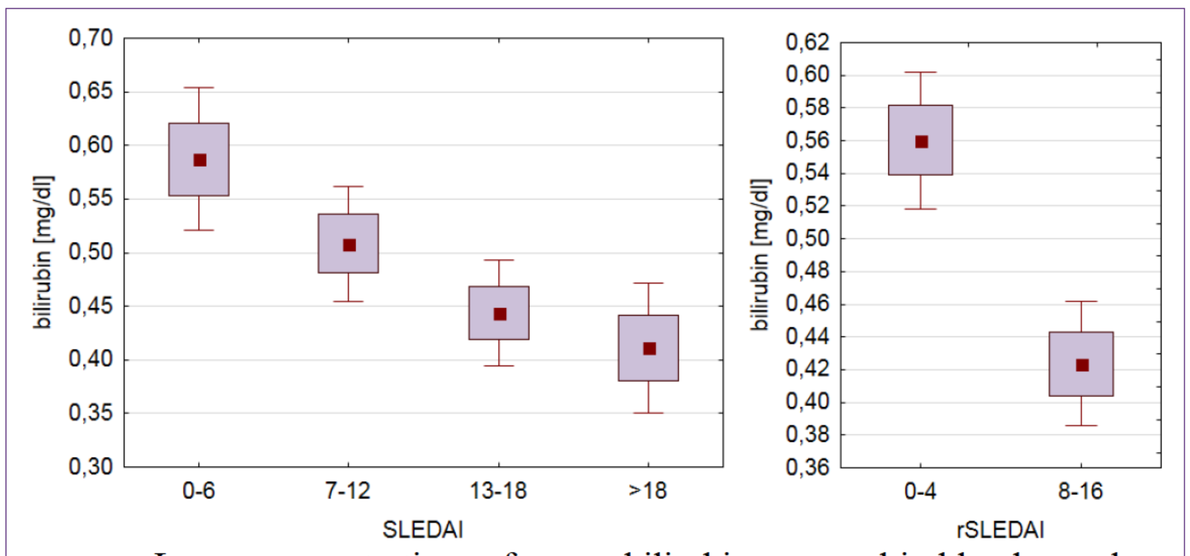
Bilirubin and the classical biomarkers of SLE activity, such as anti-double stranded DNA antibodies (anti-dsDNA), complement hemolytic activity (CH50), erythrocyte sedimentation rate (ESR), serum creatinine, protein, albumin and daily proteinuria were measured using commercially available tests. The disease activity was estimated by SLE Disease Activity Index (SLEDAI) and features of renal involvement (rSLEDAI), including daily proteinuria greater than 0.5g, hematuria, leucocyturia and the presence of heme-granular or red blood cell casts.

RESULTS

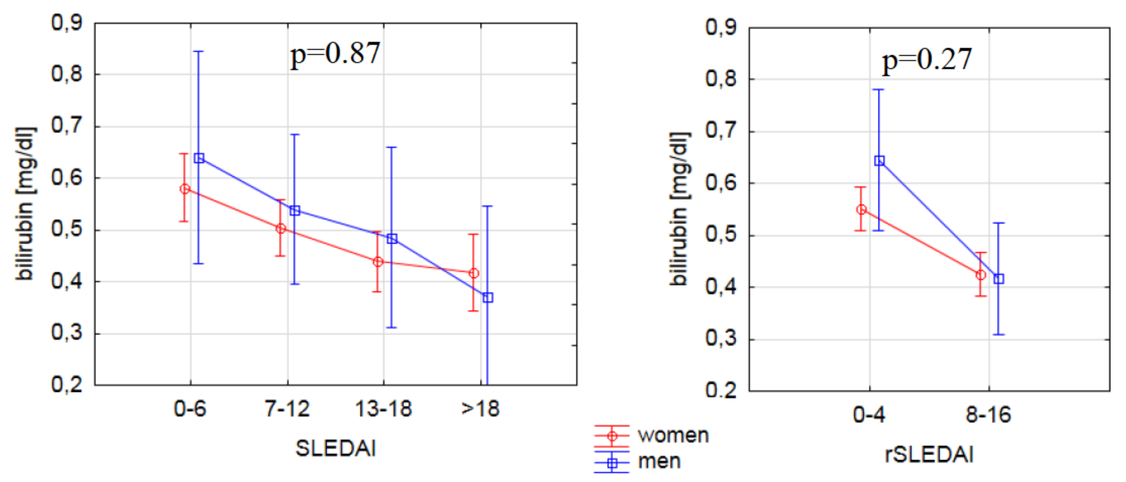


Lower concentrations of serum bilirubin were characteristic for patients with renal involvement (0.47±0.24 mg/dl) compared to patients with non-renal SLE (0.58±0.19 mg/dl) and with primary GN (0.58±0.3 mg/dl).

Group	Lupus nephritis	SLE without nephritis	Primary GN	p value
bilirubin [mg/dl]	0.47±0.24	0.58±0.19	0.58±0.3	**0.0002**
proteinuria[g/24 hours]	1.72±2.12	0.05±0.07	2.47±2.92	**<0.0001**
creatinine [mg/dl]	1.36±0.95	0.91±0.20	1.30±0.75	**<0.0001**
protein [g/dl]	6.04±0.97	7.13±0.75	5.92±1.2	**<0.0001**
albumin [g/dl]	3.39±0.67	4.14±0.54	3.36±0.89	**<0.0001**
cholesterol [mg/dl]	251.6±80.5	200.4±38.8	275.9±126.5	**<0.0001**
triglicerides [mg/dl]	187.3±105.5	123.8±55.3	222.8±163.2	**0.0001**



Lower concentrations of serum bilirubin occurred in blood samples from patients with more active disease assessed by SLEDAI (0-12 points: 0.54±0.25 mg/dl, ≥13 points: 0.43±0.2 mg/dl, p=0.0003) and by rSLEDAI (0-4 points: 0.56±0.24 mg/dl; ≥8 points: 0.42±0.22 mg/dl, p<0.0001). These observations were independent in relation to patients' gender.



Group	Lupus nephritis		SLE without nephritis		p value
SLEDAI	0-12	≥13	0-12	≥13	
bilirubin [mg/dl]	0.52±0.26	0.43±0.21	0.6±0.21	0.47±0.1	**0.0001**
ESR [mm/hour]	31.9±26.6	43.3±31.0	16.2±9.6	31.9±32.0	**0.0002**
CH50 [units]	76.8±24.8	57.8±24.8	72.5±19.1	56.4±43.2	**<0.0001**
anti-dsDNA [IU/ml]	196.4±221.6	331.1±292.5	170.4±196.0	135.5±96.4	**0.04**

Statistically significant differences in ESR (p=0.0001), CH50 (p<0.0001) and anti-dsDNA (p=0.04) in groups of patients divided by SLEDAI were also observed. Significant correlations between bilirubin concentrations and classical indicators of SLE activity were found – positive with CH50 (rs=0.17, p=0.02) and negative with SLEDAI (rs=-0.3, p<0.0001), rSLEDAI (rs=-0.3, p<0.0001) and with ESR (rs=-0.25, p=0.004). Moreover, there were significant relationships between bilirubin concentrations and clinical activity of nephritis, including positive with serum protein (rs=0.39, p<0.0001), albumin levels (rs=0.47, p<0.0001) and negative with daily proteinuria (rs=-0.37, p<0.0001), total cholesterol (rs=-0.34, p<0.0001) and triglicerides (rs=-0.48, p<0.0001).

CONCLUSIONS

Bilirubin relationships with clinical indicators of nephrotic syndrome severity, SLEDAI and rSLEDAI indices confirm its role as an additional, non-invasive biomarker of the systemic lupus erythematosus and lupus nephritis activity.

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