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Correlations urinary N-acetyl-beta-D-glucosaminidase with proteinuria, SLEDAI-2K (renal), Anti ds DNA antibody titre and serum C3

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Abstract
Objective: *In this study our main goal is to evaluate correlations urinary N-acetyl-beta-D-glucosaminidase with proteinuria, SLEDAI-2K (renal), Anti ds DNA antibody titre and serum C3.*
Method: *This cross-sectional prospective observational type of study was done among 60 Diagnosed lupus nephritis patients (active and inactive) at Department of Nephrology, Dhaka Medical College Hospital, Dhaka from January 2018 to December 2018. The informed written consent was taken from each patient.*
Results: *during the study, there was no significant difference in age between active and inactive lupus nephritis patients. Also, most of the patients in both groups were female and serum C3 were significantly lower in active LN than that of inactive LN. ESR, proteinuria, Anti ds DNA Ab titre and uNAG were significantly higher in active LN than that of inactive LN. Also, uNAG is more sensitive than Anti ds DNA antibody titre.*
Conclusion: *From our study we can conclude that, uNAG is a useful biomarker which had positive correlation with SLEDAI-2K (significantly), proteinuria, Anti ds DNA Ab titre. uNAG had negative correlation with serum C_3. Further large-scale study should be carried out for reaching optimal goal. There is therefore a need for larger prospective studies in Bangladesh for diabetics to evaluate this as well as its cost effectiveness in resource poor-settings.*
Keywords: *urinary N-acetyl-beta- D-glycosaminidase, SLEDAI-2K (significantly), proteinuria, Anti ds DNA Ab titre.*

Introduction

Lupus nephritis (LN) is one of the most common and most severe manifestations of SLE, affecting up to 60 % of patients at some point of the disease. The highest frequencies of renal involvement are found in juvenile onset-lupus patients (50-80%) as compared to less than 30 % in late-onset lupus (>50 years). In the SLE cohort at Karolinska University hospital, the prevalence of LN was found to be 42 %. [1] Most patients develop nephritis early in their disease (within 5 years from diagnosis), especially among children and adolescents in whom renal disease is often a presenting feature of SLE.

A recent study on LN patients followed between 1975 and 2005 found that although the overall mortality has decreased, it remained stable over the last decade and the risk for end stage renal

disease (ESRD) remained constant over the last 30 years. [2] In addition, morbidity and mortality is higher among patients with LN compared to SLE patients overall.[3]

Although the treatment of LN has improved, not all patients respond to standard immunosuppressive treatment, 35% have at least one renal relapse and 5-20% develop ESRD after 10 years.[4] In addition, treatment-related toxicity remains a concern.

In this study our main goal is to evaluate correlations urinary N-acetyl-beta-D-glucosaminidase with proteinuria, SLEDAI-2K (renal), Anti ds DNA antibody titre and serum C3.

Objective

General Objective

- In this study our main goal is to evaluate correlations urinary N-acetyl-beta-D-glucosaminidase with proteinuria, SLEDAI-2K (renal), Anti ds DNA antibody titre and serum C3.

Specific Objective

- To detect demographic profile of the patients.
- To evaluate Laboratory findings of the patients.

Methodology

Type of study	Cross-sectional prospective observational type of study
Place of study	Department of Nephrology, Dhaka Medical College Hospial, Dhaka.
Study period	January 2018 to December 2018.
Study population	60 Diagnosed lupus nephritis patients (active and inactive) of indoor and outdoor of Dhaka Medical College hospital.
Sampling technique	Purposive

Exclusion Criteria

- Patients with end stage renal disease (ESRD) and who had undergone renal transplantation.
- Pregnant patients.
- Patients with diabetes mellitus, Severe heart, lung, liver disease, urinary tract infection, chronic infection, e.g. tuberculosis, other immunological or inflammatory disorders, e.g. RA, vasculitis.
- Patients who are unwilling to participate in the study.

Study Procedure

During the study period A questionnaire was prepared considering key variables like demographic data, clinical presentation, clinical findings, predisposing factors, investigations were collected which was verified and the data was collected. After selection of the patient; aims, objectives and procedures of the study were explained with understandable language to the patient. Risks and benefits were also made clear to the patient. The patients were encouraged for voluntary participation and they were allowed being free to withdraw themselves from the study. Then, informed written consent was taken from each patient.

Data Analysis

Statistical analysis of the study was done by the Statistical Package for Social Science (SPSS-22). The results were presented in tables, figures and diagrams. Categorical data were presented as frequency & percentage and numerical data as mean & standard deviation. Confidence interval was considered at 95% level. Receiver-operating characteristics (ROC) analysis was used to calculate the area under curve (AUC) for uNAG and to find out the best cut-off value for identifying lupus nephritis activity. uNAG was compared with serum C3, C4 and anti dsDNA Ab titres. A p value of < 0.05 was considered statistically significant.

Results

In table-1 shows sociodemographic characteristic of the patients where there was no significant difference in age between active and inactive lupus nephritis patients. Also, most of the patients in both groups were female. The following figure is given below in detail:

Table I: Demographic profile of the patients (n=60)

	Lupus nephritis		Total	p value
	Active	Inactive		
Age (years)				
≤20	9 (31.0)	7 (22.6)	16 (26.7)	
21 – 30	13 (44.8)	13 (41.9)	26 (43.3)	
31 – 40	5 (17.2)	6 (19.4)	11 (18.3)	
>40	2 (6.9)	5 (16.1)	7 (11.7)	
Total	29 (100.0)	31 (100.0)	60 (100%)	
Mean SD	25.40 ± 8.07	30.13 ± 10.81	27.67 ± 9.75	0.060
Gender				
Male	0 (0.0)	4 (12.9)	4 (6.7)	0.113
Female	29 (100.0)	27 (87.1)	56 (93.3)	

In table-2 shows laboratory findings of the lupus nephritis patients. Hb and serum C3 were significantly lower in active LN than that of inactive LN. ESR, proteinuria, Anti ds DNA Ab titre and uNAG were significantly higher in active LN than that of inactive LN. The following figure is given below in detail:

Table-2: Laboratory findings of the patients (n=60)

Laboratory findings	Lupus nephritis		p value
	Active	Inactive	
Hb	9.34 ± 1.54	10.72 ± 0.96	<0.001
ESR	49.92 ± 29.18	22.25 ± 16.84	<0.001
Proteinuria	2.43 ± 1.05	0.34 ± 0.41	<0.001
Serum C_3	0.79 ± 0.38	1.21 ± 0.26	<0.001
Serum C_4	0.21 ± 0.25	0.20 ± 0.12	0.755
Anti ds DNA Ab titre	103.00 ± 66.64	54.23 ± 78.16	0.012
uNAG	104.58 ± 32.76	47.25 ± 14.73	<0.001

In figure-1 shows ROC curve of uNAG and Anti ds DNA Ab titre in diagnosis of lupus nephritis activity.

Area under curve (AUC) of uNAG=0.958 and Anti ds DNA Ab titre = 0.847. uNAG occupied more area than Anti ds DNA Antibody titre. So uNAG is more sensitive than Anti ds DNA antibody titre. The following figure is given below in detail:

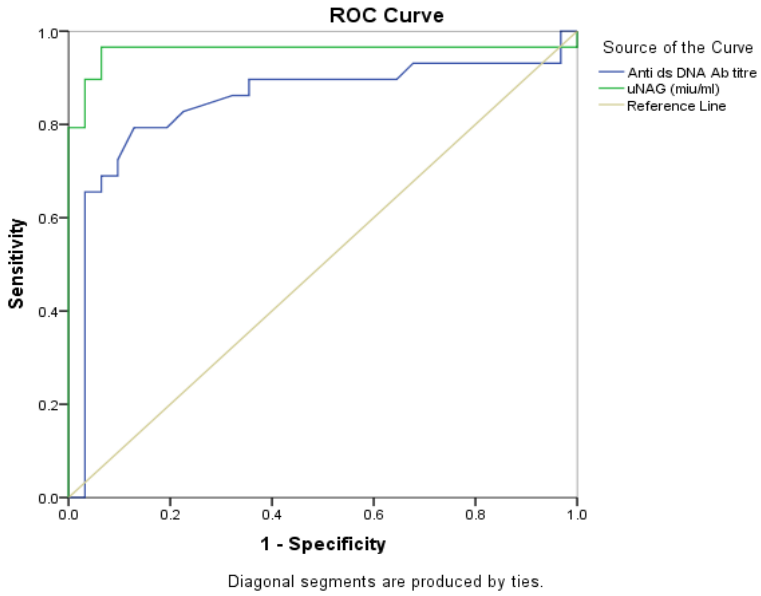

Figure 1: ROC curve of uNAG and Anti ds DNA Ab titre in diagnosis of lupus nephritis activity

In Figure 2 shows ROC curve of serum C_3 and serum C_4 in diagnosis of lupus nephritis activity. Area under curve (AUC) of serum C_4 =0.596 and serum C_3 =0.855. Here serum C_3 occupied more area than serum C_4 so serum C_3 is more sensitive than serum C_4. The following figure is given below in detail:

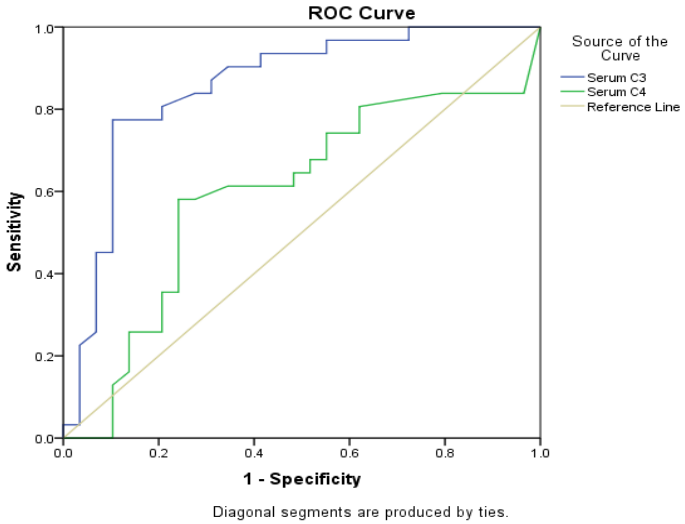

Figure 2: ROC curve of serum C_3 and serum C_4 in diagnosis of lupus nephritis activity.

In Table-2 shows correlation of uNAG with SLEDAI-2K (renal), proteinuria, serum C3 and anti ds DNA Ab titre of the patients (n=60). Above table shows uNAG had positive correlation with SLEDAI-2K (significantly), proteinuria, Anti ds DNA Ab titre. uNAG had negative correlation with serum C_3.The following table is given below in detail:

Table-2: Correlation of uNAG with SLEDAI-2K (renal), proteinuria, serum C3 and anti-ds DNA Ab titre of the patients (n=60)

	r value	p value
SLEDAI-2K (renal)	0.656	<0.001
Proteinuria	0.240	0.065
Serum C3	-0.556	<0.001
Anti ds DNA Ab titre	0.248	0.056

In figure-3 shows correlation of uNAG with SLEDAI-2K (renal) in the study subjects where uNAG positively correlated with SLEDAI-2K (renal). The following figure is given below in detail:

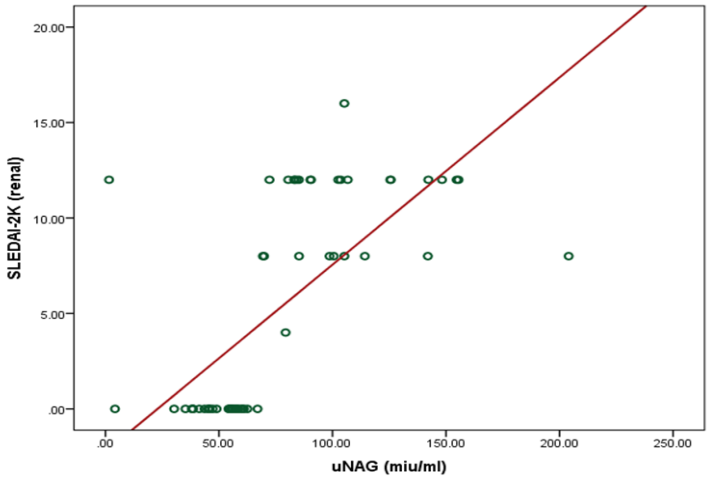

Figure-3: Correlation of uNAG with SLEDAI-2K (renal) in the study subjects.

In figure-3 shows correlation of uNAG with proteiuria in the study subjects where uNAG positively correlated with proteiuria The following figure is given below in detail:

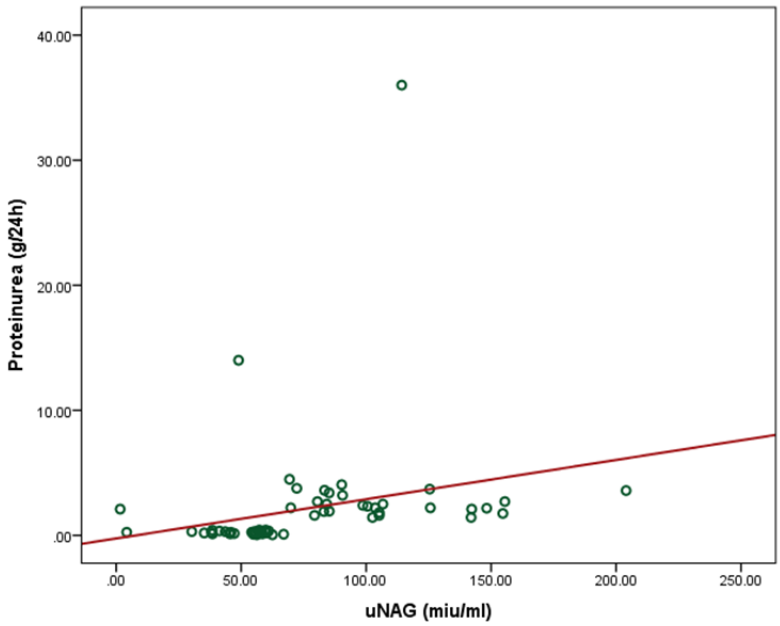

Figure-4: Correlation of uNAG with proteiuria in the study subjects

Discussion

In this study, mean age of the lupus nephritis patients in active and inactive groups was 25.40 ± 8.07 years and 30.13 ± 10.81 years respectively. There was no significant difference in age between active and inactive lupus nephritis patients. Similar finding was observed in the one study.[5]

Mean age of the lupus nephritis patients was 27.67 ± 9.75 years and female to male ratio was 14:1. Another study found that mean age of the LN patients was 34.3 ± 13.6 years and female to male ratio was 9:1.[6]

In this study, uNAG had positive significant correlation with SLEDAI-2K and proteinuria. Another study found positive correlation of uNAG with proteinuria but they did not find any correlation with SLEDAI.[7]

There was a strong positive correlation between proteinuria and urinary NAG activity ($p<0.001$, $r=0.759$). [8] uNAG had negative correlation with serum C_3 in thisstudy. Other study did not find any correlation with serum C_3.[9]

Area under curve (AUC) of uNAG was 0.958, serum C_3 was0.855, Anti ds DNA Ab titre was 0.847 and serum C_4 was 0.596 in diagnosis of lupus nephritis activity. According to this study result, uNAG is better than serum C_3, Anti ds DNA Ab titre and serum C_4 in diagnosis of lupus nephritis activity. The area under the curve (AUC) was 0.74 for the C_3, and 0.65 for C_4.[10]

uNAG showed very good agreement in diagnosis of lupus nephritis activity according to Kappa statistics. uNAG in diagnosis of lupus nephritis activity showed accuracy, sensitivity, specificity, PPV and NPV were 0.950, 0.966, 0.935, 0.933 and 0.967 respectively.

Limitations

- It was a single centered study. For better outcome and analysis multi centered study needs to done.
- Sample size was small for this study. it is not reflecting the whole country scenario.

Conclusion

From our study we can conclude that, uNAG is a useful biomarker which had positive correlation with SLEDAI-2K (significantly), proteinuria, Anti ds DNA Ab titre. uNAG had negative correlation with serum C_3. Further large-scale study should be carried out for reaching optimal goal. There is

therefore a need for larger prospective studies in Bangladesh for lupus nephritispatientsto evaluate this as well as its cost effectiveness in resource poor-settings.

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