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Nephrology

The Role of Urinary N-Acetyl-Beta- D-Glucosaminidase to Determine the Activity of Lupus Nephritis

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Abstract **Original Research Article**

Objective: In this study our main goal is to evaluate the role of urinary N-acetyl-beta- D-glucosaminidase to determine the activity of lupus nephritis. ***Method:*** This cross-sectional prospective observational type of study was conducted among 60 Diagnosed lupus nephritis patients (active and inactive) at Department of Nephrology, Dhaka Medical College Hospital, Dhaka. From January 2017 to December 2017. The informed written consent was taken from each patient. ***Results:*** during the study, 62(mIU/ml) is the best uNAG cutoff value for determination of lupus nephritis activity.Among 29 active lupus nephritis cases raised uNAG was found in 28 cases and among 31 inactive lupus nephritis cases raised uNAG was found in 2 cases.uNAG in determination of lupus nephritis activity showed accuracy, sensitivity, specificity, PPV and NPV were 0.950, 0.966, 0.935, 0.933 and 0.967 respectively. ***Conclusion:*** From our study we can conclude that, uNAG is a useful biomarker for determination of lupus nephritis activity. Further large-scale study should be carried out for reaching optimal goal.

Keywords: Urinary N-acetyl-beta- D-glucosaminidase,Systemic lupus erythematosus (SLE), lupus nephritis.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a systemic autoimmune disorder characterized by the activation of T and B lymphocytes, production of auto-antibodies and formation of immune complexes causing wide spectrum of tissue and organ damage [1]. The overall prevalence of SLE ranges from 1.4 to 21.9% cases per 100,000 people [2].

N-Acetyl-β-d-glucosaminidase (NAG) is a lysosomal brush border enzyme of proximal renal tubular cells that is normally excreted in low amounts in urine. It has been proposed as a valuable marker for renal tubular dysfunction because it's relatively large molecular weight (>130kD) precludes filtration by the glomerulus [3].

The urinary excretion of NAG is increased in subjects exposed to substances that are toxic to renal tubular cells as lead, mercury and contrast media, nephrotoxic drugs as aminoglycosides, antineoplastic drugs as methotrexate and cisplatin [4-6]. It is also increased in various human glomerular diseases, including diabetic nephropathy [7]. Moreover, it has been proposed that uNAG activity is probably an indicator of the increased lysosomal turnover that occurs when increased protein is presented to the tubular cells [3]. Increased uNAG activity in patients with glomerulonephritis and proteinuria has been suggested as indicating functional changes within the kidney, rather than renal tubular damage [6].

In this study our main goal is to evaluate role of urinary N-acetyl-beta- D-glucosaminidase to determine the activity of lupus nephritis.

OBJECTIVE

- To detect sensitivity and specificity of uNAG at different cutoff value
- To evaluate validity test of uNAG in determination of lupus nephritis activity

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 2017 to December 2017.
Study population	60 Diagnosed lupus nephritis patients (active and inactive) of indoor and outdoor of Dhaka Medical College hospital.
Sampling technique	Purposive

Inclusion criteria

- SLE patients with biopsy proven lupus nephritis.

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 fromthe 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 figure-1 shows age distribution of the patients. Mean age of the lupus nephritis patients in active and inactive LN was 25.40 ± 8.07 years and 30.13 ± 10.81 years respectively. The following figure is given below in detail:

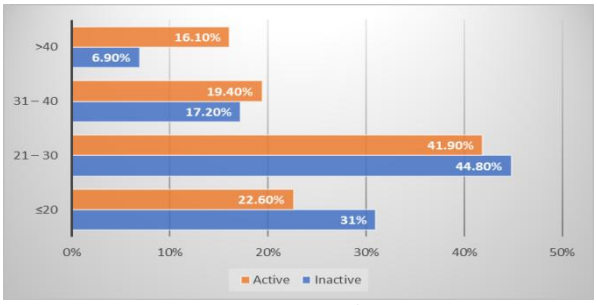

Fig-1: Age distribution of the patients

In figure-2 shows gender distribution the patients wheremost of the patients in both groups were female. There was also no significant difference in gender between active and inactive lupus nephritis patients. The following figure is given below in detail:

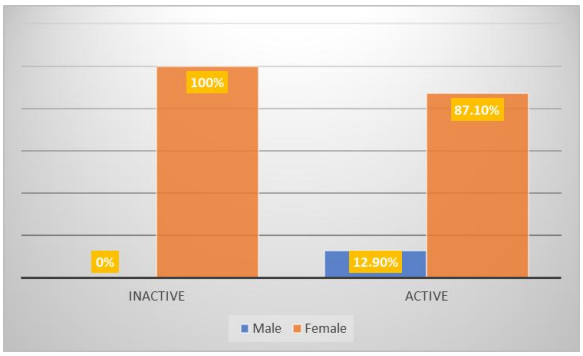

Fig-2: Gender distribution the patients

In Table-1 shows sensitivity and specificity of uNAG at different cutoff value for determination of lupus nephritis where 62(mIU/ml) is the best uNAG cutoff value for determination of lupus nephritis activity. The following table is given below in detail:

Table-1: Sensitivity and specificity of uNAG at different cutoff value for determination of lupus nephritis (n=60)

uNAG	Sensitivity	Specificity
61	0.966	0.903
62	0.966	0.935
65	0.931	0.935
68	0.897	0.935
70	0.897	0.968
71	0.862	0.968

In table-2shows lupus nephritis patients by uNAG. Lupus nephritis activity was determined by SLEDAI 2K (renal). Among 29 active lupus nephritis cases raised uNAG was found in 28 cases and among 31 inactive lupus nephritis cases raised uNAG was found in 2 cases. The following table is given below in detail:

Table-2: Distribution of lupus nephritis patients by uNAG (n=60)

uNAG	Lupus nephritis		Total
	Active	Inactive	
≥62	28 [TP]	2 [FP]	30
<62	1 [FN]	29 [TN]	30
Total	29	31	60

In table-3 shows validity parameters of uNAG in determination of lupus nephritis activity. uNAG showed very good agreement in determination of lupus nephritis activity according to Kappa statistics. uNAG in determination of lupus nephritis activity showed accuracy, sensitivity, specificity, PPV and NPV were 0.950, 0.966, 0.935, 0.933 and 0.967 respectively. The following table is given below in detail:

Table-3: Validity test of uNAG in determination of lupus nephritis activity (n=60)

Statistics	Value	Low 95% CI	High 95% CI
Kappa	0.900		
Accuracy	0.950	0.841	0.982
Sensitivity	0.966	0.853	0.988
Specificity	0.935	0.830	0.966
Positive Predictive Value (PPV)	0.933	0.825	0.965
Negative Predictive Value (NPV)	0.967	0.858	0.998

DISCUSSION

This cross-sectional study was done to evaluate the role of uNAG for the diagnosis of activity of lupus nephritis in Department of Nephrology, Dhaka Medical College Hospital. A total of 60 lupus nephritis patients in Nephrology Ward of Dhaka Medical College Hospital, Dhaka were included in this study from January 2017 to December 2017. Adult SLE patients with biopsy proven lupus nephritis were enrolled in this study.

In this study it was observed that there was a high prevalence of anaemia among the active LN patients, about 86.2% of all active patients had anaemia also found 132 cases of anaemia (122 women, 10 men) from a total of 345 screened SLE patients and the identified cases of anaemia were ACD (37%), IDA (35.6%), AHA (14.4%) and other causes (12.9%)[7].

Although ESR is a nonspecific marker of inflammation it is a useful tool in lupus nephritis management which was significantly higher in this study. One study found significant correlation of ESR with systemic lupus activity measure [8].

In this study, serum C_3 was significantly low in active LN but C_4 was almost similar in both active and inactive lupus nephritis. Another report found that serum C3 less in active LN [9]. Another study mentioned that that C3 level was more sensitive index of disease activity than those of C_4. [10]. other study identified that serum C3 level are diagnostically more sensitive and specific for systemic lupus erythromatosus activity than serum C_4 level [10].

In this study proeinuria was significantly higher in active LN but in inactive LN it was significantly lower (<500 mg/24 hours)[11]. Another study reported that urinary protein more in active lupus nephritis. Other report found that serum albumin was the parameter that was most significantly (negatively) correlated with proteinuria ($p < 0.00001$)[12].

Mean anti ds DNA ab titre in this study was 103.00±66.64 in active LN and 54.23±78.16 inactive LN which mean that high titre of anti-ds DNA ab is present in active LN than that of inactive LN. Though anti ds DNA ab titre is in this study but not statistically significant. Similar findings were observed by other study [13].

CONCLUSION

From our study we can conclude that, uNAG is a useful biomarker for determination of lupus nephritis activity. Further large-scale study should be carried out for reaching optimal goal.

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