

URINARY NEUTROPHIL GELATINASE – ASSOCIATED LIPOCALIN (uNGAL) and MONOCYTE CHEMOATTRACTANT PROTEIN-1 (uMCP-1) IN LUPUS NEPHRITIS (LN)

Sabah Mohamed Alharazy ^a, Norella CT Kong ^a, Marlyn Mohd ^b, Shamsul Azhar Shah ^c, A Halim A Gafor ^a and Arbaiyah Ba' in ^a

^a Nephrology unit, Department of Medicine, ^b Department of Immunobiology & Microbiology, ^c Department of Community Medicine, Universiti Kebangsaan Malaysia Medical Centre, Kuala Lumpur, Malaysia

Introduction

Urine neutrophil gelatinase – associated lipocalin (uNGAL) and monocyte chemoattractant protein-1 (uMCP-1) has been proposed as a potential biomarkers for lupus nephritis (LN) activity.

Objectives

We compared the urinary levels of NGAL and uMCP-1 in SLE patients with biopsy-proven LN.

Methods

This was a cross-sectional observational study in which the levels of both uNGAL (ng/mg of urinary creatinine) and uMCP-1 (pg/mg of urinary creatinine) were measured by enzyme-linked immunosorbent assay (ELISA) in SLE patients with biopsy-proven LN. Their renal function test, serum albumin, urinary parameters, lupus serology and SLEDAI-2K (global, extrarenal and renal) were also measured.

Results

A hundred patients were recruited. There were 47 patients with active and 53 with inactive LN. uNGAL levels (ng/mg creatinine) and uMCP-1 levels (pg/mg creatinine) were significantly higher in patients with active LN compared to those with inactive renal disease ($p = 0.01$ and $p < 0.001$ respectively) (Figure 1).

Both uNGAL and uMCP-1 levels were highly associated with SLEDAI -2K (renal) (uNGAL: $r = 0.32$, $p = 0.001$; uMCP-1: $r = 0.39$, $p = 0.001$). Both biomarker levels also correlated with SLEDAI-2K (global) (uNGAL: $r = 0.19$, $p = 0.05$; uMCP-1: $r = 0.27$, $p = 0.006$). However, there were no associations between uNGAL and uMCP-1 with SLEDAI-2K (extra-renal), Other important details of associations are presented in Table I.

Using receiver operating characteristic (ROC) curve, the area under the curve (AUC) for uNGAL was 0.83 (95% CI = 0.74 – 0.92, $p = 0.001$). With a cut-off value at 91.25 ng/ mg creatinine, uNGAL had a sensitivity of 0.89 and specificity of 0.67 for prediction of LN activity. Whereas, the AUC of uMCP-1 was 0.84 (95% CI = 0.75 – 0.92, $p = 0.001$). With a cut-off value at 4,247 pg/ mg creatinine, uMCP-1 had a sensitivity of 0.89 and specificity of 0.61 for early diagnosis of LN activity (Figure 2).

| Spearman's rho variable | uNGAL | | uMCP-1 | |
|---------------------------------------|-------|--------------|--------|--------------|
| | r | p value | r | p value |
| Hemoglobin | -0.19 | 0.06 | -0.11 | 0.25 |
| White blood cell | 0.07 | 0.45 | -0.06 | 0.56 |
| Platelet | 0.10 | 0.31 | 0.05 | 0.57 |
| Serum albumin | -0.11 | 0.27 | -0.35 | 0.001 |
| Serum creatinine | 0.17 | 0.09 | 0.09 | 0.38 |
| eGFR | -0.18 | 0.07 | -0.10 | 0.30 |
| C3 (mg/dl) | -0.09 | 0.34 | -0.09 | 0.34 |
| C4 (mg/dl) | -0.02 | 0.97 | 0.02 | 0.80 |
| Anti-dsDNA Ab (IU) | 0.17 | 0.09 | -0.04 | 0.64 |
| Urinary protein (mg/L) | 0.07 | 0.49 | 0.02 | 0.82 |
| Urine protein creatinine index (uPCI) | 0.34 | 0.001 | 0.39 | 0.001 |
| leucocyturia | 0.21 | 0.03 | 0.26 | 0.008 |
| Haematuria | 0.10 | 0.29 | 0.13 | 0.18 |
| Chronicity index | 0.02 | 0.82 | -0.14 | 0.25 |
| SLEDAI-2K global score | 0.19 | 0.05 | 0.27 | 0.006 |
| SLEDAI-2K renal score | 0.32 | 0.001 | 0.39 | 0.001 |
| SLEDAI-2K-extra renal score | -0.12 | 0.22 | -0.08 | 0.42 |

r: Spearman's rho Correlation Coefficient; eGFR: estimated glomerular filtration rate; C3: complement 3; C4: complement 4; anti-dsDNA : anti-double-stranded DNA; uPCI: urine protein creatinine index; Haematuria : at least 5 red blood cells/high-power field; SLEDAI-2K: Systemic Lupus Erythematosus Disease Activity Index-2K.

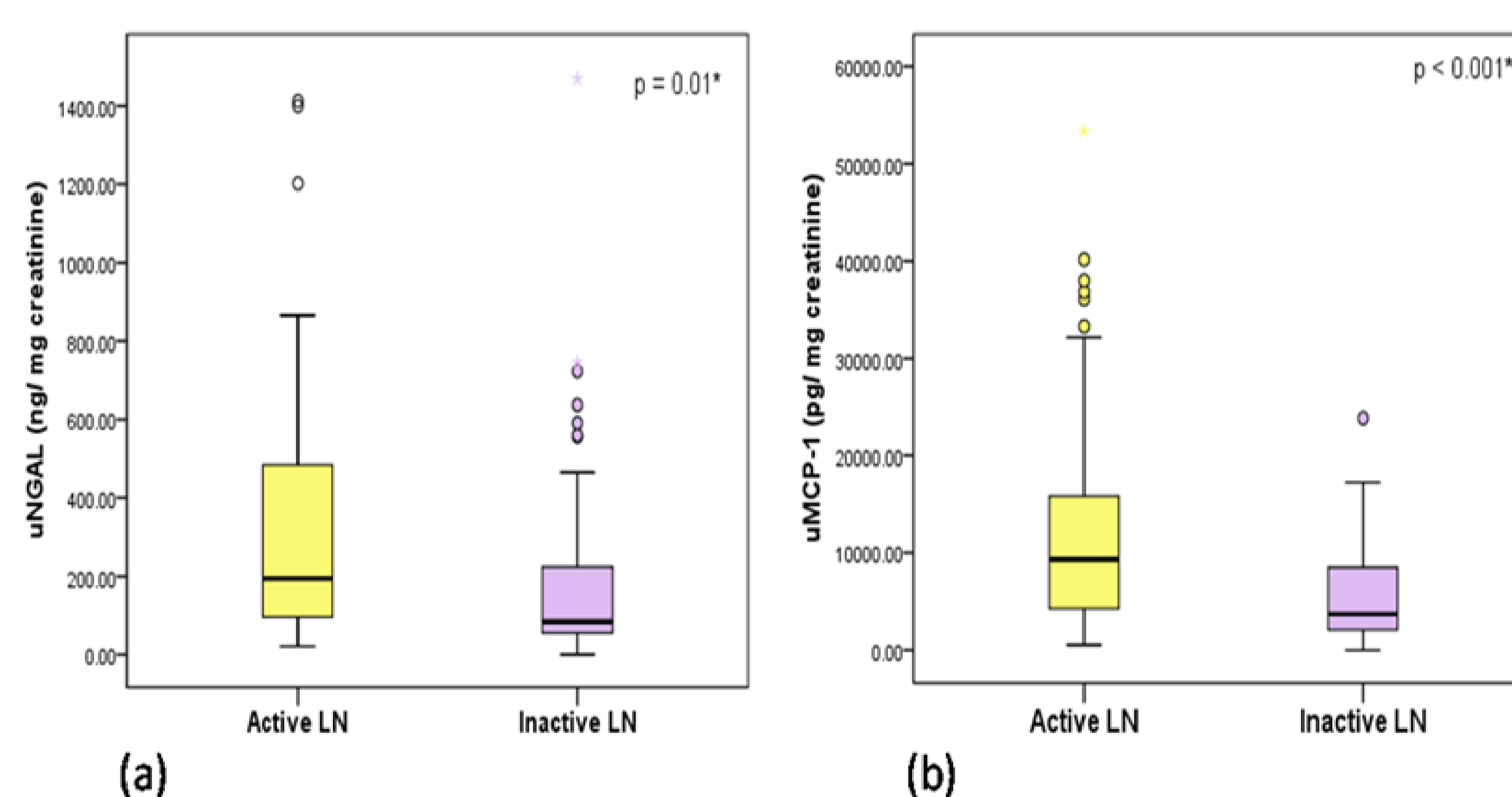


Figure 1. uNGAL AND uMCP-1 levels in patients with and without active LN.

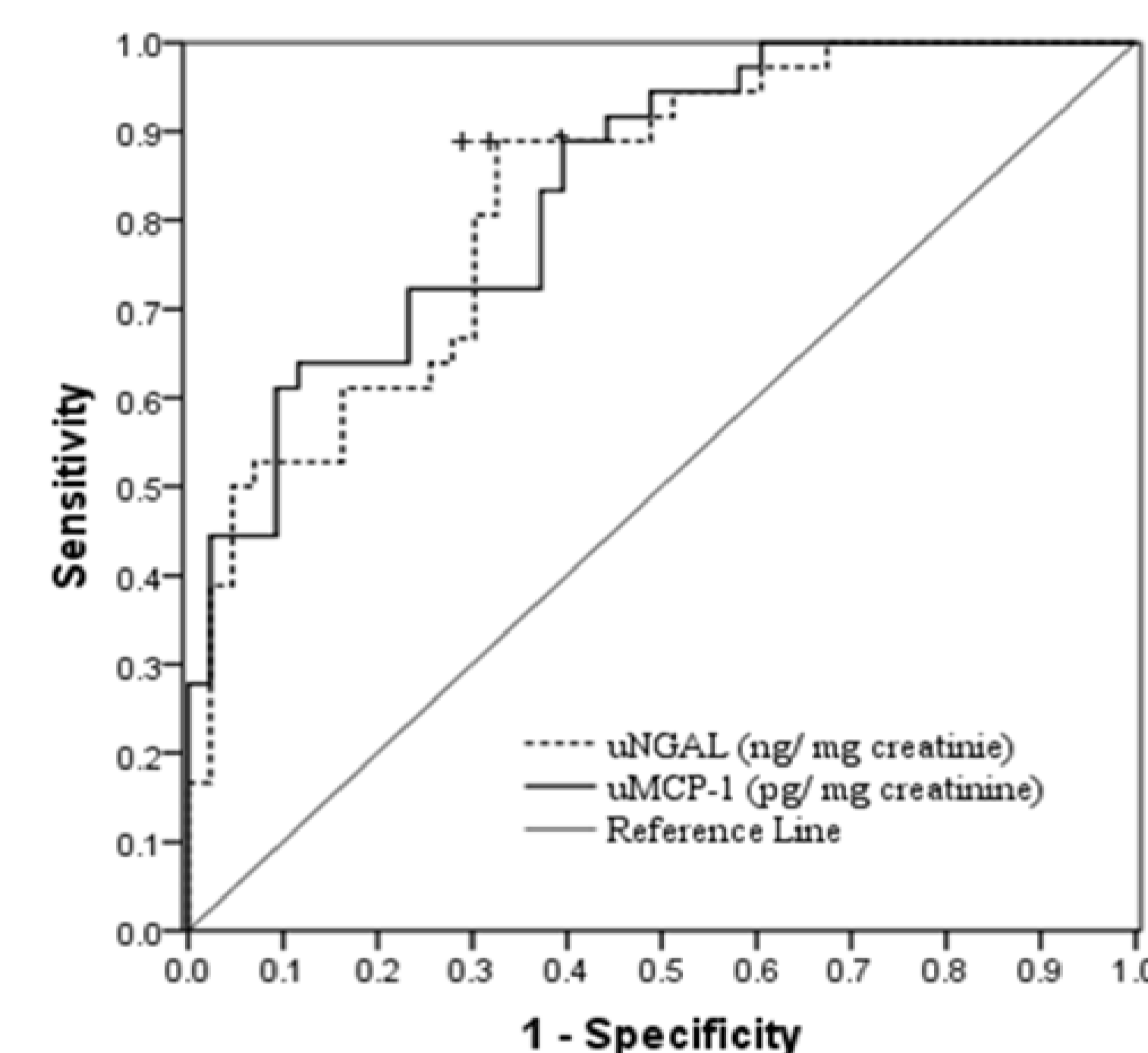


Figure 2. ROC curves of uNGAL and uMCP-1 for the diagnosis of LN activity in SLE patients.

Conclusion

Both uNGAL and uMCP-1 were highly correlated with LN activity. Serial measurements may be of value in predicting early flares of LN thus permitting earlier intervention.

References

1. Urinary neutrophil gelatinase-associated lipocalin as a biomarker of nephritis in childhood-onset systemic lupus erythematosus. *Arthritis Rheum.*
2. Urinary Lipocalin-2 Is Associated With Renal Disease Activity in Human Lupus Nephritis. *Arthritis Rheum*
3. Monitoring urinary levels of monocyte chemoattractant and activating factor reflects disease activity of lupus nephritis. *Kidney Int.*
4. Urine chemokines as biomarkers of human systemic lupus erythematosus activity. *J Am Soc Nephrol*
5. Monocyte Chemoattractant-1 as a Urinary Biomarker for the Diagnosis of Activity of Lupus Nephritis in Brazilian Patients. *J Rheumatol.*

