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## Review report

Final title: Neutrophil gelatinase-associated lipocalin is a urine-based biomarker for diagnosing active lupus nephritis

Title at submission: Neutrophil gelatinase associated lipocalin is a urine based biomarker in the diagnosis of active lupus nephritis



#### ROUND 1

Reviewer: Arifa Akram, ORCID: 0000-0001-8829-9817

The study addresses an important clinical challenge in the management of systemic lupus erythematosus (SLE), specifically the diagnosis of active lupus nephritis (LN). The exploration of urinary neutrophil gelatinase -associated lipocalin (NGAL) as a non-invasive biomarker is timely and relevant, given the complexity of diagnosing LN and the need for reliable, easily accessible diagnostic tools.

### Correspondence

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Responsible editor M Mostafa Zaman 0000-0002-1736-1342

Reviewers Arifa Akram 0000-0001-8829-9817 Rijwan Bhuiyan 0000-0003-0005-8889

SLE, lupus nephritis, urinary NGA

**Funding** 

Ethical approval

Approved by IRB of Bangabandhu Sheikh Mujib Medical University (No. BSMMU/2024/799, dated 24 Jan 2024)

Trial registration number

Not applicable

Declaration

This article encompasses MD thesis of Dr Anthony Chakma 1 Comment Expand Discussion: Elaborate on clinical implications and comparison with existing bi-

omarkers.

Address Limitations: Discuss potential confounding factors and the need for longitudinal

studies.

Future Research Directions: Suggest areas for further investigation to strengthen the evidence

base for NGAL's role in clinical practice.

This study contributes significantly to the literature on lupus nephritis diagnostics and opens

avenues for improved patient care.

Discussion is expanded and elaborated. Response

Limitations is addressed in line 164.

Future Research Directions are suggested in line 167.

Editor: M Mostafa Zaman, ORCID: 0000-0002-1736-1342

## Overview

Response

This article is a Quasi-Experimental Study on treatment response & toxicity pattern of Concurrent chemoradiation with cisplatin versus carboplatin in the treatment of locally advanced carcinoma cervix. Title seems not be self explanatory. Rationale of the study should be stated. Story telling could have been more precise. Discussion could have been more critical & comprehensive.

Please consolidate the tables. It is possible to have three comprehensive tables. 2 Comment

The word count is reduced to 1497 and references to 15.

We consolidated the tables to one. Response

Reduce the word count to 1500 and references to 15. 3 Comment

Replace the Highlights with Key Messages in a descriptive manner with no more than 50 4 Comment

The Highlights is replaced with Key Messages in a descriptive manner with 49 words. Response

## ROUND 2

# Reviewer: Rijwan Bhuiyan, ORCID: 0000-0003-0005-8889

5 Comment

Please include the objective along with the background and arrange the content descriptively. Ensure "Department" is capitalized throughout the manuscript (Page 40).

Remove "ELISA" from the keywords.

Response Objective is included along with the background and arranged descriptively.

"Department" is capitalised throughout the manuscript.

"ELISA" is removed from the keywords.

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#### 6 Comment

After Line 67, provide some information on the acute lupus nephritis disease burden in Bangladesh.

Use the short form "SLE" from Line 1 onwards, and similarly for other terms like "NGAL" after their first appearance (Line 76).

In Line 81, clarify which study you are referring to.

In Line 82: Here, you have mentioned that it is the most accurate.....but in the next sentence, it is not yet established worldwide. Please logically arrange these two sentences.

Move the content from Line 85 to the discussion section.

## Response

Information on the acute lupus nephritis disease burden in Bangladesh in line 69.

Short form "SLE" from Line 1 onwards, and similarly for short form "NGAL" after their first appearance is used.

The study is clarified.

We removed the line 'Urinary NGAL still has not established as a diagnostic marker for active lupus nephritis world-wide'

The content from Line 85 is moved to line 150 in the discussion section.

#### 7 Comment

Remove the sentence in Line 90 as it is already mentioned in the introduction: "The objective was to assess NGAL as a urine-based biomarker in the diagnosis of active lupus nephritis."

In Line 91, please mention the size estimation technique, categorization, and selection process of the cases.

Combine Lines 96 to 99 into a single sentence.

Replace "case report" with "questionnaire" in Line 100.

Move the sentence "Urine sample from each patient was collected for urinary NGAL at the department of Laboratory Medicine, BSMMU" from Line 105 to the urine measurement section.

 $Consider\ creating\ a\ separate\ paragraph\ for\ laboratory\ methods, including\ specimen\ collection\ and\ NGAL\ measurement.$ 

Describe the statistical analysis in a separate paragraph

## Response

The sentence in Line 90 is removed.

In Line 91, the size estimation technique, categorization, and selection process of the cases is mentioned.

Lines 96 to 99 are combined into a single sentence.

"case report" is replaced by "questionnaire" in Line 101.

The sentence "Urine sample from each patient was collected for urinary NGAL at the department of Laboratory Medicine, BSMMU" is removed from Line 105 to the urine measurement section.

Separate paragraphs for laboratory methods, including specimen collection and NGAL measurement are made.

The statistical analysis is described in a separate paragraph.

## 8 Comment

You mentioned creatinine clearance, proteinuria, urine sediments, anti-dsDNA, and complement levels in the introduction, but these parameters are not shown in the results section. If these were not measured, please state this in the study limitations with reasons.

Include the median in the statistical analysis along with the mean (Line 108).

Incorporate the sentence "Validity testing of urinary NGAL level in detecting active lupus nephritis in SLE patients" with the next sentence (Line 131).

# Response

They were not measured due to short time duration.

The median in the statistical analysis is included along with the mean (Line 118).

The sentence "Validity testing of urinary NGAL level in detecting active lupus nephritis in SLE patients" is incorporated with the next sentence (Line 135).

## Comment

Remove the line "This cross-sectional study was carried out in the department of Laboratory Medicine, Rheumatology and Nephrology, BSMMU with an aim to evaluate urinary NGAL as a biomarker for detection of active lupus nephritis" (Line 142).

Mention the age and its association with categories in the result section (Line 145).

Use the short forms "ROC" and "AUC" (Line 156).

## Response

The line is removed.

The age and its association with categories is mentioned in the result (Line 124).

The short forms "ROC" and "AUC" are used (Line 160).

# 10 Comment

Rephrase the sentence to include the key message: "It may be a useful biomarker for diagnosis of active lupus nephritis due to its high sensitivity and specificity."

Move the limitations to the last part of the discussion (Line 172).

Incorporate the recommendations with the conclusion (Line 176).

## Response

The sentence is rephrased to include the key message: "It may be a useful biomarker in detection of active lupus nephritis in SLE Patients due to its high sensitivity and specificity."

The limitations is moved to the last part of the discussion (Line 169).

The recommendations is incorporated with the conclusion (Line 177).

Table 1: Clarify the group information in the footnote of the table. 11 Comment

Figure 1 should have information about the lupus nephritis class descriptions at the footnote.

Table 1: The group information in the footnote of the table is clarified. Response

Figure 1 Information about the lupus nephritis classification is described at the footnote.

## Editor: M Mostafa Zaman, ORCID: 0000-0002-1736-1342

A point by point response has not been submitted. 12 Comment

A small paragraph on ethical considerations (describing how did you address the ethical issues during the study) is es-

The point by point response has been submitted. Response

Results: Provide results up to one decimal point throughout the manuscript, including tables. 13 Comment

Table 1: Clarify the group information in the footnote of the table.

Figure 1 should have information about the lupus nephritis class descriptions at the footnote.

Table and figure have been revised accordingly. Response

Discussion: Most of the contents of the Discussion section are repetition of results. Needs extensive revision to incorporate comparison of evidences (not results in verbatim), biological plausibilities and implication of the findings. Comment

Discussion is revised as per the comments. Response