

## To Assess the Correlation Between Neutrophil to Lymphocyte Ratio with hs-CRP as Inflammatory Marker in Patients with Chronic Kidney Disease

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### Abstract

**Objective:** To assess the correlation between neutrophil-to-lymphocyte ratio with hs-CRP as an inflammatory marker in patients with chronic kidney disease

**Material and Methods:** This Study was Cross-sectional study and conducted in the Department of Medical Unit-4 Services Hospital, Lahore. Duration of this study was 6 months after Synopsis approval. 115 patients with CKD (by operational definition) with peripheral edema were included in the study. A blood sample was then collected using a 5cc BD syringe under aseptic conditions. All samples were stored in a vial containing Ringer's solution. Then all samples were sent to the hospital laboratory for hs-CRP and NLR assessment. Reports were assessed and hs-CRP and NLR

**Result:** In this study, the correlation coefficient showed a weak positive correlation between hs-CRP and NLR. i.e.  $r=0.399$ ,  $p\text{-value}=0.000$ . Stratification for age, sex, BMI and duration of CKD showed a significant positive correlation between NLR and hs-CRP.

**Conclusion:** Moderately positive correlation between NLR and hs-CRP. Both markers have the potential to exclude persistent subclinical problems and may also perform risk stratification for CKD patients.

**Keywords:** Neutrophil to lymphocyte ratio, hs-CRP Chronic kidney disease.

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### Introduction

Chronic kidney disease (CKD) is a long-term kidney disease; therefore, it differs from acute kidney disease in that the reduction in kidney function must be present for more than 3 months. CKD is an internationally recognized public health problem affecting 5-10% of the world's population.<sup>1</sup> Guidelines define CKD as kidney damage or a reduced glomerular filtration rate (GFR) of less than 60mL/min/1.73m<sup>2</sup> for at least 3 months.<sup>2</sup> Chronic inflammation is a common comorbid condition in CKD and especially in dialysis patients. A number of interventions have been shown to be safe and effective in well-designed clinical trials.<sup>3</sup> Although a number of

markers have been established to measure systemic inflammation, additional markers are still required. Recently, the N/L neutrophil to lymphocyte count ratio has been investigated as a new measure of inflammation in various populations and has been shown to have prognostic and predictive values, particularly in patients with systemic inflammation.<sup>4-5</sup> In various cancer patients, the N/L ratio has been found to be a cost-effective biomarker for risk stratification of recurrence and mortality.<sup>4</sup> In cardiovascular studies, it has also been found to be a predictor of mortality in various patient groups, such as myocardial infarction and heart failure.<sup>5</sup> There are several studies on the N/L ratio and its relationship to other inflammatory markers in CKD patients.<sup>6-7</sup> One study showed that the correlation value was positive but very weak, i.e.  $r=0.264$ ,  $p=0.002$ .<sup>8</sup> Another study also showed a slightly higher positive correlation value, but also very weak, i.e.  $r=0.333$ ,  $p=0.01$ .<sup>9</sup> The rationale for this study is to assess the correlation between NLR and hs-CRP as an inflammatory marker in CKD patients. NLR is a good indicator of the inflammatory markers,

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i.e. hs-CRP. However, the literature has shown that there is a very weak correlation between NLR and hs-CRP. However, if there is a strong relationship, it will be a useful surrogate for hs-CRP to detect inflammation in CKD patients. Determination of NLR is a relatively inexpensive and time-efficient method of assessing inflammation. However, there is no local evidence in this regard. So we want to do this study so that we can achieve a local data and we can plan to screen CKD patients for inflammation to prevent the consequences of inflammation, especially to prevent cardiovascular events. Cardiovascular disease is a leading cause of morbidity, disability, and hospitalization, particularly among older adults.<sup>24</sup> Previous reports have emphasized that inflammation plays a key role in the development and progression of atherosclerosis.<sup>8,9</sup> Inflammatory cells actually contribute to the initiation and disruption of atherosclerotic lesions, which subsequently lead to acute coronary syndrome and other cardiovascular events due to instability or rupture of the atherosclerotic plaque.<sup>10,11</sup> Carotid intima-media thickness, a well-established marker of subclinical atherosclerosis, is a risk factor for cardiovascular disease and can be used to predict cardiovascular events.<sup>12</sup> To date, NLR provides information on the inflammatory state including the effects of neutrophil elevation, secondary to acute inflammation, along with lymphocyte depletion, secondary to stress-induced lymphocyte redistribution to lymphoid organs, as well as lymphocyte apoptosis.<sup>15</sup>

## Material and Methods

A cross-sectional study was conducted in the Department of Medical Unit-4 Services Hospital, Lahore. Six months after the approval of Synopsis. A sample size of 115 patients is calculated with 5% type I error, 10% type II error and the expected value of the correlation coefficient is taken, i.e.  $r=0.333$  between NLR and hs-CRP in CKD patients.<sup>9</sup> Non-probably consecutive sampling. Patients aged 16-70 years of any gender with CKD (by operational definition) with peripheral edema. Patients with active infection or inflammation (ESR>20 mm/H), atherosclerotic vascular disease, hepatitis B and C (scientific report) Impaired hepatic feature (AST>40IU, ALT>40IU), autoimmune diseases, contemporary malignancy or records of malignancy (medical report) Sufferers with diabetes mellitus (BSR>186mg/dl) Patients underwent hemodialysis (scientific document) a total of one hundred fifteen patients according to inclusion criteria were enrolled from medical OPD of Services Hospital Lahore.

Knowledgeable consent turned into received. Demographic statistics (inclusive of name, age, gender, duration of CKD) was recorded. Then blood samples were drawn with the aid of 5cc BD syringe under aseptic conditions. All samples have been stored in a vial containing ringer's lactate solution. Then all samples were dispatched to the laboratory of the health center for assessment of hs-CRP and NLR. Reviews have been assessed and ranges of hs-CRP and NLR was noted (as in line with operational definition), all the statistics were collected on a in particular designed Performa. All the collected data was entered and analyzed into SPSS version 21. Quantitative variables like age, duration of CKD, BMI, hs-CRP and NLR were presented as SD. Qualitative variables like gender become offered as frequency and percent. Pearson's correlation coefficient turned into calculated between hs-CRP and NLR. P value  $\leq 0.05$  turned into taken as variable. Statistics changed into stratified for age, gender, duration of CKD and BMI to manipulate impact modifiers. Submit-stratification, Pearson's correlation coefficient changed into calculated between hs-CRP and NLR for each stratum. P-value less than or equal to 0.05 was taken as vast.

## Results

Suggested average age of patients was  $45.70 \pm 13$  (62 years). Minimum and maximum age of patients changed into 20 and 70 years respectively. Amongst sufferers 67(58.3%) were male and 48(41.7%) were girl. BMI of 32(27.8%) was ordinary, 42(36.5%) sufferers were previously obese and 41(35.7%) patients were currently obese. Imply period of CKD became  $9.30 \pm 1.77$ . Imply cost for NLR become  $2.12 \pm 0.35$ . Minimal and maximum NLR turned into 1.70 and 3.20 respectively (**Table-1**). Mean value for hs-CRP become  $1.92 \pm 0.50$ . Minimum and maximum hs-CRP became 1.30 and 3.20 respectively (**Table-2**). Correlation coefficient shows considerable low positive correlation between NLR and hs. CRP level. i.e.  $r=0.399$ ,  $p\text{-value}=0.001$  In all age companies besides patients inside the age organization 31-40 years had confirmed fantastic correlation among NLR and hs-CRP. Furthers details can be visible in. Among male and female patient's widespread linear correlation become visible among NLR and hs-CRP stages. i.e.  $r(\text{Male})=0.367$ ,  $p\text{-value}=0.002$  &  $r=0.433$ ,  $p\text{-value}=0.002$ . Patients with regular BMI had positive slight correlation between NLR and hs-CRP, previously obese and currently obese patients had advantageous low correlation among NLR and hs-CRP sufferers.

Patients with CKD period 7-9 months for them correlation between NLR and hsCRP became slight and for sufferers whose length of CKD turned into 10-12 months amongst them correlation among NLR and hs-CRP became moderate. i.e.  $r$  (7-9 Months)=0.366,  $p$ -value=0.003 &  $r$  (10-12 months) =0.450,  $p$ -value=0.001. Correlation Coefficient ( $r$ )=0.399,  $p$ -value=0.0007: Correlation between NLR & hs-CRP stratified for age of patients.(Table-3).

**Table 1:** Descriptive statistics for NLR

<b>N</b>	<b>115</b>
<b>Mean</b>	2.12
<b>SD</b>	0.35
<b>Min</b>	1.70
<b>Max</b>	3.20

**Table 2:** Descriptive statistics for hs-CRP

<b>N</b>	<b>115</b>
<b>Mean</b>	1.92
<b>SD</b>	0.50
<b>Min</b>	1.30
<b>Max</b>	3.20

**Table 3:** Correlation between NLR and hs-CRP stratified for age

		<b>NLR</b>			
		<b>20-30 Years</b>	<b>31-40 Years</b>	<b>41-50 Years</b>	<b>&gt;50 Years</b>
<b>hs-CRP</b>	<b>r</b>	0.524	0.261	0.499	0.527
	<b>p-value</b>	0.021	0.179	0.011	0.000

**Table 4:** Correlation between NLR and hs-CRP stratified for BMI.

		<b>NLR</b>		
		<b>Normal</b>	<b>Overweight</b>	<b>Obese</b>
<b>hs-CRP</b>	<b>R</b>	0.577	0.294	0.394
	<b>p-value</b>	0.001	0.059	0.011

## Discussion

NLR has been checked in both medical and surgical floor patients it's far a prognostic marker of morbidity and mortality for numerous situations. It was these days associated with all-cause mortality in hemodialysis sufferers.<sup>23</sup> Reddan et al were the first to mention its feasible use as a biomarker in hemodialysis,<sup>7</sup> So the relationship between NLR and various other inflammatory biomarkers in patients on hemodialysis was deter-

mined in a cross-sectional analysis.<sup>21</sup>

NLR is a extensively utilized biomarker of systemic inflammation, which may be extracted easily from CBC has validated to be related to CKD and CKD sufferers has been shown to possess a low-grade inflammatory fame. A hundred and one NLR changed into discovered multiplied in patients now not simplest receiving hemodialysis but also in predialysis term.<sup>22</sup>

On this observe, correlation coefficient showed susceptible fine correlation among hs-CRP and NLR. i.e.  $r$ =0.399,  $p$ -cost=0.000. Okyay GU in his study confirmed that the cost of correlation changed into despite the fact that tremendous, however very susceptible i.e.  $r$ =0.264,  $p$ =zero.002.8 any other examine by way of Ahbap E also showed a bit higher cost of positive correlation, but additionally very vulnerable i.e.  $r$ =0.333,  $p$ =0.01.9 Although consequences of this have a look at is regular with the results of Okyay GU and Ahbap E however correlation coefficient in this look at become higher in comparison to each research. These days in 2017 Jérôme Pineault in his study said that NLR was positively correlated with CRP. i.e.  $r$  = 0.45,  $P$  < .001.10 Correlation coefficient reported by Jérôme Pineault a bit higher as compared to this study. Ahbap et al. reported that patients with higher CRP levels > three mg/d had higher NLR and PLR degrees compared to sufferers with lower CRP degrees \*NLR (three.7±0.2 vs. 2.7 ± 0.2,  $p$ < .01) and PLR one hundred fifty.7±6.9 vs. 111.eight ± 7.zero,  $p$ <0.001).9 Results of this study is up to some extent is in line with the findings of Ahbap et al.

In a study by Turkmen et al., NLR >3.5 became observed associated with increased stage of TNF- $\alpha$  however now not with CRP and IL-6 in sufferers with ESRD.<sup>7</sup> Findings of Turkmen et al. totally contradicts the effects of this take a look at as on this examine susceptible but high quality correlation was seen among hs-CRP and NLR. Stratification of age, gender, BMI and length of CKD changed into performed to manipulate these impact modifiers variables Stratification of a lot of these variables confirmed a close relationship among NLR and hs-CRP. Research have now not finished stratification for these variables. As outcomes of this have a look at have generated neighborhood significance for both of these variables and showed moderate fine correlation for every variable. It can be stated that both of those markers can be easily and successfully be used for detection of infection in CKD sufferers. Detection of increase in NLR is pretty cheap and time saving (quick) technique for assessment of inflammation. There are a few

researches showed approximately N/L ratio and its comparison with other inflammatory markers in patients with CKD. Considering N/L ratio can tell us whole results of blood sample in CKD patients. Some inflammatory markers (CRP and fibrinogen), but not all, are measured in routine clinical practice to estimate the likelihood of the presence of atherosclerotic lesions. In this regard, increasing evidence has shown that white blood cell counts and subtypes are reliable markers of inflammation.<sup>13</sup> Specifically, NLR, a rapid and simple method for assessing inflammatory status calculated as the ratio of absolute neutrophil count to absolute lymphocyte count, has recently been investigated as a novel predictor of cardiovascular risk.<sup>14</sup>

To date, NLR provides information on the inflammatory state<sup>25</sup> including the effects of neutrophil elevation, secondary to acute inflammation, along with lymphocyte depletion, secondary to stress induced lymphocyte redistribution to lymphoid organs, as well as lymphocyte apoptosis.<sup>15</sup> In fact, lymphopenia has been shown to develop secondary to stress-related cortisol release in patients with myocardial infarction.<sup>16</sup> In this regard, there was a close relationship between altered NLR and worsening prognosis of cardiovascular, metabolic, and inflammatory diseases. The aim of this study was therefore to evaluate the relationship between NLR and carotid atherosclerotic plaques, assessed by carotid doppler.<sup>17-20</sup>

## Conclusion

Consequences of this research by the look had shown superb correlation between NLR and hs-CRP. With each of those markers have the capacity to rule out the continuous subclinical problems as well as can do hazard stratification for patients with CKD.

## Conflict of Interest

*None*

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*None*

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#### **Authors Contribution**

**MAB, HF:** Conceptualization of Project

**HF, TM, KH:** Data Collection

**MQ:** Drafting, Revision

**MAB, HF:** Writing of Manuscript