A Study of Neutrophil/Lymphocyte Ratio in Chronic Kidney Disease

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ABSTRACT

BACKGROUND
Chronic Kidney Disease (CKD) is growing in complexity in both developing and developed countries. Neutrophil to lymphocyte ratio (NLR) plays a vital role in CKD. NLR can be taken as a predictor of future complications. We wanted to measure and study the correlation of NLR with renal parameters in chronic kidney disease.

METHODS
This is a control study conducted over a period of 2 months in Aarupadai Veedu Medical College Hospital, Pondicherry. During this period all consecutive subjects diagnosed with CKD were taken as cases and apparently healthy thirty adults were included as controls. Demographic data, neutrophil count, lymphocyte count, urea, creatinine, and uric acid in controls and cases were collected. The collected data was coded, entered into Microsoft Excel work sheet and exported to SPSS 21. Independent t test was used for test of significance and also correlation was calculated. NLR between controls and cases was also correlated.

RESULTS
The mean age of the study subjects was 60.7. Out of the 64 cases 46 subjects were males and 18 subjects were females; there were 14 male controls and 16 female controls. The ratio of cases to controls was close to 1:2. The mean blood urea level was 88.3 ± 52.6 for cases and 22.1 ± 5.85 for controls. The mean serum creatinine level for cases was 4.7 ± 3.1 and 0.98 ± 0.18 for controls. The mean serum uric acid level was 7.3 ± 0.5 and 3.9 ± 0.5 for cases and controls respectively. The mean difference between these two groups was significant ($p<0.001$). The correlation value between blood urea, serum creatinine & NLR among cases showed a very weak positive correlation.

CONCLUSIONS
Neutrophil Lymphocyte Ratio is simple, reliable indicator of worsening of renal function in CKD.

KEYWORDS
Chronic Kidney Disease (CKD), Neutrophil Leucocytes Ratio (NLR), Urea, Uric Acid

BACKGROUND

Chronic Kidney Disease (CKD) is a growing health complication with a prevalence of 10.8 - 16% in developed and developing countries.[1,2] Persons with CKD are at risk of progressive kidney failure, cardiovascular events, and death.[3,4] Chronic inflammation plays a vital role in the onset and progression of various diseases such as chronic kidney disease (CKD), diabetes mellitus and cardiovascular disease.[5] Patients with CKD intend to have elevated levels of inflammatory mediators.[6] These mediators arouse mesangial and glomerular cells and later cause an increase production and a decrease in the degradation of the mesangial and endothelial extracellular matrix, governing to glomerular hypertension, fibrosis and renal scarring.[7,8] Chronic inflammation is a major factor in progression of CKD so evaluating and mitigating the extent of inflammation is important to constrict the advancement of kidney dysfunction.

Non-microbial inflammation contributes to CKD progression and fibrosis.[9] the neutrophil count reflects inflammation, while the lymphocyte count indicates general stress and nutrition. The neutrophil-to-lymphocyte ratios (NLR) in CKD individuals cater information about their inflammation status.[10] Studies showed that an elevated neutrophil count coupled with a decrease in lymphocyte counts predicts mortality in hemodialysis patients[11] and peritoneal dialysis patient.[12] NLR indicates the rate of stage 4 chronic kidney disease progressing to dialysis.[13] Since NLR is readily available from complete blood count tests, its likeness as a predictor should be investigated in patients with stage 1-4 CKD. Increased NLR has been demonstrated to be related with increased mortality in hemodialysis, peritoneal dialysis, cancer, and acute coronary syndrome patients.[14,15] Whereas at the same time, increased NLR has also been associated with poor prognosis in acute pancreatitis.[16] In our study we have analyzed the correlation of NLR with renal parameters in Chronic Kidney Disease.

METHODS

This study was done as a case control study from September-October 2019 at Department of General Medicine in Aarupadai Veedu Medical College Hospital, Pondicherry. All adults above the age of 18 who were diagnosed to have CKD were included in the study as cases and apparently healthy adults were included as controls. Patients with acute illness and those not willing to give consent were excluded from the study. The collected data was coded, entered into Microsoft excel work sheer and exported to SPSS. Data was analysed using SPSS version 21. Data is presented as percentage in categories and then presented as tables and graphs. Independent t test used for test of significance and also correlation was calculated. NLR was correlated with urea, creatinine and uric acid in controls and cases. We also compared NLR between controls and cases.

RESULTS

Age Group (in years)	Cases (%)	Controls (%)
21 - 30	3 (4.7)	-
31 - 40	5 (7.8)	7 (23.3)
41 - 50	6 (9.4)	9 (30)
51 - 60	16 (25)	9 (30)
61 - 70	18 (28.1)	4 (13.3)
71 - 80	12 (18.75)	1 (3.4)
81 - 90	4 (6.25)	-
Total	64 (100)	30 (100)
Table 1. Age Distribution of Study Population		

In this study it was found that among cases maximum (28.1%) of study population was in the age group of 61 - 70 years and 25% of the study subjects were in the age group of 51 - 60 years. Around 18.75% of the cases were in the age group of 71 - 80 years. The mean age of study population among cases was 60.7 ± 15.25 years. Among controls, 30% each of the study subjects were in the age group of 41 - 50 and 51 - 60 years. Around 23.3% of study subjects were in the age group of 61 - 70 years and the mean age among controls was 50.1 ± 10.95 years.

Gender	Cases (%)	Controls (%)
Males	46 (71.8)	14 (46.7)
Females	18 (28.2)	16 (53.3)
Total	64 (100)	30 (100)
Table 2. Gender Distribution of Study Population		

Around 71.8% of cases were males and 28.2% were females and among controls 53.3% were females and 46.7% were males.

	Cases	Controls	P Value
Mean Blood urea level	88.3 ± 52.6	22.1 ± 5.85	0.001
Mean Serum Creatinine level	4.7 ± 3.1	0.98 ± 0.18	0.001
Mean Serum Uric acid level	7.3 ± 0.5	3.9 ± 0.5	0.001
Table 3. Distribution of Study Population as per Renal Parameters			

In this study it was found that mean blood urea level among cases was 88.3 ± 52.6 mg/dl and among controls it was 22.1 ± 5.85 mg/dl. The difference in the mean blood urea level among both the groups was found to be statistically significant (p value <0.001). In this study it was found that mean serum creatinine among cases was 4.7 ± 3.1 mg/dl and among controls it was 0.98 ± 0.18 mg/dl. The difference in the mean serum creatinine level among both the groups was found to be statistically significant (p value <0.001). In this study it was found that mean serum uric acid among cases was 7.3 ± 0.5 mg/dl and among controls it was 3.9 ± 0.5 mg/dl. The difference in the mean serum uric acid level among both the groups was found to be statistically significant (p value <0.001).

	Cases	Controls	P Value
Mean Neutrophil count	71.1 ± 9.13	56.4 ± 2.88	0.001
Mean Lymphocyte count	25.7 ± 7.6	40.6 ± 3	0.001
Mean Neutrophil/Lymphocyte ratio	3.16 ± 1.74	1.39 ± 0.15	0.001
Table 4. Distribution of Study Population as per Blood Parameters			

In this study it was found that mean neutrophil count among cases was 71.1 ± 9.3 cells per microliter and among controls it was 56.4 ± 2.88 cells per microliter. The difference in the mean neutrophil count among both the groups was found to be statistically significant (p value

<0.001). In this study it was found that mean lymphocyte count among cases was 25.7 ± 7.6 cells per microliter and among controls it was 40.6 ± 3 cells per microliter. The difference in the mean lymphocyte count among both the groups was found to be statistically significant (p value <0.001). In this study it was found that mean neutrophil/Lymphocyte ratio among cases was 3.16 ± 1.74 and among controls it was 1.39 ± 0.15. The difference in the mean neutrophil/Lymphocyte ratio among both the groups was found to be statistically significant (p value <0.001).
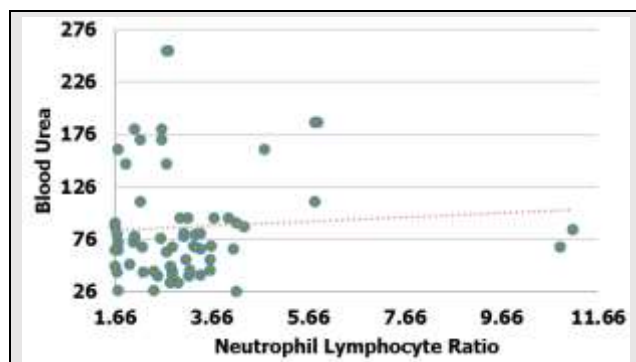

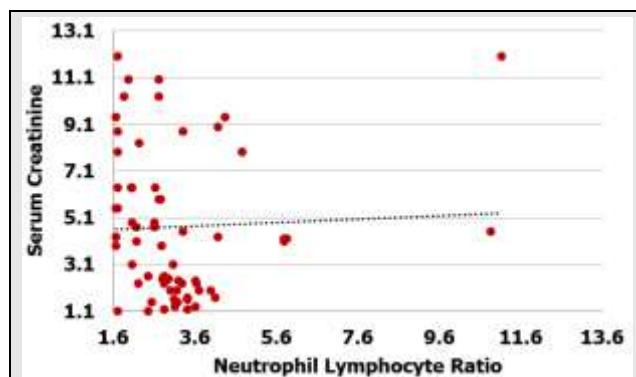*Figure 1. Correlation Between Blood Urea & NLR among Cases*

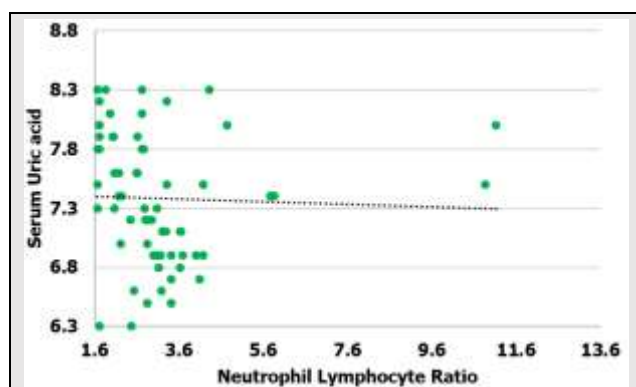*Figure 2. Correlation Between Serum Creatinine & NLR among Cases*

Figure 3. Correlation between Serum Uric Acid and NLR among Cases

The Correlation value between blood Urea & NLR among cases was 0.06. This correlation value denotes a Very weak positive correlation. The Correlation value between Serum creatinine & NLR among cases was 0.04 suggesting a Very Weak positive correlation.

The Correlation value between Serum Uric acid & NLR among cases was -0.03. This denotes a Very weak negative correlation.
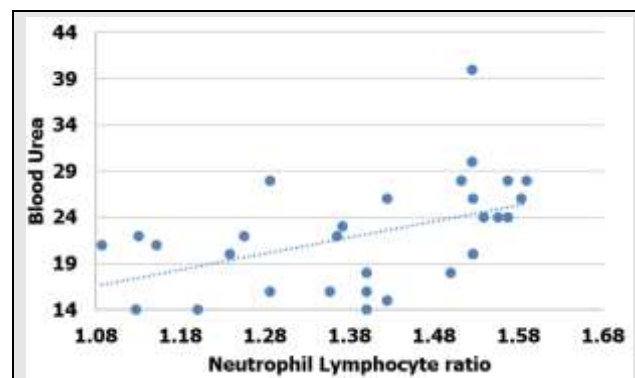

Figure 4. Correlation Between Blood Urea and NLR among Controls

The Correlation value between blood Urea & NLR among control was 0.46 which signifies a Moderate positive correlation.
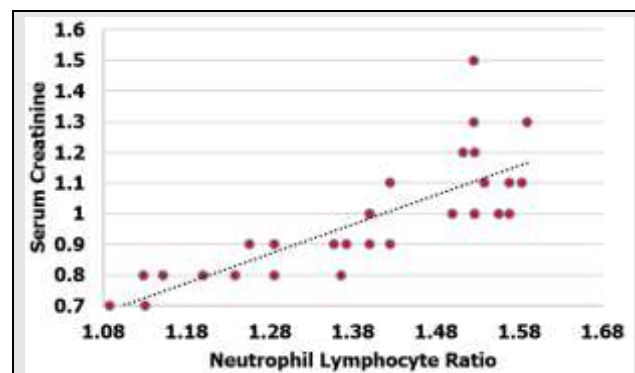

Figure 5. Correlation between Serum Creatinine & NLR among Controls

The Correlation value between Serum Creatinine & NLR among controls was 0.79 signifying a Strong positive correlation.
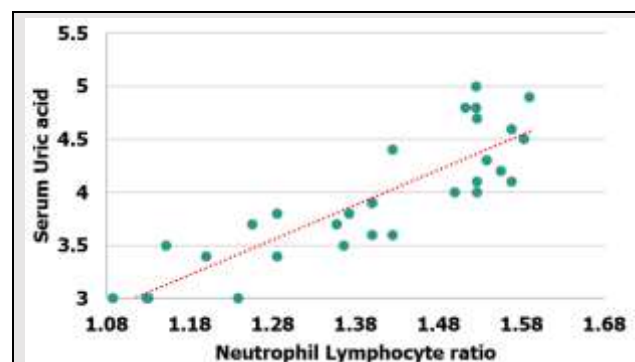

Figure 6. Correlation between Serum Uric Acid and NLR among Controls

The Correlation value between Serum Uric acid & NLR among controls was 0.86. This suggests a Very strong positive correlation.
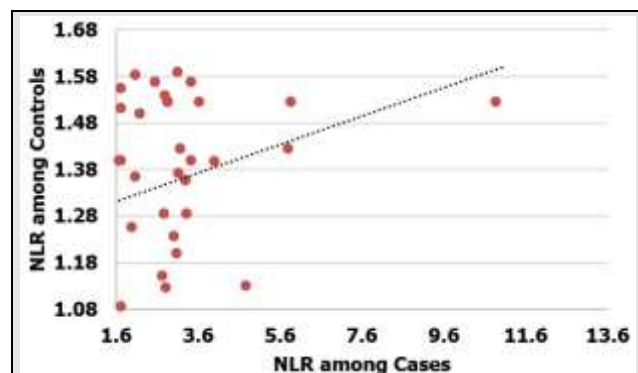
Figure 7. Correlation of NLR among Cases and Controls

The Correlation value between NLR among cases & controls was 0.13 suggesting a Weak Positive Correlation.

DISCUSSION

In the present study the mean age of study population among cases was 60.7 ± 15.25 years and the mean age among controls was 50.1 ± 10.95 years. The present study findings were comparable to a study conducted by R Yoshitomi et al in which the mean age of patients with chronic kidney disease was found to be 68 years with a range of 20 - 94 years.[17] The present study findings differed to another study conducted by Han Li et al in which the mean age of study population was 48.7 ± 10.9 years.[18] Around 71.8% of cases were males and 28.2% were females and among controls 53.3% were females and 46.7% were males. The present study findings were similar to a study by Han Li et al in which the majority of study population were males (55.6%).[18] In our study it can be concluded that mean blood urea, Serum creatinine and serum uric acid levels were significantly higher among cases as compared to healthy subjects. This findings were comparable to a study conducted by Nurhayat O S et al in which the NLR and uric acid were higher in patients with CKD stage 3 than in those with stages 1 and 2 (p = 0.013, p = 0.001 and p = 0.001, respectively).[19] In this study it was found that mean neutrophil/Lymphocyte ratio among cases was 3.16 ± 1.74 and among controls it was 1.39 ± 0.15. The difference in the mean neutrophil/Lymphocyte ratio among both the groups was found to be statistically significant (p value <0.001). The present study findings were similar to a study by Han Li et al in which the mean NLR was 3.36 ± 1.65 among patients with chronic kidney disease.[18] The present study findings differed with a study conducted by Solak Y et al in which Median NLR was 2.81.[20] In this study a weak positive correlation was found between renal parameters and Neutrophil Lymphocyte ratio. This study findings were similar to a study conducted by Kocyigit I et al in which Patients with N/L ratio =3 demonstrated high progression rate compared to patients who had N/L ratio <3 (2.6 ± 1.6 and 5.4 ± 3.3, P<.001).[21] In this study a strong positive correlation was found between Serum Creatinine & NLR among controls. A Very strong positive correlation was found between Serum Uric acid & NLR among controls. The present study findings concurred with a study conducted by Borghi C et al in which serum uric acid was found as a significant marker for the prediction of onset of renal and coronary heart disease.[22] In this study the NLR was significantly higher among cases as compared to controls and the Correlation value between NLR among cases & controls was 0.13 suggesting a Weak Positive Correlation. This finding is comparable to a study conducted by Turkmen et al in which the neutrophil to Lymphocyte ratio was found to be significantly higher in patients with end stage renal disease.[23] The present study findings were also similar to a study conducted by Okyay GU et al in which N/L ratio was significantly higher in each patient group compared to the healthy subjects (p < 0.001).[24]

CONCLUSIONS

Neutrophil Lymphocyte Ratio is simple and reliable indicator of worsening of renal function in CKD. NLR of >1.5 suggests early chronic kidney disease and an NLR of >3 suggests advanced chronic kidney disease.

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