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# Analysis of Mortality in Chronic Kidney Disease patients on maintenance Hemodialysis by neutrophil to lymphocyte ratio, Monocyte to lymphocyte ratio and platelet to lymphocyte ratio in coastal area of rural Puducherry - a cross-sectional study

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## ABSTRACT:

Chronic kidney disease is defined as a condition associated with persistent abnormality in kidney structure and function for more than 3 months duration.CKD is a global problem,16 th most common cause of mortality worldwide effecting 8-16% of population. Neutrophil to lymphocyte ratio, Monocyte to lymphocyte ratio and platelet to lymphocyte ratio help in prediction of outcome in CKD, cardiovascular diseases, rheumatic heart disease. So the present study is done to observe the Neutrophil to lymphocyte ratio, Monocyte to lymphocyte ratio and platelet to lymphocyte ratio help in prediction of outcome in CKD. A cross sectional study 82 patients for a duration of 18 months. Patients of age >18 years who were on hemodialysis for > 3months duration presented to department of Medicine, VMMC, Karaikal were included in the study. The study revealed that on comparison of sensitivity, specificity of NLR, MLR, PLR and PTH with overall mortality rate p-value of MLR with overall mortality rate is 0.039 which is statistically significant and the p-value of PTH with overall mortality is 0.030 which is statistically significant. In the present study, we established an inflammation scoring system by including NLR, MLR and PLR. We found that higher inflammation score was independently associated with all-cause mortality in HD patients. Traditionally used CRP levels doesn't have any significant association with all-cause mortality.

## INTRODUCTION:

Chronic kidney disease is defined as a condition associated with persistent abnormality in kidney structure and function for more than 3 months duration.CKD is a global problem,16 th most common cause of mortality worldwide effecting 8-16% of population. In developed countries CKD is mostly attributed by hypertension and diabetes, but very less patients<6% were aware of their disease in early stages. Over the years there will be rapid decline in kidney functioning finally leading to ESKD where the patient is subjected to hemo dialysis or peritoneal dialysis or renal transplantation to improve the

quality of living. Haemodialysis is most common method of renal replacement therapy. Even though there is wide revolution in the field of dialysis technology still the mortality rate in patients on haemodialysis is higher. It is observed in studies that death rate is around 167 per 1000 patient years (1). About 30-50% of patients on haemodialysis are having chronic inflammation (2). Chronic inflammation can lead to variety of complications like mal nutrition, Anaemia, increased risk of cardiovascular diseases thus increasing the risk of mortality in patients on hemo dialysis. It is observed in various studies that inflammation increases the risk of atherosclerosis, myocardial damage, protein-energy malnutrition, anaemia, renal bone diseases (4-6). With the advancement in science and technology there has been discovery of various prognostic markers in prediction of outcome of many diseases. Neutrophil to lymphocyte ratio, Monocyte to lymphocyte ratio and platelet to lymphocyte ratio help in prediction of outcome in CKD, cardiovascular diseases, rheumatic heart disease. During inflammation variety of cells like neutrophils, lymphocytes, monocytes and various markers levels will be elevated and this chronic inflammatory state exerts effects on blood vessels resulting in increased risk of atherosclerosis. So the present study is done to observe the Neutrophil to lymphocyte ratio, Monocyte to lymphocyte ratio and platelet to lymphocyte ratio help in prediction of outcome in CKD.

**AIM AND OBJECTIVES:**

To evaluate mortality risk in Chronic Kidney Disease patients on Hemodialysis by neutrophil to lymphocyte ratio, Monocyte to lymphocyte ratio and platelet to lymphocyte ratio in coastal area of rural Puducherry.

**MATERIALS AND METHODS:**

A cross sectional study 82 patients for a duration of 18 months. Patients of age >18 years who were on hemodialysis for > 3months duration presented to department of Medicine, VMMC, Karaikal were included in the study. Patients who were on hemodialysis for < 3 months' duration, patients with failed renal transplant and who were on dialysis were excluded from the study. After informed consent NLR, MLR, PLR ratio were calculated and the association of mortality rates with NLR, MLR, PLR was calculated.

RESULTS:

FIGURE 1: AGE DISTRIBUTION OF SRTUDY PARTICIPANTS

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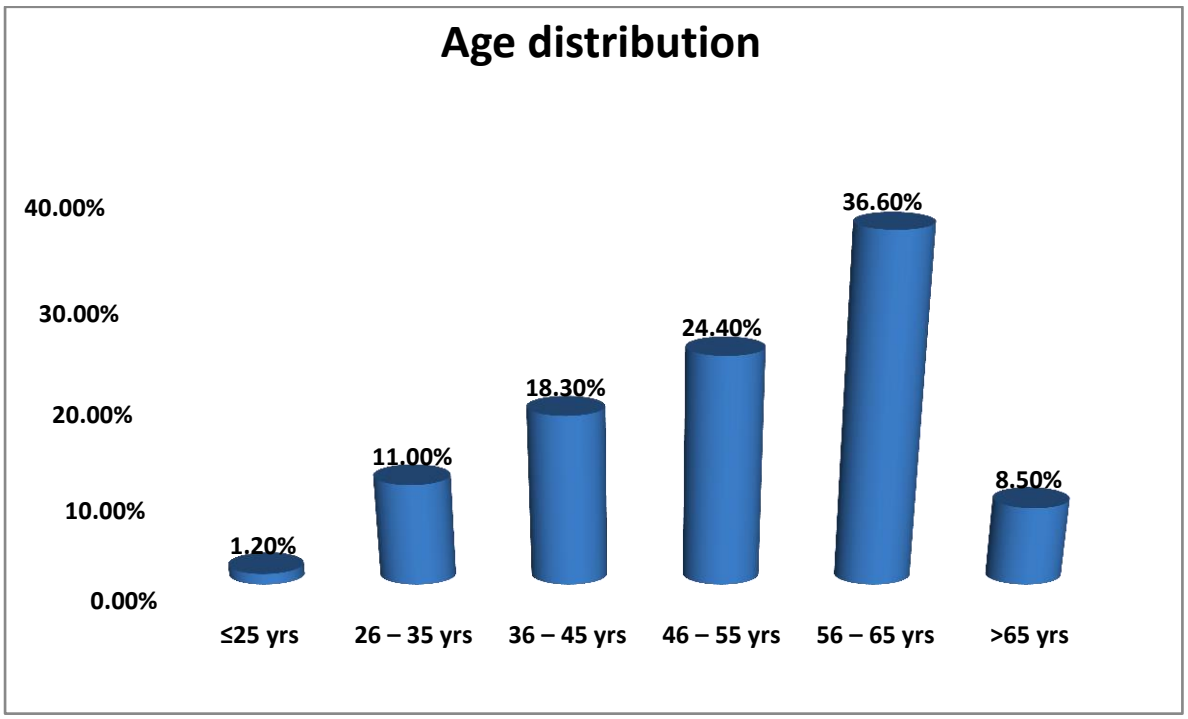


TABLE 1: Baseline Characteristics of Participants stratified by the inflammation Score:

| Variable | The Inflammation Score | | | | P value |
|---|---|---|---|---|---|
| | 0 (n=6) | 1 (n=15) | 2 (n=33) | 3 (n=28) | |
| Gender Male | 6 (7.3%) | 10 (12.2%) | 30 (36.6%) | 23 (28.0%) | 0.123 |
| Gender Female | 0 (0.0%) | 5 (6.1%) | 3 (3.7%) | 5 (6.1%) | |
| Age | 52.33 ± 10.78 | 48.93 ± 14.84 | 52.06 ± 13.48 | 54.18 ± 12.01 | 0.666 |
| BMI | 23.55 ± 2.58 | 24.43 ± 2.60 | 22.92 ± 3.28 | 23.16 ± 3.10 | 0.456 |
| T2DM | 4 (4.9%) | 11 (13.4%) | 29 (35.4%) | 22 (26.8%) | 0.488 |
| SBP | 190.00 ± 40.98 | 172.67 ± 30.58 | 157.57 ± 25.00 | 158.93 ± 22.98 | 0.023 |
| DBP | 103.33 ± 22.50 | 97.33 ± 17.51 | 88.78 ± 13.40 | 87.85 ± 15.24 | 0.053 |
| Hb | 6.38 ± 2.53 | 7.64 ± 2.41 | 8.55 ± 2.69 | 8.08 ± 1.29 | 0.151 |
| WBC | 7.15 ± 3.83 | 13.40 ± 4.72 | 13.79 ± 4.97 | 12.69 ± 5.92 | 0.045 |
| Weight | 53.83 ± 5.45 | 56.46 ± 8.13 | 54.27 ± 10.23 | 53.68 ± 8.73 | 0.807 |
| Creatinine | 6.80 ± 2.01 | 6.38 ± 2.04 | 6.27 ± 2.51 | 7.25 ± 2.66 | 0.460 |
| eGFR | 10.16 ± 4.30 | 10.80 ± 4.67 | 11.54 ± 5.99 | 10.42 ± 6.89 | 0.887 |

| | | | | | |
|---|---|---|---|---|---|
| Height | 150.66 ± 3.26 | 151.40 ± 7.18 | 153.66 ± 8.14 | 152.00 ± 5.42 | 0.595 |
| Serum Urea | 133.17 ± 62.06 | 137.57 ± 43.69 | 135.17 ± 5.36 | 145.75 ± 56.42 | 0.538 |
| Sodium | 137.28 ± 3.34 | 137.44 ± 5.51 | 135.16 ± 5.36 | 135.84 ± 3.78 | 0.426 |
| Potassium | 4.45 ± 0.58 | 4.71 ± 1.23 | 4.49 ± 1.13 | 4.28 ± 0.79 | 0.624 |
| Serum Chloride | 103.82 ± 3.22 | 100.14 ± 4.42 | 100.47 ± 4.41 | 101.29 ± 4.29 | 0.295 |
| Serum Magnesium | 2.00 ± 0.24 | 2.12 ± 0.27 | 2.25 ± 0.39 | 2.42 ± 0.38 | 0.017 |
| Serum Calcium | 8.15 ± 0.85 | 8.36 ± 0.83 | 8.87 ± 0.92 | 9.08 ± 0.89 | 0.026 |
| Serum Phosphate | 3.25 ± 0.87 | 3.75 ± 0.97 | 3.58 ± 0.82 | 3.55 ± 0.68 | 0.637 |
| MAP | 118.16 ± 23.67 | 122.00 ± 20.33 | 111.82 ± 15.42 | 112.78 ± 16.52 | 0.258 |
| Albumin | 3.96 ± 1.07 | 4.25 ± 1.07 | 4.32 ± 0.74 | 3.80 ± 0.89 | 0.127 |
| BUN | 49.15 ± 14.01 | 53.23 ± 25.67 | 56.89 ± 22.64 | 50.54 ± 16.46 | 0.639 |
| Uric Acid | 5.21 ± 1.95 | 7.69 ± 1.58 | 6.88 ± 2.12 | 7.19 ± 2.02 | 0.078 |
| NLR | 2.34 ± 1.01 | 5.07 ± 2.21 | 8.26 ± 3.12 | 9.57 ± 2.53 | 0.0001 |
| MLR | 0.23 ± 0.13 | 0.22 ± 0.09 | 0.77 ± 0.46 | 1.50 ± 0.69 | 0.0001 |
| PLR | 185.48 ± 8.94 | 200.79 ± 21.77 | 196.50 ± 13.00 | 221.02 ± 12.74 | 0.0001 |
| PTH | 61.00 ± 7.18 | 53.20 ± 10.69 | 56.93 ± 8.10 | 47.25 ± 8.47 | 0.0001 |

FIGURE 2: ALL-CAUSE MORTALITY

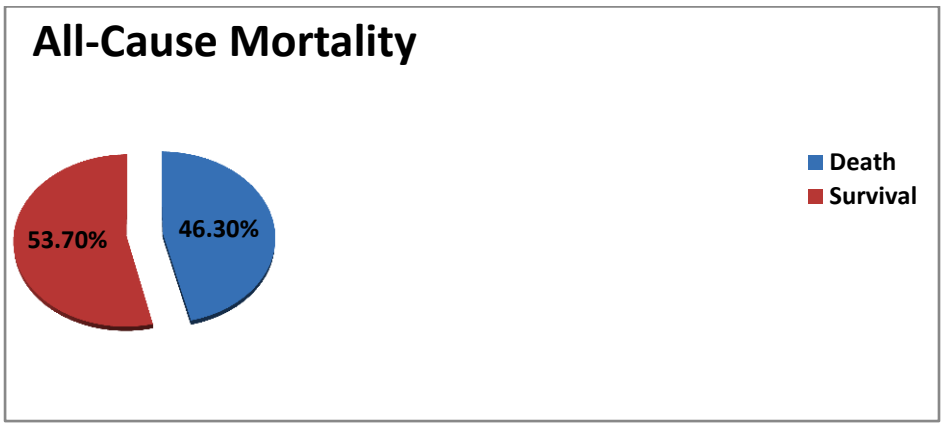


**Table:3 All-Cause mortality with inflammation Score:**

| Variable | Hazard ratio (95%CI) | P value |
|---|---|---|

| | | |
|---|---|---|
| Inflammation 0 | Reference | - |
| Inflammation 1 | 0.58 (0.007 – 0.466) | 0.001 |
| Inflammation 2 | 5.213 (1.998 – 13.606) | 0.001 |
| Inflammation 3 | 1.250 (0.501 – 3.120) | 0.632 |
| **Overall tread** | **P value** | **0.0001** |

Table 4: SENSITIVITY AND SPECIFICITY OF NLR, MLR, PLR, PTH, CPR WITH ALL-CAUSE MORTALITY

| **Variable** | **Cut-off Value** | **Area under curve** | **Sensitivity** | **Specificity** | **P value** |
|---|---|---|---|---|---|
| NLR with All-Cause Mortality | 6.64 | 0.537 | 0.579 | 0.568 | 0.564 |
| MLR with All-Cause Mortality | 0.90 | 0.633 | 0.395 | 0.386 | 0.039 |
| PLR with All-Cause Mortality | 186.40 | 0.48 | 0.842 | 0.841 | 0.616 |
| PTH with All-Cause Mortality | 35.60 | 0.360 | 0.947 | 0.977 | 0.030 |
| CPR with All-Cause Mortality | 2.50 | 0.464 | 0.737 | 0.750 | 0.571 |

FIGURE 3: SENSITIVITY AND SPECIFICITY OF NLR, MLR, PLR, PTH, CPR WITH ALL-CAUSE MORTALITY

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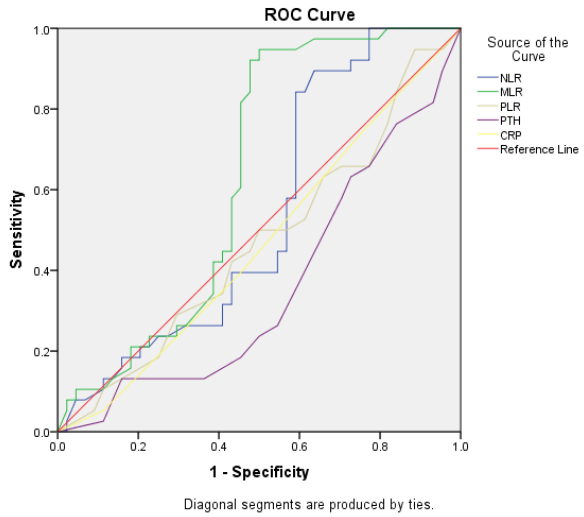


**DISCUSSION:**

The mean age group of study population is 52.23 years with a standard deviation of 12.98 years, out of 82 study participants 1 is less than 25 years,9 patients are between 26-35 years,15 patients were between 36-45 years ,20 patients were in between 46-55 years,30 patients were in between 56-65 years accounting for 36.6% of study population and 7 patients were of >65 years. p-value for age distribution is 0.666 (>0.05) which is statistically insignificant. The mean BMI of patients with inflammatory score 0 is23.55±2.58, the mean BMI of patients with inflammatory score 1 is 24.43±2.60, the mean BMI of patients with inflammatory score 2 is22.92±3.28, the mean BMI of patients with inflammatory score 2 is 23.16±3.10, p-value is 0.456 which is statistically insignificant.4 patients with inflammatory score 0 ,11 patients with inflammatory score 1,29 patients with inflammatory score2 and 22 patients with inflammatory score 3 has type 2 diabetes *mellitus*, p-value is 0.488 which is statistically insignificant. The mean SBP of the patients with inflammatory score 0 is190±40.95mmHg, mean SBP of patients with inflammatory score 1 is 172.67±30.58mmHg, the mean SBP of the patients with inflammatory score 2 is 153.66±8.14mmHg, mean SBP of patients with inflammatory score 3 is 152.00±5.42mmHg. On comparison of SBP with inflammatory scores p-value is0.023 which is statistically significant. The mean DBP of the patients with inflammatory score 0 is103±22.50mmHg, mean SBP of patients with inflammatory score 1 is 97.33±17.51, the mean SBP of the patients with inflammatory score 2 is 88.78±13.40, mean SBP of patients with inflammatory score 3 is 87.85±15.24. On comparison of SBP with inflammatory scores p-value is0.053 which is statistically insignificant. On comparison of Hb with inflammatory scores p-value is0.151 which is statistically insignificant. On comparison of WBC with inflammatory scores p-value is0.045 which is statistically significant. On comparison of creatinine with inflammatory scores p-value is0.460 which is statistically insignificant. On comparison of weight with inflammatory scores p-value is0.807 which is statistically insignificant. On comparison of eGFR with inflammatory scores p-value is0.887 which is statistically insignificant. On comparison of height with inflammatory scores p-value is0.595 which is statistically insignificant. On comparison of serum urea with inflammatory scores p-value is0.538 which is statistically insignificant. On comparison of sodium with inflammatory scores p-value is0.426 which is statistically insignificant. On comparison of potassium with inflammatory scores p-value is0.624 which is statistically insignificant. On comparison of serum chloride levels with

inflammatory scores p-value is0.295 which is statistically insignificant. On comparison of serum magnesium levels with inflammatory scores p-value is0.017 which is statistically significant. On comparison of serum calcium levels with inflammatory scores p-value is0.026which is statistically significant. On comparison of serum phosphate with inflammatory scores p-value is0.637 which is statistically insignificant. On comparison of MAP levels with inflammatory scores p-value is0.258 which is statistically insignificant. On comparison serum albumin levels with inflammatory scores p-value is0.127 which is statistically significant. On comparison BUN levels with inflammatory scores p-value is0.639 which is statistically insignificant. On comparison serum uric acid levels with inflammatory scores p-value is0.078 which is statistically insignificant .The mean neutrophil lymphocyte ratio of patients with inflammatory score 0 is 2.34±1.01, the mean neutrophil lymphocyte ratio of patients with inflammatory score 1 is 5.07±2.21, the mean neutrophil lymphocyte ratio of patients with inflammatory score 2 is 8.26±3.12,the mean neutrophil lymphocyte ratio of patients with inflammatory score 3 is 9.57±2.53 ,p-value is 0.0001 which is highly significant statistically. The mean monocyte lymphocyte ratio of patients with inflammatory score 0 is 0.23±0.13, the mean monocyte lymphocyte ratio of patients with inflammatory score 1 is 0.22±0.09, the mean neutrophil lymphocyte ratio of patients with inflammatory score 2 is 0.77±0.46, the mean neutrophil lymphocyte ratio of patients with inflammatory score 3 is 1.50±0.69, p-value is 0.0001 which is highly significant statistically. The mean platelet lymphocyte ratio of patients with inflammatory score 0 is 185.48±8.94, the mean platelet lymphocyte ratio of patients with inflammatory score 1 is 200.79±21.77, the mean neutrophil lymphocyte ratio of patients with inflammatory score 2 is 196.50±13.00, the mean neutrophil lymphocyte ratio of patients with inflammatory score 3 is 221.02±12.74, p-value is 0.0001 which is highly significant statistically. The mean PTH ratio of patients with inflammatory score 0 is 61.00±7.18, the mean PTH ratio of patients with inflammatory score 1 is 53.20±10.69, the PTH ratio of patients with inflammatory score 2 is 56.93±8.10, the mean PTH ratio of patients with inflammatory score 3 is 47.25±8.47, p-value is 0.0001 which is highly significant statistically. On comparison of p-value of inflammation score 1 and hazard ratio (0.58) it is 0.001 which is statistically significant. On comparison of p-value of inflammation score 2 and hazard ratio (5.213) it is 0.001 which is statistically significant. On comparison of p-value of inflammation score 3 and hazard ratio (1.25) it is 0.632 which is statistically insignificant. On comparison of sensitivity, specificity of NLR, MLR, PLR and PTH with overall mortality rate p-value of MLR with overall mortality rate is 0.039 which is statistically significant and the p-value of PTH with overall mortality is 0.030 which is statistically significant. In the present study, we established an inflammation scoring system by including NLR, MLR and PLR. We found that higher inflammation score was independently associated with all-cause mortality in HD patients. Chronic inflammation is most common in patients with CKD and this attributes to morbidity and death in dialysis patients [16]. Increased in neutrophils, lymphocytes, monocytes are marker of inflammation, and has been reported to predict all-cause of mortality in hemodialysis patients [3]. NLR, MLR and PLR have recently been used as indicators of inflammation. NLR has a greater predictability than total white blood cell count or neutrophil count in cardiovascular disease [8]. Neuen et al. in their study on 170 HD patients with a median follow up of 37 months have observed that NLR was independently associated with both all-cause and cardiovascular mortality. Another study on 268 HD patients showed that high NLR was an independent predictor of all-cause and cardiovascular mortality when adjusted for other risk factors. Besides neutrophil and lymphocytes, monocytes play a key role in inflammation. One study compared

the predictive values of MLR and NLR for mortality in HD patients. This is in correlation with our study where we observed a significant association between MLR and overall mortality rate in patients on hemodialysis. The results demonstrated that MLR was a strong predictor of all-cause and cardiovascular mortality among HD patients. However, NLR was not independently associated with mortality in multivariate Cox models. Platelets release pro-inflammatory mediators, such as chemokines and cytokines where in our study also we have observed significant relation between PTH and overall mortality.

CONCLUSION:

In our study we observed that the all-cause mortality of CKD patients is associated with higher inflammatory score i.e. a combination of NLR, MLR, PLR.However traditionally used CRP levels doesn't have any significant association with all cause mortality. Further studies are needed to be done in future to evaluate the impact of different treatment modalities on MLR, PLR and NLR and its prognostic outcome in CKD

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