

# Prognostic Value of the Platelet-to Lymphocyte Ratio on Cardiovascular Complications in Chronic Hemodialysis Patients

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*In Internal Medicine*

*By*

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## ***INTRODUCTION***

Chronic kidney disease (CKD) is a global public health problem. With the decline in renal function, patients with end-stage kidney disease (ESKD) can choose hemodialysis (HD), peritoneal dialysis (PD) or kidney transplantation as renal replacement therapy to improve their quality of life. Globally, HD is still the most important renal replacement therapy. With the continuous development and optimization of dialysis technology, the survival time of maintenance hemodialysis (MHD) patients is gradually prolonged. However, even in developed countries, the mortality rate of MHD patients remains high (*Saran et al., 2020*).

Many studies have shown that 30-50 percent (%) of MHD patients have chronic inflammation state (*Chavez Valencia et al., 2017*). Persistent inflammation can lead to a variety of complications, especially cardiovascular disease, malnutrition and anemia, thereby increasing the mortality of MHD patients (*Liao et al., 2022*). Although less than 5% of MHD patients die directly from inflammation, inflammation can interact with a variety of risk factors and has an important impact on the prognosis of MHD patients. Studies have found that inflammation is closely related to high-risk factors of death such as myocardial hypertrophy, ventricular dysfunction, atherosclerosis, protein energy consumption, anemia and renal bone disease (*Akchurin and Kaskel, 2015*). Therefore, the development of inflammation-related indicators has important clinical value for judging the prognosis of MHD patients and guiding early intervention. Recent studies have found that the ratios of different blood cell components are new inflammatory markers, which have good predictive value in the outcome of CKD, cardiovascular disease, rheumatic disease, etc., including platelet-to-lymphocyte ratio (PLR) (*Kurtul and Ornek, 2019*).

Previous studies have inconsistent conclusions about the predictive value of PLR on mortality of HD patients. *Xiang et al., (2108)* suggested that higher PLR is a strong and independent predictor of all-cause and cardiovascular mortality among HD patients. Another study found that PLR could independently predict all-cause mortality in these populations (*Yaprak et al., 2016*).

## ***AIM OF THE STUDY***

We hypothesized that the combination of PLR could form a new indicator for predicting the mortality of HD patients. Therefore, we incorporated PLR into an inflammation scoring system and investigated the value of inflammation score in predicting all-cause and cardiovascular mortality in HD patients.

## ***SUBJECTS AND METHODS***

This current retrospective controlled hospital based study will ***recruiting 60 ESKD patients*** who underwent MHD sessions at the HD unit of Nephrology Department of Minia University Hospital in ***the period from January 2024 to June 2024***. In addition, the study included 20 unrelated adult healthy nonsmoker subjects matched for age, gender, ethnicity and body mass index (BMI) with the HD patients to serve as control group. These subjects were carefully screened for any previous history, symptoms and signs indicative of cardiac, renal or liver diseases, neither of which were be found on both clinical examination and standard laboratory tests. Additionally, all of them were be on a regular diet without drugs or vitamin supplements at the time of the study. They were selected from the medical and paramedical staff member team of the same hospital.

### **Ethical approval and written informed consent:**

An approval of the study will be obtained from Mina University Academic and Ethical Committee. Every patient signed an informed written consent for acceptance of the operation.

### **Inclusion criteria:**

Patients undergoing HD for more than three months who will agree to be included in this study.

### **Exclusion criteria:**

We are going to exclude patients who have:

- Younger than 18 year- old or Older than 75 year-old,
- Patients with positive serum marker of anti-hepatitis C virus (anti-HCV), hepatitis B surface antigen (HBsAg) and human immunodeficiency virus (HIV).
- Alcohol or illicit drug abusers.
- Inflammatory state due to infection,

- Autoimmune diseases,
- Current malignancy or history of malignancy, ➤ Immunosuppressive therapy.

**All the study subjects will be submitted to the following:**

**I) Thorough clinical history:**

It will be taken with special emphasis on age, gender, residence, cigarette smoking, hypertension, diabetes mellitus, stroke history, peripheral vascular disease (PVD) history, dialysis duration and prescribed medications.

**II) Careful examination:**

All body systems were carefully examined with special emphasis on the cardiovascular system examination. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) measurements were taken in the supine position before and after HD session using a sphygmomanometer. In addition, body weight, height and body mass index (BMI) were carefully evaluated and calculated based on dry weight. The BMI equals body weight in kilogram (Kg) ÷ height in square meter (m<sup>2</sup>) (*Keys et al., 1972*).

**III) Dialytic session data**

As the dialysis prescriptions may act as potential confounding factors, intradialytic data were be evaluated for each patient with special emphasis on haemodialysis access, ultrafiltration (UF) volume, Kt/V (K – dialyzer clearance of urea; t – dialysis time; V – volume of distribution of urea) and urea reduction ratio (URR).

**IV) Laboratory Investigations:**

A peripheral overnight fasting period venous blood sample will be withdrawn from each subject after they will be rested in a supine position for 5 min and prior to heparinization in HD patients. The blood sample will be divided into three blood collection tubes, one containing ethylenediamine-tetra acetic acid (EDTA), one tube containing tri-sodium citrate and lastly a plane tube.

- On an EDTA containing tube, 3 ml blood will be used for determination of hemoglobinA1c (HbA1c), parathyroid hormone related protein (PTHrP) and complete blood count (CBC). The white blood cell differentiation will be detected as part of CBC, and then we will calculate platelet-to-lymphocyte ratio

- On a trisodium citrate containing tube, 1.8 ml blood will be used for determination of prothrombin time (PT) and prothrombin concentration (PC).
- On a plane tube, 4 ml blood will be left to be clotted then centrifuged. Expressed serum will be used for determination of fasting serum glucose (FSG) level, fasting serum insulin level, liver function tests (LFTs), creatinine, urea, uric acid, electrolytes [including sodium, potassium, magnesium, phosphorus and calcium], viral markers [including anti-HCV, HBsAg and HIV], iron profile [including Serum iron and total iron binding capacity (TIBC) and transferrin saturation (TSAT)], serum ferritin and high sensitive C -reactive protein (Hs CRP).

After asking the subjects to be fasting for another 4 hours or till the end of HD session, another 4 ml of peripheral venous blood sample will be taken from each subject after they adopted a supine position for 5 min. The blood sample will be collected in a new plane tube and left to be clotted then centrifuged. Expressed serum will be used to assess lipid profile.

## V) Imaging studies

1. **Lateral abdominal radiography:** It will be used to detect abdominal aortic calcifications that are defined as the presence of a longitudinal linear or strip-shaped high-density shadow at the level of the first to fourth lumbar vertebrae (*Wang et al., 2022*).
2. **Bilateral carotid duplex:** The intimal medial thickness (IMT), bilateral peak systolic velocities (PSV) and blood flow volumes will be measured for the common carotid arteries (CCA) and vertebral arteries. At the CCA, hemodynamic variables will be measured at a segment located 2 cm proximal to the bifurcation of the CCA; at the vertebral arteries, variables will be measured at the arterial segment between the transverse processes of the 4<sup>th</sup> and 5<sup>th</sup> cervical vertebrae in the sagittal plane. The diameter of the vessels at each location will be measured at each evaluation. Total cerebral blood flow will be calculated as the sum of the bilateral blood flow volumes in the CCAs and vertebral arteries (*Chung et al., 2015*).
3. **Electrocardiogram (ECG) assessment:** It will be used for detection of arrhythmias and axis deviation
4. **Transthoracic Echocardiogram (TTE) assessment:** It will be used to evaluate the following echocardiographic parameters including: interventricular septum thickness at end-diastole (IVSd), interventricular septum thickness at end-systole (IVSs), left ventricular

internal dimension at end-diastole (LVIDd), left ventricular internal dimension at end-systole (LVIDs), left ventricular posterior wall thickness at end-diastole (LVPWd), left ventricular posterior wall thickness at end-systole (LVPWs), left ventricular fractional shortening (LVFS), left atrium diameter (LAD), aortic root (AO) diameter and the ratio of the left atrial dimension to the aortic annulus dimension (LA/Ao), end-diastolic volume (EDV), end-systolic volume (ESV), left ventricular ejection fraction (LVEF), stroke volume (SV), left ventricular hypertrophy (LVH) and pulmonary arterial systolic pressure (PASP). Furthermore, the valvular structure, function and presence of calcifications will be also evaluated. Valvular calcifications were defined as a brilliant echo of >1 mm in one or more cusps of the aortic or mitral valve or mitral ring. In addition, the presence of aortic atherosclerotic changes will be evaluated (*Ellouali. et al., 2015*).

## **VI) Outcomes**

Cardiovascular events including non-fatal myocardial infarction, unstable angina, cerebrovascular events (intraparenchymal hemorrhage, subarachnoid hemorrhage, cerebral infarction), hospitalization for congestive heart failure, serious cardiac arrhythmia (resuscitated cardiac arrest, ventricular fibrillation, sustained ventricular tachycardia, paroxysmal ventricular tachycardia, an initial episode of atrial fibrillation or flutter, severe bradycardia or heart block) and peripheral arterial diseases will be evaluated after 6 months and confirmed by medical records.

### **Statistical analysis:**

Data were analyzed using Statistical Package for Social Science (SPSS) version 25.0. Quantitative data were expressed as mean  $\pm$  standard deviation (SD). Qualitative data were expressed as frequency and percentage.

For all analyses, statistical significance will be defined as p-values  $\leq 0.05$ .

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