Section: Medicine

Original Research Article

RENAL FUNCTION AND PROTEINURIA IN PATIENTS WITH POLYCYTHEMIA: A CROSS-SECTIONAL OBSERVATIONAL STUDY FROM A TERTIARY CARE CENTRE

Durga Padmanabhan[1], Sreevidhya K R[1]

[1]Assistant Professor, Department of Medicine, Government Medical College, Kottayam, Kerala, India.

Received *: 17/05/2026*
Received in revised form *: 28/06/2026*
Accepted *: 13/07/2026*

Corresponding Author:
Dr. Sreevidhya KR
Assistant Professor, Department of Medicine, Government Medical College, Kottayam, Kerala, India.
Email: sreevidhyakr86@gmail.com

DOI: 10.70034/ijmedph.2026.3.99

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2026; 16 (3); 606-611

ABSTRACT

Background: Polycythemia, encompassing both primary and secondary forms, is characterized by an increase in red blood cell mass resulting in elevated hemoglobin and hematocrit levels. Hyperviscosity, endothelial dysfunction, and thrombotic complications associated with polycythemia may adversely affect renal microcirculation, predisposing patients to chronic kidney disease and proteinuria. However, evidence regarding the burden of renal involvement among patients with polycythemia remains limited, particularly from developing countries. Early identification of renal impairment may facilitate timely intervention and improve long-term renal outcomes. The objective is to determine the prevalence of renal dysfunction and proteinuria among patients with polycythemia and to evaluate the relationship between hemoglobin concentration and renal function.

Materials and Methods: A hospital-based cross-sectional observational study was conducted among 93 adult patients diagnosed with polycythemia attending the Departments of General Medicine and Hematology of a tertiary care teaching hospital. Clinical characteristics, laboratory investigations, serum creatinine, estimated glomerular filtration rate (eGFR), urine protein-creatinine ratio (UPCR), hemoglobin, hematocrit, and other hematological parameters were recorded. Renal dysfunction was defined as eGFR <60 mL/min/1.73 m². Pearson correlation analysis was performed to evaluate the relationship between hemoglobin level and renal parameters. Statistical significance was considered at $p<0.05$.

Results: Among the 93 participants, the mean age was 54.3±12.7 years. Renal dysfunction was identified in 38.7% of patients, while clinically significant proteinuria was observed in 23.7%. Mean hemoglobin concentration was 18.8±1.9 g/dL and mean eGFR was 68.7±23.7 mL/min/1.73 m². Hemoglobin level demonstrated a statistically significant negative correlation with eGFR ($r=-0.222$, $p=0.032$), suggesting declining renal function with increasing hemoglobin concentration. No statistically significant correlation was observed between hemoglobin concentration and proteinuria ($r=0.167$, $p=0.110$).

Conclusion: Renal dysfunction and proteinuria are relatively common among patients with polycythemia. Increasing hemoglobin concentration appears to be associated with declining renal function. Routine renal evaluation including eGFR estimation and proteinuria assessment should be considered during the clinical follow-up of patients with polycythemia for early detection of kidney involvement.

Keywords: Polycythemia, Chronic kidney disease, Proteinuria, Estimated glomerular filtration rate, Hemoglobin, Renal dysfunction.

INTRODUCTION

Polycythemia is a hematological disorder characterized by an abnormal increase in circulating red blood cell mass, resulting in elevated hemoglobin concentration and hematocrit. The disorder is broadly classified into primary polycythemia, most commonly polycythemia vera, and secondary polycythemia resulting from chronic hypoxia, erythropoietin-secreting tumors, congenital disorders, or other systemic diseases.[1] Recent International Consensus Classification criteria emphasize molecular abnormalities, particularly the presence of JAK2 mutations, in the diagnosis of polycythemia vera. Despite advances in diagnosis and management, long-term complications remain a major contributor to morbidity and mortality among affected patients.[2]

The kidney plays a central role in erythropoiesis through the production of erythropoietin by peritubular fibroblasts. Consequently, renal disorders may both contribute to and result from polycythemia. Conversely, persistent erythrocytosis increases blood viscosity, impairs renal microvascular circulation, and predisposes patients to glomerular ischemia, endothelial injury, and thrombotic microangiopathy. These pathophysiological alterations may eventually lead to chronic kidney disease and progressive proteinuria.[3]

Renal manifestations in polycythemia have increasingly been recognized over the past decade. Several studies have demonstrated a higher prevalence of chronic kidney disease among patients with polycythemia vera than among those with secondary erythrocytosis.[2,3,4] Histopathological studies have described glomerular hypertrophy, focal segmental glomerulosclerosis, mesangial proliferation, chronic thrombotic microangiopathy, and ischemic glomerular changes in these patients.[4] Proteinuria has emerged as one of the earliest clinical indicators of renal involvement and may precede overt deterioration in renal function.

The mechanisms underlying renal injury in polycythemia are multifactorial. Increased hematocrit results in elevated blood viscosity, reducing renal plasma flow and oxygen delivery. Chronic endothelial activation promotes platelet aggregation and intrarenal thrombosis, while prolonged glomerular hyperfiltration and increased intraglomerular pressure contribute to structural damage. In patients with polycythemia vera, persistent activation of the JAK-STAT signaling pathway further amplifies inflammatory and fibrotic pathways, accelerating renal injury.[4]

The present study was therefore undertaken to determine the prevalence of renal dysfunction and proteinuria among adult patients with polycythemia attending a tertiary care teaching hospital and to evaluate the relationship between hemoglobin concentration and renal function.

MATERIALS AND METHODS

A hospital-based cross-sectional observational study was conducted to assess renal function and proteinuria among adult patients with polycythemia. The study was carried out in the Departments of General Medicine and Hematology of Government Medical College, Kottayam, Kerala, India. Patients attending outpatient clinics as well as those admitted to medical wards during the study period were screened for eligibility. The study was conducted over a period of three months after obtaining approval from the Institutional Review Board. Adult patients aged 18 years and above diagnosed with either primary or secondary polycythemia were included in the study.

Inclusion Criteria

- Adults aged ≥18 years.
- Diagnosed cases of primary or secondary polycythemia.
- Hemoglobin concentration >16.5 g/dL in men or >16.0 g/dL in women.

Exclusion Criteria

Patients with conditions that could independently influence renal function were excluded, including:

- Sepsis
- Long-standing diabetes mellitus (>10 years)
- Long-standing hypertension (>10 years)
- Acute coronary syndrome with heart failure
- Multiple myeloma
- Previously diagnosed nephrotic syndrome
- Previously diagnosed nephritic syndrome
- Current use of nephrotoxic drugs
- Use of sodium-glucose cotransporter-2 inhibitors

Sample Size

Sample size was estimated using the formula:

$$n = 4pq/d^2$$

Assuming a prevalence of renal impairment of 13.1% among patients with polycythemia reported in previous literature[5], with an absolute precision of 7%, the calculated minimum sample size was 93 participants, all of whom were enrolled in the present study.

Data Collection

Following written informed consent, demographic details, clinical history, comorbidities, medication history, duration of disease, blood pressure, anthropometric measurements, and physical examination findings were recorded using a structured proforma. Laboratory investigations included complete blood count, serum creatinine, hematocrit, hemoglobin concentration, urine protein-creatinine ratio, and renal ultrasonography where indicated. Estimated glomerular filtration rate (eGFR) was calculated using the Cockcroft–Gault equation.

Outcome Measures

The primary outcomes included:

- Prevalence of renal dysfunction.
- Prevalence of proteinuria.

Secondary outcomes included:

- Correlation between hemoglobin concentration and estimated glomerular filtration rate.
- Correlation between hemoglobin concentration and urine protein-creatinine ratio.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using IBM SPSS Statistics software (Version 26.0). Continuous variables were expressed as mean ± standard deviation or median with interquartile range depending on normality of distribution. Categorical variables were summarized as frequencies and percentages. Pearson's correlation coefficient was used to assess relationships between hemoglobin concentration and renal parameters. Independent sample t-test or Chi-square test was applied wherever appropriate. A p-value <0.05 was considered statistically significant.

Ethical Considerations

The study was approved by the Institutional Review Board of Government Medical College, Kottayam. Written informed consent was obtained from every participant before enrollment. Confidentiality of patient information was maintained throughout the study, and all procedures were performed in accordance with the ethical principles of the Declaration of Helsinki.

RESULTS

Table 1: Baseline demographic and clinical characteristics of study participants (n = 93)

Variable	Value
Number of participants	93
Age (years), Mean ± SD	54.27 ± 12.72
Age range (years)	24–84
Male	61 (65.6%)
Female	32 (34.4%)
Body weight (kg), Mean ± SD	66.4 ± 10.8
Duration of polycythemia (years), Mean ± SD	4.6 ± 2.9
Hemoglobin (g/dL), Mean ± SD	18.8 ± 1.9
Hematocrit (%), Mean ± SD	56.4 ± 5.3
Serum creatinine (mg/dL), Mean ± SD	1.17 ± 0.37
eGFR (mL/min/1.73 m²), Mean ± SD	68.73 ± 23.68
Urine protein-creatinine ratio	0.11 ± 0.08

A total of 93 patients with polycythemia were included in the study. The mean age of the study population was 54.27 ± 12.72 years (range: 24–84 years). Male participants constituted 65.6% (61/93) of the study population, while females accounted for 34.4% (32/93). The mean hemoglobin concentration was 18.8 ± 1.9 g/dL, mean estimated glomerular filtration rate (eGFR) was 68.73 ± 23.68 mL/min/1.73 m², mean serum creatinine was 1.17 ± 0.37 mg/dL, and mean urine protein-creatinine ratio (UPCR) was 0.11 ± 0.08.

The study population predominantly consisted of middle-aged and elderly individuals with a male predominance. Laboratory findings confirmed marked erythrocytosis, while renal function parameters demonstrated considerable inter-individual variability.

Table 2: Age distribution of study participants

Age group (years)	Number	Percentage
<40	14	15.1
40–59	42	45.2
≥60	37	39.8

Nearly 85% of patients were aged 40 years or older, indicating that polycythemia requiring tertiary care evaluation was predominantly observed among middle-aged and elderly adults.

Table 3: Prevalence of renal dysfunction and proteinuria

Variable	Number	Percentage
Renal dysfunction (eGFR <60 mL/min/1.73 m²)	**36**	**38.7%**
Normal renal function	57	61.3%
Significant proteinuria (UPCR >0.15)	**22**	**23.7%**
No significant proteinuria	71	76.3%

More than one-third of patients demonstrated impaired renal function, while approximately one-quarter exhibited clinically significant proteinuria. These findings suggest that renal involvement is relatively common among patients with polycythemia.

Table 4: Distribution of renal dysfunction according to age group

Age group	Normal eGFR	Renal dysfunction	Total
<40 years	11	3	14
40–59 years	33	9	42
≥60 years	13	24	37
Total	57	36	93

Older age was associated with a substantially greater proportion of renal dysfunction. Approximately 65% of patients aged ≥60 years had reduced eGFR compared with 21% among patients younger than 40 years, indicating an age-related decline in renal function.

Table 5: Descriptive statistics of hematological and renal parameters

Parameter	Mean ± SD	Median (IQR)	Minimum	Maximum
Hemoglobin (g/dL)	18.8 ± 1.9	18.7	16.0	24.2
Hematocrit (%)	56.4 ± 5.3	56.0	46	69
Serum creatinine (mg/dL)	1.17 ± 0.37	1.10	0.6	2.3
eGFR (mL/min/1.73m²)	68.73 ± 23.68	68	17	124
UPCR	0.11 ± 0.08	0.09	0.01	0.40

The study population demonstrated elevated hemoglobin and hematocrit levels consistent with polycythemia. Considerable variability in eGFR suggests heterogeneous renal involvement among patients.

Table 6: Correlation between hemoglobin and renal parameters

Variable	Pearson's r	p-value
Hemoglobin vs eGFR	−0.222	0.032
Hemoglobin vs UPCR	0.167	0.110

A statistically significant weak negative correlation was observed between hemoglobin concentration and eGFR (r = −0.222, p = 0.032), indicating that increasing hemoglobin levels were associated with declining renal function. No statistically significant correlation was observed between hemoglobin concentration and urine protein-creatinine ratio (p = 0.110).

Table 7: Summary of renal abnormalities among study participants

Renal parameter	Finding
Mean serum creatinine	1.17 mg/dL
Mean eGFR	68.73 mL/min/1.73 m²
Renal dysfunction prevalence	38.7%
Proteinuria prevalence	23.7%
Significant Hb-eGFR correlation	Yes
Significant Hb-UPCR correlation	No

Renal impairment was substantially more frequent than overt proteinuria. Declining eGFR appeared to be associated with increasing hemoglobin concentration, supporting the hypothesis that greater erythrocytosis may adversely influence renal function.

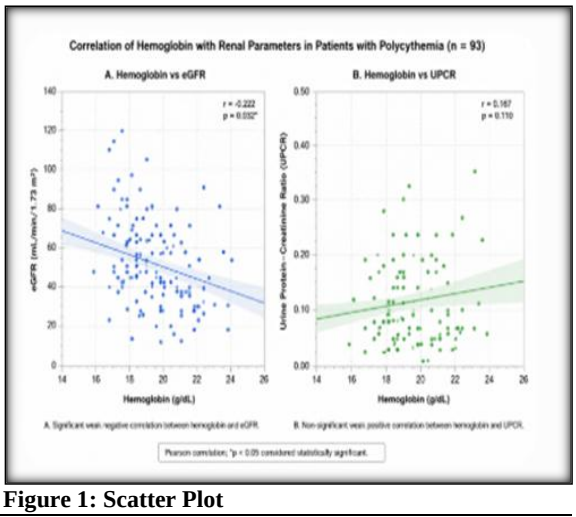

Figure 1: Scatter Plot

DISCUSSION

The present cross-sectional observational study evaluated renal function and proteinuria among 93 adult patients with polycythemia attending a tertiary care teaching hospital. The principal findings demonstrated that renal dysfunction was present in 38.7% of patients, while 23.7% exhibited clinically significant proteinuria. Furthermore, increasing hemoglobin concentration showed a statistically significant inverse relationship with estimated glomerular filtration rate (eGFR), whereas no significant association was observed between hemoglobin concentration and proteinuria. These observations indicate that renal involvement is a relatively common but frequently under-recognized complication of polycythemia and emphasize the importance of routine renal surveillance in this patient population.

One of the most important findings of the present study was that more than one-third of patients demonstrated reduced renal function. Although the

majority of patients remained asymptomatic, the observed prevalence indicates that renal impairment may occur much earlier than clinically apparent kidney disease. These findings support the concept that chronic kidney injury should be regarded as an important systemic manifestation of polycythemia rather than merely a coincidental comorbidity.

Our findings are consistent with the matched case-control study conducted by Krečak et al. (2023),[6] who demonstrated that chronic kidney disease occurred significantly more frequently among patients with polycythemia vera than among individuals with secondary polycythemia. Their study emphasized that renal dysfunction represents an independent complication of myeloproliferative disorders rather than simply reflecting aging or traditional cardiovascular risk factors. The higher prevalence observed in our study may be attributable to differences in patient selection, referral bias associated with tertiary care hospitals, inclusion of older patients, and ethnic differences in disease characteristics.

Similarly, Lucijanić et al. (2022),[5] evaluated patients with polycythemia vera and reported that impaired renal function adversely influenced long-term clinical outcomes and thrombotic risk. Their observations suggested that reduced kidney function is associated with increased disease severity and poorer prognosis.[2] Our findings reinforce these observations by demonstrating a considerable burden of renal dysfunction among Indian patients with polycythemia.

Proteinuria represents one of the earliest manifestations of glomerular injury and often precedes measurable decline in glomerular filtration rate. In the present study, approximately one-fourth of participants demonstrated clinically significant proteinuria. Although lower than the prevalence of reduced eGFR, this finding nevertheless indicates substantial glomerular involvement.

Several pathological mechanisms may explain proteinuria in polycythemia. Increased blood viscosity produces intraglomerular hypertension and endothelial injury, leading to disruption of the glomerular filtration barrier. Chronic ischemia stimulates mesangial proliferation and extracellular matrix deposition, eventually resulting in increased urinary protein excretion. Recurrent microvascular thrombosis may further aggravate glomerular injury by causing focal ischemic damage.

Our findings correspond well with those reported by Yang et al. (2022),[7] who analyzed renal biopsies from patients with polycythemia vera presenting with proteinuria. Their study demonstrated pathological findings including IgA nephropathy, focal segmental glomerulosclerosis, glomerular hypertrophy, chronic ischemic injury, and mesangial proliferative glomerulopathy. These pathological observations provide biological support for the proteinuria observed in our study.

Likewise, Büttner-Herold et al. (2021),[9] evaluated renal manifestations among patients with myeloproliferative neoplasms and found that proteinuria occurred in more than 90% of biopsy-proven renal disease cases. Histological examination consistently demonstrated mesangial sclerosis, chronic thrombotic microangiopathy, glomerular enlargement, and intracapillary hematopoietic cell infiltration. Their findings highlight that proteinuria should not be considered a benign laboratory abnormality but rather an indicator of progressive renal injury.

Perhaps the most clinically relevant finding of the present study was the statistically significant negative correlation between hemoglobin concentration and eGFR. Although the observed correlation coefficient was relatively modest ($r = -0.222$), it nevertheless suggests that increasing erythrocytosis may contribute to progressive deterioration in renal function.

Our findings are also supported by observations reported by Paule et al,[8] who described MPN-related glomerulopathy as a distinct clinicopathological entity characterized by heavy proteinuria, renal insufficiency, chronic thrombotic microangiopathy, and progressive glomerulosclerosis. Their study emphasized that chronic erythrocytosis directly contributes to renal injury rather than serving merely as an associated finding.

Experimental studies have demonstrated that increasing hematocrit beyond physiological levels results in exponential increases in blood viscosity rather than a simple linear relationship. Consequently, relatively small increases in hemoglobin concentration may produce disproportionately greater impairment in renal perfusion, particularly in older individuals and patients with pre-existing vascular disease.[10,11]

Although patients with higher hemoglobin concentrations tended to have slightly higher urine protein-creatinine ratios, the observed association did not reach statistical significance.Several explanations may account for this finding. First, proteinuria reflects glomerular permeability rather than overall renal filtration capacity. Structural glomerular injury may require prolonged exposure to hyperviscosity before measurable protein leakage develops. Consequently, reductions in eGFR may become evident before clinically significant proteinuria appears. Second, proteinuria exhibits considerable day-to-day biological variability and may be influenced by hydration status, exercise, dietary protein intake, urinary tract infection, and transient hemodynamic changes. Such variability may reduce the strength of observed correlations in cross-sectional studies.[11,12] Third, renal dysfunction in polycythemia is multifactorial. Age-related nephron loss, hypertension, smoking, vascular disease, chronic inflammation, and genetic susceptibility all contribute to proteinuria independently of hemoglobin concentration.

Clinical significance

The clinical implications of the present study are considerable. Most patients with reduced eGFR were asymptomatic, suggesting that renal impairment frequently remains undiagnosed until advanced stages. Routine assessment of serum creatinine alone may underestimate early renal injury because creatinine levels often remain within the normal range despite substantial nephron loss.

Therefore, routine estimation of eGFR together with quantitative assessment of proteinuria should become an integral component of the clinical evaluation of patients with polycythemia. Identification of renal involvement at an early stage permits optimization of hydration, aggressive control of hematocrit, management of cardiovascular risk factors, avoidance of nephrotoxic medications, and timely nephrology referral where appropriate.

The findings also support maintaining strict hematocrit targets in patients with polycythemia vera. Adequate cytoreductive therapy and therapeutic phlebotomy may reduce hyperviscosity-related renal injury and potentially preserve long-term kidney function.

Limitations

The study was conducted at a single tertiary care center, potentially introducing referral bias and limiting generalizability. The cross-sectional design precludes causal inference between elevated hemoglobin concentration and declining renal function. The relatively modest sample size may have reduced statistical power to detect weaker correlations, particularly with proteinuria. Longitudinal follow-up was not available; therefore, progression of renal dysfunction over time could not be assessed. Additionally, advanced biomarkers of renal injury such as cystatin C, urinary albumin-to-creatinine ratio, neutrophil gelatinase-associated lipocalin (NGAL), and kidney injury molecule-1 (KIM-1) were not evaluated.

CONCLUSION

The present study demonstrated that renal involvement is a frequent yet often under-recognized complication among patients with polycythemia. More than one-third of the study participants had impaired renal function, while nearly one-quarter exhibited clinically significant proteinuria, highlighting the substantial burden of kidney involvement in this population. A statistically significant inverse correlation between hemoglobin concentration and estimated glomerular filtration rate (eGFR) was observed, indicating that increasing erythrocytosis is associated with progressive deterioration in renal function. However, no significant association was found between hemoglobin concentration and proteinuria, suggesting that factors beyond elevated hemoglobin levels may contribute to glomerular injury. These findings emphasize the importance of routine assessment of renal function, including eGFR estimation and urine protein quantification, as part of the comprehensive evaluation of patients with polycythemia. Early identification of renal abnormalities may facilitate timely therapeutic interventions, prevent progression to chronic kidney disease, and improve long-term clinical outcomes.

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