International Journal of Medical Science and Health Research

Vol.9, No. 03; 2025

ISSN: 2581-3366

Diagnostic Value of Reticulocyte Hemoglobin Content (Ret-he) in Iron Deficiency Anemia Among Chronically Hemodialyzed Patients

Dr J.FARAHAT, Dr I.ELMACHI , Pr. H.ELYAHYAOUI, Pr. M.CHAKOUR
Correspondence: AVICENNA military hospital, Adresse: JXMH+VFW, Av. Al Mouqaouama, Marrakech 40000, MOROCCO
Téléphone :+212 5244-31001

doi: 10.51505/ijmshr.2025.9305 URL: http://dx.doi.org/10.51505/ijmshr.2025.9305

Received: May 04, 2025 Accepted: May 14, 2025 Online Published: May 30, 2025

Abstract

Iron deficiency anemia is a common complication in patients with chronic kidney disease (CKD) undergoing hemodialysis. This study aims to assess the relevance of measuring reticulocyte hemoglobin content (Ret-He) as a diagnostic marker of iron deficiency, compared to classical biochemical markers. A prospective descriptive study was conducted on 50 patients undergoing chronic hemodialysis in Marrakech. The results showed a strong positive correlation between Ret-He and the transferrin saturation coefficient (TSAT), and outstanding diagnostic performance of Ret-He in detecting iron deficiency anemia, independently of inflammatory processes.

Keywords: Ret-He, iron deficiency anemia, hemodialysis, chronic kidney disease, iron status.

1. Introduction

Chronic kidney disease (CKD) is increasingly prevalent, affecting approximately 10% of the global adult population. This progressive condition is marked by irreversible deterioration of kidney function, leading at an advanced stage to toxin accumulation and disruption of internal homeostasis. One of the most common consequences of CKD is anemia, especially in end-stage patients requiring regular hemodialysis. This anemia is multifactorial but is primarily due to a lack of erythropoietin (EPO) production by the kidneys and to iron deficiency, which is common in this context of chronic inflammation.

Diagnosing iron deficiency remains complex. Traditional biochemical markers such as serum ferritin and transferrin saturation (TSAT) are often skewed by the systemic chronic inflammation associated with CKD. This makes interpretation difficult and may lead to mismanagement, particularly by delaying or misadjusting iron supplementation.

In this context, measuring the hemoglobin content in reticulocytes (Ret-He) emerges as a relevant and reliable biomarker. Ret-He dynamically and directly evaluates the availability of

Vol.9, No. 03; 2025

ISSN: 2581-3366

iron for erythropoiesis, without being influenced by inflammatory processes. It is obtained directly through modern hematology analyzers at no additional cost.

The goal of this study is to assess the diagnostic value of Ret-He as a reliable parameter for iron deficiency anemia in chronically hemodialyzed patients.

2. Methods

Study Design
Quantitative descriptive study with prospective data collection.Study Setting and Population
The study included 50 patients undergoing chronic hemodialysis between January and April 2023 at the Avicenne Military Hospital in Marrakech and three private dialysis centers (Atlas, Targa, Massira).

Inclusion Criteria
Adult patients under chronic hemodialysis, receiving EPO and/or iron supplementation, and having had a complete iron status evaluation.

Biological Parameters Analyzed
- Ret-He (pg)
- Ferritin (ng/mL)
- TSAT (%)
- Hemoglobin (Hb), Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH)

Equipment
Tests were performed using Sysmex XN-1500 analyzers (hematology parameters) and Siemens Atellica Solution (iron status).Statistical Analysis
Correlations between Ret-He and other parameters were calculated (Pearson test). Diagnostic performance was evaluated using a ROC curve.

3. Results

A significant positive correlation was found between Ret-He and TSAT ($r = 0.71$, $p < 0.001$), whereas a non-significant negative correlation was observed with ferritin ($r = -0.242$, $p = 0.09$).

Vol.9, No. 03; 2025

ISSN: 2581-3366

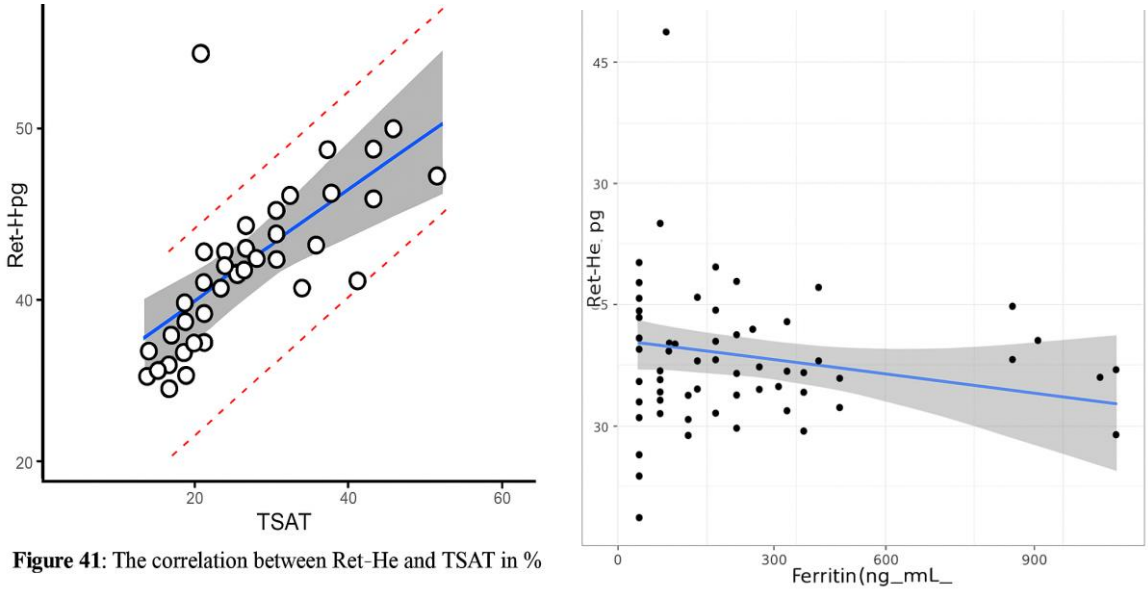


Figure 41: The correlation between Ret-He and TSAT in %

ROC curve analysis revealed the diagnostic performance of Ret-He in detecting iron deficiency anemia. The area under the curve (AUC) was 0.937, indicating excellent accuracy. The optimal threshold was 28.1 pg, with a sensitivity of 87.18% and a specificity of 100%. These results suggest that Ret-He can reliably differentiate iron-deficiency anemic patients from others.

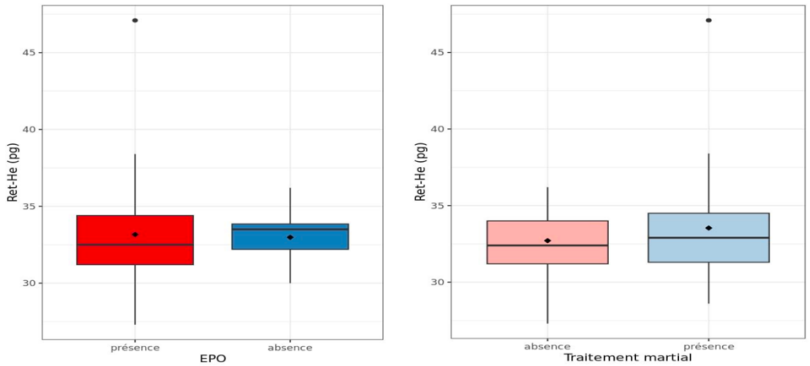
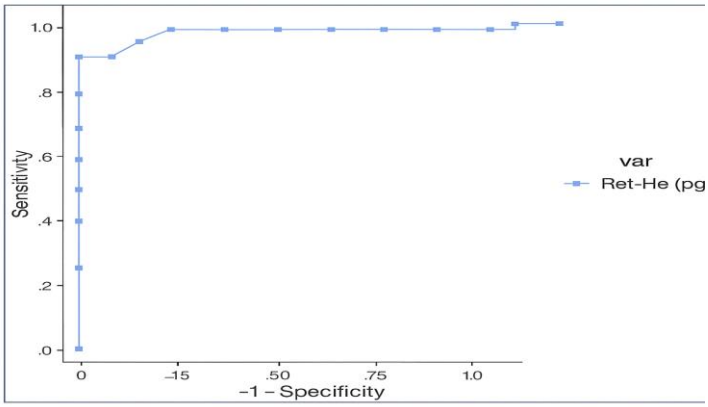


Figure 40 : distribution de Ret-He (pg) en fonction de Traitement martial et Traitement par EPO

Vol.9, No. 03; 2025

ISSN: 2581-3366



ure 38: ROC Analysis for Ret-He in the Diagnosis of Iron Deficiency A
ong Chronically Hemodialyzed Patients

4. Discussion

This study confirms the high diagnostic performance of Ret-He in detecting iron deficiency anemia among chronically hemodialyzed patients. The ROC analysis demonstrated an AUC of 0.937, indicating near-perfect precision. At this threshold, specificity reached 100%, and sensitivity was high at 87.18%, highlighting Ret-He's potential as a leading tool for the differential diagnosis of anemia in hemodialysis. These results significantly outperform classical markers such as serum ferritin and transferrin saturation (TSAT), which are frequently confounded by chronic inflammation inherent to chronic kidney disease (CKD) [1,2].

Our findings are in line with several prior studies. El Oury et al. demonstrated a rapid and significant increase in Ret-He following intravenous iron supplementation in hemodialyzed patients, confirming its utility in monitoring iron availability [3]. Similarly, Garzia et al. reported strong concordance between Ret-He and the percentage of hypochromic red cells (CHr), proposing a threshold of 30.5 pg as an indicator for initiating iron therapy [4].

Eguchi et al. evaluated Ret-He in peritoneal dialysis patients and found a significant correlation with TSAT, while also confirming that Ret-He is independent of ferritin levels, making it a more reliable marker in inflammatory contexts [5]. This is particularly important in CKD, where elevated ferritin may reflect inflammation rather than actual iron sufficiency [6].

In a larger cohort, Saito et al. highlighted the value of Ret-He not only for diagnosing iron deficiency but also as a dynamic marker responsive to treatment adjustments, with variations detectable within days after intravenous iron administration [7].

Similarly, Ogawa et al. found that Ret-He levels were significantly predictive of hematological response to iron therapy, enabling early intervention and avoiding iron overload or excessive erythropoiesis-stimulating agent (ESA) use [8].

Vol.9, No. 03; 2025

ISSN: 2581-3366

Despite these promising results, our study presents limitations. The sample size was relatively small and geographically limited to Marrakech, which may affect the external validity of the results. Moreover, although Ret-He appears to be unaffected by inflammation, further studies should explore its behavior across various inflammatory profiles, especially in patients with active infections or autoimmune diseases.

Future multicenter and longitudinal studies are warranted to validate Ret-He as a standard parameter in anemia management algorithms, particularly in dialysis patients. Integration of Ret-He into routine practice could improve decision-making regarding iron therapy and ESA use, ultimately enhancing patient outcomes and reducing treatment costs [9,10].

5. Conclusion

Measuring reticulocyte hemoglobin content (Ret-He) is a reliable, simple, and inflammation-independent method for diagnosing iron deficiency anemia in hemodialyzed patients. It enables optimization of therapeutic strategies, particularly for EPO and IV iron administration, and contributes to improved overall anemia management in the CKD context.

6. References

Weiss G, Goodnough LT. Anemia of chronic disease. N Engl J Med. 2005;352(10):1011-1023.

Locatelli F, Bárány P, Covic A, et al. Kidney Disease: Improving Global Outcomes guidelines on anaemia management in chronic kidney disease: European Renal Best Practice position statement. Nephrol Dial Transplant. 2013;28(6):1346-1359.

El Oury C, et al. Reticulocyte hemoglobin content: early marker of iron availability. Nephrol Ther. 2014;10(6):447–453.

Garzia M, et al. Reticulocyte hemoglobin content as a screening test for iron deficiency in hemodialysis patients. Int J LabHematol. 2007;29(2):113–118.

Eguchi M, et al. Reticulocyte hemoglobin equivalent as a reliable marker of iron status in peritoneal dialysis patients. Clin Nephrol. 2010;74(2):124-130.

Kalantar-Zadeh K, et al. Serum ferritin is a marker of inflammation but not iron deficiency in CKD. Am J Kidney Dis. 2006;47(1):137-145.

Saito H, et al. Monitoring iron status with Ret-He in CKD patients on hemodialysis. Clin Lab. 2012;58(5-6):423-430.

Ogawa C, et al. Predictive value of Ret-He for response to intravenous iron in hemodialysis patients. Clin Nephrol. 2020;93(1):20-27.

Macdougall IC. Intravenous iron therapy in patients with chronic kidney disease: recent evidence and future directions. Clin Kidney J. 2017;10(Suppl 1):i16–i24.

Fishbane S, et al. Iron indices and reticulocyte hemoglobin content in the diagnosis of iron deficiency. Clin J Am Soc Nephrol. 2010;5(6):1024–1029.