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Clinical Utility of New Platelet and Reticulocyte Parameters

With technological advancements including specific fluorescent markers and automation, the reliability and accuracy of measurements related to platelets and reticulocytes have improved tremendously. The current generations of hematology analyzers are more accurate in identifying cells and decreasing possible interference, to provide an accurate count reliably, particularly in patients with cytopenias.

Immature Platelet Fraction (IPF)

The first platelet count was manually performed in a cell counter chamber developed by Neubaur in 1924. Identification of nucleic acids in younger/immature platelets, termed as reticulated platelets (RP), using dyes dates back to 1969. Later, thiazole orange dye flow cytometry and “gating” strategy was introduced for better identification of RP. Current hematology analyzers have made it possible to detect newly-released immature platelets. The main clinical application of the immature platelet fraction (IPF) is evaluation of thrombopoietic activity in the bone marrow. Therefore, an elevated number of circulating immature platelets is associated with peripheral thrombocytopenia due to excessive consumption, whereas a reduced number of immature platelets is characteristic of inadequate platelet production.

A transient increase in IPF% is reported in patients after chemotherapy or hematopoietic stem cell transplant. This peak IPF% is approximately 1-11 days prior to platelet recovery ($>30 \times 10^9/L$) and is noted to be significantly earlier in those patients with peak IPF% $>10\%$ (Yamaoka G. *et. al.* Int. Jnl. Lab. Hem. 2010, 32, e208). Of note, patients with

thrombocytopenia often receive platelet transfusion. A study addressing the impact of transfusion on absolute IPF, concluded lack of significant change in the mean absolute IPF in transfused patients (Taha B. *et. al.* Transfusion. 2013 Jun;53(6):1201).

Immune thrombocytopenia (ITP) is a autoimmune disorder that effects adults and children, where autoantibodies accelerate platelet destruction. Absolute IPF is significantly lower in ITP patients than controls. Measurement of absolute IPF can be used to provide before and after assessment of therapy used. A study reported a significantly higher absolute IPF in patients receiving thrombopoietin receptor agonists compared to those managed with intravenous immunoglobulin and/or prednisolone. The number of patients investigated in this study was relatively small.

Other clinical utility of IPF includes differentiating ITP from hereditary macrothrombocytopenia (HM). A study performed concluded a significant increase in ITP in HM compared to ITP and other thrombocytopenias.

A few studies have published reference ranges (Morkis IVC *et. al.* Rev Bras Hematol Hemoter. 2016;8(4):310-313). Our reference ranges are as follows -

Reference Interval and Median for Immature Platelet Fraction

Index	Reference Range
Total (%)	1.1 – 1.7

Reticulocyte Count (RET) and Reticulocyte Hemoglobin (Ret-He)

Similar to platelets, technological advances improved availability and accuracy of parameters related to red blood cells. With availability of automation, based on size and RNA content of reticulocytes, different populations can be displayed. The reticulocyte count (RET), clinically important both for pathophysiological classification of anemia and to monitor marrow response after therapeutic intervention, includes low (LFR), medium (MFR) or high (HFR) fluorescence reticulocyte fractions. The sum of HFR and MFR correspond to immature reticulocyte fraction (IRF). And, the hemoglobin equivalent (Ret-He) parameter corresponds to the hemoglobin content of reticulocytes.

For a long time the RET count has been an underutilized parameter in clinical and laboratory practice mainly due to - 1) technical limitations in the detection of the cell, 2) the imprecision of the manual microscope method, and 3) high coefficient of variations in counts. Moreover, the RTC (expressed as %) must be corrected for the degree of anemia and for the reticulocyte maturation time. The interpretation is based on the corrected RET.

Similar to platelets, newer parameters in relation to red blood cells including IRF and Ret-He have been introduced by several manufacturers. IRF provides information similar to RET, with the advantage of the precocity of the information (includes only HFR and MFR fractions, as described above). So, for example in cases of regenerative anemia or response to replacement therapy, elevation in IRF value will precede the increase in the absolute reticulocyte count by several days. For this reason, use of IRF as an aid in the evaluation of bone marrow response during mobilization of hematopoiesis precursor cells, or as a predictor of recovery from neutropenia in autologous transplantation, is suggested.

The second parameter, Ret-He measures the content of hemoglobin of reticulocytes, which affords early detection of iron deficiency. Ret-He is more accurate than other biochemical markers such as ferritin and transferrin saturation in detecting iron-deficiency erythropoiesis in patients with inflammation or anemia of chronic disease.

Currently, the determination of Ret-He is most widely used in patients with chronic kidney disease undergoing dialysis and recombinant human erythropoiesis (rHuEPO). In this particular group of patients, biochemical dosages limit the evaluation of iron status because of the effect of inflammatory activity. Reticulocyte hemoglobin content measurement is incorporated into the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NFK-K/DOQI) guidelines to monitor rHuEPO therapy.

A few studies have been performed to determine reference ranges, which are as follows (Morkis IVC *et. al.* Rev Bras Hematol Hemoter. 2016;8(4):310-313). Our reference ranges are as follows -

Reference Interval and median for Reticulocyte Index

Index	Reference Range
IRF (%)	0.0 – 16.0
Ret-He	30.0 - 38.0

Both measurements, IPF and Reticulocyte count (includes IRF and Ret-He) are available at Saint Luke's Hospital, Saint Luke's East, Saint Luke's Barry Road, and Saint Luke's South, Monday - Sunday. Specimen requirement includes a 4 ml whole blood lavender tube (EDTA). The specimen tube fill instruction are provided at the following website:

<https://www.saintlukeskc.org/lab-test-director>

Client Services: 816-932-3850 • saintlukeskc.org

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