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Clinical utility of immature platelet fraction - an advanced parameter in laboratory hematology

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Sir,

Platelets, first described by a German anatomist as 'spherules', nearly a century ago, are multifunctional anucleated cells that play a vital role in hemostasis. They are cytoplasmic fragments of megakaryocytes with average platelet count ranging between 150 and 410 x 10^9/L. Platelets act as an initial hemostatic agent through their adhesive and cohesive properties leading to the formation of platelet plug with subsequent activation of coagulation pathways in order to consolidate the primary hemostatic plug. However, in patients with thrombocytopenia, count alone does not provide precise assessment of bleeding risk and platelet production from bone marrow. Analogous to red cell reticulocytes, immature platelets or reticulated platelets are young platelets that circulate in the peripheral blood and provide functional status of platelet production by bone marrow.

Owing to their high ribonucleic acid (RNA) content, immature platelets can be differentiated from their mature counterparts. This was first demonstrated by Kienast and Schmitz in 1990 utilizing flow cytometry. Since then, several modifications have been developed utilizing multi-color flow cytometric analysis and different flouro-chromes providing simple, rapid and precise assessment of reticulated platelets. In modern automated hematology analysers equipped with this sophisticated method, fluorescent dyes penetrate the cell membrane through a breach created by surfactant and label the RNA. It is reported as percentage of the total platelet count (%-IPF). The normal reference range for IPF ranges from 1.6 - 7.1% in adults, and 1.0 - 6.8% in children.[1]

Since IPF provides status of bone marrow thrombo-poiesis, it can be utilized for diagnosis and management of various disorders. Raised IPF levels are seen in conditions with high platelet turnover like disseminated intravascular coagulation (DIC), thrombotic thrombo-cytopenic purpura (TTP) / hemolytic uremic syndrome (HUS), immune thrombocytopenic purpura (ITP), and blood loss. Whereas, low levels are observed in individuals with bone marrow suppression such as aplastic anemia and other bone marrow failure syndromes, nutritional deficiencies and drug induced myelosuppression.

Besides its role in aiding the diagnosis of above disorders, IPF can be utilized to monitor the diseases process and to assess need of platelet transfusion. In disorders with high platelet turnover like ITP, initially high IPF values tend to decline as the disease responds to treatment. Similarly, low IPF values in drug induced myelosuppression and viral hemorrhagic fevers will return to normal range with improvement in disease process. Since IPF levels decline around 24 - 48 hours before improvement in platelet counts, unnecessary platelet transfusion can be prevented in such conditions.[2]

Several other potential uses of IPF have been documented in literature. In acute coronary syndromes, it can be used for risk stratification and for monitoring the effect of anti-platelet treatment; high IPF levels being associated with poorer prognosis.[3] Recently, a study performed in critically-ill patients suggested that IPF could be a more accurate and sensitive bio-marker of sepsis than c-reactive protein and procalcitonin.[4] A study comprising 51 patients with myelodysplastic syndrome (MDS) revealed that approximately one-fourth had IPF of more than 10%. Interestingly, this subset of patients was found to have a karyotype that predicts a poor prognosis in MDS.[5]

The sensitivity of IPF in major clinical conditions (such as ITP, TTP, DIC, dengue fever, aplastic anemia, MDS, recovery from transplant and chemotherapy) varies from 47% to 93%; whereas, specificity of 85% to 98% and positive predictive values ranging from 83% to 93% have been quoted in the literature.

IPF values tend to increase in a time-dependent fashion with formation of platelet clumps or aggregates. Additionally, presence of white cell fragments can also falsely increase the values. However, most automated analysers in use generate an abnormal platelet scatter gram flag when such abnormalities are present. In such situations, careful examination of peripheral blood film along with vigilant monitoring of these flags are required while reporting patient results.

This technique is now a part of many upcoming models of automated analysers providing accurate and valuable information of megakaryocytic activity within minutes. This simple, non-invasive and in-expensive tool assesses bone marrow thrombopoietic activity on a single blood specimen. All these properties are highly desirable specifically in pediatric settings where bone marrow examination may not always be practical.

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