

# Letter to the Editor

## Exploring platelet indices as disease biomarkers: prospective use and methodological challenges

Dear Editor,

Platelet indices have generated tremendous interests as versatile disease markers. Recently, Balkarli et al<sup>1</sup>, Yilmaz and Yilmaz<sup>2</sup>, Almis et al<sup>3</sup> and Tekin et al<sup>4</sup> have investigated platelet indices in relation to Behcet's disease, retinal vein occlusion, hepatitis A and infants with meconium-stained amniotic fluid, respectively; whereas Tulgar et al<sup>5</sup> have examined the effects of smoking on platelet indices. While the prospective use of these indices is attractive, there are certain methodological issues that are frequently overlooked by some researchers, which may limit the validity of their findings. We wish to draw attention to these important issues.

For instance, platelet indices are influenced by the type of anticoagulant used (EDTA or citrate)<sup>6,7</sup>, and platelets undergo time-dependent morphological changes, which may cause temporal alterations in the platelet indices<sup>6-8</sup>. This is especially pertinent while using EDTA tubes. Thus, measurements should be preferably performed within 2 hours from venipuncture<sup>8</sup>. But, several reports have not clearly mentioned about the anticoagulants used<sup>1,3,5</sup>, or the time delay since sample collection<sup>1,5</sup>.

Another concern is the confounding bias. Platelet indices are influenced by covariates like age, sex, serum lipids, smoking, and alcohol<sup>9,10</sup>, and also by co-morbidities like hypertension, diabetes mellitus, fatty liver disease, obesity and coronary artery disease. Many of these relevant confounders were not accounted for in some of the reports<sup>1,3</sup>.

Further, Balkarli et al<sup>1</sup> suggested neutrophil/lymphocyte ratio (NLR) as a diagnostic marker for active Behcet's disease. Given the fact that NLR is an indicator of undergoing inflammation in several conditions, it would have been better had they substantiated their results with receiver operating characteristic (ROC) curve analysis.

To conclude, platelet indices hold the promise to be valuable disease biomarkers. However, the associated pre-analytical variables, confounders and methodological challenges need to be duly addressed for realizing this potential.

### Conflict of Interest

The Authors declare that they have no conflict of interests.

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*K. Bora<sup>1</sup>, P. Borah<sup>2</sup>, A.K. Jitani<sup>3</sup>*

<sup>1</sup>North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences,  
Department of Biochemistry, Shillong, Meghalaya, India

<sup>2</sup>Bioinformatics Infrastructure Facility (BIF) and State Biotech Hub (SBT-Hub),  
College of Veterinary Science, Guwahati, Assam, India

<sup>3</sup>North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences,  
Department of Pathology, Shillong, Meghalaya, India