Absolute Immature Platelet Count As an Accessible Diagnostic Tool for Aplastic Anemia Vs. Immune Thrombocytopenia

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INTRODUCTION

- Distinguishing thrombocytopenia from a bone marrow failure disorder such as in aplastic anemia (AA) and platelet destruction due to immune thrombocytopenia (ITP) is crucial.
- Accurate differentiation is essential for making prompt treatment decisions and averting potential complications from thrombocytopenia and treatment complications.
- Hee-Jin Kim et al. showed the utility of immature platelet fraction (IPF%) in differentiating between ITP and AA, albeit with limited sensitivity of 54.0% (Kim et al., 2010)
- Complications of distinction of ITP and AA include:
  - IPF% can be influenced by platelet transfusions (Bat et al., 2013)
  - Megakaryocyte production may also be suppressed among ITP patients (McMillan et al., 2004).

AIM

- There is an urgent requirement for a more refined biomarker in the clinical realm to aid with improving diagnostic accuracy.
- We hypothesize that absolute immature platelet number (AIPN) can be a more sensitive and specific test to differentiate AA and ITP.

METHOD

- Our study cohort encompassed a diverse array of participants with ITP (n=32) and those with AA (n=15) from 2015-2023 seen at the University of Texas Southwestern Medical Center.
- We retrospectively analyzed medical records of patients at our institution with diagnosis of AA and ITP to determine IPF% collected at the time of the diagnosis and before the onset of ITP treatment as well as while on treatment, respectively.
- The AIPN was calculated by multiplying the IPF by the circulating platelet count and dividing by 100.
- This study was approved by the Institutional Review Board (IRB) at University of Texas Southwestern with reference number STU-2021-1114.

RESULTS

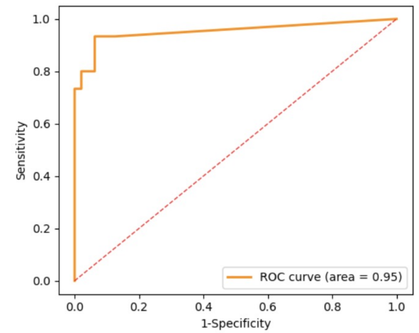
- Compared AIPN results of 15 AA subjects (M = 0.74, SD = 0.755) to 48 ITP subjects (M = 12.2, SD = 13.09)
- AA cohort consists of significantly lower AIPN values by t-test (t-value=3.4, $p<0.05$)
- Optimal threshold at which AA was classified as AIPN<=2.1 x109/L and ITP was classified as AIPN>2.1 x109/L with:
  - AUC of 0.91
  - accuracy of 94%
  - sensitivity of 93% (correct prediction of AA)
  - specificity of 94% (correct prediction of ITP).

Figure 1. Confusion matrix where threshold AIPN = 2.1 x10^9/L and AA is the positive class.

Labeled \ Predicted	AA	ITP
AA	14	1
ITP	2	30

If AIPN <= 2.1 x10^9/L, then AA; else ITP. AA, aplastic anemia. ITP; immune thrombocytopenia. Sensitivity = 0.93; Specificity = 0.94; Accuracy = 0.94; AUC = 0.95

Figure 2. AUC-ROC curve for prediction model of AA versus ITP using threshold



- Compared IPF% values of 15 AA subjects (M = 4.2, SD = 9.32) to the 48 ITP subjects (M = 20.2, SD = 230.13)
- AA cohort consists of significantly lower IPF% values by t-test (t-value=4.1, $p<0.05$)
- From various IPF% thresholds ranging from 2.1 to 12.6%, no IPF% threshold results in both sensitivity and specificity over 70%

Therefore, we infer that AIPN provides a more accurate indicator of AA versus ITP.

CONCLUSIONS

- Markedly elevated thrombopoietin (TPO) levels are specifically linked to thrombocytopenia caused by megakaryocyte hypoplasia due to bone marrow failure, as opposed to situations characterized by platelet destruction (Bat et al., 2013; Emmons et al., 1996). However, it's essential to note that measuring TPO levels is not currently a standard practice, often not readily available in local labs, and is primarily reserved for research purposes.
- In clinical scenarios, AA patients may be incorrectly diagnosed and treated for ITP. This misclassification can lead to delays in administering the appropriate treatment for AA, worsening the overall prognosis (Nakao, 2016).
- While our cohort is small and the results need to be confirmed in a larger study, our findings underscore the importance of AIPN in guiding clinicians to reliably differentiate between AA and ITP with high accuracy. The simplicity, feasibility, and accessibility of AIPN testing make it a valuable and reliable biomarker for clinical use. It serves as a tool in facilitating prompt and accurate diagnoses, thereby enhancing the overall management of patients with aplastic anemia.

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AUTHOR CONTRIBUTIONS

M.Z., P.S., A.O., and T.B. generated and conceived the study design. M.Z., P.S., and T.B. contributed to the table and manuscript; M.Z., P.S., and T.B. reviewed the clinical data, took part in patients' selection, and helped with writing the manuscript; M.Z., P.S., I.I. W.C. and T.B. reviewed clinical data and contributed to the writing of this manuscript. All authors participated in data interpretation and critical review of the final paper and submission. All authors have read and agreed to the published version of the manuscript.

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