Letter to the Editor
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Correspondence: Response to "Eliminating or Minimizing the Effects of Cold Agglutinins on the Accuracy of Complete Blood Count Results"

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Dear Editor,

We appreciate the opportunity to respond to the Letter to the Editor by La Gioia [1] regarding our comparative analysis of complete blood count (CBC) results and suggestion for correction for cold agglutinin in CBC results [2].

We agree that our study had limitations, which were clearly outlined by La Gioia [1]. Additional studies with larger sample sizes using duplicate or triplicate measurements are necessary to confirm and validate our single-case-based findings, like other recent studies [3, 4]. We expect studies in a similar setting as ours, but with large sample sizes, to be performed in the near future [5]. Furthermore, we are aware that other factors, such as the titer of cold agglutinin and the presence of underlying disease, might cause analytical interference and remain to be further assessed [6]. Another fundamental limitation of our study was that reference values were determined using an XE-2100 hematology analyzer (Sysmex, Kobe, Japan) because this was the only instrument available in our laboratory. The use of reference values determined with other analyzers would have influenced the delta percentage difference results.

However, we believe our study yielded valuable information regarding the investigation of comparative differences and relative evaluation results among the four most commonly used automated CBC analyzers. In addition, all samples were collected from only one patient with cold agglutinin disease and were tested only once at each time point. Therefore, the highest cold agglutinin titer (higher than 1:1,024) in the patient might have maximized the unique effect of cold agglutinin on CBC parameters, ruling out potential covariables.

To the best of our knowledge, this was the first study to comparatively evaluate spurious effects of cold agglutinin, using four automated hematology analyzers from three major manufacturers, including the most recently updated analyzer: XN-1000 (Sysmex). Even though all manufacturers warn users about the possibility of interfering effects of cold agglutinin, and the analyzers detect and flag spurious results caused by cold agglutinin, no other study has compared quantitative effects. Our findings—including the unreliability of results produced by automated hematology analyzers due to intrinsic factors of cold agglutinin disease—are important for clinical laboratory physicians and hematologists. In conclusion, despite its limitations, our study contributes to developing critical awareness of spurious effects of cold agglutinin in automated CBC analyses and provides an optimal protocol for accurate analysis.

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Authors' Disclosures of Potential Conflicts of Interest

No potential conflicts of interest relevant to this article were reported.

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