Article published online: 2020-02-19

Commentary

Automated hematology analyzers: Recent trends and applications

The cellular and morphological analysis is an integral part of any hematology laboratory. The hematology analyzers are being used predominantly for cell counts and differential leukocyte analysis, but in addition, these analyzers are capable of reporting many additional parameters and can provide much more information than what they are intended to provide, but unfortunately, due to lack of knowledge and propagation, they are not being optimally utilized to their potential. The new information available with these additional parameters may help the laboratory physician in the screening and diagnosis of many disease states.

Majority of the hematology analyzers are now available with an integrated reticulocyte count analysis with the routine complete blood count analysis which not only provides the reticulocyte % and absolute reticulocyte counts but also provides additional data in the form reticulocyte hemoglobin content (CHr), % hypochromic cells, % microcytic cell or microcytic anemia factor, immature reticulocyte fraction, etc. CHr is a measure of total hemoglobin content in a reticulocyte which is expressed in pg and reflects the amount of hemoglobinization in the maturing erythroid precursors. CHr is a valuable parameter and provides the status of functional iron available for erythropoiesis over the last 3–4 days. The measurement of CHr has proven to be a sensitive indicator of iron-deficient erythropoiesis. The values <27 pg are highly suggestive of iron-deficiency anemia.[1] Similarly, the measurement of this % hypochromic (defined as % of red cells with hemoglobin concentration <28 g/dl on Siemens and Advia Systems and hemoglobin concentration <17 pg on Sysmex analyzers) is a sensitive indicator for the quantification of hemoglobinization of mature red cells. The value of % hypochromic red cells >10% of all RBC's is highly suggestive of iron-deficient anemia.[2,3]

The modern day analyzers are providing five to seven parts differential white-cell analysis, based on the different technologies, such as, electrical impedance, radiofrequency conductivity, light scatter, fluorescent scatter, and cytochemistry, etc. In addition to this, they also provide additional information in the form cell population data (CPD) and Lymph Index (Beckman Coulter-LH series analyzers using the volume, conductivity, and scatter [VCS] technology) Granularity Index (Sysmex XE series), Large unstained cell population (Advia Systems) and hemoparasites which can be utilized in the screening of benign and malignant hematological conditions.

CPD is generated during the white-cell differential analysis using the VCS technology (Beckman Coulter) for each individual white cell subtype. The VCS technology of the Coulter hematology analyzer can obtain data from >8000 white blood cells in a few seconds in their near-native state, following the lysis of red cells, using impedance to measure cell volume (V) for accurate size of all cell types, radio frequency opacity to characterize conductivity (C) for internal composition-nuclear volume, nuclear-cytoplasmic details of each cell and nuclear lobulations, and a laser beam to measure light scatter (S) for cytoplasmic granularity, and nuclear structure. The data obtained from VCS technology can thus be a comparable reflection of cell morphology.[4]

Over the last few years, the CPD data generated form VCS parameters have been thoroughly investigated for their possible clinical applications. The most frequent use of this data has been done using CPD values for neutrophils for the screening of sepsis or bacterial infection. The mean volume, conductivity, and scatter are significantly increased in cases with bacterial infections and septicemia.[4] The lymphocyte CPD data have also been shown to be useful for the screening of the viral and bacterial infections. Similarly, the monocyte CPD has shown to be useful for the screening and differentiation between malaria and dengue infections on hematology analyzer by calculating malaria factor using the VCS data for the monocytes.[5,6]

In this issue of Choccalingam,[7] report lymphocyte CPD data could be useful for the screening of viral infections and lymphoid malignancies. The author has compared the lymphoid VCS data obtained from Beckman Coulter LH-780 analyzer among the normal healthy controls (n = 29), acute viral disease (AVD) (n = 23), chronic inflammatory disorders (n = 14), acute lymphoid leukemia (n = 2), and chronic lymphoid leukemia (n = 2) and also compared the histograms and scattergram among the mentioned groups. The author observed that on the histograms the trough at T1 from the patients with AVD was obliterated and the F1 curve was slightly shifted to the right. The T1 trough for the patients with acute lymphocytic leukemia (ALL) was replaced with a peak at T1 and the F1 peak was shifted to the left for patients with chronic lymphocytic leukemia Chronic lymphocytic leukemia (CLL). Among the lymphocyte CPD based on the VCS, the author reported significantly increased MLV (mean lymphocyte volume) and reduced MLV in patients with ALL and CLL, respectively, which could be attributed to the increase cell size, i.e., blast population in cases with ALL and presence of monotonous looking small lymphocytes in cases with

CLL. The author also reported increased MLV in patients with AVD, possibly because of the presence of reactive looking or activated lymphoid population in peripheral blood following a viral infection.

The conductivity, which measures the internal complexity such as the nuclear details, nuclear cytoplasmic ratio of the cells was reported to be higher in patients with CLL (MLC: 129) as compare to the normal controls (MLC: 122) owing to slightly increased nuclear cytoplasmic ratio in CLL; however, it was surprisingly reduced in ALL cases (117), although the N/C ratio is significantly elevated in patients with acute leukemia. This aspect should have been discussed. One possibility is the very small size of the study groups which is a major limitation of this study, is giving a false impression. The findings may also vary since scant literature is available over possible subjective or biological variations among the different populations in reference to the use of this CPD. The author just reported in the mean value and the difference among the various disease groups; it would have been better if the author could have proposed a cutoff for differentiating the AVD from the normal population; obviously, this would have been possible with the inclusion of more number of cases in the study groups. The similar cutoff has been proposed as lymph index using the lymphocyte CPD have been shown to differentiate between the viral and bacterial infections and defined as lymphocyte volume **X** Lymphocyte volume-standard deviation (SD)/lymphocyte scatter.[8,9] This lymph index is significantly elevated in cases with viral infections as it is associated with the presence of large reactive lymphoid cells with varying sizes (SD), thus giving a high index.

The use of CPD using the VCS definitely requires more validation to be used as an additional parameter for the screening of bacterial or viral infections or other chronic inflammatory diseases or to differentiate among the benign and malignant hematological conditions.

The user must identify the abilities and the limitations of these analyzers for better optimization in the laboratory, hence, it is the need of hour to propagate this useful information acquired from hematology analyzers, both to the clinician and laboratory physician as it may help the patients by reducing the cost to the diagnosis by avoiding other unnecessary tests and may help in timely management of the disease states.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest

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Access this article online	
Quick Response Code:	Website: www.jlponline.org
	DOI: 10.4103/JLP.JLP_124_17

How to cite this article: Chhabra G. Automated hematology analyzers: Recent trends and applications. J Lab Physicians 2018;10:15-6.