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ORAL ABSTRACTS

901.HEALTH SERVICES AND QUALITY IMPROVEMENT - NON-MALIGNANT CONDITIONS

Low-Cost Automated Microscopy and Morphology-Based Machine Learning Classification of Sickle Cell Disease and Beta-Thalassemia in Nepal and Canada

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INTRODUCTION
Sickle cell disease (SCD) is the most common inherited blood disorder, and is associated with a high mortality rate for children in low-resource settings, where the disease burden is high. Early screening and treatment options reduce morbidity and mortality. In addition to screening for SCD, screening for asymptomatic, heterozygous conditions, such as sickle cell trait (SCT) and β-thalassemia trait, is required for effective SCD and thalassemia screening programs. However, rural and remote communities lack accurate low-cost screening techniques.
The goal of this study is to augment a common low-cost screening test, the sickling test, using automated microscopy and machine learning to classify individuals with SCD (HbS/β-thalassemia and HbSS), trait conditions (HbAS and HbA/β-thalassemia), and those without common beta-globin disorders (HbAA) for implementation in Nepal. As HbC mutation is not encountered in Nepal, screening for HbSC or HbAC was not included. Additionally, we aim to evaluate the feasibility of 5 low-cost techniques to supplement/replace the local gold standard test (Hb HPLC), which is inaccessible in rural/remote settings.
METHODS
In this study (ClinicalTrials.gov Identifier: NCT05506358), blood samples were collected and tested at respective clinical sites in Nepal (Mount Sagarmatha Polyclinic and Diagnostic Center, Nepalgunj) and Canada (St. Paul's Hospital and BC Children's Hospital, Vancouver). Participants (138 total: 111 Nepal; 27 Canada) between ages 2 to 74 whose diagnoses were previously established by Hb HPLC were recruited. Five low-cost tests (our augmented sickling test, HbS solubility test, HemoTypeSC, Sickle SCAN, Gazelle Hb variant test) and Hb HPLC were performed on all participants (30 HbAA; 23 HbA/β-thalassemia; 45 HbAS; 11 HbS/β-thalassemia; 29 HbSS). Informed consent was provided by the participants or parents, according to protocols approved by institutional/national research ethics boards. For the sickling test, a sealed wet preparation of blood mixed with 2% sodium metabisulphite was imaged with a robotic microscope (Octopi) with automated scanning/focusing. The images of blood cells were segmented using Cellpose 2.0, allowing for morphological characterization of cells and morphology based classification, with an 80:20 participant-wise split of training and testing data.
RESULTS
Using high-throughput imaging, more than 300,000 de-identified images of blood films were collected, resulting in more than 1.5 trillion segmented cells. The de-identified images and processed data will be released in an open-access data repository. The frequency distribution of 11 different morphological parameters were used for machine learning based classification, resulting in testing sensitivity and specificity of 82.9% and 82.4%, respectively. The confusion matrix (Figure 1) shows that sensitivity of detecting SCD cases (HbS/β-thalassemia and HbSS) was 98.6%, and most misclassifications were between trait and normal conditions. Comparing the different low-cost techniques (Table 1), the Gazelle Hb variant test had the highest sensitivity and specificity (97.0% and 99.3%), but is more than twice as expensive than the augmented sickling test, while lateral flow assays (HemoTypeSC and SickleSCAN) had lower sensitivity (74-75%) than the augmented sickling test, due to their inability to detect β-thalassemia trait.
CONCLUSIONS

The sickling test, which is traditionally unable to distinguish between SCT and SCD, was augmented to detect SCD and trait conditions (including β-thalassemia) with an overall sensitivity of 82.4% (98.6% sensitivity for SCD detection). The preliminary results indicate that image-based classification can be a promising low-cost and automated screening tool for low-resource settings, reducing the need for highly-trained personnel for device operation and disease detection. Furthermore, the open-access image dataset can be used to improve classification in the future, as segmentation/classification algorithms improve over time.

Disclosures No relevant conflicts of interest to declare.

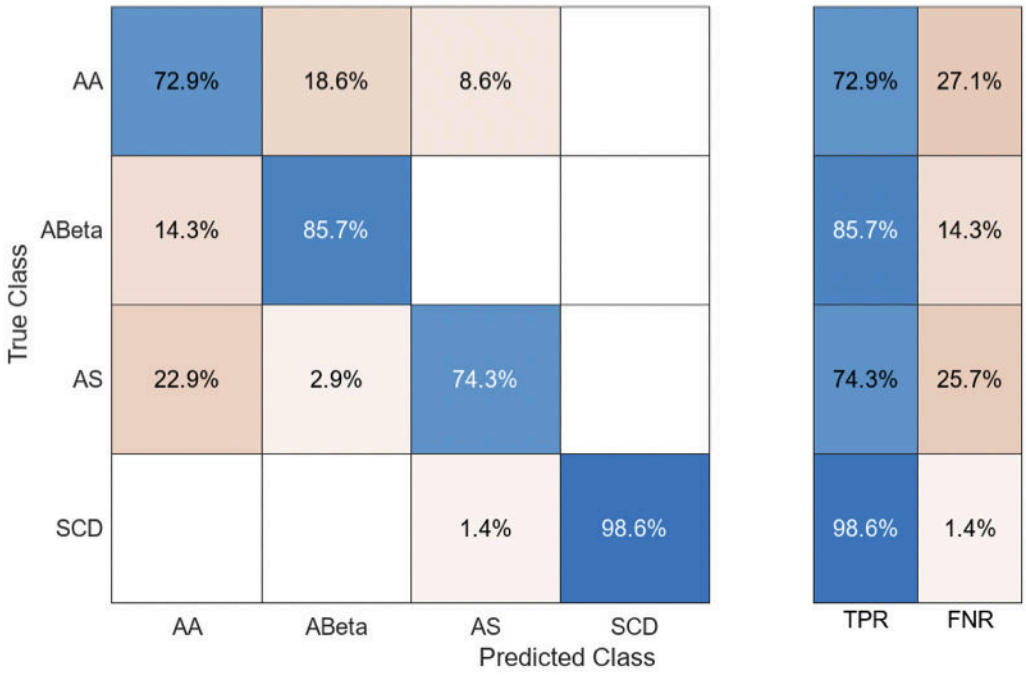

Figure 1: Confusion matrix for classification of 4 classes (HbAA – normal; HbA/β-thalassemia – β-thalassemia trait; HbAS – sickle cell trait; SCD – sickle cell disease, including genotypes HbSS and HbS/β-thalassemia), with an overall sensitivity or balanced testing accuracy of 82.9%. The diagonal values in the confusion matrix and the first column on the right (blue) represent true positive rate (TPR) or sensitivity for detection of the corresponding class, while off-diagonal values represent rates of misclassification.

Table 1: Comparison of sensitivity, specificity and material cost of low-cost point-of-care technologies for detecting sickle cell disease and β-thalassemia

Test	Sensitivity	Specificity	Material cost for 10,000 tests
Gazelle Hb variant test, Hemex Health	97.0 %	99.3 %	$ 21,000
HemoTypeSC, Silver Lake Research Corporation	74.4 %	94.4 %	$ 20,000
Sickle SCAN, BioMedomics Inc.	75.0 %	94.7 %	$ 50,000
Augmented sickling (using automated microscope, Octopi)	82.9 %	82.4 %	$ 8,000

Figure 1

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