Point-of-care diagnostic for quantification of foetal haemoglobin (Hb F) levels in monitoring hydroxyurea therapy for children with Sickle Cell Disease (SCD) in Ghana

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OBJECTIVE:

To assess the performance of the Gazelle™ Hb Variant test compared with high performance liquid chromatography (HPLC) for Hb F quantification in Ghanaian children with sickle cell disease (SCD).

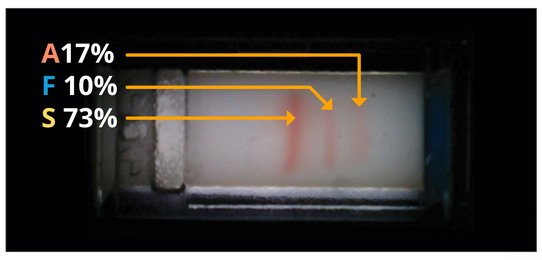
INTRODUCTION:

- Sickle cell disease (SCD) causes numerous acute and chronic complications across the lifespan of a patient.
- The majority of patients with SCD live in sub-Saharan Africa and India. 1 in 50 Ghanaian newborns have SCD.
- Foetal haemoglobin (Hb F) level is a known modulator of the severity of SCD. High levels of Hb F inhibit sickling and correlate with reduced disease morbidity and mortality.
- Hb F monitoring is also used to assess adherence and response to disease modifying (hydroxyurea) therapy.
- Standard haemoglobin electrophoretic techniques are unable to quantify HbF.
- In resource-limited settings like Ghana, the use of (HPLC) for Hb F quantification is often challenging due to the high cost and scarcity of laboratory equipment and skilled technicians.
- Gazelle™ is a fast (<8 minutes), affordable and easy-to-use test which can be performed by minimally trained personnel using only a finger-prick volume of blood.

WHY MONITORING HB F IN HYDROXYUREA PATIENTS IS IMPORTANT:

- Hydroxyurea (HU) causes the body to produce higher levels of (Hb F), a form of haemoglobin able to transport oxygen throughout the body. Hb F does not sickle, so as Hb F increases, the frequency of vaso-occlusive crises (VOCs) and the need for blood transfusions are reduced.[1]
- Hydroxyurea has been used to treat adult sickle cell patients since the 1980s and was recently approved for children by the USFDA. Hydroxyurea usage is also starting in India, Africa, and the Middle East.
- Hydroxyurea patients should be regularly monitored to help ensure that the treatment is effective, safe, and that the dosage is appropriate, but limitations on cost and availability makes this problematic today.
- Currently, patient samples usually require HPLC to be performed in a distant lab, resulting in delays in adjustments to patient dosages. In many areas, HPLC is not available.
- A point-of-care device like Gazelle that can provide Hb F quantification during the patient visit should help with patient compliance and trust in the treatment. A point-of-care device could be used to monitor Hb F levels and adjust dosage.

TECHNOLOGY:



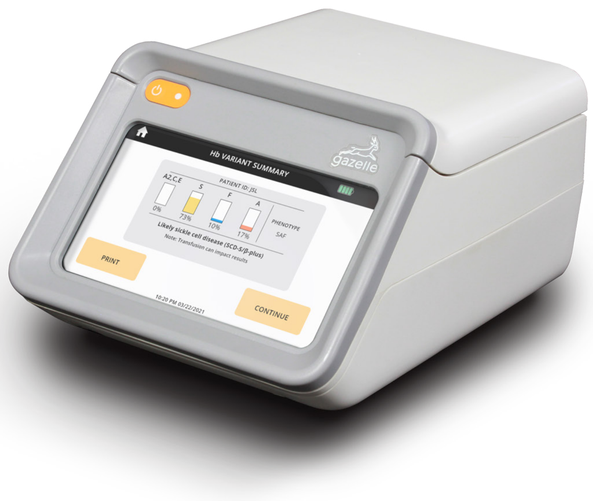


FIGURE 1: Gazelle uses a miniaturized version of the gold standard test: electrophoresis. When a disposable cartridge containing a lysed blood sample is inserted into the reader, a charge is applied to separate the haemoglobin types according to their charge. In 8 minutes, the algorithm determines the haemoglobin types and percentages, and makes the interpretation (normal, trait, disease).

MATERIALS & METHODS:

- The study was conducted at the Paediatric SCD Clinic in Korle Bu Teaching Hospital, Accra, Ghana.
- Children (age ≥ 1 year to 16 years) known to have sickle cell disease who are on or starting hydroxyurea therapy, and followed at the paediatric sickle cell clinic, were enrolled in the study.

RESULTS:

- A total of 532 children were included in the analysis. Gazelle's Hb F measurement demonstrated a correlation of 0.98 when compared to HPLC (Figure 2).

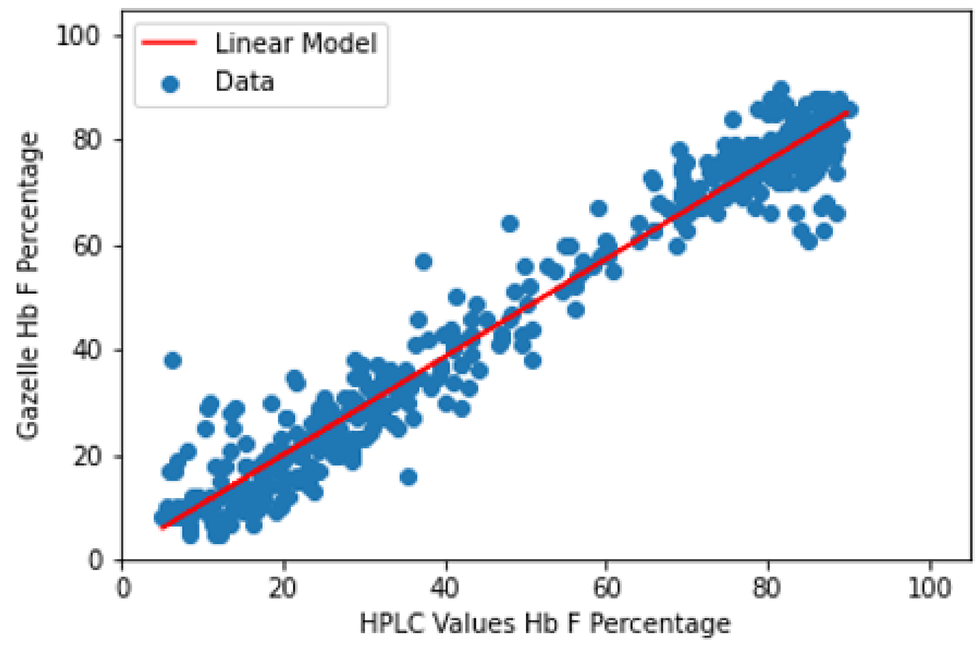


FIGURE 2: Hb Quantification Performance of Gazelle compared to HPLC

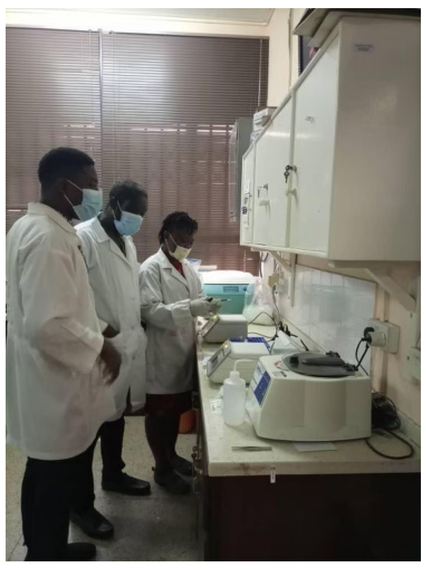


FIGURE 3: Members of the research team from Korle Bu Teaching Hospital (KBTH), Accra, Ghana, using the Gazelle Diagnostic Device. KBTH is the largest public hospital in Ghana.

FIGURE 4: Korle Bu Teaching Hospital.

DISCUSSION:

- Gazelle's foetal haemoglobin accuracy can be useful for clinicians who are monitoring hydroxyurea therapy for sickle cell disease patients.
- Gazelle's Limit of Reporting for Hb F for the following haemoglobin variants is 4%* SS, SE, SC, CC, EE, SA
- Average Pearson correlation coefficient for overall haemoglobin quantification compared to HPLC is 97.3%*

*Data from ongoing study at Korle Bu Teaching Hospital, Accra, Ghana; Study to be published.

CONCLUSION:

- **Gazelle offers the ability to monitor disease modifying therapy in SCD such as hydroxyurea, where quantification of Hb F levels is the key to assessing treatment adherence and determining response to therapy.**
- **Gazelle has the potential to be utilized as a POC test for quantification of foetal haemoglobin (Hb F) levels in monitoring hydroxyurea therapy for children with SCD, especially in limited resource settings.**

ACKNOWLEDGEMENTS:

[1] Vlassov, V. (2022, March 1). Hydroxyurea. Sickle Cell Disease News. Retrieved May 18, 2022, from https://sicklecellanemianews.com/hydroxyurea/

Gazelle™ diagnostic device has been developed by Hemex Health, USA, and India. The Gazelle Hb Variant technology was licensed from Case Western Reserve University, Cleveland, OH.
The study was funded by Hemex Health. Please contact csegbefia@gmail.com with any questons or suggestons For more informaton please visit www. hemexhealth.com
The technology in this study was supported by a Health Equity FlexGrant from The West Coast Consortium for Technology & Innovation in Pediatrics (CTIP).

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