

Premarital Screening of Thalassemia and Hemoglobinopathies with Microchip Electrophoresis (Gazelle™) Method in a Turkish Population

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OBJECTIVE

The aim of this study is to assess the performance of a low-cost, point-of-care (POC), microchip-based, cellulose acetate electrophoresis technology (Gazelle™ Diagnostic Device) as a tool to find sickle cell disease (SCD) and beta thalassemia. Gazelle was compared against high-performance liquid chromatography (HPLC) with beta gene sequencing used as a confirmatory test for both.

HAEMOGLOBINOPATHY PREVALENCE

- Haemoglobinopathies such as SCD and beta thalassemia constitute the most common recessive monogenic disorders worldwide. Recent estimates suggest that 7% of the world's population are carriers, and about 350,000 affected children are born every year.
- The prevalence of these disorders is high in the Mediterranean Basin, sub-Saharan Africa, the Middle East, India, Southeast Asia, Malaysia, and the Pacific Islands.
- In Türkiye, the overall incidence of beta thalassemia reported by Çavdar and Arcasoy was estimated to be 2.1% in 1971.^{1,2}

PREMARITAL SCREENING CAN REDUCE BETA THAL BIRTHS

- A national hemoglobinopathy prevention program was started in Türkiye in 2003 by the Ministry of Health in provinces with a high prevalence of beta thalassemia. By increasing premarital screening rates, this program achieved a 90% reduction in affected births over a ten-year period (2003-2013).
- Ongoing education and screening must continue among Turkish citizens, as well as newer immigrants and refugees, for continued progress.

THE CHALLENGE OF SCREENING FOR BETA THALASSEMIA

- Current screening methods include complete blood count (CBC), High Performance Liquid Chromatography (HPLC), or capillary electrophoresis (CE). Molecular genetic confirmation by detecting pathogenic variants establishes the diagnosis.
- These methods require trained personnel and specialized facilities, both of which may be lacking in many geographical areas where the disease is most prevalent. These standard laboratory methods also carry significant costs.
- The Gazelle™ Hb Variant Test can accurately and affordably detect sickle cell and beta thalassemia trait and disease at the point of care.

GAZELLE POINT-OF-CARE TECHNOLOGY

- Gazelle can detect sickle cell and beta thalassemia disease and trait.
- Results are available within eight minutes, allowing treatment and education to begin immediately.
- Health workers can easily take the portable Gazelle™ Diagnostic Device to any point-of-care testing site.
- PDFs of patient reports can be printed or transmitted via Wi-Fi or USB drive.



Figure 1. The Gazelle™ Hb Variant Test

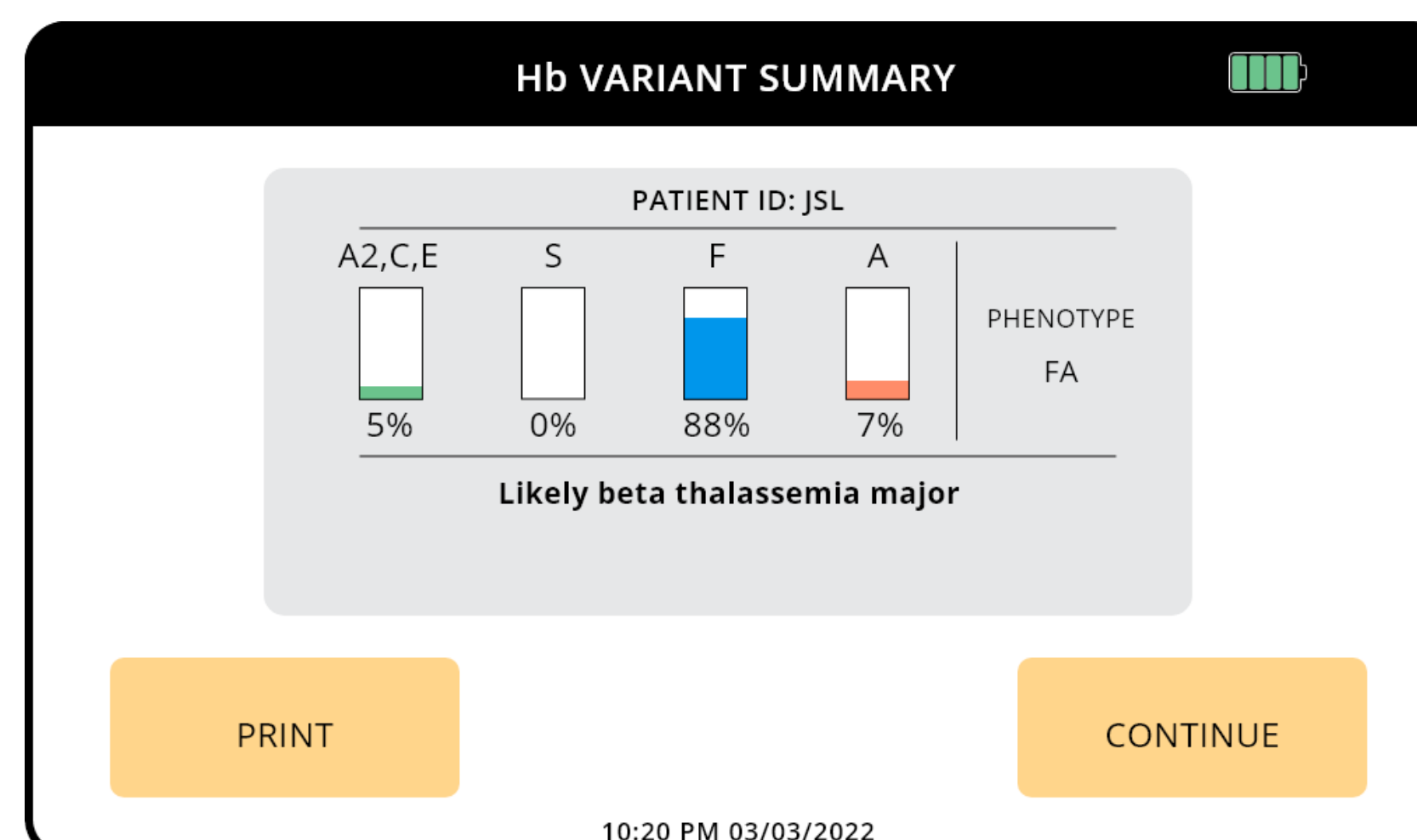


Figure 2. Results appear onscreen in 8 minutes.

METHODS

- A total of 516 study participants (couples who came to the Hemoglobinopathy Diagnosis Thalassemia Center of Mediterranean Blood Diseases Foundation (MBDF) for premarital thalassemia screening) were enrolled in the study. 284 were women (55.1%) and 232 were men (44.9%), with an average age $\pm$ SD of 32.75 ± 11.25 years.
- A control group of 81 known thalassemia carriers and 19 known sickle cell carriers were also tested. The carriers consisted of 58 women (58%) and 42 men (42%), with an average age $\pm$ SD of 26.8 ± 18.6 years.
- The participants were screened with CBC, HPLC and microchip electrophoresis (Gazelle). Beta gene sequence analysis was subsequently performed on the positive samples for confirmation.

RESULTS

- Analyses for comparing the devices were performed using IBM SPSS Version 29 software. The Kappa Analysis method was used to measure the diagnostic sufficiency of the two devices.
- Both devices (the HPLC and the Gazelle™ Diagnostic Device) were found to be 100% consistent in diagnosis.
- Among the study participants, a total of sixteen were identified with traits (3.2%), comprising 14 with beta-thalassemia trait, one sickle cell trait, and one with Hb D trait.

Statistical Data	Trait vs Normal (Gazelle vs HPLC)	Trait vs Normal (Gazelle vs Genetic analysis)	Trait vs Normal (HPLC vs Genetic Analysis)
True Positive	116	116	116
False Positive	0	0	0
True Negative	500	500	500
False Negative	0	0	0
Sensitivity	100.00	100.00	100.00
Specificity	100.00	100.00	100.00
Accuracy	100.00	100.00	100.00

Chart 1. Accuracy of the Gazelle Hb Variant Test Compared with HPLC

CONCLUSION

- The Gazelle point-of-care test provides accurate hemoglobin type identification and quantification for a broad range of hemoglobin variants, enabling accurate detection of beta thalassemia carriers.
- Gazelle has many advantages over other laboratory tests, including timely results (in <8 minutes), digital storage, wi-fi connectivity, portability, and the option to print reports.
- Gazelle is an effective replacement for HPLC.



Figure 3. Dr. Canatan (center) and his research team at Antalya Genetic Diseases Center working with the Gazelle™ Diagnostic Device

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References:

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Acknowledgements:

The Gazelle™ Diagnostic device was developed by Hemex Health, USA, and India. The Gazelle Hb Variant technology was licensed from Case Western Reserve University, Cleveland, OH. Please contact umut@case.edu for any questions or suggestions. The study was funded by Hemex Health. Please contact csegbefia@gmail.com with any questions or suggestions. For more information please visit www.hemexhealth.com. The technology in this study was supported by National Heart Lung and Blood Institute Small Business Innovation Research Program (R44HL140739) and Business Oregon [C2018320], and a Health Equity Flex Grant from The West Coast Consortium for Technology & Innovation in Pediatrics (CTIP).

Evaluation of a New Point-of-Care Diagnostic Tool for Newborn Screening in Ghana

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OBJECTIVE

To evaluate the diagnostic accuracy of Gazelle™, a microchip-based, cellulose acetate electrophoresis, point-of-care device, for point-of-care screening of newborns for sickle cell disease.

PREVALANCE AND IMPACT OF SICKLE CELL DISEASE

- Sickle cell disease (SCD) is a group of inherited disorders of haemoglobin (Hb) synthesis, first described in the medical literature by James Herrick in 1910.
- Each year about 300,000 infants are born with SCD, including more than 200,000 cases in sub-Saharan Africa alone.
- In Ghana, approximately 2% of newborns have SCD (corresponding to ~16,000 infants with SCD born per year), 98% of whom are genotypes SS and SC.

BARRIERS TO NEWBORN SCREENING

- In resource-rich countries, SCD newborn screening (NBS) performed in centralized laboratories has led to substantial reduction in SCD mortality. SCD NBS requires sensitive detection of low levels of certain haemoglobin (Hb) variants (i.e., sickle Hb, HbS) in presence of high levels of other Hb variants (i.e., fetal Hb, HbF).
- The current centralized tests used for NBS for SCD use high performance liquid chromatography (HPLC) and isoelectric focusing.
- However, in sub-Saharan Africa and central India, where >90% of SCD births occur, implementation of NBS programs has been challenging due to the cost as well as technical and logistical burden.
- There remains a need for affordable, portable, user-friendly and accurate point-of-care (POC) diagnostic tests to facilitate decentralized Hb testing in limited-resource settings for enabling nationwide NBS.



Figure 1. Korle Bu Teaching Hospital, the largest public hospital in Ghana

GAZELLE POINT-OF-CARE TECHNOLOGY

- The rugged, lightweight, battery-powered Gazelle™ Diagnostic Device can withstand high temperatures and humidity.
- Health workers can easily take Gazelle to any point-of-care testing site.
- Hemoglobin types and percentages, as well as interpreted results, are displayed onscreen within 8 minutes, and available in a detailed patient report.
- Gazelle stores test results locally, along with patient data and GPS location. Data can be uploaded to cloud applications for storage or connection to other databases.



Figure 2 (left). The Gazelle Diagnostic Device

Figure 3 (below): Hemoglobin production during prenatal and postnatal periods, demonstrating the decrease in fetal Hb and rise in sickle Hb over time

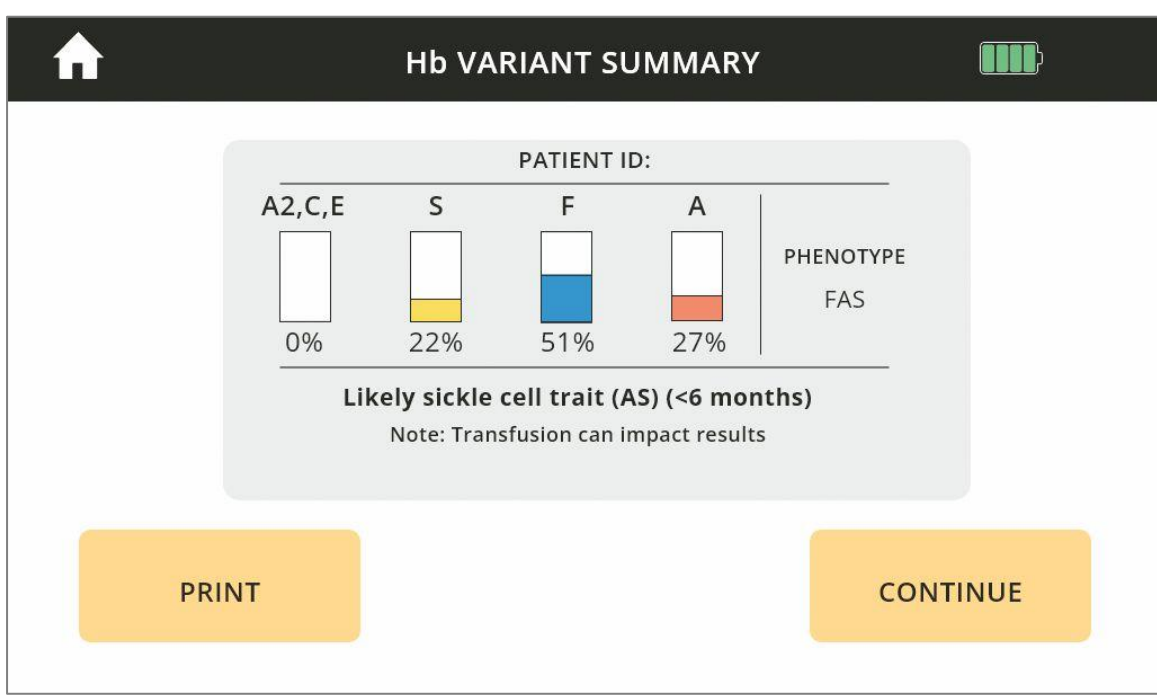
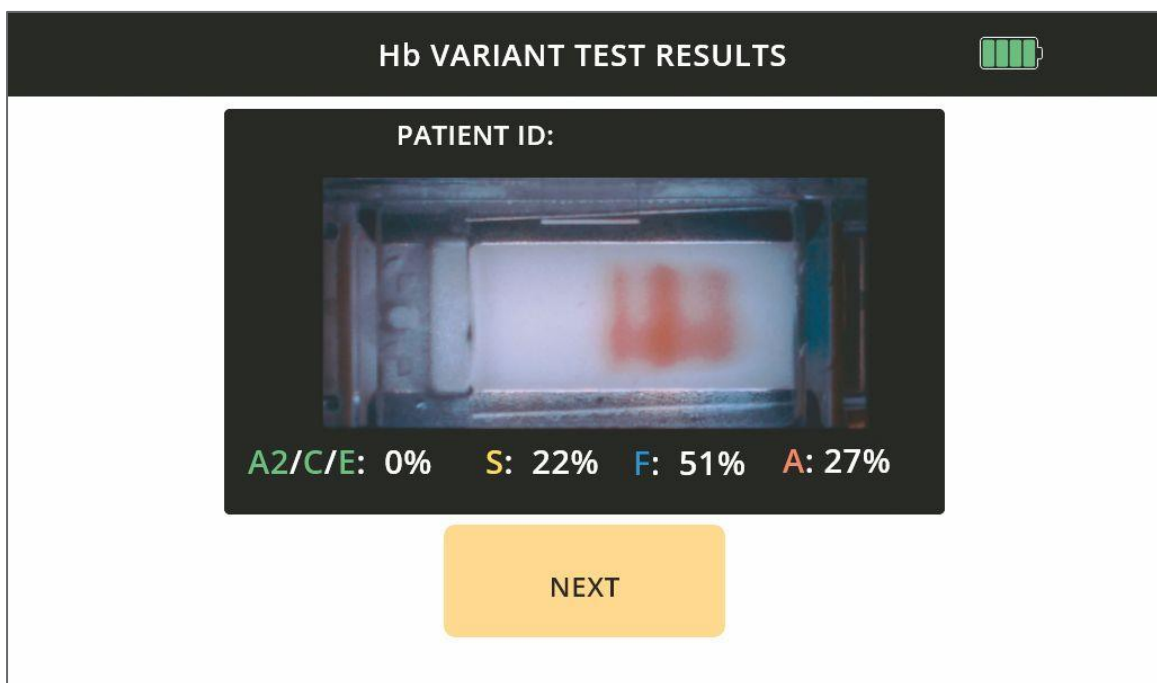
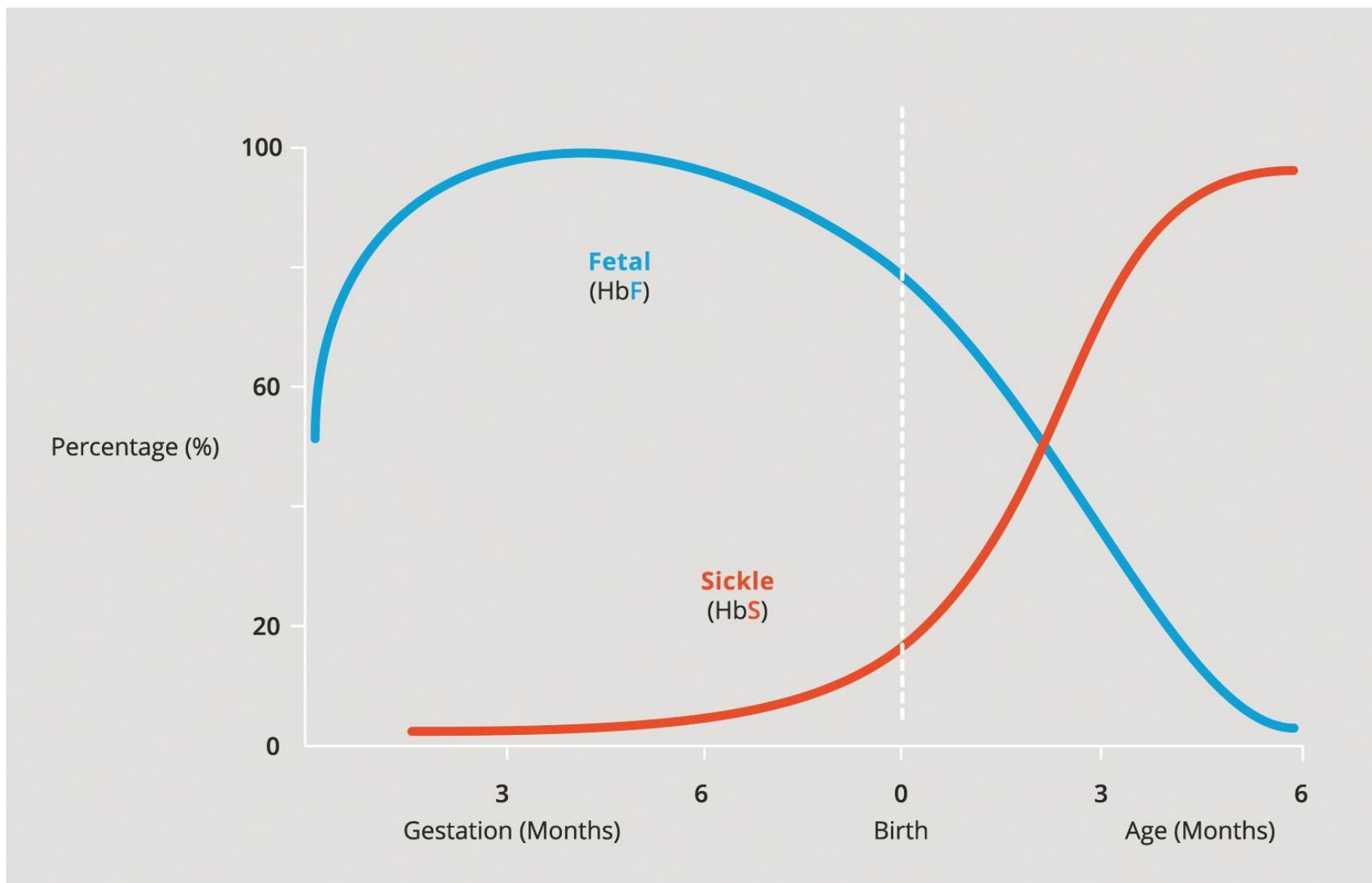


Figure 4: Gazelle test results for an infant with high HbF and sickle cell trait. Infants with the sickle cell mutation have a small concentration of Hb S present at birth. Gazelle can detect very low levels of Hb S, enabling testing of infants born as early as 37 weeks.

METHODS

- A total of 379 newborns were enrolled in the study from the postnatal ward of the Department of Obstetrics and Gynecology at Korle Bu Hospital, Accra, Ghana, which handles about 8,000 deliveries a year.
- Blood samples were collected via heel prick, tested on the Gazelle™ Diagnostic Device, and compared to High-Performance Liquid Chromatography (HPLC).

RESULTS

- Gazelle yielded high diagnostic accuracy for all Hb variants compared to standard laboratory tests (HPLC).
- Sensitivity was 100% for disease vs. normal and disease vs. trait, and 96.6% for trait vs. normal.
- Specificity was 99.7% for disease vs. normal, 100% for disease vs. trait and 95.3% for trait vs. normal.
- The Gazelle Hb Variant test displayed an overall diagnostic accuracy of 98.4% in comparison to reference standard methods for all Hb variants.

Statistical Data	Disease vs Normal	Disease vs Trait	Trait vs Normal
True Positive	4	4	56
False Positive	0	0	0
True Negative	500	500	500
False Negative	0	0	0
Sensitivity	100.00	100.00	100.00
Specificity	100.00	100.00	100.00
Accuracy	100.00	100.00	100.00

Chart 1. Summary of true positive, true, negative, false positive, false negative, sensitivity, and specificity of the clinical testing among 379 subjects conducted at Korle Bu Teaching Hospital, Korle Bu, Ghana

CONCLUSION

- Gazelle enables cost-effective and rapid identification of common Hb variants in newborns at the point of care.
- Overall, Gazelle is a versatile system that enables affordable, accurate, rapid, decentralized NBS for SCD in resource-limited settings where the prevalence of SCD is high.

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