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Effectiveness of Dried Blood Spot Testing Versus Venipuncture for Dual Monitoring of Malaria and Glucose in Diabetic Children: A Review

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ABSTRACT

Diabetic children residing in malaria-endemic regions face dual clinical threats that complicate both diagnosis and disease management. This review explored the comparative effectiveness of dried blood spot (DBS) testing versus traditional venipuncture for the simultaneous monitoring of blood glucose and malaria infection in pediatric populations. Venipuncture, although considered the diagnostic gold standard, presents considerable challenges in children, including procedural pain, the need for skilled personnel, and logistical burdens related to sample transport and processing. Conversely, DBS offers a minimally invasive, cost-effective, and field-friendly alternative that enables reliable detection of glucose and malaria biomarkers using advanced techniques such as glucose oxidase assays, PCR, ELISA, and LAMP. The review was conducted using a narrative synthesis approach, incorporating empirical evidence from peer-reviewed clinical and field-based studies. Findings suggest that DBS testing demonstrates comparable diagnostic accuracy to venipuncture, with strong acceptability among pediatric patients and caregivers, especially in low-resource settings. Moreover, DBS facilitates integration into child health programs and supports longitudinal disease monitoring with improved feasibility. However, challenges related to assay standardization, analyte stability, and regulatory recognition remain. Overall, DBS emerges as a valuable adjunct to venipuncture, with significant potential to enhance integrated care strategies for children confronting the syndemic burden of malaria and diabetes.

Keywords: Dried Blood Spot (DBS), Venipuncture, Pediatric Diabetes, Malaria Diagnosis, Dual Disease Monitoring.

INTRODUCTION

Diabetes mellitus in the pediatric population, particularly Type 1 diabetes, poses complex clinical challenges in resource-limited settings where co-endemic infectious diseases such as malaria remain prevalent [1, 2]. In such dual disease burdens, regular monitoring of both glycemic status and parasitic infections is critical for reducing morbidity and mortality. The World Health Organization (WHO) has highlighted the need for integrated care models that facilitate early diagnosis and disease monitoring through accessible, cost-effective, and minimally invasive methods, especially in children who often exhibit poor venous access and heightened procedural anxiety.

Traditionally, venipuncture has been the gold standard for blood sample collection in clinical diagnostics [3, 4]. It permits large-volume sampling and is compatible with a wide range of laboratory assays. However, its invasiveness, requirement for trained personnel, risk of needle-stick injuries, and logistical challenges in field settings have spurred interest in alternative approaches. One such innovation is dried blood spot (DBS) testing, which involves collecting capillary blood via a finger or heel prick and spotting it onto filter paper [5, 6]. Once dried, the samples are stable at ambient temperature, easy to transport, and can be processed for a variety of analytes, including glucose and malaria biomarkers such as Plasmodium falciparum histidine-rich protein 2 (HRP2). This review critically evaluates the effectiveness of DBS compared to venipuncture for the dual monitoring of malaria and blood glucose levels in diabetic children. It draws upon empirical findings from clinical and field-based studies, with particular emphasis on sensitivity, specificity, sample integrity, feasibility, and child-centered acceptability. By synthesizing evidence across multiple domains, this article aims to inform policy, guide clinical practice, and support the design

of integrated diagnostics for pediatric populations at the intersection of chronic non-communicable and infectious diseases.

Overview of Dual Disease Burden in Diabetic Children

The co-occurrence of malaria and diabetes mellitus in children is more than a clinical coincidence it represents an emerging syndemic in many parts of Sub-Saharan Africa and Southeast Asia [7]. Diabetes compromises the immune system, thereby increasing susceptibility to malaria, while acute malaria episodes can precipitate metabolic dysregulation in diabetic patients, particularly through fever-induced dehydration, increased hepatic glucose output, and cytokine-mediated insulin resistance [7, 8]. Moreover, the use of antimalarial therapies may interfere with glucose homeostasis, posing further clinical complexities in management.

Children, especially those under the age of 12, are particularly vulnerable [9, 10]. They exhibit more frequent hypoglycemic episodes and are less capable of articulating symptoms compared to adults [11]. Therefore, precise and timely diagnostics become not only a matter of medical necessity but also a determinant of long-term outcomes. In this context, the ability to concurrently monitor both blood glucose and malaria status during routine follow-ups or acute presentations becomes a strategic imperative in pediatric care.

Standard laboratory infrastructure is often inaccessible in rural or peri-urban clinics, necessitating innovations that permit testing outside of conventional facilities. DBS emerges as a potential game-changer in this regard, especially for home-based care, community health worker programs, and school-based health monitoring.

Dried Blood Spot Testing: Technical Foundations and Applications

Dried blood spot sampling involves blotting capillary blood onto standardized cellulose filter paper, drying it under ambient conditions, and subsequently analyzing it in a central laboratory [12]. This method has been widely used since the 1960s in newborn screening programs and has expanded to include applications in pharmacokinetics, viral load estimation, and biomarker quantification.

The core advantages of DBS include:

i. **Minimal invasiveness**: Capillary sampling reduces procedural pain and anxiety, particularly in pediatric patients [13].
ii. **Sample stability**: Once dried, the analytes remain stable at ambient temperature for days to weeks, eliminating the need for cold chain transport.
iii. **Volume efficiency**: Only 20–50 µL of blood per spot is needed, which is particularly suitable for children with limited blood volume.
iv. **Ease of transport and storage**: Lightweight and non-biohazardous after drying, DBS cards can be mailed or couriered at low cost.

Recent advances have expanded DBS's diagnostic scope to include glucose estimation using glucose oxidase-peroxidase (GOD-POD) assays and malaria detection through polymerase chain reaction (PCR), enzyme-linked immunosorbent assay (ELISA), and loop-mediated isothermal amplification (LAMP) techniques.

Venipuncture: Strengths and Limitations in Pediatric Settings

Venipuncture remains the clinical gold standard for many blood-based diagnostics, particularly when larger volumes are required for multiplex testing or confirmatory assays [14]. It enables real-time plasma separation and minimizes matrix effects, which are more common in whole blood or DBS samples.

However, its limitations are notable:

i. **Invasiveness and pain**: Venipuncture causes significant anxiety in children and requires restraint or sedation in some cases [15].
ii. **Technical requirements**: Skilled personnel and sterile equipment are mandatory, limiting its use in remote areas.
iii. **Risk of complications**: Hematomas, infections, and needle-stick injuries present occupational and patient-related hazards.
iv. **Sample transport constraints**: Blood samples must often be refrigerated and processed within hours to preserve analyte integrity.

In rural or community-based settings, these barriers can delay diagnosis and treatment initiation, making it imperative to consider alternatives like DBS for frontline diagnostics.

Comparative Accuracy of DBS and Venipuncture in Glucose Monitoring

Glucose monitoring through DBS has gained attention due to its non-invasive nature and practicality in field settings. Several validation studies comparing DBS glucose values to plasma glucose from venipuncture have demonstrated high correlation coefficients ($r > 0.90$), suggesting that DBS is a valid alternative when processed promptly and under controlled drying conditions [16].

Nevertheless, some limitations must be acknowledged:

i. **Hematocrit effect**: High or low hematocrit values can affect the uniformity of blood absorption onto filter paper, potentially skewing glucose quantification.
ii. **Environmental conditions**: High humidity can degrade glucose before the sample is completely dried.
iii. **Analytical variability**: Compared to automated plasma glucose analyzers, DBS methods may have higher coefficients of variation, although acceptable for screening purposes [17].

Despite these constraints, DBS is increasingly incorporated into telehealth models and school-based diabetes screening programs, where it provides reliable trend monitoring rather than point-of-care decision-making.

Comparative Performance in Malaria Diagnosis

The use of DBS for malaria detection is well-established, particularly for molecular diagnostic applications [18]. PCR and ELISA techniques have shown comparable sensitivity and specificity to venous blood samples when DBS is properly collected and stored [19]. In fact, DBS samples are frequently used in malaria surveillance programs to track parasite prevalence and genetic mutations associated with drug resistance.

A meta-analysis comparing diagnostic yields from DBS and venipuncture in children under 15 years found minimal performance discrepancies. PCR positivity rates were nearly identical, while rapid diagnostic tests (RDTs) using DBS eluates showed slightly lower sensitivity, particularly at low parasite densities. However, the ease of repeat sampling and longitudinal follow-up in children using DBS compensates for this modest diagnostic compromise.

Moreover, newer technologies such as LAMP have shown promise in enhancing malaria detection sensitivity from DBS, with the added advantage of operational simplicity and compatibility with field diagnostics.

Operational Feasibility and Acceptability in Pediatric Populations

From an implementation standpoint, DBS outperforms venipuncture in terms of feasibility, especially in resource-constrained settings. Field studies have demonstrated that community health workers with minimal training can successfully collect DBS samples with high fidelity. Additionally, parental acceptability is higher due to reduced pain, perceived safety, and shorter procedure time.

In children with chronic conditions such as diabetes, repeated venipuncture may lead to needle fatigue and reduced clinic adherence [20]. DBS offers a gentler alternative that supports more frequent monitoring without exacerbating procedural distress. This is particularly relevant in integrated care models where a single finger-prick sample can serve multiple diagnostic needs.

Cost-effectiveness studies have also favored DBS in scenarios requiring repeated surveillance, as the infrastructure and consumables required are significantly less expensive than those for phlebotomy-based systems.

Challenges and Limitations of Dried Blood Spot Testing

Despite its many advantages, DBS is not without limitations:

i. **Standardization gaps**: There is a lack of uniform protocols across laboratories for DBS processing, leading to potential variability in results [21].
ii. **Sample integrity**: Improper drying or contamination can compromise analyte stability.
iii. **Quantitative limitations**: Some assays, such as insulin or C-peptide measurements, may exhibit reduced sensitivity or accuracy in DBS format [22].
iv. **Regulatory hurdles**: In many regions, DBS-based diagnostics are not yet approved for definitive clinical decision-making, relegating them to screening or research applications.

These challenges underscore the importance of strengthening quality control mechanisms and harmonizing laboratory procedures for DBS analysis, particularly as its adoption scales in pediatric and public health contexts.

Integration into Dual Disease Management Models

The dual use of DBS for glucose and malaria monitoring represents a strategic alignment with integrated disease management paradigms. Programs such as the Integrated Management of Childhood Illness (IMCI) and the WHO's Package of Essential Noncommunicable (PEN) disease interventions for primary care could benefit from incorporating DBS diagnostics to simultaneously address infectious and metabolic conditions.

Pilot programs in Kenya, Ghana, and Uganda have demonstrated the feasibility of incorporating DBS sampling into routine child health visits [23, 24]. In these models, children presenting with fever or other nonspecific symptoms were screened for malaria and hyperglycemia using a single DBS sample. The results informed immediate management decisions and longitudinal care planning.

Such integrated diagnostics are especially valuable in areas with high disease overlap, where they can enhance case detection, reduce missed opportunities for treatment, and improve care continuity for children with comorbid conditions.

CONCLUSION

In conclusion, dried blood spot testing offers a compelling alternative to venipuncture for the dual monitoring of malaria and glucose levels in diabetic children. Its minimally invasive nature, logistical convenience, and cost-

effectiveness make it particularly suitable for pediatric populations in resource-limited and community-based settings. Empirical evidence supports its diagnostic accuracy for both glucose estimation and malaria detection, especially when standardized protocols and appropriate analytical platforms are employed. While venipuncture remains indispensable for certain confirmatory diagnostics and complex biochemical analyses, its limitations in pediatric care particularly regarding invasiveness, technical demand, and cold chain requirements highlight the need for complementary strategies like DBS. The operational advantages of DBS align well with integrated child health models and can enhance surveillance, early diagnosis, and continuity of care for children facing the dual burden of communicable and non-communicable diseases. Nonetheless, further efforts are required to refine DBS methodologies, standardize analytical procedures, and expand regulatory acceptance. Investments in capacity building, quality assurance, and technology adaptation will be critical to realizing the full potential of DBS in pediatric dual-disease management. As health systems strive for equity and innovation, DBS presents a promising pathway toward more accessible and child-friendly diagnostics.

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