Toward new diagnostic tools to improve preeclampsia care

PROBLEM

The risk a pregnant woman dies from preeclampsia (PE) in a developing country is approximately 300 times greater than in developed countries.[1] Prevention of severe clinical complications, including death, due to PE requires accurate and timely identification of women at high risk and linking them to proper care. Currently, proteinuria remains one of the primary diagnostic indicators used to identify women at increased risk for PE. However, current diagnostic tools available for proteinuria determination in developing countries have significant limitations in accuracy, in the case of the widely-used protein-only dipstick[2], or their accessibility due to the technical complexity and expense of laboratory-based reference standards such as the 24-hour urine collection.

SOLUTION – DEVELOPMENT OF NEW TOOLS

PATH has a strong track record of over 35 years in the development and introduction of innovative diagnostic solutions to support testing needs in low-resource settings. Since 2012 we have worked to improve tools for PE risk assessment and diagnosis. Our first step was analyzing the unmet needs for PE diagnosis and identifying potential solutions including assessing the potential suitability of promising host biomarker candidates for use in new screening and diagnostic devices intended for low-resource settings[3,4,5]. Next, we commenced work to accelerate development of new diagnostics. Our development strategy follows a portfolio approach, with two main efforts in parallel: (1) co-development of a near-term solution, a protein-creatinine dipstick that offers low cost, a meaningful improvement in performance over the incumbent solution, and a relatively fast route to market; (2) early-stage research to develop next-generation point- of-care diagnostics for promising PE biomarkers.

In addition to early funding to PATH from Merck for Mothers that supported initial landscape analysis, our PE diagnostics portfolio has attracted funding from several donors including two awards from USAID (Saving Lives at Birth) and support from the Bill & Melinda Gates Foundation and the Medical Research Council of South Africa. Partners are essential to the success of our work. Progress to date has been made possible by the collaboration with clinical partners including Dr. James Roberts (Magee Women's Research Institute, Pittsburgh, PA) and Dr. Peter von Dadelszen (St. Georges, University of London), and commercial partners including Louis Roux at LifeAssay Diagnostics (Cape Town, South Africa).

NEAR-TERM: A NEW PROTEIN/CREATININE DIPSTICK

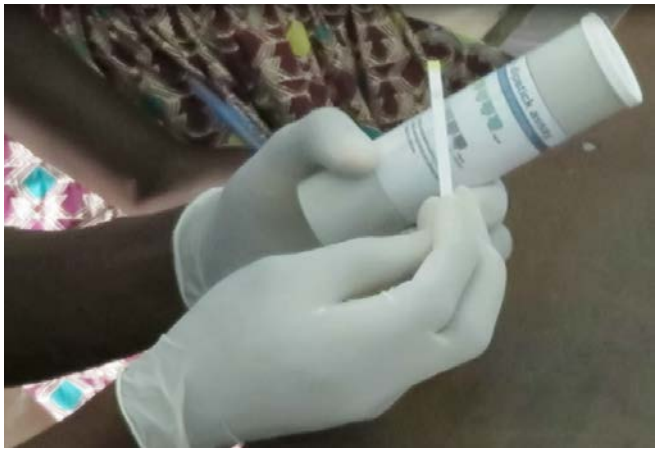
Midwife performing the LifeAssay Diagnostic Pr/Cr dipstick test during usability study in Ghana (Photo Credit: Emily Gerth-Guyette/PATH)

Spot urine tests that provide ratiometric measurement of protein-to-creatinine (Pr/Cr) can improve the accuracy of proteinuria screening compared to protein-only measurement. Unlike the protein-only dipstick, Pr/Cr testing adjusts for urine dilution--thus limiting the impact of body hydration levels on test performance. Results of Pr/Cr measurement have previously been reported to correlate well with those of the current reference standard, 24-hour urine collection, for detection of significant proteinuria[6].

In collaboration with LifeAssay Diagnostics, PATH has worked to develop a simple, inexpensive Pr/Cr ratiometric urine dipstick test with an estimated cost comparable to common protein-only dipstick products. Early laboratory-based verification of this prototype Pr/Cr dipstick test using over 500 characterized urine samples from pregnant women demonstrated performance comparable (85% sensitivity, 71% specificity*) to expensive reference laboratory-based assays for Pr/Cr determination and a current commercially-available point-of-care strip test that costs US$7 per strip. Results of recent pilot studies to assess the usability and temperature stability of the Pr/Cr test also indicated potential suitability for field use in the targeted peripheral antenatal care settings in developing countries.

LONG-TERM: NEXT-GENERATION PREDICTIVE TESTS

Diagnostics for assessing well-characterized host biomarkers for PE have great potential for earlier and more accurate identification of women at increased risk for adverse clinical outcomes[1].



Visual interpretation of the LifeAssay Diagnostics Pr/Cr dipstick during usability study in Ghana (Photo credit: Emily Gerth-Guyette/PATH)

However, current commercial test options for screening promising biomarkers, such as Placental Growth Factor, are too expensive and complex for use outside of large, well-resourced clinics. Thus access to these diagnostics to support antenatal care decisions in developing countries is likely to remain limited.

Funding through a USAID Saving Lives at Birth Seed award has supported PATH's early research and development activities for new lateral-flow immunoassay diagnostics for assessing urinary or blood biomarker candidates. We have completed early development of a new prototype rapid diagnostic test (RDT) with initial evaluation of its performance planned by the end of 2016.

The the LifeAssay Pr/Cr dipstick will be evaluated in a field-based validation for prospective use of the prototype test in an ANC program in Kintampo, Ghana for the next stage of development. This evaluation will not only build understanding of the use of the prototype but also generate pivotal data on the performance of the prototype, compared to reference testing and clinical data.

PATH is currently looking to secure funding to further advance development of this promising new PE biomarker RDT including expanded laboratory verification testing, field testing (validation and usability) and downstream technology transfer to a commercial partner.

FUTURE AVAILABILITY

With field validation set to begin in 2017 for the Pr/Cr dipstick, we estimate introduction for public-sector procurement by 2020. In our work with the prototype PE biomarker RDT, we hope to advance to transition-to-scale activities within the next 3 years, pending both funding and successful technical advancement. Based on the timing and outcome of development activities, we estimate introduction could begin by the mid-2020s or earlier.

CONTACT

Please contact Nicole Advani, Program Coordinator (nadvani@path.org), with any questions regarding this project.

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