Evaluation of the CareStart™ Glucose-6-phosphate dehydrogenase (G6PD) Rapid Diagnostic test at Community and Health Centers in Cambodia

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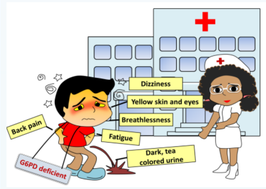
Background

Primaquine (PQ) is the only FDA-approved drug for radical cure of Plasmodium vivax *(P.v)* malaria but treatment can result in life-threatening hemolysis if given to a glucose-6-phosphate dehydrogenase deficient (G6PD***d***) patient. Therefore, the G6PD status of the patient with *P.v* must be known prior to prescribing PQ. To increase PQ access in Cambodia, performance of G6PD rapid diagnostic tests (RDTs) needs to be evaluated in healthcare workers (HCWs) and village malaria workers (VMWs).

There is insufficient data on performance of G6PD RDT **in field setting**, and whether it matches the performance demonstrated in controlled lab settings by researchers.



The G6PD RDT may enable safer application of PQ and reduce the burden of vivax malaria. Malaria workers need training on risks and benefits of PQ, G6PD testing and correct interpretation of G6PD RDT results in the field.

Objectives

- Develop training materials on G6PD and PQ to improve knowledge and acceptability of PQ use.
- Assess the HCW/VMWs' knowledge of PQ, their acceptability to test for G6PD using CareStart™, and willingness to give PQ when the G6PD status of the patient is known by RDT.

- Assess CareStart™ performance in the hands of healthcare and village malaria workers vs. expert readers both in field and laboratory settings against reference lab quantitative test (Pointe Scientific, Inc. MI).

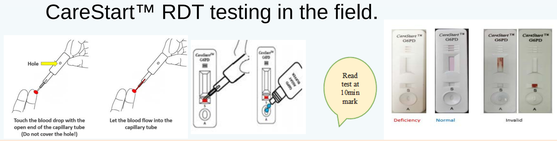
Methods

Design

- Quasi-experimental design in Oddar Meanchay province, Cambodia.
- Post-training, each of the 94 HCW/VMWs (age 18-69yrs) performed on average 10 G6PD RDT tests on 960 adult males.
- Performance of CareStart™ RDT for G6PD***d*** screening was assessed against quantitative G6PD test (Pointe Scientific, Inc. Canton MI).
- Pre/post-training questionnaires completed by HCW/VMWs and G6PD volunteers.

Blood sample collection

- Study was conducted from Dec, 2017 to Feb, 2018.
- Finger prick blood sample was obtained for CareStart™ RDT testing in the field.



- 2ml venous blood was collected in Vacutainer tubes (BD Vacutainer, Franklin Lakes, NJ) for CBC and quantitative G6PD testing in lab.

Data Collection

❖ Demographics data was collected with questionnaires
❖ Perceptions on PQ risk and benefits and willingness to use G6PD RDTs for screening was evaluated

Primary Endpoint

Assess the sensitivity, specificity, PPV and NPV of CareStart™ RDT in the field setting vs. the quantitative G6PD activity thresholds ("gold standard" for G6PD***d*** diagnosis).

The RDT test results obtained by trainees in the field were compared against the performance of the RDT test by expert readers both in field and laboratory settings

Analysis:

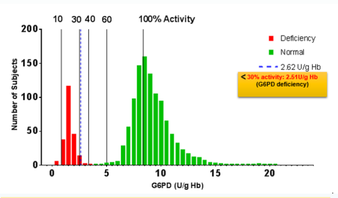
- Descriptive and inferential statistics to evaluate the acceptability and effectiveness of training.
- Stata 15, SPSS, and Graphprism 7. Standard methods for calculating sensitivity, specificity, PPV & NPV were applied to the G6PD RDT (95% CI)..

Reference standard

- The G6PD spectrophotometric quantitative analysis was performed using a Pointe G6PD reagent kit (Pointe Scientific, Inc. MI, USA).

Results

G6PD Test Results



		Quantitative Result (30% activity)	95% CI. Prevalence 16% (14%, 18.4%)
Trainee/RDT result in Field	Sensitivity (%)	96.8%	(92.6%, 98.9%)
	Specificity (%)	95.5%	(93.9%, 96.8%)
	PPV (%)	80.2%	(73.8%, 85.7%)
	NPV (%)	99.4%	(98.5%, 99.8%)
Expert (study Staff/RDT in Field)	Sensitivity (%)	96.15%	(91.8%, 98.6%)
	Specificity (%)	97.2%	(95.9%, 98.2%)
	PPV (%)	86.71%	(80.7%, 91.4%)
	NPV (%)	99.3%	(98.4%, 99.7%)
Expert/ RDT in controlled lab setting	Sensitivity (%)	94.2%	(89.3%, 97.3%)
	Specificity (%)	98.8%	(97.8%, 99.4%)
	PPV (%)	93.6%	(88.6%, 96.9%)
	NPV (%)	98.9%	(98%, 99.5%)

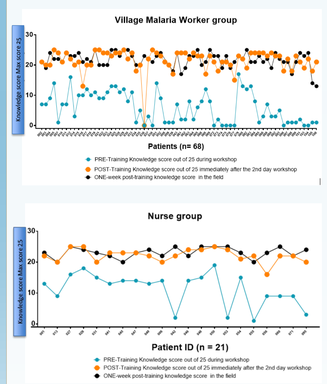
The G6PD test results were not statistically significant between the groups.

156/960 (16%) diagnosed as G6PD*d* (< 2.505)

The distribution of G6PD enzymatic activity according to spectrophotometry ranged from 0.05 to 22.57, with adjusted male median of 8.35 U/g Hb (100% activity).

G6PD RDT RESULTS	No. of G6PD normal cases read as deficient	No. of G6PD*d* cases read as normal G6PD
Trainees	37/960	5/960
Expert in field	23/960	6/960
Expert in lab	10/960	9/960

Knowledge about PQ and G6PD screening

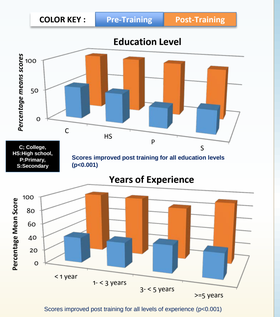


The pre/post training questionnaires assessed trainee knowledge, and perception of PQ risk and willingness to give PQ based on G6PD status by RDT.

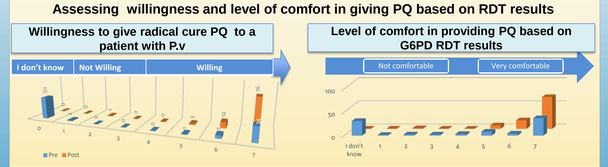
All scores improved post training

There was no statistical significance between the HCWs and VMWs

Survey Questionnaire	PRE-TRAINING	POST-TRAINING
Willingness to test for G6PD when a patient is diagnosed with malaria	56.3% (53/94)	80.8% (76/94)
Level of comfort in giving PQ based on G6PD RDT results	39.3% (37/94)	72.3% (68/94)
Level of comfort in giving PQ to a patient with *P.v* and normal G6PD test	36.1% (34/94	80.0% (76/94)
Willingness to give a patient PQ single dose for Pf without G6PD screening	20.2% (19/94)	84% (79/94)



Assessing willingness and level of comfort in giving PQ based on RDT results



The mean knowledge score pre-training was 33.86%(VMWs) and 56.4% (nurses), with a rise to 89% and 90% post training (p <0.001). The improvement in knowledge scores was independent on years of experience, profession and education level (p=0.57, p=0.38).

Conclusion

CareStart™ G6PD Rapid Diagnostic Test offered at the point-of-care will alleviate the lack of testing for G6PD***d***, thereby lowering the risk of hemolysis when PQ is prescribed.

Training tools and G6PD counseling script were very effective

Outcome of our study denoted a highly sensitive test (96.8%) with high NPV, valuable in reducing risk when PQ is prescribed.

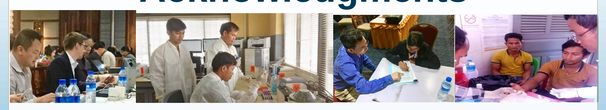
With minimal training, CareStart™ RDT is highly specific, feasible and a practical option for the identification of G6PD***d*** male patients and its use may enable safer prescribing of PQ to decrease the burden from *P.v* relapse.

Community engagement can have profound effect on PQ risk perceptions and integrating short training within community settings should be a priority with the planned deployment of PQ.

Most trainees were very receptive to the information provided about PQ and RDT testing, and were able to retain knowledge acquired during training.

Though the numbers were small, some G6PD***d*** volunteers will be misclassified as normal and therefore, patient follow up, monitoring and patient counseling will be paramount to successful deployment of PQ in Cambodia.

Acknowledgments



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