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Three-band (HRP-2/pLDH) rapid diagnostic tests for the diagnosis of severe *P. falciparum* malaria in Western Uganda

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Severe Malaria in Rural Sites

- Mortality among children with severe malaria who receive care at referral centers ranges from 10-30%, and is likely higher among those presenting to peripheral health facilities.[1,2]
- Detection of severe malaria in resource constrained settings is challenging due to requirements for laboratory infrastructure.
- There is a need for simple diagnostic tools that can be implemented in rural settings to identify severe malaria.

Study Aims

To explore the efficacy of three-band (combined HRP-2/pLDH) rapid diagnostic tests as a low-cost, scalable marker of severe malaria.

Study Overview

- Reviewed data for all malaria suspects at the Bugoye Health Health Center – Level III in the Kasese District of Western Uganda from January to March 2014

- Outcomes of interest:
  - (1) Severe anemia, defined as Hb <7g/dL
  - (2) Receipt of intravenous quinine
- Predictors of interest: two-(HRP-2) vs. three-band (HRP-2/pLDH) positive RDT result (Standard Diagnostics FK60 Malaria Ag *P. falciparum*/Pan), age, gender, distance & transmission season.
- In total, 1,509 patients underwent malaria testing with an RDT, of which 637 RDTs (42%) were positive for malaria.

Major Findings

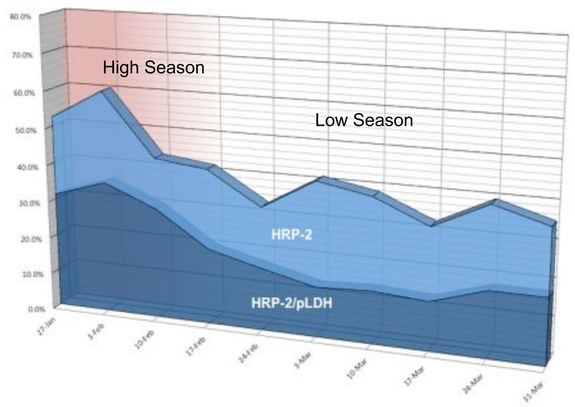
- **The majority (92%) of smears from patients with three-band positive RDT results were *P. falciparum* mono-infections.**

Table 1: Univariate comparison of patients with positive RDT by antigen category

	HRP-2 Positive	HRP-2/pLDH Positive	*p*-value
Absolute Number (%)	326 (51.5%)	307 (48.5%)	-
Sex (M/F)	124 / 202	123 /184	0.60
Mean Age (years)	38.8	36.0	0.22
Age <5 years (%)	87 (26.7%)	87 (28.3%)	0.64
Age <15 years (%)	**192 (58.9%)**	**216 (70.4%)**	**0.003**
Distant Villages (%)	33 (21.9%)	41 (30.9%)	0.069
Highest Villages (%)	**15 (4.6%)**	**5 (1.6%)**	**0.033**
High Transmission **Low Transmission**	**157 (48.2%)** **169 (51.8%)**	**203 (66.1%)** **104 (33.9%)**	**<0.001**

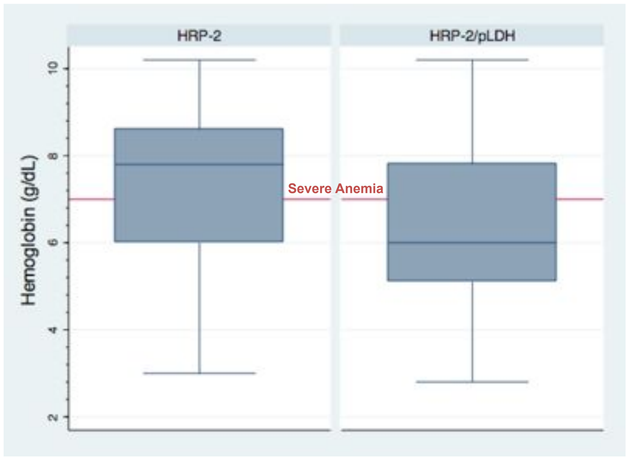
- **The proportion of three-band positive RDTs declined during the transition from high to low transmission seasons.**

Distribution of positive RDT results



- **The mean Hb was lower in patients with a three-band positive RDT than those with a HRP-2 positive RDT (P=0.055).**

Distribution of Hb levels by RDT result



- **A three-band positive RDT was the strongest predictor of severe anemia (AOR 5.25, 95%CI 0.83-33.4, P=0.08).**

Table 2: Logistic regression models for correlates of hemoglobin <7 milligrams/dL

	Univariate Model			Multivariate Model		
Characteristic	Odds Ratio	95% CI	*p*-value	Odds Ratio	95% CI	*p*-value
Female vs. male sex	1.28	0.53 - 3.13	0.58	-	-	-
Age < 15 years	3.83	1.35 - 10.84	0.011	2.35	0.37 - 14.9	0.37
Distant villages	0.18	0.02 – 1.59	0.12	0.27	0.21 - 3.31	0.30
High Transmission	1.83	0.76 - 4.44	0.18	1.22	0.029 - 1.74	0.15
3-band vs. 2-band RDT	**2.74**	**0.87 – 8.62**	**0.084**	**5.25**	**0.83 - 33.4**	**0.079**

**Explanatory variables meeting significance by a P-value of <0.25 in the univariable model were included in the multivariable model.*

- **Patients with three-band positive RDTs received treatment with anti-pyretics and parenteral quinine at a higher frequency**

Table 3: Regression models for correlates of IV quinine among patients with positive RDT

	Univariate Model			Multivariate Model		
Characteristic	Odds Ratio	95% CI	*p*-value	Odds Ratio	95% CI	*p*-value
Male vs. female	1.47	0.43 - 4.98	0.54	-	-	-
Age < 15 years	0.89	0.25 - 3.19	0.85	-	-	-
Presence of Comorbidity	0.44	0.81 - 2.43	0.35	-	-	-
Antibiotics	0.63	0.18 - 2.26	0.48	-	-	-
Distant Villages	0.68	0.072 - 6.36	0.74	-	-	-
High Season	6.52	0.80 - 52.88	0.079	5.59	0.68 - 46.0	0.11
3-band vs. 2-band RDT	**2.36**	**0.66 - 8.43**	**0.19**	**1.92**	**0.52 - 7.06**	**0.33**

**Explanatory variables meeting significance by a P-value of <0.25 in the univariable model were included in the multivariable model.*

Future Directions

If our results are corroborated, three-band RDTs, at least in environments where *P. falciparum* infections predominate, may help identify cases of severe malaria in peripheral health facilities where more advanced diagnostic testing is not available.

Limitations

- Retrospective, observational methodology
- Lack of paired microscopy and hemoglobin results for all specimens.
- Single site of observation small sample size, and a relatively short timeframe of data collection.
- Use of standard clinic and laboratory registers

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