USE OF RAPID DENGUE DIAGNOSTIC TESTS IN THE ROUTINE CLINICAL SETTING

Contact: lyda1oso@gmail.com

Lyda Osorio[1], Marcela Uribe[1], Gloria Inés Ardila[2], Yaneth Orejuela[2], Margarita Velasco[3], Anilza Bonelo[4] and Beatriz Parra[4]

GESP School of Public Health, Universidad del Valle, Cali, Colombia; 2. Laboratorio Especializado, COMFANDI, Cali, Colombia; 3. Health Services Evaluation Research Group, COMFANDI, Cali, Colombia; 4. VIREM Microbiology Department, Universidad del Valle, Cali, Colombia

Background

✓There is insufficient evidence on the performance and impact of dengue Rapid Diagnostic Tests (RDT) under routine conditions in clinical settings.

✓Evidence is required to take decisions on the implementation of dengue RDT and to inform R&D

✓We are conducting a Randomized Controlled Trial (RCT) of the validity and impact of dengue RDT in febrile subjects seeking medical care in a hyperendemic area in Colombia.

✓Our RCT does not include any educational intervention addressed to physicians or other health care staff.

Objective

To describe the patterns of use and performance of dengue RDTs in the routine clinical settings in an hyperendemic area in Colombia

Methods

✓All subjects attending 14 health care institutions in the state of Valle del Cauca in Colombia, between March and December 2012, who were clinically diagnosed with dengue or were requested a dengue test were included in the study. The latter were randomized to SD BIOLINE® Dengue IgM/IgG or SD BIOLINE® Dengue Duo NS1/IgM/IgG RDTs. Ethical approval was granted by Institutional Ethical Committees of Univalle and Comfandi.

✓Lab and clinical data was obtained from the centralized computer-based records of the health care institutions.

✓Sera samples were stored at -20ºC for quality control of RDT and measurement of Sensitivity and Specificity of RDTs against NS1 and IgM ELISA (Panbio® Alere Inc.).

✓Factors associated with requesting a dengue diagnostic test in subjects with clinically diagnosed dengue were identified with contingency tables (OR , 95% CI , chi^2 or exact tests), nonparametric tests (for quantitative variables) and multivariate logistic regression. A p-value <0.05 was considered as statistically significant.

Results

Quality control showed very high agreement of RDT results between the health care institutions and reference labs

Test	Institution / Reference Lab		Kappa Index % (95%CI)	Interpretation
	Positives	Negatives		
NS1 only	7/8	72/73	86.1 (67.3%-100%)	Almost perfect
IgM only	19/22	64/70	74.3 (58.6-90.1%)	Substancial
NS1 or IgM	18/21*1	55/60*2	70.7 (62.8%-84%)	Substancial
IgG only	27/34	53/58	71.7 (56.8%-86.5%)	Substancial

*1 Either positive *2 Both negative

Table 1. Results of quality control of dengue RDT by a reference lab

Sensitivity of IgM RDT against ELISA was low affecting the performance of DUO NS1/IgM

Component	Agreement RDT/ELISA		Sensitivity (95%CI)	Specificity (95%CI)
	Positives	Negatives		
NS1 only	25/28	310/316	89.3 (71.8-97.7)	98.1 (96-99.3)
IgM only	53/130	360/365	40.8 (32.2-49.7)	98.6 (96.8-99.6)
NS1 or IgM	42/68*1	169/174*2	54.4 (42-66.5)	97.1 (93.4-99.1)

*1 Either positive *2 Both negative

Table 2. Comparison of dengue RDT against ELISA

Results

A total of 1,039 dengue RDTs were performed in 925 subjects
35% of RDTs were Dengue NS1/IgM/IgG and 65% IgM/IgG
IgM and IgG positivity increased with time

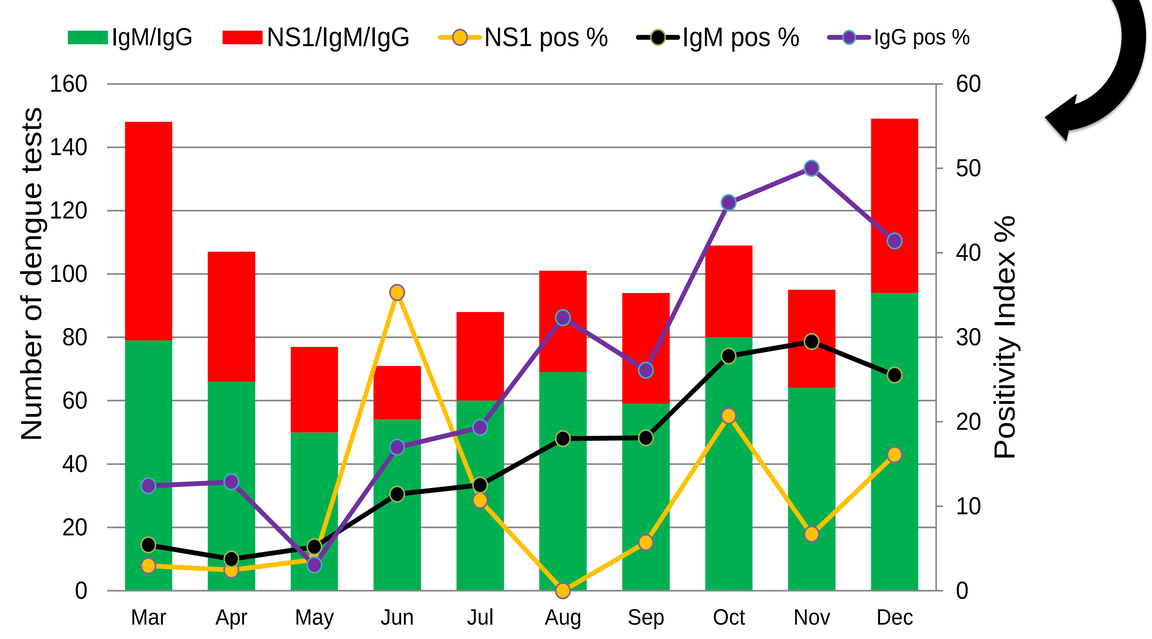
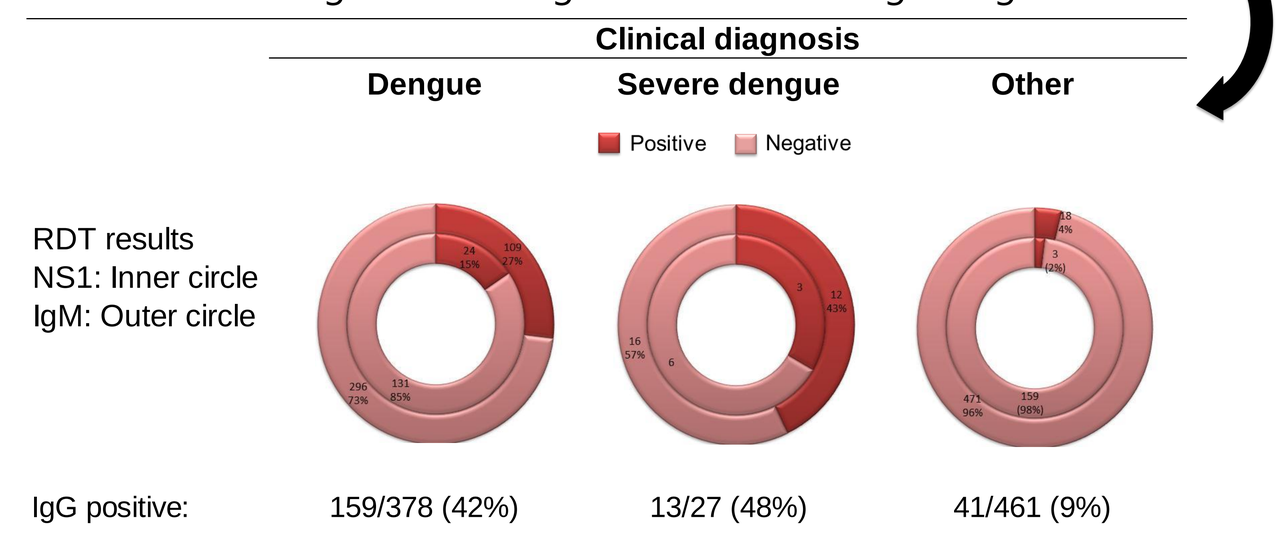


Figure 1. Trends in number of dengue RDTs requested and positive results

1 in 25 subjects whose clinical diagnosis was other than dengue had a positive dengue RDT. More than 60% of subjects with a clinical diagnosis of dengue were NS1 and IgM negative



Repeated tests: from 2 (n=43) to 5 (n=2) times. IgM seroconversion in 6 (5 with clinical dengue and 1 other diagnosis) 4/6 also serocorverted IgG , the other 2 were IgG positive in the first test

Figure 2. Dengue RDT results according to clinical diagnosis

Requesting a Dengue RDT was associated with severe dengue, seeking care in the emergency clinic, the highest level of care, and time of the year

Characteristic	Dengue test requested Yes N=386 (%)	No 392 (%)	OR (95%CI)	P-value	Adj OR (95%CI)	P-value
Sex						
Male	236 (61.1)	229 (58.4)	1			
Female	150 (38.9)	163 (41.6)	0.8 (0.7 - 1.2)	0.4		
Years of age						
Median (range)	20.8 (0.6-79)	20.9 (0.3 - 91.8)		0.3		
Dengue classification						
Non-severe	360 (93.2)	379 (96.7)	1			
Severe	26 (6.8)	13 (3.3)	2.1 (1 - 4.2)	0.03	2.2 (1.1 - 4.5)	0.02
Institution level of care						
Primary	147 (38.1)	221 (56.4)	1		*	
Secondary	93 (24.1)	104 (26.5)	1.3 (0.9-1.9)	0.09		
Tertiary	146 (37.8)	67 (17.1)	3.3 (2.2-4.7)	<0.001		
Ward						
Outpatient	171 (44.3)	237 (60.5)				
Emergency	215 (55.7)	155 (39.5)	2 (1.4 - 2.5)	<0.001	1.9 (1.4 - 2.5)	<0.001
Month						
March	46 (12)	81 (20.7)	1		1	
April	39 (10.1)	45 (11.5)	1.5 (0.8 - 2.6)	0.1	1.4 (0.7 - 2.4)	0.2
May	19 (5)	38 (9.7)	0.8 (0.4 - 1.7)	0.7	0.7 (0.4 - 1.5)	0.5
June	29 (7.5)	28 (7.1)	1.8 (0.9 - 3.4)	0.06	1.7 (0.9 - 3.3)	0.08
July	29 (7.5)	27 (6.9)	1.9 (1 - 3.5)	0.05	1.6 (0.8 - 3.1)	0.1
August	32 (8.3)	29 (7.4)	1.9 (1 - 3.6)	0.03	1.9 (1 - 3.6)	0.04
September	35 (9)	37 (9.4)	1.6 (0.9 - 3)	0.08	1.5 (0.8 - 2.7)	0.2
October	51 (13.2)	29 (7.4)	3 (1.7 - 5.5)	<0.001	3.1 (1.7 - 5.5)	<0.001
November	36 (9.3)	25 (6.4)	2.5 (1.3 - 4.7)	0.004	2.3 (1.2 - 4.4)	0.008
December	70 (18.1)	53 (13.5)	2.3 (1.4 - 3.8)	0.001	2 (1.2 - 3.4)	0.006

* Dropped from model because collinearity with ward

Table 3. Factors associated with requesting a dengue RDT in subjects with clinical diagnosis of dengue

Conclusions

✓Dengue RDT are been used for both rule in and rule out diagnosis.

✓High sensitivity in diagnostic tests is required to correctly use them to rule out diagnosis.[1] The latter is not supported by sensitivity of current dengue RDTs.[2] Hence, there is demand for improved dengue RDT sensitivity.

✓Requesting a dengue diagnostic test appears to depend on physician/institutional`s , patient and epidemiological related factors.

✓IgM and IgG positivity indexes are potentially useful for early detection of outbreaks

✓Validity of these RDT results against gold standard methods and impact of RDT are to be determined.

✓ High sensitivity, a simple quality control strategy, and automatization are priorities for R&D of dengue diagnostics.

References

1. Users' Guides to the Medical Literature: A Manual for Evidence-Based Clinical Practice. Eds. Guyatt & Rennie. Chicago, IL: JAMA, 2008 2 .Osorio L, Ramirez M, Bonelo A, et al. Comparison of the diagnostic accuracy of commercial NS1-based diagnostic tests for early dengue infection. Virol J 2010

Funding and Acknowledgements

Funds provided by: Universidad del Valle CI1685, COMFANDI, and Standard Diagnostics Inc. We thank Zoraida , Claudia Vidal, Liliana Soto , Julio and Roberto for logistic support. Dr. Martha Ramos and her team for granting access to data. Personnel of Univalle for administrative support.

Disclaimer

The present study is partially funded by Standard Diagnostics Inc. However, the diagnostic test manufacturers do not have a role, either directly or through a third party, in the gathering or analysis of data or in the preparation of this poster