A COMPARATIVE ANALYSIS ON FIVE DIFFERENT FULLY AUTOMATED ANTI-RUBELLA IgG IMMUNOASSAYS REPORTING RESULTS IN IU/mL

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OBJECTIVES

Rubella-specific IgG testing is performed either for epidemiological studies, determination of the immune status or confirmation of rubella infection (this latter together with the detection of rubella-specific IgM). Since the 1980s rubella IgG assays have been calibrated against the World Health Organization (WHO) International Standard and the test results reported in International Units per milliliter (IU/mL). Initially the cut-off for Rubella IgG assays was set at 15 IU/mL. In the mid-90s the Rubella Subcommittee of the National Committee for Clinical Laboratory Standards proposed lowering the breakpoint for rubella immunity from 15 to 10 IU/mL. Despite that, some manufacturers and some laboratories decided to maintain their cut-offs at 15 IU/mL. So, with identical results, depending on the cut-off used, patients can be considered immune or non immune. The aim of this study was to compare, in terms of sensitivity and specificity five fully automated anti-rubella IgG immunoassays that report results in IU/mL.

METHODS

The study was performed on 482 samples from pregnant women with different levels of IgG anti-rubella antibodies selected with the method currently used in the laboratory ACCESS® Rubella IgG (Beckman Coulter, Galway, Ireland):

	Negative		eqv	low pos	pos
Range IU/mL	< 5	5 - 10	10 - 15	15 - 20	> 25
N° of samples	100	100	95	87	100

All samples were tested with four commercially available immunoassays on different automated immunoassay platforms. The cut-offs stated by the manufacturers in the respective product inserts were applied to classify the samples as positive or negative. The random-access immunoassays used in the study were LIAISON® Rubella IgG (DiaSorin, Saluggia, Italy), ARCHITECT® Rubella IgG (Abbott Laboratories, Middletown, USA), IMMULITE® 2500 Rubella Quantitative IgG (Siemens Healthcare, Surrey, UK), COBAS® Rubella IgG (Roche Diagnostics GmbH, Mannheim). Samples that showed discordant results between systems were further investigated by resolution with a commercially available immunoblot. Analytical performance were calculated versus expected results obtained using a combination of the consensus and immunoblot classification.

		DiaSorin LIAISON®	Beckman ACCESS®	Abbott ARCHITECT®	Siemens IMMULITE®	Roche COBAS®
		IU/mL	IU/mL	IU/mL	IU/mL	IU/mL
Result interpretation	Negative	< 9	< 10	< 4.9	< 5	< 10
	Equivocal	≥ 9 - 11	≥ 10 - 15	5.0 - 9.9	≥ 5.0 - 10	-
	Positive	≥ 11	> 15	≥ 10.0	≥ 10	≥ 10

RESULTS

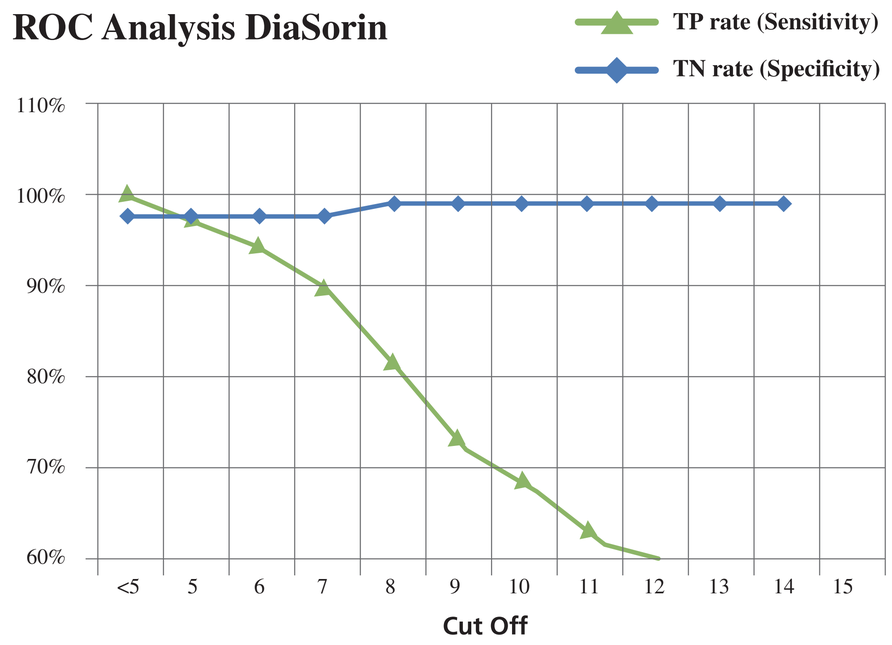
At first evaluation 88 samples were negative by all methods, 175 positive and 219 discordant. After immunoblot analysis on discordant samples, 217 were classified as positive and 2 as negative. The classified 90 negative and 392 positive samples were used to determine the sensitivity and specificity of each assay.

Assay	Cut off IU/mL	Sensitivity (%) (95% confidence limits [%]) with equivocal results assigned as:		Specificity (%) (95% confidence limits [%]) with equivocal results assigned as:	
		Positive	Negative	Positive	Negative
ACCESS®	10-15	71.4 (66.7-75.9)	47.7 (42.9-53.0)	97.8 (92.2-99.7)	100 (96.0-100)
LIAISON®	9-11	73.2 (68.5-77.5)	63.3 (58.3-68.0)	98.9 (94.0-100)	98.9 (94.0-100)
ELECSYS®	10	85.7 (81.9-89.0)	85.7 (81.9-89.0)	97.8 (92.2-99.7)	97.8 (92.2-99.7)
ARCHITECT®	5-9.9	95.2 (92.5-97.1)	68.9 (64.0-73.4)	97.8 (92.2-99.7)	98.9 (94.0-100)
IMMULITE®	5-10	99.5 (92.2-99.9)	84.9 (81.0-88.3)	97.8 (92.2-99.7)	97.8 (92.2-99.7)

ROC analysis was performed to calculate the cut-off required to achieve 95% sensitivity for the LIAISON® assay:

Cut Off to attain 95% Sensitivity (IU/mL)	
DiaSorin LIAISON®	5.80

Cut-off (IU/mL)	5	6	7	8	9	10	11	12	13	14	15
TP rate (Sensitivity)	97%	94%	90%	82%	73%	69%	63%	59%	55%	50%	47%
TN rate (Specificity)	98%	98%	98%	98%	99%	99%	99%	99%	99%	99%	99%



A wider gray zone between 5 and 10 IU/mL was applied to results of the LIAISON® assay; sensitivity and specificity were re-calculated.

Assay	Cut off IU/mL	Sensitivity (%) (95% confidence limits [%]) with equivocal results assigned as:		Specificity (%) (95% confidence limits [%]) with equivocal results assigned as:	
		Positive	Negative	Positive	Negative
LIAISON®	5-10	97.2 (68.5-77.5)	68.9 (42.9-53.0)	97.8 (92.2-99.7)	98.9 (94.0-100)

CONCLUSIONS

Even though all assays reported results in IU/mL, this study showed only a moderate correlation, particularly in terms of sensitivity. An improvement in sensitivity without impact on specificity can be observed on LIAISON® assay by use of a gray zone between 5-10 IU/mL, mainly when equivocal results were considered as positive. Due to the increase in the immunization coverage, an increasing percentage of the population show low antibody levels in comparison with those elicited by natural infection. The screening cut-off level of 10 IU/ml was determined in 1995 on the basis of early epidemiological studies and the correlates for protection now need review to support appropriate management of a young antenatal population. (L.Byrne et al., Vaccine 30 (2012) 161-167)

22nd ECCMID London, United Kingdom, 31 March-03 April 2012 P997