

DEFINITION OF THE UPPER REFERENCE LIMIT FOR THYROID PEROXIDASE AUTOANTIBODIES ACCORDING TO THE NACB GUIDELINES: COMPARISON OF SEVEN DIFFERENT AUTOMATED METHODS. PART B

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Background-Aim

Autoantibodies against thyroid peroxidase (TPOAb) are diagnostic hallmarks of autoimmune thyroid diseases. The estimation of TPOAb upper reference limit (URL) is a controversial issue because of method variability and different criteria to define the reference population. According to the NACB guidelines, TPOAb URL should be established from 120 subjects with the following features: male, younger than 30 years, biochemically euthyroid, without history of thyroid disease and non-thyroid autoimmune diseases. The aim of the study was to investigate the validity of the NACB guidelines by comparing TPOAb URLs obtained from 120 healthy males (M) and 120 healthy females (F).

Methods

In an Italian population study, 7970 subjects were screened for thyroid disease (family/personal history, function tests and neck ultrasound). Among them, 120 M and 120 F were selected. Their sera were tested for TPOAb concentration by using 12 automated immunometric methods. In this communication, we reported the results of 7 chemiluminescent methods: Architect ci4100 (ARC, Abbott), Liaison XL (LIA, Diasorin), Lumipulse G1200 (LUM, Fujirebio), Maglumi 2000 Plus (MAG, Snibe), UniCel DxI 800 (UNI, Beckman Coulter) and AIA-CL2400 (CL2, Tosoh Bioscience) and one fluorimetric method: AIA-2000 (AIA, Tosoh Bioscience) (Table 1). URL was established at 99th percentile. The non-parametric Mann-Whitney U test was used to compare TPOAb levels in M and in F within the same method. A two-sided value of $p < 0.05$ was considered statistically significant.

Company	Platform	Method/Tracer	Antigen	Abbreviation
Abbott	Architect ci4100	CLIA/Acrinium esters	recTPO	ARC
Diasorin	Liaison XL	CLIA/Isoluminol derivative	recTPO	LIA
Fujirebio	Lumipulse G 1200	CLIA/AMPPD	recTPO	LUM
Snibe	Maglumi 2000 Plus	CLIA/N-(aminobutyl)-N-(ethyl)-isoluminol	natTPO	MAG
Beckman Coulter	UniCel Dx880i	CLIA/Alkaline phosphatase-Lumiphos 530	recTPO	UNI
Tosoh Bioscience	AIA-2000	FIA/4-methyl-umbelliferyl phosphate	recTPO	AIA
Tosoh Bioscience	AIA-CL2400	CLIA/DIFURAT	nd	CL2

Table 1. Companies, platforms and methods involved in the study.

Abbreviations. AMPPD: Alkaline phosphatase-aminantyl-methoxy-phosphoryloxy-phenyl-dioxetane; CLIA: chemiluminescence immunoassay; DIFURAT: 3-(5-tert-Butyl-4,4-dimethyl-2,6,7-trioxabicyclo[3.3.2]hept-1-yl) phenylphosphate disodium salt; FIA: fluorimetric immunoassay; TPO: thyroid peroxidase.

Results

Value distributions were not Gaussian with a positive skew both for M and F (Figure 1). A statistically significant difference between M and F was observed for UNI and AIA but not for the other five methods (Table 2) (Figures 2-8). URLs were different according to the method and the gender (Table 2). Such URLs were generally lower than those stated by the manufacturers.

Platform	Sex	No.	Mean (C.I. 95%)	SD	Median	CV	p	URL	Package Insert cut-off
ARC	M	120	0.6 (0.62-0.74)	0.3	0.6	45.7	0.8	1.6	5.6
	F	120	0.7 (0.65-0.78)	0.4	0.6	51.3		2.0	
LIA	M	120	3.2 (2.62-3.87)	3.4	1.9	106.0	0.8	14.2	16.0
	F	120	3.2 (2.56-3.87)	3.9	1.7	111.3		17.9	
LUM	M	120	2.5 (2.28-2.63)	1.0	2.2	39.3	0.8	5.5	6.9
	F	120	2.4 (2.29-2.75)	0.9	2.2	37.7		5.2	
MAG	M	120	5.5 (4.28-6.66)	6.5	2.7	119.8	0.8	24.6	30.0
	F	120	4.9 (3.78-6.10)	6.2	2.2	126.3		25.4	
UNI	M	120	1.1 (0.91-1.37)	1.2	0.7	108.7	<0.05	7.0	9.0
	F	120	1.5 (1.16-1.74)	1.6	1.0	108.9		8.5	
AIA	M	120	0.4 (0.40-0.44)	0.1	0.4	25.9	<0.05	0.8	3.2
	F	120	0.5 (0.44-0.50)	0.2	0.4	32.7		1.0	
CL2	M	120	0.3 (0.23-0.33)	0.3	0.2	101.9	0.8	1.6	3.0
	F	120	0.3 (0.19-0.36)	0.3	0.2	104.7		1.5	

Table 2. Main statistical parameters of TPOAb, measured by the five different methods in males and females.

Median, URL and package insert cut-off are expressed in IU/mL; CV is expressed in %. Abbreviations. M: males; F: females; CV: coefficient of variation; URL: upper reference limit

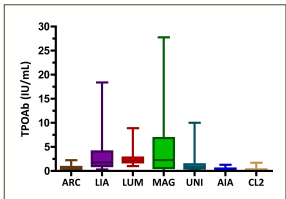


Figure 1. Value distribution of TPOAb (120 M and 120 F) measured by the five methods.

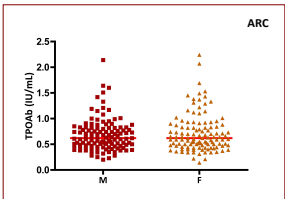


Figure 2. Comparison between values of TPOAb in males and in females (Architect ci 4100). Red line: median.

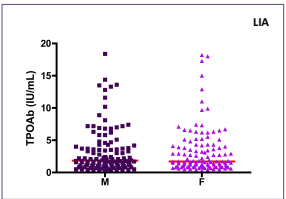


Figure 3. Comparison between values of TPOAb in males and in females (Liaison XL). Red line: median.

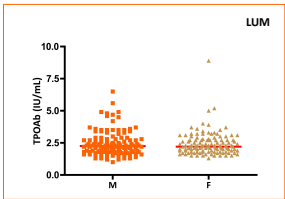


Figure 4. Comparison between values of TPOAb in males and in females (Lumipulse G 1200). Red line: median.

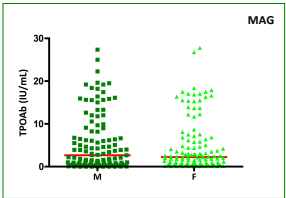


Figure 5. Comparison between values of TPOAb in males and in females (Maglumi 2000 Plus). Red line: median.

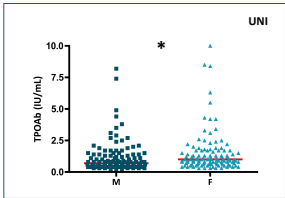


Figure 6. Comparison between values of TPOAb in males and in females (UniCel Dx880i). Red line: median. * $p < 0.05$

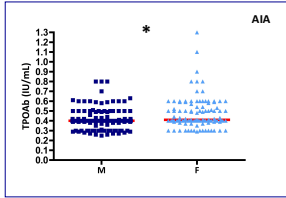


Figure 7. Comparison between values of TPOAb in males and in females (AIA-2000). Red line: median. * $p < 0.05$

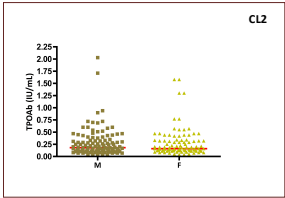


Figure 8. Comparison between values of TPOAb in males and in females (AIA-CL2400). Red line: median.

Conclusions

TPOAb URLs were method- and gender-dependent and they were similar or lower than those proposed by manufacturers, which do not distinguish between sexes. Therefore, unlike what is indicated by the the NACB guidelines, laboratories have the opportunity to use gender-specific reference intervals.