The increased prevalence of celiac disease: what is the contribution of an improved diagnostic accuracy?

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Anil K. Verma,[1] Simona Gatti,[1,2] Elena Lionetti,[1,2] Tiziana Galeazzi,[1] Chiara Monachesi,[1] Elisa Franceschini[1,2], Linda Balanzoni,[3] Novella Scattolo,[4] Mauro Cinquetti,[3] Carlo Catassi[1]

[1]Celiac Disease Research Laboratory, Department of Pediatrics, Università Politecnica delle Marche, Ancona ,ITALY
[2]Department of Pediatrics, Università Politecnica delle Marche, Ancona ,ITALY
[3]Department of Pediatrics, Ospedale "G.Fracastoro", San Bonifacio (Verona),Azienda ULSS 20, Scaligera, ITALY
[4]Laboratorio Analisi, Ospedale "G.Fracastoro", San Bonifacio (Verona),Azienda ULSS 20, Scaligera, ITALY

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Introduction

- In current time IgA class of anti tissue transglutaminase antibody (IgA anti tTG ab) is the most reliable serological marker for the celiac diseae (CD)
- IgA anti gliadin ab (AGA) was used as a reliable CD sero-marker for several years
- AGA serology was used as a sole test to screen CD cases during 90's
- In the last years an increase in frequency of celiac disease (CD) has been observed
- A previous multicenter Italian AGA based study in school age children found an overall CD prevalence of 0.54%, with a ratio of known to undiagnosed CD cases of 1 in 7

Catassi et al. Acta Paediatr Suppl 1996

AIM

To evaluate the rate of "potentially missed CD cases" by screening studies based on anti-gliadin (AGA) IgA antibodies in order to compare CD prevalence rates from current studies (based on IgA anti tTG ab or anti-endomisium –EMA antibodies)

Methodology

sera samples were collected from a large CD serological screening project perfomed in Italian school-age children 5-10 years during the years 2015-2016

Selection of study materials:

- Untreated CD (n=46): Sera of IgA tTG, EMA positive, and HLA DQ2/DQ8 predisposed children already detected in a screening project in Italy were considered
- Healthy controls (n=92): For each untreated CD, two IgA tTG, EMA negative, HLA predisposed subjects were tested as matched controls (same sex, age and ethnicity)
- Celiac disease was diagnosed according to the ESPGHAN 2012 criteria. Children with IgA-deficiency were excluded

Test Procedure:

- IgA AGA was analyzes by a commercially available sandwich-type enzyme immunoassay α-GliaPep IgA (Eurospital, Trieste, Italy)
- IgA anti tTG ab was analyzed by Quanta Flash® h-tTG (Inova Diagnostics, San Diago CA, USA)
- EMA was performed by Nova Lite ® monkey Esophagus (Inova Diagnostics, San Diago CA, USA)
- HLA DQ2/DQ8 genotyping was charecterised by, «Celiac Gene Screen rapid HLA DQ typing test» developed by BioDiagene S.R.L. (Palermo, Italy)

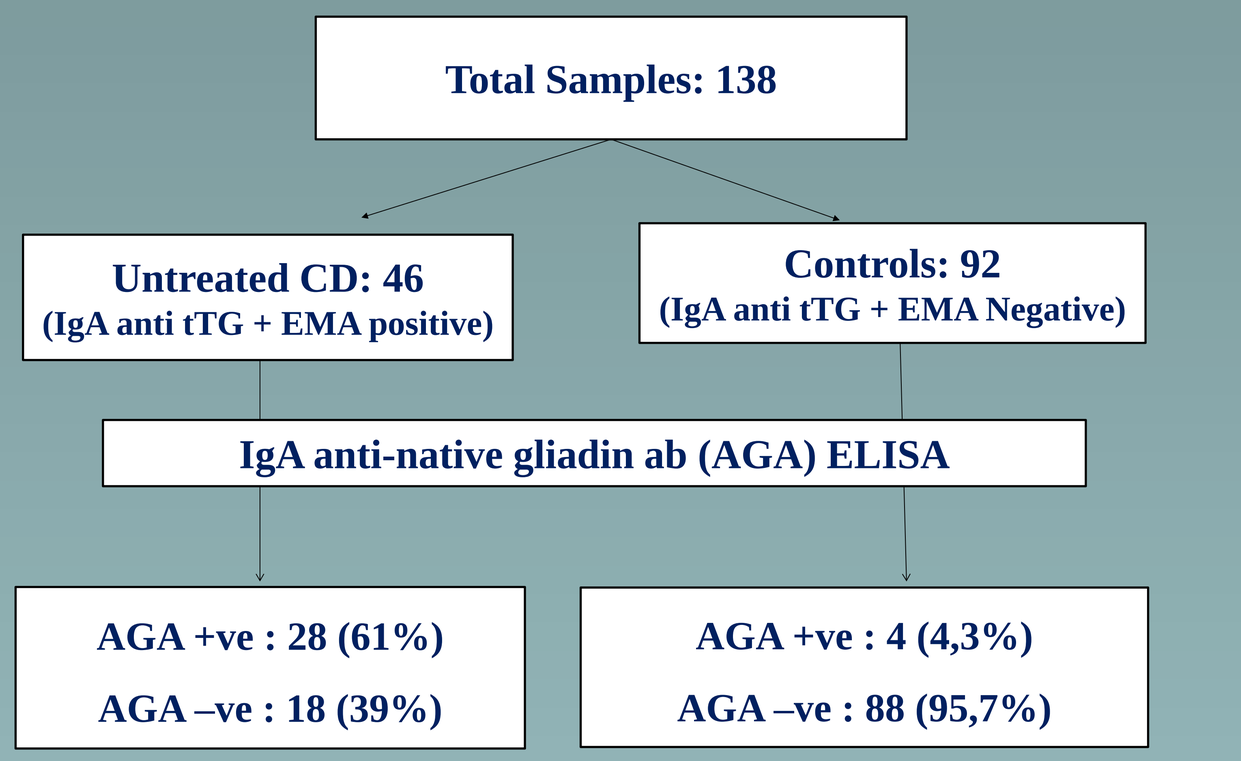
Manufacture's guidelines were followed for all laboratory test preocedures

Statistical Analysis

The sensitivity, specificity, negative and positive predictive values of the IgA AGA and the 95% confidence interval (CI) were calculated. Data analysis were performed using IBM Software Program Stata System (SPSS), version 25

Results

Fig.1 : IgA AGA status in children with untreated-CD and unaffected controls



CD: Celiac Disease; tTG: anti-transglutaminase antibodies; EMA: anti-endomisium antibodies; AGA: anti-native gliadin antibodies

Table1: Results of IgA AGA determination in the study samples

Samples (HLA DQ positive)	Total no.	AGA Positive (%; 95%CI)	AGA Negative (%; 95% CI)
Untreated CD (anti tTG, EMA positive)	46	28 (61%; 47-75)	18 (39%; 25-53)
Control (anti tTG, EMA negative)	92	4 (4.3%; 0,2-8,4)	88 (95.7%; 94-100)

CD: Celiac Disease; tTG: anti-transglutaminase antibodies; EMA: anti-endomisium antibodies; AGA: anti-native gliadin antibodies

Table 2: Sensitivity , specificity positive and negative predictive values of IgA AGA

Statistical analysis	Value in percentage
Sensitivity	61%
Specificity	96%
Positive predictive value	87,5%
Negative predictive value	83%

Conclusions

- There is 39% genetically predisposed individuals having anti tTG IgA positve but AGA –ve
- Thees cases would have missed if AGA would be the final screening tool as in used to be in 90's
- previous prevalence studies based on AGA IgA as the initial screening test would have underestimated the prevalence of CD
- This discrepancy should be taken into account when comparing current prevalence of CD (based on EMA as screening technique) to previous figures

Anil K Verma, UNIVPM, Italy
Email: anilkrvermaa@gmail.com ; a.k.verma@pm.univpm.it

The authors declare no conflict of interest