Effect Of the Gluten Free Diet on Serum Zonulin Levels and Autoimmune Biomarkers in Both Treated and Untreated Celiac Disease Patients

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Background: It is well known that Celiac Disease (CD) can be associated with other autoimmune diseases (AD). It is however still unclear whether the CD-associated risk of other AD is related to ongoing gluten ingestion or simply depends on common genetic background. Zonulin, which is responsible for the modulation of intestinal permeability, is up regulated in CD and other AD, such as Type 1 diabetes. Our hypothesis is that the loss of barrier function secondary to zonulin increase in CD can be involved in the high risk for AD co-morbidity. **Aim**: To establish the changes of serum zonulin levels and serum autoimmune antibodies in patients with newly diagnosed CD and after treatment with the gluten-free diet (GFD). Patients and Methods: They were 54 patients diagnosed with CD (20 M and 34 F; mean age: 39y; biopsy-proven: 42/54). Associated AD were found in 7 subjects (1 Type 1 diabetes, 1 Graves's disease, 5 rheumatoid arthritis). Serum samples were collected at diagnoses and after a mean period of 17 months of GFD (range 10-49). All serum samples were measured for auto-antibodies related to CD (anti-transglutaminase - tTG, anti-endomysial - EMA), Type 1 diabetes (IA-2: tyrosine phosphates, IAA: anti-insulin antibodies, GAD: glutamic acid decarboxilase), thyroiditis (TPO: thyreoperoxidase antibodies, TG: thyreoglobulin antibodies), and zonulin levels. **Results:** at CD diagnosis increased serum zonulin were found in 76 % and autoantibodies were detected in 39 % (TPO: 21.7%, TG 19.6%, GAD 6.5%, ICA 4.4% and IA-2 2.5 %). After GFD, EMA and zonulin remained altered in 13% of patients, and tTG in 35% of the subjects. Some autoantibodies decreased (TPO: 10.9%, GAD 4.4%), while other remained unchanged (TG 23.9%, ICA 4.4%, and IA-2 2.2 %). Seven out of 53 patients did not start the GFD. These subjects had altered zonulin, EMA, and tTG and 14% of them were auto-antibodies positive. In these subjects, both zonulin levels and serum auto-antibodies did not change at the follow-up evaluation. **Conclusions:** Untreated CD typically show zonulin up-regulation and increased prevalence of serum auto-antibodies. After treatment with GFD, serum zonulin levels tend to normalize, a situation that is associated with a decreased prevalence of some auto-antibodies (especially TPO). These results indirectly suggest that recovery of the intestinal barrier function can decrease the risk of associated autoimmune phenomena.

Background

It is well known that Celiac Disease (CD) can be associated with other autoimmune diseases(AD). It is however still unclear whether the CD-associated risk of other AD is related to ongoing gluten ingestion or simply depends on common genetic background.

Zonulin, which is responsible for the modulation of intestinal permeability, is up regulated in CD and other AD, such as Type 1 diabetes. Our hypothesis is that the loss of barrier function secondary to zonulin increase in CD can be involved in the high risk for AD co-morbidity.

Aim

To establish the changes of serum zonulin levels and serum autoimmune antibodies in patients with newly diagnosed CD and after treatment with the gluten-free diet (GFD).

Patients and Methods

Fifty four patients diagnosed with CD (20 M and 34 F; mean age: 39y; biopsy-proven: 42/54) were enrolled. Associated AD were found in 7 subjects (1 Type 1 diabetes, 1 Graves's disease and 5 rheumatoid arthritis). Serum samples were collected at diagnoses and after a mean period of 17 months following GFD (range 10-49 months). All serum samples were measured for auto-antibodies related to CD (anti-tissue transglutaminase - tTG, anti-endomysial - EMA), Type 1 diabetes (IA-2: tyrosine phosphates, IAA: anti-insulin antibodies, GAD: glutamic acid decarboxilase), thyroiditis (TPO: thyreoperoxidase antibodies, TG: thyreoglobulin antibodies), and zonulin levels.

Results:

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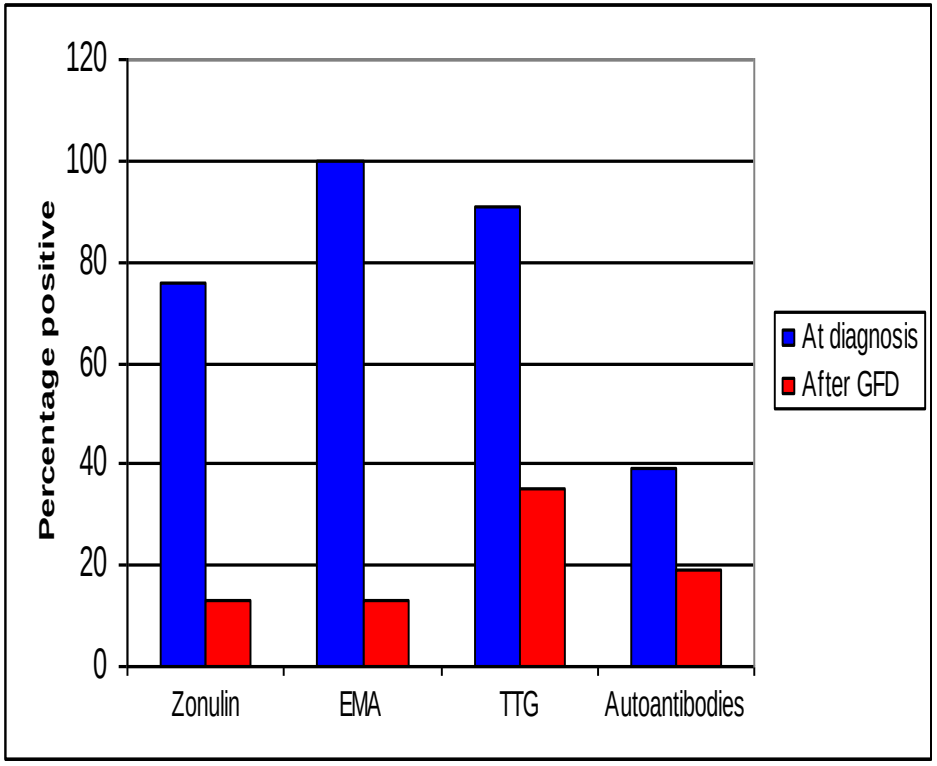
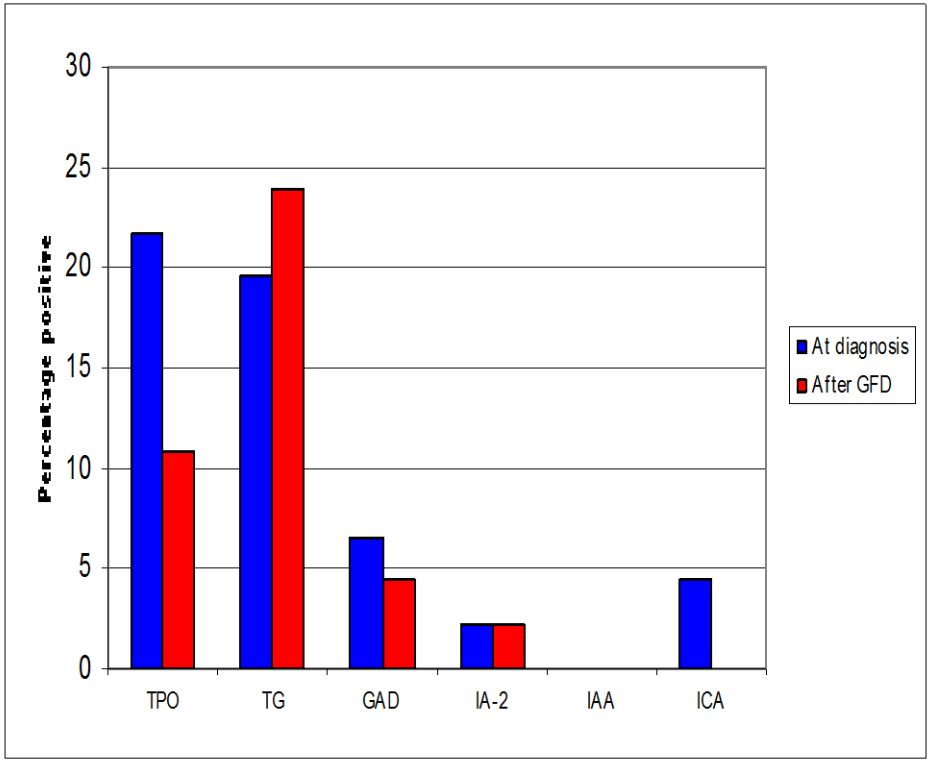
Celiac Disease Prospective Study:

Celiac Disease Patients that Complied to the Diet

Celiac disease Biomarkers



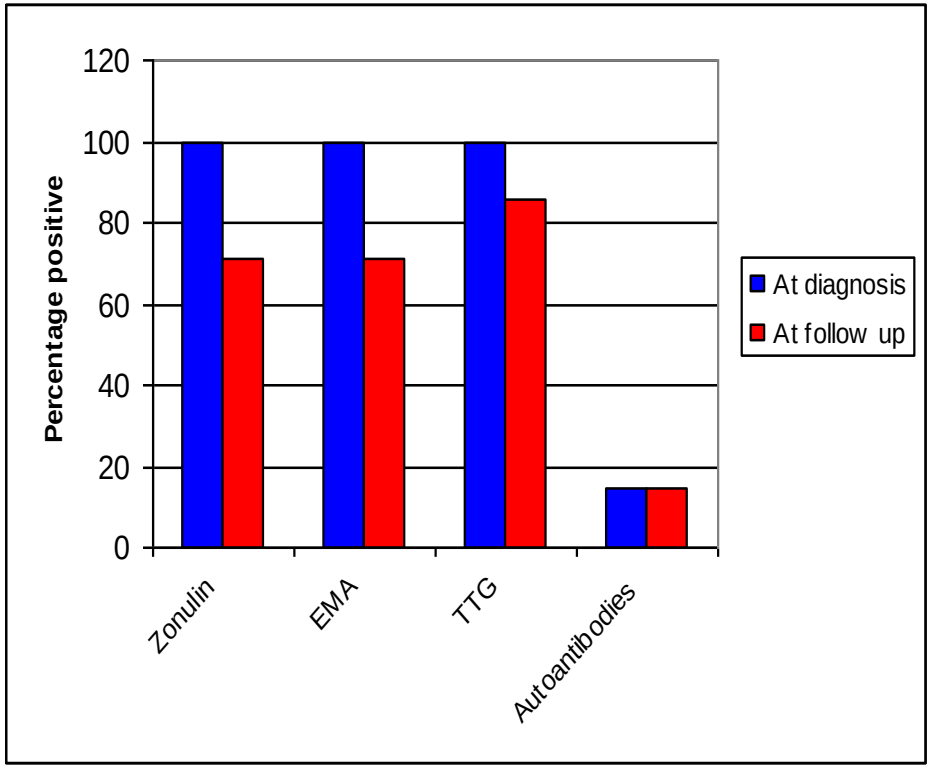
Autoantibodies



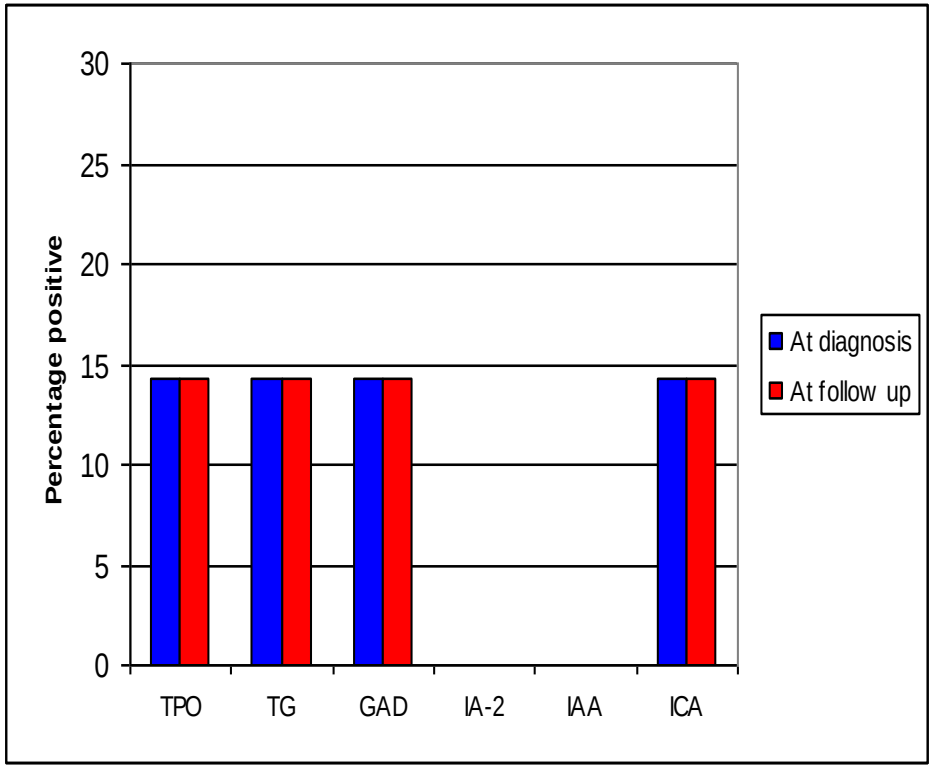
Celiac Disease Prospective Study:

Celiac Disease Patients that Did Not Comply to the Diet

Celiac disease Biomarkers

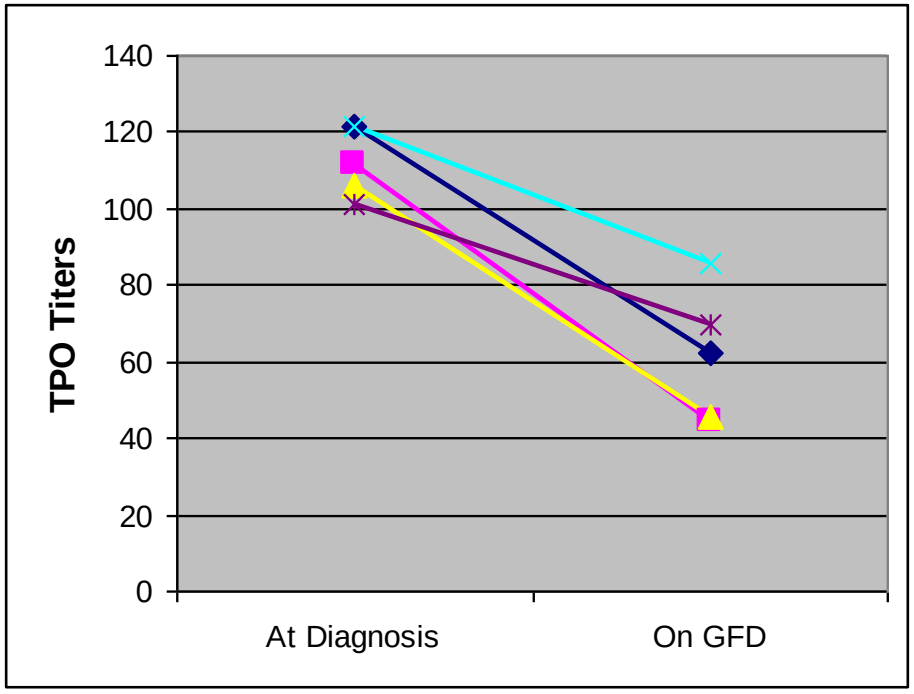


Autoantibodies

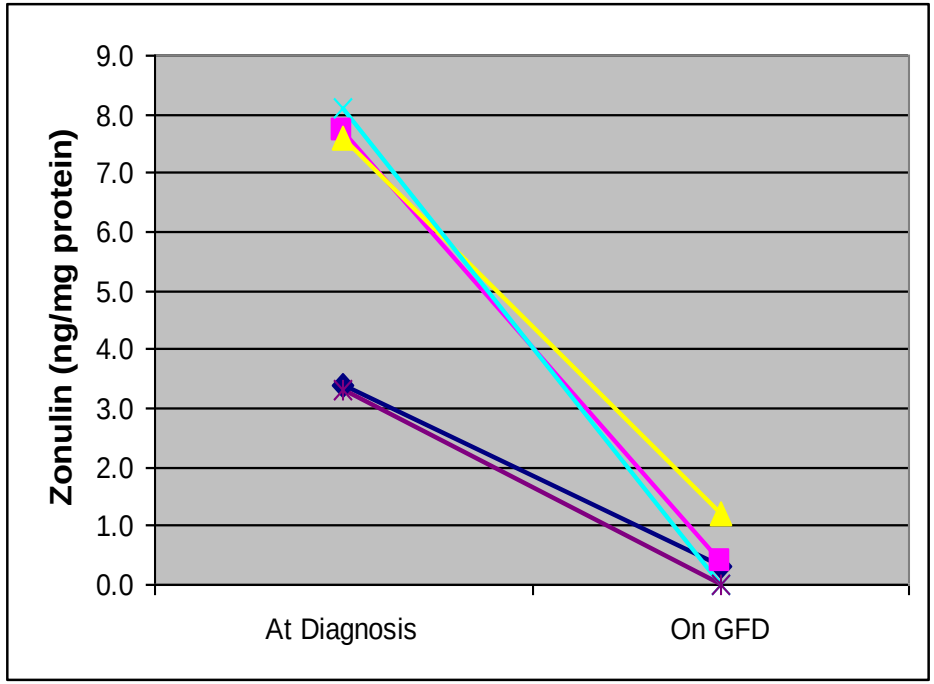


TPO Titers and Zonulin Serum Levels in Subjects That Responded to the GFD

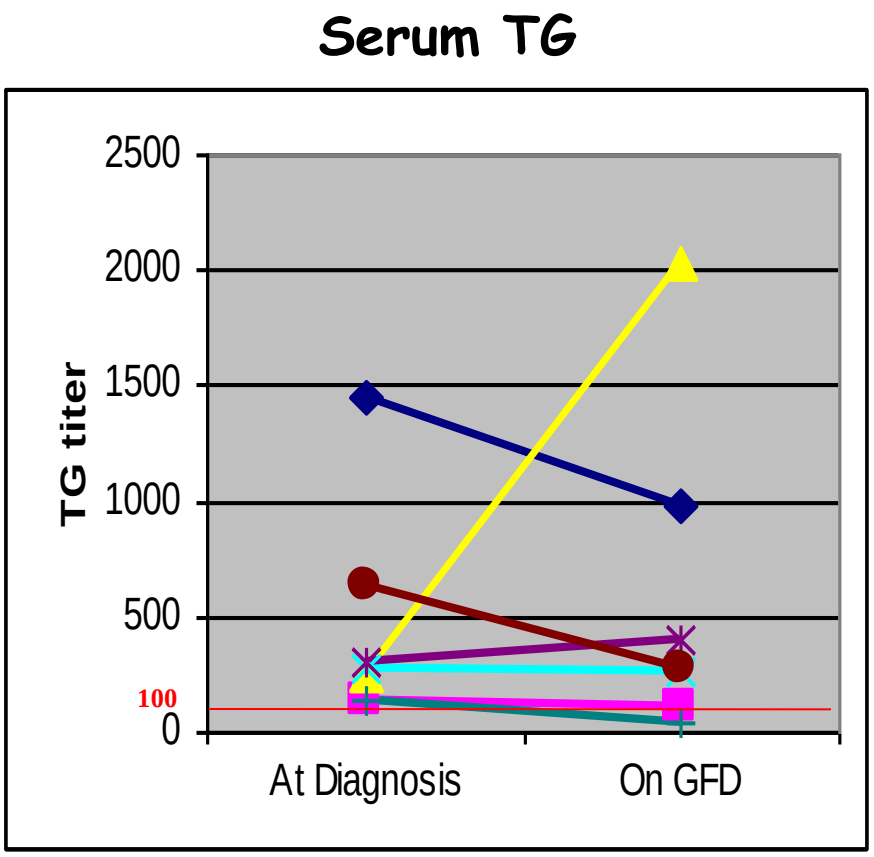
Serum TPO

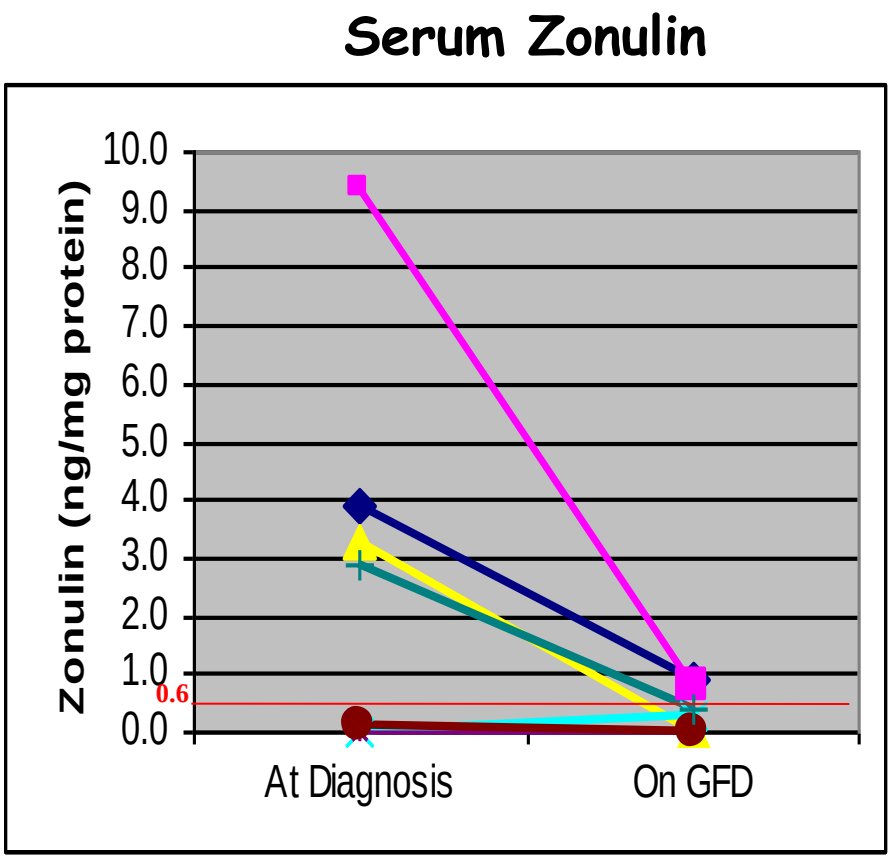


Serum Zonulin



TG Titers and Zonulin Serum Levels in Subjects That Responded to the GFD



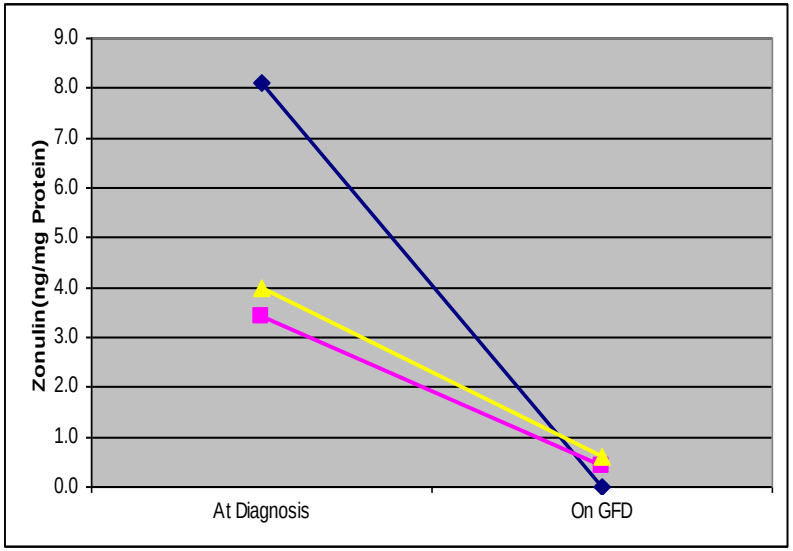


ICA Titers and Zonulin Serum Levels in Subjects That Responded to the GFD

Serum ICA

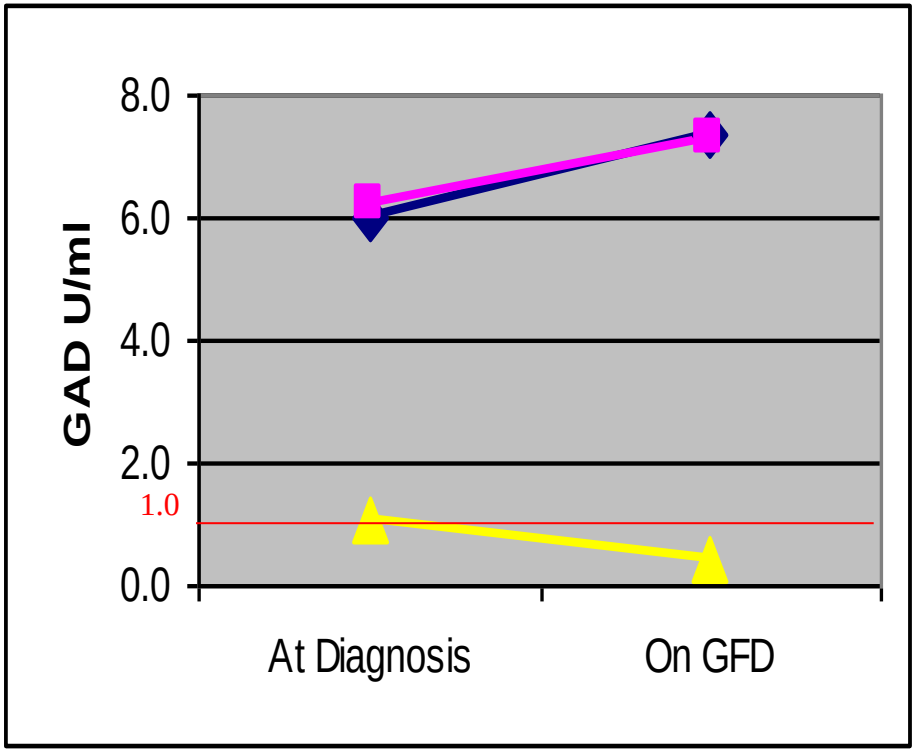
- All 3 of the Subjects with positive ICA titers, seroconvered to negative titers on the GFD.

Serum Zonulin

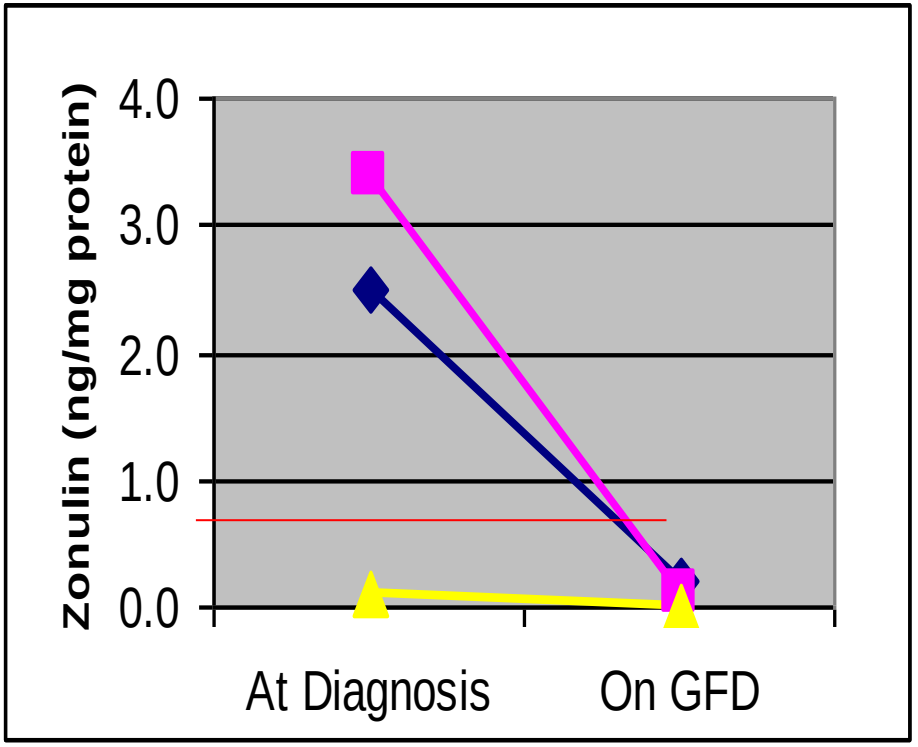


GAD Titers and Zonulin Serum Levels in Subjects That Responded to the GFD

Serum GAD



Serum Zonulin



Other Data of Interest:

- Incidence of Ab based on the age
- HLA and Ab
- Ab in subjects with pre-existing autoimmune disease
- CC zonulin AB

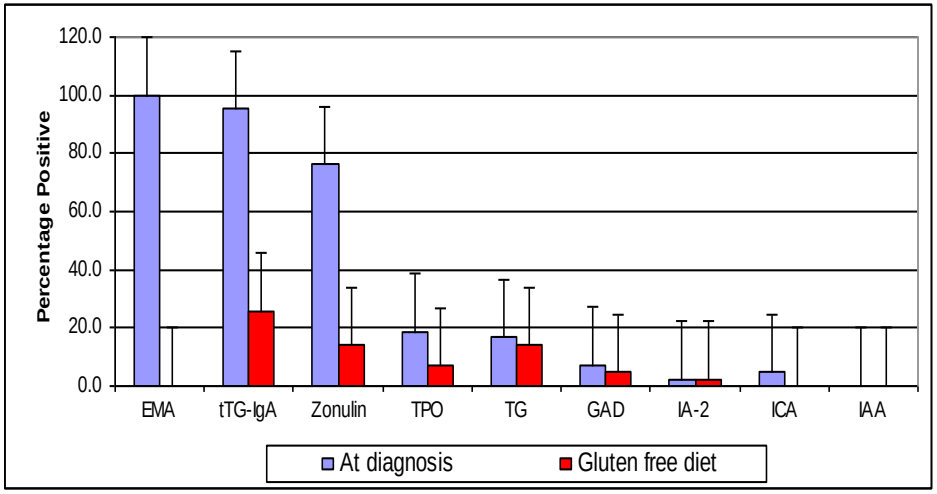
Conclusions

- Untreated CD patients typically show zonulin up-regulation and increased prevalence of serum auto-antibodies.

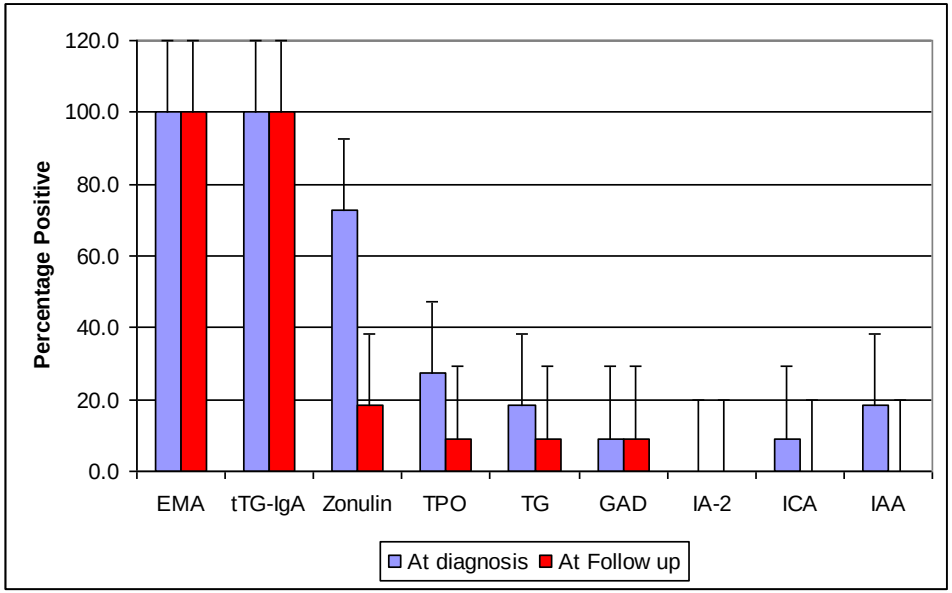
- After treatment with GFD, serum zonulin levels tend to normalize, a situation that is associated with a decreased prevalence of some auto-antibodies (TPO and ICA).

- These results indirectly suggest that recovery of the intestinal barrier function can revert the autoimmune response in subjects genetically predisposed, so decreasing the risk of autoimmune co-morbidity in celiac disease patients.

43 on GFD

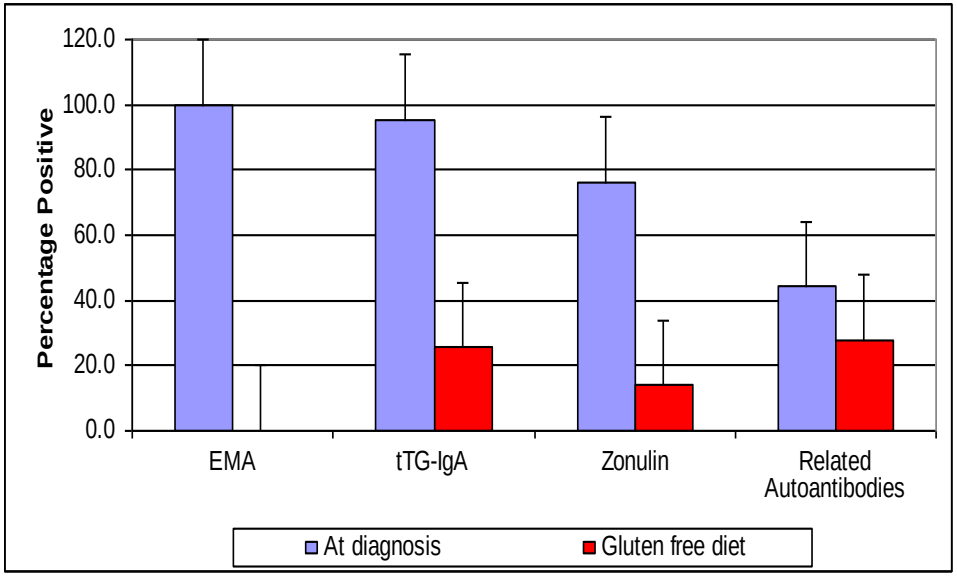


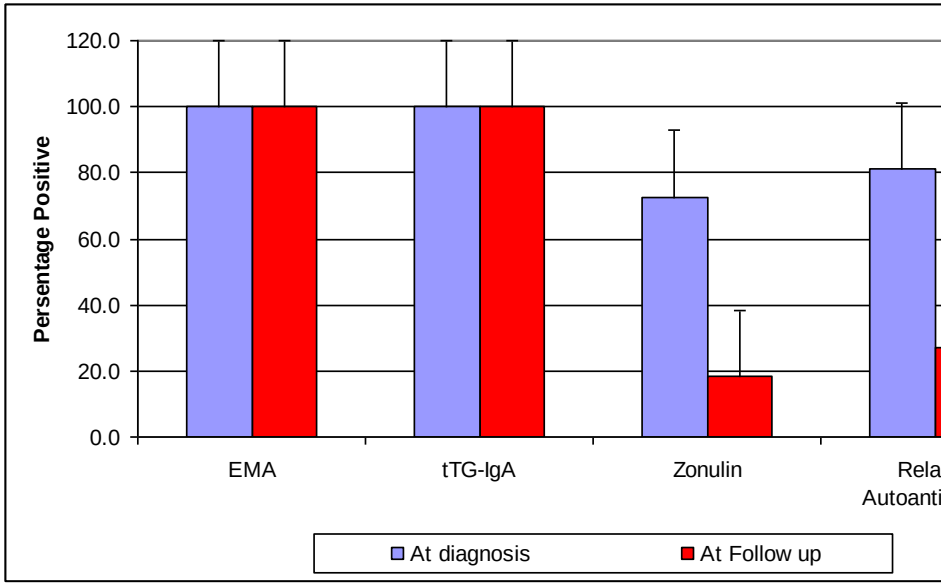
11 no GFD



43 on GFD

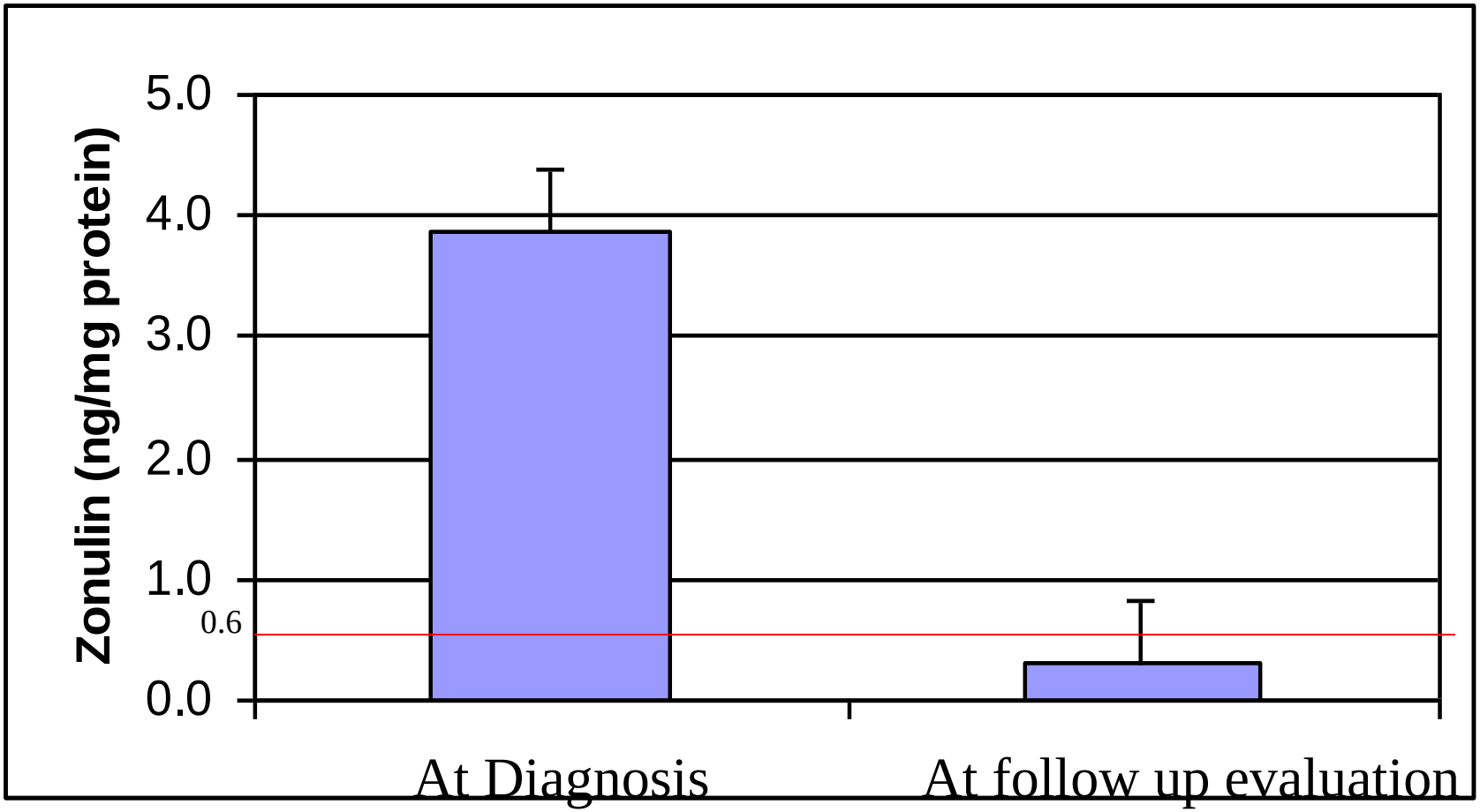
11 no GFD





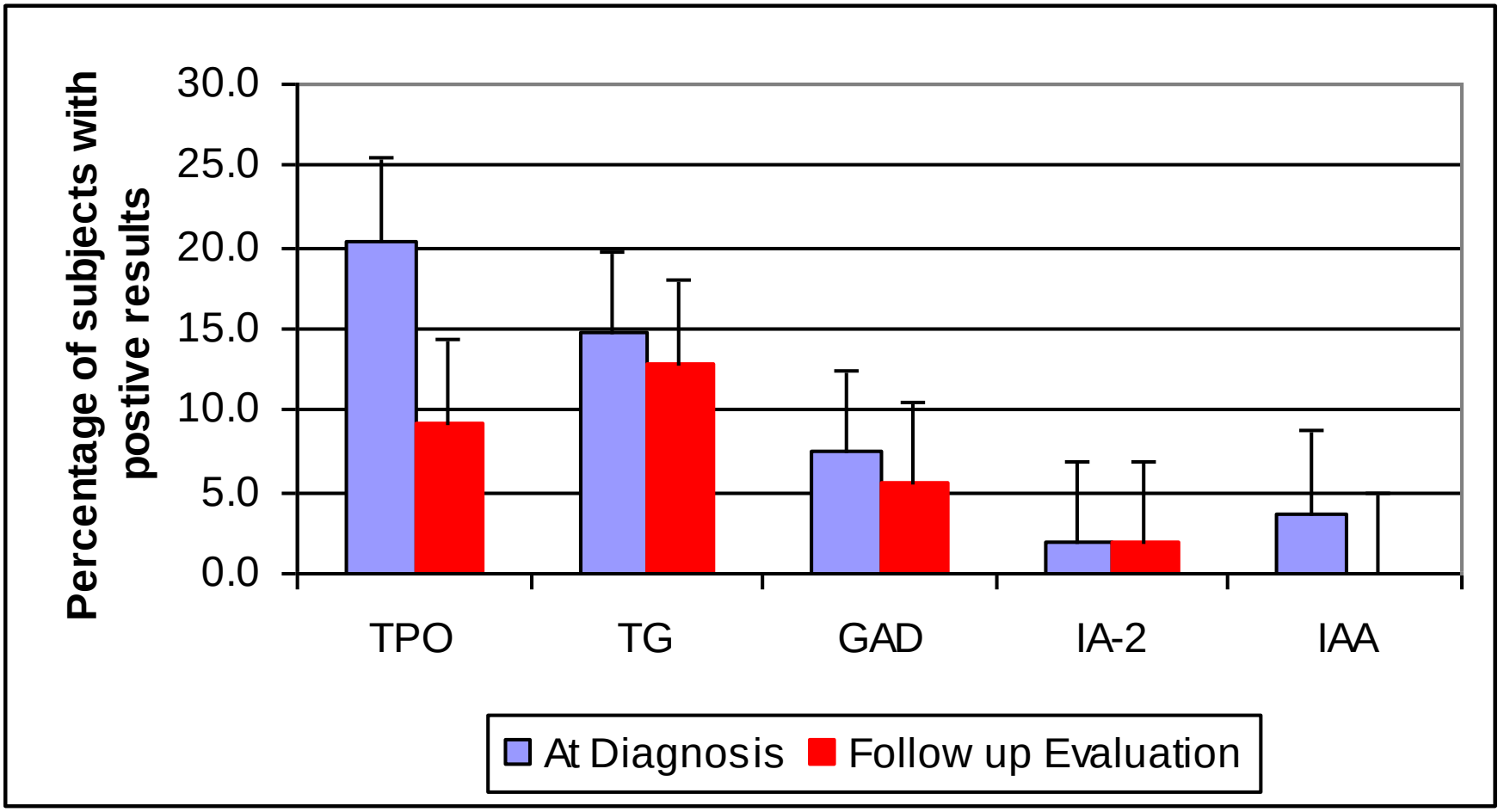
Averaged Zonulin levels of all for participants

mean period of 17 months



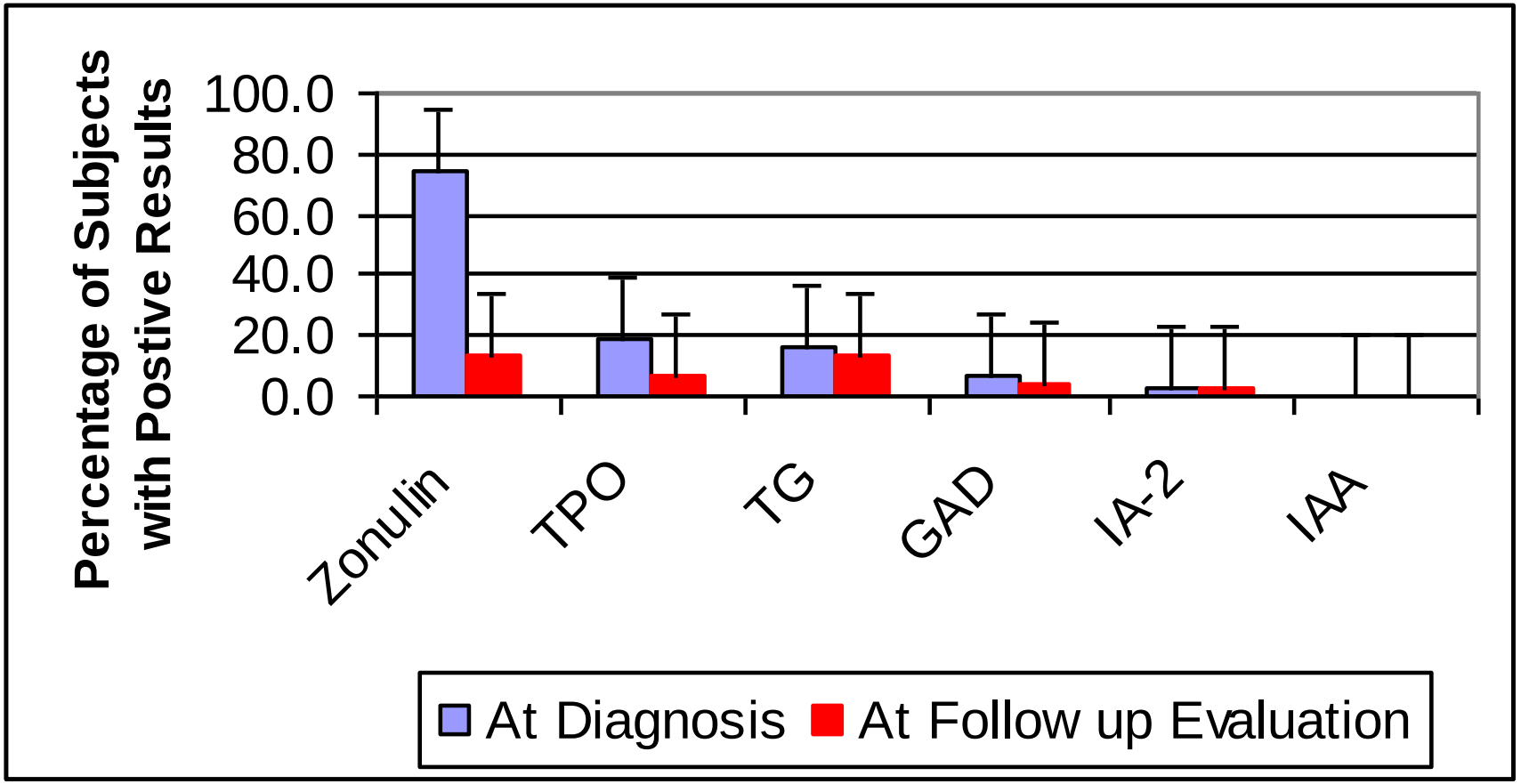
Autoimmune antibodies of all for participants

mean period of 17 months



Antibody levels for Subject who went on a GFD

mean period of 17 months



Antibody levels for Subject who were not on a GFD

EMA and tTG-IgA are all positive