

BACKGROUND

IgA is the most produced antibody in the body and is abundantly present in the serum. There are two major forms of IgA, monomeric serum IgA and dimeric mucosal (secretory) IgA. Increasing evidence suggests that IgA is not only involved in gut homeostasis, but also plays an important role in the regulation of immune responses. Elevated serum IgA has been sporadically reported in autoimmune diseases including type 1 diabetes (T1D), although its role in T1D is not understood.

PURPOSE

Here, we aimed to analyze serum IgA and clinical parameters in children with new onset T1D.

METHODS

- We analyzed 612 children with new onset T1D diagnosed between 1/2008-2/2012. Serum IgA values above age-adjusted normal ranges were defined as elevated serum IgA. Demographic and clinical variables were analyzed.
- Summary statistics were stratified by normal and elevated IgA, and compared using the Wilcoxon rank sum test, or Pearson Chi-square. A significance level of 0.05 was used. **(Table 1)**
- Univariable logistic regression was used to identify baseline characteristics that were significantly associated with elevated IgA (vs. normal IgA). Multiple logistic regression was used to include all the significant factors from the univariable model.

	Characteristics	Normal IgA	High IgA	P value	
IgA level (mg/dL)*		143 [101-186]	300 [226-358]	<0.001	
Age (years)*		10.1[6.9-13.0]	8.9[5-11.8]	0.007	
Gender	Male	245 (51%)	74 (58%)	0.150	
	Female	239 (49%)	54 (42%)		
Ethnicity	Caucasian	302 (63%)	48 (40%)	<0.001	
	Hispanic	76(16%)	45 (38%)		
	African American	74 (16%)	21 (17%)		
	Asian	18 (4%)	6 (5%)		
	Mixed	7 (1%)	0		
Puberty	Pre-pubertal	261 (58%)	75 (65%)	0.640	
	Post-pubertal	189 (42%)	41 (35%)		
Labs*	pH	7.34 [7.22-7.38]	7.29 [7.16-7.36]	<0.001	
	BOHB (mmol/L)	3.8 [1.2-7.5]	6.4 [3.0-8.6]	<0.001	
	Glucose (mg/dL)	356 [256-495]	416 [341-548]	<0.001	
	HbA1C (%)	11.8 [10.2-13.4]	12.4% [10.8-13.9]	0.016	
DKA		153 (33%)	57 (47%)	0.021	
	Antibody positive	GAD	402 (83%)		93 (74%)
	IAA	167 (35%)	59 (47%)		
	IA2	377 (79%)	105 (83%)		
	TTG	433 (90%)	108 (85%)	0.14	
BMI percentile*		76 [50-90]	80 [55-90]	0.22	

Table 1: Clinical characteristics of patients with normal IgA level vs. with elevated IgA level at onset of T1D. [p<0.05]

*Median [Interquartile range]

RESULTS

- At the onset of T1D, elevated serum IgA was present in 21% (128/612) of the children [p<0.001].
- By multivariable logistic regression analysis, compared with children with normal IgA, those with elevated serum IgA were more likely to be of Hispanic ethnicity, had a higher hemoglobin A1c (A1c) and insulin autoantibody (IAA) level at diagnosis [p<0.05]. They also had lower odds of having GAD antibody positive. [p<0.05] **(Figure 1)**
- On the other hand, in the multivariable logistic regression model, elevated serum IgA was not significantly associated with age, glucose level or presence of DKA.

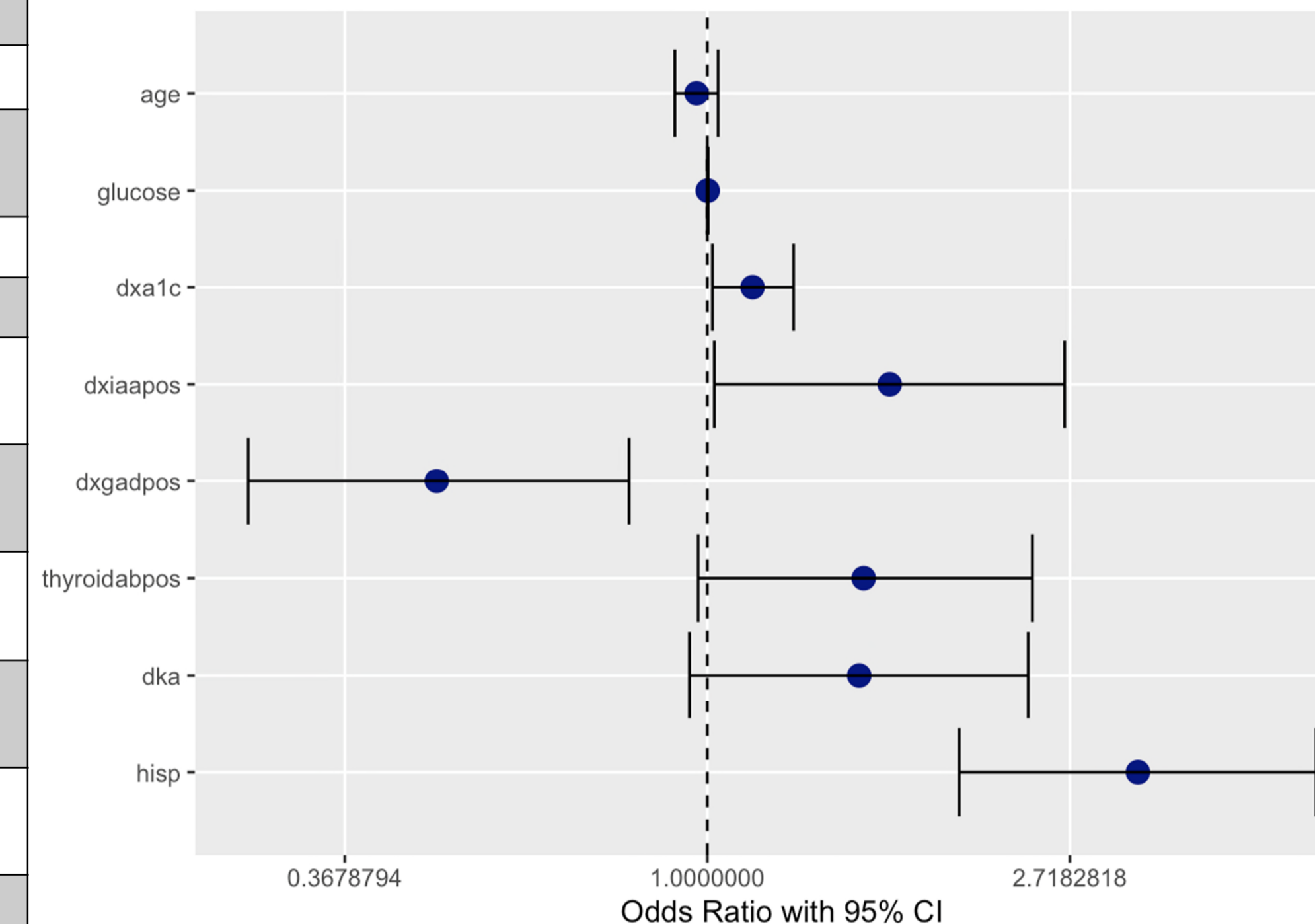


Figure 1: Multivariable logistic regression analysis of patients with elevated IgA at onset of T1D. [p<0.05]

CONCLUSION

- Our findings suggest patients with high serum IgA level at diagnosis of T1D could have more severe insulin deficiency at diagnosis and be associated with specific islet autoimmunity.
- Further studies are warranted to investigate the IgA response, its role in T1D pathogenesis and whether they persist over time.
- Given that current tools to prevent T1D are limited, improved understanding of the natural history of the disease may lead to new targeted strategies to preserve or improve beta-cell function in individuals with clinical or pre-clinical T1D.
- The authors are currently working on a prospective case control study to test the association between elevated serum IgA and gut dysbiosis at onset of T1D in children.