Anti-glycan antibodies are significantly increased in Crohn's disease patients and their first-degree relatives.

Iris Dotan[1,3,4], Hadar Meringer[1,4], Aaron Lerner[5], Noya Horowitz[1,3,4], Timna Naftali[6], Ayala Yaron[2,3,4], Shoshana Schwartz [1,3], Ilana Goldiner[1,3], Shimon Reif[2,3,4], Zamir Halpern[1,3,4]

[1]IBD Center, Department of Gastroenterology and Liver Diseases, [2]Department of Pediatrics, [3]Tel Aviv Sourasky Medical Center, [4]Sackler Faculty of Medicine, Tel Aviv University [5]Pediatric Gastroenterology and Nutrition Unit, Carmel Medical Center, Rappaport School of Medicine, Technion-Israel Institute of Technology, Haifa, [6]Institute of Gastroenterology and Liver Diseases, Meir Hospital, Kfar Saba, Israel.

Background:

- Disease specific antibodies have been described in patients with inflammatory bowel diseases (IBD) and their first-degree relatives (FDR).
- The recently described anti-glycan antibodies: anti-laminaribioside, anti-chitobioside and anti-mannobioside (ALCA, ACCA and AMCA, respectively) and anti-*Saccharomyces cerevisiae* antibodies (gASCA) specifically favor a Crohn's disease (CD) diagnosis and prediction of disease behavior.
- ASCA was detected in 20-30% of FDR in multiple CD families.
- Little is known about the prevalence of anti-glycan antibodies in healthy FDR of IBD patients and its significance.

Aim:

To investigate whether anti-glycan antibodies identify a specific IBD patients subgroup as well as their FDR.

Methods:

- IBD patients and their healthy FDR and control patients undergoing investigation due to gastrointestinal symptoms, and their FDR (FDR-C) were included.
- Demographic and disease data were recorded.
- Inflammatory markers (C-reactive protein, ESR) were detected.
- Anti-glycan antibodies were detected by ELISA (IBDX®, generously supplied by Glycominds Ltd, Israel).

Conclusions:

- Anti-glycan antibodies are more prevalent and significantly increased in CD patients compared to controls.
- A third of the FDR of IBD patients had positive anti-glycan antibodies.
- gASCA levels best differentiated between CD and their FDR.
- CD patients who are anti-glycan antibody positive are younger and tend to have a shorter disease duration compared to anti-glycan antibody negative CD patients.
- Anti-glycan status in IBD patients and their FDR correlate. The correlation between CD patients and FDR seropositivity may support either genetic anticipation or similar environmental exposure.

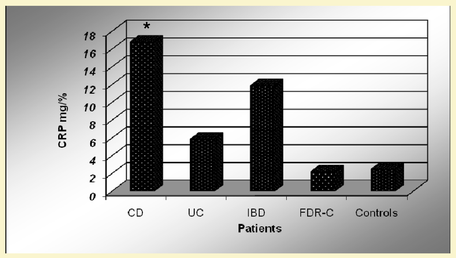
Table 1: Study Groups

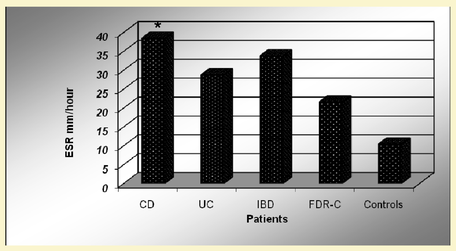
		IBD patients (n =34)	FDR-IBD (n =38)	Controls (C) (n =39)	FDR-C (n =68)
Age (years)		15 ±29.3	47.7±15.8	10.7± 7.8	41± 4.8
Gender	Male	15	16	16	33
	Female	19	22	23	35
Smoker		5 (16%)	10 (28%)	0	2 (3%)

Table 2: IBD Patients Demographic and Clinical Data

		IBD PATIENTS (N =34)
Age (years)		29.3±15
Disease type	Crohn`s disease	18
	Ulcerative colitis	11
	Pouch	5
Gender	Male	15
	Female	19
Age at diagnosis (years)		22.4± 11
Disease duration (years)		6.68±8.3
Extraintestinal manifestations		12 (37.5%)
Smoker		5 (16%)
Family histoty of IBD		16 (47%)
Disease type of family relative	UC	12
	CD	4
Medications	Antibiotic+ 5ASA	17
	Steroids	3
	Immunomodulators	9
	Biologics	5

Figure 1: Inflammatory Markers

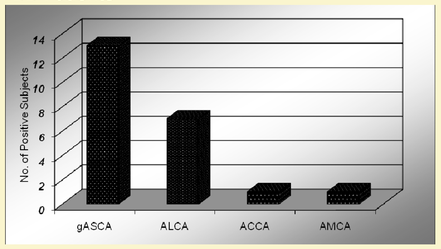




CRP (16.8±22.6 mg/dl) and ESR (38.4±24.6 mm/hour) levels were increased in CD patients compared to IBD-FDR (p=0.063), controls (p=0.02) and FDR-C (p=0.02).

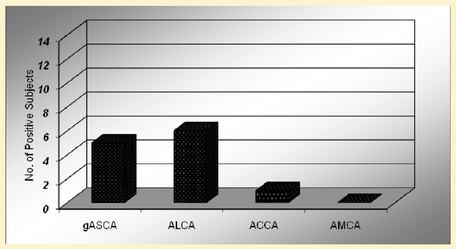
Figure 2: Anti-glycan Antibody Distribution

IBD Patients



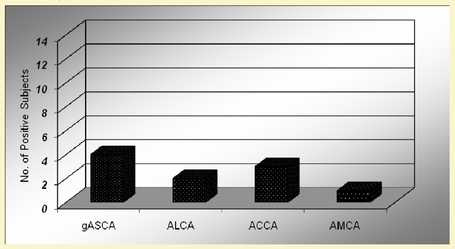
Anti-glycan antibodies were detected in 15 (44%, 12 CD) IBD patients:
13 gASCA, 7 ALCA, 1 ACCA, 1 AMCA
Double positive anti-glycan antibodies were detected only in the CD patients group.

FDR-IBD



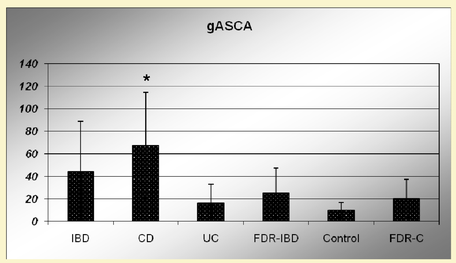
Anti-glycan antibodies were detected in 12 IBD-FDR (32%, 6 CD-FDR):
5 gASCA, 6 ALCA, 1 ACCA, 0 AMCA. P=0.4 vs. the IBD group.

FDR-C



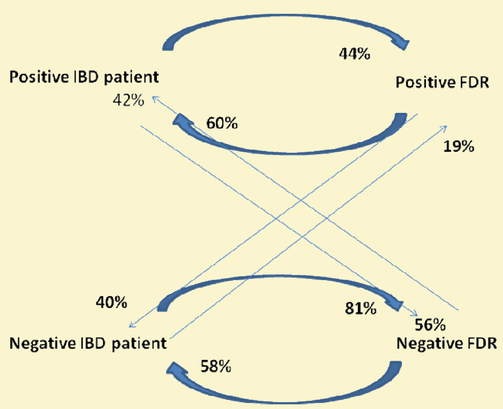
Anti-glycan antibodies were not detected in the control group, but were detected in 9 FDR-C (13%):
4 gASCA, 2 ALCA, 3 ACCA, 1 AMCA

Figure 3: Anti-glycan Antibody Levels



- gASCA levels were significantly increased in CD patients compared to UC, FDR-IBD, controls and FDR-C (p<0.001).
- ALCA and AMCA levels were significantly increased in CD patients compared to controls and FDR-C (p<0.001 and p=0.015, respectively).
- Positive compared to negative anti-glycan antibody CD patients were significantly younger at diagnosis: 23.2±8.3 vs. 33±17.6 years (p=0.04) and had shorter disease duration: 3.6±4 vs. 8±8.3 years (p=0.06).
- Immunomodulators/biologics had no effect on serologic response, however, more CD negative patients were treated with immunomodulators/biologics (67 vs. 33%, p=0.4).

Figure 4: Correlation in Serologic Status in IBD Patients and their FDR



- Anti-glycan antibody negative IBD patients have a greater chance to have an anti-glycan antibody negative, compared to positive, FDR.
- Anti-glycan antibody positive IBD patients have a similar chance to have a positive or negative FDR.
- FDR have a greater chance to have a similar serologic status as their relatives with IBD.