Research article Available online www.ijsrr.org ISSN: 2279–0543

International Journal of Scientific Research and Reviews

Study of Association of Anti-*Saccharomyces Cerevisiae* Mannan Antibodies in Patients of Ankylosing Spondylitis

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ABSTRACT

Inflammatory bowel disease especially Crohn's disease is associated with presence of IgG and IgA antibodies against the phosphor-peptidomannan of the *Saccharomyces cerevisiae.* Various studies have assessed the association of anti-*Saccharomyces cerevisiae*antibodies **(**ASCA) with several autoimmune diseases postulating molecular mimicry as a possible link between ASCA and autoimmunity.This study was done to find out the prevalence of ASC Ain serum of patients of Ankylosing Spondylitis (AS) patients. A case control study was conducted to find the association of ASCA with AS in 232 cases of AS and 100 age and sex matched controls. The presence of anti-*Saccharomyces cerevisiae* mannan antibodies was estimated using commercial ELISA kit. ASCA IgA and IgG antibodies were significantly increased in AS patients as compared to control. 8.6% of AS patients were positive for ASCA IgA and 9.5% were positive for ASCA IgG while in control only 1 case of AS was positive for ASCA IgA but no case was positive for ASCA IgG. This study showed a significant correlation between AS patients and prevalence of ASCA suggesting a possible pathognomonic association.

KEYWORDS: Ankylosing Spondylitis, Saccharomyces cerevisiae, HLA-B27

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INTRODUCTION

Ankylosing Spondylitis (AS) is a disease of unknown etiology with interplay of various genetic and environmental factors. In this disease, innate immunity could be disturbed making individuals prone to abnormal reactions after bacterial infections. Though the role of infections is established in reactive arthritis but so far serological studies have not confirmed a chlamydial involvement in AS. A hypothesis has already been proposed that HLA-B27 promotes the continued existence of bacterial components, may be because of similarities between HLA-B27 and Gram-negative bacteria.[1]

An increase in circulating antibodies to certain bacterial antigens has been observed in Inflammatory bowel disease(IBD), including anti-*Saccharomyces cerevisiae*mannan antibodies (ASCA) suggesting intolerance to normal bowel flora.[2] In AS patients too, IBD associated serologic markers are present, compared with healthy controls, indicating a potential loss of tolerance to commensal bacteria similar to that observed in IBD patient.[3-6]Because of the IBD-like mucosal changes that occur in a substantial percentage of AS patients, a hypothesis has been put forward that serologic activity normally used to detect loss of tolerance to enteric antigens related to mucosal deregulation in IBD may be detectable in levels higher than normal controls in AS patients.

The aim of this study was to investigate the presence of Anti *Saccharomyces cerevisiae*antibodies (ASCA) in serum of AS patients and compare with healthy control.

MATERIALS AND METHODS

This study was carried out in a tertiary care hospital and samples from patients were collected from outdoor and indoor of the Rheumatology division of Department of Medicine and Department of Orthopedics' of the hospital.All patients of age >10 years who fulfilled ASAS criteria for Axial spondyloarthropathies from June 2012 to June 2016 were included in the study.[7] In all cases detailed clinical history was taken and diagnosis was established by rheumatologist.

Written informed consent were taken from each patient or their attendants if age of patient was less than 18 years. In every patient, details of clinical features were recorded.

Similar data was generated for normal control. Healthy controls had not any present and past history of any joint pain. 100 age and sex matched healthy controls were studied. The study was approved by Institute of Medical Sciences, Human Research Ethics Committee, Banaras Hindu University, Varanasi, India.

The presence of Anti-*Saccharomyces cerevisiae* (ASCA) antibodies IgA and IgG antibody was done by the kit of Blue Well, Dtek, Belgium based on the principle of Enzyme linked

immunosorbentassay (ELISA).For ASCA IgA and IgG antibody value of >25 U/ml were taken as positive

STATISTICAL ANALYSIS

All data were analyzed using Statistical Package for Social Sciences (SPSS, Chicago, Illinos, USA), version 16. Pearson's Chi-square and Fisher exact test were used to compare differences between the frequencies as per the requirement. A p-value <0.05 was considered significant for all analysis.

RESULTS AND DISCUSSION

Total 232 patients of AS who fulfilled the inclusion criteria were enrolled in study. Anti-*Saccharomyces cerevisiae* IgA and IgG antibodies were significantly increased in AS patients as compared to control. About 8.6% of AS patients were positive for ASCA IgA and 9.5% were positive for ASCA IgG while in control only 1 case of AS was positive for ASCA IgA but no case was positive for ASCA IgG. (Table 1)

Table 1: Correlation of Anti-*Saccharomyces cerevisiae* antibodies (ASCA) IgA and IgG antibodies positivity in AS patients and Control

Group(No of Cases)	ASCA Ig A				ASCA Ig G			
	Positive		Negative		Positive		Negative	
	No	%	No	%	No	%	No	%
AS (n=232)	20	8.6	212	91.4	22	9.5	210	90.5
Control (n=100)	1	1	99	99	0	0	100	100
Fisher's exactp value	0.006*				0.000*			

*statistically significant (p<0.05)

Our studies showed that level of ASCA IgA and IgG antibodies were not statistically different in both HLA-B27 positive and negative patients of AS. (Table 2)

Table 2: Showing correlation of ASCA IgA and IgG with HLA-B27 positivity in AS patients.

Group(No of Cases)	ASCA Ig A				ASCA Ig G			
	Positive		Negative		Positive		Negative	
	No	%	No	%	No	%	No	%
HLA-B27 positive (162)	11	6.8	151	93.2	14	8.6	148	91.4
HLA-B27 Negative (70)	9	12.9	61	87.1	8	11.4	62	88.6
$\chi 2$	2.28				0.44			
p value	0.131				0.506			

*statistically significant (p<0.05)

No significant differences were found for Anti- *Saccharomyces cerevisiae* antibodies between males and females' patients of AS. (Table 3)

Table 3: Correlation of ASCA (IgA, IgG) antibodies with the gender of AS patients

Gender	No	ASCA IgA		ASCA IgG	
		No	%	No	%
Male	190	17	8.9	17	8.9
Female	42	3	7.1	5	11.9
χ^2		0.14		0.35	
p-value		0.706		0.554	

*statistically significant ($p<0.05$)

Spondyloarthritis (SpA) is a musculoskeletal inflammatory disease associated with immune responses to intestinal micro biota and subclinical intestinal ulcerations that are closely related to IBD. Anti – *Saccharomyces cerevisiae*antibodies (ASCA) are associated with intestinal inflammation in both Crohn's disease and SpA. Evidence of intestinal inflammation, had been reported in 65% of patients with Spondyloarthritis (SpA).[8-9]

Anti- *Saccharomyces cerevisiae* are directed against the cell wall of *Saccharomyces cerevisiae*, commonly known as Bakers or Brewer's yeast. ASCA have been suggested as a serological marker for the diagnosis of undetermined IBD.[10] Studies have found that increased concentration of ASCA are found in patients with Crohn's disease.[11-13]Nowadays, ASCA is regarded more as a marker of increased gastrointestinal permeability than a serological autoimmune marker of intestinal inflammatory disease as it has also been found in patients with celiac disease. [14]

In our study, ASCA IgA and IgG antibodies were significantly increased in AS patients as compared to control. 8.6% of AS patients were positive for ASCA IgA and 9.5% were positive for ASCA IgG while in control only 1 case of AS was positive for ASCA IgA but no case was positive for ASCA IgG.(Table 1) No significant differences were found for Anti- *Saccharomycescerevisiae* antibodies between males and females' patients of AS. (Table 3)

Contrary to our data, in a previous report, Mundwiler*et al.*(2009*)* found no major difference in positivity rates for IgG and IgA ASCA in AS patients and controls.[3] Further, another group, investigating ASCA in SpA found that ASCA IgA, but not IgG, levels were higher in AS than in healthy controls but in our findings both IgG ASCA, IgA ASCA were increased in AS compared to healthy control.[15]Another study reporting the prevalence of ASCA IgA, ASCA IgG antibodies in 52 AS patients without IBD to be higher than in our study at 19%, 8% respectively.[16] Hoffmann *et al.*(2003) showed that ASCA IgA levels were significantly increased in patients with AS in comparison with healthy control.[15]Ferna´ndez-Sueiro*et al.*(2005)studied only HLA -B27 positive patients and found elevated levels of IgG-ASCA in AS whereas our studies showed that level of ASCA IgA and IgG antibodies were not statistically different in both HLA-B27 positive and negative patients of AS. [17]

CONCLUSION

We confirmed previous reports that ASCA IgA and IgG levels are raised in AS in comparison with healthy controls. Thus, our study suggested that ASCA might be a prognostic or etiological marker in AS.

ACKNOWLEDGMENT

This work was supported by the Institute of Medical Sciences, University Grant Commission (UGC), New Delhi, India, in the form of Junior and Senior research fellowships to Niladri Chaudhry. We would like to thanks late Dr. N. K. Singh, Professor of Medicine, IMS,BHU for his contribution to the study.

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