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ASSOCIATION BETWEEN PSORIASIS AND COELIAC DISEASE RELATED ANTIBODIES

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Background: Psoriasis is a common, chronic, disfiguring, inflammatory and proliferative condition of skin manifested by red, scaly, sharply demarcated, indurated plaques present particularly over the extensor surfaces and scalp. The disease has been found to be associated with celiac disease related antibodies with variable frequencies in different populations of the world. The subset of patients showing this association have a higher psoriasis severity and also respond well to cost effective way of gluten free diet. There is a need to work out the frequency of these antibodies in our local psoriatic patients. **Methods:** The study was carried out in Department of Dermatology, Military Hospital Rawalpindi from 4th June to 4th December, 2008. A total of 80 patients of both gender, aged more than 15 with a clinical diagnosis of psoriasis attending dermatology outpatient department were selected. Relevant history and thorough physical examination was performed and disease characteristics like previous treatments received and history of arthropathy were obtained. Coeliac disease related antibodies were assessed on serum by indirect immunofluorescence and data was analysed using software SPSS-13. **Results:** From the study of 80 patients, celiac disease related antibodies were found in none of the cases. All the severe and mild to moderate patients of psoriasis were negative for IgA antigliadin antibodies, IgG antigliadin antibodies and IgA anti-reticulin antibody. **Conclusion:** This study concludes that celiac disease related antibodies are not present in psoriatic patients irrespective of severity of disease in our local population.

Keywords: Psoriasis, coeliac disease, celiac disease associated antibodies, gluten free diet

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INTRODUCTION

Psoriasis is a common, chronic, disfiguring, inflammatory and proliferative condition of skin manifested by red, scaly, sharply demarcated, indurated plaques present particularly over the extensor surfaces and scalp.[1] While the cause is uncertain, susceptibility to psoriasis is inherited and the disease is influenced by environmental factors such as stress, infection and diet.[2]

In coeliac disease (CD), the ingestion of gluten-containing cereals results in small bowel mucosal inflammation and villous atrophy with crypt hyperplasia resulting in malabsorption syndrome with symptoms such as diarrhoea and abdominal distension. It is assumed that gluten-sensitive enteropathy commonly manifests with minimal or no gastrointestinal symptoms termed as latent gluten sensitivity. IgA and IgG antibody testing against various antigens including gliadin, transglutaminase, endomysin and reticulin can be used to identify this gluten-sensitive patients.[3]

Psoriasis has been found to be associated with celiac disease related antibodies. In a British study by Woo *et al*. IgG antigliadin antibody (IgG AGA), IgA antigliadin antibody (IgA AGA) and IgA antitransglutaminase antibody (TGA) were found to be positive in 3.8%, 8.5% and 7.7% psoriatic patients respectively while 2 patients(out of a total of 130) were found to be positive for IgA antiendomysial antibody (EmA).[4] The proportion of IgA and IgG AGA positivity in psoriatic patients was found to be even higher (16%) in another population as compared to the rate reported in Italy by Cardinali *et al* (5%).[5,6] Hereditary, socioeconomic and cultural factors seem to lie behind relatively different frequencies of antibodies in these different population groups.[7]

The presence of these antibodies also reflected a higher psoriasis activity, as indicated by necessity for second line treatment in such patients, used for more difficult-to-control lesions.[4] The severity of psoriatic arthritis is also found to be associated with higher CD associated antibody levels.[8]

All the currently available remedies for psoriasis including immune suppressants, topical treatments and photo-chemotherapy are difficult and incomplete.[9] Gluten free diet has been found to improve psoriasis in a trial of 3–6 months in patients with elevated AGA evidenced by significant reduction in mean Psoriasis Area severity index and reduced AGA values, while worsening was observed with resumption of ordinary diet.[2] There has also been a case report of a patient with coeliac disease and psoriasis not responding to specific therapies, in

whom skin lesions improved shortly after starting a gluten free diet.[10]

The purpose of my study was to investigate association between psoriasis and coeliac disease related antibodies in our local population as no work has been done on this association in our part of the world and secondly, in the event of significant antibody positivity in severe cases of psoriasis in our local population, the cost effective way of gluten free diet as compared to expensive therapies, may change the face of future interventions.

MATERIAL AND METHODS

The cross-sectional study was carried out in the Department of Dermatology, Military Hospital Rawalpindi. The study was conducted from 4 June 2008 to 4 December 2008 (6 months). Patients of both genders, aged more than 15 years with a clinical diagnosis of psoriasis attending dermatology outpatient department were included in the study. Patients who refused to participate in study, patients having a histological or antibody related diagnosis of coeliac disease and patients of dermatitis herpetiformis were excluded from the study.

Permission from hospital ethical committee was obtained and 80 patients attending dermatology outpatient department meeting both inclusion and exclusion criteria were selected. Informed consent of all subjects was taken on a printed *pro forma* and personal information of patients was kept confidential. Relevant history and thorough physical examination was performed and disease characteristics like presence or absence of arthropathy and previous treatment by methotrexate, eterinate, cyclosporin, PUVA, UVB or topical steroids were recorded in patients *pro forma.* Clinical severity was measured by body surface area (BSA) involvement. BSA involvement of less than 10% was taken as mild, 10-20% moderate and more than 20 % as severe. 3 ml of venous blood was taken, serum was separated and was assessed for antibodies including IgA antireticulin antibodies (IgA ARA), IgA antigliadin antibody (IgA AGA), IgG antigliadin antibody (IgG AGA) simultaneously by indirect immunofluorescence using in house prepared tissue sections of mouse kidney. Sera with Antibody titer of ten (dilution 1:10) were considered as positive. Positive sera were further evaluated by double dilution method for quantitative analysis. Results were recorded as positive or negative for individual antibodies and titer was also mentioned in positive cases.

Data collected was analysed using SPSS-13. Mean and SD for numerical variables i.e., age and was calculated. Frequency and percentage were presented for categorical variables, i.e., gender, previous treatment, arthropathy, severity and celiac disease associated antibodies (IgA antigliadin antibodies, IgG antigliadin antibodies and IgA antireticulin antibodies). Severe (>10% of BSA involvement) and non-severe cases (<10% of BSA involvement) were compared by using chi Square test in celiac disease associated antibody positive patients of psoriasis. *p*-value of less than 0.05 was taken as significant.

RESULTS

Amongst the 80 patients included in this study, there were 55 male (68.8%) and 25 female patients (31.3%) with a mean age of 39.23±16.062. Clinically 31 cases had severe (38.8%) disease while 49 were having mild to moderate (61.3%) psoriasis. All the severe and non-severe cases were found to be negative for IgA antigliadin antibodies, IgG antigliadin antibodies and IgA antireticulin antibodies. In 25 (36%) cases Arthropathy was present whereas it was absent in the rest of 45(64%) cases. Moreover, the frequency and percentage of various previous treatment modalities is shown in table-1. Chi-square test was not done as all cases were negative for all antibodies.

Table-1: Frequency and percentage of previous treatment modalities

Previous treatment modalities	Frequency	Percentage
Topical	49	61
UVB	10	13
Methotrexate	12	15
Eterinate	3	4
Cyclosporin	6	7
Total	**80**	**100**

DISCUSSION

Psoriasis has been found to be associated with celiac disease related antibodies. This association signifies the cost effective way of use of gluten free diet as opposed to expensive therapies in psoriatic subjects showing the presence of these antibodies. In our study, celiac disease related antibodies were seen in none out of 80 patients of mild to moderate and severe psoriasis.

In literature, there are many studies showing variable frequency of celiac disease associated antibody positivity. In a British study by Woo *et al*. IgG antigliadin antibody (IgG AGA), IgA antigliadin antibody (IgA AGA) and IgA antitransglutaminase antibody (TGA) were found to be positive in 3.8%, 8.5% and 7.7% psoriatic patients respectively while 2 patients (out of a total of 130) were found to be positive for IgA antiendomysial antibody (EmA).[4] Michaelsson *et al* reported 16% frequency of IgA type antibodies to gliadin in psoriatic patients.[11] Similarly in a Turkish study by

A. Kalayciyan and A. Kotogyan, 16.5% of patients with psoriasis had serum levels of IgA antibodies to gliadins compared to that of control group (9.6 %).[7] Despite being a relatively high percentage when compared with those of the control group and the general population, it was not a statistically significant increase; however, the result of Michaelsson *et al* were significantly higher than the frequency of IgA type antigliadin antibodies of their own population. This association has also been confirmed by Ojetti *et al* who showed a higher prevalence of celiac disease in psoriatic patients than controls.[3]

Conversely, the rate report by Cardinali *et al* on Mediterranean subjects was lower (5%). Out of 39 cases of the psoriasis, two serum samples were positive for IgG AGA, one was border line for anti-tTG antibodies (5.22), and none was positive for EMA or IgA AGA. Healthy donors were negative for all such screenings.[6] Similarly, a case of severe psoriasis in a patient with CD has been described that did not respond to specific therapies for psoriasis. [5] EmA was absent, and IgA and IgG AGA serum levels were not raised. Diagnosis of CD was performed by jejunal biopsy, which showed atrophy of the intestinal villi. A gluten-free diet (GFD) was started, with rapid improvement of the duodenal mucosa and skin lesions. This case shows not only the absence of celiac disease related antibodies but also highlights that gluten sensitivity may even still be present with antibody negative results.

Different frequencies of these antibodies ranging from nil (as also seen in my study) to 16% in different population groups seem to be caused by different hereditary, socioeconomic and cultural factors. For instance, the fact that the Turkish diet is based mainly on cereals such as wheat may explain the higher frequency of antigliadin antibodies in individuals than in other populations with different diets. This fact can be substantiated by noting higher prevalence of these antibodies (9.6%) even in the control group. The results of my study could have been better validated if normal population would have also been evaluated for antibody profile

Antigliadin and antireticulin are the only antibodies tested in my study, while they have been seen to be less sensitive predictor of gluten sensitivity in psoriatic patients. The sensitivity of anti-endomysial and anti-tissue transglutaminase antibodies are close to 100%, while the sensitivity of antigliadin IgA and IgG is 89%.[12] The specificity of anti-endomysial was 100% while anti-TTG was 97% in a study. Antigliadin IgA was 96% and antigliadin IgG 78%. However, the most important predictive value has been shown by anti-endomysial antibodies 97%, whereas it was considerably lower for anti-TTG and antigliadin IgA and IgG antibodies.[13] A study by cardinally *et al* also revealed increased frequency of anti endomyseal anti body positivity.[6] My study can be criticized on this basis but antigliadin and antireticulin antibodies were included based on availability and cost effectiveness. This non inclusion of more sensitive and specific tests might also be the reason for absolute antibody negative profile seen in my results. This demands testing of more sensitive and specific antibodies in future studies. 38.8 % of the my patients have been found to have severe disease but none of them showed antibody positivity while Michaelsson *et al*. commented that 14% of their psoriasis patients with raised AGA were on methotrexate or etretinate treatment, compared with 7% of patients with normal levels. He inferred that the presence of CD-associated antibodies reflect greater disease activivty, as the requirement for second-line therapeutic agents indicates that their psoriasis was more difficult to control.[14] In parallel with his findings, Lindqvist *et al*. found that the severity of psoriatic arthritis correlated with CD-associated antibody levels.[8] Patients with raised serum IgA AGA had significantly more pronounced inflammation, as evidenced by higher erythrocyte sedimentation rate, C-reactive protein and longer duration of morning stiffness. Woo *et al* investigated Patients with psoriasis (n=130) for serum IgG and IgA AGA, IgA antitransglutaminase antibody and IgA antiendomysial antibody.[4] Disease characteristics and associated bowel and joint symptoms were determined. All patients were invited to undertake endoscopy with duodenal biopsy. A significantly higher proportion of patients with elevated CD-associated antibody levels were currently on or had previously required systemic immunosuppressants (methotrexate, ciclosporin or etretinate or psoralen plus ultraviolet A phototherapy. One case of CD was diagnosed. It was concluded that the presence of CD-associated antibodies in psoriasis patients correlates with greater disease activity. On the other hand, patients requiring systemic immunosupressents in my study were all negative for CD associated antibodies. This may be either due to straight forward absence of this association in our society or this may be apparent negativity due to inclusion of less number of very severe cases, probably caused by less outpatient reporting of severe psoriatic group on account of constraints by poor socioeconomic conditions, psoriatic morbidity and weak community support and health services system of our society.

Michaelsson *et al*. evaluated the effect of a 3-month gluten-free diet in 33 AGA-positive and six AGA-negative patients with psoriasis.[14] Thirty patients with AGA completed the gluten-free diet period and showed a highly significant decrease in

mean PASI. No improvement was found in the AGA-negative patients. He concluded that patients with psoriasis with raised AGA may improve on a gluten-free diet. As none of my patients has shown AGA positivity, they are likely to be unresponsive to gluten free diet trial, if employed in future.

There has been no pre-existing data or study regarding this aspect in our population. It can be commented that this association may not even exist here or may be very weak, considering our relatively less number of cases, which may not be the clear representative of the general overall psoriatic population. Thus a larger scale study is recommended to quantify this likely weak association in our part of the world.

CONCLUSION

Coeliac disease associated antibodies are not present in mild to moderate and severe patients of psoriasis in our local population. Large scale study with full list of sensitive as well as specific serological markers followed by a trial of gluten free diet in positive cases should be undertaken to ascertain this association.

Conflict of interest: The study was carried out purely for research purpose and there was no conflict of interest.

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