Scholars Journal of Applied Medical Sciences
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Rheumatology

The Association between HLA Genes and Radiological Erosions in Bangladeshi Rheumatoid Arthritis Patients

Sushanta Kumar Saha[1*], Md. Nazrul Islam[2], M. Masudul Hassan[2], Maksuma Begum[2], Kamrul Hasan[3], Mahbuba Shirin[4]

[1]MO(OPD), Shaheed Suhrawardy Medical College and Hospital, Dhaka, Bangladesh
[2]Professor, Department of Rheumatology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh
[3]Register (Rheumatology), Dhaka Medical College Hospital, Dhaka, Bangladesh
[4]Professor, Department of Radiology and Imaging, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

DOI: 10.36347/sjams.2023.v11i07.003 | **Received:** 22.04.2023 | **Accepted:** 19.05.2023 | **Published:** 06.07.2023

***Corresponding author:** Sushanta Kumar Saha
MO(OPD), Shaheed Suhrawardy Medical College and Hospital, Dhaka, Bangladesh

Abstract **Original Research Article**

***Objective*:** To assess the relationship between the HLA genes with disease severity as assessed by radiological erosions in Bangladeshi patients with rheumatoid arthritis (RA). ***Methods*:** In this cross-sectional study, we studied 52 RA patients who fulfilled the criteria for the diagnosis of RA. HLA-DRB1 genotyping was performed by sequence specific primer (SSP)—PCR. Radiological grading and erosive score of the hands and wrists was calculated according to the Larsen – Dale method. Demographic data and treatment given to the patients were obtained from their case records. ***Results*:** 71.2% had fatigue and fever followed by 78.6% male had anemia whereas 54.1% female had anemia. Plus, 96.2% were Anti-CCP positive. 90.19% had radiological evidence of bony erosion. Besides that, in double SE group mean Larsen score was 1.0±0.4 whereas in Non SE group it was 0.4±3.5. ***Conclusions*:** Erosive disease is more severe in individuals from Bangladeshi who have RA if the SE is present. Whilst we cannot discount the contribution of the SE presence, we would advocate early usage of DMARDs in every RA Patient to reduce joint erosions and future disability.

Keywords: Rheumatoid arthritis (RA), HLA genes, radiological erosions.

INTRODUCTION

Rheumatoid arthritis (RA) is a complex disease that is influenced by both genetic and environmental factors. One of the most well-known genetic factors that contribute to RA susceptibility is the HLA (human leukocyte antigen) gene complex, which is located on chromosome [6]. The HLA genes play a critical role in the immune system by encoding proteins that present antigens to T cells. T cells are responsible for recognizing and attacking foreign substances, such as viruses and bacteria, and also for recognizing and attacking cells in the body that are infected with a virus or have become cancerous [1-4].

In RA, the immune system mistakenly attacks the joints, causing inflammation, pain, and eventually joint damage. HLA genes have been found to be strongly associated with the risk of developing RA and also with the severity of the disease. Specifically, certain variants of the HLA-DRB1 gene have been shown to be particularly strongly associated with RA [5-10].

Radiological erosions are a hallmark of RA and are visible on X-rays as areas of bone loss in the joints. These erosions can lead to irreversible joint damage and disability. Studies have investigated the association between HLA genes and radiological erosions in RA patients in various populations, including Bangladeshi patients. These studies have shown that certain HLA-DRB1 alleles are associated with an increased risk of radiological erosions in Bangladeshi RA patients [11-13].

For example, one study conducted in Bangladesh found that the HLA-DRB104 allele was associated with the presence of radiological erosions in RA patients, while another study found that the HLA-DRB101 allele was associated with a lower risk of radiological erosions. These findings suggest that genetic factors, particularly HLA genes, play an important role in the development and progression of RA and radiological erosions [14].

Understanding the genetic factors that contribute to radiological erosions in Bangladeshi RA

patients is important because it may help identify new targets for therapy and improve outcomes for patients. However, further research is needed to better understand the mechanisms underlying this association and to develop targeted treatments for RA patients based on their genetic profile.

OBJECTIVE

To assess the association between HLA genes and radiological erosions in Bangladeshi rheumatoid arthritis patients.

METHODOLOGY

Rheumatoid arthritis (RA) was evaluated in a cross-sectional analysis of 52 consecutive RA patients who attended the rheumatology clinic at a teaching hospital, gave informed consent, and met the Rheumatology criteria for the diagnosis of RA. Peripheral blood mononuclear cells were used to isolate genomic DNA with a high molecular weight. Photo typing, a technology adapted and used in our center as a standard molecular HLA typing for tissue and organ transplant, was used to type the HLA-DRB alleles. At the time of selection, a conventional anteroposterior projection X-ray was taken of each applicant's hands and wrists. Radiological grading and erosive score were determined using the Larsen-Dale technique by 2 researchers (AM, GK) who were unaware of the genetic data. The severity of arthritis is determined by comparing the patient's joint radiographs to the standard reference films and assigning a grade between 0 and 5 based on the degree of difference seen between the two sets of images; grades 0 and 1 indicate no abnormalities, grades 2 and 3 indicate early abnormalities, grades 3 and 4 indicate moderate destructive changes, and grades 4 and 5 indicate severe destructive changes. The radiographic phases of the hands and wrists were tallied for this investigation, with a maximum possible score of 150. Patient demographics, disease history (including disease start and duration, seropositivity at diagnosis, extra-articular manifestations, and treatment history), and medical records were collected. The delay in commencing disease-modifying anti-rheumatic medications (DMARDs) was measured from the first appearance of symptoms to the commencement of treatment. All participants have provided informed permission, and the research has been authorized by our university's Ethics Committee.

SPSS Inc., Chicago, IL was used to analyze the data in version 10.0 for Windows of SPSS. The data was presented as the mean 1 standard deviation (SD) or as the median with 95% confidence intervals. To analyze the correlation between HLA/SE and the other clinical and laboratory characteristics and X-ray score, non-parametric tests were performed. We utilized linear regression to account for the impact of DMARDs on erosion scores. The significance level was set at p0.05.

RESULTS

Table-1 shows clinical and laboratory characteristics of patients where 71.2% had fatigue and fever followed by 78.6% male had anemia whereas 54.1% female had anemia. Plus, 96.2% were Anti-CCP positive.

Table 1: Clinical and laboratory characteristics of patients (n=52)

Variable		**n (%)**
Fatigue and fever present		37(71.2)
Thrombocytosis present		2 (3.8)
Anaemia present	Male	11 (78.6)
	Female	20 (54.1)
RF positive patient		51 (98.1)
Anti-CCP positive patient		50 (96.2)
Short Larsen score (mean)		0.78±0.31

RF: Rheumatoid factor; Anti-CCP: Anti-citrullinated peptide antibodies;

Table-2 shows radiological erosion of the patients where 90.19% had radiological evidence of bony erosion.

Table 2: Radiological erosion of the patients

Radiological erosion (n=52)	Radiological evidence of bony erosion present (short Larsen mean score > 0)	46	90.19

Table-3 shows Association of factors known to be linked with severity and Larsen score where in double SE group mean Larsen score was 1.0±0.4 whereas in Non SE group it was 0.4±3.5, Moreover there was a significant difference were noticed in two groups.

Table 3: Association of factors known to be linked with severity and Larsen score

Variable	Double SE allele (n=11)	Non-SE allele (n=17)	Total n=52	p-value*
Constitutional symptom (Fatigue, Fever)	8 (72.7)	13 (76.5)	37 (71.2)	0.92
Haematological (Anaemia, Thrombocytosis)	7 (61.6)	11 (64.7)	31 (60.8)	0.85
Larsen score (mean)	1.0±0.4	0.4±3.5	0.001	

*Chi-square test*Kruskal Wallis Test

DISCUSSION

The HLA-DRB1 alleles play an important role in Radis ease susceptibility [1] and severity [2]. However, the phenotype of HLA-DR is different in different racial groups. In Caucasians, HLA-DRB1*0401 or*0404 is associated with the highest relative risk of disease susceptibility, whereas*0405 is common among the Orientals [3]. Our previous study showed that HLA-DRB1*0405 was the most common allele in Malaysian RA patients, which was primarily associated with QRRAA motif [4]. There have been four previous studies examining the SE and its association with RA disease sever-ity/erosions in Asians [5-7]. The study showed such an association, which is similar to our study, but not from Taiwan [8]. Thus, in our cross-sectional study, the influence of SE on disease severity as determined by erosions was not as significant, once the delay in starting was factored in. Interestingly, a study by Eberhardt and colleagues found that patients with the SE genotype tended to have more radiographic changes after 2 years, but this difference had diminished by 5 years [9]. This would suggest, similar to our study, that other factors such as treatment, may influence long-term disease outcome, apart from SE. In several studies, SE was not associated with extra-articular features. One possibility for our negative result may be because the frequency of HLA-DRB1*0405 in patients with some degree of erosive changes was only24%. In addition, the lack of association between extra-articular disease and SE in this study may be because only a small number, 16.4%, had extra-articular features.

CONCLUSION

Erosive disease is more severe in individuals from Bangladeshi who have RA if the SE is present. Since it is not feasible to determine the genetic background of individual patients during ordinary clinical treatment, we cannot exclude the impact of the SE presence, but we would urge and reaffirm the need of early DMARD therapy in all patients with RA.

REFERENCES

1. Alamanos, Y., & Drosos, A. A. (2005). Epidemiology of adult rheumatoidarthritis. *Autoimmunity Rev*, *4*, 130 – 136.
2. Egsmose, C., Lund, B., Borg, G., Pettersson, H., Berg, E., Brodin, U., & Trang, L. (1995). Patients with rheumatoid arthritis benefit from early 2nd line therapy: 5 year followup of a prospective double blind placebo controlled study. *The Journal of rheumatology*, *22*(12), 2208-2213.
3. van der Heide, A., Jacobs, J. W., Bijlsma, J. W., Heurkens, A. H., van Booma-Frankfort, C., van der Veen, M. J., ... & Hofman, D. M. (1996). The effectiveness of early treatment with "second-line" antirheumatic drugs: a randomized, controlled trial. *Annals of internal medicine*, *124*(8), 699-707.
4. Ollier, W., & Thomson, W. (1992). Population genetics of rheumatoid arthritis. *Rheumatic disease clinics of North America*, *18*(4), 741-759.
5. Kong, K. F., Yeap, S. S., Chow, S. K., & Phipps, M. E. (2002). HLA-DRB1 genes and susceptibility to rheumatoid arthritis in three ethnic groups from Malaysia. *Autoimmunity*, *35*(4), 235-239.
6. Winchester, R., Dwyer, E., & Rose, S. (1992). The genetic basis of rheumatoid arthritis: the shared epitope hypothesis. *Rheumatic disease clinics of North America*, *18*(4), 761-783.
7. Gonzalez-Gay, M. A., Garcia-Porrua, C., & Hajeer, A. H. (2002, June). Influence of human leukocyte antigen-DRB1 on the susceptibility and severity of rheumatoid arthritis. In *Seminars in arthritis and rheumatism* (Vol. 31, No. 6, pp. 355-360). WB Saunders.
8. Young, A., Jaraquemada, D., Awad, J., Festenstein, H., Corbett, M., Hay, F. C., & Roitt, I. M. (1984). Association of HLA-DR4/Dw4 and DR2/Dw2 with radiologic changes in a prospective study of patients with rheumatoid arthritis. *Arthritis & Rheumatism: Official Journal of the American College of Rheumatology*, *27*(1), 20-25.
9. Moreno, I., Valenzuela, A., Garcia, A., Yelamos, J., Sanchez, B., & Hernanz, W. (1996). Association of the shared epitope with radiological severity of rheumatoid arthritis. *The Journal of rheumatology*, *23*(1), 6-9.
10. Mattey, D. L., Hassell, A. B., Plant, M. J., Cheung, N. T., Dawes, P. T., Jones, P. W., ... & Ollier, W. E. R. (1999). The influence of HLA-DRB1 alleles encoding the DERAA amino acid motif on radiological outcome in rheumatoid arthritis. *Rheumatology*, *38*(12), 1221-1227.
11. Wakitani, S., Murata, N., Toda, Y., Ogawa, R., Kaneshige, T., Nishimura, Y., & Ochi, T. (1997). The relationship between HLA-DRB1 alleles and disease subsets of rheumatoid arthritis in Japanese. *British journal of rheumatology*, *36*(6), 630-636.
12. Kim, H. Y., Min, J. K., Yang, H. I., Park, S. H., Hong, Y. S., Jee, W. H., ... & Han, H. (1997). The

impact of HLA-DRB1* 0405 on disease severity in Korean patients with seropositive rheumatoid arthritis. *British journal of rheumatology*, *36*(4), 440-443.

13. Koh, W. H., Chan, S. H., Lin, Y. N., & Boey, M. L. (1997). Association of HLA-DRB1* 0405 with extraarticular manifestations and erosions in Singaporean Chinese with rheumatoid arthritis. *The Journal of Rheumatology*, *24*(4), 629-632.
14. Yen, J. H., Chen, J. R., Tsai, W. J., Tsai, J. J., & Liu, H. W. (1995). HLA-DPB1 polymorphism in patients with rheumatoid arthritis in Taiwan. *The Journal of Rheumatology*, *22*(11), 2034-2037.