Major Histocompatibility Complex gene Polymorphism in Systemic Lupus Erythematosus Patients

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Abstract

The major histocompatibility complex (MIC) is one of the MHC class I related genes which related with autoimmune diseases , the present study aims to investigated association between MIC gene polymorphism class I in systematic lupus erythrymatous patients within Hilla city, the present study implemented using whole blood genomic DNA and single strand DNA conformation polymorphism (SSCP) for detection gene polymorphisms and haplotypes frequency, The results of present study show that 183 bp of MIC gene and it has three haplotypes (A, B, and C) each of these haplotypes consist of two bands, non-significant differences between patient and control in haplotypes frequency, B haplotype was more frequent in patinas than others (20%) while A was more frequents in control than others (22.8%). The present study concluded that MIC gene may be contributed in immune response of SLE and can be used in pre diagnosis of disease. This study was one of the serious investigators deal with several immune genes in this disease in Iraqi SLE.

Key words : *The major histocompatibility complex, systematic lupus erythrymatous, single strand DNA conformation polymorphism.*

Introduction

An autoimmune disease is one of the most common health problem in last decades that observed in Iraqi population, different types of Chronic autoimmune diseases were recorded, SLE is one of these types, the SLE is complex inflammatory dieses which multifactorial contributed in etiology of disease [(1).] The pathogenesis of SLE is not well understood, several studies suggested dysfunction of immune system, and determined self-antigens resulted to chronic inflammation cusses destruction in tissue and organ damage[(2)] . One of the factors involved in the pathogenicity of SLE disease is genetic alteration, some genes mutations have been determined which related with SLE [(5,6)] .

The major histocompatibility complex (MIC) is found in the chromosome 6 at the short arm [(3)] , it be found that About 40% of the expressed MHC genes encode proteins related to immune defense [(4)] .

The relation of MHC and autoimmune diseases was documented since 1970s in some studies, its considered as strongest risk factors of autoimmune diseases. When wide-screen genotyping platforms and imputation pipelines developed , the genetic map of were performed for different population like European and Asian in some disease included , systemic lupus erythematosus (SLE) [(9,10,11)] .Studies exhibit that the major histocompatibility complex (MHC) is One of the genetic risk factors for the development of immune-mediated diseases like SLE [(7,8,12).]

Materials and Methods

Study design and subjects; present study is one of the sequential projects deal with genetic polymorphisms in some genes in SLE patients in Hilla city, A case-control study was implemented enrolled 30 Iraqi patients suffered from systemic lupus erythematosus (SLE) and

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35 of healthy subjects as control group, that attendance to Merjan teaching hospital in Babylon – Iraq, All patients were diagnosed by a specialist dr. Ali Al-kazaz, patients group consist of (28 female and 2 male) with age (10-60 year), the control group consist of 35 individuals (20 male and 15 female) apparently healthy with age (20-65 year) , All subjects in this study were taken written consent before participation in this study.

Inclusion Criteria the diagnosis of SLE patients was conducted according to observed 4 criteria of The Systemic Lupus International Collaborating Clinics (SLICC) criteria which consist of clinical manifestations like malar rash, discoid rash photosensitivity, oral ulcers, arthritis, serositis, renal disorder, neurologic disorder, hematologic disorder, immunologic disorder, antinuclear antibody [13].

1- PCR condition : the gene segments was amplification using MIC-A5F 5′CCTTTTTTTCAGGGAAAGTGC-3 and MIC-A5R, 5′CCTTACCATCTCCAGAAACTGC-3 [14] . under the condition 95Cº /5 min, (95Cº /30 sec. 57Cº /30 sec, 72Cº /20 sec) for 30 times finally 72 /10 min, The products were detected by electrophoresis in garose 1% , 70 v , 20 Ma for 90 min. SSCP technique implemented according to Al-Terehi et al., [15]

Static analysis : the static analysis was conducted using Odd ration, confidence Intervals 95% at P value 0.05.

Results and Discussion

This study deal with polymorphism of MIC gene in SLE disease, the SSCP was used to determine the gene polymorphism, the results show there were 183 bp of amplification products for all patients and control group (figure 1 A), three haplotypes represented as two bands for each one were observed after SSCP electrophoresis pattern, these haplotypes were A, B, and C (figure 1 B). as a results of high incidence SLE in Iraqi population at last year sequential studies were suggested to investigated some genes polymorphisms in SLE patients like mitochondrial, APRIL gene and micro-RNA, the results of these studies were varying.

In spite of poorly understood of SLE pathogenicity, numerous environmental and genetic [16] factors have been postulated, the major risk is genetic predisposition which well documented Some genes now are reported to SLE contributed [17] .and these genes impact on the immune pathways and processing like C2 and C4 related to the MHC [18] .

Table (1) haplotypes frequency of MIC gene polymorphism in study subjects

Allele descript	SLE patients (30)	Control (35)	Odd ration CI95%	P value
A	13%	22.8%	1.9259 0.5168 to 7.1774	0.3288
B	20%	8.57%	1.8621 0.4231 to 8.1942	0.4109
C	3.33%	8.57%	2.7188 0.2676 to 27.6189	0.3978

The statics analysis show that B haplotypes was more frequent in patient than control in non-significant differences it was appeared in 20% and 8,57% for patients and control respectively (OR 1.8621, CI 95% 0.4231 to 8.1942). A allele found in 22.8% of control while 13% in patients (OR 1.9259, CI 95% 0.5168 to 7.1774). Finally haplotype C appeared in 8.57% in control and 3.33% in patients in non-significant differences (OR 2.7188c CI 95% 0.2676 to 27.6189).

The polymorphism in present study restricted by 183 bp represented by A, B and C, a study clarified that the the MHC in human genome is the more gene-dense locus , also its high polymorphic genes. It included more than 120 functional genes, pseudo-genes [19] . The variation in SSCP electrophoresis pattern showed more than the three haplotypes which documented in this study , all these variations were don't dependent in present study because it frequent in all study subjects. The non-significant may be because the sample limitation number in present study, here we are announced that all patients of SLE in Hilla city were enrolled in our projects at the time of sample collection and they are followed up with rheumatology unit in Marjan hospital .

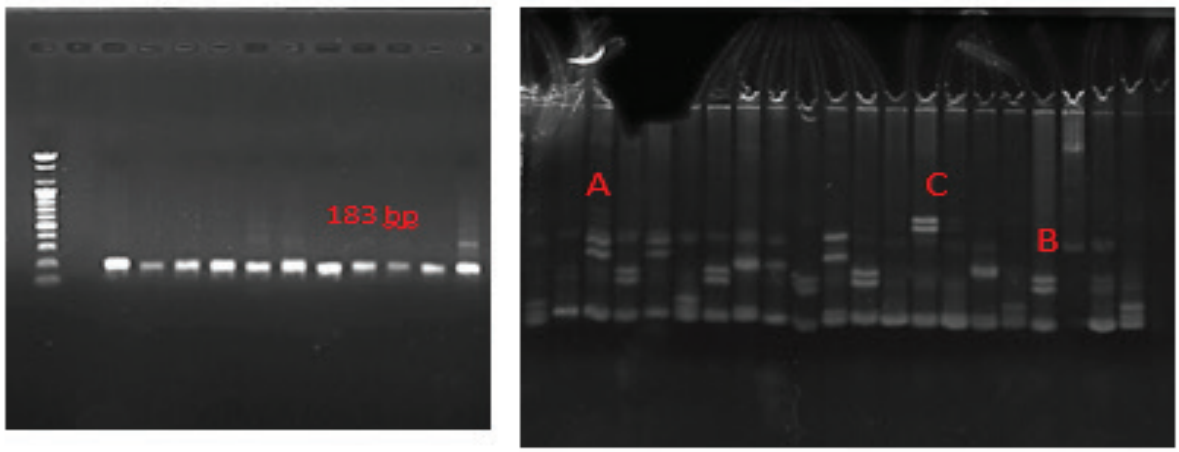

Figure (1) A the left electrophoresis pattern of MIC PCR products 183 bp for patients and control at 20mA, 70 V and 90 min. B the right electrophoresis pattern of SSCP technique show three haplotypes A, B, and C.

The present study show related polymorphisms with SLE disease, same results proved by Gambelunghe et al., [20] that found three major markers (DR3-DQ2, MICA5 and MICA5.1) were strongly associated to confer genetic risk of SLE. Also Ping et al.,[21] observed *MICB*009N* allele might be a SLE risk factor while the *MICB*014*, *MICA*010* and *MICB*002* alleles were correlated with decreased SLE incidence, however MIC gene need more investigation to prove its role in immune response in SLE patients and further gene sequencing. We concluded from this observation that MIC gene polymorphisms can be used in pre diagnosis of SLE disease in genetic predisposition family to avoid accumulate environment factor effect that lead to trigger disease.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both MOH and MOHSER in Iraq

Conflict of Interest: Non

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