REVIEW ARTICLE

The Genotyping Impact of X-ray Repair Cross-Complementing Group 1 Gene in Systemic Lupus Erythematosus

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ABSTRACT

DNA repair genes have a vital role in a variety of diseases. The present investigates deal with X-ray repair cross-complementing group 1 gene (XRCC1 Arg399Gln) in systemic lupus erythematosus (SLE). PCR-CTPP method used to detect polymorphism, the results show two alleles (A and G) and three genotyping (AA, AG, and GG), the present analysis shows that non-significant association between (AG and GG) with SLE patients (p = 0.3964), strong association with absent AA in patients than control (10%) in significant differences (p = 0.0322). can be concluded that the XRCC1 Arg399Gln may be affected in the SLE in Iraqi patients.

Keywords: DNA repair, XRCC1, Arg399Gln, Genotyping, Systemic Lupus Erythematosus.

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INTRODUCTION

The B-cell hyperactivity is a feature of SLE, which is a multi-factorial autoimmune illness, and the generation of autoantibodies antinuclear components and other self-antigens.[1] SLE is resulted from a combination of genetic, hormonal, and environmental factors. Infection with a virus and ultraviolet (UV) light exposure, for example, is both significant environmental influences.[2]

Genetic abnormalities can induce abnormality in inflammation, cytokine generation, and inadequate clearance of apoptotic cells or immune complexes, resulting in anti-self-immune reactions.[3]

Despite advances in knowledge of possible molecular pathways because to SNPs typing, the specific interaction of environmental variables with genetic variations in SLE remains largely obscure.[4] Hypersensitivity to irradiation via UV is a common diagnosis in SLE cases. Defects in the capacity to repair DNA injury, as well as the resulting excessive amounts of apoptotic bodies, have recently been identified as causal for SLE agent.[5,6] Clinical investigations have also revealed that certain SLE patients have severe deoxyribonucleic acid (DNA) repair deficiencies, indicating that genetic differences in the DNA repair protein genes have a role in SLE susceptibility. The X-ray repair cross-complementing (XRCC) gene family, which participates in repair of DNA pathways, has been linked to shielding mammalian cells from DNA damage.[7,8]

At DNA damage sites, XRCC1 serves as a scaffold protein, forming a compound with human polynucleotide kinase, polymerase b DNA and ligase. The allele frequency of the mutation at codon 280 is similarly bind to a reduction in DNA repair activity.[8,9] The impact of XRCC1 Gene (Arg399Gln) Genotyping on Systemic Lupus Erythematosus was investigated in this study.

MATERIAL AND METHODS

This study was conducted in the DNA lab at the University of Babylon's biology department, with 40 SLE patients (that diagnostic by Dr. Ali Alkzaz in a clinic of chronic disease in the Marjan Hospital City). Their age ranged from 30 to 65 years old and 20 healthy subjects (30–65 years old). All samples were collected with the approval of Iraq's environment and health ministry.

- Genomic DNA from white blood cells (WBCs) was isolated using a DNA extraction kit (Favorgen), and the DNA concentration of the samples was measured using a spectrophotometer for both SLE patients and controls (Nanodrop).
- The primer of XRCC1 gene was used: F1: TCC CTGCGC CGC TGC AGT TTC T R1: TGG CGT GTGAGG CCT TAC

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CTC C F2 TCG GCG GCT GCCCTC CCA R2 AGC CCT CTG TGA CCT CCCAGG C. The PCR-CTPP amplicons size are the G allele (399Arg), A allele (399Gln) amplify bands were 447- and 222-bp, respectively and 630-bp common band.[10]

- *Data Analysis:* The data were analyzed statically by Qi Square analysis at a level of significance (0.05)

RESULTS

The present study was a case-control deals with patients' systemic lupus erythematosus, this study involved 40 samples, additionally healthy control group 20 samples. In this study, we detected the Impact of XCRR1 Genotyping with Systemic Lupus Erythematosus.

The result of the Polymerase chain reaction for XRCC1 gene showed two alleles (A, G) and three genotyping's (AA, AG and GG), the results show two alleles (A and G) and three genotyping (AA, AG, and GG), the present analysis shows that non-significant association between (AG and GG) with SLE patients (p = 0.3964), strong association with absent AA in patients than control (10%) in significant differences (p = 0.0322) as shown in Figure 2.

DISCUSSION

Studies reported that exposure to UV is a strong stimulation of SLE and that an individual's vulnerability to the development of SLE is determined by genetic variation. The Leucocytes cells in SLE patients had a higher spontaneous single strand breaks level and oxidative DNA injury than those from healthy people.[11] In this study we found that the XRCC1 Arg399Gln may be affected in the SLE in Iraqi patients, our study agreement with the study in the Polish population conducted by Warchoł *et al*., reported that the XRCC1 399Gln gene polymorphism considered as a risk factor for SLE happened in a sample.[12] Furthermore, meta-analysis of some populations reported that this gene polymorphism related to incidence of SLE.[13,14]

Another study found that the XRCC1 AG genotyping at codon 399 may be a risk of SLE disease, This A/G genotype was also linked to malar rash and photosensitivity, both of which are connected to a decreased ability to resist UV irradiation, suggesting that XRCC1 SNPs play a significant role in SLE development.[13]

Any DNA breaks along with nuclear proteins have recently been discovered to be powerful immunogens for evoking auto-reactive antibodies in SLE patients, suggesting that DNA repair capacity in cells is a deciding factor in the development of SLE.[15,16] The XRCC1 399 Gln polymorphism variation has also been identified as a genetic alteration for enhancing the production of DNA adducts and DNA damage which is caused by exposure to cigarette smoke, aflatoxin B1, metabolites and several molecules.[17] The XRCC1 protein is an important part of the DNA damage repair mechanism called a base excision repair (BER). Although XRCC1 lacks enzymatic activity. It serves as a scaffold to regulate the action of other BER machinery proteins such as glycosylases, an endonuclease (APE1), Poly (ADP-ribose) Polymerases (PARP1 and PARP2) and DNA polymerase b.[18]

Endogenous variables such as reactive oxygen species, such as exogenous ones like chemicals and ionizing radiation, can cause DNA damage, either directly or indirectly during BER.[19,20] The UV irradiation exposure may lead to DNA destruction and is a powerful trigger SLE in susceptible cases.[21] In susceptible cases with the XRCC1 399 Gln protein variation who have been exposed to DNA injury causes, poor DNA repair may trigger an autoimmune response, nucleoprotein complexes containing new composites or conformation epitopes, as well as their destruction products, which may include immunocryptic peptides that trigger autoreactive T cells, may be formed as a result of DNA damage.[22,23] In conclusion our genetic analysis exhibits the possible contribution of the XRCC1 gene variant to SLE development.

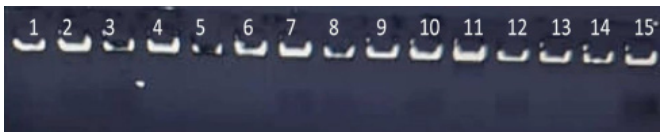

Figure 1: Electrophoreses pattern of DNA extracted from whole blood of SLE patient and control, 1% Agarose, 75 v, 20 mA for 45 minutes, lane 1-10 DNA of patient, 11-15 DNA of control.

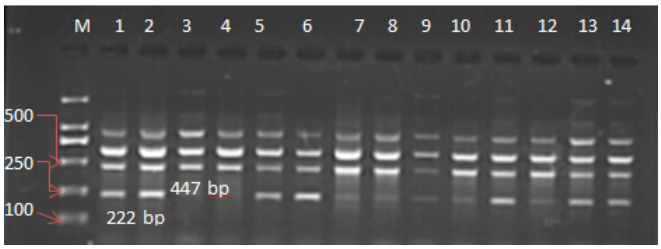

Figure 2: Genotypes pattern of XRCC1 gene, this amplification product was 222 bp and 447bp, and 630bp 1% agarose, 75v, 20 mA for 45 min (5 μ*L* in each well). Lane (1–9) PCR product of patients and (10-14) PCR product of control.

Table 1: Genotyping and allele frequency among study group

Genotyping	*Patients*	*Control (%)*	*Odd ratio*	*Sig*
AG	21 (52.5)	46.66	1.2716 0.7297–2.2159	p = 0.3964
GG	19 (47.5)	43.33	22.9310 1.3044–403.1228	p = 0.0322
AA	0	10	Reference group	

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