International Research Journal of Pharmacy and Medical Sciences
ISSN (Online): 2581-3277

Role of MiRNA-146a and IL- 23 Level in Patients with Systemic Lupus Erythematosus

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Abstract*—Systemic lupus erythematosus a complex an autoimmune chronic illness with a broad range of symptoms. The primary characteristic of the illness is the generation of many autoantibodies due to a lack of immunological tolerance. One hundred people participated in a case-control research. involve 60 SLE patient (30 females and 30 males) and 40 control matched with patient in age and gender. Rang between 21to 51 years.at the time of sampling, the hematological parameters that evaluate the quantity of proteinuria, erythrocyte sedimentation rate, and complete blood count were measured. Using an ELISA kit, the Amount of IL-23 in the blood of both subjects and controls was determined. Extraction of micro RNA from whole blood By using the kit of Trans Zol Up, micro RNA was extracted from whole blood samples. A Using a quantitative real-time polymerase chain reaction analyze miR-146a activity.*

***Keywords*—** *Systemic lupus erythematosus, pro-inflammatory cytokines, miR-146a.*

I. Introduction

Systemic lupus erythematosus is complex long-term inflammatory illness of a broad range complaints [1].The primary characteristic in the illness is the generation of a broad range of self-antibody due to the loss of immunological tolerance, which triggers an attack on self-antigens like DNA, cellular parts, immunological assemblies, and host nuclei antigens.[2][3].The development of SLE is significantly influenced by genetic factors[4].Despite being non-coding and crucial in the control of gene expression, microRNAs (miRNAs) are tiny RNAs with a single chain (21–25 nucleotides) that make up 30% of transcripts in people [5].

With a length of 22–25 nucleotides, A significant member of the family of micro-ribonucleic acids (miRs) is microRNA-146a (miR-146a).Theirs is a type of non-codin single-stranded RNA molecule that breaks down or inhibits translated messenger RNA to take role in transcriptional control [6]The release of inflammatory mediators, immune response, and hematopoietic cell proliferation and differentiation are all influenced by the immunological and hematopoiesis-related miRs.[7]MiR-146a expression is dysregulated in a number of autoimmune diseases, such as psoriasis, (RA), and Lupus erythematosus systemic.[8]SLE is a complicated, diverse immunologic condition with a wide range of analytical and medical symptoms. It is brought on by environmental and genetic elements that lead to a decrease in tolerance to self-antigens[9]. One A component of the mediator family IL-12 is interleukin-23 (IL-23). The IL-12p40 and IL-23p19 subunits make up this heterodimer.T lymphocytes, blood vessel cellular, and cells that carry antigens combine to create ofp19 subunit IL-23[10]. Tumor necrosis factor alpha, IL6, certain Cytokines, metalloproteinases, and the attraction of macrophages to tissues implicated in the development of SLE are just a few of the proinflammatory cytokines that IL17 induces. IL23plays a vital role in the proliferation of Th17 cells that produces IL17[11].

II. Methodology

A case-control study was conducted on one hundred involve 60 SLE patient (30 females and 30 males) and 40 control matched with pateint in age and gender. Rang btween 21to 51 years. Referrals to the outpatient clinic were made attend tothe Al-Sador A hospital and Al-Najaf Hospital (the Rheumatology Unit) from October 2024 – to February 2025. The rheumatologists at the unit clinic diagnosed SLE using the EULAR/ACR (European League against Rheumatism/American College of Rheumatology) diagnostic standards. During the blood sample, the doctor directly calculated the activity of each patient's systemic lupus erythematosus. Fourty healthy controls this study included. Both groups are matched in age and gender.

Laboratory Investigations

Each patient's medical record was used to gather demographic data and clinical manifestations. The immunological and standard tests were evaluated using laboratory examinations. At this Timing of sample, all hematological parameters involving proteinuria, Full blood count (CBC) and rate of erythrocyte sedimentation (ESR) were assessed. Autoimmune profile tests, including anti–ds DNA antibodies and the enzyme linked immunosorbent assay (ELISA) method was used to measure the anti-nuclear autoantibody (ANA) (Human Company, Germany).

Measurement of (IL-23) in SLE Patients' Serum

Using an ELISA kit, the amount of cytokine in the serum of patients and controls was determined. Five milliliters of venous peripheral Blood samples were taken from each patient and a healthy control group. Each sample was given three milliliters in a sterile gel tube to obtain serum, then serum samples were stored after being separated by centrifugation at –20°C prior to examination the levels of cytokine (pg/ml), the levels of IL-23 was measured. The ELISA reader-controlling software was used to transform the digital data of the raw absorbance values into a standard curve.

Hind Fouaad AL-Hammami, "Role of MiRNA-146a and IL- 23 Level in Patients with Systemic Lupus Erythematosus," *International Research Journal of Pharmacy and Medical Sciences (IRJPMS)*, Volume 9, Issue 2, pp. 25-27, 2026.

International Research Journal of Pharmacy and Medical Sciences
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Detection of miR-146a

The remaining (2ml) of blood was transported into a tube with EDTA and stored at -20°C until using real-time PCR analysis. Extraction of micro RNA from whole blood By using the kit of Trans Zol Up, micro RNA was extracted from whole blood samples by the use company's instructions, A one percent agarose gel electrophoresis was used to confirm the RNA's quality. miR-146a expression was measured using a qPCR.

Reverse transcription: involve miR-146a was reversibly transcribed in accordance with the manufacturer's instructions using the miScript II RT Kit (Qiagen), In a conventional PCR thermal cycler, After The samples were heated for one hour at 37°C to 95°C. for 5 minutes. The complementary DNA that was not diluted was stored at -20°C until it was processed further.

Real-time PCR: was employed to quantify the blood miR-146a levels in both patients and controls by the GoTaq® Probe 1-Step RT-qPCR System allows for the detection and relative quantification of RNA expression levels by a one-step RT-qPCR.

Statistical analysis

The current study employed version 22 of the Scientific Statistical Package (SPSS)to handle the collected data. In addition, this chi-square test is used for analyses, and correlations between various research parameters were examined using Spearman correlation. A P-value of less than 0.05 was used to determine the significance level, and a 0.01 or less P-value was regarded as highly significant. The miR-146a cutoff values as a possible SLE signal for diagnosis were calculated using the Receiver Operating Characteristic (ROC) curve. Sensitivity and specificity calculations were used to assess the miR-146a.

III. Results

The patient and control groups' demographic characteristics are displayed in (Table 1) Characteristics of controls and SLE patients Fourty healthy controls and 60 SLE patients were enrolled in this study. Both groups are matched in age and gender. The mean age of SLE patients and controls were 21.60 ± 8.40 and years, respectively.

TABLE 1: Patient and Normal Parameters

Properties	Patients (n=60)	Control (n=40)	*P*-value
Age ,mean±SD	21.60 ± 8.40	26.21 ± 9.80	0.239
Male	30 (50.%)	20 (50.%)	0.094
Female	30 (50.5%)	20(50%)	

IL-23 of Participants' serum levels were noticeably higher than those of normal.

(*P*<0.001)The mean serum levels of IL23was 3.64* ± 1.34 in patients versus 2.54 ± 0.55 in controls. This was a significant increase in serum IL23 levels in patients of SLE compared with controls at P=0.004 this shown in (Table 2) Figure (1).

Receiver operator characteristic (ROC) curve analysis was used to assess the IL- 23 cutoff value and predict SLE disease as diagnostic tests. The area under the curve (AUC) value was 68.7with 95% CI: 0.5–0.88 (p equal 0.05) versus the control. The results are displayed in Table (3) and Figure (2).

TABLE 2: Comparing of IL23 (Pg/Ml)of Participants and Controls

Parameter	Mean ± SD		P-value
	Patients	Control	
IL 23	3.64* ± 1.34	2.54 ± 0.55	0.004

Notes: SD mean±standard deviation, * *P*-value is significant, ie,<0.001.

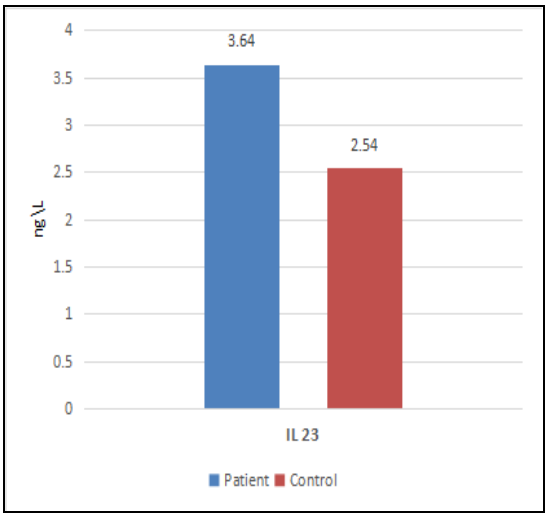

Figure (1) IL23 levels in patients of SLE compared with controls

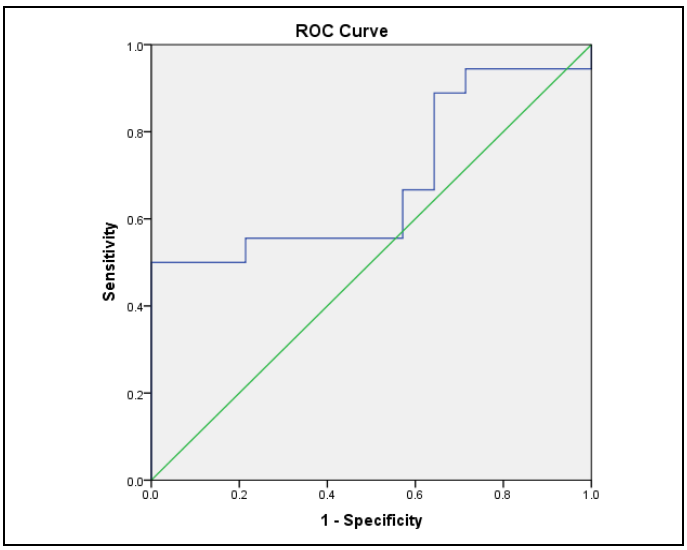

Figure (2): IL-23 ROC characteristic study to determine a potential diagnostic cutoff value

TABLE 3: Specificity and sensitivity of IL-23 level in SLE disease

AUC	Sensitivity	Specificity	Asymptotic 95% CI		P-value
			Lower Bound	Upper Bound	
68.7	55.6	78.6	0.5	0.88	0. 05

CI: Confidence interval, AUC: Area under curve

The mean serum levels of miR-146a was 0.4-14.1in patients versus0.03-7.40 in regulates. Serum miR-146aSLE patients' levels were noticeably greater than those of controls at P< 0.001 (Table 4)

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TABLE 4: Compared miR-146a level between healthy control and SLE patients

Parameter	Mean ± SD		P-value
	SLE Patients	Control	
mRNA 146 a	0.4±14.1	0.03±7.40	<0.001

n: Number of Participants; SD: Standard deviation; significant at P ≤ 0.001

IV. Discussion

The current study. Showed there was no statistically significant difference was seen in mean age (P= 0.239) and sex between patients with Systemic lupus erythematosus and control subjects, while in other study The study's findings point to a predictive factor for female age and gender in the source of SLE.[13] that women with SLE have a greater predominance compared to men after puberty because of elevated estrogen levels in the blood [14]The current study's findings showed that SLE patients' serum levels of IL23 were noticeably higher than those of healthy controls. These findings were consistent with numerous previous research that demonstrated higher Serum levels of IL23 in SLE patients versus healthy controls.[15]Immune complexes cause the production of many cytokines the results in this study showen role of cytokine in Systemic lupuserythematosus development this agree with Certain cytokines have been demonstrated to be directly linked to the pathophysiology of SLE.[16]

These findings suggested that IL23 may be connected to clinical characteristics and play a part in the pathophysiology of SLE. IL23 is essential for Th17 cells to turn into IL17. [17] The axis of IL23/IL17, that supports Chronic illness and autoimmune is correlated with both IL23 and IL17, which play essential roles in inflammation.[18]The findings indicated a correlation among microRNA-146a transcript and the likelihood developing lupus. Thus, in high-risk populations, miRNA-146a may beutilized as a potential biomarker for the diagnosis of SLE, as these findings were validated by earlier research[19]

In agreement, with [20]discovered that when SLE patients' urine was compared to healthy controls, The most expressed miR-146a was elevated, a hundredfold difference. According to the other research the amount of miRNA-146a was linked to an increased danger of SLE. Consequently, in high-risk individuals, miRNA-146a may be a utilized like a potential indicator for SLE identification. The expression of miRNA-146a and the danger of SLE did not significantly differ, according to a prior meta-analysis. Perhaps as a result of using limited sample sizes.[21]

V. Conclusion

The present study is involved examine miR-146a and pro-inflammatory cytokine expression (IL-23) together in the same patients SLE, Data demonstrated that miR-146a had significantly increased.

In SLE sufferers. Additionally, describe how pro-inflammatory cytokines and miR-146a contribute to the immunopathology of SLE. Patients with SLE possess higher serum levels of IL23, which is connected to SLE activity and may be crucial to the pathophysiology and activity of the illness.

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