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ORIGINAL ARTICLE

The Role of Nuclear Enriched Abundant Transcript 1 (NEAT1) as a Novel Marker in Diagnosis of Systemic Lupus Erythematosus Disease in Benha University Hospital

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Key words:
Systemic lupus erythematosus (SLE), Nuclear enriched abundant transcript 1 (NEAT1), Long non-coding ribonucleic acid (LncRNA), Disease activity index (SLEDAI), and biomarker.

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ABSTRACT

Background: *A persistent autoimmune condition with a variety of symptoms is systemic lupus erythematosus. Reliable biomarkers that support diagnosis and reflect disease activity remain clinically valuable* ***Objectives:*** *Our study pointed out to assess Nuclear enriched abundant transcript 1 (NEAT1) expression as a diagnostic marker for SLE and to explore association with activity and severity of the disease.* ***Methodology:*** *Twenty age and sex-matched healthy controls and thirty SLE patients who met SLICC criteria were included in this case-control study. NEAT1 expression was relatively quantified in PBMCs utilizing quantitative real-time PCR. Standard laboratory indices (ESR, CRP, complements, ANA) were assessed and anti-dsDNA was detected by using indirect immunofluorescent test (IIFT) also SLEDAI score was used to measure disease activity.* ***Results:*** *Females predominated among SLE cases (83.3% vs 70.0% in controls; P=0.311) with no significant age difference (33.60±11.04 vs 31.15±10.26 years; P=0.367). Expression level of NEAT1 was higher in cases than controls (9.62±29.02 vs 8.41±19.55; P=0.010). NEAT1 positively correlated with 24-hour proteinuria (P <0.001) and to high ESR and low C3/C4 (P<0.001). NEAT1 level was increased in cases with high SLEDAI and anti-dsDNA titers (P<0.001). ROC curve analysis revealed AUC=0.717 (P=0.010)., sensitivity was 83.33% and specificity 70.0% (accuracy 78.0%). In multivariate ordinal regression, anti-dsDNA level and NEAT1 expression levels predicted higher disease activity.* ***Conclusions:*** *NEAT1 is upregulated in SLE patients and this makes it useful as a supportive marker for diagnosis of the disease. In addition, its level reflects the activity and severity of the disease. Therefor NEAT1 can be used as an additional biomarker alongside other tests.*

INTRODUCTION

A collapse in tolerance to self-antigens is a hallmark of SLE, multiple immune system abnormalities, and elevated levels of autoantibodies directed against nuclear components. [1] Its development is complex, with both genetic predisposition and environmental influences playing important roles in its onset.[2]

Non-coding RNAs make up over 98% of the human genome.[3] Although some of these molecules may encode short peptides with particular biological roles, they often lack the ability to code proteins.[4]

The pathophysiology of autoimmune disorders is significantly influenced by lncRNAs.[5] They may increase the production of IFN-I, TNF-α, IL-1β, IL-6, IL-8 and participate in inflammatory pathways linked to autoimmune disorders.[6] Furthermore, lncRNAs are highly stable in plasma and serum and are broadly distributed in different bodily fluids, which makes them potential biomarkers for a number of autoimmune illnesses, including SLE.[7]

NEAT1 regulates the release of inflammatory cytokines, changing B- and T-cell immunological responses and leading to occurence of SLE. NEAT1 increasingly recognized as regulator of chronic inflammation and autoimmune diseases pathogenesis. Elevated NEAT1 levels have been observed in SLE which leads to dysregulated cytokine networks and impaired immune tolerance. By modulating type I interferon signaling, TLR pathways, and immune cell activation, NEAT1 appears to amplify pathogenic immune responses.[8] NEAT1 influences the transcriptional stability of interferon-stimulated genes (ISGs), leading to sustained activation of the IFN pathway. This persistent IFN signaling contributes to autoantigen presentation, stimulation of innate immunity, subsequent tissue damage.[9] NEAT1 is positively connected with disease activity and may be a target for both diagnosis and therapy.[10]

SLE is mainly manifested and represented by anti-nuclear antibodies in blood due to defects in humoral and cell mediated immunity.[11] Detection of these autoantibodies is widely utilized to diagnose SLE. Early patients diagnosis, followed by prompt and appropriate treatment, can significantly enhance their prognosis and extend their survival rates.[12]

Patients' serum testing has revealed that there are some autoantibodies as anti-SM, ANA, anti-rRnp, anti dsDNA and others which is the cause of inflammation and detection of these autoantibodies is widely carried out in SLE diagnosis.[13]

The specificity of anti-dsDNA antibodies exceedes 97% in SLE diagnosis, moreover, their positivity rate is significantly higher during active disease compared to the inactive phase which also indicates the disease activity.[14]

Therefore, the aim of our research was to ascertain the duration of non-coding RNA Nuclear-Enriched Abundant Transcript 1 (NEAT1) in the diagnosis of SLE and to examine its correlation with disease activity and severity.

METHODOLOGY

Design and population

This case-control study was carried out at Medical Microbiology and Immunology Department Faculty of Medicine Benha University. Between December 2023 and April 2025, thirty participants were recruited from the Rheumatology, Rehabilitation, and Physical Medicine Department's Inpatient and Outpatient Clinics at Benha University Hospital and twenty age and sex matched healthy individuals.

Prior to participation, each subject provided written informed permission. The study was conducted in compliance with the ethical guidelines authorized by the Ethics Committee of the Benha Faculty of Medicine (MD 23-11-2022).

Patient Selection

Patients who satisfied the systemic lupus international Collaborating Clinics Classifcation Criteria (SLICC) categorization criteria for SLE and age- and sex-matched healthy persons who were enlisted as controls were included in the inclusion criteria. The study did not include patients having a history of connective tissue illnesses, cancer, or other autoimmune disorders.

The SLICC classification criteria for SLE encompass both clinical and immunologic components. Oral or nasal ulcers, non-scarring alopecia, acute or subacute cutaneous lupus, synovitis affecting two or more joints, serositis, kidney and nervous system involvement, haemolytic anaemia, leukopenia (<4,000/mm³) or lymphopenia (<1,000/mm³), and thrombocytopenia (<100,000/mm³). The immunologic criteria include the presence of antiphospholipid antibodies, low complement levels, a positive direct Coombs' test, and ANA, anti-dsDNA, and anti-Sm antibodies.[15] A definitive SLE classification requires ≥4 cumulative criteria, including at least one clinical and one immunologic criterion; these criteria do not need to be present at the same time.

Grouping

All subjects were divided into 2 groups:

Group I: thirty people who has SLE.

Group II: twenty individuals matched for age and sex and appeared to be in good health.

Full history taking

A comprehensive history was obtained from each patient, including personal data (age, sex, residence, marital status). The history of present illness was taken chronologically to define symptoms onset, course, duration, initial manifestations, and potential triggers (e.g., infection, sun exposure, surgery, stress), with systematic screening for constitutional, musculoskeletal, cutaneous, urinary, cardiac, respiratory, gastrointestinal, neuropsychiatric, ocular, hematological, and vascular symptoms. Past history of comorbidities, prior operations/trauma, hospital admissions, and detailed treatment history (especially steroids and DMARDs), including dose, duration, discontinuation , efficacy, and adverse effects.

Clinical examination

All SLE patients underwent general examination with attention to features . A full systemic examination was performed, including chest examination, cardiovascular examination, abdominal examination, and musculoskeletal examination.

SLEDAI

SLE activity was measured by SLEDAI. Based on their score, patients were categorised into four groups: no activity (score = 0), mild (from 0– to 10), moderate (from11– to 20), severe (from 21– to 45), and extremely severe (>45). The SLEDAI is a weighted scoring system that integrates significant clinical and laboratory criteria to provide a consistent evaluation of disease activity.[16]

Laboratory investigations and NEAT1 analysis

Routine laboratory investigations:

All patients underwent blood testing . Urinary casts , haematuria , pyuria were all included in the urine assessment. Also chemical tests were done.

Serology: Indirect immunofluorescence was used in serological examinations to detect ANA . ELISA was used to measure anti-dsDNA antibodies. Immunodiffusion plate method was used to measure complement levels. Antiphospholipid antibodies were assessed.

LncRNA NEAT1 analysis: For NEAT1 analysis, 2 ml of peripheral blood was collected for PBMC isolation and RNA extraction using QIAamp RNA Blood Mini Kit (QIAGEN ®; Germany) according to manufacturer's instructions,[17] followed by complementary DNA (cDNA) preparation by using RT mix Solarbio

according to manufacturer's instructions , then relative quantification of NEAT1 level was done by quantitative real-time polymerase chain reaction using specific NEAT1 primer pairs which are 5' TGGCTAGCTCAGGGCTTTCAG-3,' 5' TCTCCTTGCCAAGCTTCCTTC-3' that designed and tested for efficiency and accuracy with glyceraldhyde-3-phosphayte dehydrogenase (GAPDH) as a house keeping gene with cycling conditions as follow: enzyme activation at 95 °C for 20 s, followed by 40 cycles of denaturation at 95 °C for 3 s then annealing and extension at 60 °C for 30s. Relative quantitation was performed with the results expressed in the linear form by using the formula $2^{-\Delta\Delta}$CT and expressed as relative units using Rotor-Gene Q real-time PCR machine (QIAGEN ®; Germany) .

Anti-dsDNA by IIFT: Anti-dsDNA was also assessed using indirect immunofluorescence on Crithidia luciliae using AESKU.DIAGNOSTICS, AESKUSLIDES® nDNA, Germany according to manufacturer's instructions, based on binding of patient antibodies to kinetoplast DNA and detection using Fluorescin isothiocyanate (FITC) labeled anti-human antibodies, with fluorescence microscopy used for result interpretation.

Statistical methods

IBM SPSS Statistics for Windows (Version 25.0; IBM Corp., 2017) and the Handbook of Medical Statistics were used to examine the data. The comparative Ct methodology was used to quantify relative gene expression, which was then calculated using the 2−ΔΔCt method and normalised to a housekeeping gene.[18] Numerical data were reported as mean ± standard deviation (and standard error when applicable). For nonparametric continuous variables, the Mann-Whitney U or Kruskal-Wallis test was employed; for categorical variables, the Chi-square or Fisher's exact test was utilised. Correlations were assessed using Spearman's rho. Diagnostic performance was evaluated using ROC curve analysis, and the area under the curve (AUC) was utilised for interpretation.

RESULTS

This study included 30 patients divided into 5 males and 25 females with SLE with higher percentage in females (83.3%) than males (16.7%). Age of studied patients was between 19-58 years with a mean of 33.60 ± 11.04 years **.**

The vast majority of patients (70.0%) had mouth ulcers and malar rash. Arthritis affects all patients (100.0%). Nephritis was seen in 66.7% of patients, with the majority being grade IV (40.0%) and hematuria 3.3%. Other clinical symptoms include alopecia, cutaneous rash, skin rash represented (13.3%), (16.7%), (30%) respectively.

Analysis of ESR and CRP in the SLE group revealed that the mean CRP was (11.50 mg/L) and the mean ESR was (51.0 mm/h). According to table (1) , 46.7% of SLE patients had normal ESR and CRP values, whereas 53.3% had high levels. Additionally, complement protein C3 and C4 levels were lower in 66.7% and 60% of SLE patients, respectively, whereas all controls had normal values. SLE patients were substantially linked to reduced C3 and C4 and higher CRP and ESR. The immunologic indicators showed that the SLE and control groups varied significantly. The titers of anti-dsDNA antibodies were 1/160 in 46.7%, 1/320 in 26.7%, 1/640 in 20%, and 1/1280 in 6.6% of SLE patients. **(Table 1) and figure (1).**

Table 1: ESR, CRP, C3, C4, and Anti ds-DNA between the studied participants

Variable		SLE(n=30)	Control (n=20)	P value
ESR (mm/h)	Value	51.0 ± 26.49	11.55 ± 1.88	**<0.001***
	Normal	14 (46.7%)	20 (100%)	
	High	16 (53.3%)	0 (0%)	
CRP (mg/L)	Value	11.50 ± 10.09	1.2 ± 0.47	**<0.001***
	Normal	14 (46.7%)	20 (100%)	**<0.001***
	High	16 (53.3%)	0 (0%)	
C3	Normal	10 (33.3)	20 (100)	**<0.001***
	Decreased	20 (66.7)	0 (0)	
C4	Normal	12 (40.0)	20 (100)	**<0.001***
	Decreased	18 (60.0)	0 (0)	
Anti ds-DNA	Negative	0 (0.0)	20 (100.0)	**<0.001***
	Positive	30 (100.0)	0 (0.0)	
Anti ds-DNA titre	1/160	14 (46.7)	NA	–
	1/320	8 (26.7)	NA	
	1/640	6 (20.0)	NA	
	1/1280	2 (6.6)	NA	
	Mean ± SD	373.3 ± 306.9	NA	

Data was presented as Means ± SD or n (%), *: p value less than0.05 is considered significant.

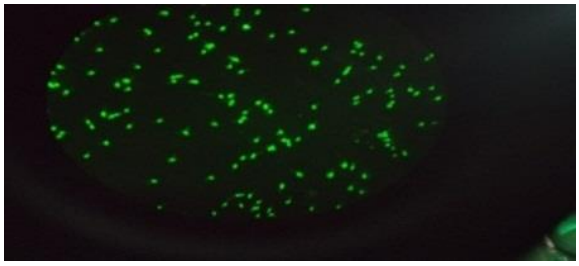

Fig. 1: Positive Anti dsDNA sera at titre of 1/80

NEAT1 gene expression was significantly higher in the SLE group than in the control group (9.62 ± 29.02 vs 8.41 ± 19.55; P = 0.010). **Figure 2**, **Figure 3, figure 4**

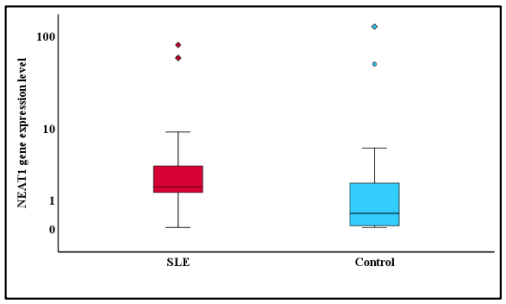

Fig. 2: Boxplot chart for comparison between SLE and the control group regarding NEAT1 gene expression level.

Fig 3: CT analysis of cases and controls

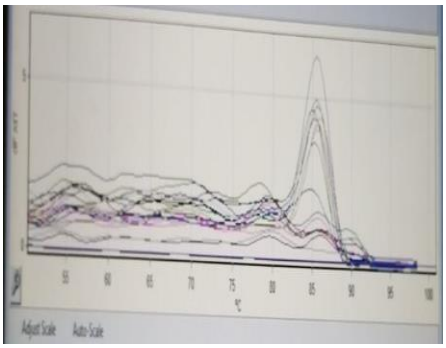

Fig. 4: Melting Curve

The correlation analysis demonstrated that NEAT1 gene expression levels showed significant positive correlations with proteinuria (p-value <0.001). While NEAT1 gene expression did not significantly correlate with other investigations studied among the SLE patients as liver function and kidney function tests. **(Table 2)**

Table 2: Correlation between NEAT1 gene expression level and different parameters among patients with SLE group

	NEAT1 gene expression level	
	ρ	p
AST	-0.279	0.135
ALT	-0.118	0.535
Serum urea	0.219	0.245
Creatinine	0.258	0.169
24h urinary protein	0.997	**<0.001***

ρ, Spearman's rho correlation coefficient.

Table (3) showed that NEAT1 expression level had no significant relationship with CRP levels in SLE patients with a p-value of 0.608. Furthermore, there was remarkable association between higher NEAT1 expression with low C3, C4 levels and high ESR (p-value <0.001). The relationship between NEAT1 gene expression levels and SLEDAI scores showed that individuals with very severe disease activity had highest NEAT1 expression, whereas those with moderate activity had the lowest median. (The p-value of <0.001) This implies that worse disease activity and increased NEAT1 expression were significantly correlated. as evaluated by SLEDAI score. Also NEAT1 expression levels were correlated significantly among anti-dsDNA titers, with the highest median in the 1/1280 group and the lowest in the 1/160 group. **(Table 3)**

Validity assessment of NEAT1 gene expression levels in differentiating SLE patients from the control group revealed an AUC of 0.717, suggesting modest discriminatory capacity. A p-value of 0.010 indicated that this result was statistically significant. The ideal threshold for NEAT1 expression was >0.624, demonstrating a 70.0% specificity and an 83.33% sensitivity. With an overall accuracy of 78.0%.

These findings indicated that NEAT1 gene expression could function as an effective biomarker for distinguishing SLE patients from healthy individuals. **Figure (5)**

Table 3: Connection between NEAT1 gene expression level with ESR, CRP,C3,C4, severity of SLE according to SLEDAI scores, and Anti-ds-DNA among patients with SLE.

Variable		NEAT1 gene expression level	P
ESR	<45 (n=14)	1.067± 0.761	**<0.001***
	≥45 (n=16)	14.838± 25.381	
CRP	Normal (n=14)	7.81 ± 20.72	0.608
	High (n=16)	8.94 ± 19.14	
C3	Normal (n=10)	0.816± 0.681	**<0.001***
	Decreased (n=20)	12.209± 23.189	
C4	Normal (n=12)	0.986± 0.74	**<0.001***
	Decreased (n=18)	13.361± 24.227	
SLEDAI	Moderate (n=9)	0.69 ± 0.63	**<0.001***
	Severe (n=21)	8.34 ± 17.04	
Anti ds-DNA	Negative (n=0)	-	-
	Positive (n=30)	8.411±19.552	
	1/160 (n=14)	0.99 ± 0.65	**<0.001***
	1/320 (n=8)	2.39 ± 1.13	
	1/640 (n=6)	26.23 ± 33.52	
	1/1280 (n=2)	30.95 ± 38.36	

Data was presented as Means ± SD, *: p<0.05 is considered significant.

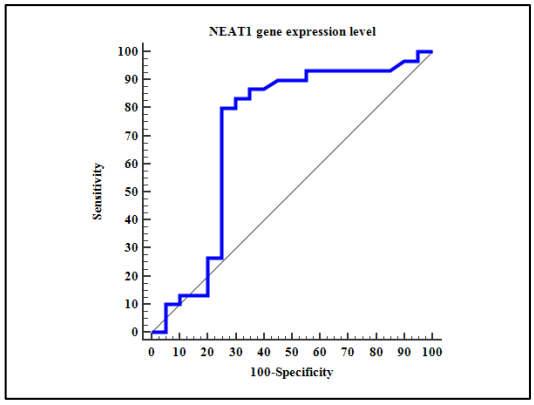

Fig. 5: ROC Curve for NEAT1 gene expression level for discrimination between SLE and the control group.

The ordinal regression analysis indicated several factors that may affect SLEDAI scores. The univariate analysis revealed significant relationships between higher ESR, anti-dsDNA, NEAT1 gene expression level and decreased C3 and C4, with p-values <0.05. Only increased anti-dsDNA and NEAT1 gene expression were considered independent markers of increased activity in the multivariate analysis. There were no significant relationships found between SLEDAI scores and other variables including age, sex, or any laboratory values. **(Table 4)**

Linear regression analysis revealed that longer disease duration was significant predictors of SLICCS scores. Additional variables, including age, sex, ESR, CRP, C3, C4, anti-dsDNA and NEAT1 gene expression level exhibited no significant relations with SLICCS scoresas shown in **Table 5**

Table 4: Ordinal regression analysis for prediction of SLEDAI.

	SLEDAI					
	Univariate			Multivariate		
	P	OR	95% CI	P	OR	CI 95%
Sex	0.518	1.473	0.455-4.766			
Age	0.393	1.017	0.978-1.059			
Disease duration	0.189	0.964	0.912-1.018			
ESR	**0.029***	1.024	1.002-1.046	0.848	1.001	0.994-1.007
CRP	0.362	1.021	0.976-1.069			
C3 and C4 decreased	**<0.001***	1.286	1.151-1.436	**<0.001***	1.814	1.304-2.523
Anti ds-DNA	**0.023***	1.002	1.000-1.005	**0.012***	1.012	1.030-1.065
NEAT1 gene expression level	**0.013***	1.004	1.001-1.007	**0.046***	1.009	1.000-1.017

CI, confidence interval. OR: Odd Ratio *: Significant when p value <0.05.

Table 5: Use of linear regression for predicting SLICCS.

	SLICCS	
	β	p
Sex	0.271	0.147
Age	0.291	0.119
Disease duration	0.492	**0.006**
ESR	0.243	0.196
CRP	- 0.157	0.409
Decreased C3 and C4	0.068	0.723
Anti dsDNA	0.263	0.160
NEAT1 gene expression level	0.122	0.521

β Standardized Coefficients.

DISCUSSON

SLE is a complicated autoimmune condition, and in order to avoid irreversible organ damage, early diagnosis and precise evaluation of disease activity are essential. The goal of our study was to assess NEAT1 role in diagnosis of SLE and discover its connection to the severity and activity of the disease. Thirty SLE patients and twenty age and sex matched controls were gathered from Benha University Hospital.

Our study showed that the average ages in cases group was 30.6±7.1 years old (19 – 58Y), females represented 83.3%, while males represented (16.7%) in this cases group. This was in correlation with a study done by Ramírez et al. [19] stated that 87% from1226 cases were females and 13% of them were males. Also, Gui et al. [20] included that the prevalence of SLE in men (9.1%) and in women (90.9%). Another work done by Borrelli et al. [21] demonstrated that the majority of the cases were females who represented 89.9% compared to males who represented 10%.

Our study showed a mean disease duration of 8.13 years and a median of 5.0 years, with a wide range of disease duration (0.42 to 43 years). The vast majority of patients (70.0%) have mouth ulcers and malar rash. Arthritis affects all patients (100.0%). Nephritis was seen in 66.7% of patients, with the majority being grade IV (40.0%) and hematuria (3.3%). Other clinical symptoms include alopecia, cutaneous rash, skin rash represented by (13.3%),(16.7%),(30%) respectively. In approval with our study, Elera-Fitzcarrald et al. [22] who reported that the disease duration was 7.3 years. Also a study by Mendoza-Pinto et al. [23] found that the average disease duration was 6 years, Another study by El-Badawy et al. [24] found that the average disease duration was 10.9 years. Wen et al. [25] reported that malar rash affect 76% of patients with SLE. Lu et al. [26] found that 54.4% of SLE patients had lupus nephritis.

Also in the current study, the mean ESR level was 51.0 mm/h and a mean CRP level was (11.50 mg/L). The normal levels of ESR and CRP were present in (46.7%) while elevated levels of them were present in (53.3%) of SLE patients. This result was agreeing with the study done by Abdel Magied et al.[27] who stated that mean value of ESR is (54.2mm/h) and the mean value of CRP is (25.3mg/dl). Another study done by Littlejohn et al. [28] stated that ESR mean value was (50.7mm/h) and CRP mean value was (7.2 mg/dl). Elevated fibrinogen and acute phase proteins produced by the liver during inflammation leads to increase RBCs aggregation and elevated ESR levels. Also SLE patients have increased immunoglobulins which enhances rouleaux formation of RBCs . High CRP level because of severe inflammation as pleuritis, synovitis and also due to tissue damage and necrosis.

In our study, 66.7% of SLE patients had decreased amount of complement protein C3 and 60% of them showed decreased levels of C4, while all controls have normal values. This was agreeing with a study done by Ceasovschih et al. [29] who stated that C3 and C4 were lower in 62% of cases. Also, Ambrose et al.[30] stated that there was drop in C3and C4 in (62%) of patients with SLE. Another study done by Lu et al. [26] stated that (82%) of cases had low level of C3 and C4. Chedid et al. [31] reported that there was low levels of C3and C4 in (88%) of SLE patients. Also, Wen et al. [25] reported that there was decreased C3 in (69.3%), decreased C4 in (58.2%) in SLE patients.

In SLE levels of complement decrease because it is included in the antibody defense mechanisms in the tissues ,there is consumption of C3 and C4 in activation of classical and lectin pathways which associated with increased disease activity and with the flares.[32]

ANA and anti-dsDNA antibodies were positive in all SLE patients, whereas the control group were negative. This result was consistent with another study done by Al-Mughales [33] and Wang et al. [34] and Ajasllari et al.[35] who reported that Anti dsDNA was positive for all 495 (100%) cases. Also, Abdel-Magied et al. [27]stated that Anti dsDNA was positive in all SLE patients. Another study done by El sayed [36] who reported that Anti ds DNA were positive in 87.5% of patients, ANA were positive in 97.5% of all cases.

Most cases of SLE have positive Anti ds DNA that is because SLE disease involves loss of the self tolerance to the body antigens specially nuclear antigens released from dying cells. The combination of genetic predisposition with the over active immune response and failure to clear nuclear material from dead cells create a viscous circle where self DNA act as immunogen leading to widespread production of ANA , Anti ds DNA antibodies.

In the current study the average of NEAT1 gene expression level was considerably higher in the SLE group with a mean of (6.49), whereas in the control group was (3.57), with a p-value of 0.010 suggesting a statistically significant difference. A study done by Jiang et al. [37] who mentioned that LncRNA NEAT1

expression in SLE group (97 cases) was crucially more elevated than the control group (50 healthy people) with (p- value <0.05). Also Li et al.[38] reported that the expression of LncRNA NEAT1 in cases with SLE (75 cases) was more elevated than in healthy control (40 people) with p=0.006. Also Xiang et al.[39] reported that the NEAT1 expression levels were remarkably elevated in monocyte and dendritic cells of SLE patients compared to healthy controls (p<0.01). Another study done by Zhang et al.[10] who reported that NEAT1 expression in PBMCs was significantly higher in patients than control. This could be due to that NEAT1 acts as a competing endogenous RNA(ceRNA), effectively binding to microRNAs such as miR-365a-3p.This prevents the microRNA from performing its normal function of inhibiting the expression of target genes like interleukin6.The resulting high levels of IL6 promote inflammation and B cell differentiation into autoantibody producing plasma cells. Also high NEAT1 expression enhance secretion and production of B cell activating factor (BAFF), this enhance abnormal secretion of the INF-1 signaling pathways in B cells which is the key driver of the IFN signature which is linked to autoantibody production and disease progression.

In the current study NEAT1 gene expression levels displayed remarkable positive corresponding with ESR (p less than 0.001), also there were significant associations between higher NEAT1 expression and low C3 and C4 levels (p <0.001). A study was performed by Li et al. [38] who found that there was significant association between higher NEAT1 expression with elevated ESR (p=0.001), low C3and low C4 (p=0.037).

In our study the association between NEAT1 gene expression levels and SLEDAI scores showed that individuals with very severe disease activity had the highest NEAT1 expression, whereas those with moderate activity had the lowest level with (p-value less than 0.001) which indicated that there was crucial relationship between higher NEAT1 expression and worse disease activity, as evaluated by SLEDAI score. This result was in agreement with another study conducted by Li et al. [38] and Xiang et al.[39] who reported that there was significant relation between expression of LncRNA NEAT1 and disease activity (p<0.001), (p=0.04), respectively. This is because NEAT1 phosphorylates C-Jun N- terminal kinases (JNK) and Extra- cellular Signal regulated- kinases (ERK), thus activating these proteins and enhancing the expression of interleukin 6 (IL-6), C-C motif ligand 2 (CCL2) and CXC motif chemokine ligand 10 (CXCL10), leading to secretion of IFN-γ which promotes B cell class switching and stimulates pathogenic autoantibody production. Levels of IFN-γ are elevated in patients with SLE compared to controls and positively correlate with SLE disease activity index (SLEDAI) scores .

Our study demonstrated that NEAT1 levels were correlated significantly with anti-dsDNA titers, with the highest median level in the 1/1280 group and the lowest level in the 1/160 group, with p-value less than 0.001.

According to our study the validity assessment of NEAT1 gene expression levels in differentiating SLE patients from the control group revealed an AUC of 0.717, showing modest discriminatory capacity. A p-value of (0.010) provided that this result was statistically crucial. The ideal threshold for NEAT1 expression was >0.624, displaying 83.33% sensitivity and 70.0% specificity. Similarly, Li et al. [38] showed that an AUC of NEAT1 was 0.633, displaying sensitivity 62.2% and specificity of 92.5% with P value=0.024. Mohammed et al.[40] stated that NEAT 1 had an area under curve of 0.692 with sensitivity 69.2% and specificity of 100%.

Limitations: This study was limited by being performed at a single center and by its moderately small size of sample, which may reduce applicability of the results to many population and reduce the accuracy of the estimated effects. The case–control design didn't establish temporal or causal relationships, and NEAT1 was assessed at a single time point without longitudinal follow-up to evaluate changes preceding flares or treatment response.

CONCLUSION

NEAT1 plays a major role in the pathogenesis of SLE, disease activity and severity. NEAT1 turns out to be an important marker with good sensitivity. Measurement of NEAT1 level helps in guiding a prompt diagnosis and treatment of SLE.

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