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Evaluation of depression and general health assessment among systemic lupus erythematosus patients in relation to disease activity and damage

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Abstract

Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune illness defined by involvement of several systems and a variety of clinical symptoms among them the neuropsychiatric manifestations. The purpose of the study was to evaluate the presence of depression and to assess overall health in individuals with SLE, as well as their relation to SLE disease activity and damage. Sixty adult SLE patients were enrolled, along with sixty age and sex-matched controls. For the presence of major depression, all patients were examined using the Beck Depression Inventory (BDI-II) and the General Health Questionnaire (GHQ-12) for mental distress. Antinuclear antibody, anti-ds DNA, complements 3 and 4, and anti-ribosomal P antibody were performed for SLE patients. The SLEDAI-2 K and SLEDDI were assessed.

Results: The 60 patients were 52 (86.7%) females and 8 (13.3%) men, with a mean age of 32.5 ± 11.5 years and disease duration of 3.57 ± 3.55 years. Patients with depression accounted for 43 (71.6%) of the total, whereas controls accounted for just 14 (23.3%). Patients with substantial depression had significantly higher SLEDAI-2 K, SLEDDI, and illness duration than those without major depression ($p = 0.047$, $p = 0.043$, and $p = 0.033$, respectively). The patients' mean GHQ-12 score was 17 ± 5.96 , whereas the control group's was 10.0 ± 6.30 , with a p value of 0.002. SLEDAI-2 K, SLEDDI, and depression score had a substantial positive association ($p = 0.001$, $p = 0.042$), while BDI-II and GHQ-12 had a significant positive correlation ($p = 0.001$).

Conclusions: Depression and psychological distress were both common in SLE patients. Depression severity was linked to illness duration, activity, and damage.

Keywords: Depression, Systemic lupus erythematosus, SLEDAI-2 K, General health

Background

Systemic lupus erythematosus (SLE) is a chronic autoimmune illness defined by involvement of several systems with variety of clinical manifestations as a result of autoantibody production and immune complex

deposition. During their reproductive years, females are nine times more likely than males to be afflicted [1].

In patients with SLE, neuropsychiatric SLE (NPSLE) refers to a diverse range of neurological and psychiatric symptoms caused by involvement of the central, peripheral, and autonomic nervous systems [2, 3]. Seizures, mood disorder, psychosis, headache, neuropathy, and stroke were among the neuropsychiatric symptoms of SLE documented in Egyptian patients [4]. Cognitive impairment was also discovered to be a common symptom in SLE Egyptian patients [5].

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Prevalence, initiation time, complexity, resolution rates, and recurrence of neuropsychiatric episodes vary [6]. The majority of the events are linked to a decrease in self-reported health-related quality of life [7]. In a recent research of Egyptian SLE patients, quality of life was shown to be severely impaired, particularly in those who were obese [8].

Mood disorders, particularly depression, are common in SLE patients and are important neuropsychiatric manifestations of the illness, in addition to their high incidence and possible deleterious influence on disease progression [9].

SLE depression is complex, with neurotransmitter dysfunction and immunological activation (lymphocyte abnormalities and cytokine production) being two possible causes [10, 11]. Depression exacerbates pain, tiredness, psychological stress, and reduces treatment adherence in SLE patients, resulting in a considerable worsening in quality of life and job disability [12, 13].

The goal of this study was to evaluate the occurrence of depression and its contributing factors, as well as overall health assessment in patients with SLE, and to determine their relation with disease activity and damage.

Methods

Sixty adult SLE patients who met the 2012 Systemic Lupus International Collaborating Clinics (SLICC) criteria were included in this research [14]. Patients were recruited from the Rheumatology Unit of Alexandria University Hospital's Internal Medicine Department. As controls, sixty healthy adults were enlisted who were age and sex matched to the patients. Exclusion criteria included patients with history of depression prior to the onset of SLE, uncooperative patients, antiphospholipid syndrome, other autoimmune rheumatic diseases, and pregnant lupus patients. After receiving clearance from the institutional ethics committee, the study was carried out in accordance with the Declaration of Helsinki's ethical criteria, and each subject gave their informed consent.

Age, gender, domicile, marital status, educational level, and work status of the participants were all taken into account. All SLE patients had a history taking, a clinical examination, and a disease activity evaluation using the SLE disease activity index (SLEDAI-2k) [15], with scores ranging from "inactive" (scores ≤ 4) to mild-moderate (5–9) to high (≥ 10). The Systemic Lupus Collaborating Clinics/ACR damage index (SLICC/ACR DI) was also used to quantify disease damage [16].

Complete blood count, creatinine, urinary protein to creatinine ratio (PCR), alanine transaminase, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) were performed.

Serological tests included antinuclear antibodies (ANA), anti-double-stranded DNA (anti-ds DNA), anti-ribosomal-p antibody, and complement C3 and C4 were among the laboratory tests performed for the patients.

The Beck Depression Inventory Score (BDI-II) was applied to assess the presence of depression in the patients and control group, and we used the Arabic version (Additional file 1), which is one of the most extensively used tools for measuring depression symptoms and severity [17]. It has 13 items, each of which is assessed on a four-point Likert scale ranging from 0 (not likely to happen) to 3 (always or mostly happen). The total number of components in the patient's score ranges from 0 to 39. There are four levels of depression: no depression (0 to 4), mild cases (5 to 7), moderate instances (8 to 15), and severe cases (≥ 16).

The General Health Questionnaire-12 (GHQ-12) [18] was used to conduct psychometric testing for general health and psychological distress. The GHQ-12 is a 12-item questionnaire with a score range of 1 to 36, with mild cases falling between (1 to 12), moderate cases (13 to 24), and severe cases (25 to 36).

Statistical analysis

IBM-SPSS statistical program version 22 was used to analyze the data. The Mann-Whitney or Student *t*-test was used to analyze continuous data, while the chi-square test was employed to assess categorical ones. The Spearman coefficient was used to determine the correlation between quantitative variables. Logistic regression analysis was used to determine risk factor for presence of depression among SLE patients. The significance of the acquired results was assessed at a 5% level. The *p* value of 0.05 was used to determine statistical significance.

Results

The 60 patients had a mean age of 32.5 ± 11.5 years and illness duration of 3.57 ± 3.55 years, with 52 (86.7%) females and 8 (13.3%) men (F to M 6.5:1). Table 1 shows the socio-demographic characteristics of SLE patients and controls. Table 2 shows the patients' clinical features and immunological profiles. In terms of SLE disease activity, 11 patients had inactive disease, 32 patients had mild-moderate disease activity, and 17 patients had high disease activity.

The neuropsychiatric manifestations were observed in 15 patients (25%) and included seizures 3 patients (20%), cranial neuropathy 2 patients (13.4%), psychosis 3 patients (20%), cognitive dysfunction 4 patients (26.6%), headache 3 patients (20%), and peripheral neuropathy 2 patients (13.4%).

The medications that were used by the patients included the following: hydroxychloroquine 52 patients

Table 1 Sociodemographic data of SLE patients and the control group

	Group I SLE patients		Group II Control		<i>p</i>
Age					
Range	15–55		16–65		0.236
Mean	32.56		34.63		
S.D.	11.51		12.12		
Sex					
Male	8	13.3	16	26.7	0.101
Female	52	86.7	44	73.3	
Residence					
Rural	24	40.0	26	43.3	0.39
Urban	36	60.0	34	56.7	
Education					
Not educated	8	13.3	3	5.0	0.107
Read and write	22	36.7	8	13.3	
Preparatory	6	10.0	6	10.0	
Secondary	14	23.3	21	35.0	
University	10	16.7	22	36.7	
Marital status					
Single	16	26.7	12	20.0	0.256
Married	33	55.0	37	61.6	
Divorced	7	11.6	5	8.4	
Widow	4	6.7	6	10.0	
Occupation					
Unemployed	39	65.0	32	53.3	0.09
Employed	21	35.0	28	46.7	
Socioeconomic status					
High	2	3.4	8	13.3	0.211
Moderate	8	13.3	39	65.0	
Low	28	46.6	6	10.0	
Very low	22	36.7	7	11.7	

(86.6%), glucocorticoids 48 patients (80%), azathioprine 21 (35%), mycophenolate mofetil 9 patients (15%), cyclophosphamide 12 patients (20%), methotrexate 5 patients (8.4%), and cyclosporin 4 patients (6.7%).

According to the BDI-II, 43 (71.6%) of patients experienced depression, with a mean score of 14.94 ± 7.3 , whereas 14 (23.3%) of the control group's had depression, with mean score of 7.1 ± 3.62 (Fig. 1), with a *p* value of 0.0019.

The SLE patients with depression were classified as following: 17 patients with high disease activity (10 patients in severe depression, 5 patients in moderate depression and 2 patients in mild depression), while 24 patients with mild-moderate activity (2 patients in severe depression, 12 patients in moderate depression and 10 patients in mild depression) and 2 patients were

Table 2 Clinical characteristics, immune profile, and disease activity of systemic lupus erythematosus patients

Parameter	SLE patients (<i>n</i> = 60)	
	No.	%
Clinical		
Mucocutaneous	31	51.7
Musculoskeletal	28	46.7
Hematological	16	26.7
Renal	24	40.0
Neuropsychiatric	15	25.0
Cardiovascular	9	15.0
Respiratory	13	21.6
Immune profile		
ANA	Mean \pm SD	
Anti-ds DNA	179.74 \pm 191.36	
C3	269.47 \pm 229.35	
C4	54.57 \pm 26.15	
Anti-ribosomal p antibody	12.64 \pm 8.91	
SLEDAI-2K	46.48 \pm 74.76	
SLEDAI-2K		
	Mean \pm SD	
	16.9 \pm 9	
SLICC/ACR DI		
	Mean \pm SD	
	3.17 \pm 1.3	

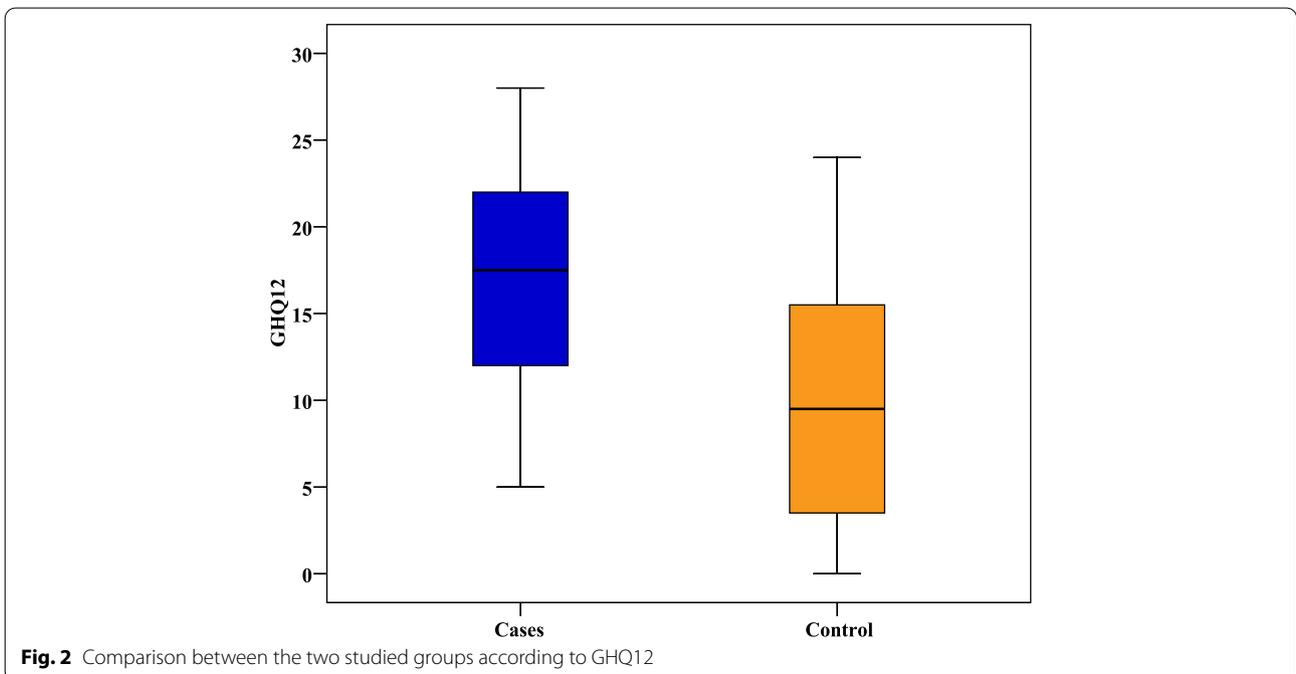
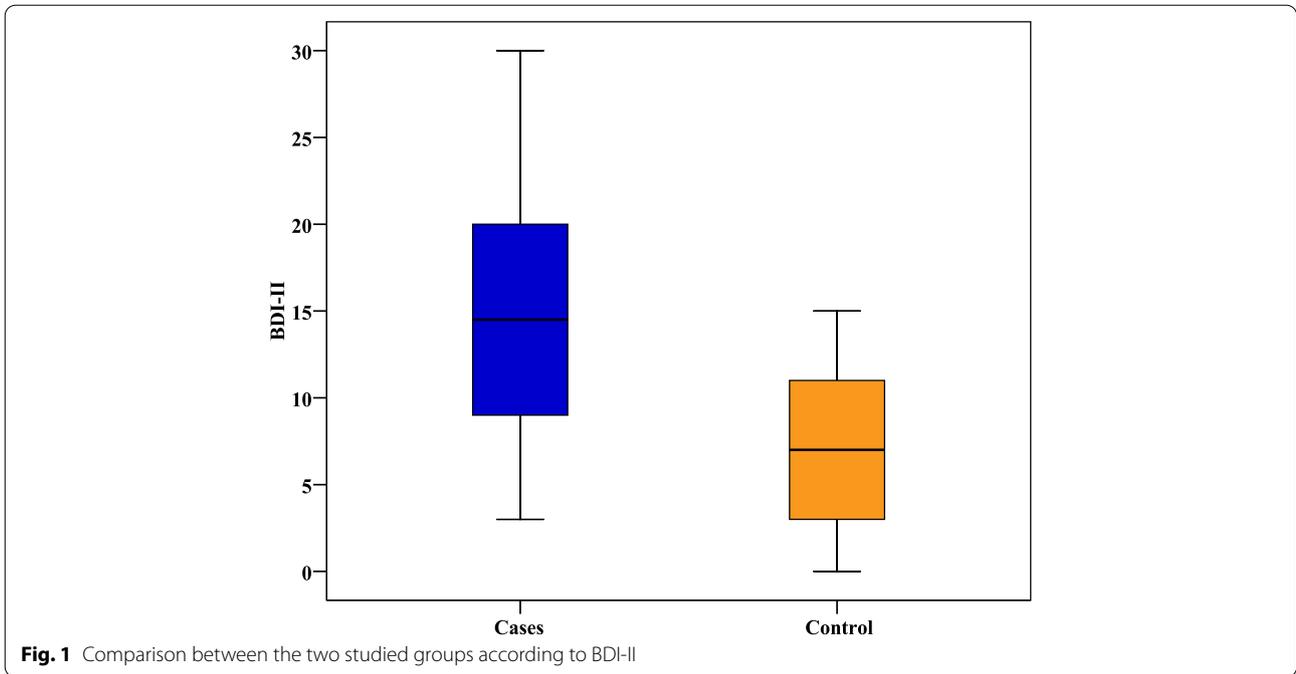
inactive disease had mild depression. Based on the degree of their depression, the patients were separated into three groups: there were 14 individuals with mild depression, 17 with moderate depression, and 12 with severe depression. In addition, there was a substantial distinction between the two groups as regard GHQ-12 with *p* value = 0.0021 (Fig. 2).

The sociodemographic status of SLE patients with and without depression did not differ substantially, although they did differ considerably in terms of illness duration, SLEDAI-2K, and SLEDDI (*p* = 0.033, *p* = 0.047, and *p* = 0.043, respectively).

SLEDAI-2K had a substantial positive connection with BDI-II and GHQ-12 scores (*p* 0.001, *p* 0.001), as shown in Fig. 3. SLEDDI was also shown to be associated with depression score (*p* = 0.042) and GHQ-12 severity (*p* = 0.026). Furthermore, there was a significant positive connection between the BDI-II and GHQ-12 (*p* < 0.001).

Anti-ribosomal P antibody testing was positive in 23.3% of SLE patients in this investigation, with a mean titer of 46.48 U/ml. Furthermore, there was a high statistical correlation between anti-ribosomal P antibody and depression score (*p* = 0.0472), as well as SLEDAI-2K (*p* = 0.001).

Multivariate regression analysis was done to determine the predictors of depression in SLE patients. We found that disease activity, damage, and disease duration were significant predictors for depression (Table 3).



Discussion

SLE has a significant influence on people’s quality of life, posing several obstacles, particularly for young people who are frequently impacted. Involvement of the central nervous system (CNS) in SLE is linked to a variety of neurological and psychiatric symptoms and is one of the leading causes of morbidity and disability [19, 20].

The majority of the SLE patients in this study reported significant depressive symptoms. According to the BDI-II score, 43/60 (71.6%) of the patients had depression, while only 14/60 (23.3%) of the control group had depression. This is consistent with Raafat et al. [21], who found that 64% of their study patients had depression, while Stoll et al. [22] found that the prevalence of depression

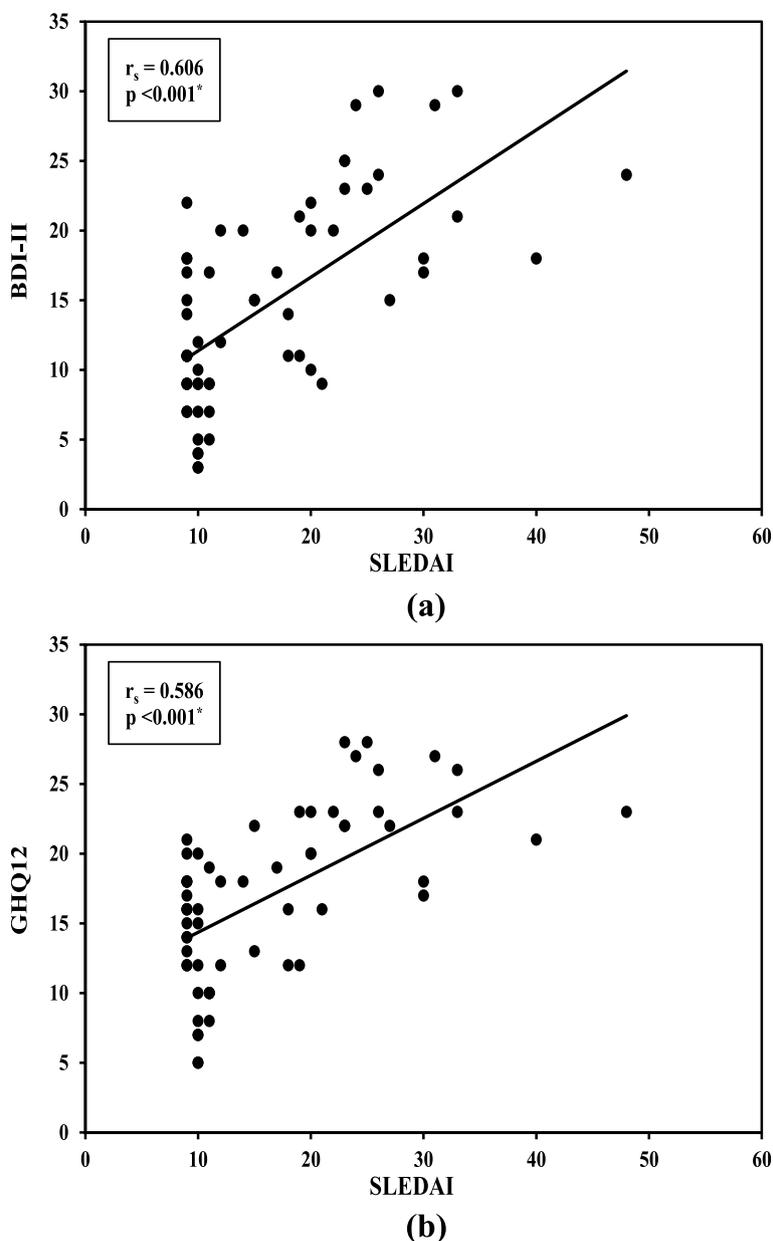


Fig. 3 a Correlation between SLEDAI-2K with BDI-II in SLE patients ($n = 60$). b Correlation between SLEDAI-2K with GHQ12 in SLE patients ($n = 60$)

was as low as 16%. Our sample had a larger proportion of patients with depression than previous research, which might be related to different methodology, different evaluation tools, patient samples, sample sizes, and different social and economic factors and cultural backgrounds.

GHQ-12 has become one of the most commonly used tools for detecting psychological distress. It carries advantage when compared to other version like GHQ-28, being brief, easily scored. In addition to level of

symptoms present (Likert type scoring). It is composed of positive and negative phrased items that cover the multiple dimension of mental health including social dysfunction, anxiety, depression, and loss of confidence [23].

Patients with depression had a higher SLEDAI-2K score than those without, and there was a strong positive connection between SLEDAI-2K score and depression severity. These findings back up the theory that disease activity may be a risk factor for the

Table 3 Multiple logistic regression analysis of different risk factors affecting depression

Model	Unstandardized Coefficients		Standardized Coefficients	Test	
	B	Std. error	Beta	t	p-value
(Constant)	4.239	0.748		5.666	0.000
Age	-0.003	0.012	-0.058	-0.264	0.794
Sex	-0.083	0.337	-0.047	-0.247	0.807
Disease duration	0.022	0.037	0.126	-2.591	0.046*
SLEDAI score	0.023	0.020	0.219	3.104	0.028*
SLEDDI score	0.401	0.173	0.406	2.580	0.0433*

**p* value ≤ 0.05 statistical significance

presence and severity of depression in SLE patients. This was in line with the findings of Zakeri et al. [24], who found that 60% of patients reported depression, with the severity of depression being related to disease activity. Nery et al. [25] likewise came up with similar results.

Patients with higher disease activity are more likely to experience impairments in daily living activities, which can contribute to depression and a deterioration in health-related quality of life (HRQOL) [26]. This might be explained by the two-dimensional association between chronic illness activity influences emotional condition, or by the fact that depression induces more disease activity, as documented by Beckerman et al. [27].

Anti-ribosomal P antibody testing was positive in 23.3% of the patients in this research, and there was a significant correlation with depression score ($p = 0.0472$). This is in line with the findings of Arnett et al. [28], who discovered strong links between lupus psychosis and depression and serum anti-ribosomal P antibodies. Furthermore, Reichlin et al. [29] and Schneebaum et al. [30] have verified the anti-ribosomal P antibody's capacity to distinguish people who have nervous system involvement owing to SLE illness from those who have it as a consequence of therapy or merely as an associated condition.

Disease activity, damage, and disease duration were all found to be predictors of depression in SLE patients in regression analysis. Higher disease activity at baseline was predictive of depression, psychosis, and cognitive impairment, according to Mikdashi et al. [31]. Stoll et al. [22] also showed a high total SLICC/ACR DI score during the first years of disease is a strong predictor of depression and other neuropsychiatric manifestations.

Conclusions

Depression is quite common among SLE patients. Disease activity, damage, and disease duration were all found to be predictive of the occurrence and severity of depression. Anti-ribosomal P antibody was found to be positive in considerable number of patients with a significant correlation with depression score. The early identification and treatment of depression may have a significant influence on the patient's quality of life.

Abbreviations

ANA: Antinuclear antibodies; anti-ds DNA: Anti-double-stranded DNA; BDI-II: Beck Depression Inventory; CNS: Central nervous system; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; GHQ-12: General Health Questionnaire; HRQOL: Health-related quality of life; NPSLE: Neuropsychiatric SLE; PCR: Protein to creatinine ratio; SLE: Systemic lupus erythematosus; SLEDAI-2k: SLE disease activity index; SLICC/ACR DI: Systemic Lupus Collaborating Clinics/ACR damage index; SLICC: Systemic Lupus International Collaborating Clinics; SLEDDI: Systemic lupus erythematosus disease damage index.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s43166-022-00113-5>.

Additional file 1.

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Authors' contributions

Ahmed Shaaban: software, writing original draft. Manal Tayel: supervision, conceptualization. Eman Hassan: conceptualization, methodology. Medhat Salah: methodology, resources. Mohamed Ibrahim: investigations. Walaa Saide: software, investigations. The author(s) read and approved the final manuscript.

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Availability of data and materials

Data is available from Ahmed Shaaban (corresponding author).

Declarations

Ethics approval and consent to participate

After receiving clearance from the institutional ethics committee, the study was carried out in accordance with the Declaration of Helsinki's ethical criteria, and each subject gave written informed consent.

Consent for publication

All authors revised the manuscript and approved the publication.

Competing interests

The authors declare that they have no competing interests.

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