

Review Article

# Systemic Lupus Erythematosus and Depression Overview

Ahmed Shaaban<sup>1\*</sup>, Nourelhouda Said<sup>2</sup> and Hoda Afifi<sup>3</sup>

<sup>1</sup>Associate Professor of Internal Medicine, Rheumatology & Immunology Division, Faculty of Medicine, Alexandria University, Egypt

<sup>2</sup>Internal Medicine and Rheumatology Consultant, MD (PhD), Faculty of Medicine, Alexandria University, Egypt

<sup>3</sup>Lecturer of Internal medicine, MD (PhD), Faculty of medicine, Ain Shams University, Egypt

## Abstract

Systemic lupus erythematosus (SLE) is a chronic inflammatory multisystem disorder that commonly affects females during their reproductive years. It is characterized by the presence of autoantibodies and immune complex deposition, the etiology is not known but the interaction of an environmental agent in a genetically susceptible individual is thought to be fundamental. SLE most frequently involves the skin, joints, lungs, heart, kidney, and neuropsychiatric manifestations that may occur during the course of the disease. Mood disorders among SLE patients, particularly depression, are common and important psychiatric manifestations of the disease, in addition to their high incidence and possible deleterious influence on disease progression, so early identification and treatment of depression may have a significant influence on the patient's quality of life.

## Introduction

Systemic lupus erythematosus (SLE) is a chronic multisystem autoimmune disease that affects many organs with a variety of clinical manifestations due to the production of autoantibodies and deposition of the immune complex. The course of the disease is unpredictable, with periods of disease activity alternating with remissions [1]. Women of childbearing age are more commonly affected than men with a ratio of 9: of 1.

SLE is characterized by widespread inflammation with the generation of autoantibodies. Despite the specific etiology of SLE is unknown, there are many factors that are associated with the disease development, including genetic, epigenetic, environmental, and hormonal factors. As well immune disturbances affecting both innate and acquired immune systems, occur in SLE [2].

The SLE patients may present with different manifestations. The general symptoms include fatigue, fever, headache, malaise, arthralgias, and myalgias, in addition to organ-specific manifestations including; skin, kidney, lung, and heart as well as neuropsychiatric syndromes.

The neuropsychiatric manifestation of SLE (NPSLE) is considered one of the major and most serious presentations. It includes a wide spectrum of neurological syndromes affecting all parts of the nervous system (central, peripheral,

and autonomic nervous systems), as well as psychiatric syndromes [3].

Mood disorders among SLE patients, particularly depression, are common and important psychiatric manifestations of the disease, in addition to their high incidence and possible deleterious influence on disease progression [4].

## Prevalence of depression in SLE

There is a dual relationship between depression and chronic diseases. The biological changes and complications of chronic diseases may precipitate episodes of depression. On the other hand, the psychobiological changes and adverse health risk behaviors associated with depression might increase the risk for chronic medical conditions.

Comorbid depression has deleterious effects such as increased burden of medical symptoms, functional limitation, medical costs, and poor adherence to the regimens, in addition to increased risk of morbidity and mortality among patients with chronic medical disorders. Depression may worsen the course of the disease due to its effect on proinflammatory factors, metabolic factors, autonomic nervous system, and hypothalamic-pituitary axis in addition to its association with a higher risk of obesity, smoking, sedentary lifestyle, and poor adherence to mediations [5].

Depression is common among SLE patients, just like depression is common in all chronic illnesses. It is common

## More Information

### \*Address for correspondence:

Ahmed Shaaban, Associate Professor of Internal Medicine, Rheumatology & Immunology Division, Faculty of Medicine, Alexandria University, Egypt, Email: ahmedabourayba@yahoo.com

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in the general population as well. About 10% of the general population will become depressed, in any given year [6].

Recent evidence suggests that the prevalence of depression in SLE patients is between 11.5% and 47% in a cross-sectional study that examined 150 persons with SLE done by the American College of Rheumatology in 2011 [6].

Also Shaaban, et al. [7] in their study of Egyptian SLE patients in 2022, found that the prevalence of depression was (71.6%), while Stoll, et al. [8], found that the prevalence of depression was as low as 16%. These different results might be related to different methodologies, patient sample sizes, different evaluation tools, and different social and economic factors and cultural backgrounds.

The higher prevalence of depression in patients with (SLE) may be due to the psychosocial impact of this chronic disease as well as from central nervous system (CNS) lesions [6].

### Etiology and risk factors of depression in SLE

Depression among SLE patients can be related to physical or psychological reactions to lupus or its medications or maybe a combination of these factors, or the depression can be independent.

Psychosocial factors have been considered the most frequent possible cause of depression in SLE, including environmental factors, and psychological reactions to both SLE disease and social stress [9]. Major depression in active lupus is a CNS manifestation related to the disease, mediated by an autoimmune mechanism, principally anti-ribosomal P antibodies have been identified as potentially involved in the pathogenesis of NPSLE in some studies. Other autoantibody specificities have been examined, such as antineuronal and antiphospholipid antibodies [10].

### Pathophysiology of depression in SLE

The evidence in the literature refers to the participation of neurophysiological and biochemical changes, induced by cytokines, in the occurrence of neuropsychiatric manifestations. Through activation of the enzyme indoleamine 2,3-dioxygenase (IDO), the change of neurotransmitters' bioavailability, and the overstimulation of certain neural circuits, inflammatory cytokines might cause mood swings and depression [11].

In addition to the immune deregulation that occurs in SLE, the Hypothalamic-Pituitary-Adrenal (HPA) axis dysfunction correlates with neuronal and physiological changes involved in depression. Moreover, autoantibodies that are present in the cerebrospinal fluid, such as anti-ribosomal P, can cause significant damage to neurons in specific areas of the brain which are related to humor and behavior, subsequently leading to the occurrence of depression. On the other hand, limbic system lesions present in SLE patients, although their etiology

is unclear, suggest impairment of cerebral achievement in behavioral and emotional functions. Recently, depression in SLE has a biological basis which has been confirmed, under the influence of multiple factors [12].

There are few studies that used brain magnetic resonance imaging (MRI) in depressed SLE patients, no correlation between depression and brain abnormalities has been found with brain MRI, while, on the contrary, SPECT analysis showed that SLE patients with depression present cerebral blood flow reductions in discrete frontal and temporal areas that may account for symptoms of depression. Further research is highly needed in this field. To date, the research in this area is scarce [12].

### Relation of depression to disease activity

Despite increasing awareness of psychiatric manifestations among physicians and other healthcare professionals, little research explores the different aspects of depression among SLE. Lupus patients with neuropsychiatric syndromes encounter a relapsing and remitting course of the disease and the side effects from several medications might deteriorate their quality of life and precipitate depression. In addition, the burden of lupus associated with depression may increase the suicidal risk [13].

In a recent study, there was a significant correlation between socioeconomic status including (work status, income, marital status, and level of education) and anxiety/depression in SLE patients. Also, gender and menstrual history were considered some risk factors for depression. In addition, there was a significant positive correlation between anxiety/depression severity and disease activity score [14]. Previous studies have shown that impaired quality of life and functional limitation were independent risk factors of psychological diseases [15,16].

Depression is highly prevalent in SLE and there is a significant risk of suicide among lupus patients with psychiatric syndromes, comprehensive assessment is mandatory to provide proper diagnosis and adequate care should be an essential part of SLE patients' evaluation protocol, and globally accepted and validated assessment tools should be established and translated into clinical practice, as well as widely experienced therapeutic regimens. In addition, a high priority should be given to the identification of SLE-specific biomarkers of depression [4].

### Manifestations of depression in SLE

The commonest manifestations of depression reported in SLE are fatigue and weakness (88.2%) which might be closely related to the main symptoms of SLE. Also, irritability (82.3%), sadness (77.6%), somatic preoccupation (76%), and trouble falling asleep (70%) were frequently encountered. Among the previous studies that were initially identified, only two evaluated the prevalence of suicide ideation and found

that prevalence rates ranged from 10% to 34%, which is much higher when compared to the general population [17].

Future studies are needed to clarify the commonest manifestations of depression and identify the most common subtype of depressive symptoms in SLE as well as methodological guidelines to address this aspect. Few studies and methodological limitations are present in the current literature and a definitive subset of depressive symptoms is difficult to determine [17].

## Prevention of depression in SLE

### Primary prevention [18]

- Early detection and diagnosis of SLE.
- Awareness of doctors, and nurses dealing with SLE about psychiatric disorders and psychological problems of SLE including depression (e.g., lectures, pamphlets, workshops, and videos).
- Screening for depression, those with mild, moderate, and severe depression are to be referred to a psychologist or psychiatrist for reassessment.
- Supportive therapy to those who did not develop major depressive disorder but are at high risk (with few symptoms of depression) by trained doctors and specialized nurses.
- Regular monitoring of those at high risk of depression every 1-3 months [18].

### Secondary prevention [19]

Treatment options available include lifestyle changes, therapy, and medications.

## Pharmacological treatment

**Selective Serotonin Reuptake Inhibitor (SSRI's):** SSRIs are currently the most common group of medications used to treat depression. All the SSRIs are very similar in their treatment efficacy. They take several weeks to start their actions and have relatively mild adverse events such as gastrointestinal upsets and minimal weight gain. Overall, the SSRIs are safe, so they are commonly prescribed [19].

**Serotonin-Norepinephrine Reuptake Inhibitor (SNRI's):** SNRIs have the added benefit of treating pain. These drugs essentially have "double duty" and may help to alleviate feelings of depression as well. These medications may be difficult to withdraw from, however, and it must be done slowly. One of the adverse effects of both SSRIs and SNRIs is sexual dysfunction [19].

## Nonpharmacological treatment

**Cognitive Behavioral Therapy (CBT):** CBT is a focused short-term psychotherapy during which a therapist works

with the patient on examining his behavior patterns and current negative thoughts. It is based on the understanding that patient thinking plays a vital role in how he feels and what he does. The therapy sessions are structured and within a set length of time, in addition, the therapist will often assign homework. CBT is considered an active therapy as it requires the patient to work on issues between sessions. It has been shown to be effective with SLE patients and it is a good therapeutic option for people who are more solution-focused [20].

## Psychodynamic therapy

This is a type of therapy where the patient explores his feelings, attitudes, and early life experiences and how these have influenced his current relationships, attitudes, and feelings. The duration of therapy can range from a few months up to a longer time. This is a good match for a person who is more self-exploratory [20].

## Interpersonal therapy

Interpersonal therapy is a short-term intervention that emphasizes the interpersonal context as well as building interpersonal skills. It is not performed alone, rather it is integrated into CBT or psychodynamic therapy. While depression is not caused by interpersonal stressors, depression can be made worse by interpersonal conflict, and this type of therapy works to improve this domain [20].

## Mindfulness-based therapies

This type of therapy consists of talk therapy and the practice of meditation. It is a structured 8-10 week course in a group that involves talking, meditation, and body scanning, in addition to homework assignments. The focus of the therapy is on alleviating pain and improving physical and mental well-being [20].

## Combined treatment

Combination of both pharmacological and non-pharmacological treatment.

### Tertiary prevention [21]

- Reducing the long-term effects of SLE (damage and complications) by focusing on mental, physical, and social rehabilitation and treatment of complications.
- Improve quality of life by preventing complications in the future.
- Restoring the health and functions of patients affected by disease complications (restoring normal daily functions as much as possible).
- Maximize the remaining capabilities and functions of disabled patient [21].



## Conclusion

SLE is a chronic autoimmune disorder defined by the involvement of multiple systems and a variety of clinical symptoms among them the neuropsychiatric manifestations. Depression is quite common among SLE patients, with neurotransmitter dysfunction and immunological activation being two possible causes. Depression exacerbates pain, tiredness, and psychological stress, and reduces treatment adherence in SLE patients, so early identification and treatment of depression may have a significant influence on the patient's quality of life.

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