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Systemic Lupus erythematosus - An autoimmune disorder in comparison with unani medicine - A review

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Abstract

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disorder characterized by widespread inflammation and multi-organ involvement, driven by immune system dysregulation. It presents with a wide spectrum of clinical manifestations, including joint pain, skin rashes, fatigue, and renal dysfunction, which vary in severity among patients. The pathogenesis of SLE involves a complex interplay of genetic, epigenetic, and environmental factors, such as sunlight exposure, infections, and certain drugs, which trigger autoimmune responses. Modern medical research has identified key genetic contributors, including variants in HLA, IRF5, and STAT4 genes, alongside complement system deficiencies, which underline the disorder's complex etiology. While advancements in biomedical science have enhanced diagnostic and therapeutic strategies for SLE, its multifaceted nature continues to challenge effective management.

Unani medicine, a holistic healthcare system with Greco-Arabic roots, provides an alternative framework for understanding SLE through the lens of humoral theory and temperament (Mizaj). Unani scholars describe a condition analogous to SLE, termed "Waram-e-Mufassil," characterized by systemic inflammation, skin lesions, and joint pain. According to Unani principles, SLE results from an imbalance in Safra (Yellow bile) and Sauda (Black bile), often exacerbated by dietary, lifestyle, and environmental factors. Unani therapeutic approaches aim to restore humoral balance through dietotherapy, herbal remedies like *Withania somnifera* and *Curcuma longa*, regimental therapies such as cupping and venesection, and stress management techniques. By integrating Unani concepts with modern medical insights, this article explores the potential for a comprehensive approach to the diagnosis, management, and treatment of SLE, bridging traditional knowledge with contemporary advancements.

Keywords: Systemic lupus erythematosus, unani medicine, autoimmune diseases, humoral imbalance

Introduction

Systemic lupus erythematosus is a complex and heterogeneous autoimmune disease that can affect multiple organ systems. It is characterized by the production of autoantibodies that target a wide range of self-antigens, leading to inflammation and tissue damage. Autoimmune diseases, which comprise a broad spectrum of complicated conditions, including rheumatoid arthritis, ankylosing spondylitis, systemic lupus erythematosus, idiopathic inflammatory myopathy, systemic sclerosis, and Sjögren's syndrome, have become a major public health concern, with clinical manifestations ranging from mild skin rashes to severe multiple organ dysfunction. The pathogenesis of autoimmune diseases involves abnormal regulation of the immune system and cellular activity, and further understanding of the underlying molecular mechanisms and identification of crucial regulators in these conditions are essential for early diagnosis and effective treatment.

Unani literature has mentioned a disease condition similar to Lupus Erythematosus called "Waram-e-Mufassil," which is characterized by skin lesions, joint pains, and systemic involvement. Unani physicians have described the pathogenesis and management of this condition, which may provide valuable insights into the understanding and treatment of systemic lupus erythematosus.

Unani medicine, an ancient and holistic system of healthcare, originated from the Greco-Arabic tradition and has been practiced for centuries, particularly in South Asia, the Middle East, and parts of Europe. It is based on the principles laid down by Hippocrates, Galen, and

later refined by notable scholars such as Ibn Sina (Avicenna). The Unani system emphasizes maintaining a balance between the four humors: Dam (Blood), Balgham (Phlegm), Safra (Yellow bile), and Sauda (Black bile). Health is perceived as the equilibrium of these humors, and disease arises when this balance is disrupted.

Systemic Lupus Erythematosus (SLE) is a chronic, autoimmune inflammatory disorder that affects multiple organs. The disease presents with a wide range of symptoms, including joint pain, skin rashes, fatigue, and kidney dysfunction. Modern medicine identifies SLE as a consequence of immune system dysregulation; however, the Unani system interprets it as a result of humoral imbalance, particularly involving Balgham and Sauda.

Pathogenesis

The pathogenesis of systemic lupus erythematosus is complex and involves the interplay of genetic, epigenetic, and environmental factors. Genetic susceptibility plays a crucial role in the development of autoimmune diseases, and several genes have been associated with an increased risk of SLE. Epigenetic modifications, such as DNA methylation, histone modifications, and the regulation of long non-coding RNAs, have also been implicated in the pathogenesis of autoimmune diseases, including SLE. Environmental triggers, such as sunlight, drugs, and infections, can also contribute to the development of SLE by altering the immune system and triggering autoimmune responses.

Key genetic changes in SLE

HLA class II genes ^[21]

The Human Leukocyte Antigen (HLA) region is the most significant genetic contributor to SLE susceptibility. Variants of HLA-DR2 (HLA-DRB115:01) and HLA-DR3 (HLA-DRB103:01) are commonly associated with an increased risk of SLE. These alleles are involved in antigen presentation and influence immune tolerance.

TNFAIP3 (A20) polymorphisms ^[22]

TNFAIP3, a gene coding for a key regulator of inflammation, has polymorphisms linked to SLE. The rs2230926 polymorphism reduces the regulatory function of A20, leading to increased inflammation and autoimmunity.

IRF5 gene variants ^[23]

The IRF5 gene encodes the Interferon Regulatory Factor 5, which is involved in the type I interferon pathway. Variants like rs2004640 and rs10954213 are associated with increased interferon signaling, which is a hallmark of SLE pathology.

PTPN22 gene polymorphisms ^[24]

The PTPN22 gene, which encodes a lymphoid-specific phosphatase, regulates T-cell activation. The rs2476601 variant is associated with increased susceptibility to SLE.

BLK (B-lymphoid tyrosine kinase) variants ^[25]

Variants in BLK affect B-cell receptor signaling and have been linked to SLE. The rs13277113 polymorphism in BLK reduces expression levels of the protein, leading to altered B-cell activity.

Complement component genes (C1Q, C4A, C4B) ^[26]

Deficiencies in C1Q and deletions in C4A and C4B are strongly associated with SLE. These complement proteins

play a role in clearing immune complexes and apoptotic cells.

STAT4 gene polymorphisms ^[27]

The STAT4 gene encodes a transcription factor involved in cytokine signaling. Variants like rs7574865 increase SLE risk by enhancing T-helper 1 immune responses.

Unani concept of SLE pathophysiology

In Unani medicine, diseases are caused by an imbalance in the humors, Mizaj, environmental factors, diet, and lifestyle. Autoimmune diseases like SLE are viewed as an imbalance of Aklat arbah, leading to chronic inflammation, fatigue, and multisystem involvement.

Mizaj (Temperament) in SLE ^[5]

In Unani medicine, each individual has a distinct mizaj (temperament), which is a balance of qualities such as hot, cold, moist, and dry. In diseases like SLE, there is a disruption in an individual's temperament. Based on clinical symptoms of SLE, such as joint pain, rashes, fatigue, and inflammation, the following Mizaj changes are typically observed:

Hot and dry Mizaj: The inflammatory processes in SLE may be associated with an excessive heat and dryness imbalance (Yubusat wa Hararat).

Cold and dry Mizaj: The chronic, debilitating aspects (fatigue, joint stiffness) can indicate a disturbance towards cold and dry temperament (Burudat wa Yubusaat).

Akhlat (Humors) and SLE

The Unani system identifies four humors (Akhlat Arba'a), which are:

- Dam (Blood): Hot and moist.
- Balgham (Phlegm): Cold and moist.
- Safra (Yellow bile): Hot and dry.
- Sauda (Black bile): Cold and dry.

Dam-e-ghair tabai (Abnormal blood) ^[11]

Nature: Blood becomes excessively thick, thin, or contaminated.

Causes: Overconsumption of rich foods, lack of exercise, excessive bleeding, or improper digestion.

Diseases: Hemorrhagic conditions, skin disorders, and infections.

Balgham-e-ghair tabai (Abnormal phlegm) ^[6]

Nature: Phlegm becomes excessively cold, thick, or watery.

Causes: Excessive intake of cold and moist foods, lack of physical activity, overconsumption of dairy, and poor digestion.

Diseases: Respiratory issues, joint stiffness, lethargy, and digestive disorders.

Safra-e-ghair tabai (Abnormal yellow bile) ^[6]

Nature: Yellow bile becomes excessively hot, thin, or dry, leading to irritability.

Causes: Excess consumption of hot, spicy, and fried foods, anger, and stress.

Diseases: Jaundice, skin rashes, inflammation, and fevers.

Sauda-e-ghair tabai (Abnormal black bile) ^[10, 15]

Nature: Black bile becomes excessively cold, thick, or dry.

Causes: Excessive intake of dry, heavy, and burnt foods, stress, and chronic illnesses.

Diseases: Melancholia, joint disorders, chronic constipation, and tumors.

Causes of abnormal humors (Asbab-e-ghair tabai akhlaat)

Abnormal humors are produced due to a combination of dietary, lifestyle, environmental, and psychological factors. Some key causes include:

Dietary causes (Asbab-e-ghizaiya) ^[1]

- Consumption of foods that are not suitable for the individual's temperament (Mizaj).
- Excessive intake of processed, heavy, or spoiled foods.
- Overeating or malnutrition.

Lifestyle causes (Asbab-e-aamaliya) ^[2]

- Sedentary habits, lack of exercise, or overexertion.
- Improper sleep patterns (e.g., staying awake late at night).

Environmental causes (Asbab-e-muheetiya) ^[2]

- Exposure to extreme heat, cold, or humidity.
- Seasonal changes impacting humoral balance (e.g., summer increasing Safra).

Psychological causes (Asbab-e-nafsaniya) ^[4]

- Emotional disturbances such as anger, grief, anxiety, and stress.

Digestive causes (Asbab-e-hazmiya) ^[1]

- Weak digestion (Zo'f-e-Hazm), leading to improper formation of humors.

Types of humoral corruption ^[5]

Unani scholars classified humoral corruption into several types:

Kammiyati fasād (Quantitative corruption)

- Excess or deficiency in the quantity of humors.
- Example: Excess blood leading to hypertension.

Kaifiyati fasād (Qualitative corruption)

- Alteration in the normal quality of humors.
- Example: Excessively hot Safra causing fever.

Maqami fasād (Local corruption)

- Abnormal humors accumulating in specific organs.
- Example: Accumulated Balgham in lungs causing pneumonia.

In SLE, the imbalance of these humors plays a significant role ^[6]

Imbalance of safra (Yellow bile) ^[3]

Inflammation, skin rashes, fever, and heat-related symptoms

can be due to an excess of Safra. The dominance of Safra is associated with heat and dryness, leading to inflammatory responses.

Imbalance of sauda (Black bile) ^[3]

Joint pain, fatigue, and chronic symptoms may be due to an excess of Sauda, leading to dryness and coldness in the body.

Mixed humoral disturbance ^[3]

SLE often shows a mixed humoral imbalance involving Safra and Sauda, leading to complex symptoms affecting multiple systems.

Pathophysiology in SLE according to unani scholars ^[1]

Inflammation and heat: The chronic inflammatory nature of SLE aligns with Hiddat (heat) due to excess Safra.

Joint pain and fatigue: These symptoms reflect the predominance of Sauda, resulting in dryness and rigidity of tissues.

Clinical features of SLE in the unani context

Fever (Humma)

- Chronic low-grade fever is a common symptom in SLE.
- In Unani, fever is linked to humoral imbalance, particularly excess Safra (bile) or Dam (blood).

Joint pain (Waja' al-Mafasil) ^[15]

- Arthritis or arthralgia, presenting as pain and swelling in the joints.
- Seen as a result of excess Balgham (phlegm) or cold temperament affecting joints.

Hip pain (Waja' al-Warik) ^[7]

- Pain in hip region, and feel discomfort.
- Seen as a rest of excess Safra or hot temperament, which produce humidity and cause dryness of fluid.

Skin rash (Hasat or bagharaj) ^[16]

- The characteristic "butterfly rash" and photosensitivity.
- Interpreted as heat (Hararat) in the blood or altered Safra.

Fatigue (Khunuq) ^[8]

- Persistent tiredness and weakness.
- Related to imbalance in Mizaj (temperament), particularly cold and dry states.

Alopecia (Saqt al-Sha'r) ^[17]

- Hair loss due to systemic inflammation.
- Associated with weakened body temperament and poor nourishment.

Renal symptoms (Zof-i-Kulya) ^[9]

- Lupus nephritis leading to proteinuria and kidney dysfunction.
- Seen as excess Balgham or Safra affecting kidney function.

Neurological symptoms (Sara' or waja al-dimagh) ^[10]

- Seizures, psychosis, or mood disorders.
- Linked to disturbances in Dam and Sauda affecting the brain.

Oral ulcers (Qala') [17]

- Painless sores in the mouth or nose.
- Attributed to heat and dryness (Hararat and Yubusat) in the mucosa.

Raynaud's phenomenon (Alaqat al-barud) [17]

- Cold-induced changes in fingers or toes.
- Seen as cold temperament affecting peripheral blood flow.

Systemic inflammation (Warim) [4, 12]

- Manifested as swelling in various organs and tissues.
- Considered a result of humoral imbalance causing inflammation.

Therapeutic Approaches in Unani Medicine**Dietotherapy (Ilaj-Bil-Ghiza)** [2, 13]

- Warm, light foods to counteract excess Balgham.
- Avoidance of cold, damp foods that worsen humoral imbalances.

Herbal medicine (Ilaj-bil-dawa) [14, 19, 20]

- Use of anti-inflammatory herbs like Asgandh (*Withania somnifera*) and Banafsha (*Viola odorata*).
- Formulations such as Majoon Suranjan for joint pain and Habbe Gule Aakh for systemic inflammation.

Regimental therapy (Ilaj-bil-tadbeer) [11, 18]

- Detoxification methods, including Hijama (Cupping therapy) and Fasd (Venesection).
- Physical therapies like Dalak (Massage) and Hammam (Steam baths) to improve circulation and reduce inflammation.
- Apply Roghan and Zimad to improve Blood circulation.

Psychotherapy (Ilaj-bil-nafsiyat)

- Managing stress and emotional well-being to reduce disease flares.

Conclusion

Systemic Lupus Erythematosus (SLE) is a multifaceted autoimmune disease with significant clinical and therapeutic challenges. Modern medicine attributes its pathogenesis to complex interactions between genetic, epigenetic, and environmental factors, resulting in immune dysregulation and multisystem involvement. Despite advances in understanding its molecular mechanisms and developing targeted therapies, SLE remains a chronic condition with no definitive cure.

Unani medicine offers a complementary perspective, viewing SLE as a manifestation of humoral imbalances, particularly involving Safra (yellow bile) and Sauda (black bile), and disruptions in Mizaj (temperament). Its holistic approach emphasizes restoring balance through dietary adjustments, herbal remedies, regimental therapies, and stress management. The Unani framework aligns with modern medicine in recognizing the role of inflammation and immune dysfunction while contributing unique insights into disease management.

The integration of Unani principles with contemporary biomedical approaches could provide a more comprehensive understanding of SLE and its management. Exploring Unani therapies such as anti-inflammatory herbs, detoxification

methods like cupping (Hijama), and lifestyle modifications offers promising avenues for adjunctive care. This interdisciplinary approach underscores the importance of blending traditional wisdom with modern science to enhance patient outcomes and quality of life. Further research is warranted to validate Unani therapies and incorporate them effectively into mainstream healthcare systems.

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