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REVIEW ARTICLE OPEN ACCESS

An Overview & Update of Systemic Lupus Erythematosus (SLE)

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Abstract
Systemic Lupus Erythematosus (SLE) is a chronic autoimmune inflammatory disease. In this disease, the immune cell attacks its own genetic material which is supposed to protect. The cause of disease is unknown but it may be the result of combination of environmental, genetic and hormonal factors. It can affect person of any age or gender, affection ratio is higher in females than that of males. The SLE shows geographical variations and mostly found in people of Asia, Africa and Caribbean islands. It is difficult to evaluate the nature of lupus. General symptoms of SLE are skin rashes, joint pain, fatigue etc. It can affect any part of body. There is not specific test that is used to diagnose SLE. There is no cure for SLE but some changes in lifestyle and medications can control the symptoms of disease. There has been improvement in quality of life of people living with SLE since last two decades.

KEY WORDS: NSAIDs, immunosuppressants, antibodies, genetic factors, inflammation.

1. INTRODUCTION

SLE is a chronic autoimmune inflammatory disease. In this, reddening of skin resembles like wolf's bite. Immune system protects the body from invaders but in lupus it acts differently. It is autoimmune disease which means immune cells attack the tissues which they supposed to protect. Lupus can target any tissue or organ in the body like brain, skin, joints, kidneys and other parts of the body[1]. The diagnosed ratio of SLE is approximately 20-150 persons per 100,000[2]. It can affect person of any age whether he or she is male or female, however it is mostly observed in females of child bearing age[2,3]. The SLE affection ratio of female to male is 9:1; however, the risk of SLE in women decreases after menopause, but still, it is higher than men[4]. Geographically, it is mostly found in people of Asia, Africa and Caribbean islands. It is less common in European and Caucasian population[3,5,6]. So, this disease shows geographic variations. It is unknown that why this disease develops and like most diseases it is the result of genetic, hormonal and environmental factors, so diagnose of SLE is challenging part[7]. If one of the twins is affected from SLE

than the chances that the other twin is also affected is 24%[1]. It is difficult to evaluate the nature of lupus as symptoms may appear and disappear.

CLINICAL FEATURES

Butterfly rash or molar rash over the cheeks and on the bridge of nasal is the most common symptom of SLE. Rashes on the parts which are exposed to UV radiations like interphalangeal spaces, phalangeal and metaphalangeal joints could be seen[8]. Renal failure is also observed in 45-50% of SLE patients and this is known as lupus nephritis[9]. Inflammation of serous tissues of body like in lungs it causes pleuritis, in heart it causes pericarditis etc. Oral ulcers and non-erosive arthritis are also observed in some cases[10, 11]. Photosensitivity is the most common feature among all SLE patients. The blood disorder features are Leukopenia, Lymphopenia, Thrombocytopenia but the most common is autoimmune hemolytic anemia. There is generation of antinuclear antibodies due to loss self-tolerance. Immunological manifestations include anti Smith antibody and anti-double stranded DNA antibody[1,12]. Neurological manifestations include headache, mood disorders, seizures, cognitive dysfunction and many more[13].

A data of Canadian study shows that the most common causes of death in SLE patient's renal diseases, cerebrovascular diseases, cardiovascular diseases, neoplasm and respiratory diseases[14,15].

PATHOGENESIS

The exact pathophysiology of SLE is still unknown. Suppose the susceptible cell is subjected to UV radiations. This will

damage the DNA of susceptible cell. Then the cell tries to repair them, if they can't then they undergo programmed cell death called APOPTOSIS. A normal response of immune system will clear apoptotic cell from body, but sometimes cell is not cleared effectively due to some factors like excess amount of apoptotic cell. Then unclear apoptotic cell is presented to dendritic cell as antigen which is recognized by T cell. Then T cell triggers the B cell and it forms auto antibodies[16,17]. These auto-antibodies attack own nuclear material. Now immune system is sensitized to its own nuclear material so it attacks other cells of the body. Thus, SLE developed. Now the disease is developed so certain environmental factors are enough to trigger or flare up the disease[18,19].

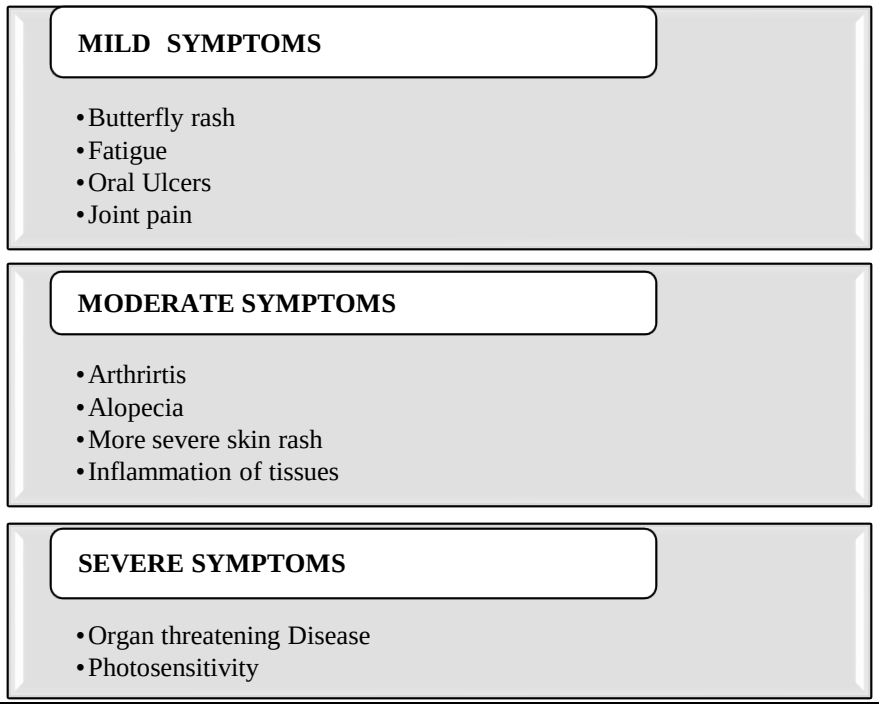

Figure 1. Symptoms of SLE

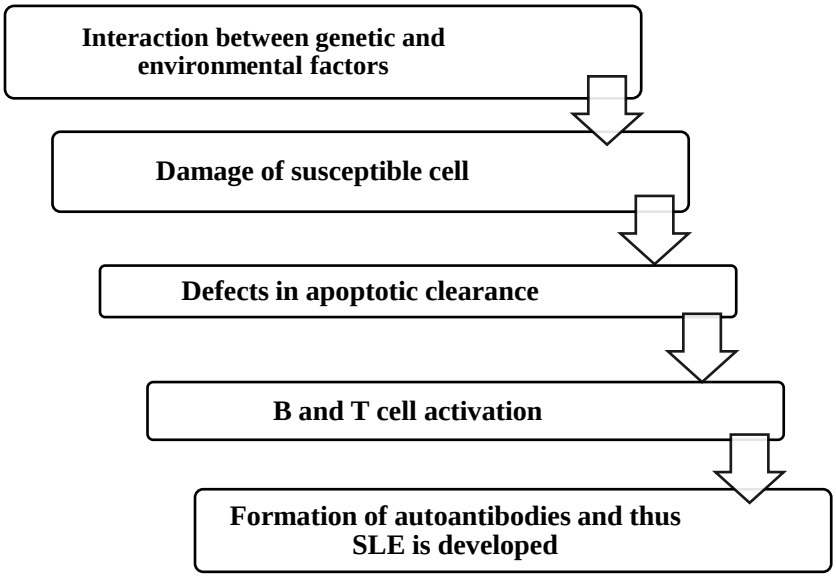

Figure 2. Flow chart of Pathogenesis of SLE

DIAGNOSIS

Family history of patient is checked, whether the SLE is related to genetic factors or not. If clinical features of SLE are present in suspected then laboratory tests help in diagnosis[20]. Laboratory screening tests like Erythrocyte's sedimentation rate which is high for SLE patients.

Leucopenia, Thrombocytopenia and Anemia can be observed in blood count test. Presence of RBCs, high level of protein and sugar in urine are observed in SLE. If Lupus cell attacks kidneys, then there will be increased serum creatinine level. ANA (Anti-nuclear antibodies) test and Anti dsDNA (double-stranded DNA) test are positive for lupus patients[21, 22].

TREATMENT

There is no cure for SLE[23]. Ongoing treatments focus on improving quality of life of people with lupus by controlling symptoms.

Medicinal approach:

i. Non-steroidal anti-inflammatory drugs (NSAIDs): NSAIDs work by inhibiting the chemicals that causes inflammation in the body. These common drugs like Aspirin, Ibuprofen, Naprosyn or Indomethacin helps reducing swelling, stiffness and pain. For people with very mild lupus, NSAIDs alone are enough to control symptoms. But these drugs increase the risk of allergic reactions, kidney injuries and hepatoxic effects[24]. NSAIDs increases the risk of kidney injury in lupus nephritis and can cause death in patients at end stage of kidney disease[25].

ii. Hydroxychloroquine: Hydroxychloroquine is used to treat malaria and researchers have found that this drug also helps with lupus flares. These drugs can help ease lupus symptoms such as joint swelling and skin rashes[24,26]. It can be taken in the form of pills or liquid. Hydroxychloroquine work by accumulating in lysosomes and inhibit the functions by increasing the PH. Hydroxychloroquine lowers the risk of organ damage, prevent blood clots and reduce the dosage of steroids[27]. Antimalarials act as daily multivitamins for lupus patients[28]. It also lowers the risk of cholesterol in people with antiphospholipid antibodies. But therapy of hydroxychloroquine increases the risk of visual disturbance and can cause photophobia[24,29]. Therefore, annual screening of eyes from ophthalmologist after five years of treatment is required. This drug can also be prescribed to pregnant women[27].

iii. Belimumab: Belimumab is a humanized monoclonal antibody that inhibits B cell activating factor[30]. It was approved for SLE treatment by US food and drug administration and European Medicines Agency in 2011. It is the only biological agent that is approved for treatment of SLE. It is added on therapy for people with SLE who are receiving standard treatment. But it is not indicated in SLE with lupus nephritis and central nervous system involvement. It plays an important role in suppression of B cell and production of autoantibodies. It begins action in 8 weeks of administration and show improved clinical manifestations in 16 weeks[31]. Infection, rash, Arthralgia, headache and diarrhea are common adverse reactions of Belimumab. Serious Infections and suicide due to depression were also seen in some cases[32].

iv. Corticosteroids: Oral steroids such as prednisone and prednisolone can be a lifesaving treatment for people with lupus. They work by inhibiting the action of overactive white blood cells. High doses of steroids can quickly control symptoms during serious lupus flares. Side effects are weight gain, mood changes, depression, osteoporosis, diabetes etc. so corticosteroids should never be taken without consultation with doctor[24]. The goal of steroids is to get the person onto the lowest possible dose necessary to control symptoms. After the lowest safe dose corticosteroids should be withdrawn when possible[33]. For mild diseases, lower doses are enough to control the symptoms and higher doses of corticosteroids are given in life threatening lupus[24].

Dose Grading	Prednisolone dose (mg)	Indications
Low Dose	<7.5	Maintenance
Medium Dose	7.5-30	Mild diseases; muscuskeletol, hematological symptoms
High Dose	30- 100	Induce remission of severe disease
Very High Dose	>100	

Table 1. Steroid dose and indications in SLE[24]

i. Immunosuppressive drugs: As lupus is a disease caused by an overactive immune system, drugs that suppress the immune system can help relieve symptoms. These drugs include Mycophenolate mofetil, Cyclophosphamide, Azathioprine etc. These are used in people who have severe lupus, when corticosteroids do not work properly. But the use of immunosuppressants in SLE carries a risk of infection. The treatment of SLE with Cyclophosphamide carries higher risk of incidence of infection than that of Mycophenolate mofetil. Mycophenolate Mofetil or Cyclophosphamide when given in combination with corticosteroids shows a greater action in suppressing the immune system against microorganisms. Thus, ability of body to fight with infection is decreased[34]. Immunosuppressants are also used to reduce the dose of steroids and prevent the undesirable effects of steroidal therapy. For this reason, Immunosuppressants are also known as "steroid-sparing" medications[35].

i. **Other medications:** Because lupus can affect any organ of body, so many people need other medications to control symptoms depending on their organ of affection. These can include diuretics, anti-hypertensive, Anticoagulants, stimulants, antibiotics and others[24].

NON-MEDICINAL APPROACHES

LIFESTYLE CHANGES FOR LUPUS

- **Eating a healthy diet:** Lupus patients should have a well-balanced diet that includes whole grains, plenty of fruits and vegetables, which are rich in antioxidants. They should avoid unhealthy fatty diet. Although, no food can cure SLE but healthy diet is a part of treatment of SLE. In SLE, healthy diet can reduce inflammation and helps to combat the side effects of medications given during treatment such as corticosteroids increases the risk of osteoporosis so, having diet rich in calcium and vitamin D will be very beneficial[36].

- **Exercise:** Exercise is the key if you have lupus. It can help improve your mood, boost energy, lower your risk of heart diseases and sharpen your mind. Most preferable exercises for lupus patients are stretching, yoga, Pilates

and aerobic exercises like dancing, swimming, walking, cycling etc. But it is important to consult with your doctor as some movements or postures could be harmful during joint pain and swelling and also tolerance of each SLE patient is different. Exercise not only provides physical health but also improves mental health, reduces the risk of depression and anxiety. Exercise also combat and prevents the side effects of medications during treatment[37].

- **Reduction in stress:** In many people, stress can trigger lupus flares. Use techniques like meditation, yoga and breathing exercises to cut down on stress[37,38]. Morning and Evening walk is also very beneficial to decrease stress.

- **Rest:** People with lupus might need more rest than an average person. If you can build time for rest into day and allow for 8 to 10 hours sleep at night. Some patients need rest after performing each activity, this allows them to regain the energy and feel good. Alcohol and caffeine drinks should be avoided before sleep. Development of good sleeping habits is necessary for SLE patients[39].

- **Sun protection:** Most of the patients with SLE are having skin involvement in the disease. The protection from sunlight is necessary for them as exposure to UV lights can cause skin rashes and flare up the symptoms. Covering the body by wearing full sleeves clothes when go outside in day time, use of sun protection lotion or cream with sun protection fairness (SPF) greater than 25 is very helpful for the avoidance of sunlight in lupus patients[38].

DIET OF LUPUS PATIENTS

There is not specific diet for lupus patients, but some supplements can help in relieving symptoms: -

i. **Omega 3 fish oil:** Omega 3 fish oil helps in decreasing inflammation. It also decreases the risk of heart failure. Taking this supplement in daily routine relieves lupus symptoms[36].

ii. **DHEA (Dehydroepiandrosterone):** DHEA is a hormone, lupus patients have low level of DHEA, so taking DHEA supplements can suppress SLE. Various studies have found that DHEA supplements help in reduction of fatigue, depression, Obesity, Lupus and other mental problems. It is also keeping the skin moisturizing and healthy[40].

iii. **Antioxidants:** Having a diet rich in fruits, vegetables and whole grains are a good source of antioxidants which are natural healers. Berries and sweet potatoes are also rich in antioxidants[36].

iv. **Vitamins:** Vitamin C can boost the immunity which is good for fighting infections. Lupus patients need to avoid sun, this decreases the absorption of vitamin D from lupus patients, so vitamin D supplements is also beneficial. Vitamin E, vitamin A and vitamin B are also good for lupus diet[41].

SLE IN PREGNANCY

Most of the autoimmune disorders have high rate of incidence in women in their reproductive age and SLE is one of them. So, SLE interferes in pregnancy. In some cases, SLE doesn't interfere with pregnancy and the SLE outcome is negative. But if a pregnancy is diagnosed with SLE, they need to consult with their doctors for the good pregnancy results. The presence of SLE in pregnant women increases the risk of preeclampsia, still birth, preterm birth and fetal growth restriction[42]. These risks can be controlled by regular monitoring of blood tests and urine tests during visits to the doctor[43]. Medications in SLE can have adverse impact on fetus so an ultrasound scan can help whether the fetus developing without structural abnormalities or with abnormalities[42]. Assessment of development risk of preeclampsia is also done in pregnant women. Risk of preeclampsia is higher in patients with prescribed Aspirin[44]. For the good pregnancy result, a communication between Rheumatologist and Obstetrician with regular monitoring is required in SLE pregnant patients[42]. Pregnancy loss risk in SLE has been reduced from 43% in 1960s to 17% in last decade. Corticosteroids and hydroxychloroquine are used to control disease activity by preventing flares of lupus[45]. A recent study suggests that continuation of hydroxychloroquine in pregnancy lower the risk of preterm birth, pregnancy loss and prevent lupus flares[45,46]. Immunosuppressive drugs are not prescribed in SLE during pregnancy. Aspirin and heparin are also contraindicated for the prevention of fetal abnormalities and damage[2].

CONCLUSION

There is no cure for SLE but there are medicines available which can control the flares of lupus. SLE being chronic disease needs long time and regular treatment which include regular visit to the doctor, blood tests, urine tests and medications. People in Asia, Africa and Caribbean islands are at high risk of developing SLE due to higher exposure to UV radiation. The professionals of health care are helping the SLE patients by educating them about the need of treatment, adverse reactions of the disease and monitoring the status of disease in them. The quality of life of people living with SLE is improving every year with the development of more accurate monitoring tests and treatments. Role of immune system in causing diseases is becoming better understood through research. This knowledge is applied to design safer and more effective treatment methods. People with SLE are improving their long-term health by learning characteristics of disease and monitoring their health with doctors. The mortality ratio has reduced in last 20 years and the survival rate of SLE patients has increased.

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