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SYSTEMIC LUPUS ERYTHEMATOSUS

***Batchu Pavani, T. Neha, G. Manoj Sai, G. Sushmitha, V. Tejaswi , G. Ramesh**

Vignan Pharmacy College (Approved by Aicte and Affiliated to Jntuk-Kakinada Vadlamudi (V), Chebrolu (M), Guntur (Dt.) - 522213).

***Corresponding Author: Batchu Pavani**

Vignan Pharmacy College (Approved by Aicte and Affiliated to Jntuk-Kakinada Vadlamudi (V), Chebrolu (M), Guntur (Dt.) - 522213).

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ABSTRACT

Systemic Lupus Erythematosus is autoimmune and a complicated disease which is very difficult to treat and diagnose. The exact cause / Aetiology of abnormal autoantibody production and development of SLE is still unknown. It occurs more in women when compared to men. The SLE effects many organs which include Cardio-vascular system, renal damage, neurological system, gastro-intestinal tract etc. Typically four or more of the following criteria must be present to make a diagnosis of SLE. There is no cure for SLE. The main aim of the treatment is to prevent flares and minimise organ damage and complications. The medications which are mainly used in the treatment includes NSAID'S, Corticosteroids, and Immuno-suppressants etc.

KEYWORDS: Systemic lupus erythematosus, auto antibody production, organ damage.

INTRODUCTION

Systemic lupus Erythematous is a multi-system inflammatory disorder characterised by auto antibody production and other immune system abnormalities. The hall mark of SLE is the development of auto-antibiotics,[1] to cellular nuclear components that leads to chronic inflammatory auto immune disease. The immune system attacks the body's cells and tissue resulting in inflammation and tissue damage. It is not surprising that SLE was first recognised as a skin disorder because cutaneous manifestation constitute one of the most common clinical features of the disease . The recurrent inflammation affects many organ systems including the joints, kidneys, skin, lungs, heart, and brain[2]

EPIDEMOLOGY

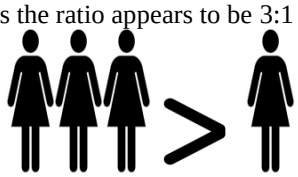
Incidence

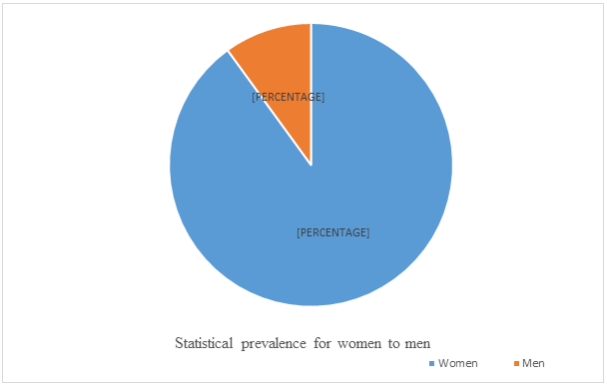
The incidence of SLE is estimated that there are approximately seven new cases of SLE diagnosed per 100000 population each year. The disease can occur in all races, but is seen more frequently in blacks and Asians. Ninety percent[3] of SLE patients are women and the onset of their disease occurs between the ages of 15 and 25. SLE is reported to be less prevalent in whites than in other ethnic groups including blacks, Hispanics, native American's and Asians.

Prevalence

The prevalence in the general population is about 1 in 1000.[4] At age 30 years, the ratio of women to men is 9:1.

At age 65 years the ratio appears to be 3:1





Etiology

The aetiology of abnormal autoantibody production and development of SLE is still unknown Genetic, environmental and hormonal factors[5-6] play a role in loss of self – tolerance and expression of disease.

- **Genetic factors:** Siblings of SLE patients are approximately 30 times more likely to develop SLE

compared with individuals without an affected sibling.

- **Epigenetic effects:** The risk for SLE may be influenced by epigenetic effects such as DNA methylation and post translational modifications of histones, which can be either inherited or environmentally modified.
- **Environmental factors:** Sunlight is the most obvious environmental factor that may exacerbate SLE.
- **Hormonal factors**

Pathogenesis

SLE affects many organ systems with in the body. Much of the damage is thought to be due to the action of circulating immune complexes that fix complement and produces tissue damage where the complexes are deposited, such as in the skin and kidney

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It is thought that DNA, which is released into the circulation, combines with anti-DNA antibodies and forms immune complexes that lodge in tissues and produce damage from the inflammatory reaction

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In addition, antibodies are produced directly against antigens on cell membranes

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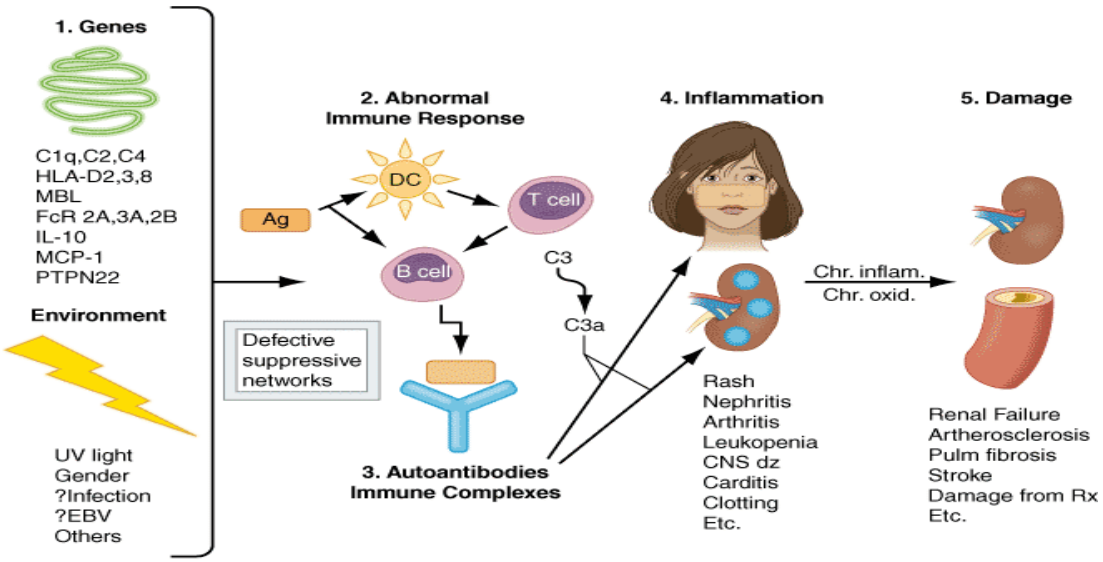
Immuno-globulins, specific antibodies such as anti-DNA and complement components are often found at the sites of tissue damage.[7-9]



Clinical Presentations

Dermatologic symptoms

Dermatologic symptoms are present in approximately 70-80%of SLE patients. The most characteristic skin lesion is the butterfly rash. The rash usually affects the checks bilaterally involves the bridge of nose and is characterized by the erythema and oedema. The rash occurs frequently after exposure to the skin. Maculopapular rash is another common dermatologic finding. This occurs following sun exposure, and is therefore most commonly seen on areas of the body exposed to the sunlight. Vasculitis skin lesions such as petechiae, purpura, and ecchymosis are often associated with severe serologic abnormalities. Alopecia commonly occurs in patients with SLE.

Renal symptoms

Hypertension may develop as a result of the renal damage with its resultant increase in the morbidity and mortality of the disease. The pathologic renal abnormalities in SLE are divided into 4 main categories

1) Minimal lupus nephritis
2) Focal (mild) lupus nephritis
3) Diffuse (severe) proliferative nephritis
4) Membrane lupus nephritis

- Patients with minimal lupus nephritis either have no observable urinary abnormalities or have transient proteinuria and minimal haematuria, but have immune deposits in renal biopsy.
- Patients with focal lupus nephritis have segments of glomeruli involved, with other areas that are unaffected. These patients usually have urinary abnormalities including haematuria and proteinuria, but the nephrotic syndrome is rare.
- Patients with diffuse proliferative lupus nephritis have moderate to heavy proteinuria, haematuria, red cell casts and mild to moderate renal insufficiency. Proteinuria is frequent but haematuria may not always be seen. A complication from the renal damage is the development of hypertension.

Neurological symptoms

Primary central nervous system (CNS) lupuses include both neurological and psychiatric disorders. The cranial nerves are less frequently involved and facial paralysis is

uncommon. Seizures may also be caused by SLE. Generalised tonic-clonic seizures are the most frequent seizure, although other seizure disorders may be seen. Difficulties in memory, perception and intellectual function may be seen. Severe headache are another neurological symptoms that may be produced by SLE. Psychological abnormalities such as depression and less commonly anxiety may also be caused by SLE. Both organic brain syndrome and central neurologic involvement excluding seizures have the worst prognosis

Cardiac symptoms

Cardiac manifestations are most frequent in SLE than in other autoimmune disorders. The most frequent manifestation is pericarditis, which is found in approximately 25% patients. Pericardial tamponade is a rare complication. Myocardial damage may also occur in SLE. The valvular damage may be due to non -infectious endocarditis called Libman-Sacks endocarditis in which there are areas of proliferating and degenerating valve tissue with fibrin and platelet thrombi Gastro intestinal symptoms.

The gastro intestinal symptom of SLE includes crampy abdominal pain. Mesenteric arteries can also occur in SLE. Pancreatitis may recur during exacerbations of the disease in some patients. Hepatomegaly, Splenomegaly, Lymphadenopathy are other known gastrointestinal manifestations that can produce by SLE.[10-17]

Mild to moderate anaemia is very common and is usually normochromic and normocytic. The anaemia caused by SLE is due to impaired erythropoiesis.

Diagnosis

Typically four or more of the following criteria must be present to make a diagnosis of SLE

The "Eleven Criteria"[18-21]

1) **Malar rash:** Flat or raised, Fixed erythema, butterfly-shaped rash across cheeks and nose
2) **Photosensitivity:** When exposed to Ultra –Violet light skin rash is observed
3) **Discoid (skin):** rash
4) **Arthritis:** Swelling
5) **Immunologic disorder:** Positive LE cell preparation or anti-Sm or false positive serologic disorder.
6) **Renal disorder:** Proteinuria or cellular casts
7) **Neurological disorder:** Seizures or Psychosis
8) **Oral Ulcers:** Painless
9) **Serositis:** Pleuritic or pericarditis
10) **Hematologic disorder:** haemolytic anaemia or leukopenia or Lymphopenia or Thrombocytopenia
11) **Anti- nuclear:** antibody (ANA)

Treatment

There is no cure for the SLE

Treatment plans are mainly based on patient age, sex, health, symptoms and lifestyle

The main goals of treatment are to

1) Prevent flares
2) Treat flares when they occur
3) Minimize organ damage and complications

Exposure to sunlight is usually restricted for SLE patients

The main class of drugs that are used to treat SLE are

1) Anti –inflammatory drugs
2) NSAID'S
3) Corticosteroids
4) Anti-malarial
5) Immune-suppressants
6) Anticoagulants
7) Monoclonal antibodies

Anti-inflammatory drugs

Anti-inflammatory medications help to relieve many of the symptoms of lupus by reducing inflammation and pain.

1) **Aspirin:** Pain reducer with anti-inflammatory and anti-coagulant properties
2) **Side effects:** Stomach irritation
3) **Acetaminophen:** In rare cases, causes acute liver failure.

Does not help with inflammation and cannot control lupus disease activity

NSAID'S

- NSAID'S provides symptomatic relief from
- Headache
- Arthralgias
- Fever
- Mild serositis
- Especially useful for joint pain and stiffness

Drug	Dose	Moa	Adverse effects	Drug interactions
Ibuprofen	400-	Inhibits the inflammatory	Abdominal pain	Ibuprofen –Rivaroxabane

(MOTRIN)	800 mg	reactions and pain by decreasing prostaglandins	Heartburns Indigestion	May increase the risk of bleeding including severe and sometimes fatal haemorrhage
Indomethacin (INDOCIN)	25-50 mg	Inhibits both COX-1 and COX-2	Chest pain Shortness of breath Bloody stools Dark urine	Indomethacin-Diflunisal increase the effect of indomrthacin
Celecoxib (CELEBREX)	100-200 mg	Reduces pain and inflammation by blocking COX-2	Upset stomach Diarrhoea Bloating Sore throat Runny nose	Celecoxib-Cidofovir increase the risk of kidney failure
Naproxen (NAPROSYN)		NSAID'S inhibit the generation of prostaglandins By blocking COX-1 and COX-2	GI disturbances Belching bleeding	NSAID'S reduce renal blood flow and thereby decrease the efficacy of diuretics[22]

Side effects: Abnormal urine test results

- NSAID'S are available over the counter and by prescription (for high dosage)

Corticosteroids

Ex: Prednisolone and methyl prednisolone

- Corticosteroids are prescribed for auto-immune diseases
- Steroid medication work quickly to decrease the swelling, warmth, tenderness and pain that re associated with inflammation
- Most people take steroids in pill form, but topical creams or gels are often used for cutaneous (skin).
- Steroids in liquid for are sometimes injected into muscles or directly into joints and in some cases into skin lesions

  Side effects: Acne, moon shaped face, weight gain, fluid retention and a redistribution of fat, leading to a swollen face and abdomen but thin arms

Immuno-suppressants

- Immune-suppressants medications are prescription drugs used to control inflammation and the overactive immune system.
- Immunosuppressive drugs reduce body's ability to fight off infections and increase the chances that could develop viral infections such as Chicken pox or herpes zoster.

Drug	Dose	Moa	Adverse effects	Drug interactions
Methotrexate (RHEUMATREX)	2.5-5 mg/dl	Inhibits the DNA synthesis through a blockage of the biosynthesis of thymidylate and purines	Myelosuppression Nausea Alopecia	Salicylates and sulphonamides inhibit the renal tubular secretion of methotrexate and may displace it from plasma proteins
Cyclophosphamide (CYTOXAN)	3.5-5 mg/kg/day orally	Formation of cross links within DNA due to a reaction of the two chloro-ethyl moiety of cyclophosphamide with adjacent nucleotide bases.	Bone marrow suppression Alopecia Fibrosis	Cyclophosphamide-Clozapine lowers the WBC count

Anti-malarial

- Anti-malarial are prescription drugs used in combination with steroids and other medications, to reduce the dose required of the other drugs
- Anti-malarial are most often prescribed for skin rashes, mouth ulcers and joint pain, but also can be effective in mild forms of lupus where inflammation and blood clotting are a concern
- Two types of anti-malarial most often prescribed are:

1) Hydroxychloroquine (Plaquenil)
2) Chloroquine (Aralen)

Drug	Dose	Moa	Adverse effects	Drug interactions
Chloroquine (ARALEN)	250mg (chloroquine base is 150mg)	It controls the conversion of toxic heme to hemozoin[23] by inhibiting the biocrystallization of hemozoin, thus poisoning the parasite through excess level of toxicity	Pruritis Nausea Vomiting Anorexia Abdominal pain Confusion seizures	Chloroquine-auranofin can cause blood disorder and other severe side effects

Anti-coagulants

Drug	Dose	Moa	Adverse Effects	Drug interactions
Heparin (Calciparine)	Iv bolus 5,000-10,000U	Heparin binds and accelerate the activity of plasma anti-thrombin III Anti – thrombin III inhibits the activated clotting factors Xa, IIa, IXa, XIIa, XIIIa by forming stable complexes thus prevents further thrombus formation	Bleeding Hypersensitivity reactions Heparin induced thrombocytopenia	Heparin-argatroban increase the risk of bleeding
Warfarin (COUMADIN)	10-15mg followed by 2-10 mg per day	These are vitamin K antagonist	Abdominal pain Bleeding gums Bloody stools	Warfarin-clopidogrel Can increase the risk of bleeding complications

Monoclonal antibodies

Belimumab (BENLYSATE) was developed to disrupt activation of B lymphocytes by interfering with BLyS a protein required for B cell activation.

CONCLUSION

Systemic Lupus Erythematosus is autoimmune disease which is very difficult to treat and diagnose. There is no proper treatment for SLE. The redness of the skin can aggravate when exposed to sun so patient is advised to apply sun screen lotion prior to exposure to sun light. During the flares of their disease it may be necessary to temporarily stop vigorous exercise. Avoiding the exposure to allergic substances is encouraged.

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