SYSTEMIC LUPUS ERYTHEMATOSUS – AN IMMUNOLOGICAL DISORDER: CLINICAL PRESENTATIONS AND THERAPEUTIC OPTIONS

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ABSTRACT
Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by production of numerous autoantibodies and damage to multiple organs and systems. SLE most often affects heart, joints, skin, lungs, blood vessels, liver, and kidneys. SLE is seen in young women of childbearing age (20 – 40 years) but it may occur at any age. Like other autoimmune disorders etiology of SLE is unknown, but it includes many components such as genetic, environmental, hormonal, drugs, etc. Immune responses against endogenous nuclear antigens are characteristic of SLE. SLE is diagnosed on the basis of classification criteria established by the American College of Rheumatology (ACR). The conventional treatment of SLE includes non-steroidal anti-inflammatory drugs (NSAIDS), anti-malarial agents, corticosteroids and other immunosuppressive medications. New treatment options for SLE include Belimumab, Mycophenolate mofetil, intravenous immunoglobulins, Rituximab, Atacicept etc. Main purpose of addition of new treatment modalities is prevention of complications of conventional treatment and to look for better therapeutic options.

Keywords: Systemic lupus erythematosus, immunological disorder, clinical manifestations, therapy.

INTRODUCTION
Systemic Lupus Erythematosus (SLE) is prototypic multi organ autoimmune disorder (Miah et al, 2008). The word lupus means wolf in Latin, as the destructive injuries of the disease resemble bites of this animal. The history of lupus can be divided into three periods: the classical period which includes description of cutaneous disorder, neoclassical period which shows description of systemic or disseminated manifestations of lupus, and the modern period which shows discovery of LE cell in 1948 (Blotzer et al, 1983). SLE shows a broad spectrum of clinical presentations involving almost all organs and tissues (Miah et al, 2008). Due to the heterogeneity of disease, SLE is proposed as a syndrome and not a single disease (Bertsias et al, 2008).

Epidemiology
The incidence of SLE in the USA ranges from 2.0 to 7.6 cases per 100,000 persons per year (Bongu et al, 2002). Prevalence of lupus is estimated to be as high as 51 per 100,000 people in the USA (Bertsias et al, 2008). The highest prevalence of SLE is reported in Brazil with 20 to 150 cases per 100,000 populations (George et al, 2011). Estimated incidence of SLE ranges from 2 to 8 per 100,000 per year in North America, South America, and Europe (Bertsias et al, 2008). The incidence of SLE has almost tripled worldwide in the last 4 decades and is increasing as the disease is recognized more readily and the survival rate has increased (George et al, 2011).

SLE is more common in people of African – Caribbean and Asian origin than in white population (Rahman et al, 2008). The overall prevalence of SLE in UK is approximately 28 per 100,000, and it is about 200 per 100,000 in African – Caribbean patients (Johnson et al, 1995). Sixty five percent of SLE patients have disease onset between 16 – 55 years, 20% before the age of 16, and 15% over the age of 55 (Bertsias et al, 2008). SLE affects all age groups but young women of childbearing age (20 – 40 years) are affected more commonly. The overall female: male ratio is 9:1. In pediatric population and in those who develop lupus over the age of 50 years, female to male ratio is 4:1 (Teresa et al, 2011).

Etiology
Etiology of SLE includes many components such as genetic, environmental, hormonal, drugs etc (Helen et al, 1999).

Genetic factors
During the last few years, by using hundreds of thousands of single nucleotide polymorphism (SNP) markers, understanding of genes involved in the pathogenesis of SLE has increased (Bertsias et al, 2008). Most of the SNPs associated with SLE fall within non-coding DNA regions of immune response – related genes (Harley et al, 1998). Certain SNPs linked to SLE have...
been identified for genes whose products may contribute to abnormal T-cell function in SLE. A large scale replication study confirmed some of these associations and identified TNIP1, PRDM1, JAZF1, UHRF1, BP1, and IL10 as risk loci for SLE (Gateva et al, 2009).

SLE may be associated with the deficiency of a single gene, e.g., complement components Cq and C4 (Moser et al, 2009, Tsokos et al, 2000) but the disease more commonly results from the combined effects of variants in a large number of genes (Roozendaal et al, 2007), whereas lack of C1q leads to deficient elimination of necrotic material (Manderson et al, 2004).

**Hormonal factors**

Through unknown mechanisms, in women hormones contribute to the increased prevalence of SLE (Duarte et al, 2011). The X chromosome may contribute independently from hormones in the severity of SLE. In experiments carried out in castrated female and male mice that have been genetically manipulated to express XX, XO (female), XY, or XXY (male) combinations, it was observed that the presence of two X chromosomes was associated with increased severity of SLE (Smith – Bouvier et al, 2008). Increase in estrogen or prolactin can lead to autoimmunity with an increase in mature high – affinity auto-reactive B cells (Bertsias et al, 2008).

Men and women suffering from SLE have different metabolisms of estrogen and androgen. For example, women with SLE metabolize estrogen to 16α-hydroxyestrone which is a more potent form as compared to 2 – hydroxyestrone which is produced by non SLE women and therefore they may have increased risk of miscarriage and irregular menstruation cycles (McAlindon et al, 2000).

**Environmental factors**

Environmental triggers of SLE include ultraviolet light, demethylating drugs, and infections. Sunlight is the most obvious environmental factor that may exacerbate SLE (Bertos et al, 2008).

Epstein – Barr virus (EBV) has been identified as a possible factor in the development of lupus. EBV may reside in and interact with B cells and promotes interferon α (IFNα) production by plasmacytoid dendritic cells (pDCs), suggesting that elevated IFNα in lupus may be at least in part due to aberrantly controlled chronic viral infection (MH et al, 2009).

**Drugs**

Up to 10% of SLE patients may actually have drug induced lupus (DIL), and approximately 80 percent of drugs have been implicated in causing DIL. Hydralazine, Procainamide and isoniazid inhibit DNA methylation and can induce manifestations of lupus in healthy persons (Ballester et al, 2006). All of these medications undergo acetylation as part of their metabolism; therefore patients who are slow acetylators tend to have more problems with DIL compared with those who have normal or fast acetylation (Teresa et al, 2011). Another potential cause of DIL involves hapten-like reactions where the drug or its metabolites bind to proteins rendering them foreign to the body (Teresa et al, 2011).

**Pathogenesis**

Immune responses against endogenous nuclear antigens are characteristic of SLE. Auto-antigens released
Table 1: American College of Rheumatology (ACR) criteria for the classification of systemic lupus erythematosus.

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Definition</th>
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<tr>
<td>1. Malar Rash</td>
<td>Fixed erythema, flat or raised, over the malar eminences, tending to spare the nasolabial folds</td>
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<tr>
<td>2. Discoid rash</td>
<td>Erythematous raised patches with adherent keratotic scaling and follicular plugging; atrophic scarring may occur in older lesions</td>
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<tr>
<td>3. Photosensitivity</td>
<td>Skin rash as a result of unusual reaction to sunlight, by patient history or physician observation</td>
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<tr>
<td>4. Oral ulcers</td>
<td>Oral or nasopharyngeal ulceration, usually painless, observed by physician</td>
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<tr>
<td>5. Non-erosive Arthritis</td>
<td>Involving 2 or more peripheral joints, characterized by tenderness, swelling, or effusion</td>
</tr>
<tr>
<td>6. Pleuritis or Pericarditis</td>
<td>Pleuritis – convincing history of pleuritic pain or rubbing heard by a physician or evidence of pleural effusion. Or Pericarditis – documented by electrocardiogram or rub or evidence of pericardial effusion</td>
</tr>
<tr>
<td>7. Renal Disorder</td>
<td>Persistent proteinuria &gt; 0.5 grams per day or &gt; than 3+ if quantitation not performed. Or Cellular casts – may be red cell, hemoglobin, granular, tubular, or mixed</td>
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<tr>
<td>8. Neurologic Disorder</td>
<td>Seizures – in the absence of offending drugs or known metabolic derangements; e.g., uremia, ketoacidosis, or electrolyte imbalance. Or Psychosis – in the absence of offending drugs or known metabolic derangements, e.g., uremia, ketoacidosis, or electrolyte imbalance.</td>
</tr>
<tr>
<td>9. Hematologic Disorder</td>
<td>Hemolytic anemia – with reticulocytosis Or Leukopenia – &lt; 4,000/mm³ on ≥ 2 occasions Or Lymphopenia – &lt; 1,500/ mm³ on ≥ 2 occasions Or Thrombocytopenia – &lt; 100,000 / mm³ in the absence of offending drugs</td>
</tr>
<tr>
<td>10. Immunologic Disorder</td>
<td>Anti-DNA: antibody to native DNA in abnormal titer. Or Anti-Sm: presence of antibody to Sm nuclear antigen Or Positive finding of antiphospholipid antibodies on: an abnormal serum level of IgG or IgM anticardiolipin antibodies, a positive test result for lupus anticoagulant using a standard method, or a false – positive test result for at least 6 months confirmed by Treponema pallidum immobilization or fluorescent treponemal antibody absorption test</td>
</tr>
<tr>
<td>11. Positive Antinuclear Antibody</td>
<td>An abnormal titer of antinuclear antibody by immunofluorescence or an equivalent assay at any point in time and in the absence of drugs</td>
</tr>
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</table>

For the purpose of identifying patients in clinical studies, a person must have SLE if any of the 4 or more of the 11 criteria are present, serially or simultaneously, during any interval of observation. (Adapted from Tan EM, Cohen AS, Fries JF et al. The 1982 revised criteria for the classification of SLE. Arthritis Rheum 1982; 25: 1271-7)

by apoptotic cells are presented by dendritic cells to T cells leading to their activation. Activated T cells in turn help B cells to produce antibodies to these self – constituents by secreting cytokines such as interleukin 10 (IL₁₀) and IL₂₃ and by cell surface molecules such as CD₂₉L and CTLA₄. In addition to this antigen – driven T cell – dependent production of autoantibodies, recent data supported T cell – independent mechanisms of B cell stimulation via combined B cell antigen receptor (BCR) and TLR signaling (Bertsias et al, 2008).
The pathogenesis of SLE involves a multitude of cells and molecules that participate in apoptosis, innate and adaptive immune responses. Increased amounts of apoptosis – related endogenous nucleic acids stimulate production of IFNα and promote autoimmunity by breaking self – tolerance through activation of antigen presenting cells. Once initiated, immune reactants such as immune complexes amplify and sustain inflammatory response (Bertsias et al., 2008).

SLE activity has three patterns: flare, chronic, and long quiescence. A flare or relapsing remission is an exacerbation that occurs suddenly and unpredictably; patients are usually in good health between flares. Factors that may trigger a disease flare-up include stress, excessive work, emotional crisis, sunlight, ultraviolet light, infection, injuries, surgery, pregnancy, abrupt discontinuation of medications, treatment noncompliance, medications, and immunizations (Miah et al., 2008). Serologic tests are not helpful in predicting flares because serologic activity of SLE may occur without clinical manifestations. Chronic cases of SLE have persistent activity such as chronic synovitis, chronic cytopenias, or active discoid lupus. This chronic activity may or may not require treatment. Patients with long quiescence have a long remission period before having additional flare-up (Gladman et al., 1999). Patients can also have comorbid conditions associated with SLE e.g., nephritis and neuropsychiatric involvement (Teresa et al., 2011).

Several validated global and organ-specific activity indices are widely used in the evaluation of SLE patients (Urowitz et al., 1998). These include European Consensus Lupus Activity Measure (ECLAM), British Isles Lupus Assessment Group Scale (BILAG), Lupus Activity Index (LAI), National Institutes of Health SLE Index Score (SIS), Systemic Lupus Activity Measure (SLAM), and SLED is a Disease Activity Index (SLEDAI). SLEDAI is more convenient for use in daily practice as shown in Table 2.

### Table 2: Systemic Lupus Erythematosus Disease Activity Index (SLEDAI).

<table>
<thead>
<tr>
<th>Score</th>
<th>Descriptor</th>
<th>Definition</th>
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<tr>
<td>8</td>
<td>Seizure</td>
<td>Recent onset. Exclude metabolic, infectious, or drug – related causes</td>
</tr>
<tr>
<td>8</td>
<td>Psychosis</td>
<td>Altered ability to function in normal activity due to severe disturbance in the perception of reality. Includes hallucinations; incoherence; marked loose associations; impoverished thought content; marked illogical thinking; bizarre, disorganized or catatonic behavior. Exclude the presence of uremia and offending drugs</td>
</tr>
<tr>
<td>8</td>
<td>Organic brain syndrome</td>
<td>Altered mental function with impaired orientation or impaired memory or syndrome other intellectual function, with rapid onset and fluctuating clinical features. Includes a clouding of consciousness with a reduced capacity to focus and an inability to sustain attention on environment, and at least two of the following: perceptual disturbance, incoherent speech, insomnia or daytime drowsiness, increased or decreased psychomotor activity. Exclude metabolic, infectious, and drug – related causes</td>
</tr>
<tr>
<td>8</td>
<td>Visual</td>
<td>Retinal changes from systemic lupus erythematosus: cytoid bodies, retinal hemorrhages, serous exudates or hemorrhages in the choroid, optic neuritis (not due to hypertension, drugs, or infection).</td>
</tr>
<tr>
<td>8</td>
<td>Cranial nerve</td>
<td>New onset of a sensory or motor neuropathy involving a cranial nerve.</td>
</tr>
<tr>
<td>8</td>
<td>Lupus headache</td>
<td>Severe, persistent headache; may be migranous; unresponsive to narcotics.</td>
</tr>
<tr>
<td>8</td>
<td>Cerebrovascular accident</td>
<td>New syndrome. Exclude arteriosclerosis.</td>
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</table>
Clinical presentation

Clinical presentation of SLE can be nonspecific e.g. fever, malaise, arthralgias, myalgias, headache, and loss of appetite and weight. Fatigue, fever, arthralgia, and weight changes are the most common symptoms in new or in recurrent active SLE. Fatigue is the most common constitutional symptom and it can be due to active SLE, medications, lifestyle habits, comorbid fibromyalgia or affective disorders. Fatigue due to active SLE generally occurs in concert with other clinical and laboratory markers. Fever, another common yet nonspecific symptom of SLE, may also result from many causes, the most common of which include active SLE, infection, and drug fever. The specific symptoms of SLE are photosensitivity, malar rash, oral ulcer, alopecia, serositis etc (D’Cruz et al, 2007).

Musculoskeletal features

Ninety percent of SLE patients have joint inflammation such as arthralgia, arthritis, tendinitis, or early morning stiffness that is generally in knees, wrists, and hands. Joint inflammation does not cause permanent damage. Men with SLE tend to have less arthritis, but serositis can be more predominant in men than in women (Amissah – Arthur et al, 2009).

Cutaneous involvement

Common skin manifestations include malar or butterfly rash, with sun-induced macules or papules occurring on the face, or generalized rash on the body, which may or may not be sun induced. Discoid lupus presents as a hyperkeratotic lesion associated with atrophy, scarring, and hypopigmentation (D’Cruz et al, 2007). Diffuse alopecia can generally occur when the disease is active and is usually reversible during remission. Patchy alopecia, on the other hand, may lead to scarring and can become permanent (Cervera et al, 2003).
Another common feature, occurring in 50% of SLE is mucosal ulceration; usually oral. Since methotrexate can also cause these ulcerations, it can be difficult to determine if the ulceration is induced by SLE or it is drug induced (Teresa et al, 2011).

Cardiovascular features
Cardiovascular and respiratory symptoms are also common and include chest pain on inspiration due to pleurisy or pericarditis. Cardiovascular disease (e.g. myocardial infarction) can be exacerbated in SLE but mostly these are secondary to accelerated atherosclerosis and other risks i.e. hypertension, hypercholesterolemia, hypertriglyceridemia, diabetes, and heart failure. The risk of hospitalization for an acute myocardial infarction was 2.27 times greater for lupus patients between aged 18 to 44 years than for non-lupus patients (Aranow et al, 2000).

Renal complications
Although it is almost common in SLE that there are deposits of immunoglobulin in the glomeruli, but only one half of the patients present with the features of clinical nephritis (Ben – Menachem et al, 2010). Lupus nephritis (LN) is a common and potentially devastating manifestation of SLE. In general, LN occurs in more than half of SLE patients. LN is primarily caused by the deposition of immune complexes. The classification of LN is based on renal biopsy. If possible, a biopsy should be obtained from patients who are suspected of renal impairment. Renal biopsy need not to be made routinely in patients with normal creatinine values and normal urine analysis (Petri et al, 2007).

Neuropsychiatric manifestations
Neurological manifestations of lupus are reported in 25 to 75% of patients and can involve all parts of the nervous system (D’Cruz et al, 2007). Incidence of elevated anti-phospholipid (APL) antibodies in patients with neurological symptoms is approximately two times higher than in those without neurological symptoms. Moreover, APL antibodies antedated neurologic symptoms in 81% of patients (Ben – Menachem et al, 2010).

Pulmonary manifestations
Pulmonary manifestations of SLE may manifest acutely or indolently that include many complications such as serositis, which can affect both cardiac and pulmonary systems and cardiac and pulmonary serositis often coexist. Serositis can be due to pericardial or pulmonary effusions, pulmonary embolism, lupus pneumonia, chronic lupus interstitial lung disease, complement – mediated pulmonary leukoaggregation, or infection may be related to lupus disease. Pleurisy with pleuritic chest pain with or without pleural effusion is the most common feature of acute pulmonary involvement in SLE. Shortness of breath or dyspnea may be due to many causes (Ben – Menachem et al, 2010).

Ocular manifestations
Ocular manifestations of lupus are reflection of systemic disease and therefore these manifestations should alert the clinicians for the presence of disease activity elsewhere as well. The most common ocular manifestation of SLE is keratoconjunctivitis sicca (KCS) that occurs in approximately 25% of patients (Arevalo et al, 2002). Conjunctivitis, interstitial keratitis, episcleritis and diffuse or nodular scleritis are less common. The severity of episcleritis and scleritis may closely mirror the activity of systemic disease. Necrotizing scleritis is rare in patients with SLE. Retinal involvement in SLE is the second most common ocular manifestation after KCS (Peponis et al, 2006).

Hematologic manifestations
Patients with SLE have a complex array of abnormalities of immune system. Among other etiologies, history of multiple cytopenias such as leukopenia, lymphopenia, anemia, or thrombocytopenia may suggest SLE. Leukopenia and more specifically lymphopenia are common in SLE and along with this decreased complement levels may predispose people with SLE to frequent infections (Manole et al, 2011).

Treatment of SLE
Management of SLE often depends on disease severity and disease manifestations (Hahn et al, 2005). Duration of therapy is also highly variable and it depends upon the disease severity in an individual and is based on the patient’s response (Chaichian et al, 2013).

Conventional therapy: Conventionally, patients of SLE are treated with non-steroidal anti-inflammatory, anti-malarial, glucocorticoids and immunosuppressive drugs including cyclophosphamide, azathioprine, methotrexate, and Mycophenolate mofetil. In addition to anti-inflammatory effects, inhibitors of cyclooxygenase promote the death of auto-reactive T cells. The anti-malarial agent hydroxychloroquine has therapeutic value and limited toxicity. It inhibits the function of toll – like receptors that contribute to autoimmunity (Karlsson et al, 2007). Every month or bimonthly at lower dose intravenous infusions of cyclophosphamide is effective for the treatment of LN, although there are serious potential side effects, including bone marrow suppression, infections, and gonadal suppression (Illei et al, 2001). Mycophenolate mofetil has considerable therapeutic value with few side effects (Radhakrishnan et al, 2010) but its long-term effects with respect to the preservation of kidney function are under trial (Boumpas et al, 2010).

New drugs and treatment options
The development of new modalities is important for
the prevention of complications of current treatment options and it is believed that they have better therapeutic outcomes (Chaichian et al., 2013). New potential drugs for SLE therapy are as follows.

**Belimumab (Benlysto):** Belimumab (human immunoglobulin IgG) is a selective inhibitor of soluble protein B lymphocyte stimulator (BLyS). The protein BLyS is essential for B cell maturation, proliferation, survival and antibody production. High serum levels of soluble BLyS are found in SLE and are associated with high autoantibody levels and active disease (Chaichian et al., 2013). Belimumab binds to soluble BLyS and inhibits its biological activity. Therefore, autoantibodies are not produced and do not damage tissues of the body (Navarra et al., 2011).

**Mycophenolate mofetil (Cellcept):** Mycophenolate mofetil (MMF) inhibits the action of an enzyme that is vital for the proliferation and maturation of white blood cells (Chaichian et al., 2015). LN which is one of the life-threatening complications of SLE is associated with kidney failure that needs treatment with dialysis. A common treatment employed for grade IV LN (diffuse proliferative glomerulonephritis) is a combination of corticosteroids and immunosuppressive drugs, mainly intravenous cyclophosphamide (CYC). This combination is used to achieve and maintain remission in disease activity. The administration of CYC is limited by significant toxic effects, including premature ovarian failure, sterility, infections, bladder toxicity and malignancies (Netta et al., 2014).

**Intravenous immunoglobulins (IVIG):** IVIG is a biologic therapy of antibodies obtained from pooled human plasma donors. The mechanism is not entirely clear, but several mechanisms are suggested, including suppression of white blood cells, inhibition of immune system activation, and neutralization by antibodies causing damage to organs. IVIG treatment is effective for treating moderate to severe SLE and IVIG can be used as an adjuvant therapy (Netta et al., 2014).

**Rituximab (Mabthera):** Rituximab is a chimeric monoclonal antibody that selectively depletes CD20-positive B cells. Rituximab changes immune system activity, thus decreasing the degree of damage to vital organs including the kidneys. Rituximab is given to lupus patients that are resistant to standard therapy (Merrill et al., 2010).

**Atacicept:** Atacicept is a soluble, fully human, recombinant fusion protein that inhibits both BLyS and a proliferation – inducing ligand (APRIL) unlike belimumab which selectively blocks BLyS activity (Ginzler et al., 2012).

**Abetimus:** It is a synthetic toleragen molecule consisting of four double-stranded oligo-deoxy-ribo-nucleotides attached to non-immunogenic polyethylene glycol. It is an immune – modulating agent that induces tolerance in B cells directed against double-stranded DNA (dsDNA). The presumed mechanism of action is rapid decrease in anti-dsDNA antibody levels through clearance of drug-antibody complexes and development of tolerance among anti-dsDNA – specific B cells (Alarcón – Segovia et al., 2003).

**Ocrelizumab:** A humanized anti-CD20 monoclonal antibody, has also been evaluated in SLE (Chaichian et al., 2013).

**Antibody against CD22:** B cell depletion using CD22 as a target has been studied as a potential therapy in SLE. Epratuzumab is a humanized monoclonal antibody against CD22. Unlike anti-CD20 medications such as rituximab and ocrelizumab, epratuzumab affects B cell activity without fully depleting peripheral B cell stores (Wallace et al., 2010).

**Abatacept:** Abatacept binds to B7 (CD80/86) molecule on the surface of antigen – presenting cells and B lymphocytes to inhibit co-stimulation of T cells (Merrill et al., 2010).

**Rapamycin:** Mitochondrial abnormalities in T cells of SLE patients, leading to oxidative stress have also been the subject of clinical investigation. Rapamycin regulates mitochondrial transmembrane potential and calcium flow. It is safe and effective in reducing disease activity (Fernandez et al., 2006).

**N-acetylcysteine:** N-acetylcysteine is a precursor of glutathione that inhibits the mammalian target of rapamycin (mTOR) activity in T lymphocytes (Lai et al., 2012).

**Spleen tyrosine kinase (Syk) and CD40 ligand blockade:** Syk acts downstream of mTOR. R788 which is an orally bio available Syk inhibitor, has been effective in treating nephritis and skin disease in mouse models of lupus (Deng et al., 2010).

**Oral quinoline-3-carboxamide (Laquinimod):** Small molecules have also drawn interest as possible therapies in SLE. Laquinimod alters T helper cell response in favor of TH2 over TH1 cells, leading to suppression of pro-inflammatory cytokines and promotion of several anti-inflammatory cytokines (Chaichian et al., 2013). Other drugs which are under clinical trials include Sifalimumab which is a fully human IgG,K monoclonal antibody that binds strongly to IFN – alpha and inhibits IFN – alpha signaling through its receptor. Rontalizumab; a humanized IgG, monoclonal antibody inhibits IFN, Tocilizumab; humanized monoclonal antibody against IL6 receptor, B-N, murine anti-IL20 monoclonal antibody, Infliximab; chimeric TNF – alpha inhibitor and Etanercept; soluble TNF – receptor fusion protein (Chaichian et al., 2013).

It is concluded that SLE is an autoimmune dise-
case that predominantly affects women and typically has manifestations in multiple organs including skin, kidneys and CNS. Immune – system aberrations, genetic, hormonal, and environmental factors contribute in organ damage. Immune complexes, auto-antibodies, auto reactive lymphocytes, dendritic cells, and local factors are all involved in clinical manifestations of SLE. Biologic therapies and small – molecule drugs that can correct aberrant immune – cell function are being developed in the hope that they will be more effective and would have less toxic effects as compared to the current treatment options. The lack of consistency in disease activity indices due to various therapies employed in the clinical trials of SLE has made comparison of targeted therapies more challenging. Numerous B-cell, T-cell, and anti-cytokine targets have been studied (Chaichian et al, 2013). The new treatment options e.g rituximab, atacicept, abetimus etc. available for SLE patients have shown to improve disease activity parameters, increased disease free period and to have a steroid sparing effect. Therefore, they can be considered as an alternative treatment options in patients who cannot be treated with cytotoxic agents or in those who would like to avoid side effects of standard treatment. A number of these possible therapeutic targets e.g. rituximab, atacicept, abetimus etc have shown promise in early trials and it is likely that the approach to lupus management will undergo significant change in the coming years and it is hoped that further targeted therapies will meet success in the near future(Chaichian et al, 2013).

Author’s contributions:
All the authors contributed equally to this work.

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