International Journal of Healthcare Sciences ISSN 2348-5728 (Online)
Vol. 4, Issue 2, pp: (443-448), Month: October 2016 - March 2017, Available at: www.researchpublish.com

Systemic Lupus Erythematosus (SLE), prevalence, disease characteristics and treatment options: Systematic review

[1]Ammar Mohammed Afif Alhaqli, [2]Mahmood Abdullrahman Najmi, [3]Ammar yasser shanou, [4]Mohammed Salem A Alqurashi, [5]Abdulrahman Ali J Walibi, [6]Arwa meshal alshaikh, [7]Jumana ahmed jabber, [8]Abdolmalek mohammad alghamdi

Abstract: **Systemic lupus erythematosus (SLE) is an auto-immune inflammatory illness credited to environmental and genetic factors causing the dysfunction of T cells, B cells, and dendritic cells and the production of antinuclear autoantibodies that affects multiple systems of the body. This study was aimed to overview the prevalence and characteristics and therapeutic management of the Systemic lupus erythematosus (SLE). MEDLINE (via PubMed), EMBASE, and the Cochrane Library were searched on 29 November 2016, using search terms (Medical Subject Heading [MeSH], EMTREE, and/or free text) from three categories: 1) systemic lupus erythematosus (lupus erythematosus, systemic, systemic lupus erythematosus, lupus, SLE); 2) prevalence, disease characteristics, management, and outcomes (characteristic*, disease attributes, flare*, guideline*, health care need, health planning guidelines, health services needs and demand, management, mortality, needs assessment, patient care, practice guideline, prevalence, population characteristics, quality of life, recommendation*, remission, remission induction, therap*, and treatment. The pathogenesis of SLE is Numerous genes provide vulnerability to disease development. Interaction of sex, hormonal milieu, the HPA axis, and malfunctioning immune guideline, such as clearance of immune complexes and apoptotic cells, modify this vulnerability. The loss of immune tolerance, increased antigenic load, excess T cell aid, defective B cell suppression, and moving of Th1 to Th2 immune responses cause cytokine imbalance, B cell hyperactivity, and the production of pathogenic autoantibodies. Lupus continues to present many unanswered questions.**

Keywords: **Systemic Lupus Erythematosus.**

1. INTRODUCTION

Systemic lupus erythematosus (SLE) is an auto-immune inflammatory illness credited to environmental and genetic factors causing the dysfunction of T cells, B cells, and dendritic cells and the production of antinuclear autoantibodies that affects multiple systems of the body [(1,2,3,4)]. Worldwide quotes of the prevalence of SLE vary from 4.3 to 150 per 100,000 population, [(5,6,7)] with higher occurrence in females, especially those of childbearing age, and particular ethnic groups [(1,2)]. The manifestations of SLE differ considerably and can be intermittent, making the disease tough to identify and treat. Typical symptoms consist of a characteristic red "butterfly" rash on the face, arthritis, myalgia, serositis, and nephritis [(1,2)]. Patients with SLE are at increased danger of death from infections and, later on in life, atherosclerotic heart disease [(1,2)].

The pathogenesis of SLE is incompletely comprehended and existing therapies largely relying on making use of corticosteroids and cytotoxic anti-proliferative drugs have limited efficacy and bring significant risks of toxicity. A logical approach for therapeutic style needs an in-depth understanding of disease pathogenesis. Independent lines of evidence have actually implicated environmental aspects and genetic factors of the host in the causation of the disease [(8)].

Genome-wide association studies (GWAS) have identified various chromosomal loci that may harbor vulnerability genes [(9)]; nevertheless, the functional significance of these GWAS-derived polymorphisms is currently unknown. A systematic

characterization of the cellular and molecular basis of signaling problems within the immune system that leads to autoreactivity and swelling and their relationship to regulation of gene expression remain critical for understanding of disease pathogenesis [10].

This study was aimed to overview the prevalence and characteristics and therapeutic management of the Systemic lupus erythematosus (SLE).

2. METHOD (SEARCH STRATEGIES)

MEDLINE (via PubMed), EMBASE, and the Cochrane Library were searched on 29 November 2016, using search terms (Medical Subject Heading [MeSH], EMTREE, and/or free text) from three categories: 1) systemic lupus erythematosus (lupus erythematosus, systemic, systemic lupus erythematosus, lupus, SLE); 2) prevalence, disease characteristics, management, and outcomes (characteristic*, disease attributes, flare*, guideline*, health care need, health planning guidelines, health services needs and demand, management, mortality, needs assessment, patient care, practice guideline, prevalence, population characteristics, quality of life, recommendation*, remission, remission induction, therap*, and treatment. Search terms were combined using "OR" and "AND", and results limited to human studies and English-language articles published since 1990. All MeSH and EMTREE terms were exploded.

3. RESULTS AND DISCUSSION

Prevalence of SLE

several studies [6,11,12] investigated and address the incidence of SLE varies amongst ethnic groups and by geographical place, sex, and age. The reported occurrence of SLE in the basic population is roughly 20 to 150 cases per 100,000 persons [6,11,12].

Geographical frequency, A report submitted by the National Arthritis Data Working Group approximated that SLA impacts 250,000 Americans [13]. The prevalence of SLE in the United States shows an unique elevation among Asian, Afro-American, Afro-Caribbean, and Hispanic-Americans compared to Americans of Eastern European descent [14,15]. The frequency of SLE amongst Caucasian patients in Rochester, Minn., is around 40 cases per 100,000 individuals, compared with Hispanic patients in Nogales, Arizona, where the rate is 100 cases per 100,000 persons [16,17].

Black individuals in Africa have a much lower occurrence of SLE than African-Americans in the U.S [18]. The incidence of SLE in various populations (e.g., rural versus urban locations) is likewise a subject in need of more examination. Epidemiologic data using lupus windows registries indicate the requirement for larger, population-based studies with a large patient base. Such data are presently doing not have because of potential obstacles, such as differing case meanings, small-source populations, and differing demographic group targets [19].

Sex and Age, SLE is more common in ladies, especially those of child-bearing age. This increased occurrence might be credited to hormones, particularly estrogen, as research studies have revealed ladies who had an early menarche or who used contraceptive pills or hormone treatments had actually an increased risk of SLE [20,21]. The lower danger in men resembles that in prepubertal or postmenopausal women. Klinefelter's syndrome, which includes an additional X chromosome in males, is connected to a raised occurrence of SLE, therefore providing more assistance for the association between SLE and a possible hormone pathogenesis [22].

Characteristics of SLE

Two studies [23,24] have actually approved that eruthematous rash on the cheeks aross the nasal bridge (butterfly rash) unique charactristics for SLE. purpura and urticarial rash over the idea of the fingers and nail folds. These are brought on by vasculitis (vasculitic rash). there will be other skin modifications like Livedo reticularis and periungual erythema. Patient may also develop plantar and palmar rashes. Patients may establish a erythematous rash in confront with well-defined margins. there plques can eventually lead to scarring and colorings (Discoid rash). In Subacute cutaneous lupus erythematosus, there is a migratory, non-scarring, papulosquamous/ annular rash [23,24].

About involvements of cardiovascular conditions, three case control studies [25,26,27] validated that atherosclerosis develops prematurely, separately of traditional danger factors for cardiovascular disease. Lupus itself appears to be a danger aspect

for the development of atherosclerosis, and a reasonable theory recommends that inflammatory disease activity over long periods leads to vascular and endothelial damage, which sets the scene for atherosclerosis. In addition to intensive management of disease activity, aggressive danger element decrease will be essential to improving result. One consisted of research study [28] have suggested guidelines for managing risk factors and they propose that this disorder must be considered as a coronary artery disease equivalent, in much the same way as is diabetes mellitus. The contribution of antiphospholipid antibodies to accelerated atherosclerosis in systemic lupus erythematosus stays unclear.

Due to the cardiac participation and with the possibility of arterial and venous thrombus development with vasculitis, patients are at danger of developing organ hypoperfusion. Eg: Brain strokes can take place providing functions of paralysis, paresthesia and cranial nerve palsy. In spinal cord, functions of infarction like limb paralysis, paresthesia, bladder/ bowel dysfunction. In bones, ischemic pain at site of the joint/back pain and fractures following long bone infarction can be seen. Myocardial infarctions can occur following hypoperfusion of the myocardium (chest pain, problem in breathing, dizziness). In lungs there will be shortness of breath and pleuritic type chest pain. In mesentry, intense stomach pain will be the discussion. In digits, agonizing fingers and toes with small bone infarction. In kidneys infarction of medulla with papillary necrosis might lead to stop working in focusing urine triggering high urine output, dehydration and nighttime enuresis. Chronic liver failure with micro infarction triggering anorexia nervosa, yellowish discoloration of eyes. Splenic infarction leads to frequent infections like upper/ lower respiratory system infections and diarrheal illnessess [29,30].

Central nervous system lupus CNS disease in lupus stays difficult in regards to treatment, pathogenesis, and assessment. A research study by DeGiorgio and coworkers [31] revealed that antiDNA antibodies acknowledge a pentapeptide that is also present in the extracellular domain of murine and human N-methyl-Daspartate (NMDA) receptor subunits NR2a and NR2b, which bind the neurotransmitter glutamate. They showed that the NR2 receptor is identified by both murine and human antiDNA antibodies and that these cross reactive antiDNA anti bodies can induce neuronal apoptosis. In an extension of their work, they showed that cerebrospinal fluid from a patient with systemic lupus erythematosus and progressive cognitive decrease included these antibodies and also mediated neuronal death via an apoptotic path. Hence, lupus antibodies can crossreact with DNA and NMDA receptors, gain access to cerebrospinal fluid, and can lead to irregularities of the CNS [31].

Management and treatment of SLE

The approach to the treatment of signs and symptoms of lupus depends on the type and the intensity of disease. General recommendations for all patients include sun protection, proper diet and nutrition, workout, smoking cessation, suitable immunizations, and management of comorbid conditions. In patients with mild-to-moderate lupus, NSAIDs, anti-malarial agents, and corticosteroids are commonly utilized to treat signs and indications. As the disease advances and scientific manifestations intensify, high-dose corticosteroids and immunosuppressive agents are used to help control disease development. A list of drugs typically utilized to deal with SLE exists in (**Table1**) [32,33]. NSAIDs might be utilized to relieve musculoskeletal pain, swelling, and pains. These drugs have pain-reducing, anti-inflammatory, and anticoagulant properties, which are advantageous in treating typical lupus-associated symptoms; however, the capacity for negative effects (see **Table 1**) must be thought about prior to clinicians recommend NSAIDs for a patient with lupus [32,33]

Table1: Commonly Used Medications in the Treatment of Systemic Lupus Erythematosus [32,33]

Drug Class	Mechanism of Action	Commonly Used Agents and Dosage	Potential Adverse Effects	Common Monitoring Parameters
NSAIDs (including salicylates)	Block prostaglandin synthesis through inhibition of cyclooxygenase enzymes, producing anti-inflammatory, analgesic, and antipyretic effects	Various agents and dosages	Gastrointestinal irritation and bleeding, renal toxicity, hepatic toxicity, hypertension	Nausea, vomiting, abdominal pain, dark/tarry stool; baseline and annual CBC, SCr, LFTs, urinalysis

Antimalarials	Unclear; may interfere with T-cell activation and inhibit cytokine activity; also thought to inhibit intracellular TLRs	Hydroxychloroquine PO 200–400 mg daily	Macular damage, muscle weakness	Funduscopy and visual field examination at baseline and every 6 to 12 months
Corticosteroids	Multiple effects on immune system (e.g., blocking cytokine activation and inhibiting interleukins, γ-interferon and tumor necrosis factor-α)	Prednisone PO 0.5–2 mg/kg per day Methylprednisolone IV 500–1,000 mg daily for 3 to 6 days (acute flare)	Weight gain, hypertension, hyperglycemia, hyperlipidemia, osteoporosis, cataracts, edema, hypokalemia, muscle weakness, growth suppression, increased risk of infection, glaucoma	Baseline blood pressure, bone density, glucose, potassium, lipid panel; glucose every 3 to 6 months; annual lipid panel and bone density
Immunosuppressants	Multiple suppressive effect on immune system (e.g., reduction of T-cell and B-cell proliferation; DNA and RNA disruption)	Cyclophosphamide PO 1–3 mg/kg per day or 0.5–1 g/m^2 IV monthly with or without a corticosteroid Azathioprine PO 1–3 mg/kg per day Mycophenolate PO 1–3 g daily	Myelosuppression, hepatotoxicity, renal dysfunction, infertility, increased risk of infection and cancer	Baseline and routine CBC, platelet count, SCr, LFTs, and urinalysis (depends on individual drug)
Monoclonal antibodies	Block binding of BLyS to receptors on B cells, inhibiting survival of B cells, and reducing B-cell differentiation into immunoglobulin-producing plasma cells	Belimumab IV 10 mg/kg (over a period of 1 hour), every 2 weeks for the first three doses, then every 4 weeks	Nausea, diarrhea, pyrexia, nasopharyngitis, insomnia, extremity pain, depression, migraine, gastroenteritis, infection (e.g., pneumonia, UTI, cellulitis, bronchitis)	Gastrointestinal complaints, infectious signs and symptoms, mood or behavioral changes, infusion reactions

BLyS = B-lymphocyte stimulator protein; CBC = complete blood count; DNA = deoxyribonucleic acid; IV = intravenous; LFTs = liver function tests; NSAIDs = nonsteroidal anti-inflammatory drugs; PO = by mouth; RNA = ribonucleic acid; SCr = serum creatinine; TLRs = toll-like receptors; UTI = urinary tract infection.

Other Treatment Options

two studies [34,35] have actually been particularly interested in the use of stem-cell hair transplant to introduce healthy cells into the body in order to help restore the immune system. Both DHEA and rituximab have actually been studied in medical trials and have supplied improvements in patients' lifestyle. DHEA is thought to assist in the regulation of sex hormones, whereas rituximab decreases the variety of B cells and may be most useful in patients who do not respond to the other generally utilized immunusuppressants [34,35].

4. CONCLUSION

The pathogenesis of SLE is Numerous genes provide vulnerability to disease development. Interaction of sex, hormonal milieu, the HPA axis, and malfunctioning immune guideline, such as clearance of immune complexes and apoptotic cells, modify this vulnerability. The loss of immune tolerance, increased antigenic load, excess T cell aid, defective B cell

suppression, and moving of Th1 to Th2 immune responses cause cytokine imbalance, B cell hyperactivity, and the production of pathogenic autoantibodies. Lupus continues to present many unanswered questions. No treatment has actually been found for this autoimmune disease, numerous medications are offered to help manage flares, to keep remission, and to handle signs. Pharmacists and other healthcare specialists can play a crucial function in treatment by educating patients, monitoring their healing programs, and determining preventable drug-associated unfavorable events.

REFERENCES

[1] Maidhof W, Hilas O. Lupus: an overview of the disease and management options. P T 2012; 37: 240-249.

[2] Askanase A, Shum K, Mitnick H. Systemic lupus erythematosus: an overview. Soc Work Health Care 2012; 51: 576-586

[3] Kyttaris VC, Juang YT, Tsokos GC. Immune cells and cytokines in systemic lupus erythematosus: An update. Curr Opin Rheumatol. 2005;17:518–522.

[4] Fox RI. Sjogren's syndrome: Immunobiology of exocrine gland dysfunction. Adv Dent Res.1996;10:35–40.

[5] Chakravarty EF, Bush TM, Manzi S, Clarke AE, Ward MM. Prevalence of adult systemic lupus erythematosus in California and Pennsylvania in 2000: estimates obtained using hospitalization data. Arthritis Rheum 2007; 56: 2092-2094.

[6] Pons-Estel GJ, Alarcon GS, Scofield L, Reinlib L, Cooper GS. Understanding the epidemiology and progression of systemic lupus erythematosus. Semin Arthritis Rheum 2010; 39: 257-268.

[7] Jakes RW, Bae SC, Louthrenoo W, Mok CC, Navarra SV, Kwon N. Systematic review of the epidemiology of systemic lupus erythematosus in the Asia-Pacific region: prevalence, incidence, clinical features, and mortality. Arthritis Care Res (Hoboken) 2012; 64: 159-168.

[8] Steinberg AD, Gourley MF, Klinman DM, Tsokos GC, Scott DE, Krieg AM. Systemic lupus erythematosus. Ann Intern Med. 1991;115:548–559.

[9] Harley JB, Alarcon-Riquelme ME, Criswell LA, Jacob CO, Kimberly RP, Moser KL, et al. Genome-wide association scan in women with systemic lupus erythematosus identifies susceptibility variants in ITGAM, PXK, KIAA1542 and other loci. Nat Genet. 2008;40(2):204–210.

[10] Kyttaris VC, Krishnan S, Tsokos GC. Systems biology in systemic lupus erythematosus: Integrating genes, biology and immune function. Autoimmunity. 2006;39(8):705–709.

[11] Lawrence RC, Helmick CG, Arnett FC, et al. Estimates of the prevalence of arthritis and selected musculoskeletal disorders in the United States. Arthritis Rheum. 1998;41:778–799.

[12] Chakravarty EF, Bush TM, Manzi S, et al. Prevalence of adult systemic lupus erythematosus in California and Pennsylvania in 2000: Estimates obtained using hospitalization data. Arthritis Rheum.2007;56:2092–2094.

[13] Helmick CG, Felson DT, Lawrence RC, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States: Part 1. Arthritis Rheum. 2008;58(1):15–25.

[14] Hochberg MC. The incidence of systemic lupus erythematosus in Baltimore, Maryland, 1970–1977. Arthritis Rheum. 1985;28:80–86.

[15] Serdula MK, Rhoads GG. Frequency of systemic lupus erythematosus in different ethnic groups in Hawaii. Arthritis Rheum. 1979;22:328–333.

[16] Uramoto KM, Michet CJ, Jr, Thumboo J, et al. Trends in the incidence and mortality of systemic lupus erythematosus, 1950–1992. Arthritis Rheum. 1999;42(1):46–50.

[17] Balluz L, Philen R, Ortega L, et al. Investigation of systemic lupus erythematosus in Nogales, Arizona. Am J Epidemiol. 2001;154(11):1029–1036.

[18] Symmons DP. Frequency of lupus in people of African origin. Lupus. 1995;4:176–178.

[19] Lim S, Drenkard C, McCune W, et al. Population-based lupus registries: Advancing our epidemiologic understanding. Arthritis Rheum. 2009;61(10):1462–1466.

[20] Costenbader KH, Feskanich D, Stampfer MJ, Karlson EW. Reproductive and menopausal factors and risk of systemic lupus erythematosus in women. Arthritis Rheum. 2007;56:1251–1262.

[21] Buyon JP, Petri MA, Kim MY, et al. The effect of combined estrogen and progesterone hormone replacement therapy on disease activity in systemic lupus erythematosus: A randomized trial. Ann Intern Med. 2005;142:953–962.

[22] Scofield RH, Bruner GR, Namjou B, et al. Klinefelter's syndrome (47, XXY) in male systemic lupus erythematosus patients: Support for the notion of a gene–dose effect from the X chromosome. Arthritis Rheum. 2008;58:2511–2517.

[23] KOLE AK, GHOSH A. CUTANEOUS MANIFESTATIONS OF SYSTEMIC LUPUS ERYTHEMATOSUS IN A TERTIARY REFERRAL CENTER Indian J Dermatol [online] 2009, 54(2):132-136

[24] WYSENBEEK AJ, GUEDJ D, AMIT M, WEINBERGER A. Rash in systemic lupus erythematosus: prevalence and relation to cutaneous and non-cutaneous disease manifestations. Ann Rheum Dis [online] 1992 Jun, 51(6):717-719

[25] Roman MJ, Shanker BA, Davis A, et al. Prevalence and correlates of accelerated atherosclerosis in systemic lupus erythematosus. N Engl J Med 2003; 349: 2399–406.

[26] Asanuma Y, Oeser A, Shintani AK, et al. Premature coronary-artery atherosclerosis in systemic lupus erythematosus. N Engl J Med 2003; 349: 2407–15.

[27] El-Magadmi M, Bodill H, Ahmad Y, et al. Systemic lupus erythematosus: an independent risk factor for endothelial dysfunction in women. Circulation 2004; 110: 399–404.

[28] Wajed J, Ahmad Y, Durrington PN, Bruce IN. Prevention of cardiovascular disease in systemic lupus erythematosus—proposed guidelines for risk factor management. Rheumatology (Oxford) 2004; 43: 7–12.

[29] Cooper GS, Dooley MA, Treadwell EL, St Clair EW, Gilkeson GS. Hormonal and reproductive risk factors for development of systemic lupus erythematosus: results of a population-based, case-control study. Arthritis Rheum 2002; 46: 1830–39.

[30] Mok CC, Lau CS,Wong RW. Use of exogenous estrogens in systemic lupus erythematosus. Semin Arthritis Rheum 2001; 30: 426–35.

[31] DeGiorgio LA, Konstantinov KN, Lee SC, Hardin JA, Volpe BT, Diamond B. A subset of lupus anti-DNA antibodies cross-reacts with the NR2 glutamate receptor in systemic lupus erythematosus. Nat Med 2001; 7: 1189–93.

[32] American College of Rheumatology Ad Hoc Committee on Systemic Lupus Erythematosus Guidelines. Guidelines for referral and management of systemic lupus erythematosus in adults. Arthritis Rheum.1999;42:1785–1796.

[33] Bertsias GK, Ioannidis JPA, Arlinger M, et al. EULAR recommendations for the management of systemic lupus erythematosus. Report of a Task Force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics. Ann Rheum Dis. 2008;67:195–205.

[34] Thatayatikom A, White AJ. Rituximab: A promising therapy in systemic lupus erythematosus. Autoimmun Rev. 2006;5:18–24.

[35] Lu TY, Ng KP, Cambridge G, et al. A retrospective seven-year analysis of the use of B cell depletion therapy in systemic lupus erythematosus at University College London Hospital: The first fifty patients. Arthritis Rheum. 2009;61:482–487.