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A Review on Awareness and Knowledge Gaps of Systemic Lupus Erythematous

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Abstract

➢ *Background:*
Severe multisystem autoimmune illnesses known as Systemic Lupus Erythematosus (SLE) can harm nearly all body systems. Although it is regarded as a typical case of autoimmunity, but very little is known about it.

➢ *Objective:*
Immunosuppressive medication treatment is difficult since unexpected flare-ups and remissions, characterize the underlying illness and many of the medications are somewhat vague. Based on recent research, this review offers a thorough and up-to-date overview of SLE. This synopsis of fundamental and translational science also comprises the causes of *lupus nephritis*, the current global mortality rate of SLE patients and problems experienced by pregnant SLE women.

➢ *Study design:*
Current recommendations and treatment options, as well as improvements in diagnosis and categorization, are included in this clinical science overview. An analysis of the clinical trials of the last five years' worth of SLE is also included in this report.

➢ *Conclusion:*
Potential future directions and current known and unknown are reviewed and included the findings in this article. Cost of the treatment of SLE in various nations is denoted as another challenge in this illness. All this evaluation has been done to create an awareness among the people about the updated state of the disease for a better control of this disease.

Keywords: *Systemic Lupus Erythematosus (SLE), Awareness, Treatment, Patient Care, Cost, Mortality, Risk in Pregnancy.*

I. INTRODUCTION

Systemic Lupus Erythematosus (SLE) is a heterogeneous autoimmune disease that causes immune system dysfunction. Antinuclear antibodies that bind self-antigens produce immune complexes that accumulate in tissues, causing inflammation and damage to several organs. This is how SLE develops.[1] Even within the same organ, heterogeneity in inflammatory pathways and clinical presentations might delay diagnosis and make it more difficult to generate objective disease activity measurements and plan effective therapeutic trials.[2] Its onset is often insidious, with clinical evident developed over the years, mostly between 3 to 7 years. At early stages, many patients present with only a few features that can resemble other autoimmune, infectious, or hematological diseases. Diagnostic delay of these may lead to delayed treatment initiation, which may increase the likelihood of organ damage and affect short- and long-term outcomes.[3] Even with some significant advances in the understanding of SLE, the prevalence of the disease remains unexplained, with a 1:9 male-female ratio, and it has also been found that the incidence of SLE is highest in women during their early reproductive years.[4] From 2000 to 2015, SLE was listed as the underlying or contributing cause of death in 28,411 female fatalities. SLE was

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included as one of the top 20 causes of mortality for females aged 5 to 64. SLE was listed as an underlying or contributing cause of death in 28,411 women from the period of 2000 to 2015 and included as one of the top 20 causes of death for women aged 5 to 64 years.[5]

This article aims to raise awareness among people so that patients can be diagnosed early and save their lives, to inform about the recent discoveries of the treatment systems of this disease and to improve the quality of life of SLE patients.

II. METHOD

In this review, a search was conducted across literature databases published between 2019 and 2024. The information's were evaluated after collected from Embase, MEDLINE, SUB Library, A meta-analysis article, newspapers, ScienceDirect, PubMed, Google Scholar, and other related books as well as original research papers and analysis review papers.

➢ *Survey Analysis of the Databases*

There are four (04) types of Lupus. Systemic lupus erythematosus (SLE), drug-induced lupus, cutaneous lupus, and neonatal lupus are the four primary forms of lupus. The most prevalent kind of lupus is SLE. Since SLE is a chronic ailment, if it is not well treated, it will become worse. Some drugs can cause drug-induced lupus, which symptoms are comparable to those of SLE, but they disappear when the patient stops taking the medication. Cutaneous lupus results, when the immune system attacks the skin and sun exposure damages skin cells. Children born from mothers with autoimmune diseases like Sjogren's syndrome or lupus can develop neonatal lupus.[6]

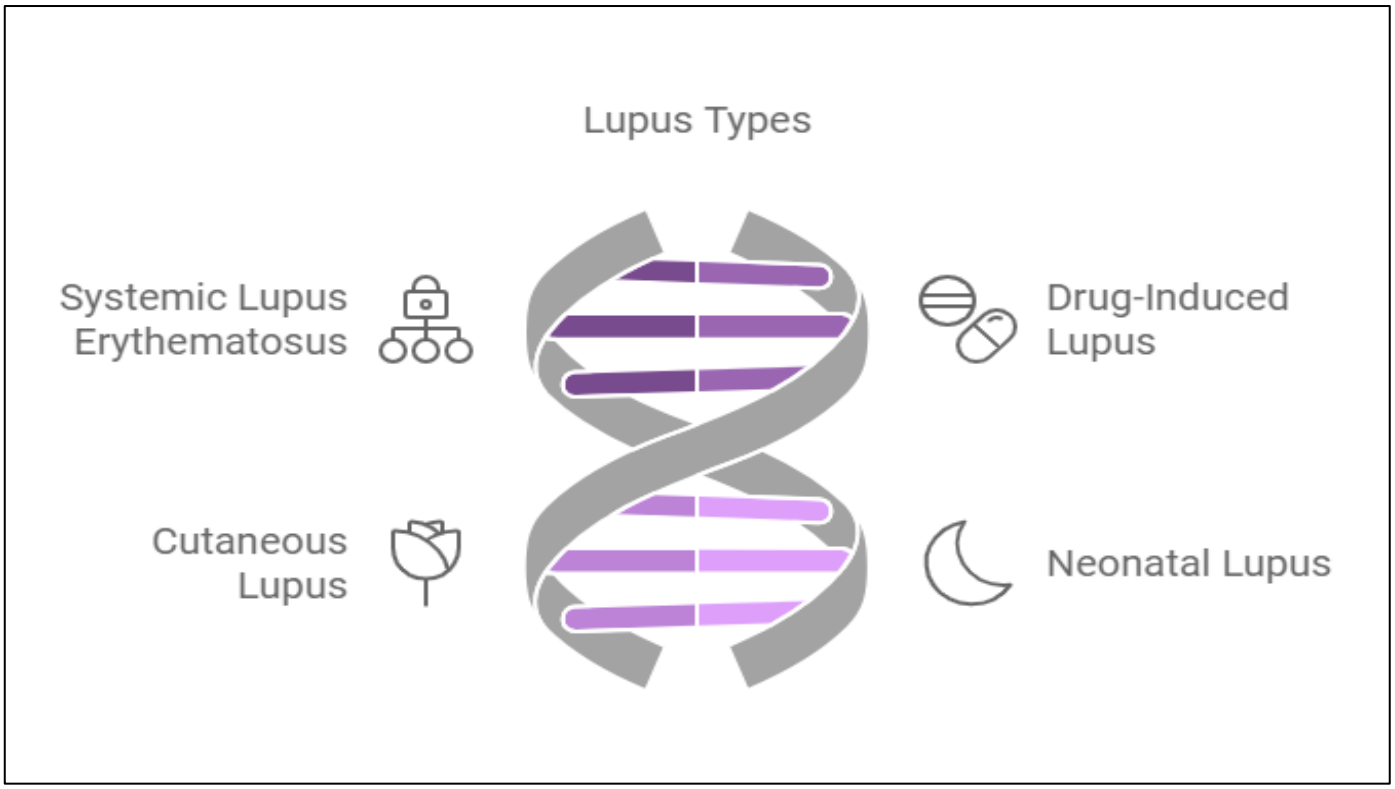

Fig 1 Survey Analysis of the Databases

Lupus has a complex etiology that includes hormonal, environmental, and genetic variables.[7] Autoimmune dysfunction is the etiology of SLE, which results in inflammation. Anemia, lymphopenia, exhaustion, mental symptoms and involvement of several organs are among the symptoms, which lead to a worse quality of life and a higher use of health services.[8] Renal problems, pleuritis, pericarditis, joint discomfort, and ocular symptoms including keratitis, keratoconjunctivitis sicca, and retinal abnormalities like cotton wool patches are also the most common manifestation of SLE.[9] The nervous system is one of the major organs affected in patients with systemic lupus erythematosus (SLE). One challenge that clinicians often face in the diagnosis and management of patients with NPSLE is that its presentation can be highly variable, ranging from common and nonspecific features, such as headache, cognitive abnormalities and mood disorders, to rare presentations including Guillain–Barré syndrome and autonomic dysfunction.[10] Systemic lupus erythematosus (SLE) can also cause by an apoptotic malfunction that produces autoantibodies. Myocarditis and an elevated risk of myocardial infarction as a result of immunological onslaught and persistent inflammation are among the symptoms.[11] Psychological symptoms associated with lupus, such as acute confusional state, mood disorders, anxiety disorders, psychosis, and cognitive impairment. Although the precise causes of lupus are unknown, they may include immunological dysregulation, adverse drug reactions, and psychological stresses, such as systemic symptoms, cutaneous lesions, and butterfly rash.[12] Anti-phospholipid antibodies, complement deficits, and autoimmune reactions are among the causes, which can

result in various clinical manifestations and possible consequences.[13]

In addition, when lupus autoantibodies affect parts of the kidneys named Lupus nephritis. This causes swelling and irritation of the kidneys, called inflammation. It might lead to blood in the urine, protein in the urine, high blood pressure, kidneys that don't work well or even kidney failure. According to the International Society of Nephrology/Renal Pathology Society (ISN/RPS) 2003 classification system lupus nephritis classified into six classes. These are, Class I: Minimal mesangial lupus nephritis, Class II: Mesangial proliferative lupus nephritis, Class III: Focal lupus nephritis. Class IV: Diffuse lupus nephritis. Class V: Lupus membranous nephropathy. Class VI: Advanced sclerosing lupus nephritis.[14]

III. TREATMENT AND MANAGEMENT

Currently some biologic medicines such as belimumab and rituximab, corticosteroids, methotrexate, cyclophosphamide, mycophenolate mofetil, and azathioprine are available for the treatment of lupus. Biologics have shown promise, but more researches are necessary to ensure the best possible therapy outcomes.[15] Although the information presented does not provide exact efficacy rates. Recent studies on belimumab, voclosporin, obinutuzumab, and anifrolumab in lupus nephritis and SLE indicate enhanced efficacy through better research designs.[16] The only FDA-approved drugs for treating cutaneous lupus erythematosus are hydroxychloroquine and glucocorticoids. There are several off-label therapies are also available, but their effectiveness varies, and many of them are not covered by insurance in developed countries, which puts a financial strain on patients.[17] Some other treatment options for SLE include immunosuppressants, antimalarial drugs, and NSAIDs. The need for better therapeutic approaches is revealed by the fact that conventional medicines may not work for all individuals and might result in serious organ damage.[18]

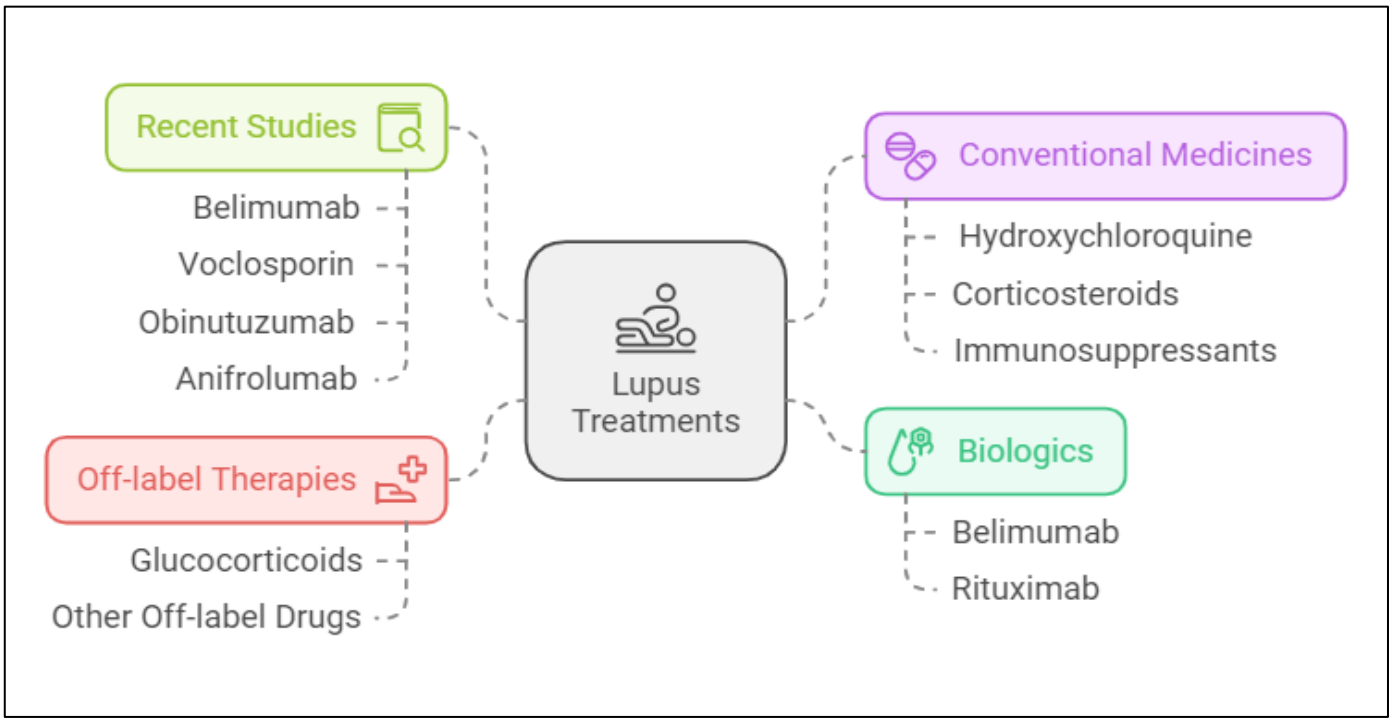

Fig 2 Treatment and Management

➢ *Mortality Rate in SLE*

According to current trends, systemic lupus erythematosus (SLE) patients' 5-year mortality risk is declining with time, although excess mortality still exists, especially in those under 50, where the 10-year relative risk is still greatest.[19] Throughout the research periods, the 10-year relative risk of younger patients rose from 3.6 to 4.9, indicating the persistence of excess mortality.[20] Age-related increases in risk are evident in the death rate for SLE, which is 1,262.62 per 100,000 person-years with notable variation, such as 520.47 for teenagers (10–19 years) and peaking at 7,252.06 for elderly patients (70–79 years).[21] According to the study, 21% of the cohort passed away, and the reasons for mortality had a bimodal distribution. Cardiovascular illness was connected to later deaths, but cancer, and infection were linked to early deaths in SLE, which were more prevalent in men.[22] Adult-onset SLE has a higher standardized mortality rate (SMR) of 1.8, but juvenile-onset SLE has a peak SMR of 7.2, which falls as diagnostic age increases.[23] There are no statistically significant variations in the overall death rate across the various age groups of patients with SLE, which is 2.09 cases/ 100 patient-years for men and 1.39 cases/100 patient-years for females.[24] SLE patients in the research had an overall in-hospital death rate of 25.5%. 75% of the observed mortality cases were caused by infection, making it the most prevalent cause of death.[25] The study found that the death rates varied significantly depending on disease activity, with low-moderate disease activity having a rate of 7.7/1000 person-years and severe activity having a rate of 14.0/1000 person-years.[26] Lupus nephritis was the cause of 8,899 fatalities between 1999 and 2019. Compared to

other demographic categories, females, older adults, and non-Hispanic Black people had much higher age-standardized mortality rates, especially in big central metro regions.[27]

According to the study, the mortality rate for lupus patients in Bangladesh was 2.17%; neither infection nor cancer were cited as causes of death. This is less than the global norm, where a variety of problems can cause fatality rates to surpass 10%.[28]

Males had a greater death rate (2,718.86) than females (1,060.57) for Korean patients with SLE, which was 1,262.62 per 100,000 person-years. The primary cause of mortality was SLE itself.[21]

➢ *Systemic Lupus Erythematosus (SLE) in Pregnancy*

Maternal mortality, antiphospholipid syndrome problems, preeclampsia, and flare-ups of the illness are common pregnancy consequences of lupus.[29] Premature delivery, Polyhydramniosis, and gestational diabetes mellitus are all examples of lupus during pregnancy.[30] Preterm labor, hypertension, placental insufficiency, and fetal death are also common pregnancy problems associated with lupus.[31] Renal impairment, opportunistic infections, sepsis, preeclampsia, IUGR, IUFD, stillbirth, preterm delivery, and congenital heart disorders are all associated with lupus during pregnancy.[32] To protect the safety of both the mother and the fetus, management entails prompt relapse therapy, distinguishing preeclampsia from lupus nephritis, and providing specialized care for antiphospholipid syndrome.[29] For individuals with lupus nephritis, management entails continued use of hydroxychloroquine, low-dose corticosteroids, aspirin, and effective contraception.[33] To reduce risks and guarantee the health of both the mother and the fetus, management involves careful observation and cooperation between medical professionals.[30]

➢ *Mortality Rate in Pregnancy*

In pregnancies with SLE, the reported fetal fatality rate is 19.5%. There has been no change in the overall death rate over time, suggesting that worries about the fetal outcomes of SLE pregnancies have not gone away.[34] In a study, 17 maternal fatalities occurred in pregnant women with SLE and lupus nephritis; the reasons were pulmonary embolus (11.8%), infection (41.2%), illness flare-up (29.4%), adrenal failure (5.9%), and cardiomyopathy (5.9%).[35] The research found two infant fatalities preterm delivery time, in 84 pregnant women.[36] Although there has been progress but the rate of fetal death is still alarming. About 19.5% of fetal loss in pregnancies.[37] Some studies show a decrease in maternal mortality rates, with in-hospital fatalities falling from 442/100,000 admissions (1998-2000) to fewer than 50/100,000 (2013-2015), even though SLE pregnancies are still regarded as high-risk due to possible complications.[38]

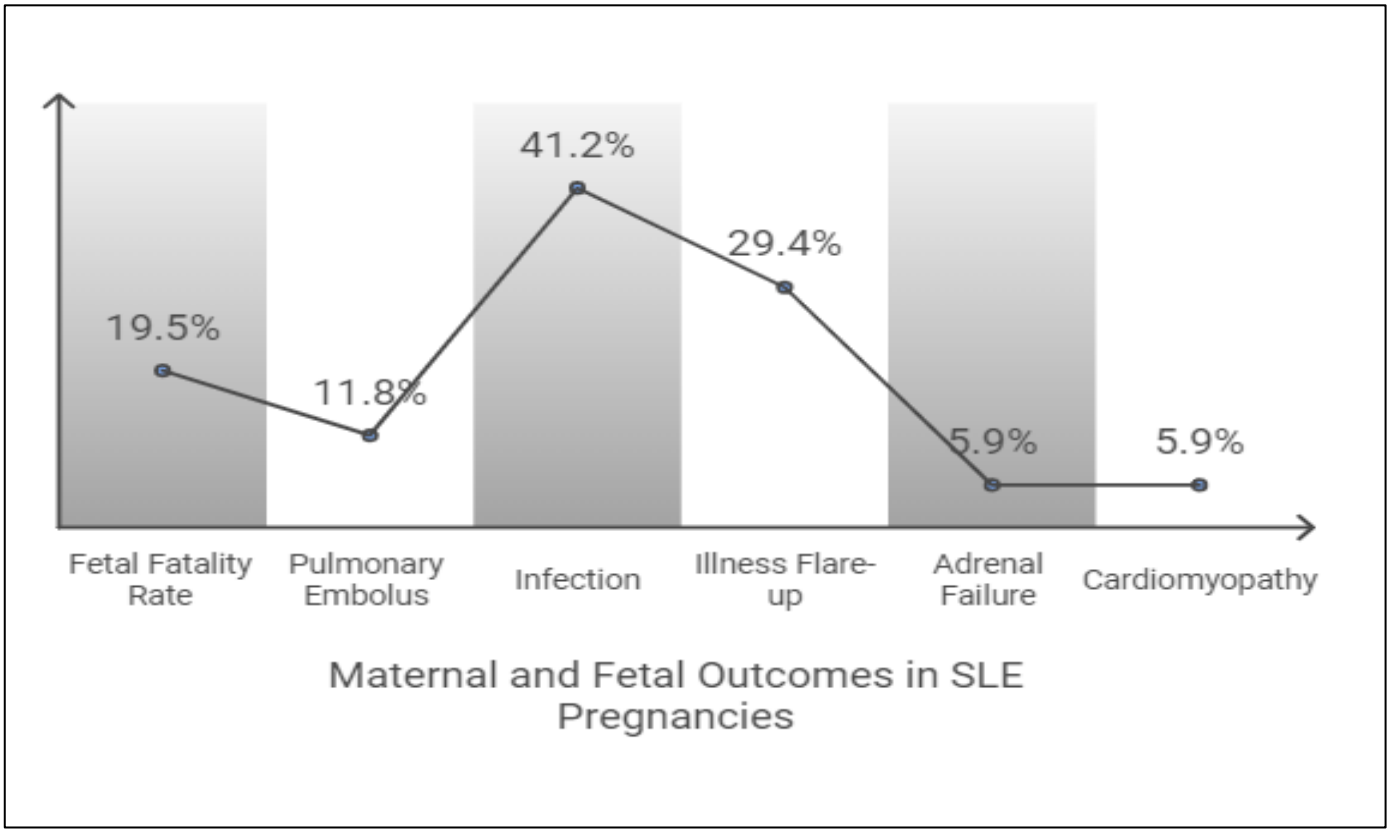

Fig 3 Mortality Rate in Pregnancy

➢ *Diagnosis of Lupus*

Common diagnostic challenges include clinical heterogeneity, unpredictable disease course, and lack of pathognomonic features. Overcoming these pitfalls requires careful clinical evaluation, awareness of serologic autoimmunity indicators, and reliance on updated classification criteria to support accurate diagnosis. Early diagnosis of SLE remains a significant challenge.[39] Diagnosis of SLE using a magnetic bead-based immunofluorescence assay (IFA) with human-derived

double-stranded DNA antigens, achieving 71.9% accuracy, surpassing the conventional chemiluminescent immunoassay (CIA) accuracy of 65.3%. But CIA has low specificity due to varied dsDNA sources.[40] It focuses on the lupus band test (LBT), which shows a sensitivity of 56.5% and specificity of 88.2% for diagnosing SLE in inconclusive cases.[41] Serologic assays that monitor disease activity and validate lupus diagnosis include ANA, anti-dsDNA, and complement levels. The role of laboratory testing in diagnosing and determining organ involvement is the main focus, with little particular attention paid to imaging techniques.[42]

Women are 9 times more likely to develop lupus than men. Lupus can be caused by genetic or hereditary factors, environmental factors, air pollution, smoking, taking birth control pills, hormonal influences, and infection with certain viruses that increase the risk of developing lupus. The hereditary contributions to the disease's gender bias are highlighted, with little attention paid to hormonal influences.[43] Estrogen is thought to be harmful in SLE and boosts type I immunological responses, which increases the risk of developing the illness. In females, hormonal changes throughout the menstrual cycle and pregnancy might change the activity for the disease and worsen symptoms of SLE.[44] The immune system's control is greatly influenced by sex hormones, especially estrogen, which is why SLE is more common in women.[45] Estrogen boosts immunological responses, which may protect males against autoimmune illnesses. One of the hormonal elements leading to SLE is men's decreased estrogen levels, which are linked to immune-stimulatory effects. Genetic variables include the X chromosome, which increases a woman's vulnerability to autoimmune illnesses like lupus when it is overexpressed.[46]

- *Prevention of SLE*

Systemic lupus erythematosus (SLE) can be avoided by using natural plant metabolites as immunomodulators and intracellular signaling regulators. These metabolites provide a comprehensive therapeutic strategy by focusing on signaling cascades, proinflammatory cytokine generation, and B-T cell co-stimulation.[47] Omega-3 polyunsaturated fatty acids (PUFAs) have been proposed as a viable preventative measure for SLE, emphasizing their ability to improve neuromotor, cardiovascular, depressive, and inflammatory symptoms, thereby increasing patient quality of life and overall disease management.[48] A secretum produced from mesenchymal stem cells that successfully protects lupus by reducing proteinuria, increasing body weight, and encouraging anti-inflammatory cytokines such as TGF-β1 and IL-10, while also reducing inflammatory cell activity and lupus nephritis.[49] Minimizing immunosuppressive agents to reduce infection risk, routine vaccinations to prevent infections, vigilant screening for cardiovascular disease, and addressing osteoporosis. These strategies aim to effectively manage long-term comorbidities and complications associated with SLE.[50] By determining organ involvement and tracking the effects of the disease and treatment, laboratory tests including antinuclear antibody, anti-dsDNA, as well as imaging techniques like chest X-rays and CT scans, are crucial for diagnosing lupus.[51]

- *The Role of Vitamin D in Pediatric SLE*

The percentage of SLE patients with vitamin D levels < 20 ng/ml is around 41.5%.[52] According to current knowledge, hypovitaminosis D may enhance oxidative stress, intensify inflammatory processes, and modify immunological function, all of which may increase the frequency and severity of lupus flares in children with pSLE.[53] Given that vitamin D insufficiency is common in female SLE patients and is linked to higher levels of inflammatory activity and the degree of organ damage, there may be a connection between low vitamin D levels and flare-ups of lupus that merits more research.[54] Genetically determined SLE has a detrimental impact on vitamin D levels, indicating that vitamin D deficiency may be linked to SLE rather than lupus flares.[55] The pathophysiology and activity of SLE are significantly influenced by vitamin D deficiency and treatment may improve inflammatory and hemostatic indicators, improving clinical outcomes and lowering flare-ups of SLE.[56] Low vitamin D levels may be linked to more lupus flares, especially in patients receiving steroid therapy, since there is a negative correlation between vitamin D deficiency and disease activity in childhood-onset SLE.[57] There may be a connection between low vitamin D levels and more lupus flares since vitamin D deficiency is linked to greater disease activity (SLEDAI) and damage accrual (SDI) in individuals.[58]

- *Cost of SLE Treatment*

According to 2002, in Canadian currency, the average cumulative direct expenses per patient over four years in the tri-nation study were CAD 15,845 in Canada, CAD 17,647 in the UK, and CAD 20,244 in the USA.[59] The annual cost of treating SLE in Brazil is US$ 3,123.53 per patient, with notable geographical variations caused by behavioral, social, and biological variables.[60] In 2014, the average yearly direct cost of lupus treatment in Colombia was 2,865 for expectant mothers and young individuals with SLE may incur annual expenses of up to US$ 14,944 in the USA.[61] In the five nations under study—France, Germany, Italy, Spain, and the UK—the average yearly cost of lupus treatments varied from €1436 in Spain to €2542 in France, accounting for 29.7% to 68.1% of overall medical expenses.[62] US$ 42,213 in the UK, underscoring the large disparities in expenses linked to reduced labor market engagement across both nations.[63] The US$ 5,062 yearly medical expenses for SLE patients in Canada. However, because it only considers the Canadian context, it does not reveal typical expenses of lupus therapy in other nations or areas.[64] The average annual per-patient expenditures for lupus treatment were US$ 4853 in Canada, US$ 5285 in the United States, and US$ 4760 in the United Kingdom, after adjusting for demographics, disease duration, activity, damage, and health status.[65]

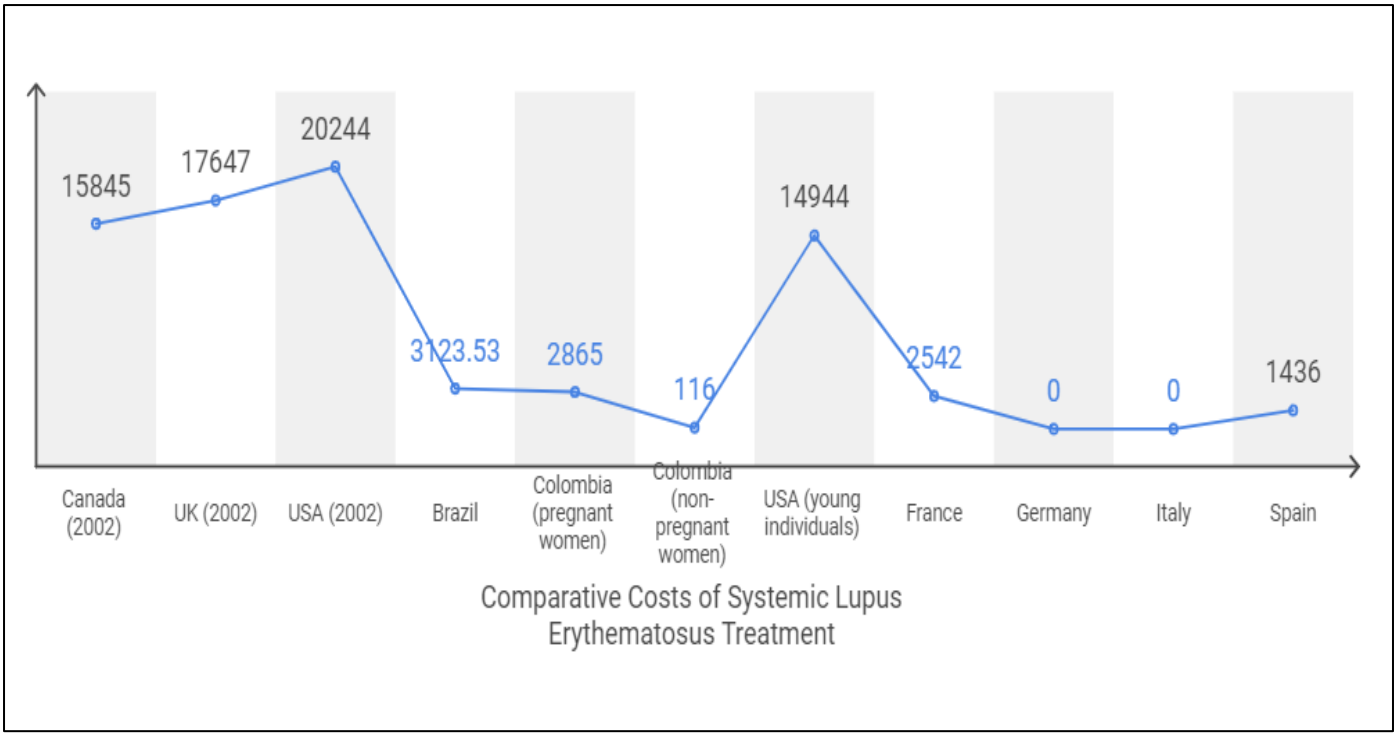

Fig 4 Cost of SLE Treatment

➢ *Systemic Lupus Erythematosus Patient Care*

E-Health interventions have improved health outcomes in patients with SLE, particularly in disease management and emotional status. However, further high-quality studies are needed to assess long-term effects and refine these strategies.[66] Effective strategies for improving health outcomes in lupus patients include targeted immunotherapies, such as monoclonal antibodies and CAR-T therapy, alongside gut microbiota modulation techniques like fecal microbiota transplantation, which may restore immune balance and enhance treatment efficacy.[67] The most effective strategies for improving health outcomes in lupus patients include a multidisciplinary approach involving rheumatologists, gynecologists, psychologists, and nurses, focusing on disease management during pregnancy, enhancing quality of life, and addressing psychological impacts through coordinated care.[68] Effective strategies for improving health outcomes in lupus patients include targeting anti-dsDNA antibodies through B cell-targeted biologics, immunoadsorption, and synthetic mimic peptides, which can reduce autoantibody levels, ameliorate symptoms, and improve renal pathology without significant adverse effects.[69] Omega-3 supplementation, vitamin D supplementation, turmeric supplementation, and a low glycaemic index diet are effective strategies for improving health outcomes in lupus patients, as they reduce inflammation, disease activity, and oxidative stress, while promoting weight loss and reducing fatigue.[70] Ideas and suggestions for better care in the context of SLE, such as prompt diagnosis, information availability, integrated care teams, and extensive treatment choices to improve patients' quality of life.[71]

➢ *Awareness of SLE Patients*

When patients are informed about lupus, they may take part in decision-making, which improves treatment results and adherence. Support from family and caregivers is essential for promoting patient engagement and education.[72] Given the disease's sneaky beginning, prompt medical action can result from awareness of lupus symptoms and the value of early diagnosis.[73] When compared to conventional techniques, new diagnostic tools like the AVISE test have demonstrated an increased probability of an accurate diagnosis and the start of therapy.[74] Specifically, discuss how awareness affects lupus patients' diagnosis and course of therapy. On the other hand, more knowledge could help with early diagnosis and better care, enhancing the overall prognosis and efficacy of therapy.[75]

IV. FINDINGS

Lupus is a deadly disease. There is no warning among people about it. Even developing countries, like Bangladesh, India, Pakistan, and Nepal know less about the treatment. Therefore, they cannot provide better treatment. Many patients die every year because of not knowing the severity of lupus. SLE is a long-term autoimmune condition. Although up to 20% of patients 50 years of age or older may have it, it primarily affects younger women. During pregnancy, SLE can cause high life risk. Women are more affected than men because of the estrogen hormone.

V. DISCUSSION

Nearly every bodily system is impacted by SLE, albeit to differing degrees. The American College of Rheumatology's criteria serve as the basis for the diagnosis. Individualized care is provided based on the symptoms that are exhibited. There is no prevention or vaccine for SLE yet. Since it is an autoimmune disease, it can be treated to strengthen the immune system. A weak immune system is responsible for SLE. Awareness can prevent this phenomenon to a greater extent.

VI. CONCLUSION

We need to create awareness about SLE, especially for women, who face this disease very badly. Most women are not careful and aware about SLE. It's important for not only women but also humans. During pregnancy, pregnant women should adhere to medication while maintaining healthy lifestyles.

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