

# Cardiovascular Manifestations and Therapy Options for Systemic Lupus Erythematosus: A Systemic Literature Review

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## Abstract

Systemic lupus erythematosus (SLE) is an autoimmune multi-systemic disease; it is a controlled disease but is not curable. SLE affects different systems in the body, such as cardiac, renal, respiratory, hematology, neurology, and rheumatology. It can cause various problems in the heart, lungs, and joints. This Systemic review researched articles from 3 databases: PubMed, Google Scholar, and PubMed Central in June 2022. We did this systemic review using Prisma guidelines. We collected this systemic review in the last five years. Free full articles randomized controlled trial (RCT), systemic review articles, and English language included. Other languages and articles earlier than 2017. Joanna Briggs Institute (JBI) checklist, Assessment of Multiple Systemic Reviews 2 (AMSTAR), and Scale for the Assessment of Multiple Systemic Reviews 2 (SANRA) are used to check for quality assessment. In the systemic review, the initial search generated 516 articles. They included 13 in the final selection; six were case reports, two were systemic reviews, three of them retrospective studies, and two were literature reviews.

In this Systemic review, we will focus on the cardiac manifestations associated with systemic lupus erythematosus and use Hydroxychloroquine to prevent the deterioration of systemic lupus erythematosus and decrease the incidence rate cardiac problems. It discovered a decrease in the incidence rate of cardiac manifestations. It found that hydroxychloroquine is effective in the treatment of systemic lupus erythematosus patients. Not only that, but they found that Hydroxychloroquine effectively treats systemic lupus erythematosus patients and limits cardiac risk factors. We need further studies and research to understand the effect of systemic lupus erythematosus on the cardiac system and the effects of Hydroxychloroquine on decreasing the impact of systemic lupus erythematosus on the heart.

**Keywords:** SLE; Lupus; Discoid lupus erythematosus; Autoimmune disease; Hydroxychloroquine; Immune suppressive; Anti-malarial; Plaquenil; Pericarditis; Constrictive pericarditis; Diffuse ST elevation; Pericardiectomy

**Categories:** Internal Medicine, Rheumatology, pharmacological treatment

## Introduction

Autoimmune systemic lupus erythematosus (SLE) is a chronic autoimmune and multi-systemic disease affecting the skin, joints, kidneys, brain, and heart. There is a higher rate of SLE in women compared to men. Systemic lupus erythematosus (SLE) is a multi-systemic disease that impacts the skin, joints, kidneys, brain, and heart. There is a higher rate of SLE in women than men 15:1. Sometimes, SLE presents with initial symptoms such as fever, joint pain, and rash, which affect the speed of diagnosis [1].

Pericardium, myocardium, coronary arteries, and valves, but acute pericarditis is the most common cardiac problem that can affect SLE patients [2].

Cardiac symptoms are different, which include pain, dyspnea, fatigue, leg swelling, and palpitations [3].

They consider lupus myocarditis a rare manifestation of SLE. Still, it is life-threatening, and corticosteroid usage treats SLE if it is mild, but it requires mechanical support if it is severe [4].

Half of SLE patients get cardiac manifestation and 1/3 of dying causes in SLE patients due to cardiac diseases [5].

Lupus myocarditis can be the first manifestation during a follow-up visit, mainly if the patient isn't treated well [6].

Also, some articles report that SLE patients could present with cardiac manifestation symptoms [[7\_13]. As systemic lupus erythematosus (SLE) is more common in females, males are more likely to have aggressive symptoms; there are not enough studies to prove that [14].

Intravenous Immunoglobulin (IVIG) is helpful in the treatment of autoimmune diseases, so it is beneficial for SLE patients [15].

Because of the cardiac problems that can happen in SLE patients and how it is more common to occur as a lethal cause in young SLE patients, hence, it is essential to know more about the cardiac effect on SLE patients and how we can limit it by using Hydroxychloroquine.

Although many studies support the use of Hydroxychloroquine in SLE patients and how it decreases the cardiovascular risk factors, on the other hand, many studies focus on the cardiac side effects of Hydroxychloroquine, and others reduce the beneficial impact of hydroxychloroquine as sudden withdrawal of it does not flare SLE manifestations.

In this systemic review, we focus on the Hydroxychloroquine effect on SLE patients and how it improves cardiac outcomes and decreases the mortality rate due to cardiac risk.

### Method

This systemic review conducts based on the selected reporting items for systemic reviews and Meta-Analyses (PRISMA) 2020 guidelines.

### Eligibility criteria

The studies were selected based on the elements of patients, intervention, and outcomes (PIO). Patients (Systemic lupus erythematosus patients), intervention (Hydroxychloroquine use), and the results (Hydroxychloroquine effects on systemic lupus erythematosus patients)

Inclusion criteria in the study are English-language, free full-text articles Published between 2017 and 2022, randomized controlled trials (RCT), and Systemic reviews and Meta-Analyses.

**Exclusion criteria:** Languages other than English and articles published before 2017.

### Databases and search strategy

The search was collected systematically using PubMed, PubMed Central, and Google Scholar. The research was done in June 2022. This systemic review did a search based on the keyword. The study was done in June 2022. This systemic review did a search based on the keywords used in the previous literature and through Medical Subject Headings (Mesh), depending on the three databases used, as seen in the table below.

**Table 1:** The bibliographic search strategy in 3 databases with their filters.

Databases	Keywords	Search strategy	filters	Search results
PubMed	SLE, lupus, discoid lupus erythematosus, autoimmune disease, hydroxychloroquine, immune suppressive, anti-malarial, Plaquenil, pericarditis, constrictive pericarditis, diffuse ST elevation, pericardiectomy	#1 SLE OR lupus OR discoid lupus erythematosus OR auto immune disease OR ( "Lupus Erythematosus, Systemic/complications"[Mesh] OR "Lupus Erythematosus, Systemic/drug therapy"[Mesh] OR "Lupus Erythematosus, Systemic/pathology"[Mesh] OR "Lupus Erythematosus, Systemic/physiopathology"[Mesh] OR "Lupus Erythematosus, Systemic/prevention and control"[Mesh] OR "Lupus Erythematosus, Systemic/therapy"[Mesh] ) #2 Hydroxychloroquine OR immune suppressive OR anti-malarial OR Plaquenil OR ( "Hydroxychloroquine/administration and dosage"[Mesh] OR "Hydroxychloroquine/adverse effects"[Mesh] OR "Hydroxychloroquine/pharmacokinetics"[Mesh] OR "Hydroxychloroquine/therapeutic use"[Mesh] ) #3 pericarditis OR constrictive pericarditis OR diffuse ST elevation OR pericardiocentesis OR pericardiectomy OR ( "Pericarditis/diagnosis"[Mesh] OR "Pericarditis/diagnostic imaging"[Mesh] OR "Pericarditis/etiology"[Mesh] OR "Pericarditis/physiology"[Mesh] OR "Pericarditis/physiopathology"[Mesh] ) OR "Pericarditis/prevention and control"[Mesh] ) #4 #1 AND #2 AND #3 -1054	Last five years, free full text	444
Google Scholar	Systemic lupus erythematosus hydroxychloroquine pericarditis	Systemic lupus erythematosus AND hydroxychloroquine. AND pericarditis -6120	2017-2022	28
PubMed Central	Systemic lupus erythematosus hydroxychloroquine pericarditis	Systemic lupus erythematosus AND hydroxychloroquine AND pericarditis -176	2017/6/30-2022/6/30	57

The studies, in the beginning, were reviewed based on abstracts and titles, and irrelevant articles were excluded. Because of the lower number of systemic reviews, narrative reviews, and meta-analysis reviews in the study, the researchers decided to include them. All references were gathered and alphabetized using Microsoft Excel 365 for duplicate removal.

### Risk of Bias in each study

All included studies assess for quality checks and the probability of risk bias by assess for quality checks and the likelihood of risk bias by using tools depending on each study: case report study, Joanna Briggs Institute (JBI) Critical Appraisal Checklist[17].

Systemic reviews and Meta-analyses, Assessment of Multiple Systemic Reviews 2 (AMSTAR)[18]. cohort studies, Newcastle Ottawa (NOS) [19], and Narrative reviews and Scale of the assessment of Narrative review Articles 2 (SANRA2)[20]. Each quantity assessment tool has its own criteria and scoring. Give 1 point when scoring minimal risk is (yes) or (partial yes) and give 2 points if two points are required.

**Table 2:** Quality assessment of all the studies included in this systemic review

Quality Assessment Tool	Type of study	Items and their characteristics	Total score	Accepted score (>70%)	Accepted studies
JBI	Case report	Eight items: 1. Were the patient's demographic characteristics clearly described? 2. Was the patient's history clearly described and presented as a timeline? 3. Was the current clinical condition of the patient in the presentation clearly described? 4. Were diagnostic tests or assessment methods and the results clearly described? 5. Was the intervention(s) or treatment procedure(s) clearly described? 6. Was the post-intervention clinical condition clearly described? 7. Were adverse events (harms) or unanticipated events identified and described? 8. Does the case report provide takeaway lessons?	8	6	Antonius Anis, 2022 Hannah Jethwa, 2019 Neil P Larson, 2019 Nicole Marjjanovich and Alexandra Halalau, 2018 Jaydeep J Raval, 2021 Sohaib Tariq, 2017

Quality Assessment Tool	Type of study	Items and their characteristics	Total score	Accepted score (>70%)	Accepted studies
AMSTAR 2	Systemic review and Meta-analysis	Sixteen items: 1. Did the research questions and inclusion criteria for the review include the components of PICO? 2. Did the report of the review contain an explicit statement about the established review methods prior to the conduct of the review and did the report justify any significant deviations from the protocol? 3. Did the review authors explain their selection of the study designs to include in the review? 4. Did the review authors use a comprehensive literature search strategy? 5. Did the review authors perform the study selection in duplicate? 6. Did the review authors perform data extraction in duplicate? 7. Did the review authors provide a list of excluded studies and justify the exclusions? 8. Did the review authors describe the included studies in adequate detail? 9. Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review? 10. Did the review authors report on the sources of funding for the studies included in the review? 11. by performing meta-analysis, did the review authors use methods for statistical combination of results? 12. By performing meta-analysis, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis? 13. Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review? 14. Did the review authors satisfactorily explain, and discussion of, any heterogeneity observed in the results of the review? 15. If they performed quantitative synthesis, did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its impact on the results of the review? 16. Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	6	12	Dan Liu, 2018 Suliyah Hu, 2021
NOS	Cohort study	Eight items: 1) Representativeness of the exposed cohort 2) Selection of the non-exposed cohort 3) Ascertainment of exposure 4) Demonstration that outcome of interest was not present at start of study 5) Comparability of cohorts based on the design or analysis 6) Assessment of outcome 7) Was follow-up long enough for outcomes to occur 8) Adequacy of follow up of cohorts	8	6	Risa Wakiba, 2020 Rubi Fernandez Ruiz, 2020 Guillemette Thomas, 2017
SANRA 2	Narrative review	Six items: 1. Justification of the article's importance to the readership 2. Statement of concrete aims or formulation of questions 3. Description of the literature search 4. Referencing 5. Scientific reason 6. Appropriate presentation of the data	6	4	Kayla Meridor, 2021 Mohammed Ezat Amin, 2021

- JBI: Joanna Briggs Institute
- AMSTAR 2: Assessment of Multiple Systemic Reviews 2
- NOS: Newcastle Ottawa Scale
- SANRA: Scale for the Assessment of Multiple Systemic Reviews 2
- ROB: Risk of Bias

### Data Collection and Analysis

Due to the difference Between the trials regarding the participants, interventions that did, and results and outcomes, we analyzed all the studies in this systemic review. We differentiated them into clinical trials and reviews.

### Results

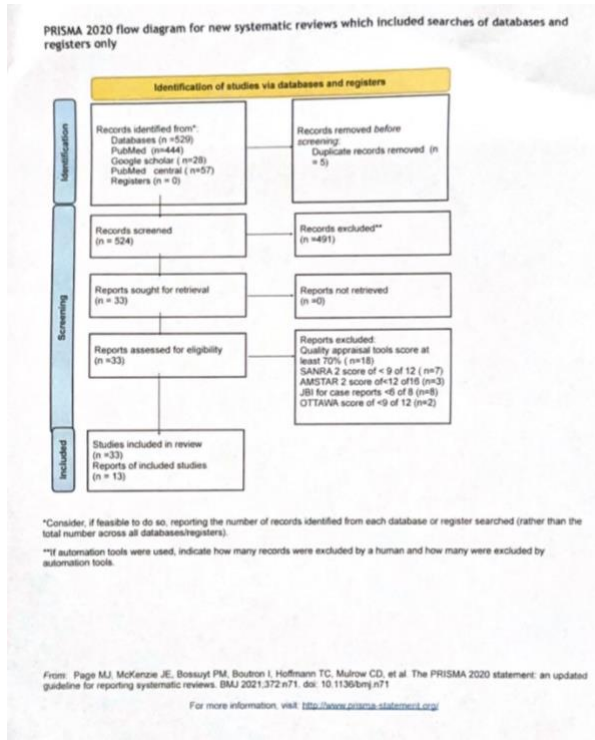
The figure below shows the Prisma flow diagram for this systemic review. In this systemic review, the total number of articles is 529, collected from three databases PubMed, Google Scholar, and PubMed Central. After that, we removed five duplicates. After that, 491 articles were excluded by titles. After that, we did the quality check on the remaining 33 articles. 20 papers excluded by the quality check and 13articles used in this systemic review. Six studies were case reports, four systemic reviews and meta-analyses, three cohort studies, and two narrative reviews.

Number of the study	Title of the study	Result
1.	Cardiac Tamponade in an 18-year-old Male with Undiagnosed Systemic Lupus Erythematosus	An 18-year-old previously healthy male who visited the emergency room complaining of abdominal pain and hematochezia was the subject of this investigation. After further testing, the diagnosis of SLE was confirmed. The first workup revealed a significant pericardial effusion with tamponade pathogenesis, necessitating an urgent pericardiocentesis. Although SLE frequently shows no symptoms at all, the disease may first manifest as cardiac tamponade.

2.	Hemorrhagic Tamponade as Initial Manifestation of Systemic Lupus with Subsequent Refractory and Progressive Lupus Myocarditis Resulting in Cardiomyopathy and Mitral Regurgitation	Higher corticosteroid doses are frequently administered as intravenous boluses in more severe cases or when cardiac tamponade is present, for example, 1 gram of methylprednisolone daily for three days. Chronic immunosuppression with methotrexate, azathioprine, or mycophenolate mofetil, along with intravenous immunoglobulin usage, may be advantageous in individuals with recurrent pericarditis. While using azathioprine in our case, the patient's underlying condition gradually worsened. With the help of mycophenolate mofetil, the disease's general development was stopped, but the myocardium's active inflammation persisted. The patient's underlying myocardial inflammation didn't disappear until after undergoing cyclophosphamide therapy, which improved her ejection fraction and level of mitral regurgitation.  The use of earlier and more aggressive immune therapy justifies itself in patients who present with severe, life-threatening cardiac involvement because doing so will help achieve and maintain disease resolution and improvement in ejection fraction.
3.	SLE strikes the heart! A rare presentation of SLE myocarditis presenting as cardiogenic shock	Myocarditis, which can gradually lead to cardiac shock, can be a symptom of systemic lupus erythematosus. However, both immune therapy and supportive care can improve this symptom.

4.	Myocarditis due to systemic lupus erythematosus associated with cardiogenic shock	The most popular kind of treatment for lupus myocarditis is high-dose corticosteroid therapy. However, there are very few instances of lupus myocarditis presenting as cardiogenic shock requiring mechanical support, despite the fact that it seems to be an effective first treatment leading to an improvement in left ventricular function in hemodynamically stable patients. Azathioprine, cyclophosphamide, rituximab, and intravenous immunoglobulins are further medications utilized in therapy. Rituximab, glucocorticoids, and intravenous immunoglobulins were used to treat our patient, but minimal improvement in left ventricular function was seen as a result.
5.	Cardiovascular System involvement in systemic lupus erythematosus (SLE)	exercise and resting ECGs are the most common methods for finding CAD in lupus. Atherosclerotic plaque imaging is thought to aid in diagnosis as well. Imaging procedures can be both invasive and non-invasive. The best imaging method that is invasive is angiogram. The non-invasive methods include MRI, CT, and B-mode ultrasound.
6.	Lupus Myocarditis: Initial Presentation and Longterm Outcomes in a Multicentric Series of 29 Patients	Lupus myocarditis is a severe manifestation of SLE. It can be the first manifestation of the disease, or it can occur during follow-up, in particular in untreated patients. However, the Longterm prognosis is typically positive. Patients with less severe disease exhibited good left ventricular ejection fraction (LVEF) recovery without cyclophosphamide (CYC).
7.	Lupus acute cardiomyopathy is highly responsive to intravenous immunoglobulin treatment	Within a few days to a month after therapy, heart function improved clinically and according to echocardiography. This case series leads to the conclusion that IVIg is crucial in the treatment of lupus acute cardiomyopathy. Particularly in extreme circumstances, one should think about this safe, well-tolerated optional treatment.
8.	<a href="#">MSSA Pericarditis in a Patient with Systemic Lupus Erythematosus Flare</a>	<p>Due to the significant prevalence of various pericarditis etiologies, the diagnosis of bacterial pericarditis needs a high index of suspicion. In this instance, the patient's SLE flare was to blame for her pericarditis. The infectious work up was triggered by the patient's fever on day 15 of hospitalization. Later, once MSSA was grown in the pericardial fluid culture, MSSA pericarditis was identified. Delay in diagnosis might be harmful since individuals may develop cardiac tamponade quickly.</p> <p>Surgery drainage for source control is necessary throughout treatment, coupled with antibiotics. In this scenario, the patient needed a drain to be placed for 13 days and a pericardial window to be opened. Subxiphoid pericardiostomy and full drainage are advised in cases of bacterial pericarditis because the purulent fluid tends to re-accumulate.</p> <p>If adhesions form, intrapericardial thrombolysis treatment may be necessary in some circumstances. The survival rate can reach 85% when antibiotics are administered properly (8).</p> <p>Conclusion</p> <p>Even though bacterial pericarditis is a very uncommon infection in the age of antibiotics, certain people are nonetheless at risk of contracting it. Patients can have successful results despite the high death rate if bacterial pericarditis is identified and treated quickly.</p>

9.	Chloroquine and hydroxychloroquine are associated with reduced cardiovascular risk: a systematic review and meta-analysis	Our findings revealed that chloroquine/hydroxychloroquine (CQ/HCQ) was linked to a lower risk of cardiovascular disease (CVD) in rheumatological disease patients.
10.	The Biological Disease-Modifying Antirheumatic Drugs and the Risk of Cardiovascular Events: A Systematic Review and Meta-Analysis	Use of biological disease-modifying antirheumatic drugs (bDMARDs) may be linked to lowered chances of CV events, particularly in RA patients. In bDMARD users with TNF-inhibitors or follow-up beyond a year, the CV events may be less common. To validate findings, more research is required.
11.	Efficacy and Safety of Hydroxychloroquine Therapy for Systemic Lupus Erythematosus Patients Depend on Administration Dose	Patients with SLE who are in the maintenance phase benefit from extra hydroxychloroquine (HCQ) therapy. The skin involvement and composite disease activity indicators were able to be improved by the extra HCQ therapy at both dosages. It's possible that the standard dose of HCQ will have greater results than a smaller dose in lowering the immunological activity of SLE. But in order to prove that the standard dose of HCQ is preferable to low-dose HCQ, big studies are necessary.
12.	Discontinuation of hydroxychloroquine in older patients with systemic lupus erythematosus: a multicenter retrospective study	Withdrawal did not significantly raise the incidence of flares in this retrospective investigation of elderly stable SLE patients on long-term HCQ.
13.	Constrictive Pericarditis as the First Presentation of Systemic Lupus Erythematosus	<p>Despite the fact that infectious or idiopathic conditions are the most frequent causes of constrictive pericarditis, this case shows that connective tissue disorders should also be taken into consideration as a differential diagnosis, particularly in cases where there is no known cause and no improvement after receiving antimicrobial or antiviral medication. Even though constrictive pericarditis is an uncommon symptom of SLE, individuals who have increasing shortness of breath after a normal first echocardiography should be treated with a high index of suspicion. A cardiac MRI and assessment from a cardiologist may be helpful in certain situations to find hidden problems.</p> <p>Five (71%) of patients in this study were male; it is well known that SLE has a female preponderance though male patients with SLE frequently have more severe disease, which may account for the higher proportion of male patients with constrictive pericarditis in our literature review. However, it is difficult to draw conclusions regarding gender prevalence when only seven cases have been reported. Even though corticosteroid medication may partially relieve the symptoms in such individuals with constrictive pericarditis, a pericardiectomy is likely to be necessary for effective treatment. Although a pericardial biopsy may show ambiguous signs of acute or chronic inflammation, it should be carried out whenever feasible to rule out underlying infections.</p>



**Figure 1:** Prisma 2020 flow diagram [16].

- SANRA / Scale of Assessment of Narrative Review Articles 2
- AMSTAR 2/ Assessment of Multiple Systemic Reviews 2
- JBI/Joanna Briggs Institute
- NOS/ Newcastle Ottawa Scale

**Table 3:** Risk of a bias summary of case report studies by review authors

First Author, Year	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8
Sohaib Tariq,2017	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Nicole Marijanovich, 2018	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Hannah Jethwa,2019	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Neil P Larson,2019	Yes	Yes	Yes	Yes	Yes	Yes	NO	Yes
Jaydeep J. Raval, 2021	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

**Table 4:** Results of bias summary of systemic review and Meta-analysis

First author, year	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Item 12	Item 13	Item 14	Item 15	Item 16
	Dan Liu, 2018	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No
Sui yuan Hu, 2021	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	Yes

**Table 5:** results summary of critical risk for cohort studies

First author, year	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8
Guillemette,2017	1	1	1	1	1	1	1	1
Risa Wakiya, 2020	1	1	0	1	1	1	1	1
Ruth Fernandez Ruiz, 2020	1	1	0	1	1	1	1	1

**Table 6:** results summary for critical risk of narrative review.

First author, year	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6
Mohammed Ezzat Amin, 2021	2	1	2	2	2	2
Katya Meridor, 2021	2	2	1	2	2	2

## Discussion

We reviewed many articles that said pericarditis is possible in Systemic lupus erythematosus patients. Also, there are many studies about using hydroxychloroquine in systemic lupus erythematosus patients with cardiac manifestations and how it improves the outcome and decreases the number of hospitalizations. Pericarditis is a prevalent cardiac manifestation and can progress to pericardial effusion and cardiac tamponade. Delay in the treatment of Cardiac tamponade could be fatal, so it is essential to know more about pericarditis to be more aware. Not only does pericarditis happen as a cardiac manifestation in SLE patients, but also myocarditis, valvular disease, and coronary artery disease (CAD) can happen. Myocarditis is rare but fatal; in one study, 2/3 of the patients died because of myocarditis. Hydroxychloroquine is non biological disease-modifying antirheumatic drugs (non bDMARD) that helps control cardiovascular risk factors, so it decreases the incidence of cardiovascular diseases in SLE patients. It is essential to know how Hydroxychloroquine decrease and control cardiovascular risk factors. It is also crucial to know more about other medications and if it is more helpful than Hydroxychloroquine. This systemic review will try to learn more about these subheadings and connect them.

### Pericarditis in SLE patients

Although pericarditis is rare in SLE patients, it can be fatal if it is not diagnosed and treated promptly. Pericarditis can be caused by a variety of factors, including immune suppressants the patient takes or bacterial infections that might occur due to lowered immunity. There are different causes of bacterial infection, which could be Staphylococcus aureus, Mycobacterial tuberculosis, and Neisseria meningitis. The case reported by Anis et al. presented several days of chest pain; she is a 31 -year- old SLE patient; her blood pressure was 204/130 mm. She has normal

swelling in her legs. Her labs showed she had low C3, low C4, high Anti DS Abs, high Anti-Smith, high anti double-strand DNA ( Anti DS Abs), high anti nuclear antibody (ANA) , and high erythrocyte sedimentation rate (ESR), which is 60, creatinine was 1.8, and troponin was normal in 3 separate readings. The transthoracic echo (TTE) and computed tomography angiography (CT angiography ) revealed that she has pericardial effusion. The chest pain, the increase in erythrocyte sedimentation rate ( ESR) , the average troponin level, and the pericardial effusion suggest that she has pericarditis secondary to the SLE flare. In the hospital, treating patient, the patient was treated with antihypertensive drugs, three days of methylprednisolone 0.5 mg/ kg, and then tapered. On day 16 in the hospital, the severity of pain increased, and the troponin level was 2. Another Echo was done, which showed that the size of the pericardial effusion increased, and there was right ventricular collapse during diastole, so she had tamponade. The pericardial window is done and drained of 500cc of purulent fluid. When she left the hospital, she was well and had no complications [21].

Pericarditis can happen in systemic lupus erythematosus patients and can cause pericardial effusion and tamponade, which can cause death if not treated well. These things can happen quickly, as in this case, from the start of pain, and the tamponade is just several days.

Another case reported by Jethwa et al. was a 49-year-old man who presented with a productive cough, lethargy, decreased appetite, and weight loss. His labs showed that he must increase erythrocyte sedimentation rate(ESR) , and His Echo showed he had pleural and pericardial effusion. Misdiagnosed as he had pulmonary tuberculosis, which is caused by pleural and pericardial effusion, he started on Anti-tuberculosis medications and prednisone 30 mg but still has the same problem. Many tests were done, which revealed that he has increased anti-nuclear antibodies (ANA) , anti double strand DNA (Anti-DS Abs), and the ratio of protein to creatinine. A renal biopsy showed that he had lupus nephritis. Echocardiography revealed that he had pericardial effusion, which progressed to cardiac tamponade.

Treatment with hydroxychloroquine increases the prednisone dose to 60 mg and colchicine to 0.5 mg twice daily. After that, the patient becomes well and does not have any complications. But he is still complaining of constrictive effusion pericarditis and needs pericardiectomy [22].

Treating pericardial effusion from the beginning decreases the need for pericardiectomy and if it doesn't treat causes thickening and scarring of the pericardium. These things affect the heart's function and cause it not to work correctly, so it requires pericardiectomy to relieve the stress on nature and improve the pump blood pump.

The incidence of SLE in males is 4%-22% of all patients of SLE, but males are more reliable to get serositis as SLE starts with nonspecific symptoms that cause a delay in the diagnosis. The average age to get the symptoms of SLE is between 26-38.4 and diagnosed between the ages of 26-55.

Another case reported by Larson et al was an 18-year-old male who presented with chest pain, and his PMHx was gastroesophageal reflux disease (GERD) only; neither his chest x-ray nor his Echocardiography was remarkable. His troponin, complete blood count (CBC), and basic metabolic panel (BMP) were normal, and then he was diagnosed with gastritis regarding the history taken. After ten days, he came back with different systems. His computerized tomography scan (CT scan) showed that he had pericardial effusion and his electrocardiogram (ECG) revealed sinus tachycardia with electrical alternans. His labs showed that he has positive anti double strand DNA (Anti-DS DNA) and anti-nuclear antibody (ANA) and low levels of c3 and c4 complement. So, the patient was diagnosed with pericardial effusion with SLE. So, the first hospitalization was pericarditis which causes pericardial effusion. Pericarditis is not common in this age, gender, and rapid presentation. [1]

SLE patients sometimes present with serositis as an initial symptom, and the investigations confirm that the patient has SLE. Pericarditis is the most common type of serositis and cardiac manifestation in SLE patients.

Another case reported by Marijanovich et al. was a 21-year-old female with PMHx of deep venous thrombosis (DVT); she was on Warfarin and presented with sharp chest pain, which is increased by taking deep breaths and relieved by moving forward. She has tachycardia and tachypnea. Her chest X-ray showed that she had cardiomegaly. Echocardiography and chest computerized tomography scan (CT) showed that she had pericardial effusion with hemorrhage. Her labs showed an elevation of her erythrocyte sedimentation rate (ESR) and c reactive protein (CRP). Her anti double strand DNA (anti-DS DNA) level, anti nuclear antibody (ANA), anti-sjogren's syndrome-related antigen A autoantibodies (SSA), anti-sjogren's syndrome type B (SS B), anti-phospholipid antibody syndrome (APS), and Anticardiolipin increased, so she was diagnosed with pericarditis with effusion as a cardiac manifestation of SLE. She received plasma and blood; after that, her international normalized ratio (INR) decreased from 5.4 to 2.1. Pericardiocentesis was done 500 cc 120 ccs drained. Treatment with three days of Methylprednisolone 100 mg \*2, prednisone 40 mg, Hydroxychloroquine 200 mg\*2, colchicine 0.6\*2, and ibuprofen 400 mg \*4. \*4. Pericarditis with effusion progressed to myocarditis, but she continues improving on her medications.

Pericarditis causing pericardial effusion can be presented as a first presentation, diagnosed by chest X-ray as global heart enlargement. There is a possibility that pericarditis causes cardiac tamponade, which is a

cardiac emergency that needs treatment urgently. Cardiac tamponade is hemodynamically unstable because it affects the pumping of the heart of a patient on antiplatelet medications and causes hemorrhagic pericardial effusion.

Another case reported by Raval et al. was 20-year-old male who presented with a nonproductive cough, pleuritic chest pain, dyspnea, fever, and skin rash. He was diagnosed with SLE 6 months ago. Lab tests showed that there is an increase in inflammatory and cardiac markers. His blood culture showed that he is optimistic about methicillin-sensitive staphylococcus aureus (MSSA). The lower level of complements levels confirmed that he had SLE flare. A Chest computerized tomography scan (CT scan) revealed that he has pleural and pericardial effusion. His Echocardiography showed that he had generalized ST elevation without ischemic changes. Transesophageal and transthoracic Echocardiography showed that his left ventricular ejection fraction (LVEF) was 45% and with no valvular changes. Echocardiography revealed that he has endocarditis. The patient responded to the antibiotic, but his Echocardiography revealed that his left ventricular ejection fraction (LVEF) was <10%. His endomyocardial biopsy revealed that he has diffuse myofiber inflammation and degeneration. A skin biopsy showed that he has lichenoid dermatitis with a granular pattern. These things showed that the patient has SLE myocarditis, which is a response to aggressive therapy of SLE [3].

Myocarditis can happen during an SLE flare. Myocarditis takes one of two ways, the first one, the most common, is asymptomatic and self-limiting. Still, the other one, which is rare, is the rapid, severe progression and causes deterioration of the cardiac function and causes cardiogenic shock. There is a difference between the outcome of myocarditis complications and severe myocardial infarction, which is reversible and irreversible.

Another SLE case reported by Tariq et al. was a 41-year-old male who presented with signs and symptoms of myocarditis with cardiogenic shock and had a biventricular failure.

He needed an Intra-aortic balloon pump and vasopressor, but he did not respond to them. He needs a cardiac transplant; he has no complications after the surgery. SLE associated with myocarditis could be because of multi factors [4].

The most crucial vasopressor used in cardiogenic shock is norepinephrine. If it is not working, dopamine use increases the kidney reabsorption of sodium, increasing systemic blood pressure. If vasopressors are not working so, we may reach cardiac transplantation.

A literature review by Ezzat et al. about the risk factors that cause cardiovascular disease in SLE patients: the disease flare rate, hyperlipidemia, hypertension, and renal failure. Corticosteroid use in SLE is also considered



a risk factor if used over a long time and at a high dose [5].

SLE increases the cardiac risk factors, which cause atherosclerosis and coronary disease, increasing mortality and premature death.

Author, Year Of Publication	Organ Considered	Type Of Study	Conclusion
Tariq et al, 2017 [4]	Heart	Case report	Cardiac Involvement Is Seen In SLE Patients
Marijanovich et al, 2018 [2]	Heart	Case report	Cardiac Involvement in SLE Patient Is Seen
Jethwa et al, 2019 [22]	Heart	Case report	Cardiac Involvement In SLE Patients In Seen
Larson et al, 2019 [1]	Heart	Case report	Cardiac Involvement SLE Patient In Seen
Raval et al, 2021 [3]	Heart	Case report	Cardiac Involvement In SLE Patient Is Seen
Ezzat et al, 2021 [5]	Heart	Literature	Cardiac Involvement Is Seen In SLE Patients
Anis et al., 2022 [21]	heart	Case report	Cardiac Involvement In SLE Patients Is Seen

## Hydroxychloroquine in SLE patient

A systemic review by Liu et al. showed that chloroquine/ hydroxychloroquine had improved cardiovascular risk rarely recommended for an annual ophthalmologist visit after five years of use. The adverse effects happen in < 1% in 10 years of less than 5 mg/kg use. Many studies

in the past were different; some said there were positive effects of using chloroquine/ hydroxychloroquine and cardiovascular outcomes, and others said there were no effects [23].

Hydroxychloroquine decreases the cholesterol level and the risk of thrombosis and arrhythmia, decreasing the risk of card diseases in SLE patients.

Another systemic review done by Hu et al. compare biological disease modifying Anti rheumatologic drug ( bDMARD ) and non-biological disease modifying antirheumatic drug ( non- DMARD ) regarding the effect on cardiovascular diseases , which shows that although non-biological disease modifying antirheumatic drug ( non- bDMARD ) Decreases the risk of cardiovascular decreases, using biological disease modifying antirheumatic drug ( bDMARD ) significantly decreases the risk of myocardial infarction, stroke, and cardiac death as compared with non-biological disease modifying antirheumatic drugs ( non-bDMARD ). It also shows that the risk decreases more with annual follow-up and the use of tumor necrosis factor (TNF) inhibitors [24].

Biological disease modifying antirheumatic drug ( bDMARD ) causes stabilization of the plaque and stops forming new plaque. This beneficial effect will stop with the sudden stop of biological disease modifying antirheumatic drugs ( bDMARD ).

In a retrospective study done by Wakiya et al. to compare the effect of the usual dose of Hydroxychloroquine and a low dose of Hydroxychloroquine for three months, 61 patients participate, 45 of them on an adequate amount of Hydroxychloroquine and 15 on an amount lower than the effective dose. The cutaneous LE disease area severity index (CLASI) activity decreases in both groups, but it is more in the group with the adequate amount. The complements level was lower in the group with the effective dose of Hydroxychloroquine. The systemic lupus erythematosus disease activity index (SLEDAI) reveals the disease activity decreased in the group that used an adequate amount of Hydroxychloroquine. The side effects of the group that uses an effective dose of Hydroxychloroquine are more than those that use a lower than effective dose [25].

The usual dose of Hydroxychloroquine is 200 mg once a day or 400 mg once a day or divided into two doses. We are saving Hydroxychloroquine in a closed container at a room temperature of up to 30 C.

Author name	Name of the study	Medication used	Conclusion
Liu et al, 2018 [23]	Systemic review and meta-analysis	Antimalarial (hydroxychloroquine and quinolone)	Improve we see the cardiovascular risk factors

Weslye et al., 2020 [25]	Retrospective study	Hydroxychloroquine	Decrease the disease activity of SLE with the usual dose of SLE
Hu et al., 2021 [24]	Systemic review and	BDMARD	Improvement: we saw the cardiovascular risk factors

### Withdrawal of Hydroxychloroquine

Ruiz et al. did a retrospective study to find the effect of the withdrawal of Hydroxychloroquine on the flare rate. In this study, 49 patients participated; 26 stopped Hydroxychloroquine, and the rest continued. After a while, five patients from each group get a flare, but it is not severe. A flare occurs in the skin and musculoskeletal system. The cause of withdrawal mostly (42.3%) because of ocular toxicity that it causes, then because of the patients' desire (34.6%), then because of other side effects that occur (15.4%), then ophthalmologist advice (3.8%), and lastly rheumatologist advice [26].

Other research revealed a sudden stop of Hydroxychloroquine or a decrease in the dose, lower education people, and patients who are studying showed a sudden halt of Hydroxychloroquine or a reduction in the dose, lower education people, and patients who are on corticosteroid or immunosuppressive therapy increase the risk of flare.

Author	Name of the study	Number of patients	Name of medication	Conclusion
Ruiz et al., 2020 [26]	Retrospective study	49	Hydroxychloroquine	No difference in the rate of flare between the group that continued hydroxychloroquine and the group that stopped taking hydroxychloroquine

### Myocarditis in SLE patients

In a retrospective study by Thomas et al. to check the presentation of myocarditis as a first symptom in SLE. 29 patients took part in this study; 17 of them had myocarditis as a first symptom, and 19 of them had left ventricular ejection fraction (LVEF) <45%. They started the SLE treatment and followed for a specific period; after one month of starting the treatment, ten patients of 23 patients there left ventricular ejection fraction (LVEF) > 55%; during this study, three patients died, and 2 of them died because of myocarditis[6].

Any autoimmune disease can affect the body's immune system, so it could affect anybody's system. The presentation of myocarditis could be asymptomatic or symptomatic. If it presents symptoms, the patient presents signs of infection such as fever, fatigue and

headaches, chest pain, shortness of breath, and leg swelling, as it causes heart failure.

Author	Number of patients	Name of the study	Organ	Conclusion
Thomas et al., 2017 [6]	29	Retrospective study	heart	Seen Myocarditis as the first symptom of SLE.

### Intravenous immunoglobulin (IVIG) in SLE patients

A literature review by Meridor showed that five females took part in the effect of IVIG on SLE patients. They responded rapidly to IVIG and improved the outcomes [15].

IVIG mechanism in SLE patients is an anti-idiotypic effect for anticardiolipin and anti-DNA. They found IVIG helps treat SLE and Anti phospholipid syndrome and improves the level of antibodies.

Author	Name of the study	Number of patients	Name of medication	conclusion
Meridor et al., 2021 [15]	Literature review and case series	5	IVIG	Improvement of the outcome in SLE patients is seen with the use of IVIG

### Limitation:

Because of the limited number of studies that report the cardiac involvement in SLE patients and how Hydroxychloroquine can improve these cardiac manifestations, this systemic review of the research done between 2017-2022 includes only the English language of study. Data collection from just three databases (PubMed, Google Scholar, and PubMed Central). There need to be more studies to reveal the exact dose of Hydroxychloroquine that helps decrease the risk of pericarditis, and if stopped, it can cause flare and increase the risk of pericarditis. The follow-up time after Hydroxychloroquine is differs and the number of samples is short. Regarding all these things, we need more studies with many participants, long follow-ups, and the same period to understand it more thoroughly.

### Conclusion

Cardiac manifestations are considered the most common and dangerous complication in SLE patients. These cardiac manifestations include pericardial, myocardial, valvular, and coronary artery disease. Hydroxychloroquine is an effective medication used in SLE to improve the risk factors that can cause cardiovascular disease in SLE. So, this study revealed that it is helpful to use Hydroxychloroquine in SLE patients; it is effective in treating SLE patients, decreasing the risk of pericarditis and the risk of flare. More studies are required to know more about the effectiveness of Hydroxychloroquine, its side effects, and if it affects SLE outcomes.

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