Journal of Advances in Medicine and Pharmaceutical Sciences
p-ISSN: 2964-268X, e-ISSN: 2963-4253

Case Report Paper

Impact of Off-Label Drug Side Effects on Healthcare Costs in Systemic Lupus Erythematosus Patients

Jamsuwan Pornpromlikit[1*], **Komhom Suchart**[1]

[1] *Department of Clinical Science, School of Medicine, Walailak University. Thaiburi, Thailand.*

Article History
Received:
09.07.2024

Revised:
03.08.2024

Accepted:
15.08.2024

***Corresponding Author:**
Jamsuwan Pornpromlikit

Abstract: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disorder that predominantly affects women and often requires treatment with off-label medications. These medications, although effective in managing SLE symptoms, can cause adverse drug reactions that increase healthcare costs and complicate patient management. This study aimed to assess the incidence of adverse drug reactions from off-label medication use in SLE patients in Thailand and analyze the resulting impact on healthcare expenditure. A cross-sectional and retrospective approach was used, involving 100 SLE patients receiving off-label medications at various hospitals in Thailand. Data were collected through patient interviews and medical record reviews, with a focus on adverse drug reactions and associated costs. The findings revealed that the most common adverse events included bone and joint problems, gastrointestinal problems, and metabolic changes. These adverse events led to increased healthcare costs for 65% of patients, mainly due to additional medications and hospital visits. Patients who experienced adverse reactions incurred 30-40% higher medical costs than those who did not experience adverse events. The results are in line with global trends but also reflect the unique health care context in Thailand, where access to medical resources and reliance on traditional medicine may influence treatment outcomes. Future research should explore prospective trials, evaluate alternative treatments to reduce side effects, and develop comprehensive guidelines for safer off-label drug use.

Keywords: Autoimmune Disorders, Drug Side Effects, Healthcare Costs, Off-Label Drug Use, Systemic Lupus Erythematosus.

1. Introduction

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease characterized by the immune system attacking healthy tissue, leading to inflammation and damage to multiple organs. The complexity of SLE arises from its heterogeneous clinical manifestations and unpredictable disease course, making its management challenging for healthcare providers [1]. In Thailand, the prevalence of SLE continues to increase, necessitating effective treatment strategies to manage this condition [2] [3].

To manage the symptoms of SLE, healthcare providers often use off-label medications, prescribing medications outside of their approved indications. This practice is common in Thailand due to the limited number of approved therapies for SLE and the need for a personalized treatment approach [4] [5]. However, off-label medication use carries inherent risks, including the potential for adverse side effects that may not be well documented.

The occurrence of adverse effects from off-label medications poses a significant challenge, as it can worsen patients' health conditions and lead to increased healthcare utilization. As a result, it results in a significant economic burden for patients and the healthcare system. Understanding the impact of these adverse events is critical to developing strategies to reduce associated costs and improve patient outcomes.

1) Systemic Lupus Erythematosus

Systemic Lupus Erythematosus (SLE) is a complex autoimmune disease in which the immune system attacks the body's tissues, leading to inflammation and damage to various organs, including the skin, kidneys, heart, and joints. The pathophysiology of SLE is multifactorial, involving genetic predisposition, environmental triggers, and hormonal factors, with autoantibody production playing a major role. These autoantibodies form immune complexes that deposit in tissues, leading to inflammation and subsequent organ damage [6]. The clinical presentation of SLE is highly variable, with symptoms ranging from mild manifestations such as fatigue and joint pain to more severe symptoms including nephritis and neurological involvement [7].

The epidemiology of SLE suggests that the disease predominantly affects women, particularly those of childbearing age, with a female to male ratio of approximately 9:1. In addition, ethnic variation in the prevalence of SLE has been documented, with higher incidence and severity reported among African, Asian, and Hispanic populations [8]. The burden of this disease is enormous, as SLE can significantly impair quality of life, leading to frequent hospitalizations and the need for long-term treatment, which in turn results in high direct medical costs [6]. In Thailand, the challenges in diagnosing and managing SLE are further compounded by limited health care resources and socioeconomic disparities, which can affect timely diagnosis and optimal disease management [9].

The clinical impact of SLE includes multisystem involvement, requiring a multidisciplinary approach to treatment. Commonly affected organs include the kidneys, skin, joints, and cardiovascular system. Relapses and remissions contribute to the unpredictable nature of the disease. Chronic organ damage, particularly renal impairment, can significantly impact a patient's long-term prognosis, requiring lifelong management [10]. As SLE is often associated with remissions and relapses, careful management is essential to reduce organ damage and optimize patients' quality of life [11].

The economic burden of SLE is high due to the chronic nature of the disease and its associated complications. Direct costs include medical visits, hospitalizations, medications, and diagnostic tests, while indirect costs result from lost productivity, disability, and reduced quality of life. The costs associated with SLE management are compounded by the need for long-term care and frequent adjustments to therapy as the disease progresses [8]. In Thailand, healthcare costs associated with SLE are increasing, posing challenges in allocating resources effectively within the public health system [9].

2) Off-Label Drug Use in SLE Management

Off-label drug use is common in SLE management due to the limited availability of specific drugs approved for this condition. Drugs such as hydroxychloroquine (HCQ), corticosteroids, and immunosuppressants are often used off-label to manage various manifestations of SLE. HCQ, originally approved for malaria, has shown significant efficacy in reducing disease activity and preventing flares in SLE patients. Corticosteroids, although highly effective in controlling inflammation, have significant side effects, including weight gain, hypertension, and increased susceptibility to infections [12].

Immunosuppressants such as mycophenolate mofetil and azathioprine are also commonly used off-label, especially in managing severe manifestations of SLE such as lupus nephritis. These drugs suppress the immune response to prevent tissue damage but carry their own set of risks, including gastrointestinal problems, bone marrow suppression, and increased risk of infection [12]. Off-label use of drugs in the treatment of SLE is often driven by clinical judgment, as physicians balance the potential benefits of disease control with the risks of side effects [13].

Although off-label drug use provides therapeutic benefits in the management of SLE, it is not without risks. Side effects of corticosteroids, such as osteoporosis, weight gain, and diabetes, can significantly affect patient outcomes. Immunosuppressive drugs commonly used in the management of SLE can also increase the likelihood of infection, requiring careful monitoring and management. Hydroxychloroquine, although generally well tolerated, can cause side effects such as gastrointestinal upset and, in rare cases, retinal toxicity [14]. Therefore, it is important for healthcare providers to weigh the risks and benefits of off-label drug use in the management of SLE.

In Thailand, off-label prescribing is influenced by factors such as drug availability, clinical practice guidelines, and physician expertise. Given the complex nature of SLE and its diverse symptoms, physicians often rely on off-label drugs to address specific needs, especially in severe cases or when other treatments have failed. However, greater clarity is needed in clinical guidelines to ensure the safe and effective use of off-label drugs, especially with regard to monitoring and management of side effects [13].

Furthermore, healthcare providers should educate patients about the potential risks of off-label medication use, ensuring that they are aware of potential side effects and understand the importance of regular follow-up and monitoring. This is particularly important in countries such as Thailand, where healthcare access and resources may be limited, potentially impacting patient adherence and outcomes [15]. Ultimately, while off-label medication use offers significant benefits in managing SLE, its safety profile must be continually assessed through pharmacovigilance and patient education.

3) Healthcare Costs of Chronic Diseases

Chronic diseases such as SLE place a significant financial burden on healthcare systems due to the long-term nature of the disease and the need for ongoing treatment and care. Direct costs of chronic diseases include medical consultations, diagnostic tests, hospitalizations, and medications, while indirect costs result from lost productivity and disability [16]. Adverse side effects from medications used to manage chronic diseases can exacerbate these costs, as they can lead to additional medical interventions, longer hospitalizations, and increased healthcare resource utilization.

In the context of SLE, the use of corticosteroids and immunosuppressants often results in side effects that can increase overall health care costs. For example, long-term corticosteroid use is associated with conditions such as osteoporosis, hypertension, and diabetes, which may require additional treatment and monitoring [12]. The use of immunosuppressive drugs also increases the risk of infections, leading to more frequent hospitalizations and additional medical costs [14]. Thus, the side effects of these medications contribute to increased overall health care costs, underscoring the importance of effectively managing the disease and its treatment-related complications.

Previous studies have examined the economic impact of adverse drug reactions in chronic diseases, including autoimmune conditions such as SLE. These studies have shown that adverse drug reactions not only increase direct medical costs but also reduce patient productivity due to prolonged illness or disability. In the case of SLE, the financial burden is further increased by the need for routine monitoring, laboratory tests, and imaging, which are essential for detecting and managing adverse events associated with long-term drug use [16].

In Thailand, where health care resources may be limited, the additional costs associated with managing adverse events from off-label drug use in SLE patients are of increasing concern. The economic impact of SLE management is compounded by challenges in accessing specialty care and the high costs associated with imported drugs. Efforts to reduce health care costs associated with SLE may benefit from more targeted interventions, such as early detection of adverse events and optimization of drug regimens to minimize adverse reactions [9].

In addition, studies have shown that improving patient education and adherence to treatment regimens may help reduce the costs of managing SLE and its associated complications. Educating patients about the importance of medication adherence and regular check-ups can help prevent complications, potentially reducing the need for hospitalization and expensive treatments.

Furthermore, the use of generic and biosimilar drugs can help reduce the cost burden on patients and the healthcare system, making SLE care more affordable and accessible [17].

Overall, healthcare costs for chronic diseases such as SLE are influenced by multiple factors, including direct costs of care, the impact of drug side effects, and indirect costs associated with disability and lost productivity. In countries such as Thailand, where healthcare resources are limited, optimizing treatment strategies and effectively managing side effects are critical to reducing the overall financial burden of SLE management.

This study aimed to identify adverse events associated with off-label drug use in SLE patients in Thailand and analyze their impact on healthcare costs. By examining patient records and healthcare expenditure data, this study sought to provide insight into the economic implications of adverse drug reactions. The primary objective is to inform health care policy and optimize off-label prescribing practices to improve patient safety and reduce the financial burden on the health care system.

Understanding the risks associated with off-label drug use in the treatment of SLE is critical for healthcare professionals to make informed prescribing decisions. This study provides valuable data on the prevalence and economic impact of adverse events, assisting clinicians in balancing therapeutic benefits with potential risks.

The findings are also relevant to policymakers in the healthcare sector, offering evidence to guide the development of regulations and guidelines that ensure the safe and cost-effective use of off-label drugs. Implementing such policies could lead to more efficient resource allocation and improved healthcare delivery. For SLE patients in Thailand, this study highlights the importance of monitoring and managing side effects associated with their treatment regimen. By raising awareness, patients can engage in informed discussions with their healthcare providers, leading to better adherence to treatment plans and improved quality of life.

2. Method

This study adopts cross-sectional and retrospective analysis designs. The cross-sectional design is used to assess the prevalence of adverse drug reactions related to off-label drug use in SLE patients at a specific point in time. Meanwhile, retrospective analysis provides insight into the historical impact of these adverse events on healthcare costs.

The population for this study consists of SLE patients treated at selected hospitals and clinics in Thailand, focusing on major hospitals in Bangkok, such as Siriraj Hospital and Chulalongkorn Hospital, as well as clinics in Chiang Mai and Phuket. A convenience sampling method is used to select participants, ensuring a representative sample of SLE patients treated with off-label drugs.

1) Data Collection

Data is collected through the following methods:

1) Secondary Data
   SLE patient medical records are reviewed to identify instances of off-label drug use and any documented adverse events. This data includes demographic information, clinical details, and medication history.
2) Patient Interviews
   Interviews are conducted with participants to understand the personal impact of adverse drug reactions on their quality of life. Questions focus on symptoms, adverse events experienced, and any healthcare interventions sought due to these adverse events.
3) Healthcare Cost Analysis
   A cost analysis is conducted to measure the financial burden of adverse drug reactions. This includes direct medical costs such as additional medications, hospital visits, and treatment for adverse events.

2) Inclusion and Exclusion Criteria

- Inclusion Criteria: SLE patients who have been prescribed off-label drugs as part of their treatment regimen and are willing to participate in this study.
- Exclusion Criteria: Patients with severe comorbid conditions (such as psychiatric disorders or speech disorders) or patients who withdraw from the study at any time.

3. Finding and Discussion

3.1. Respondent Characteristics

In this study, the majority of SLE patients treated with off-label drugs were female (85%), consistent with the known gender prevalence in SLE, where females are more frequently affected. Age distribution showed that most patients were aged between 26-45 years (50%), followed by 46-65 years (30%), and the youngest group (12-25 years) comprised only 15% of respondents. This suggests that SLE typically manifests during the reproductive years and early adulthood, demographic groups that are frequently prescribed off-label drugs. Regarding education, 60% of participants had at least a high school education, with 40% having a college degree, indicating that these patients are generally well-informed and potentially better aware of the risks and benefits associated with their treatment regimen. 4.2 Incidence of Off-Label Adverse Drug Effects

A variety of adverse effects were identified among participants, primarily bone and joint problems (45%), gastrointestinal problems (30%), and metabolic changes, such as weight gain and moon face (25%). The most commonly used medications were corticosteroids (eg, methylprednisolone), immunosuppressants (eg, azathioprine), and antimalarials (eg, hydroxychloroquine). The incidence of adverse effects was categorized as follows: Possible (40%), Definitely (35%), Possible (20%), and None (5%).

- Bone and Joint Problems
  These were the most common, with patients reporting osteoporosis and fractures, which are often associated with long-term corticosteroid use.
- Gastrointestinal Effects
  These included ulcers, nausea, and abdominal pain, likely related to the use of corticosteroids and other immunosuppressants.
- Metabolic Changes
  Weight gain and moon face have been associated with corticosteroid therapy in particular. These cosmetic adverse effects have a significant impact on patients' quality of life.

These findings are consistent with previous literature on corticosteroid side effects in autoimmune diseases, highlighting the potential risks of long-term off-label drug use. The higher incidence of bone-related problems is particularly concerning in an already vulnerable population due to the nature of the disease and the common use of corticosteroid therapy in the treatment of SLE.

3.2. Impact on Health Care Costs

Health care costs for patients with SLE are significantly increased due to off-label drug side effects. Of patients who reported side effects, 65% experienced an increase in their health care expenditures, primarily due to additional hospital visits, diagnostic testing, and treatment for the side effect itself. The most common additional costs included:

- Medications
  42% of participants required additional medications to manage side effects, such as calcium and vitamin D supplements for bone health and proton pump inhibitors for gastrointestinal problems.
- Hospital Visits
  38% of patients had to visit the hospital for follow-up or emergency care related to side effects.
- Care for Side Effects
  20% of patients required treatment for side effects, primarily for fractures or severe gastrointestinal problems.

Comparative analysis of patients with adverse drug reactions versus those without showed a significant difference in overall health care costs. Patients who experienced adverse drug reactions incurred costs that were 30-40% higher on average than those who did not report any adverse drug reactions. These findings are important for health policymakers, as they suggest that while off-label drugs may be effective in managing SLE, the financial burden of adverse drug reactions may outweigh the benefits if not managed properly.

3.3. Comparative Analysis with Previous Studies

When compared with studies conducted in other countries, such as the United States and the United Kingdom, the findings of this study are consistent with global trends regarding the economic burden of adverse drug reactions. For example, a study in the United Kingdom found that corticosteroids in autoimmune conditions cause similar problems, such as bone loss and gastrointestinal complications, which contribute to higher health care costs. However, local factors in Thailand, such as health care infrastructure and access to medical resources, may have influenced the magnitude of these costs. In Thailand, where access to health care can vary, especially in rural areas, patients may experience delays in managing side effects, which worsens their health outcomes and health care costs.

In addition, the cultural context in Thailand, where patients often rely on traditional medicine in addition to conventional care, may contribute to different patterns of side effects or additional health care costs. It is also worth noting that the health care system in Thailand, which offers both public and private health care options, may influence the economic burden depending on the type of insurance or out-of-pocket costs incurred by patients. 4.5 Policy and Practice Implications

Based on the findings of this study, several policy and practice recommendations can be made to improve patient care and reduce the financial burden of off-label drug use in patients with SLE:

- Regulation of Off-Label Drug Use
  Stricter guidelines and protocols for prescribing off-label drugs, especially corticosteroids and immunosuppressants, may help minimize unnecessary risks. Physicians should be provided with clear, evidence-based guidance on the long-term effects and cost implications of these medications.
- Patient Education and Counseling
  Improving patient education programs about the potential side effects of their treatments and the importance of monitoring their health can empower patients to better manage their condition. Regular counseling sessions about the risks of side effects, combined with regular checkups, may also reduce adverse health outcomes and health care costs.
- Better Monitoring and Early Intervention
  Routine monitoring of patients taking off-label drugs for early detection of side effects, such as bone loss or gastrointestinal problems, may prevent long-term damage and reduce hospitalizations. In addition, the use of alternative therapies or adjunct medications may reduce these side effects and lower costs.
- Cost-Effective Treatment Strategies
  Given the significant cost burden, healthcare systems should explore more cost-effective treatment alternatives for SLE, including the use of biologics that may reduce the need for off-label medications.

This study highlights the critical need to improve the management and oversight of off-label medication use in patients with SLE, not only to ensure patient safety but also to reduce the financial burden on healthcare systems. By integrating patient education, monitoring, and improved regulatory measures, healthcare providers can help reduce the risks associated with off-label medication use, ultimately resulting in better outcomes for patients and healthcare systems.

4. Conclusion

This study investigated the adverse effects of off-label drug use in patients with Systemic Lupus Erythematosus (SLE) in Thailand, highlighting its significant impact on healthcare costs. Findings showed that the majority of patients, particularly females aged 26–45 years, experienced common adverse effects such as bone and joint problems, gastrointestinal problems, and metabolic changes. The increase in healthcare costs due to these adverse effects was substantial, with patients reporting 30–40% higher medical costs compared to those without adverse reactions. These additional costs stemmed from the need for medications, hospital visits, and treatment for adverse effects, indicating the financial burden associated with off-label drug use in managing SLE.

This study provides valuable insights into the management of SLE patients in Thailand, particularly the financial and clinical implications of off-label drug use. This study underscores the need for stronger healthcare policies to address the risks of off-label drugs, such as corticosteroids and immunosuppressants, in managing autoimmune diseases such as SLE. It also highlights the importance of patient education, regular monitoring, and development of cost-effective treatment strategies. These findings have significant implications for policymakers and clinicians in the healthcare sector, as they emphasize the importance of improving regulatory oversight and providing clear guidelines for off-label drug prescribing to prevent unnecessary risks and reduce the economic burden on the healthcare system.

Future research should focus on conducting prospective trials or population-based studies to better understand the long-term effects of off-label drug use in SLE patients across different demographic groups. Investigating alternative treatment options and therapies that minimize side effects, such as biologics, may also help reduce healthcare costs. Furthermore, developing comprehensive, evidence-based guidelines for safer and more effective off-label drug use in autoimmune diseases such as SLE is essential. Greater exploration of culturally relevant patient education models and integration of traditional medicine with conventional medicine may also provide valuable insights to improve patient outcomes and reduce the overall healthcare burden.

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