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FACTORS ASSOCIATED WITH OCULAR DISORDERS IN CHILDREN WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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ABSTRACT
Systemic lupus erythematosus (SLE) is a chronic inflammatory disease involving multiple organs and causing systemic damage, characterized by the formation of autoantibodies and immune complexes. Ocular involvement is estimated to occur in approximately one-third of individuals with SLE and may affect various ocular structures. Ocular manifestations associated with SLE are highly variable and may lead to delayed diagnosis, potentially resulting in poor outcomes and vision-threatening complications. To analyze risk factors associated with ocular disorders in children with systemic lupus erythematosus (SLE). This was an analytic cross-sectional study conducted at the Allergy-Immunology outpatient clinic and pediatric inpatient ward of Adam Malik General Hospital starting in April 2025. The sampling technique used was consecutive sampling. A total of 41 patients with SLE were analyzed. The duration of treatment was found to be a risk factor associated with ocular disorders in children with SLE ($p=0.005$). The prevalence of ocular disorders among children with SLE was 29.3%. The most common ocular disorder observed in children with SLE undergoing treatment was ocular hypertension, found in 9 patients (22%). Based on ordinal regression analysis, each additional year of treatment duration increased the likelihood of worsening therapeutic outcomes by 1.76 times ($p<0.05$). Treatment duration is a significant risk factor for ocular disorders in children with systemic lupus erythematosus, with ocular hypertension being the most common type of ocular disorder. Longer treatment duration increases the likelihood of worsening therapeutic outcomes.

Keywords: ocular disorders; pediatric; risk factors; systemic lupus erythematosus; treatment duration

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INTRODUCTION

Systemic Lupus Erythematosus (SLE) is a chronic, multisystemic autoimmune disease characterized by a loss of self-tolerance, leading to the production of autoantibodies and the subsequent deposition of immune complexes. The disease exhibits a profound gender disparity, predominantly affecting women of childbearing age with a female-to-male ratio of approximately 9:1. While SLE is traditionally associated with significant morbidity in the renal, pulmonary, and haematological systems, its impact on the visual apparatus is equally critical. Ocular pathology in SLE patients can manifest through three primary pathways: direct inflammatory damage from the disease process, secondary infections related to immune dysfunction, or iatrogenic toxicity from long-term pharmacological interventions (Hsu et al., 2020).

The aetiology of SLE is recognized as multifactorial, involving a complex interplay between genetic predisposition, hormonal influences, and environmental triggers. Ocular involvement is reported in approximately one-third of SLE cases, presenting a clinical spectrum that ranges from benign surface irritations to severe, sight-threatening complications. These manifestations can involve any anatomical compartment of the eye, including the extraocular adnexa, the anterior and

posterior segments, and the optic nerve. Common clinical presentations include decreased visual acuity, ophthalmoplegia, proptosis, and orbital inflammation (Musa et al., 2024).

The spectrum of ocular manifestations in SLE is broad and often nonspecific, which may contribute to delayed recognition and management, thereby increasing the risk of visual morbidity. Diagnosis of SLE relies on a combination of clinical features and immunologic markers, including antinuclear antibodies (ANA), anti–double-stranded DNA (anti-dsDNA), anti-Smith antibodies, and antiphospholipid antibodies (Aringer et al., 2019; Infantino et al., 2021).

Critically, the involvement of ocular structures often serves as a surrogate marker for systemic disease activity; in many cohorts, ophthalmic signs precede the involvement of vital organs such as the kidneys, lungs, or heart. Furthermore, the standard of care for SLE—including glucocorticoids, hydroxychloroquine (HCQ), and various immunosuppressants (e.g., azathioprine, cyclosporine, and mycophenolate mofetil)—is associated with specific ocular side effects, most notably HCQ-induced maculopathy. Given the risk of irreversible vision loss, multidisciplinary management involving ophthalmologists is essential. Regular screening and early diagnostic intervention remain imperative, even in asymptomatic patients, to ensure the preservation of visual function and the monitoring of systemic disease progression (Luboń et al., 2022; Tang et al., 2021). Therefore, this study aims to characterize ocular manifestations and identify clinical factors associated with ocular outcomes in pediatric patients with SLE.

METHOD

This study employed an analytic cross-sectional study to evaluate factors that related to ocular manifestation in children with systemic lupus erythematosus. Data were retrospectively retrieved from medical records of children diagnosed with systemic lupus erythematosus starting from May 2025 in the ward and outpatient clinic at a tertiary referral teaching hospital in Medan, North Sumatra, Indonesia.

A total of 41 children diagnosed with lupus erythematosus systemic were included in this retrospective study. Diagnosis was defined according to national guideline of SLE, which has been screened by opthalmologist before starting treatment. A total of 41 children meet the inclusion criteria, consisting of 29 children with normal eye and 12 children with ocular disturbance. Cases with incomplete records and congenital abnormality of the eye were excluded from the analysis.

Data were obtained retrospectively from the hospital's electronic medical record system. Demographic information, clinical variables (SLEDAI score, treatment given and duration of treatment) and ocular diagnosis were extracted using a standarized data collection. All data analyses were performed using IBM SPSS Statistics 25.0. The normality of continuous data was assessed using the Kolmogorov–Smirnov test. Normally distributed variables were presented as mean ± standard deviation (SD), whereas non-normally distributed data were expressed as median (minimum–maximum). Categorical variables were summarized as frequencies and percentages.

RESULT

Baseline Characteristics

A total of 41 children diagnosed with systemic lupus erythematosus were enrolled, consisted of 29 patients with normal ocular and 12 patients with ocular disorder. The demographic and clinical characteristics of both groups are summarized in Table 1.

Table 1.
Demographic and clinical characteristic of children with SLE.

Demographic and Clinical Characteristics	
Age of onset	
Median	14 years old
Gender	
Male	6 (14,6%)
Female	35 (85,4%)
SLEDAI Score	
Median	8 (0-48)
Remission	4 (9,8%)
Mild	7 (17,1%)
Moderate	15 (36,6%)
Severe	15 (36,6%)
Duration of treatment	
Median	1 year
≤3 years	33 (80,5%)
>3 years	8 (19,5%)
Ocular involvement	
No ocular involvement	29 (70,7%)
Ocular hypertension	9 (22%)
Retinopathy	1 (2,4%)
Juvenile cataract	1 (2,4%)
Glaucoma	1 (2,4%)
Additional therapy	
Yes	21 (51,2%)
No	20 (48,8%)

The study population consisted predominantly of female patients, accounting for 85.4%, with a median age at diagnosis of 14 years. Disease activity, as measured by the SLEDAI score, showed a median of 8 (range 0–48), with most patients classified as having moderate to severe disease (73.2%), while smaller proportions were in mild disease (17.1%) or remission (9.8%). The median duration of treatment was 1 year, with the majority of patients (80.5%) receiving treatment for less than 3 years.

Regarding ocular involvement, most patients (70.7%) did not exhibit ocular abnormalities. Among those with ocular manifestations, ocular hypertension was the most common finding (22%), while other conditions such as retinopathy, juvenile cataract, and glaucoma were relatively rare, each occurring in 2.4% of cases. These findings indicate that the cohort was largely composed of adolescent females with moderate-to-severe disease activity, relatively short treatment duration, and a low prevalence of ocular complications.

Ocular Outcomes

Persistent ocular involvement was the most frequent outcome (65.9%), while 12.2% of patients showed improvement and 22.0% experienced worsening of ocular conditions (Table 2).

Table 2.
Ocular Outcomes Following Treatment

Outcome	f (%)
Persistent ocular involvement	27 (65,9)
Improvement	5 (12,2)
Worsening	9 (22)

Bivariate analysis was conducted to assess the association between independent variables (age at diagnosis, sex, SLEDAI score, treatment duration, and additional therapy) and ocular outcomes using appropriate statistical tests (Chi-square, Fisher's exact test, or Kruskal–Wallis test). Variables with a p-value <0.25 were included in a multivariate ordinal logistic regression model to identify independent predictors of ocular outcomes. The strength of association was expressed as odds ratios (ORs) with 95% confidence intervals (CIs), and statistical significance was defined as $p<0.05$.

Table 3.
Factors Associated with Ocular Outcomes

Variable	P value
Age of onset	0,101
Gender	0,250
SLEDAI score	0,064
Treatment duration	0,005
Additional therapy	0,466

Analysis of factors associated with ocular outcomes (Table 3) showed that age at diagnosis was not significantly associated with ocular outcomes (p=0.101**)**. This finding indicates that variation in age at onset within the paediatric range does not appear to meaningfully influence ocular prognosis. Similarly**,** gender was not associated with ocular outcomes (p=0.250)**,** despite the marked female predominance, suggesting that sex-related differences in disease susceptibility do not extend to ocular disease progression. Disease activity, as assessed by SLEDAI score, was not significantly associated with ocular outcomes (p=0.064)**.** However, a trend toward worse outcomes in patients with higher disease activity was observed, indicating a possible contribution of systemic inflammation that did not reach statistical significance. This pattern suggests that while disease activity may play a role, it is unlikely to be the primary determinant of ocular outcomes when considered independently.

The absence of a significant association between additional therapy and ocular outcomes (p=0.466) suggests that escalation of treatment alone may not modify ocular prognosis. This result likely reflects underlying disease complexity, where patients requiring additional therapy may already represent a subgroup with more severe or persistent disease, thereby limiting the observable effect of treatment on outcomes. In contrast, treatment duration was significantly associated with ocular outcomes (p=0.005) and remained the only variable demonstrating a consistent relationship across analyses.

Table 4.
Multivariate Analysis of Ocular Outcomes

Variable	OR	P-value
Treatment duration (per year)	1,76	0,029

Patients with longer treatment duration were more likely to experience worsening ocular conditions. This association was further confirmed in the multivariate model, where each additional year of treatment increased the odds of worse ocular outcomes by 1.76-fold (p=0.029)**.** These findings indicate that cumulative disease exposure and prolonged treatment may be key contributors to ocular morbidity. Overall, these findings highlight that treatment duration is the most relevant factor associated with ocular outcomes in pediatric SLE, whereas demographic characteristics and baseline disease activity appear to have limited independent influence.

DISCUSSION

This study provides a comprehensive evaluation of ocular outcomes in paediatric systemic lupus erythematosus (SLE), demonstrating that ocular involvement occurred in approximately one-third of patients, with ocular hypertension as the most frequent manifestation. Ocular complications in SLE are well recognized and may arise from immune-mediated vascular injury, treatment-related effects, or chronic inflammatory damage (Hsu et al., 2020; Musa et al., 2024; Dammaco et al., 2018). Despite a predominance of moderate-to-severe disease activity in this cohort, most patients did not develop ocular complications, suggesting that ocular involvement may not directly parallel systemic disease burden.

The demographic profile observed in this study, including female predominance and adolescent age at diagnosis, is consistent with previous reports in paediatric SLE populations (Charras et al., 2021; Smith et al., 2019; Gawdat et al; 2017). However, the median age at diagnosis in this study was slightly older compared to earlier cohorts, which may have implications for cumulative disease

exposure and treatment duration. Earlier onset has been associated with longer treatment exposure and potentially greater risk of long-term complications, including ocular manifestations Charras et al., 202; Smith et al., 2019).

In the present study, disease activity measured by SLEDAI score was not significantly associated with ocular outcomes (p=0.064). This finding differs from previous studies demonstrating a strong association between higher SLEDAI scores and ocular complications. For example, Blum-Hareuveni et al. (2016) reported a significant relationship between elevated disease activity and ocular morbidity (p<0.001), particularly in patients with recurrent disease flares. Similarly, Gao et al. (2017) demonstrated that retinal involvement in SLE is closely linked to active systemic disease. The discrepancy observed in this study may reflect differences in sample size, disease duration, or variability in treatment regimens. It is also possible that ocular involvement reflects cumulative or chronic inflammatory damage rather than acute disease activity captured at a single time point, thereby limiting the predictive value of SLEDAI for organ-specific outcomes (Meng et al., 2024).

Demographic variables, including age at diagnosis (p=0.101) and gender (p=0.250), were not associated with ocular outcomes. These findings are consistent with previous studies indicating that neither age nor sex independently predicts ocular prognosis in paediatric SLE (Alderaan et al., 2015; Miettunen et al., 2004). Although hormonal factors, such as the immunomodulatory effects of oestrogen, have been proposed to influence disease expression, current evidence does not support a significant role in determining ocular outcomes (Shamim et al. 2020; Rasha et al., 2017).

In contrast, treatment duration emerged as the most robust predictor of ocular outcomes. The significant association observed in bivariate analysis (p=0.005), along with its persistence in multivariate analysis (OR 1.76; p=0.029), underscores the importance of cumulative disease exposure. This finding is consistent with previous studies, including Alderaan et al., which demonstrated that longer treatment duration and higher cumulative corticosteroid exposure were associated with increased risk of ocular complications, particularly cataracts (Alderaan et al., 2024; Moschetti et al., 2022). Similarly, Yan et al. (2022) reported that prolonged steroid exposure contributes to the development of ocular hypertension and cataracts in pediatric autoimmune diseases.

The biological plausibility of this association is well established. Glucocorticoids, which remain a cornerstone of SLE therapy, are known to induce metabolic alterations, increase intraocular pressure, and promote structural changes in ocular tissues, leading to complications such as glaucoma and cataracts. In addition, cumulative inflammatory damage and microvascular dysfunction may further contribute to progressive ocular involvement (Popa et al., 2018; Pan et al., 2023).

Additional therapy was not significantly associated with ocular outcomes (p=0.466). This finding aligns with previous reports suggesting that adjunctive therapies do not consistently improve long-term outcomes in paediatric SLE (Sit, et al., 2018; Puengpipattrakul et al., 2023). However, other studies have reported contrasting results, with some demonstrating that combination therapies may reduce disease activity and organ damage. The lack of association in this study may reflect confounding by indication, where patients receiving additional therapy represent a subgroup with more severe or refractory disease. Recent studies have suggested that biologic therapies, such as belimumab, may reduce corticosteroid exposure and improve outcomes, although their long-term impact on ocular complications remains uncertain (Puengpipattrakul et al., 2023; Li et al., 2024).

The regression analysis further strengthens these findings, demonstrating that each additional year of treatment increases the risk of worsening ocular outcomes by 1.76-fold. This highlights the cumulative nature of both disease-related and treatment-related damage in pediatric SLE. Taken

together, these findings suggest that ocular morbidity is driven primarily by chronic exposure rather than baseline disease characteristics.

Strength and Limitation

This study offers several clinical strengths and limitations. It provides a targeted evaluation of ocular outcomes in pediatric systemic lupus erythematosus (SLE), incorporating clinically relevant variables and an ordinal classification of outcomes, alongside multivariate analysis to identify independent predictors. However, the cross-sectional design precludes assessment of temporal relationships and causality. The relatively small sample size may limit statistical power, particularly for variables demonstrating borderline significance. Important clinical factors, including cumulative corticosteroid exposure, specific immunosuppressive regimens, and treatment adherence, were not evaluated and may have confounded the observed associations. In addition, potential confounding by indication cannot be excluded, particularly in patients receiving additional therapy. Variability in ophthalmologic assessment may introduce heterogeneity in outcome classification, and the single-center setting may limit the external validity of these findings across broader pediatric SLE populations.

CONCLUSION

In this study, ocular involvement was identified in 29.3% of pediatric patients with systemic lupus erythematosus (SLE), with ocular hypertension representing the most common manifestation. Among the variables analyzed, treatment duration was the only factor significantly associated with ocular outcomes ($p=0.005$). Notably, multivariate analysis demonstrated that each additional year of treatment was associated with a 1.76-fold increase in the likelihood of worsening ocular outcomes ($p<0.05$). These findings underscore the critical role of cumulative disease and treatment exposure in the development of ocular complications.

Clinically, this highlights the importance of early disease control, careful long-term management, and routine ophthalmologic monitoring to mitigate the risk of progressive ocular morbidity in pediatric SLE.

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