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Original Research Article

Evaluation of Glaucomatous Changes in Systemic Lupus Erythematosus Patients Undergoing Combined Steroid and Immunosuppressive Therapy: An Observational Study

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Abstract:

Background: Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease that often requires long-term systemic corticosteroids and immunosuppressive agents for disease control. These treatments, while effective, may have ocular side effects including the development or exacerbation of glaucomatous features. This study aimed to assess the impact of systemic steroids combined with immunosuppressive therapy on intraocular pressure (IOP) and other glaucomatous changes in SLE patients.

Methods: A prospective observational study was conducted over at the Department of Ophthalmology, Sri Krishna Medical College Hospital, Muzaffarpur, Bihar, India from October 2024 to January 2025. A total of 80 patients diagnosed with SLE and undergoing systemic steroid and immunosuppressive treatment were enrolled. Comprehensive ophthalmic evaluations including intraocular pressure measurement, optic disc assessment, gonioscopy, and visual field analysis were performed at baseline and at 3-month intervals. Patients with pre-existing glaucoma or ocular hypertension were excluded.

Results: Among the 80 patients, 32.5% developed elevated IOP during the follow-up period, with 18.75% exhibiting early glaucomatous changes on optic disc examination. Visual field defects consistent with glaucoma were detected in 12.5% of cases by the end of the study. The risk of developing ocular hypertension was significantly higher in patients receiving systemic steroids for more than 6 months. A positive correlation was observed between cumulative steroid dose and IOP elevation ($p<0.01$). No significant differences were observed between various types of immunosuppressive agents used.

Conclusion: Systemic corticosteroid therapy, especially when prolonged, significantly increases the risk of developing ocular hypertension and glaucomatous changes in SLE patients. Regular ophthalmologic screening and timely intervention are crucial for the early detection and management of steroid-induced glaucoma in this high-risk population.

Keywords: Systemic Lupus Erythematosus, Corticosteroids, Immunosuppressants, Glaucoma, Intraocular Pressure, Steroid-Induced Ocular Hypertension, Optic Neuropathy.

Introduction

Systemic lupus erythematosus (SLE) is a chronic, relapsing autoimmune disorder characterized by the production of autoantibodies and immune complexes that can affect virtually any organ system, including the eyes. It primarily affects young women in their reproductive years and manifests with diverse clinical features, such as cutaneous lesions, arthritis, nephritis, and neuropsychiatric symptoms [1]. The complex pathophysiology of SLE often necessitates long-term immunomodulatory treatment, with systemic corticosteroids forming the cornerstone of therapy. In moderate to severe cases, additional immunosuppressive agents such as azathioprine, cyclophosphamide, or mycophenolate mofetil are frequently used to achieve disease control and minimize organ damage [2].

While these therapies are often life-saving and crucial for disease management, they are not without adverse effects. One of the significant ocular complications associated with long-term corticosteroid use is the development of ocular hypertension and secondary open-angle glaucoma [3]. Steroid-induced glaucoma is a well-documented condition wherein corticosteroids elevate intraocular pressure (IOP) through altered trabecular

meshwork function, leading to increased resistance to aqueous outflow. If unrecognized and untreated, this pressure elevation can result in progressive optic nerve damage and irreversible visual field loss [4].

In patients with SLE, the ocular system may already be vulnerable due to vasculitic and inflammatory changes. When systemic corticosteroids are introduced, the risk of developing glaucomatous damage may be further potentiated. Despite this, ocular monitoring often takes a backseat to systemic disease management, leading to delayed diagnosis of steroid-induced ocular hypertension or glaucoma. Complicating this scenario further is the concurrent use of immunosuppressive agents, whose impact on ocular tissues and intraocular pressure remains inadequately explored [5]. Although these agents are not primarily known to induce IOP elevation, their role in modulating inflammatory pathways could potentially influence ocular dynamics either positively or negatively.

Several studies have addressed the ocular manifestations of SLE, including retinopathy, optic neuritis, and dry eye disease. However, limited literature exists specifically examining the cumulative effect of systemic corticosteroids and immunosuppressants on glaucomatous changes in this population [6]. Most existing studies have been retrospective or focused narrowly on one treatment agent or disease manifestation, leaving a gap in our understanding of real-world outcomes.

This study was therefore designed to prospectively evaluate the impact of combined systemic corticosteroid and immunosuppressive therapy on intraocular pressure, optic disc morphology, and glaucomatous visual field changes in patients diagnosed with SLE. The objective was to generate comprehensive clinical data over a 12-month follow-up period to inform better surveillance strategies and early intervention approaches in this high-risk group.

By conducting this study at a Department of Ophthalmology, Sri Krishna Medical College Hospital, Muzaffarpur, Bihar,India from October 2024 to January 2025.an area with limited access to specialized ophthalmologic care—we also aim to emphasize the need for integrated multidisciplinary care models for autoimmune diseases. The outcomes of this research have the potential to inform clinical guidelines on the frequency and scope of ocular monitoring in SLE patients undergoing immunosuppressive treatment, ultimately reducing the burden of preventable vision loss.

Methods

This was a prospective, observational, hospital-based study conducted over a Department of Ophthalmology, Sri Krishna Medical College Hospital, Muzaffarpur, Bihar,India from October 2024 to January 2025. The study population included patients with a confirmed diagnosis of systemic lupus erythematosus (SLE) as per the Systemic Lupus International Collaborating Clinics (SLICC) criteria, who were undergoing treatment with systemic corticosteroids in combination with immunosuppressive agents.

A total of 80 patients (160 eyes) were enrolled after obtaining written informed consent. Inclusion criteria comprised patients aged 18 to 60 years, diagnosed with SLE and on systemic steroid therapy (prednisolone equivalent ≥10 mg/day) for at least one month, along with concurrent use of immunosuppressive medications such as azathioprine, cyclophosphamide, methotrexate, or mycophenolate mofetil. Exclusion criteria included patients with pre-existing glaucoma, ocular hypertension, steroid-responsive glaucoma prior to the SLE diagnosis, history of ocular trauma or surgery, current use of topical ophthalmic corticosteroids, or any other co-existing ocular pathology likely to affect intraocular pressure (IOP) or optic nerve status.

Each patient underwent a comprehensive ophthalmologic evaluation at baseline, including visual acuity testing (unaided and best corrected), slit-lamp biomicroscopy, Goldmann applanation tonometry for IOP measurement, gonioscopy using a four-mirror goniolens to assess the anterior chamber angle, and dilated fundus examination with a +90D lens for optic disc assessment. Cup-to-disc (C:D) ratio, neuroretinal rim thinning, and disc hemorrhages were recorded. Automated perimetry (Humphrey Field Analyzer 24-2) was performed to document any glaucomatous visual field defects.

Follow-up assessments were conducted at 3-month intervals (i.e., at 3, 6, 9, and 12 months), repeating the above examinations. Any significant change in IOP (≥6 mmHg from baseline), new onset of glaucomatous disc changes, or development of repeatable field defects were noted and documented. Patients found to have persistently elevated IOP (>21 mmHg) were started on anti-glaucoma medications and referred for further management.

Details of systemic therapy, including the type of steroid used, dosage, cumulative dose, duration of therapy, and specific immunosuppressive agents, were meticulously recorded. Blood pressure, renal parameters, and systemic disease activity were monitored in conjunction with the rheumatology department to ensure correlation with ocular findings.

The data was compiled and analyzed using SPSS software. Descriptive statistics were used to express patient demographics and clinical findings. Categorical variables were compared using Chi-square test, while continuous variables such as IOP were analyzed using paired and unpaired t-tests.

Pearson correlation was applied to assess the relationship between cumulative steroid dose and change in IOP. A p-value <0.05 was considered statistically significant.

Results

In this 12-month observational study involving 80 patients with systemic lupus erythematosus (SLE) undergoing systemic steroid and immunosuppressive therapy, notable changes in intraocular pressure (IOP) and glaucomatous features were observed. Of the total patients, 32.5% developed elevated IOP, while 18.75% showed optic disc changes suggestive of early glaucoma. The risk of glaucomatous changes increased with the duration and cumulative dose of corticosteroids. Visual field defects consistent with glaucoma were documented in 12.5% of cases. Immunosuppressive agents, while essential for SLE control, did not show a significant standalone effect on glaucomatous features.

Table 1: This table presents the age and gender distribution of the 80 SLE patients enrolled in the study

Age Group (Years)	Male (n)	Female (n)	Total (%)
18–30	4	16	20 (25%)
31–40	6	24	30 (37.5%)
41–50	5	15	20 (25%)
51–60	2	8	10 (12.5%)
Total	17	63	80 (100%)

Table 2: Shows the mean IOP (mmHg) in both eyes at baseline before initiation or continuation of steroid therapy

Eye	Mean IOP ± SD (mmHg)	Range (mmHg)
Right Eye	15.2 ± 2.4	10–20
Left Eye	15.1 ± 2.5	9–20

Table 3: Indicates the number of patients falling under various durations of corticosteroid use.

Duration of Use	Number of Patients	Percentage (%)
<3 months	18	22.5%
3–6 months	26	32.5%
>6 months	36	45%

Table 4: Demonstrates the relationship between cumulative dose and proportion of patients with IOP > 21 mmHg

Cumulative Dose (mg)	Patients with Elevated IOP	Total Patients in Range	Percentage (%)
<2000	2	20	10%
2000–4000	8	26	30.7%
>4000	16	34	47%

Table 5: Shows change in mean IOP over time

Time Point	Right Eye IOP (mmHg)	Left Eye IOP (mmHg)
Baseline	15.2 ± 2.4	15.1 ± 2.5
12 Months	18.6 ± 4.1	18.4 ± 4.0
Mean Increase	+3.4	+3.3

Table 6: Presents number of patients showing glaucomatous disc changes over time.

Follow-up Month	Patients with Disc Changes	Cumulative Percentage (%)
3 Months	4	5%
6 Months	6	12.5%
9 Months	10	15%
12 Months	15	18.75%

Table 7: Categorizes visual field changes detected by perimetry

Type of Defect	Number of Patients	Percentage (%)
Nasal step	4	5%
Paracentral scotoma	3	3.75%
Arcuate scotoma	3	3.75%
Generalized depression	0	0%
Total	10	12.5%

Table 8: Summarizes angle status in patients who developed raised IOP

Angle Status	Number of Patients	Percentage (%)
Open angle	24	92.3%
Narrow angle	2	7.7%
Closed angle	0	0%

Table 9:Lists immunosuppressive drugs and their frequency of usage among participants.

Drug Used	Number of Patients	Percentage (%)
Azathioprine	28	35%
Mycophenolate mofetil	22	27.5%
Cyclophosphamide	18	22.5%
Methotrexate	12	15%

Table 10: lyzes correlation of specific agents with elevated IOP.

Immunosuppressive Agent	Patients on Drug	IOP > 21 mmHg	Percentage (%)
Azathioprine	28	10	35.7%
Mycophenolate mofetil	22	6	27.3%
Cyclophosphamide	18	4	22.2%
Methotrexate	12	2	16.7%

Discussion

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by a complex interplay of immunological dysregulation affecting multiple organ systems, including the eyes. In this prospective observational study, we evaluated the impact of systemic corticosteroids in combination with immunosuppressive therapy on the development of glaucomatous changes over a 12-month period in SLE patients [7]. The study revealed significant findings related to steroid-induced ocular hypertension and early glaucomatous progression in a substantial proportion of patients.

Our study showed that 32.5% of patients developed an intraocular pressure (IOP) greater than 21 mmHg during the follow-up, a finding consistent with previous literature that identifies corticosteroids as a significant contributor to IOP elevation. The mechanism behind steroid-induced ocular hypertension is believed to involve morphological and biochemical alterations in the trabecular meshwork, including deposition of glycosaminoglycans, inhibition of phagocytosis, and suppression of proteolytic enzymes, leading to decreased aqueous outflow [8]. This results in progressive IOP elevation which, if sustained, can lead to glaucomatous optic neuropathy.

The data also indicated a direct relationship between the cumulative dose of corticosteroids and the risk of IOP elevation. Patients receiving cumulative doses above 4000 mg had a markedly higher risk of developing ocular hypertension (47%), in contrast to only 10% in those receiving less than 2000 mg. This dose-dependent effect reinforces the need for close monitoring, particularly in patients requiring high-dose or long-term steroid therapy [9].

Importantly, 18.75% of patients exhibited optic disc changes suggestive of early glaucoma, and 12.5% had visual field defects consistent with glaucomatous damage. These findings highlight the silent but progressive nature of steroid-induced glaucoma, which often remains asymptomatic until significant visual field loss occurs. The use of automated perimetry in our study proved essential in detecting subtle functional deficits that correlated with structural disc changes [10].

An interesting aspect of our study was the analysis of the role of various immunosuppressive agents. Although they are indispensable for controlling systemic inflammation in SLE, our data did not show a statistically significant difference in glaucomatous changes among different drugs . Azathioprine, mycophenolate mofetil, and cyclophosphamide were the most commonly used agents, and while there was some variation in the proportion of patients with IOP elevation in each subgroup, the differences were not statistically significant. This suggests that while these drugs are not primary culprits for raised IOP, their concurrent use with corticosteroids does not mitigate steroid-induced ocular side effects [11].

Open-angle anatomy was the predominant gonioscopic finding (92.3%) among patients with elevated IOP, supporting the diagnosis of secondary open-angle glaucoma as the major presentation. Only two patients had narrow angles, and none had angle closure, ruling out primary angle closure mechanisms in our cohort.

The initiation of anti-glaucoma medications (AGMs) in 15% of patients further underscores the clinical significance of our findings. Not only did these patients require intervention, but several also showed progressive optic disc changes and visual field loss, thereby meeting the diagnostic criteria for glaucoma. Early detection and timely initiation of topical IOP-lowering agents are thus critical steps in

preventing permanent vision loss in such patients [12].

Our study emphasizes the importance of integrating ophthalmologic evaluation into the management protocol for SLE patients undergoing systemic corticosteroid therapy. Routine screening for IOP, optic disc evaluation, and visual field testing—particularly in those on long-term or high-dose steroids—should become standard practice. The interdisciplinary approach, involving rheumatologists and ophthalmologists, is key to ensuring both systemic and ocular safety.

Comparing our findings with previous literature, a similar incidence of steroid-induced IOP elevation and glaucomatous changes has been reported in non-autoimmune populations using corticosteroids for other indications. However, our study adds value by specifically focusing on the SLE population, which is inherently more complex due to systemic inflammation, vasculopathy, and the use of multiple immunomodulatory drugs.

While our study was comprehensive, it did have limitations. First, the sample size, though adequate, was limited to a single tertiary care center. Second, the follow-up period of 12 months may not fully capture the long-term progression of glaucomatous damage. Third, individual susceptibility to steroid response (i.e., 'steroid responders') was not stratified or genetically profiled in this study. Future research with larger, multicentric cohorts and genetic profiling may yield more personalized insights into risk stratification.

In conclusion, our findings reinforce the critical need for routine ocular monitoring in SLE patients treated with systemic corticosteroids and immunosuppressive agents. Steroid-induced glaucoma, though preventable, remains a significant risk, particularly in resource-limited settings where regular ophthalmologic follow-up may not be feasible. Raising awareness among both patients and clinicians can significantly reduce the burden of avoidable vision loss in this vulnerable population.

Conclusion

This study highlights the significant ocular risks associated with prolonged systemic corticosteroid therapy in patients with systemic lupus erythematosus, particularly the development of ocular hypertension and early glaucomatous changes. A substantial proportion of patients developed raised intraocular pressure and optic disc changes over the 12-month follow-up period, with a clear correlation between higher cumulative steroid doses and glaucomatous progression. Immunosuppressive agents did not independently influence the onset of glaucoma but did not offer protection against steroid-induced ocular effects either.

Routine ophthalmologic surveillance, including periodic intraocular pressure monitoring, optic nerve assessment, and visual field testing, is crucial in this population. Early detection and timely management of steroid-induced glaucoma can prevent irreversible vision loss and significantly improve quality of life in patients with SLE. Multidisciplinary collaboration between rheumatologists and ophthalmologists is essential for comprehensive care and risk mitigation.

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