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Ocular Manifestations of Stevens-Johnson Syndrome: A Two-Year Clinical Study

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ABSTRACT

Stevens-Johnson Syndrome (SJS) is a rare but severe inflammatory disorder that affects the skin and mucous membranes, including the eyes, and may result in vision loss. This study aimed to assess the clinical characteristics, ocular manifestations, and management of patients with SJS at Dr. M. Djamil General Hospital, Padang. A retrospective cross-sectional study was conducted using medical records of 17 patients with ocular involvement caused by SJS, TEN, and SJS/TEN overlap who referred to the ophthalmology department from January 2021 to August 2023. A total of 65% presented in the acute/subacute phase and 35% in the chronic phase. Visual acuity in acute/subacute cases ranged from 6/6 to better than 6/60, with no symblepharon. Chronic-phase patients had poorer outcomes, including five eyes with vision worse than 1/60 and ocular complications such as symblepharon, corneal ulceration, opacity, neovascularization, and conjunctivalization. All patients received medical therapy, and three required surgical interventions, including symblepharon release and amniotic membrane transplantation. In conclusion, early ophthalmologic assessment and timely intervention are crucial to prevent severe ocular complications. Patients referred in the chronic phase experienced significantly worse visual outcomes.

Keywords: Ocular Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), symblepharon, ocular manifestation

INTRODUCTION

Stevens-Johnson Syndrome (SJS) is a rare, acute, multisystem inflammatory disorder that affects the skin and mucous membranes, including the conjunctiva. The condition manifests as an acute vesiculobullous eruption that causes peeling of the skin and mucosal surfaces. The condition is considered a hypersensitivity reaction, most commonly triggered by medications such as antibiotics, anticonvulsants, and nonsteroidal anti-inflammatory drugs, although infectious agents have also been implicated. The annual incidence of SJS is estimated at 2 to 6 cases per million population, with a significant mortality rate, particularly when it progresses to toxic epidermal necrolysis (TEN). Clinically, SJS presents with fever, malaise, and flu-like prodrome followed by the development of painful erythematous or purpuric macules, blisters, and mucosal erosions involving the oral, respiratory, gastrointestinal, and genitourinary tracts. Due to its multisystem involvement, SJS often results in long-term sequelae and requires multidisciplinary management during the acute phase. [1,2]

Among mucosal surfaces, the conjunctiva and oropharynx are most commonly involved. Ocular involvement in patients with SJS has been reported in approximately 69% to 81% of cases. The typical acute ocular manifestations include conjunctivitis with the presence of membranes or pseudomembranes, along with varying degrees of conjunctival and corneal epithelial desquamation. Chronic effects of SJS may include conjunctival cicatrization resulting in symblepharon formation, dry eye, trichiasis, keratinization of the eyelid margin, and limbal stem cell deficiency. The combination of these complications can lead to corneal ulcers, scarring, and decreased visual acuity. [1–3]

Ophthalmic intervention during the acute phase primarily consists of supportive therapy, including lubrication, prophylactic topical antibiotics, and the lysis of adhesions. These interventions form the

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cornerstone of ocular management in patients with SJS/TEN and can help improve ocular prognosis. The use of amniotic membrane transplantation on the ocular surface during the acute phase has also been shown to reduce inflammation and prevent long-term complications. [1,2,4–6]

Given the importance of early detection and management of ocular involvement, it is crucial to understand the clinical manifestations of SJS/TEN during both acute and chronic phases. Therefore, the authors were motivated to conduct this study, which aims to examine the characteristics of ocular manifestations in patients diagnosed with or having a history of SJS at Dr. M. Djamil General Hospital, Padang, during the period from January 2021 to August 2023.

METHOD

This study is a descriptive observational research using a retrospective cross-sectional approach. The data were recorded from secondary sources, specifically from the patients' medical records, and focused on cases referred to the Infection and Immunology Subdivision of the Ophthalmology Department at Dr. M. Djamil General Hospital in Padang.

The research was conducted between July and September 2023 at the ophthalmology outpatient clinic of Dr. M. Djamil General Hospital, Padang. The study population included all patients diagnosed with Stevens-Johnson Syndrome (SJS) or with a history of SJS who were referred to the Infection and Immunology Subdivision during the period from January 2021 to August 2023. All individuals who met the inclusion criteria were selected as study samples, making this a total sampling study.

The inclusion criterion for this study was patients who had been diagnosed with SJS or had a documented history of SJS in their medical records. Patients were excluded if their medical records were incomplete in key areas such as age, gender, SJS classification, ophthalmologic status, or treatment information.

In this study, operational variables were clearly defined. Age was defined as the patient's life span measured in years and categorized into ≤17 years, 18–44 years, and >44 years, based on data from medical records. Gender referred to the biological characteristics differentiating male and female patients, and was determined through recorded medical data. Laterality was assessed by identifying whether the ocular manifestations occurred in one or both eyes. The classification of SJS was based on the extent of skin involvement and was recorded as SJS, SJS/TEN overlap, or TEN. The onset of SJS referred to the time interval from the first diagnosis or history of SJS to the initial ophthalmologic consultation during the study period, and was classified as acute (<2 weeks), subacute (<6 months), or chronic (≥6 months). Drug history was assessed through prior medication intake suspected to trigger SJS, as documented in the medical records. Ocular manifestations were defined as clinical findings observed during the initial ophthalmology visit, including the condition of the eyelids, conjunctiva, cornea, and visual acuity. Lastly, treatment referred to the ocular management provided, whether solely medical or a combination of medical and surgical interventions.

This study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was not required as the study involved a retrospective review of anonymized medical records/data without any patient intervention or identification.

RESULT

A total of 17 patients (34 eyes) diagnosed with or having a history of Stevens-Johnson Syndrome (SJS) with ocular involvement were included in this study, based on data from polyclinic and consular visits to the Infection and Immunology Subdivision of the Ophthalmology Department at Dr. M. Djamil General Hospital, Padang, during the period of January 2021 to August 2023. All patients met the predetermined inclusion and exclusion criteria.

Table 1. Patient characteristics based on age, sex, and laterality

Age (years)	Gender		Lateralites		Total
	Man	Woman	Unilateral	Bilateral	
Age					
? 17	1	4	-	5	5 (29%)
18-44	6	2	-	8	8 (47%)
> 44	2	2	-	4	4 (24%)
Total	9 (53%)	8 (47%)	-	17 (100%)	17 (100%)

Table 1 presents the demographic characteristics of the patients. The majority were in the 18–44 year age group (47%). The gender distribution was slightly male-predominant, with 53% males and 47% females. All patients exhibited bilateral ocular involvement; no unilateral cases were recorded.

Table 2. Patient characteristics based on SJS classification

SJS Classification	Number (people)	Percentage (%)
SJS	12	70%
SJS/TEN *overlap*	2	12%
TEN	3	18%
Total	17	100%

Table 3. Patient characteristics based on the onset of SJS

Onset SJS	Number (people)	Percentage (%)
Acute	8	47%
Subakut	3	18%
Kronik	6	35%
Total	17	100%

Table 2 shows the distribution based on the clinical classification of SJS. Most patients (70%) were diagnosed with SJS, followed by 18% with Toxic Epidermal Necrolysis (TEN), and 12% with SJS/TEN overlap. Table 3 summarizes the onset of ocular manifestations. The majority of patients (47%) presented in the acute phase (<2 weeks from onset), followed by 35% in the chronic phase (≥6 months), and 18% in the subacute phase (<6 months). Table 4 displays the suspected drug-induced etiology of SJS. The most common drug group implicated was analgesics (18.5%), followed by antibiotics (14.8%) and anticonvulsants (14.8%). Notably, 29.6% of patients were unable to recall or determine the drugs consumed prior to SJS onset.

Table 4. History of drug consumption suspected to be the cause of SJS

Drug Name	Quantity (%)
Antibiotic	**4 (14,8)**
Ceftriaxone	1 (3,7)
Cefixime	1 (3,7)
Metronidazole	1 (3,7)
Amoxicilin	1 (3,7)
Anticonvulsant	**4 (14,8)**
Phenobarbital	3 (11,1)
Carbamazepine	1 (3,7)
Analgetik	**5 (18,5)**
Paracetamol	4 (14,8)
Sodium Diklofenac	1 (3,7)
Antihistamin	**2 (7,4)**
Ranitidine	1 (3,7)
Cetirizine	1 (3,7)
Other Medications	**4 (14,8)**
Sulfadoxine+Pyrimethamine	1 (3,7)
Asetilsistein	1 (3,7)
Omeprazole	1 (3,7)
Donepezil	1 (3,7)
Unknown	**8 (29,6)**
Total	**27 (100)**

*Patients can use >1 medication

Table 5 outlines the ocular manifestations observed in different phases. In the acute phase, all patients retained relatively good visual acuity (6/6–6/18). Similarly, in the subacute phase, visual acuity remained generally good, with the worst acuity recorded being in the <6/18–6/60 range. In contrast, chronic-phase patients showed significantly worse visual outcomes, with five eyes exhibiting visual acuity worse than 1/60 to light perception.

Ocular surface involvement varied by phase. In the acute phase, manifestations were limited to palpebral and conjunctival inflammation, including secretion/crust formation and conjunctival hyperemia. In the chronic-phase, patients demonstrated more severe and extensive damage condition, extended to the cornea, with findings such as blepharitis, simblepharon, corneal epithelial erosions, infiltrates, and opacification. Corneal neovascularization and conjunctivalization were also noted in several chronic cases.

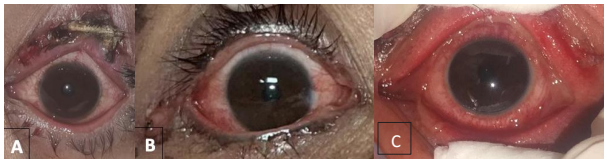

Figure 1. Acute-phase ocular manifestations. A. secretion/crust formation, B. conjunctival hyperemia, C. palpebral inflammation

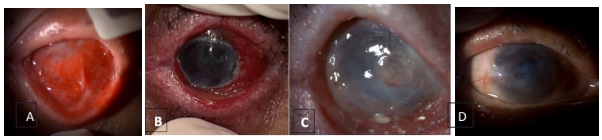

Figure 2. Chronic-phase ocular manifestations. A. symblepharon, B. corneal erosions, C. corneal infiltrat, ulcer and neovascularization, D. corneal scarring, neovascularization and opasification

Figure 1 shows acute-phase findings, including conjunctival hyperemia, palpebral inflammation and secretion/crust formation. Figure 2 demonstrates chronic-phase sequelae, such as symblepharon formation, corneal scarring, corneal erosions, neovascularization and opacification. These images provide a visual representation of the clinical progression of ocular involvement in Stevens–Johnson Syndrome and highlight the differences between acute and chronic manifestations

Regarding treatment, all patients received medical therapy. There patients additionally underwent surgical intervention, consisting of symblepharon release (symblepharectomy) and multilayer amniotic membrane transplantation (ML AMT), due to restricted ocular motility or persistent corneal complication

Table 5 Ocular manifestations of SJS patients in the acute phase

Variabel	Clinical findings	Onset Acute	Subakut	Kronik
Visual acuity	6/6 – 6/18	16	1	5
	< 6/18 – 6/60	-	5	2
	< 6/60 – 3/60	-	-	-
	< 3/60 – 1/60	-	-	-
	< 1/60 – PL	-	-	5
	NPL	-	-	-
Pelpebra	Secretion/crust	14	4	1
	Edema	4	-	2
	Meibomitis/blepharitis	2	2	2
	Trichiasis/Dystichiasis	-	-	4
	Madarosis	2	2	2
	Margo Irregulate	-	-	4
Conjunctive	Hyperemis	16	6	11
	Conjunctival membrane	-	-	-
	Subconjunctival hemorrhage	-	-	-
	Simblefaron	-	3	8
	Fornix foreshortening	-	-	-
Kornea	Epithelial erosion	-	4	2
	Infiltrate	-	2	2
	Corneal ulcer	-	-	2
	Corneal opasification	-	2	2
	Neovasculariosis	-	-	3
	Conjunctivalization	-	-	3

*PL = perception of light, NPL = no perception of light. All values presented refer to the number of affected eyes.

DISCUSSION

This study analyzed 17 patients (34 eyes) diagnosed with Stevens-Johnson Syndrome (SJS) or Toxic Epidermal Necrolysis (TEN) with ocular involvement at Dr. M. Djamil General Hospital, Padang, between January 2021 and August 2023. The majority of patients in this study were adults aged 18–44 years, which is consistent with the findings of Sutedja et al., who reported that most SJS patients were adults within the age range of 25–44 years.[7]

Gender distribution in this study showed a slight male predominance (53%), which supports the findings by Rahayu et al.[7] However, contrasting results were reported by Abrol et al., who observed a higher incidence among females in their cohort.[8] These differences suggest that gender may not be a consistent risk factor for SJS, as the condition is primarily triggered by immunological reactions irrespective of sex.[1]

All patients in this study presented with bilateral ocular manifestations of SJS. Similarly, Abrol et al. also reported that all patients with SJS in their study had bilateral ocular involvement.[8] This finding is consistent with the literature, which describes that SJS typically affects the skin and mucous membranes, with the conjunctiva of both eyes being the most frequently involved mucosal site. Although both eyes are usually affected, the severity can differ between eyes, highlighting the need for careful evaluation of each eye individually.[9] This difference in severity may also serve as the basis for tailored management strategies for each eye in the same patient.[1,2,8–11]

Most cases in this study were classified as SJS (70%), followed by TEN (18%) and SJS/TEN overlap (12%). This finding is consistent with

those of Wijanto et al., Abrol et al., and Chen et al., who also reported that the majority of patients were classified as SJS rather than TEN or SJS/TEN overlap. However, it differs from the findings of Sutedja et al., who reported that TEN was the most commonly observed classification.[7,8,12,13] The majority of patients presented in the acute phase of the disease, emphasizing the importance of early ophthalmologic referral and evaluation.

Drug-induced reactions were the most suspected etiology, with analgesics being the most commonly implicated (18.5%), followed by antibiotics and anticonvulsants (each 14.8%). Approximately 29.6% of patients had no clear history of preceding drug use. These results echo those of Abrol et al., who identified non-steroidal anti-inflammatory drugs (NSAIDs), antibiotics, and anticonvulsants as common triggers of SJS/TEN.[8] Although infections and genetic predispositions are also acknowledged risk factors, their evaluation was limited in this study due to incomplete data.

Visual acuity in the acute phase was generally preserved, except in cases where assessment was hindered by the patient's systemic condition. This is consistent with literature stating that the acute phase typically involves the eyelids and conjunctiva, sparing the cornea.[1,2,10,11] In contrast, patients in the chronic phase exhibited poorer visual outcomes, with five eyes recording visual acuity worse than 1/60 to light perception. Corneal pathologies such as infiltrates, ulcers, and conjunctivalization were prominent in these patients.

Ocular involvement progressed with disease phase. In the acute phase, manifestations were limited to conjunctival hyperemia and palpebral secretions. Subacute and chronic phases showed more severe findings, including blepharitis, simblepharon, corneal erosions, opacification, neovascularization, and conjunctivalization. These findings are consistent with the progressive cicatricial changes described in chronic SJS. [1,2,10,11]

All patients received medical treatment. In line with previous studies, acute-phase therapy involved lubrication, topical antibiotics, and mechanical separation of adhesions to prevent symblepharon.[2,5,14] Three patients with advanced ocular complications underwent surgical intervention, including symblepharon release (symblepharectomy) and multilayer amniotic membrane transplantation (ML AMT). Indications for surgery included restricted ocular motility and corneal damage (erosions and ulcers). These interventions are supported by literature, which advocates ML AMT in managing cicatricial ocular surface disease and restoring ocular integrity in severe cases.[2,4,5,15]

CONCLUSION

Steven-Johnson Syndrome (SJS) is an acute inflammatory reaction caused by a delayed-type hypersensitivity response, characterized by vesiculobullous lesions affecting the skin and mucous membranes, including the conjunctiva. SJS/TEN can occur in both males and females, predominantly in adults, and ocular manifestations are more commonly bilateral. Among its classifications, SJS is more frequently encountered than TEN or SJS/TEN overlap. The most commonly suspected causative agents are medications, particularly analgesics, followed by anticonvulsants and antibiotics. In the acute phase, ocular manifestations typically involve the conjunctiva and eyelids, while in the subacute and chronic phases, the involvement may extend to the cornea. All cases of SJS/TEN require medical management; however, some patients may require surgical intervention such as symblepharon release (symblepharectomy) and/or multilayer amniotic membrane transplantation (ML AMT) for more severe ocular complication

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest related to this study.

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