

Understanding the Gap Between Acute Complications and Long-Term Sequelae in Patients with Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis in Bandung, West Java, Indonesia: Experience from Two Institutions

Endang Sutedja¹, Oki Suwarsa¹, Miranti Pangastuti¹, Chaerani Pratiwi Firdaus¹, Reiva Farah Dwiyanita¹, Trustia Rizqandar¹, Arief Akhdestira Mustaram², Patriotika Muslima², Ayu Adzani Sabila¹

¹Department of Dermatology and Venereology, Faculty of Medicine, Universitas Padjadjaran Dr. Hasan Sadikin General Hospital, Bandung, West Java, Indonesia; ²Department of Ophthalmology, Faculty of Medicine, Universitas Padjadjaran Cicendo Eye Hospital, Bandung, West Java, Indonesia

Correspondence: Ayu Adzani Sabila, Department of Dermatology and Venereology, Faculty of Medicine, Universitas Padjadjaran - Dr. Hasan Sadikin General Hospital, Jl. Pasteur 38, Bandung, West Java, 40161, Indonesia, Tel +6282118094129, Email ayu12002@mail.unpad.ac.id

Introduction: A severe skin reaction called Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN) can cause a number of short-term and long-term problems that affect many organ systems.

Objective: To describe acute complications and long-term sequelae in patients with SJS/TEN in two tertiary referral hospitals in West Java.

Methods: A retrospective study was conducted in patients with SJS/TEN treated from January 1st, 2022, to July 31st, 2024, at Dr. Hasan Sadikin General Hospital Bandung and Cicendo Eye Hospital Bandung.

Results: The study included a total of 28 patients, 11 males and 17 females. The study diagnosed patients with SJS (33%), SJS/TEN overlap (31%), or TEN (36%). The age range of the majority of patients was 25–44 years (32%). The most commonly implicated medication was acetaminophen, accounting for 43% of the cases. The average length of hospitalization for SJS was 8±3.29 days, for SJS/TEN overlap was 15.12±18.42 days, and for TEN was 13±9.01 days. The highest SCORTEN was 4. Among SJS and SJS/TEN overlap patients, cheilitis was the most frequent complication, while hypokalemia was the most common acute complication in TEN patients (17%). Long-term skin sequelae include hypopigmentation in five patients and hyperpigmentation in eleven. The most common long-term eye sequelae, dry eye, affected 3 patients.

Conclusion: Common acute complications include extensive cheilitis, hypoalbuminemia, hypocalcemia, acute conjunctivitis, and acute kidney injury. Hyperpigmentation and hypopigmentation were found as the most frequent long-term skin complications, and dry eyes were the most frequent long-term eye sequelae. Further studies on the physical sequelae of SJS/TEN are necessary to enhance our understanding of the condition and improve treatment for survivors.

Keywords: acute complications, long-term sequelae, Stevens-Johnson syndrome, toxic epidermal necrolysis

Introduction

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are severe, life-threatening mucocutaneous eruptions, most often triggered by a severe allergic drug reaction.^{1–3} Both conditions are characterized by the development of blisters and the detachment of the epidermal layer.^{1,4} The main difference between SJS and TEN is the extent of epidermal detachment. SJS involves 0–10% of total body surface area (BSA), SJS/TEN overlap affects 10–30% BSA, and TEN affects more than 30% BSA.^{1,4,5}

In Japan, the yearly prevalence per million was 2.5 for SJS and 1 for TEN.⁶ Indonesia has reported several studies on SJS/TEN. In 2016, Dr. Hasan Sadikin General Hospital in Bandung conducted a study from 2009 to 2013, which found 39 cases of SJS, 7 cases of SJS/TEN overlap, and 11 cases of TEN.⁷ Isaac et al⁸ in 2019 conducted a study at Dr. Soetomo Hospital in Surabaya and found 28 cases of SJS/TEN, consisting of 24 SJS patients (85.7%), 3 TEN patients (10.7%), and 1 patient with SJS/TEN overlap (3.5%).⁸ SJS/TEN has a high mortality and morbidity rate.^{1,9}

Reports of various acute complications and long-term sequelae from SJS/TEN are widely available.¹⁰ Acute complications can affect multiple organs, such as the kidneys, lungs, and eyes, and can even lead to sepsis.^{1,11} Other acute complications that may occur in SJS/TEN patients include acute interstitial nephritis (AIN), respiratory failure, gastrointestinal bleeding, and oral ulceration.^{10,12} Acute eye complications occur in 50–88% of cases and mainly result in visual disturbances.¹³ Acute skin complications can lead to secondary infections.^{1,9} Laboratory tests may show low levels of albumin or protein, signs of an electrolyte imbalance, a lack of white blood cells or leukocytosis, high levels of creatinine or urea in the blood, or high levels of liver enzymes.^{14,15} Many acute complications can develop into long-term sequelae,¹¹ which can affect the patient's quality of life.¹⁶

Long-term sequelae on the skin can include post-inflammatory pigmentation changes (both hyperpigmentation and hypopigmentation), scarring, nevus eruptions, telogen effluvium, chronic pruritus, hyperhidrosis, and photosensitivity. In the study by Hoffmann et al¹⁷ 84.3% of patients had cutaneous sequelae that comprised irregular pigmentation, eruptive nevi, alopecia, chronic eczema, and pruritus. Nearly all SJS/TEN cases result in nail complications. These may include nail deformity, nail loss, nail dystrophy, or onychodystrophy, pterygium, and anonychia.^{1,10}

A third of acute eye complications in SJS/TEN progress into long-term sequelae, often due to inadequate management during the acute phase.¹³ Dry eyes, trichiasis, keratopathy, limbal stem cell deficiency, blepharitis, corneal ulcers, Meibomian and lacrimal gland obstruction, symblepharon, corneal opacification, and neovascularization are some of the long-term effects that can happen.^{3,18} Saka et al¹⁹ reported eye complications in SJS/TEN patients such as decreased vision (14.1%), symblepharon (12.7%), photophobia (12.7%), and dry eyes (9.9%). Untreated eye involvement can persist and worsen, severely impacting the patient's quality of life.^{12,20} The aim of this study was to describe acute complications and long-term sequelae in patients with SJS/TEN in tertiary referral hospitals in West Java, Indonesia.

Patients and Methods

This was a retrospective study of SJS/TEN conducted at Dr. Hasan Sadikin General Hospital and Cicendo Eye Hospital in Bandung, Indonesia, between January 1st, 2022, and July 31st, 2024. Medical records of patients treated at the Dermatology and Venereology Department were inclusion criteria for this study. We determined the sample size using the total sampling technique, which included all medical records that met the inclusion criteria. Medical records with highly incomplete data or those that were inaccessible were considered exclusion criteria in this study. The total number of collected medical records was 31, of which 3 were excluded, resulting in a final analysis of 28 medical records.

We reviewed the medical records to identify the following: demographic characteristics, previous drug exposures, hospitalization duration, SCORTEN (Severity of Illness Score for Toxic Epidermal Necrolysis), acute complications, and long-term sequelae. When we analyzed the causative drugs, we included all suspected medications based on the information recorded in the medical records without using the Naranjo scale assessment. Data were manually extracted from electronic medical records, and statistical analysis was performed using SPSS software (version 29.0.2), generating descriptive statistical data.

Acute complications were defined as clinical conditions affecting specific organs that arise at the onset of the disease, alongside primary manifestations such as epidermolysis and lesions. We defined long-term sequelae as abnormalities in specific organs that arose during the resolution phase of SJS/TEN or the acute phase of SJS/TEN and did not improve for at least one month after the resolution of SJS/TEN. This study restricted them to the skin, nails, and eyes. We obtained eye complications from the electronic medical records at Cicendo Eye Hospital, which included patients previously diagnosed with SJS/TEN and hospitalized at Dr. Hasan Sadikin General Hospital during the study period.

Results

Twenty eight patients (11 males and 17 females) were admitted to Hasan Sadikin General Hospital and had a discharge diagnosis of SJS (33%), SJS/TEN overlap (31%), or TEN (36%) during the 2-year study period (Table 1). The majority of patients were in the age range of 25–44 years (32%) (Table 1). Adverse reactions to medication were the most likely causative factor in all patients. Acetaminophen was the most commonly suspected implicated drug, affecting 12 patients (43%), followed by carbamazepine and cotrimoxazole, each affecting 4 patients (14%), as shown in Table 2. Please note that one patient may have multiple medications suspected as the cause.

The characteristics based on the duration of hospitalization for patients with SJS, SJS/TEN overlap, and TEN can be seen in Figure 1. In this study, the average length of hospitalization for SJS was 8 ± 3.29 days, for SJS/TEN overlap was 15.12 ± 18.42 days, and for TEN was 13 ± 9.01 days. This study recorded the shortest length of care at 4 days, and the longest at 60 days. We calculated the SCORTEN for each patient to assess prognosis. Out of 28 patients, there were two who did not have their SCORTEN values recorded in the medical records. Two patients (7%) with TEN had the highest SCORTEN, which was recorded at 4. Mean SCORTEN in this study for SJS was 1.8 ± 1.09 , SJS/TEN overlap was 1.8 ± 2.49 , and TEN was 1.6 ± 2.07 (Figure 2).

Multiple acute complications may occur in a single patient. Extensive cheilitis was the most frequent acute consequence in our study, occurring in 7 patients (28%), of which 4 were SJS patients and 3 were SJS/TEN overlap

Table 1 Demographic and Baseline Characteristics of SJS, SJS/TEN Overlap, and TEN

Variable					Total (28)	
	SJS n(%)	SJS/TEN Overlap n(%)	TEN n(%)	Mean±SD	n	%
Gender						
Male	3 (11)	4 (14)	4 (14)	1.61±0.497	11	39
Female	6 (22)	5 (17)	6 (22)		17	61
Age at diagnosis (year)						
≤18	0	3 (11)	3 (11)	2.86±1.297	6	22
18–24	2 (7)	2 (7)	0		4	14
25–44	4 (14)	2 (7)	3 (11)		9	32
45–64	3 (11)	1 (4)	2 (7)		6	22
≥ 65	0	1 (4)	2(7)		3	11

Table 2 Suspected Etiology of SJS/TEN

Drugs	Diagnosis			Total n (%)
	SJS n (%)	SJS/TEN Overlap n (%)	TEN n (%)	
Antibiotics	4 (21)	7 (36)	4 (16)	15 (23)
Cotrimoxazole	1 (5)	3 (15)	0	4 (14)
Ceftriaxone	0	0	2 (8)	2 (7)
ATT FDC (rifampicin, isoniazid, pyrazinamide,ethambutol);	0	2 (10)	0	2 (7)
Cefadroxil	1 (5)	0	0	1 (4)
Fradiomycin Sulfate	1 (5)	0	0	1 (4)
Amoxicillin	0	0	1 (4)	1 (4)
Cefotaxime	0	1 (5)	0	1 (4)
Cefixime	0	0	1 (4)	1 (4)
Levofloxacin	1 (5)	0	0	1 (4)
Metronidazole	0	1 (5)	0	1 (4)

(Continued)

Table 2 (Continued).

Drugs	Diagnosis			Total n (%)
	SJS n (%)	SJS/TEN Overlap n (%)	TEN n (%)	
Antiepileptics	1 (5)	3 (15)	2 (8)	6 (9)
Carbamazepine	1 (5)	2 (10)	1 (4)	4 (14)
Phenytoin	0	1 (5)	0	1 (4)
Lamotrigine	0	0	1 (4)	1 (4)
Analgesics	6 (31)	7 (36)	7 (28)	20 (31)
Acetaminophen	3 (15)	5 (26)	4 (16)	12 (4)
Ibuprofen	0	1 (5)	1 (4)	2 (7)
Aspirin	1 (5)	0	1 (4)	2 (7)
Tramadol	1 (5)	1 (5)	0	2 (7)
Caffeine	1 (5)	0	0	1 (4)
Mefenamic Acid	0	0	1 (4)	1 (4)
Cold Drugs	3 (15)	0	3 (12)	6 (9)
Dextromethorphan	1 (5)	0	1 (4)	2 (7)
Tremenza® (pseudoefedrin, tripolidine)	1 (5)	0	1 (4)	2 (7)
Hufagrip™ (Pseudoephedrine HCl, CTM)	0	0	1 (4)	1 (4)
Phenylephrine	1 (5)	0	0	1 (4)
Other Drugs	5 (26)	2 (10)	9 (36)	16 (25)
ARV (efavirenz, lamivudine,tenofovir)	0	2 (10)	0	2 (7)
Amlodipine	1 (5)	0	1 (4)	2 (7)
Atorvastatin	1 (5)	0	0	1 (4)
Eperisone	0	0	1 (4)	1 (4)
Allopurinol	0	0	1 (4)	1 (4)
N-acetylcysteine	0	0	1 (4)	1 (4)
Amitriptyline	1 (5)	0	0	1 (4)
Mecobalamine	1 (5)	0	0	1 (4)
Chlorpromazine	1 (5)	0	0	1 (4)
Omeprazole	0	0	1 (4)	1 (4)
Furosemide	0	0	1 (4)	1 (4)
Yellow tablet	0	0	1 (4)	1 (4)
Green yellow capsule	0	0	1 (4)	1 (4)
Red blue capsule	0	0	1 (4)	1 (4)

Abbreviations: ATT, Antituberculosis therapy; FDC, Fixed drug combination; CTM, Chlorpheniramine maleate.

patients (Table 3). Hypokalemia was the most frequent acute consequence among TEN patients, occurring in 5 of them (17%) (Table 3). Two patients in the TEN group died due to sepsis, which was the most severe acute complication.

The dermatology clinic at Dr. Hasan Sadikin General Hospital recorded 16 patients with long-term skin sequelae, including hypopigmentation in 5 patients (18%) and hyperpigmentation in 11 patients (39%) (Table 4). Meanwhile, the medical records at Cicendo Eye Hospital identified long-term sequelae related to the eyes in only three patients, all of whom were children, out of seven who experienced acute eye complications. We lost the other four patients to follow-up. The most common long-term ocular sequela was dry eyes, affecting 3 patients (Table 4). Other long-term ocular sequelae found in this study included cicatricial entropion, blepharitis, trichiasis, and keratoconjunctivitis. The electronic medical records did not record any long-term sequelae related to the nails.

Discussions

Although previously thought to be the primary trigger for keratinocyte apoptosis, the precise pathogenesis of SJS/TEN remains unclear. Recent research indicates that cytotoxic T lymphocytes and natural killer (NK) cells produce granulysin,

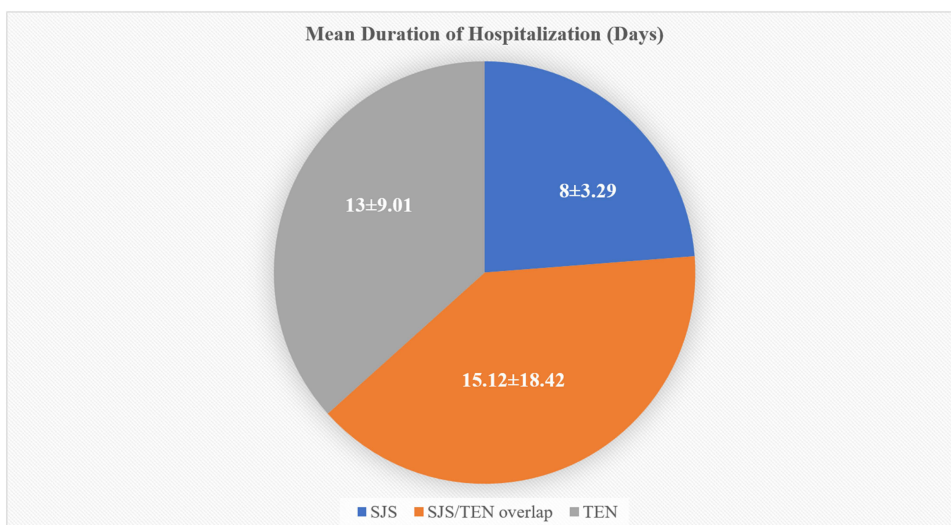


Figure 1 Mean duration of hospitalization.

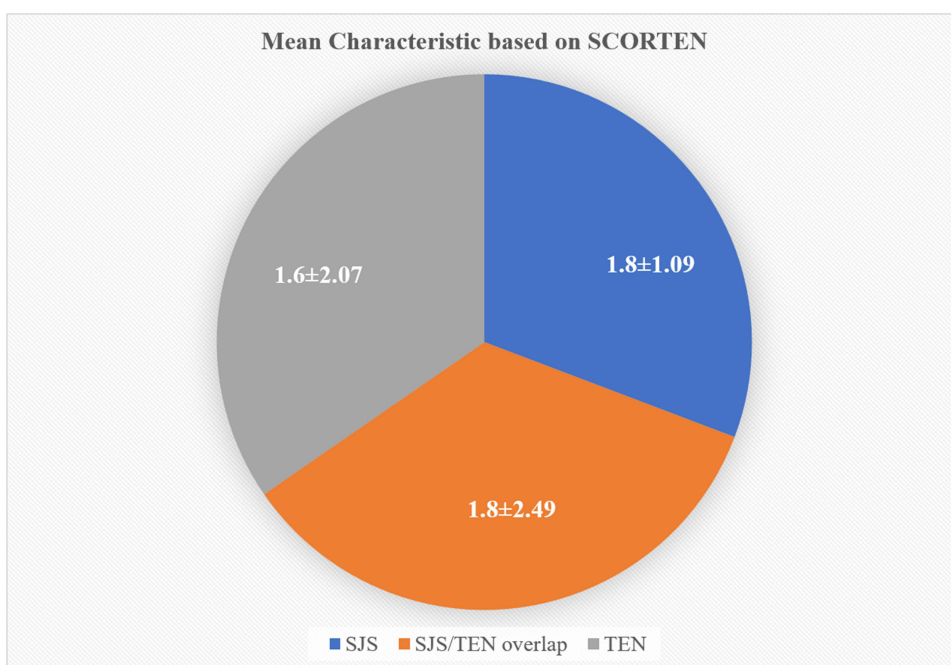


Figure 2 Mean SCORETEN.

a cytotoxic protein, which triggers widespread apoptosis in keratinocytes. The involvement of cytotoxic T cells, tumor necrosis factor-alpha, and Fas-FasL interactions is still considered relevant in these diseases. A cytotoxic protein released by cytotoxic T cells or NK cells is now known to play a major role in the death of many keratinocytes in SJS and TEN.^{1,4,7}

According to a study by Sunaga et al⁶ it was found that patients with SJS were more commonly female than male, with a total of 550 female patients compared to 380 male patients. The findings are also in line with a 2015–2020 study on SJS/TEN in the United States (US) that discovered a 57.2% female prevalence.²¹ Based on medical record data from 2017–2023, another unpublished study at Dr. Hasan Sadikin General Hospital found that there were more female patients with SJS/TEN than male patients.²² Those studies were similar to our findings.

Table 3 Acute Complications of SJS/TEN

	Diagnosis			Total n (%)
	SJS n (%)	SJS/TEN Overlap n (%)	TEN n (%)	
Electrolyte Imbalances	4 (15)	3 (15)	9 (45)	16 (24)
Hypocalcemia	2 (7)	1 (5)	3 (15)	6 (22)
Hyponatremia	2 (7)	2 (10)	1 (5)	5 (17)
Hypokalemia	0	0	5 (5)	5 (17)
Eye Complications	7 (26)	5 (25)	6 (3)	18 (27)
Acute Conjunctivitis	3 (11)	2 (10)	1 (5)	6 (22)
Ectropion	1 (3)	0	0	1 (4)
Conjunctivitis	0	0	1 (5)	1 (4)
Conjunctival Haemorrhage	1 (3)	0	0	1 (4)
Dry eye	0	1 (5)	0	1 (4)
Corneal abrasion	0	1 (5)	0	1 (4)
Symblepharon	0	0	1 (5)	1 (4)
Oropharyngeal Complications	10 (38)	6 (30)	0	16 (24)
Extensive Cheilitis	4 (15)	3 (15)	0	7 (28)
Intraoral Erosive Lesion	2 (7)	2 (10)	0	4 (14)
Mucositis	1 (3)	1 (5)	0	2 (7)
Xerostomia	1 (3)	0	0	1 (4)
Acute Tonsillopharyngitis	1 (3)	0	0	1 (4)
Pharyngitis	1 (3)	0	0	1 (4)
Other Complications	5 (19)	6 (3)	5 (25)	16 (24)
Hypoalbuminemia	2 (7)	2 (10)	2 (10)	6 (22)
Transaminitis	1 (3)	2 (10)	2 (10)	5 (17)
DILI	1 (3)	1 (5)	0	2 (7)
Acute Kidney Injury	2 (7)	1 (5)	3 (15)	6 (22)
Sepsis	0	0	1 (5)	2 (7)

Abbreviation: DILI, Drug induced liver injury.

Table 4 Long-Term Sequelae of SJS/TEN

	Diagnosis				Total n (%)
	SJS n (%)	SJS/TEN Overlap n (%)	TEN n (%)	Mean±SD	
Skin sequelae					
Hyperpigmentation	3 (19)	6 (38)	2 (12)	2.67±1.966	11 (68)
Hypopigmentation	2 (12)	3 (19)	0		5 (31)
Eye sequelae					
Dry Eyes	0	2 (28)	1 (14)	0.47±0.640	3 (43)
Cicatricial Entropion	0	1 (14)	0		1 (14)
Blepharitis	0	1 (14)	0		1 (14)
Trichiasis	0	1 (14)	0		1 (14)
Keratoconjunctivitis	0	0	1 (14)		1 (14)

Although the precise etiology of SJS/TEN is still unknown, medications are the main contributing factor.^{1,23} Numerous studies revealed that drugs are responsible for nearly 90% of SJS/TEN cases, making them the primary cause.²⁴ The investigation has implicated over 100 distinct medications. Antibacterial sulfonamides, aromatic antiepileptic medications, lamotrigine, nevirapine, nonsteroidal anti-inflammatory medications, and allopurinol are among these

high-risk medications.^{1,23–25} In addition to the previously mentioned drugs, new antimicrobial agents, such as antifungals and antivirals, have also been reported as causes of SJS-TEN.^{26,27} The most often implicated drug in a prior study by Suwarsa et al⁷ at Dr. Hasan Sadikin General Hospital was acetaminophen, which accounted for 16.56%. In the study conducted by Finkelstein et al²³ it was indicated that the most frequent causative agents for SJS/TEN were antiepileptic drugs, such as carbamazepine.²³ The results of this study correlate with those of previous studies, indicating that acetaminophen (43%) is the most common cause of SJS/TEN, followed by carbamazepine (4%). Reports regarding acetaminophen may be due to its widespread prescription and over-the-counter availability.²⁸

A study of Japanese and Thai people found a strong link between HLA-A33:03, HLA-B44:03, and HLA-C*07:01 and SJS/TEN caused by acetaminophen.²⁹ Studies in Han Chinese populations from Taiwan have demonstrated a strong correlation between HLA-B1502 and carbamazepine-induced SJS-TEN, as well as between HLA-B5801 and allopurinol-induced SJS-TEN. This association of HLA-B*1502 with carbamazepine-related SJS-TEN has been validated in multiple Southeast Asian countries but has not been observed in Japan or Korea.^{1,2,4} However, based on the authors' knowledge, no studies have been conducted in Indonesia investigating the association between acetaminophen and HLA in the context of SJS-TEN. In addition, further research is needed to investigate the association between acetaminophen and HLA genotyping in SJS-TEN patients within the Indonesian population, considering that acetaminophen was the most common causative agent in this study and HLA genotyping is not yet routinely performed in our center due to facility limitations.

The average length of hospitalization for patients in the Wasuwanich et al²¹ study was seven days. Yoo et al²⁵ showed that the duration of treatment in the SJS group, SJS/TEN overlap, and TEN were 16.5, 20.4, and 21.4 days, respectively. In this study, the average length of hospitalization for SJS was 8 ± 3.29 days, for SJS/TEN overlap was 15.12 ± 18.42 days, and for TEN was 13 ± 9.01 days.

Predictive scoring systems such as SCORTEN and ABCD-10 are vital in evaluating and treating patients with SJS-TEN. ABCD-10 (age, bicarbonate, cancer, dialysis, 10% body surface area) is a newer risk prediction scoring system compared to SCORTEN.³⁰ However, in this study, the scoring system used is SCORTEN because the use of ABCD-10 is not yet common in our center. SCORTEN uses seven independent risk factors to predict the risk of death: age, malignancy, heart rate, epidermal detachment, serum urea, glucose, and bicarbonate at admission.^{1,28} A higher risk of daily fluctuating mortality during the first five days of hospitalization is associated with the SCORTEN.^{28,30} For the first five days following its hospital admission, it has performed well.³⁰ The study by Yoo et al²⁵ showed that in the groups with antibiotic and allopurinol etiologies, the average SCORTEN scores were 2.1 and 1.9, respectively. In this study, the highest SCORTEN, 4, was recorded for two patients (7%) with TEN, and it was not associated with any specific etiology. Unfortunately, this study only analyzed the SCORTEN at the time of admission rather than daily, which may have limited its ability to predict mortality.

A study by Micheletti et al³¹ in 2018 reported acute complications in 377 patients with SJS/TEN in the United States, including acute kidney injury (130 cases, 34.5%), respiratory failure (89 cases, 23.6%), pneumonia (57 cases, 15.1%), sepsis (48 cases, 12.7%), and secondary infections (30 cases, 8%). Monteiro et al³² in 2016 found that the most common complications were sepsis (20%) and kidney failure (13.3%). Suwarsa et al⁷ in 2016 in Bandung found 16 cases of SJS, 1 case of SJS TEN overlap, and 2 cases of TEN were reported, with elevated liver enzymes, respiratory issues, and sepsis. In 1922, Stevens and Johnson provided the first description of the illness, which included acute oral involvement. Since then, studies have reported involvement of the oral mucous membranes in 71–100% of patients. We have thoroughly examined the acute pathologic alterations, including ulceration and fibrinous exudative inflammation.¹² The most frequent acute consequences in this study were extensive cheilitis (28%), followed by hypoalbuminemia, hypocalcemia, acute conjunctivitis, and acute kidney injury, each at 22%. Furthermore, this study noted transaminitis, hyponatremia, and hypokalemia in 17% of patients.

In a study by Weisz et al¹¹ in 2020 in Spain involving 6 patients with TEN, 3 patients were found to have post-inflammatory hyperpigmentation. Saka et al¹⁹ in 2019, in their research on 177 patients with SJS/TEN, reported that 42.3% experienced long-term sequelae affecting the skin, with the most common being pigmentary disturbances (38%). Rahmawati et al³³ conducted a study in Indonesia and found that 7 patients experienced hypopigmentation complications, while 19 patients experienced hyperpigmentation. Sometimes a person has both hyperpigmentation and

hypopigmentation after inflammation. This study observed hyperpigmentation in 39% of patients and hypopigmentation in 18%. Three patients in this study experienced both hypopigmentation and hyperpigmentation simultaneously.

Inflammation and necrosis of the conjunctiva, along with swelling and loss of skin on the eyelids, can cause membranous conjunctivitis and loss of goblet cells in the lacrimal ducts, which can make the eyes dry all the time.^{1,10,18,19} Inflammation and erosion of the lacrimal ducts can also leave scarring, which may cause adhesions of the eyelids, leading to malposition, entropion, and ectropion. This can alter eyelash growth, a condition known as trichiasis.^{18,19} A 2017 study by Olteanu et al³⁴ in Canada, which included 17 individuals with either SJS or TEN, revealed that 67% of these individuals had long-term ocular sequelae, with dry eyes accounting for the majority at 44%. Symblepharon (33%), chronic ocular surface inflammation (33%), blurred vision (22%), conjunctivitis (22%), tarsal conjunctival keratinization (22%), blindness (11%), trichiasis (11%), ectropion (11%), and corneal neovascularization (11%) were among the other signs found in the study. Finkelstein et al²³ conducted a study on pediatric patients and found that 15 children (27%) had long-term ocular sequelae, such as uveitis, keratitis, corneal defects, and chronic conjunctivitis. All patients who experienced long-term ocular sequelae in this study were children. The most common long-term ocular sequela in this study was dry eyes, affecting 3 patients, in line with previous studies. However, this number may not accurately reflect the actual prevalence of long-term ocular sequelae, as some patients were lost to follow-up.

We suspect that the extent of skin involvement during the acute phase correlates with the severity of long-term ocular sequelae.^{19,20} In this study, long-term effects were more common in people who had SJS/TEN overlap and TEN. This is thought to be because they had a lot of inflammation in the eye's epithelium and had previous acute eye problems.

The main limitations of our study were its retrospective design and the limited usefulness for providing definite proof of causality for suspected agents. However, virtually all SJS and TEN studies share this limitation, as the patients are too sick to undergo rechallenge with suspected drugs. We did not conduct the SCORTEN assessment daily, which could have resulted in less accurate death estimates. We only gathered long-term sequelae data from electronic medical records. Additional follow-up and direct physical examination would yield more thorough and reliable patient data. Another limitation is the incomplete data in medical records, particularly the absence of documented nail-related sequelae. Thus, obtaining information on nail abnormalities in SJS-TEN patients in this study is challenging. This could be due to patients not experiencing such sequelae or the frequent overlooking of nail examinations.

Conclusions

SJS/TEN is a multi-organ condition that necessitates multidisciplinary care involving various specialists. The key findings revealed that nearly all SJS/TEN survivors in our study suffered from physical complications; however, the majority of these patients did not receive ongoing medical follow-up. Common acute complications included extensive cheilitis, hypoalbuminemia, hypocalcemia, acute conjunctivitis, and acute kidney injury. The most common long-term skin complications are hyperpigmentation and hypopigmentation, while the most common long-term eye sequelae are dry eyes. Patients with SJS/TEN require continuous follow-up to maintain their quality of life. Additionally, we should always conduct and document a thorough physical examination for SJS/TEN survivors to ensure more comprehensive patient management. Further studies on the physical sequelae of SJS/TEN are necessary to enhance our understanding of the condition and improve treatment for survivors. In addition, further research is needed to investigate the association between acetaminophen and HLA genotyping in SJS-TEN patients within the Indonesian population, considering that acetaminophen was the most common causative agent in this study and HLA genotyping is not yet routinely performed in our center due to facility limitations.

Ethics Approval

This study had obtained ethical clearance from the Research Ethics Committee of Dr. Hasan Sadikin General Hospital Nu. DP.04.03/D.XIV.6.5/484/2024 and the Research Ethics Committee Cicendo Eye Hospital Nu. DP.04.03/D.XXIV.16/16584/2024. All patients provided informed consent to participate in the study, in accordance with the Declaration of Helsinki.

Consent for Publication

Written informed consent was obtained from the patient for publication of this study. Approval has been obtained from Dr. Hasan Sadikin General Hospital and Cicendo Eye Hospital to publish the study.

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References

1. Mockenhaupt M, Claude-Roujeau J. Epidermal necrolysis (Stevens-Johnson syndrome and toxic epidermal necrolysis). In: Kang S, Ma A, Bruckner AL, Enk AH, Margolis DJ, McMichael AJ, editors. *Fitzpatrick's Dermatology in General Medicine*. 9th McGraw Hill; 2019:733–748.
2. Kinoshita S, Ueta M. Editorial: the updated understanding of Stevens-Johnson syndrome and toxic epidermal necrolysis. *Front Med*. 2021;8:811570.
3. Chang WC, Abe R, Anderson P, et al. SJS/TEN 2019: from science to translation. *J Dermatol Sci*. 2020;98(1):2–12. doi:10.1016/j.jdermsci.2020.02.003
4. Hasegawa A, Abe R. Stevens-Johnson syndrome and toxic epidermal necrolysis: updates in pathophysiology and management. *Chin Med J*. 2020;612:1–12.
5. Necrolysis E, Bastuji-Garin S, Rzany B, et al. Clinical classification of cases of toxic syndrome, and erythema multiforme. *Arch Dermatol*. 1993;129(1):92–96. doi:10.1001/archderm.1993.01680220104023
6. Sunaga Y, Kurosawa M, Ochiai H, et al. The nationwide epidemiological survey of Stevens-Johnson syndrome and toxic epidermal necrolysis in Japan, 2016–2018. *J Dermatol Sci*. 2020;100(3):175–182. doi:10.1016/j.jdermsci.2020.09.009
7. Suwarsa O, Yuwita W, Dharmadji HP, Sutedja E. Stevens-Johnson syndrome and toxic epidermal necrolysis in Dr. Hasan Sadikin general hospital Bandung, Indonesia from 2009-2013. *Asia Pac Allergy*. 2016;6(1):43–47. doi:10.5415/apallergy.2016.6.1.43
8. Andrew Isaac W, Fatimah N, Nurul Hidayati A. The profiles of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) patients in tertiary hospital. *J Univ Airlangga*. 2021;33(2):116–122.
9. Yang CW, Cho YT, Chen KL, Chen YC, Song HL, Chu CY. Long-term sequelae of Stevens-Johnson syndrome/toxic epidermal necrolysis. *Acta Derm Venereol*. 2016;96(4):525–529. doi:10.2340/00015555-2295
10. Lee HY, Walsh SA, Creamer D. Long-term complications of Stevens–Johnson syndrome/toxic epidermal necrolysis (SJS/TEN): the spectrum of chronic problems in patients who survive an episode of SJS/TEN necessitates multidisciplinary follow-up. *Br J Dermatol*. 2017;177(4):924–935. doi:10.1111/bjd.15360
11. Cabañas Weisz LM, Miguel Escuredo I, Ayestarán Soto JB, García Gutiérrez JJ. Toxic epidermal necrolysis (TEN): acute complications and long-term sequelae management in a multidisciplinary follow-up. *J Plast Reconstr Aesthet Surg*. 2020;73(2):319–327. doi:10.1016/j.bjps.2019.07.015
12. Saeed H, Mantagos IS, Chodosh J. Complications of Stevens-Johnson syndrome beyond the eye and skin. *Burns*. 2016;42(1):20–27. doi:10.1016/j.burns.2015.03.012
13. Kohanim S, Palioura S, Saeed HN, et al. Acute and chronic ophthalmic involvement in Stevens-Johnson syndrome/toxic epidermal necrolysis - A comprehensive review and guide to therapy. II. ophthalmic disease part I (systemic disease). *Ocul Surf*. 2016;14(2):168–188. doi:10.1016/j.jtos.2016.02.001
14. Wambier CG, Hoekstra TA, Wambier SPDF, et al. Epidermal necrolysis: SCORTEN performance in AIDS and non-AIDS patients. *An Bras Dermatol*. 2019;94(1):17–23. doi:10.1590/abd1806-4841.20196864
15. Khurana A, Sharma MK, Sardana K. Sepsis assessment in SJS/TEN: an important point overlooked? *An Bras Dermatol*. 2019;94:773–774. doi:10.1016/j.abd.2019.06.002
16. Reilly PO, Walsh S, Bunker CB, et al. The quality-of-life impact of Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) on patients' lives: an interpretative descriptive qualitative study. *Br J Dermatol*. 2024;00:1–7.
17. Hoffman M, Chansky PB, Bashyam AR, et al. Long-term physical and psychological outcomes of Stevens-Johnson syndrome/toxic epidermal necrolysis. *JAMA Dermatol*. 2021;157(6):712–715. doi:10.1001/jamadermatol.2021.1136
18. Ma DHK, Tsai TY, Pan LY, et al. Clinical aspects of Stevens-Johnson syndrome/toxic epidermal necrolysis with severe ocular complications in Taiwan. *Front Med*. 2021;12(8):1–9.
19. Saka B, Akakpo AS, Tecloussou JN, et al. Ocular and mucocutaneous sequelae among survivors of Stevens-Johnson syndrome and toxic epidermal necrolysis in Togo. *Dermatol Res Pract*. 2019;2019:1–7.

20. Cekić S, Canitez Y, Yuksel H, et al. A comprehensive assessment of long-term complications in patients with Stevens-Johnson syndrome and toxic epidermal necrolysis. *Int Arch Allergy Immunol.* 2023;184(10):994–1002. doi:10.1159/000531366
21. Wasuwanich P, So JM, Chakrala TS, Chen J, Motaparathi K. Epidemiology of Stevens-Johnson syndrome and toxic epidermal necrolysis in the United States and factors predictive of outcome. *JAAD Int.* 2023;13:17–25. doi:10.1016/j.jdin.2023.06.014
22. Lamsu G. *Komplikasi Akut Dan Long-Term Sequelae Pada Pasien Sindroma Stevens Johnson Dan Nekrosis Epidermal Toksik Di RSUP Dr. Hasan Sadikin Dan PMN Rumah Sakit Mata Cicendo Bandung Periode Januari 2017–Oktober 2020* [thesis]. Bandung: Universitas Padjadjaran; 2021.
23. Finkelstein Y, Soon GS, Acuna P, et al. Recurrence and outcomes of Stevens-Johnson syndrome and toxic epidermal necrolysis in children. *Pediatrics.* 2011;128(4):723–728. doi:10.1542/peds.2010-3322
24. Wang L, Varghese S, Bassir F, et al. Stevens-Johnson syndrome and toxic epidermal necrolysis: a systematic review of PubMed/MEDLINE case reports from 1980 to 2020. *Front Med.* 2022;9:1–18.
25. Yoo HW, Kim HY, Shin K, Kim SH. Clinical characteristics of drug-induced Stevens-Johnson syndrome and toxic epidermal necrolysis: a single-center study. *Asia Pac Allergy.* 2022;12(2):1–10. doi:10.5415/apallergy.2022.12.e17
26. Das A, Sil A, Mohanty S. Itraconazole-induced Stevens-Johnson syndrome and toxic epidermal necrolysis overlap: report of a rare incident. *Dermatol Ther.* 2020;33(6). doi:10.1111/dth.14311
27. Sen SS, Sil A, Chakraborty U, Chandra A. Stevens-Johnson syndrome-toxic epidermal necrolysis: a fatal cutaneous adverse reaction to oral Acyclovir. *BMJ Case Rep.* 2020;13(8):e238555. doi:10.1136/bcr-2020-238555
28. Patel TK, Barvaliya MJ, Sharma D, Tripathi C. A systematic review of the drug-induced Stevens-Johnson syndrome and toxic epidermal necrolysis in Indian population. *Indian J Dermatol Venereol Leprol.* 2013;79(3):389–398. doi:10.4103/0378-6323.110749
29. Jongkhajornpong P, Ueta M, Lekhanont K, et al. Association of HLA polymorphisms and Acetaminophen-related Steven-Johnson syndrome with severe ocular complications in Thai population. *Br J Ophthalmol.* 2022;106(6):884–888. doi:10.1136/bjophthalmol-2020-317315
30. Koh HK, Fook-Chong S, Lee HY. Assessment and comparison of performance of ABCD-10 and SCORTEN in Prognostication of epidermal necrolysis. *JAMA Dermatol.* 2020;156(12):1294–1299. doi:10.1001/jamadermatol.2020.3654
31. Micheletti RG, Chiesa-Fuxench Z, Noe MH, et al. Stevens-Johnson syndrome/toxic epidermal necrolysis: a multicenter retrospective study of 377 adult patients from the United States. *J Invest Dermatol.* 2018;138(11):2315–2321. doi:10.1016/j.jid.2018.04.027
32. Monteiro D, Egipto P, Barbosa J, et al. Nine years of a single referral center management of Stevens-Johnson syndrome and toxic epidermal necrolysis (Lyell's syndrome). *Cutan Ocul Toxicol.* 2017;36(2):163–168. doi:10.1080/15569527.2016.1218501
33. Rahmawati YW, Indramaya DM. Studi retrospektif: sindrom Stevens-Johnson dan nekrosis epidermal toksik (A retrospective study: Stevens-Johnson syndrome and toxic epidermal necrolysis). *J Univ Airlangga.* 2016;28(2):68–76.
34. Olteanu C, Shear NH, Chew HF, et al. Severe physical complications among survivors of Stevens-Johnson syndrome and toxic epidermal necrolysis. *Drug Saf.* 2018;41(3):277–284. doi:10.1007/s40264-017-0608-0

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