

# Profile And Risk Factors of Stevens Johnson Syndrome–Toxic Epidermal Necrolysis on Adult Patients in Dr. Moewardi General Hospital Surakarta from January 2019 – December 2022

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## Abstract

**Background:** Steven Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are acute and life-threatening skin diseases, commonly induced by medications. Study on SJS/TEN in Indonesia was still limited, hence knowledge about the profile and risk factors of SJS/TEN patients is still required to provide appropriate management and reduce patient mortality rate. This study aimed to determine the profile and risk factors of adult SJS/TEN patients in the inpatient installation of RSDM Surakarta. **Methods:** We conducted a cross sectional study using secondary data from medical records of SJS/TEN patients at the inpatient installation of Dr. Moewardi hospital, Surakarta from 2019 – 2022. Correlation tests on characteristics, comorbidity with length of stay (LoS) and discharge status were analyzed. **Results:** Of the total 147,531 inpatients, 35 (0.02%) of them were diagnosed with SJS/TEN, dominated by females (57.14%) with the mean of 45.74 years old. Most subjects were diagnosed with SJS (48.57%), followed by SJS/TEN (40.0%) and TEN (11.43%). The mean LoS was  $\pm 8$  days. Most subjects were discharged alive (85.71%). Paracetamol was the most common causative drug (25.71%), followed by cefadroxil (11.43%). Acute kidney injury (AKI) was the most common comorbidity (14.29%,  $p = 0.040$ ). Spearman Rank test obtained no correlation between comorbidities and LoS ( $r = 0.028$ ;  $p = 0.842$ ) as well as discharge status ( $r = 0.063$ ;  $p = 0.651$ ). **Conclusion:** SJS/TEN is rare case with high mortality rate. Patients' comorbidities have a very weak correlation with LoS and discharge status. Initial knowledge of the patient's profile and risk factors including comorbidity and causative drugs can optimise comprehensive therapy for SJS/TEN patients.

**Keywords -- SJS, TEN, comorbidities, drug triggers**

## Abstrak

**Latar Belakang:** Sindrom Steven Johnson (SSJ) dan Nekrolisis Epidermal Toksik (NET) merupakan penyakit kulit yang sering dipicu oleh obat-obatan, serta bersifat akut dan mengancam jiwa. Penelitian mengenai SSJ/NET di Indonesia relatif sedikit, sehingga pengetahuan terhadap profil dan faktor risiko pasien SSJ/NET masih dibutuhkan agar dapat memberikan tatalaksana yang tepat dan menurunkan angka mortalitas pasien. Penelitian ini bertujuan untuk mengetahui profil dan faktor risiko pasien SJS/TEN dewasa dewasa di instalasi rawat inap RSDM Surakarta. **Metode:** Penelitian ini merupakan penelitian deskriptif retrospektif dengan menggunakan data sekunder dari rekam medik pasien SSJ/NET di instalasi rawat inap RSUD Dr. Moewardi (RSDM) Surakarta pada periode tahun 2019 – 2022. Komorbiditas dan lama perawatan, serta komorbiditas dengan status pasien saat pulang turut dianalisis dalam penelitian ini dengan menggunakan SPSS Ver. 26.0. **Hasil:** Subjek penelitian adalah 35 pasien dari total 147.531 pasien rawat inap, dengan mayoritas jenis kelamin perempuan (57,14%) dan rerata usia 45,74 tahun. Dari keseluruhan subjek penelitian, pasien dengan SSJ ditemukan sejumlah (48,57%), diikuti SSJ overlap NET (40,0%) dan NET (11,43%). Rerata waktu perawatan yang didapatkan subjek penelitian ialah 8 hari. Parasetamol merupakan obat penyebab paling sering (25,71%),

diikuti sefadroksil (11,43%). Sebagian besar pasien pulang dalam keadaan hidup (85,71%). Acute kidney injury (AKI) merupakan komorbid yang paling banyak ditemukan (14,29%) disusul epilepsi (11,43%). Analisis statistik uji spearman menunjukkan korelasi yang sangat lemah dan tidak signifikan antara komorbiditas dengan lama perawatan dan komorbiditas dengan status pasien saat pulang. **Kesimpulan:** Penyakit SSJ/NET merupakan penyakit yang jarang terjadi dengan angka mortalitas yang cukup tinggi. Komorbiditas pasien memiliki korelasi yang sangat lemah dan tidak signifikan dengan lama rawat dan status saat pulang. Pengetahuan awal mengenai profil pasien dan faktor risiko termasuk komorbiditas dan obat penyebab dapat mengoptimalkan terapi yang komprehensif untuk pasien SSJ/NET

**Kata Kunci -- SSJ, NET, komorbid, obat pencetus**

## I. INTRODUCTION

*Steven Johnson Syndrome* (SJS) and *toxic Epidermal Necrolysis* (TEN) are acute and potentially life-threatening skin reactions. These diseases cause reactions in the form of rashes, blisters, and epidermolysis of the skin and mucous membranes that systemic symptoms can accompany.<sup>1</sup> This condition can lead to complications such as sepsis and death, especially in cases of TEN.<sup>2</sup> SJS and TEN cases have similar pathophysiology and are differentiated based on the body surface area (BSA) affected, namely SJS (<10% body area), SJS overlap TEN (SJS/TEN) (10-30% body area) and TEN (>30% body area).<sup>3</sup> However, there was no specific incidence rate of SJS/TEN in Indonesia. A retrospective study at an Indonesian referral hospital mentioned that from the records of 150 patients diagnosed with SJS, SJS/TEN overlap, and TEN during 2009–2013, a total of 101 medical records were included in the study.<sup>4</sup> According to the study, the primary causing medication of SJS/TEN was analgesic-antipyretic drugs.<sup>4</sup>

Globally, SJS/TEN cases were estimated to affect 2-7 people per one million population annually,<sup>3</sup> with reported incidences varying widely by location.<sup>5</sup> The incidence of SJS, SJS/TEN and TEN cases in the adult population in the United States was 9.2; 1.6; and 1.9 cases per one million population per year from 2009-2012. Although the incidence is considered quite rare, the mortality of SJS/TEN cases was high, with SJS mortality at 4.8-9%, followed by SJS/TEN at 19.4-29% and TEN at 14.8-48%.<sup>5</sup>

Approximately 5-20% of SJS/TEN cases were idiopathic, but SJS/TEN is thought to result from a combination of immune predisposition and stimulus interactions such as drugs.<sup>3,6</sup> SJS and TEN have a genetic predisposition across age, gender and ethnicity but are more common in the

elderly, women and individuals with Human Immunodeficiency Virus (HIV) infection.<sup>3,7</sup> The clinical symptoms of SJS/TEN are divided into two phases, namely the acute phase and the late phase with sequelae. In the acute phase of SJS/TEN, patients may experience flu-like symptoms followed by a painful rash, blisters, and skin shedding, affecting mucous membranes and leading to complications such as sepsis and respiratory distress.<sup>8</sup> During the late phase with sequelae, patients can suffer from long-term complications such as skin hyperpigmentation or hypopigmentation, nail dystrophies, and serious ocular issues like severe dry eyes and vision loss.<sup>8</sup> In SJS/TEN, the lesions will initially appear as erythema to blackish red macules, purpuric macules, irregularly shaped which will progressively confluence and there are atypical lesions in the form of 'target' lesions. The location of skin involvement is not limited to the body and face. More than 90% of patients have buccal mucosal involvement with typical clinical features of haemorrhagic crusts on the oris, genital and/or ocular lesions.<sup>6</sup> Some cases also involved the respiratory and gastrointestinal mucosa.<sup>9,10</sup>

Known risk factors involved in the development of SJS/TEN include drugs, infection and genetics. Drug exposure is most commonly involved in the development of this disease, which is around 50-95%. The most common drugs are penicillin and sulfonamide group antibiotics, followed by analgesics, Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) and antituberculous.<sup>3,5</sup> SJS/TEN patients with comorbidities are also considered to be at risk of worse disease progression and higher mortality.<sup>11</sup> Various comorbidities are thought to be associated with SJS/TEN cases, such as Acute Kidney Injury (AKI),<sup>12</sup> epilepsy,<sup>13</sup> metabolic-endocrine diseases such as diabetes mellitus, or malignancies such as hepatic cirrhosis and metastases.<sup>11</sup>

Although SJS/TEN was rare on a global scale, it has a high mortality rate especially in vulnerable groups, such as those with older age or comorbidities. Early knowledge of a patient's profile and risk factors for SJS/TEN is crucial because it enables the prompt identification and discontinuation of the offending agent, significantly reducing disease progression, morbidity, and mortality.<sup>14</sup> Additionally, understanding these factors helps in tailoring patient management to prevent disease recurrence and manage complications effectively, thereby improving patient outcomes and quality of life.<sup>14</sup> Thus, the study aimed to determine the profile and risk factors of adult SJS/TEN patients in the inpatient installation of RSDM Surakarta for the period January 2019 - December 2022.

## II. METHODS

This study cross sectional study was conducted using secondary data from the medical records of adult SJS / TEN patients at the Dr. Moewardi hospital, Surakarta inpatient installation in the period January 2019 - December 2022. This study met the ethical feasibility issued by Dr. Moewardi Hospital (ID S202202002). The subjects were retrieved using the total sampling method with inclusion criteria, which were patients aged  $\geq 18$  years, patients with a diagnosis assessment of SJS, SJS/TEN and TEN based on the International Classification of Disease (ICD10 L51.1, L51.2, L51.3) at the RSDM inpatient installation in the period January 2019 - December 2022. We excluded patients with incomplete medical records. The study characteristics including age, gender, comorbidities, diagnosis of SSJ, SSJ-NET and NET, penetrant drugs, length of stay, discharge status were collected and included in the study. The relationship between comorbidities and length of stay, and comorbidities and discharge status were analysed in this study using Statistical Program for Social Science (SPSS) Ver.

26.0. All results in this study were compiled in tables and explained descriptively.

## III. RESULTS

### A. CHARACTERISTICS OF STUDY SUBJECTS

The total number of patients hospitalized in the last 4 years was 147,531. There were 43 hospitalization visit histories included in the ICD10 diagnosis codes L51.1, L51.2, L51.3. The data was tidied up according to the inclusion and exclusion criteria of the study, duplicates were removed and then 35 patients were obtained as research subjects. The prevalence was found to be 0.02% of the total patients admitted to the inpatient installation at RSDM in a 4-year period. The mean age of the study subjects was 45.74 years old with the youngest age being 20 years old and the oldest being 85 years old, with the majority of subjects dominated by women (57.14%). The study subjects received treatment with different durations, ranging from 1 to 16 days of treatment with an average of 8 days. The number of patients diagnosed with SJS was 48.57%, followed by SJS-TEN at 40.0% and TEN at 11.43%. Most of the treated patients were discharged alive (85.71%), with a mean SCORTEN score of 1.43. The SCORTEN value per case was greater in TEN and SJS-TEN cases followed by SJS. Based on the patient's condition at discharge, the case fatality rate showed a value of 14.29%, namely 5 out of 35 patients treated were declared dead. The overall characteristics of the study subjects can be seen in Table 1.

**TABLE 1. CHARACTERISTICS OF STUDY SUBJECTS**

Parameter s	SJS		SJS- TEN		TEN		Total		p-value
	n	(%)	n	(%)	n	(%)	n	(%)	
Total	17	48,57	14	40,0	4	11,43	35	100	
Gender									
Male	6	64,71	7	50,0	2	50,0	15	42,86	0,408
Female	11	35,29	7	50,0	2	50,0	20	57,14	
Age									
18-35	8	57,1	4	28,6	2	14,6	14	100	0,245
36-65	7	50,0	5	35,7	2	14,3	14	100	

>65	2	28,6	5	71,4	0	0,0	7	100
SCORTEN (mean ± SD)	1 ± 1		2 ± 1		2 ± 1		1 ± 1	
Length of stay (mean)	8 days		8 days		9 days		8 days	
Discharge status	15	88,24	12	85,71	3	75	30	85,71
Live	2	11,76	2	14,29	1	25	5	14,29
Died								

### B. COMORBID CHARACTERISTICS OF STUDY SUBJECTS

This study identified the comorbidities of the study subjects and grouped them into several categories based on system involvement. The study subjects had the most comorbidities in the urogenital system (22.85%) with the most common type of disease being acute kidney injury (AKI) (14.29%) and followed by comorbidities from the cardiovascular system (20%), namely hypertension. Based on the type of disease, AKI was the most common comorbidity at 14.29% and statistically significant with p value = 0,040, followed by epilepsy at 11.43% (Table 2). This study also analyzed the relationship between comorbidities and length of stay. Both of these had a very weak correlation (r = 0.028) and were not significant (p = 0.842). Analysis of the relationship between comorbidities and patient status at discharge, which showed a weak correlation (r=0.063) and was not significant (p=0.651).

TABLE 2. COMORBID CHARACTERISTICS OF STUDY SUBJECTS

Parameter	SJS (n=17)		SJS-TEN (n=14)		TE N (n=4)		Total (n=35)		p value
	n	%	n	%	n	%	n	%	
Orbital Tumor			1	7,14			1	2,86	
Psychiatry									
Bipolar	1	5,88					1	2,86	
Schizophrenia	1	5,88					1	2,86	
Respiration System									0,221
Asthma	1	5,88					1	2,86	
COPD	1	5,88					1	2,86	
Pneumonia			1	7,14			1	2,86	
Nervous System									1,000

Epilepsy	2	11,76	2	14,29			4	11,43	
Cardiovascular System									1,00
Hypertension	1	5,88	2	14,29			3	8,57	
Hypertensive heart failure (HHF)	1	5,88					1	2,86	
Hypertensive heart disease (HHD)			1	7,14			1	2,86	
Congestive heart failure (CHF)	1	5,88					1	2,86	
Atrial fibrillation (AF)			1	7,14			1	2,86	
Gastrointestinal System									0,197
Hepatitis			1	7,14			1	2,86	
Post hepatic jaundice			1	7,14			1	2,86	
Elevated transaminase enzymes	2	11,76	1	7,14			3	8,57	
Uroreproductive System									0,040
AKI	1	5,88	4	28,57			5	14,29	
CKD	3	17,65					3	8,57	
Endocrine System									1,000
DM	1	5,88	2	14,29			3	8,57	
Immune System									
HIV infection	1	5,88	1	7,14			2	5,71	
Hematology System									
Thrombocytopenia			1	7,14			1	2,86	

### B. CHARACTERISTICS PRECIPITATING DRUGS BASED ON THE DRUG HISTORY

Triggering drugs for SJS, SJS-TEN and TEN in the study subjects were also identified. The antipyretic analgesic group was the highest type of precipitating drug (42.85%) found in our study subjects with paracetamol as the most common type of drug (25.71%). While the second highest triggering drug class was followed by antibiotics (40%), with the most common drug type being cefadroxil (11.43%). Data regarding the triggers in this study were obtained based on the patient's medication history (Table 3).

**TABLE 3. CHARACTERISTICS OF THE STUDY SUBJECTS' PRECIPITATING DRUGS BASED ON THE DRUG HISTORY**

Parameter	SJS (n=17)		SJS- TEN (n=14)		TE N (n =4)		Total (n=35)		value
	n	%	N	%	n	%	n	%	
Anticonvulsants									0,129
Valproic acid			1	7,14			1	2,86	
Phenytoin	1		2	14,29			3	8,57	
Carbamazepine	2		1	7,14			3	8,57	
Lamotrigine	1	5,88					1	2,86	
Antibiotics									0,176
Amoxicillin	1	5,88	2	14,29			3	8,57	
Levofloxacin			2	14,29			2	5,71	
Clindamycin	1	5,88					1	2,86	
Metronidazole	1	5,88					1	2,86	
Cefadroxil	2		2	14,29			4	11,43	
Thiamphenicol					1	25	1	2,86	
						,0			
Moxifloxacin	1	5,88					1	2,86	
Isonicotinylhydrazide (INH)	1	5,88					1	2,86	
Antihypertension									
Candesartan	1	5,88					1	2,86	
Clonidine	1	5,88					1	2,86	
Antipyretic analgesics									0,848
Paracetamol	2	11,76	5	35,71	2	50	9	25,71	
						,0			
Ibuprofen			1	7,14	1	25	2	5,71	
						,0			
Na Diclofenac			1	7,14			1	2,86	
Meloxicam			1	7,14			1	2,86	
Metamizole	1	5,88	1	7,14			2	5,71	
Antiangina									
Isosorbide dinitrate (ISDN)	1	5,88					1	2,86	
Expectorant mucolytics									
Acetylcysteine	1	5,88					1	2,86	
Glyceryl guaiaacolate					1	25	1	2,86	
						,0			
Antiretroviral									0,346
Zidovudine	1	5,88					1	2,86	
Lamivudine	1	5,88					1	2,86	
Nevirapine	1	5,88	1	7,14			2	5,71	

#### IV. DISCUSSION

Stevens Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are cases of skin emergencies, which are acute and potentially fatal reactions involving the skin or mucosa with or without systemic symptoms.<sup>5,15</sup> SJS and TEN conditions are the result of type IV hypersensitivity reactions mediated by cytotoxic T cell lymphocytes.<sup>3,6</sup> SJS and TEN cases are differentiated based on the

body surface area affected, namely SJS (<10% body area), SJS-TEN (10-30% body area) and TEN (>30% body area).<sup>3,6</sup>

Sousa-Pinto et al's study found that there was no significant difference between genders regarding the incidence of SJS/TEN cases.<sup>16</sup> However, another study reported that the female population (54%) was found to be more than men in their study.<sup>17</sup> The results of our study also showed harmony, that our research subjects were dominated by women (57.14%). This is in line with a study by Pratiwi et al in Indonesia, that women dominated their research subjects.<sup>18</sup> The involvement of gender with SJS/TEN is still uncertain, but one hypothesis states that there is a possibility that the male immune system is able to suppress slow-type hypersensitivity reactions that protect this group from the incidence of SJS/TEN, so the majority of SJS/TEN patients are dominated by women.<sup>17</sup>

Age is one of the risk factors that increase the incidence of SJS/TEN, especially in the age group > 60 years.<sup>19</sup> This is expected because elderly people tend to use a variety of drugs (polypharmacy) for several types of diseases.<sup>19</sup> In this study, 34.29% of the subjects involved were > 60 years old. The mean age of the patients in this study was 45.74 years, similar to the findings in other studies which found a mean of 45+18 years.<sup>20</sup> Older age is associated with higher complications and mortality.<sup>19</sup>

Comorbidity in patients with SJS/TEN is a risk factor for patient mortality in the hospital.<sup>11</sup> In a study conducted by Lee et al, 30.7% SJS/TEN patients experienced AKI. Patients with SJS/TEN significantly increased the incidence of AKI.<sup>12</sup> Meanwhile, patients with comorbid AKI experienced more severe complications, require longer hospital stays, also have a greater 1-year mortality rate.<sup>12</sup> In another study, epilepsy comorbidity was associated with the use of antiepileptic drugs (OAEs)

which is one of the most common causes of SJS/TEN cases,<sup>21</sup> especially in new OAE users.<sup>13</sup> Other studies conducted by Ezaldein et al and Sangwan et al found that diabetes mellitus (25.4%) was the most common comorbidity.<sup>11,22</sup> In addition, other comorbidities that are considered to significantly increase the mortality rate of patients in the hospital are liver cirrhosis (14.58%) and metastatic disease (10.62%).<sup>11</sup> In this study, AKI was found to be the most common comorbidity at 14.29% so that comprehensive management is needed to prevent mortality in SJS/TEN patients we treated. The second most common comorbidity in this study was epilepsy (11.43%). Regarding comorbidities, statistical analysis of comorbidities with length of treatment and comorbidities with patient status at discharge, showed a very weak correlation and insignificant statistical analysis results.

Stevens Johnson syndrome can be caused by several precipitating factors, such as the use of drugs, bacterial, fungal and viral infections.<sup>23,24</sup> As many as 65% of SJS/TEN cases are caused by the use of drugs and followed by infection. In addition, vaccination can also cause SJS/TEN although it is less common.<sup>24</sup> Drugs that are often associated with SJS/TEN are antibiotics, anticonvulsants or antiepileptic drugs (OAEs) and NSAIDs.<sup>25,26</sup> More specifically, Patel et al and Deore et al mentioned that SJS/TEN is most commonly caused by cotrimoxazole and other sulfonamide class antibiotics followed by cephalosporins.<sup>27,28</sup> The next drug class is OAEs, which are OAEs. The next group of drugs are OAEs, namely carbamazepine and phenytoin,<sup>27,29</sup> and the last is NSAID drugs such as paracetamol and oxycam derivatives.<sup>22</sup> Wijanto et al's study based in Indonesia obtained similar results to other studies that SJS/TEN was caused by OAEs, especially carbamazepine and phenytoin, followed by NSAIDs such as paracetamol and finally caused by antibiotics. But in this

case, the dominating antibiotics were from the quinolone group such as ciprofloxacin.<sup>26</sup> Different from Wijanto et al, the causative antibiotic in Pratiwi et al's study which was also based in Indonesia, was dominated by amoxicillin.<sup>18</sup> Overall, the classes of drugs found to contribute to the incidence of SJS/TEN in this study included anticonvulsants, antibiotics, antihypertensives, analgesics and antipyretics, anti-angina, mucolytic expectorants and antiretrovirals. Of all these groups, the analgesic group was the most SJS/TEN trigger in the subjects of this study, with paracetamol as many as 9 (25.71%) patients and cefadroxil which is an antibiotic of the cephalosporin group causing SJS/TEN in 4 (11.43%) patients. The high incidence of SJS/TEN caused by paracetamol may be due to its common use in managing non-specific symptoms, its ease of obtaining, and its relatively affordable.<sup>29,30</sup> Paracetamol is also often used in infectious conditions, such as viral infections. In this case, the virus is able to trigger drug metabolism, present drug molecules to lymphocytes and produce cytokines/chemokines. Immune cells in the body are then activated by various signals, including molecular patterns related to pathogens and bacteria, thus triggering a T cell response. This immune response can later cause SJS/TEN.<sup>31</sup> In this study, the drugs mentioned were obtained based on the patient's treatment history before the symptoms of SJS/TEN appeared and not through the results of drug patch tests.

Based on data per case, the average length of treatment for TEN cases is longer than SJS and SJS-TEN cases. The average length of treatment for TEN cases was 9 days, while the other two case groups had an average of 8 days. Research by Dilokthornsakul et al. found a longer length of stay in their study of  $10.1 \pm 13.2$  days. Their study also found that SJS cases required longer treatment than TEN cases, assuming that there is a possibility that TEN patients have a more severe severity than SJS so that mortality in

a shorter time is quite high.<sup>32</sup> In this study, the length of stay ranged from 1-16 days, with a mean length of stay of 8 days. Length of hospitalization was found to be associated with the number of chronic diseases and the number of organs involved. A study conducted by Derek et al. found that the strongest predictor of length of hospitalization in patients with SJS-TEN was the number of chronic conditions the patient had. If the chronic conditions of patients with SJS-TEN are multiple, this will prolong the duration of hospitalization.<sup>33</sup> In this study, the analysis of the relationship between length of hospitalization with comorbidities showed a very weak and insignificant correlation strength. This dissimilar result may occur due to the lack of sample size used in the study.

Basically, the main therapy in treating SJS/TEN cases is to stop the triggering drug, and provide therapy to help manage the patient's condition. One of the therapies used in SJS-TEN cases is systemic corticosteroids. The administration of this therapy is recommended to start with high doses as early as possible and for a short time, with administration for 3 days can be an option and adjusted to the patient's clinical response.<sup>34</sup> Therapy that starts as early as possible will improve the prognosis of the patients.<sup>35</sup> The administration of corticosteroids, especially methylprednisolone, is considered to be able to reduce the levels of pro-inflammatory cytokines which will improve the survival of patients.<sup>34</sup> The combination of corticosteroids with IVIG shows a lower mortality rate when compared to corticosteroid monotherapy.<sup>35</sup> The dose of corticosteroids was found to be different in each study with a dose range of methylprednisolone of 160 mg - 1000 mg/day and its equivalents.<sup>34</sup> Our study subjects received therapy in the form of high-dose methylprednisolone intravenously starting from 125 mg/24 hours and then tapering off according to the length of stay

and patient response to therapy. This administration is based on the literature that recommends the administration of corticosteroids as therapy for SJS/TEN cases.<sup>36</sup> Corticosteroid administration is equivalent to a dose of prednisone 3-4 mg/KgBB,<sup>36</sup> which is then converted into a dose of methylprednisolone in giving to patients we adjust to the preparations available at RSDM. The subjects of this study received topical therapy such as NaCL compress with gauze for 10-15 minutes and then kenalog in orabase on the lip area which usually has hemorrhagic crusts. In epidermolysis lesions or peeling skin, topical vaseline album and topical corticosteroids such as mometasone furoate 0.1% cream and desoxymethasone 0.025% cream were given. Topical corticosteroid administration is as crucial as systemic corticosteroids to reduce inflammation.<sup>37,38</sup>

The limitations of this study were that it was conducted in only one study center so that the sample data was small and there was no special data recording management related to SJS/TEN. Data on precipitating drugs were obtained from the patient's treatment history and not from the results of the drug patch test. The strength of this study is to analyze the profile and risk factors of SJS/TEN patients in RSDM and the correlation between patient comorbidities with length of stay and discharge status. Future research will be better if the trigger drug is obtained through drug patch test results and there is a special data recording management related to SJS/TEN so that the incidence rate, profile, and patient risk factors for certain cases can be better analyzed.

## V. CONCLUSION

In this study, we highlighted the profile and risk factors of adult SJS/TEN patients in the inpatient installation of RSDM Surakarta. We found 35 adult SJS/TEN patients with an average length of stay of 8 days in the 4-year period. The number of female patients was



more than male with an average age of 45.74 years. In this study, the most common comorbidity was acute kidney injury (AKI) and the most common precipitating drug was paracetamol. The correlation of comorbidities with length of stay and discharge status was very weak and there was no statistically significant relationship. Knowledge of patient profiles and risk factors including comorbidities can be a concern for the potential occurrence of SJS / TEN related to the drugs given.

#### REFERENCES

- [1]. Labib A, Milroy C. Toxic epidermal necrolysis. Statpearls. 2022.
- [2]. Anwar AND, Carolia N, Hamzah MS. Stevens johnson syndrome - toxic epidermal necrolysis overlap disebabkan oleh drug eruption obat anti tuberkulosis. Medical Faculty of Lampung University. 2017;7(9):8–14.
- [3]. Oakley AM, Krishnamurthy K. Stevens-Johnson Syndrome. 2023;1–10.
- [4]. Abdulah R, Suwandiman TF, Handayani N, Destiani DP, Suwantika AA, Barliana MI, et al. Incidence, causative drugs, and economic consequences of drug-induced SJS, TEN, and SJS-TEN overlap and potential drug-drug interactions during treatment: a retrospective analysis at an Indonesian referral hospital. *Ther Clin Risk Manag.* 2017;13:919–25.
- [5]. Frantz R, Huang S, Are A, Motaparathi K. Stevens-johnson syndrome and toxic epidermal necrolysis: A review of diagnosis and management. *Medicina (Lithuania).* 2021;57(9):1–15.
- [6]. Zimmerman D, Dang NH. Stevens-johnson syndrome (SJS) and toxic epidermal necrolysis (TEN): Immunologic reactions. *Oncologic Critical Care.* 2019;267–80.
- [7]. Fakoya AOJ, Omenyi P, Anthony P, Anthony F, Etti P, Otohinoyi DA, et al. Stevens - Johnson syndrome and toxic epidermal necrolysis; extensive review of reports of drug-induced etiologies, and possible therapeutic modalities. *Open Access Maced J Med Sci.* 2018;6(4):730–8.
- [8]. Harr T, French LE. Toxic epidermal necrolysis and Stevens-Johnson syndrome. *Orphanet J Rare Dis.* 2010 Dec;5:39.
- [9]. Dewi CC. Tinjauan atas Stevens-Johnson Syndrome dan Toxic Epidermal Necrolysis. *Cermin Dunia Kedokteran.* 2019;46(7):55–9.
- [10]. Rahmasari AT, Indramaya DiM, Lestari P. Profile And Treatment Steven Johnson Syndrome Patients In Inpatient Kemuning I And II RSUD DR. Soetomo Period 2011-2015. *Nusantara Medical Science Journal.* 2019;4(2):32.
- [11]. Ezaldein H, Totonchy M, Chow C, Samuel A, Ventura A. The effect of comorbidities on overall mortality in Stevens- Johnson Syndrome: an analysis of the Nationwide Inpatient Sample. *Dermatol Online J.* 2017;23(4):1–7.
- [12]. Lee TH, Lee CC, Ng CY, Chang MY, Chang SW, Fan PC, et al. The influence of acute kidney injury on the outcome of Stevens–Johnson syndrome and toxic epidermal necrolysis: The prognostic value of KDIGO staging. *PLoS One.* 2018;13(9):1–12.
- [13]. Trivedi B, Darji N, Malhotra S, Patel P. Antiepileptic Drugs-induced Stevens-Johnson syndrome: A case Series. *J Basic Clin Pharm.* 2017;8(1):42.
- [14]. Hasegawa A, Abe R. Recent advances in managing and understanding Stevens-Johnson syndrome and toxic epidermal necrolysis. *F1000Res.* 2020;9.
- [15]. Wolff K, Johnson RA, Saavedra AP. Fitzpatrick's Color Atlas and Synopsis of Clinical Dermatology. Treatment of Skin Disease: Comprehensive Therapeutic Strategies. 2017. 448–450 p.
- [16]. Sousa-Pinto B, Araújo L, Freitas A, Correia O, Delgado L. Stevens-Johnson syndrome/toxic epidermal necrolysis and erythema multiforme drug-related hospitalisations in a national administrative database. *Clin Transl Allergy.* 2018;8(1):1–10.
- [17]. Duplisea MJ, Ziemer CM, Laughon SL, Williams FN. Characteristics associated with disease prevalence, SCORTEN, length of stay, and mortality in hospitalized SJS/TEN patients: A single-center, eleven-year experience. *Burns Open.* 2022;6(3):110–5.
- [18]. Primisawitri PP, Mawardi P. The Correlation of Neutrophil–Lymphocyte Ratio and Eosinophil Count with SCORTEN in SJS/TEN. *Clin Cosmet Investig Dermatol.* 2022;15(March):547–56.
- [19]. Ubukata N, Nakatani E, Hashizume H, Sasaki H, Miyachi Y. Risk factors and drugs that trigger the onset of Stevens–Johnson syndrome and toxic epidermal necrolysis: A population-based cohort study using the Shizuoka Kokuho database. *JAAD Int.* 2023 Jun;11:24.
- [20]. Isaac WA, Damayanti D, Fatimah N, Hidayati AN. The Profiles of Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) Patients in Tertiary Hospital. *Berkala Ilmu Kesehatan Kulit dan Kelamin.* 2021;33(2):116.
- [21]. Frey N, Bodmer M, Bircher A, Rüegg S, Jick SS, Meier CR, et al. The risk of Stevens-Johnson syndrome and toxic epidermal

- necrolysis in new users of antiepileptic drugs. *Epilepsia*. 2017;58(12):2178–85.
- [22]. Sangwan. Controversies in the Management of Cutaneous Adverse Drug Reactions Systemic Corticosteroids in the Management of SJS / TEN: Is it Still. *Indian J Dermatol*. 2018;63(2):125–30.
- [23]. Imatoh T, Saito Y. Associations Between Stevens–Johnson Syndrome and Infection: Overview of Pharmacoepidemiological Studies. *Front Med (Lausanne)*. 2021;8(March):1–6.
- [24]. Mawson AR, Eriator I, Karre S. Stevens-johnson syndrome and toxic epidermal necrolysis (SJS/TEN): Could retinoids play a causative role? *Medical Science Monitor*. 2015;21:133–43.
- [25]. Lebrun-Vignes B, Guy C, Jean-Pastor MJ, Gras-Champel V, Zenut M. Is acetaminophen associated with a risk of Stevens–Johnson syndrome and toxic epidermal necrolysis? Analysis of the French Pharmacovigilance Database. *Br J Clin Pharmacol*. 2018;84(2):331–8.
- [26]. Queena Maureen Wijanto J, Damayanti Dr, Fathul Qorib M, Anggraeni S, Rosita Sigit Prakoeswa C. Risk Factors for Stevens Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) in Dr. Soetomo General Hospital Surabaya. *International Journal of Research Publications*. 2021;92(1):361–8.
- [27]. 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 May;79(3):389.
- [28]. Deore SS. Drug Induced - Stevens Johnson Syndrome- A Case Report.pdf - Google Drive. *International Journal of Scientific Study*. 2014;2:2–5.
- [29]. Eric. HHS Public Access Author manuscript *Epilepsia*. Author manuscript; available in PMC 2019 December 01. Published in final edited form as: *Epilepsia*. 2018 December ; 59(12): 2318–2324. doi:10.1111/epi.14591. Stevens-Johnson Syndrome and Toxic Epidermal Necro. *Physiol Behav*. 2017;176(5):139–48.
- [30]. Rajput R, Sagari S, Durgavanshi A, Kanwar A. Paracetamol induced Steven-Johnson syndrome: A rare case report. *Contemp Clin Dent*. 2015;6:S278–81.
- [31]. Ban GY, Ahn SJ, Yoo HS, Park HS, Ye YM. Stevens–johnson syndrome and toxic epidermal necrolysis associated with acetaminophen use during viral infections. *Immune Netw*. 2016;16(4):256–60.
- [32]. Dilokthornsakul P, Sawangjit R, Inprasong C, Chunhasewee S, Rattanapan P, Thoopputra T, et al. Healthcare utilization and cost of Stevens-Johnson syndrome and toxic epidermal necrolysis management in Thailand. *J Postgrad Med*. 2016;62(2):109–14.
- [33]. Hsu DY, Brieva J, Silverberg NB, Silverberg JI. Morbidity and Mortality of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis in United States Adults. *Journal of Investigative Dermatology*. 2016;136(7):1387–97.
- [34]. Gupta L, Martin A, Agarwal N, D’Souza P, Das S, Kumar R, et al. Guidelines for the management of Stevens-Johnson syndrome/toxic epidermal necrolysis: An Indian perspective. *Indian J Dermatol Venereol Leprol*. 2016;82(6):603–25.
- [35]. Hsieh MH, Watanabe T, Aihara M. Recent Dermatological Treatments for Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis in Japan. *Front Med (Lausanne)*. 2021;8(July):1–9.
- [36]. 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):43–7.
- [37]. Matsumoto K, Ueta M, Inatomi T, Fukuoka H, Mieno H, Risa T-M, et al. Topical Betamethasone Treatment of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis with Ocular Involvement in the Acute Phase. *Am J Ophthalmol*. 2023;253:142–51.
- [38]. Wilken R, Li CS, Sharon VR, Kim K, Patel FB, Patel F, et al. Topical clobetasol for the treatment of toxic epidermal necrolysis: Study protocol for a randomized controlled trial. *Trials*. 2015;16(1):1–10.