Original Article

Thai Journal of Pharmaceutical Sciences

# Investigation of drug reaction with eosinophilia and systemic syndrome and its management in a tertiary care hospital of South India

**S. Shridhar[1], B. Suresh[1], S. Ojha[1], S. Seshadri[2], Mallayasamy Surulivelrajan[1], S. Elstin Anbu Raj[1], V. Rajesh[1]**

*[1]Department of Pharmacy Practice, Manipal College of Pharmaceutical Sciences, Manipal College of Academy of Higher Education, Manipal, Karnataka, India, [2]Department of Medicine, Kasturba Medical College, Manipal College of Academy of Higher Education, Manipal, Karnataka, India*

**Corresponding Author:**
V. Rajesh, Department of Pharmacy Practice, Manipal College of Pharmaceutical Sciences, Manipal College of Academy of Higher Education, Manipal - 576 104, Karnataka, India.
Phone: +91-9538417313
E-mail: rajesh.v@manipal.edu

**Received:** Dec 31, 2020
**Accepted:** Feb 01, 2021
**Published:** Sep 01, 2021

## ABSTRACT

**Introduction:** Drug reaction with eosinophilia and systemic syndrome (DRESS) is also known as drug hypersensitivity syndrome or drug-induced hypersensitivity syndrome, is a rare, potentially life-threatening drug reaction that affects multiple organ systems simultaneously. **Objective:** The objective of the study was to investigate the DRESS syndrome and its management in a tertiary care hospital in the department of medicine. **Materials and Methods:** A retrospective evaluation of 227 medical records was conducted among the patients admitted in medicine units. Causality assessment was carried out using Naranjo's scale and two specific scoring systems. RegiSCAR 1 was utilized to confirm the diagnosis of DRESS syndrome. **Results:** A total of 86 cases were identified. The mean age of patients was 43.96 years (SD = 17.05). The gender distribution was almost equal with males constituting 52% with females constituting 48%. Probability of reactions was found to be occurring in 37.4% of the patients. The condition was managed symptomatically and using topical agents for the treatment of skin reactions. **Conclusion:** The study was one of its kind in South Indian population that identified the burden of DRESS in a tertiary care hospital and its respective treatment pattern. Future studies considering the human leukocyte antigen sequencing should be designed to identify the patients falling under risk and for vigilant reporting of DRESS.

**Keywords:** Adverse drug reaction, drug reaction with eosinophilia and systemic syndrome, investigation, South India, tertiary care hospital

## INTRODUCTION

The use of drug therapy predisposes one to certain side effects, some of which are self-limiting while others require medical intervention.[1] These unintended, negative effects expressed as a result of drug therapy at normal doses are collectively known as adverse drug reactions (ADRs). The World Health Organization defines adverse drug reactions as "*a response to a drug, which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease, or for the modification of physiological function*."[2] The skin, being the largest organ in the human body, may be solely affected or concomitantly affected with other systemic manifestations following administration of certain medications.[3] Although every drug has the potential to elicit a cutaneous drug reaction, some drugs are more likely than others to do so. A major contributing factor is the failure to detect and monitor skin-related adverse reactions affecting outpatients.[4] Drug reaction with eosinophilia and systemic syndrome (DRESS) is also known as drug hypersensitivity syndrome or drug-induced hypersensitivity syndrome (DIHS), is a rare, potentially life-threatening drug reaction that affects multiple organ systems simultaneously. It encompasses a wide range of clinical manifestations including cutaneous eruptions lymphadenopathy, hematological abnormalities, and internal organ involvement.[5]

The clinical presentations of DRESS syndrome are characterized by fever, widespread skin lesions, internal organ involvement, a long latent period after intake of the inciting

drug, a prolonged and protracted clinical course, and possible sequential reactivation of various human herpesvirus.[6] The diagnosis of DRESS has been adequately challenging due to its relatively long latency period ranging from 2 to 8 weeks between the exposure to the suspected drug and the onset of the reaction.[7] Incidence of DRESS syndrome is extremely limited but is alleged to be approximately 1 in 1000–10,000 drug exposures. The cases in adults are found to be high compared to children.[8]

A defined therapy is very much necessary as the incidence of disease ranges from 10% to 20% resulting in several mortalities.[9] Although a wide range of drugs causes DRESS syndrome, data on incidence, diagnostic criteria, and management are exceedingly limited.[10] Incomplete information on the disease makes the physician difficult to diagnose the condition.[11] This has led to a lack of awareness among health-care professionals as the reaction could go unnoticed or managed inappropriately. If the condition is not properly identified with relevant suspected drugs, its use might be continued unabated leading to further complications.[12] The previous studies and case reports have been reported based on individual class of drugs and the reaction pattern.[13] The current study was designed to investigate the DRESS syndrome and its management in a tertiary care hospital in the department of medicine.

## MATERIALS AND METHODS

### Study Designs

A retrospective evaluation of medical records was conducted among the patients admitted in the medicine unit in Kasturba Hospital, Manipal. The study was conducted from October 2016 to March 2017. The study was approved by the Institutional Ethical Committee (IEC 690/2016).

### Population and Samples

The patient files falling under ICD Codes L27.0 (generalized skin eruption due to drug and medicine) and T88.7 (unspecified adverse effect of drug and medicine) and admitted in the medicine department during the year 2013–2015. Patients with non-drug-related skin manifestations (e.g., burn patients) were excluded from the study.

### Study Instruments

Causality assessment was carried out using Naranjo's scale[14] and a specific scoring systems. RegiSCAR 1 was utilized to confirm the diagnosis of DRESS syndrome as per the literature.[15] Based on the individual scoring, the cutaneous reactions were distinguished as definite ADR (≥9), probable ADR (5–8), possible ADR (1–4), and doubtful (0). The ADRs were classified based on the RegiSCAR 1 scores (<2 = excluded; 2–3 = possible; 4–5 = probable; or >5 = definite). Definite and probable groups were considered for further analysis. A pre-designed case record form (CRF) was utilized to collect the data retrospectively from the files.

### Data Collection

A pre-designed CRF was used for the data collection. The records were screened manually by the authors for the required data. The patients fulfilling the criteria were included in the study. The demographics, suspected drugs, and the type of reaction were noted based on the reported outcomes. The collected data were entered into Microsoft Excel 2016 and later exported to SPSS version 20.0 (IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp. IBM Corp. Released 2012) for further analysis.

### Statistical Analysis

The data were analyzed using descriptive statistics. The categorical data were presented as frequency and percentage and the continuous data were presented as Mean±SD. The frequency data were plotted as graphs for better representation.

## RESULTS

The retrospective screening yielded a total of 227 patients falling under the inclusion criteria. The patient's demographic data were collected through a pre-designed CRF. The mean age of patients was 43.96 years (SD = 17.05). The eligible participants mostly consisted of age ranging from 41 to 60 years that constituted 41.4% of the whole study sample. The detailed demographics of the patients diagnosed with skin reactions are represented in Table 1. Most of the patients did not have any history of sensitivity to any other allergens. The average length of stay of the patients admitted was 7.46 days. The patients who developed the reaction had a fever which was observed in 77 patients. Although the data were available for only 120 patients, most of the participants reported fever as a common symptom. Furthermore, the onset of the reaction was widely seen before admission than in people who were admitted to the hospital.

### Demographics of DRESS Patients

The eligible patients were further assessed using the RegiSCAR 1 scale to classify them under DRESS diagnosis and a total of 86 patients were identified as DRESS. The demographics of the DRESS diagnosed patients were further categorized to differentiate from the overall population. The same is depicted in Table 2. The DRESS population was equally distributed in terms of gender with 45 (52.32%) males and females 41 (47.67%) females. The causality assessment of individual patients was carried out using the Naranjo's scale. Most of the reactions were categorized as possible ADRs 44 (51.2%) followed by probable ADRs 36 (41.9%). The reaction was categorized as a possible case (2–3) in 34 patients, probable (4–5) in 8 patients, and as atypical DIHS (5) in 4 patients based on the RegiSCAR 1 scale. Majority of the patient's condition had a score below 2 (40) in the DRESS group.

### Laboratory Investigations

The eosinophil measure was of great value in detecting the presence of DRESS.[16] Eosinophil count and absolute eosinophil count (AEC) were documented in the study cases. Eosinophil counts were found to be 4% in the DRESS population which was in the normal range as per the reference values. Whereas, the AEC value was found to be higher than the normal range, that is, $0.4*10^9$/L.

### Clinical Manifestation

The DRESS patients had reactions all over the body and a few were restricted to certain parts. The reaction was bound

**Table 1:** Patient demographics of the overall population

| Category | Group | Overall population, *n* (%) |
|---|---|---|
| Age (Mean±SD) | | 43.96±17.058 |
| Age groups | ≤ 20 | 24 (10.6) |
| | 21–40 | 68 (29.9) |
| | 41–60 | 94 (41.4) |
| | >60 | 41 (18.1) |
| Gender | Male | 120 (53) |
| | Female | 107 (47) |
| Occupation | Homemaker | 73 (32.1) |
| | Agriculture | 31 (13.6) |
| | Business | 15 (6.6) |
| | Student | 34 (14.98) |
| | Service sector | 22 (9.69) |
| | Labor | 20 (8.81) |
| | Retired | 10 (4.4) |
| | Office employee | 2 (0.88) |
| | Teacher | 20 (8.81) |
| Previous allergies | Yes | 93 (40.96) |
| | No | 134 (59.03) |
| Length of stay (Mean±SD) | | 7.46±7.381 days |
| Onset of reaction* | Before admission | 111 (48.89) |
| | After admission | 19 (8.37) |
| Fever associated with rash* | Yes | 77 (33.92) |
| | No | 53 (23.34) |
| More than 1 causative drug* | Yes | 24 (10.57) |
| | No | 96 (42.29) |
| Causality assessment by Naranjo's scale | Doubtful ADR | 92 (40.52) |
| | Possible ADR | 74 (32.59) |
| | Probable ADR | 53 (23.34) |
| | Definite ADR | 2 (0.88) |

*Data were not available

**Table 2:** Demographics of patients diagnosed with DRESS

| Category | Group | DRESS population, *n* = 86 (%) |
|---|---|---|
| Age groups | ≤20 | 10 (11.62) |
| | 21–40 | 24 (27.9) |
| | 41–60 | 39 (45.34) |
| | >60 | 13 (15.11) |
| Gender | Male | 45 (52.32) |
| | Female | 41 (47.67) |
| RegiSCAR 1 | Not meeting criteria | 139 (61.23) |
| | Meeting the criteria | 86 (37.88) |
| Clinical manifestation | Body | 61 (70.93) |
| | Face | 30 (34.88) |
| | Groin and genitals | 8 (9.30) |
| | Hands and feet | 53 (61.62) |
| | Abdomen | 35 (40.69) |
| | Oral cavity | 10 (11.62) |
| Causative drug | Antibiotics | 30 (34.88) |
| | Antiepileptics | 22 (25.58) |
| | NSAIDs | 12 (13.95) |
| | Unknown | 6 (6.97) |
| | Others | 16 (18.60) |
| Laboratory values | Eosinophil count (%) | 4 |
| | AEC^ (L)* | $0.04\times10^9$/L |
| Choice of treatment | Antibiotics | 30 (34.88) |
| | Antiemetics | 20 (23.25) |
| | Antifungals | 6 (6.97) |
| | Antihistamines | 67 (77.90) |
| | Emollients | 35 (40.69) |
| | Soaps and shampoo | 12 (13.95) |
| | Systemic corticosteroids | 42 (48.83) |
| | Topical corticosteroids | 27 (31.39) |

DIHS: Drug-induced hypersensitivity syndrome patients presented with clinical manifestation in multiple sites, ^data represented as median, *higher range values. ADR: Adverse drug reaction; AEC: Absolute eosinophil count; DIHS: Drug-induced hypersensitivity syndrome; DRESS: Drug reaction with eosinophilia and systemic symptoms. NSAIDs: Nonsteroidal anti-inflammatory drugs

to commonly affect the skin, body, face, groin and genitals, hands, feet, abdomen, and oral cavity.

The major body parts affected by DRESS are represented in Table 2. Itching, generalized rash, erythematous rash, and maculopapular rashes were the major types of skin reactions presented in most patients. Other reactions included hyperpigmentation, clustered plaques, desquamation, lesions, and ulcers. The detailed description of the skin reactions is represented in Supplementary Table 1.

## Causative Drugs

DRESS caused by individual drugs was categorized based on the causality assessment by Naranjo's scale. The reaction presented by various drugs as identified as probable and some had a mere possibility to cause ADRs. The causative drugs were one or more in number in the present population. In fewer cases, the causative drug was left unidentified. The drugs causing DRESS mostly belonged to the class of antibiotics followed by antiepileptics and nonsteroidal anti-inflammatory drugs. The drugs were classified based on the drug class and are represented in Table 2. The individual drugs causing DRESS were phenytoin, anti-tubercular therapy (ATT), and diclofenac followed by others, respectively, as represented in Figure 1.

## Treatment Pattern

There are no standard treatment guidelines for DRESS. The condition was mostly managed symptomatically and using topical agents for the treatment of skin reactions. The

antibiotics usage was seen for the prevention of infection or in patients who presented with fever. The treatment was initiated after stopping the suspected causative drug. The treatment constituted various classes of drugs based on the presenting symptoms. The most used class of drugs was systemic corticosteroids to reduce the inflammation or to reduce immune response. The skin reaction was managed using antihistamines which were projected as allergic reactions. The major agents used to manage the reactions are presented in Figure 2.

## DISCUSSION

DRESS is a rare condition accompanied by severe rashes or fever with or without internal organ dysfunction.[17] The diagnosis of the disease is solely based on the RegiSCAR scoring, which was utilized to classify the disease condition.[18] These reactions occur during the general administration of the drugs and are not specific to any pharmacodynamic effect. DRESS is mostly underreported due to their unidentified mechanisms. In several scenarios, the disease condition is provisionally diagnosed as drug hypersensitivity disorder then gets as DRESS through confirmation.[19] No patients in the study were diagnosed with DRESS at initial admission. The differential diagnosis is difficult due to insufficient analysis techniques, thus making it a rare disorder.

The incidence of DRESS is yet to be known. Literature has shown the estimated incidence of DRESS to be 1 in 1000–1 in 10,000 drug exposures.[20] Even though the incidence varies among the population, the studies have shown a similar incidence in Asian population when compared to other studies.[21] As reported, the sample size in our study was more in number compared to other studies, the reason being the usage of RegiSCAR 1 as a major diagnostic method than RegiSCAR 2. For analysis, RegiSCAR 1 was considered in the current study as per the evidence from the literature.

DRESS was seen as more common syndrome in middle-aged adults than in older adults and the young.[22] The current study showed similar results on the development of DRESS in patients with age group of 41–60 years. A study conducted by Lam *et al.* which were a retrospective evaluation of vancomycin causing DRESS reported a similar age group with 49 years as median age. The male-to-female participants were reported to be similar in number in our study and this observation was noted in other studies as well.[22]

The clinical manifestation of DRESS was likely to spread all over the body. Skin being soft tissue in nature is more prone to allergic reactions and rashes in various severities. In the present study, the clinical manifestation of DRESS was classified based on the body parts affected. The skin was the major part to be affected as it was sensitive to diverse reactions. The presence of itching, generalized rash, erythematous rash, and maculopapular rashes was the major type of skin reactions seen in our study population. Cacoub *et al.* reviewed the literature and reported the clinical manifestation of DRESS from previously published studies. The major reactions were maculopapular rash, generalized erythematous rash, and facial edema. The occurrence of facial edema was not seen in our study which was a common reaction in other studies.[23]

The current study mainly focused on determining the clinical manifestation and treatment pattern of DRESS in South Indian population; thus, the study was more specific to the above

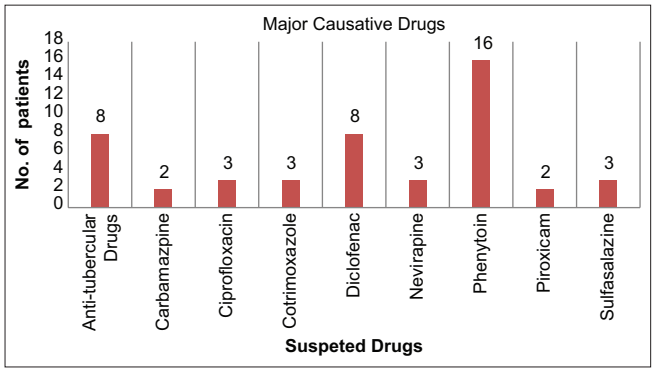


**Figure 1:** Suspected drugs causing drug reaction with eosinophilia and systemic syndrome

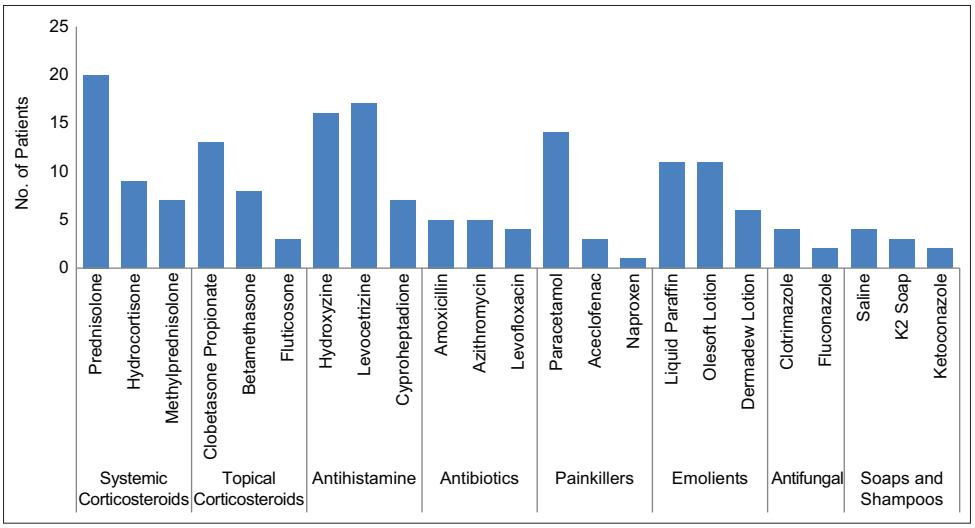


**Figure 2:** Prescription pattern for the treatment of drug reaction with eosinophilia and systemic syndrome

objective for which RegiSCAR scale was given more importance than the laboratory tests. The median eosinophil was found 4% in our study and the AEC was $0.4*10^9$/L. The obtained eosinophil was below normal whereas, the AEC was found to be high in number showing the presence of eosinophilia in the diagnosed patients as compared to existing studies.[24]

The causative drugs are to be identified to avoid severe reactions. The unavailability of appropriate treatment options also adds up to the burden of physicians in treating this syndrome.[25] In our study, the major causative drugs identified were antibiotics, antiepileptics, and anti-tubercular drugs. The drugs associated with DRESS in our study were found to be similar to other reports.[26,27] Accordingly, ATT had a high probability of causing DRESS as observed in the current study.[28,29]

The treatment pattern of DRESS was mostly based on the withdrawal of the causative agent and symptomatic treatment for the concerned condition. The treatment involved antibiotics in the presence of fever or to prevent further skin infections. Systemic or topical steroids were used in case of skin reactions. The study categorized treatment based on their pharmacological activity. A retrospective evaluation taken up by Wongkitisophon *et al.* that included 27 patients diagnosed with DRESS. The treatment pattern consisted of oral prednisolone and i.v dexamethasone which were the widely used steroids in the DRESS population.[30] In our study, the major drugs used were oral prednisolone or i.v methylprednisolone. The DRESS population was seen to be reviving after the removal of the suspected drug. Thorough knowledge of the disease is required to design effective treatment guidelines for DRESS as the pattern of disease changes based on the causative drugs.[31] The study had its own limitations in collecting the data and reporting. The study failed to interpret and correlate the laboratory data due to their unavailability. The data did not include organ infected and other added parameters that are required to define DRESS.

Future studies targeting the laboratory data and human leukocyte antigen (HLA) typing are necessary to explore the disease pattern of DRESS. Awareness on DRESS among the physicians for the right diagnosis should be emphasized to prevent mortality. The treatment pattern utilized in many studies should be well discussed to develop standard treatment guidelines for the fair treatment of the disease.

## CONCLUSION

The study was one of its kind in South Indian population that identified the burden of DRESS in a tertiary care hospital and its respective treatment pattern. The incidence of the reaction was like other Asian studies. The major causative drugs were identified as phenytoin, ATT, and diclofenac in the studied population. The treatment pattern commonly involved systemic or topical corticosteroids followed by antihistamines and antibiotics. Future studies considering the HLA sequencing should be designed to identify the patients falling under risk and for vigilant reporting of DRESS.

## ACKNOWLEDGMENTS

The authors are grateful to all students for their contributions in this study.

## REFERENCES

1. Abubakar AR, Simbak NB, Haque M. Adverse drug reactions: Predisposing factors, modern classifications and causality assessment. Res J Pharm Technol 2014;7:14.
2. Edwards IR, Aronson JK. Adverse drug reactions: Definitions, diagnosis, and management. Lancet 2000;356:1255-9.
3. Alomar MJ. Factors affecting the development of adverse drug reactions (Review article). Saudi Pharm J 2014;22:83-94.
4. Larson E, Girard R, Pessoa-Silva CL, Boyce J, Donaldson L, Pittet D. Skin reactions related to hand hygiene and selection of hand hygiene products. Am J Infect Control 2006;34:627-35.
5. Omairi NE, Abourazzak S, Chaouki S, Atmani S, Hida M. Drug reaction with eosinophilia and systemic symptom (DRESS) induced by carbamazepine: A case report and literature review. Pan Afr Med J 2014;18:9.
6. Cho YT, Yang CW, Chu CY. Drug reaction with eosinophilia and systemic symptoms (DRESS): An interplay among drugs, viruses, and immune system. Int J Mol Sci 2017;18:1243.
7. Shiohara T, Iijima M, Ikezawa Z, Hashimoto K. The diagnosis of a DRESS syndrome has been sufficiently established on the basis of typical clinical features and viral reactivations. Br J Dermatol 2007;156:1083-4.
8. Fiszenson-Albala F, Auzerie V, Mahe E, Farinotti R, Durand- Stocco C, Crickx B, *et al*. A 6-month prospective survey of cutaneous drug reactions in a hospital setting. Br J Dermatol 2003;149:1018-22.
9. Bohan KH, Mansuri TF, Wilson NM. Anticonvulsant hypersensitivity syndrome: Implications for pharmaceutical care. Pharmacotherapy 2007;27:1425-39.
10. Riaz M, Ragsdale BD, Rahman ZU, Nigam G. Drug rash with eosinophilia and systemic symptoms (DRESS) caused by phenytoin. BMJ Case Rep 2017;2017:bcr2017220835.
11. Fleming P, Marik PE. The DRESS syndrome: The great clinical mimicker. Pharmacotherapy 2011;31:332.
12. Jurado-Palomo J, Cabanas R, Prior N, Bobolea ID, Fiandor- Roman AM, Lopez-Serrano MC, *et al*. Use of the lymphocyte transformation test in the diagnosis of DRESS syndrome induced by ceftriaxone and piperacillin-tazobactam: Two case reports. J Investig Allergol Clin Immunol 2010;20:433-6.
13. Aagaard L, Strandell J, Melskens L, Petersen PS, Hansen EH. Global patterns of adverse drug reactions over a decade: Analyses of spontaneous reports to VigiBase™. Drug Saf 2012;35:1171-82.
14. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, *et al*. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther 1981;30:239-45.
15. Kardaun SH, Sidoroff A, Valeyrie-Allanore L, Halevy S, Davidovici BB, Mockenhaupt M, *et al*. Variability in the clinical pattern of cutaneous side-effects of drugs with systemic symptoms: Does a DRESS syndrome really exist? Br J Dermatol 2007;156:609-11.
16. Wong SS, Bekker HL, Thornton JG, Gbolade BA. Choices about abortion method: Assessing the quality of patient information leaflets in England and Wales. BJOG 2003;110:263-6.
17. Adwan MH. Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome and the rheumatologist. Curr Rheumatol Rep 2017;19:3.
18. Kardaun SH, Sekula P, Valeyrie-Allanore L, Liss Y, Chu CY, Creamer D, *et al*. Drug reaction with eosinophilia and systemic symptoms (DRESS): An original multisystem adverse drug reaction. Results from the prospective RegiSCAR study. Br J Dermatol 2013;169:1071-80.
19. Sasidharanpillai S, Riyaz N, Khader A, Rajan U, Binitha MP, Sureshan DN. Severe cutaneous adverse drug reactions: A clinicoepidemiological study. Indian J Dermatol 2015;60:102.
20. Shiohara T, Kano YJ. Review of drug-induced hypersensitivity: Special emphasis on drug-induced hypersensitivity syndrome.

Expert Dermatol 2012;7:539-47.
21. Ang CC, Wang YS, Yoosuff EL, Tay YK. Retrospective analysis of drug-induced hypersensitivity syndrome: A study of 27 patients. J Am Acad Dermatol 2010;63:219-27.
22. Lam BD, Miller MM, Sutton AV, Peng D, Crew AB. Vancomycin and DRESS: A retrospective chart review of 32 cases in Los Angeles, California. J Am Acad Dermatol 2017;77:973-5.
23. Cacoub P, Musette P, Descamps V, Meyer O, Speirs C, Finzi L, *et al*. The DRESS syndrome: A literature review. Am J Med 2011;124:588-97.
24. Blumenthal KG, Youngster I, Rabideau DJ, Parker RA, Manning KS, Walensky RP, *et al*. Peripheral blood eosinophilia and hypersensitivity reactions among patients receiving outpatient parenteral antibiotics. J Allergy Clin Immunol 2015;136:1288- 94.e1.
25. Brockow K, Przybilla B, Aberer W, Bircher AJ, Brehler R, Dickel H, *et al*. Guideline for the diagnosis of drug hypersensitivity reactions: S2K-guideline of the German society for allergology and clinical immunology (DGAKI) and the German dermatological society (DDG) in collaboration with the Association of german allergologists (AeDA), the German society for pediatric allergology and environmental medicine (GPA), the German contact dermatitis research group (DKG), the Swiss society for allergy and immunology (SGAI), the Austrian society for allergology and immunology (ÖGAI), the German academy of allergology and environmental medicine (DAAU), the German center for documentation of severe skin reactions and the german federal institute for drugs and medical products (BfArM). Allergo J Int 2015;24:94-105.
26. Bermeo-Ovalle A. Making rash decisions in epilepsy: Evaluating hypersensitivity reactions to anti-seizure medications. Epilepsy Curr 2019;19:96-8.
27. Ihtisham K, Ramanujam B, Srivastava S, Mehra NK, Kaur G, Khanna N, *et al*. Association of cutaneous adverse drug reactions due to antiepileptic drugs with HLA alleles in a North Indian population. Seizure 2019;66:99-103.
28. Coster A, Aerts O, Herman A, Marot L, Horst N, Kenyon C, *et al*. Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome caused by first-line antituberculosis drugs: Two case reports and a review of the literature. Contact Dermatitis 2019;81:325-31.
29. Czapka M, Shukla S, Slosar-Cheah M. Urine trouble: Genitourinary tuberculosis and subsequent DRESS syndrome. BMJ Case Rep 2017;2017:bcr2017220440.
30. Wongkitisophon P, Chanprapaph K, Rattanakaemakorn P, Vachiramon V. Six-year retrospective review of drug reaction with eosinophilia and systemic symptoms. Acta Derm Venereol 2012;92:200-5.
31. Sim DW, Yu JE, Jeong J, Jung JW, Kang HR, Kang DY, *et al*. Variation of clinical manifestations according to culprit drugs in DRESS syndrome. Pharmacoepidemiol Drug Saf 2019;28:840-8.