e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2022; 14(12); 326-334

Original Research Article

A Prospective Study on Drug Reaction with Eosinophilia and Systemic Symptoms

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Received: 10-10-2022 / Revised: 13-11-2022 / Accepted: 09-12-2022

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Conflict of interest: Nil

Abstract

Introduction: "Drug reaction with eosinophilia and systemic symptoms" (DRESS) disease is a severe dermal as well as comprehensive medication answer with numerous problems, a long way, and a 10% humanity rate. In addition to this, the physician needs to take into account numerous different serious nerves, search for good quality materials and impeding functionalities of the DRESS symptoms, and differentiate it from other serious severe skin bad effects (SCARs) such as "Stevens-Johnson syndrome/toxic epidermal necrosis" (SJS/TEN) and exertional modified exanthemata's pustulosis. Body temperature, skin infection, eosinophilia, atypical lymphocytosis, lymphadenopathy, as well as hepatitis are the classic symptoms of DRESS syndrome. However, pneumonitis, kidneys, and other physiological injuries are all potential complications that could arise, and they might be substantial.

Aims and Objectives: To evaluate the spectrum of clinical features of DRESS and further analyze their demographic features.

Methods: A prospective study was conducted on 30 patients who visited the outpatient department of our hospital. A detailed medical history of the patients was taken and examined and diagnosed. All the patients were analyzed for various parameters, based on DRESS and SJS.

Results: The study also found that 45.7% of the DRESS cases had probable casualty and AED accounted for 80% of the probable drug cases. Further, the study found 93.33% of people had a fever of at least 38.5°C, whereas 7% had a fever of 38.0-38.5°C, and 21% had multiple episodes of fever of at least 38.0°C. In 86.67% of cases, lymphadenopathy was seen. Every case (100%) displayed one or more hematopoietic abnormalities. Absolute eosinophil counts below 700 L1 and above 1500 L1 were both detected in 46.67% and 73.33% of cases with eosinophilia, respectively. There were abnormal lymphocytes in 8 instances (53.34%).

Conclusion: The study has validated the scoring system for DRESS which is considered to be a severe adverse drug reaction involving many organs, presenting combinations of features. Delayed diagnosis or management will reduce the chance of survival and hence, prompt treatment and early diagnosis are required which can only be possible if awareness can be made among the patients and also hospital staff.

Keywords: severe adverse reaction, drug reaction, eosinophilia

Introduction

"Drug reaction with eosinophilia and systemic symptoms" (DRESS) disease is a severe dermal as well as comprehensive medication answer with numerous problems, a long way, and a 10% rate [1]. The disease is unusual but still not rare; nonetheless, it is not widely known about and cannot be easily caught; as a consequence, it is susceptible to obtaining an incorrect decision. This illness, which has also been given the name substance acute illness, has been known for quite some time. The illness was primarily documented in the 1930s in linked with phenytoin, and for numerous ages, it must have been believed to be related to that medication [2]. The identification of new pharmacological risk factors and the significant improvement in one's knowledge of pathogenesis and progression managed the growth of a change of different terms and groups [3]. The physician must be able to identify DRESS disease from the numerous acne that appears during severe sickness, diagnose it to be a drug reaction, and separate it all from milder adverse drug events. In addition to this, the physician needs to take into account numerous different serious nerves, search for good quality materials and impeding functionalities of the DRESS symptoms, and differentiate it from other serious severe skin bad effects (SCARs) such as "Stevens-Johnson syndrome/toxic epidermal necrosis" (SJS/TEN) and exertional modified exanthemata's pustulosis [4].

The medication response defined by symptoms or signs and clinical signs condition affects individuals of all ages, including both children and adults. It is expected that it occurs anywhere between once per 1000 and once per 10,000 times, a drug is exposed [5, 6]. The main aspect is a slightly deferred start, which is most common approximately 2 and 6 weeks after alcohol's original conception, earlier on re-exposure, and now and then as long as 8 to 16 weeks [7]. This is most common over 2 and 6 weeks after alcohol's original conception, with emphasis on re-exposure, and now and again as late as 8 to 16 weeks. Both the symptoms and the treatment of the condition could be extended if the disease has a long-term and progressive course [8]. Although a delayed start can help patients in identifying DRESS disease from those other drug outbreaks, it can also be easier for them to miss the diagnosis of a drug-related adverse effect altogether. In addition, the chronic duration of the condition, which can include development and flare-ups even when the harmful medication has been taken, might also complicate or delayed clinical diagnosis.

Body temperature, skin infection, eosinophilia, atypical lymphocytosis, lymphadenopathy, as well as hepatitis are the classic symptoms of DRESS syndrome. However, pneumonitis, kidneys, and other physiological injuries are all potential complications that could arise, and they might be substantial [8]. There have been cases of extremely high flu symptoms in up to 90 percent of individuals, and these illnesses can appear many days even before the outbreak [9]. The outbreak is often irritating, and pain may appear before the release itself. The DRESS disease can occur in a variety of different ways on the skin. A most typical manifestation is a method as a means of rash [2]. There is a possibility that issues which arise will be prevalent; an initial concentration on the face, neck, proximal trunk, and arms might be joined by an increase of the focus on the legs. The reaction may have become widespread, raised or infused, modifying or maybe even purpuric, along with dissolution, scales, water loss, and peeling. In severe cases, the outbreak may even turn purpuric.

Edema is a major factor, and it most often appears on the face, where it can be quite

significant and indicate increased presence. In certain instances, the outbreak can persist for decades, and even when the harmful chemical has been removed, a continuous duration of the disease may experience remission followed by a return. It is estimated that abscess is present in around 75% of individuals [9]. People could feel regional or widespread lymphadenopathy, most strongly in the neck, axilla, and groin, along with the painfully metastatic disease. Ang et al. stared at 27 cases of DRESS symptoms and found that although nearly 80% of people used to have the systems have a lot of outbursts over the face, trunk, and limbs, and a third used to have face edema, a third also had mucositis, 7% evolved pustules, and another 7% showcased target-type growths. These findings were found after the researcher asked 27 patients with DRESS symptoms [10].

It is a hereditary form with a 0.9/100,000 annual incidence [11]. In DRESS syndrome, the latency between both initiations of therapy as well as the onset of skin rash is 2-8 weeks, which is longer than in most other drug reactions. Anti-epileptic medications like carbamazepine, lamotrigine, or phenytoin account for 35% of all incidents, NSAIDs account for 13%, sulfonamides like sulfasalazine, dapsone, trimethoprim-sulfamethoxazole, or sulfadiazine profile for 12%, and bacteria like vancomycin, minocycline, and related proteins The process of pathophysiology is diverse and complex. They describe the results of systematic research in which individuals with no illnesses who had a medication event characterized by symptoms or signs and widespread signs 4 weeks later taking drugs to participate.

Materials and Methods

Study design

A prospective study was conducted on patients who came to the outpatient department of our hospital from November 2021 to November 2022, with Stevens-Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN), acute generalized exanthematouspustulosis (AGEP), and DRESS, including the collection of biological samples. A detailed medical history of the patients was taken and examined and diagnosed. All the patients were analyzed for various parameters, based on DRESS and SJS. The study considered 30 patients in total.

Inclusion and exclusion criteria

Patients who were hospitalized, reported to the national investigators, and who met three or more of the inclusion criteria (acute rash, fever over 38 °C, lymph node enlargement in at least 2 sites, involvement of at least one internal organ, or abnormal blood counts) were sequentially enrolled as potential cases of DRESS. Patients who visited the hospital's outpatient department completed the study protocol and provided informed consent were included.

Patients who did not follow the study protocol did not finish it, or did not provide consent were not included in the study.

Statistical analysis

The researchers used the web-based remote data entry system MACRO to enter all of the obtained data into a centralized database at the University Medical Center Freiburg, Germany (Oracle, version 8.1.7 (8i), Redwood Shores, CA, U.S.A.) (version 3.0, InferMed, London, U.K.). The software program SAS (version 9.2, Cary, NC, U.S.A.) was utilized for subsequent data processing, including routine data checks, preparation, and analysis. The software packages SAS, SPSS (version 16, SPSS, Chicago, IL, U.S.A.), and MS Excel Data Analysis were utilized for statistical analysis. Absolute numbers and percentages were used to display categorical and dichotomous variables, whereas mean, standard deviation, or, when more appropriate, median and interquartile range, were used to show continuous variables.

Ethical approval

The authors gave the patients a thorough explanation of the study. The patients' permissions have been gotten. The concerned hospital's ethical committee has accepted the study's methodology.

Results

In table 1 while 21 individuals' reactions began in the hospital, 30 patients were community cases who were admitted as a result of the reaction. Six patients, one of whom had previously undergone a DRESS episode due to the same medicine, had previously encountered a cutaneous adverse drug reaction. Particularly in patients whose reaction was related to antibiotics (median 39 vs. 51 years), females predominated and were somewhat younger than men (P = 0.05), whereas no difference was seen for allopurinol (median 63 vs. 61 years) and antiepileptics (median 40 vs. 39 years). The treatment's indication did not differ based on gender. Epilepsy was the comorbidity that occurred 20–0% of the time.

Table 1: Demographics, comorbidities, concomitant medication

Characteristics	DRESS n= 15 N (%)	SJS/TEN n= 15 N (%)
Sex, male/female ratio	7/8	6/9
Age all (median, interquartile range)	49 (31-63)	51 (29-69)
Age male (median, interquartile range)	57 (35-67)	48 (31-63)
Age female (median, interquartile range)	45 (30-58)	52 (29-73)
Community cases	12 (80%)	15 (100%)
Earlier cADR	3 (20%)	2(13.33)
Comorbidities		
Collagen vascular disease	2(13.33)	3(20)
Conclusive disorders	4(26.67)	2(13.33)
Diabetes mellitus	3(20)	1(6.67)
Pre-existing liver disorder	1(6.67)	1(6.67)
Pre-existing kidney disorder	1(6.67)	2(13.33)
Recent cancer b	1(6.67)	2(13.33)
Radiation therapy	0	2(13.33)
HIV	1(6.67)	2(13.33)
Acute infections (4 weeks before the onset of reaction)	4(26.67)	7(46.67)
Concomitant medication		
Immunosuppressive or immunomodulating agents C		
Corticosteroids ≤ 8 weeks/ > 8 weeks	2(13.33)	3(20)
Other ≤ 8 weeks/ > 8 weeks	1(6.67)	3(20)

cADR, cutaneous adverse drug reaction. aEuro SCAR-study. recent cancer: diagnosed during the last 2 years before the index date or, if diagnosed earlier, still being treated. cNot including colchicine, combined with allopurinol ≤8 weeks in four cases; four patients using corticosteroids were also using other immunosuppressive or immunomodulating agents.

As seen in Table 2, 93.33% of people had a fever of at least 38.5°C, whereas 7% had a fever of 38.0-38.5°C, and 21% had multiple episodes of fever of at least 38.0°C. In 86.67% of cases, lymphadenopathy was seen. Every case (100%) displayed one or more hematopoietic abnormalities. Absolute eosinophil counts below 700 L1 and above 1500 L1 were both detected in 46.67% and 73.33% of cases with

eosinophilia, respectively. There were abnormal lymphocytes in 8 instances (53.34%). We also discovered other haematological anomalies, however, they were not factored into the validation score. 66.67% had lymphocytosis while 80% had leucocytosis. While monocytosis (66.67%) occurred later in the reaction, neutrophilia (80%) predominated in the early stages. Thrombocytopenia (66.67%), thrombocytosis (60%), and lymphopenia (5%, data not shown) were uncommon.

A severe skin eruption occurred in all of the patients. 70% of cases had a morphology that met two or more criteria that suggested DRESS, while 86.67% had skin involvement that surpassed 50% of the body's surface area. In 40% of cases, the rash was monomorphic maculopapular, occasionally confluent and/or oedematous erythema, whereas in the remaining cases, it was polymorphous and included additional varying combinations of other lesions like pustules or tense blisters with, save for two cases, negligible detachment. More frequently (81%) than scorching or pain (35%), itching. Facial edema was seen in 86.67% of cases. Most often, the liver (53.33%), kidney (46.67%), and lung (40%) were impacted by the reaction.

Table 2: Characteristics of definite cases of DRESS

Characteristics	Study Sample n=15	Percentage	95% CI
Fever ≥ 38.5 degrees centigrade	14	93.33	84-96
Lymphadenopathy	13	86.67	44-65
Haematological abnormalities	14	93.33	96-100
Eosinophilia	12	80.00	90-98
Grade 2 ($\geq 1500\mu L-1$)	11	73.33	
Grade 1 (700-1499 $\mu L-1$)	7	46.67	
Atypical lymphocytes	10	66.67	56-75
Leucocytes > 10000 $\mu L-1$	12	80.00	90-99
Netrophilia> 7000 $\mu L-1$	12	80.00	68-86
Lymphocyte> 4000 $\mu L-1$	13	86.67	43-61
Thrombocytosis > 400 000 $\mu L-1$	9	60.00	13-28
Monocytosis> 1000 $\mu L-1$	10	66.67	58-80
Thrombocytopenia < 100 000 $\mu L-1$	10	66.67	4-15
Skin	15	100.00	96-100
Extent of rash > 50%	13	86.67	71-88
Suggestive rash	12	80.00	57-78
Facial edema	13	86.67	68-84
Monomorphic maculopapular	6	40.00	
Polymorphous maculopapular	14	93.33	
Exfoliative	3	20.00	
Urticarial	3	20.00	
Lichenoid	1	6.67	
Pustules	11	73.33	
Infiltrated plaques	8	53.33	
Purpura	9	60.00	
Blisters	6	40.00	

Target-like lesions	4	26.67	
Eczema-like lesions	3	20.00	
Duration exanthema ≥ 15 days	12	80.00	83-98
Mucosal involvement	13	86.67	46-67
mouth/throat/lips	12	80.00	
Eyes	5	33.33	
Genitalia	3	20.00	
Other	3	20.00	
Internal organ involvement	13	86.67	86-97
1 organ involved	13	86.67	
2 organs involved	6	40.00	
> 2 organs involved	5	33.33	
Kidney	7	46.67	
Liver	8	53.33	
Lung	6	40.00	
muscle/heart	3	20.00	
Spleen	4	26.67	
Pancreas	2	13.33	
Other	2	13.33	
Duration DRESS ≥ 15 days	14	93.33	95-100

Table 3 displays the findings of the expert judgment on drug causality. In total, 316 distinct therapeutically active ingredients from 636 different drugs were used in the month before the likely index day. The time course had the effect of significantly reducing the number of suspicious medicines following elimination. In 25 instances, just one (13) or two (12), most frequently one drug with a high level of renown. All patients whose use of highly infamous drugs was discontinued due to prolonged use were exposed to a different highly infamous drug during the selected period. In 34.3% of the cases, aromatic antiepileptic drugs were held responsible. With an initial daily dose of 300 mg in 9 patients, 200 mg in 2 patients, and 100 mg in 4 patients, allopurinol (40%) was given for hyperuricemia in 3 patients and gout in 3 patients. Miscellaneous antibiotics, primarily vancomycin, and minocycline, were suspected in 3 patients, antimicrobial sulfonamides or dapsone (sulfas) in 26.67%, and other medications in 13.34%. The study also found that 45.7% of the DRESS cases had probable casualty and AED accounted for 80% of the probable drug cases.

Table 3: Culprit drugs and time relation of drugs taken within 1 month before the reaction among DRESS patients

Exposure	**Cases**	**Median**	**Interquartile range**
At least one drug	14 (93.34%)		
Total number of drugs	25	5	2-8
Casualty	**Cases**	**Drugs**	
Very probable	12 (34.3%)	40	
Probable	16 (45.7%)	56	
Possible	3 (8.6%)		
Undetermined	2 (5.7%)		

Unlikely	2 (5.7%)		
No drug use	1 (2.8%)		
Associated very probable drugs		**Median latency**	**Interquartile range**
AED	12 (80%)		
Carbamazepine	6	30	21-37
Phenytoin	2	30	26-38
Lamotrigine	2	26	21-35
Oxcarbazepine	1	n.a.	n.a.
Phenobarbital	1	n.a.	n.a.
Allopurinol	6 (40%)	21	16-31
Sulfonamides	4 (26.67%)		
Sulfasalazine	1	21	17-26
Dapsone	1	n.a.	n.a.
Sulfamethoxazole-trimethoprim	1	n.a.	n.a.
Sulfadiazine	1	n.a.	n.a.
Antibiotic	6(40%)		
Vancomycin	1	18	12-20
Minocyclin	2	21	16-25
Amoxicillin	2	n.a.	n.a.
ampicillin/ sulbactam	1	n.a.	n.a.
Other drugs	2 (13.34%)	27	24-29

n.a., not applicable, AED, aromatic antiepileptic drugs. equally suspected highly notorious drugs in the same case: allopurinol/fluindione, oxcarbazepine/ phenobarbital, and carbamazepine/ phenytoin. Two equally suspected aromatic antiepileptic drugs in two cases. cFlavoxate, fluindione, nevirapine, phenylephedrine-acetaminophen, strontium ranelate.

Discussion

Jorg et al. (2020) investigated and reported on 46 people with DRESS who were regarded in the aversion partition of the "Inselspital, Bern University Hospital". Drug-related relapses stayed examined about the occurrence and whether conceivable sensitization to the new drugs was detected using skin examinations and/or "lymphocyte transformation tests" (LTT). A subset of patients was also evaluated for drug tolerance. There were 56 relapses in 27 of 46 DRESS patients (58.7%). 30 drug-related declines were appraised using a cover test and/or a lymphocyte alteration examination, accounting for 33 (58.9%) of these relapses. Sensitization to the new drug was observed in 8/30 (26.7%) drug-related relapses, indicating the rise of a "multiple drug hypersensitivity syndrome" (MDH). 14 people had 22 medicine-related declines with no visible sensitization and only 1/6 advanced new indications after re-exposure. Medicine-related declines were public among DRESS people. Half of the people who experienced medicine-related declines advanced an MDH with demonstrated sensitivities not only to the DRESS-inducing drugs but also to newly introduced medicine. Drugs indicated in drug-related declines could be restored if not explained. In this paper, they suggest a process for medicine challenging and future drug-related relapse organization in DRESS [13]. People with the disease with DRESS are at risk of developing another severe DHR from new drugs. As a result, it is critical to better understand and possibly

avoid an MDH course. According to our findings, drug-related relapses and MDH were shared difficulties in DRESS. The popular of drug-related relapses was not related to an obvious immune response. When not sensitized, involved drugs can be managed over. To evade the growth of an MDH, it is best to limit the administration of new drugs as much as possible during a DRESS response. All medicine implicated in declines should be confirmed, even if used advanced in the DRESS plan.

Soria et al. (2020) investigated and reported on the delayed occurrence of DRESS and the culprit drugs. In this case series, individuals who had an initial incident of DRESS and for whom the medicine was a strong suspicion would be included if they were treated in one of three medical clinics. Based on how much time it took for DRESS signs to manifest, patients were classified into two groups some that presented themselves soon and those that presented them much after. The experiment had a minimum of 41 DRESS symptoms, with 14 participants classified to the faster category and 27 people assigned to the slow category. In the faster category, the most prevalent causes of illness were medicines. Carbamazepine (number of patients: 4/4), lamotrigine (number of patients: 6/6), allopurinol (number of patients: 8/8), and sulfasalazine (number of patients: 2/2) constituted the only medications in the premature group. It is standard procedure to attribute DRESS to the introduction of medication 15 days or lower before the appearance of skin negative impacts. The start of DRESS might be delayed or accelerated based on the drugs that are used [14].

Sasidharanpillai et al. (2019) researched and examined "Drugs response with symptoms or signs and systemic symptoms" (DRESS) is a major negative medicine response that can impact anyone. DRESS therapy epidemiology in kids was studied prospectively. They examined all 12-year-olds treated in the paediatrics and dermatological department of a tertiary hospital with possible or proven DRESS, as described by RegiSCAR, over three years. Analyzing eleven people. Penicillin and lamotrigine (four patients) were the two most common causes (three patients). Lamotrigine-induced DRESS may have been enhanced by not following conventional protocols for induction and progressive adjustment to prescribed levels. Medication use and drug reaction happen quickly in antibiotic-induced DRESS [15]. Significant internal organ contact and drug-induced sensitivity response are the most severe types of DRESS, which is a range condition. Research findings are also consistent with Soria et al that a short delay before drug use and adverse reactions would not rule out DRESS if other analytical standards are pleased.

Conclusion

The study has validated the scoring system for DRESS which is considered to be a severe adverse drug reaction involving many organs, presenting combinations of features. Cutaneous features are observed primarily, which also include other symptoms, that are severe and acute in manifestation. As DRESS involves a plethora of symptoms, the management of all can be troublesome and may indicate symptomatic treatment. Early diagnosis and prompt management are the decisive steps in alleviating the condition. The authors also concluded that there is a need to spread awareness about DRESS which is important for early management. Delayed diagnosis or management will reduce the chance of survival and hence, prompt treatment and early diagnosis are required which can only be possible if awareness can be made among the patients and also hospital staff. Although this study can be considered clinically significant in the prevention and management of DRESS, however, the limited sample of this study may not result in a conclusion that can be reflected upon the population at large. Therefore, more similar studies involving

larger samples should be conducted to bring out more acceptable conclusions.

Reference

1. Oelze LL, Pillow MT. Phenytoin-induced drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome: a case report from the emergency department. J Emerg Med. 2013;44:75–78.
2. Husain Z, Reddy BY, Schwartz RA. DRESS syndrome: part I. Clinical perspectives. J Am AcadDermatol. 2013;68:693.e1–693.e14.
3. Bocquet H, Bagot M, Roujeau JC. Drug-induced pseudolymphoma and drug hypersensitivity syndrome (drug rash with eosinophilia and systemic symptoms: DRESS). Semin Cutan Med Surg. 1996; 15:250–257.
4. Darlenski R, Kazandjieva J, Tsankov N. Systemic drug reactions with skin involvement: Stevens-Johnson syndrome, toxic epidermal necrolysis, and DRESS. ClinDermatol. 2015;33:538–541.
5. Chiou CC, Yang LC, Hung SI, et al. Clinicopathological features and prognosis of drug rash with eosinophilia and systemic symptoms: a study of 30 cases in Taiwan. J Eur Acad Dermatol Venereol. 2008; 22:1044–1049.
6. Fiszenson-Albala F, Auzerie V, Mahe E, et al. A 6-month prospective survey of cutaneous drug reactions in a hospital setting. Br J Dermatol. 2003;149:1018–1022.
7. Cacoub P, Musette P, Descamps V, et al. The DRESS syndrome: a literature review. Am J Med. 2011;124:588–597.
8. Irga N, Kosiak W, Jaworski R, et al. Pediatrician! Do you know the symptoms of DRESS syndrome? A case report of a 4-year-old girl. Pediatr Emerg Care. 2013;29:504–507.
9. Kardaun SH, Sekula P, Valeyrie-Allanore L, 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;169:1071–1080.
10. Ang CC, Wang YS, Yoosuff EL, et al. Retrospective analysis of drug-induced hypersensitivity syndrome: a study of 27 patients. J Am AcadDermatol. 2010;63:219–227.
11. Husain Z, Reddy BY, Schwartz RA. DRESS syndrome: part I. Clinical perspectives. J Am AcadDermatol. 2013 May;68(5):693.e1–14.
12. Kardaun SH, Sekula P, Valeyrie-Allanore L, Liss Y, Chu CY, Creamer D, et al.; RegiSCAR study group. Drug reaction with eosinophilia and systemic symptoms (DRESS): an original multisystem adverse drug reaction. Results from the prospective RegiSCAR study. Br J Dermatol. 2013 Nov;169(5):1071–80.
13. Jörg L, Helbling A, Yerly D, Pichler WJ. Drug-related relapses in drug reaction with eosinophilia and systemic symptoms (DRESS). Clinical and translational allergy. 2020 Dec;10(1):1-8.
14. Soria A, Bernier C, Veyrac G, Barbaud A, Puymirat E, Milpied B. Drug reaction with eosinophilia and systemic symptoms (DRESS) may occur within 2 weeks of drug exposure: a retrospective study. J Am Acad Dermatol. 2020; 82:606-611.
15. Sasidharanpillai S, Sabitha S, Riyaz N, et al. Drug reaction with eosinophilia and systemic symptoms in children: a prospective study. Ped Dermatol. 2016;33(2):e162-e165.
16. Chakroborty B., Parvin S., Hossain M. M., & Hossain M. J. Self- Examination of Breast of the Students of Nursing College in Bangladesh. Journal of Medical Research and Health Sciences. 2022; 5(12): 2339–2344.