Review article

Dermatological emergency and life threatening skin conditions.

Mohammed Saiful Islam Bhuiyan[1]

1. Associate Professor, Department of Dermatology & Venereology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

Abstract

Dermatology is known to be a non-emergency cool discipline, but many dermatological entities really deserve special immediate intervention. Some of them also have significant disease related fatality. Understanding the etiopathogenesis and disease course of these conditions are very important to save patient's life. Among them severe drug reactions, acute urticaria, angioedema, anaphylaxis, erythroderma, flare of pre-existing inflammatory dermatoses, bullous diseases and infections including staphylococcal scalded skin syndrome (SSSS), necrotizing fasciitis (NF) etc. Failure of timely diagnose and intervene against many of these conditions may lead to acute skin failure and multiorgan failure. This article is aimed to discuss dermatological emergencies, their etiopathogenesis, consequences, diagnosis and management.

Keywords: Dermatology, Emergency, Dermatological emergency, Acute skin failure.

Introduction:

Dermatological diseases are the fourth leading cause of nonfatal burden in global disease burden (GBD).[1] Cutaneous and subcutaneous diseases were responsible for 41.6 million Disability-Adjusted Life years (DALY) and 39.0 million Years loss due to disability (YLD) in 2013.[2] Dermatological diseases imposes physical disability, discomfort, disfiguration, psychological distress and even death. As skin lesions are readily visible and present mostly with pruritus, it creates significant impact on daily quality of life.[3-4] Though dermatology is generally considered as a cool and non-emergency discipline but very often some situations demand emergency care. All over the world a good proportion of patients come to emergency room for their skin problems. Sometimes skin is primarily involved and in other situations skin manifests some signs of dreadful internal diseases. In emergency department 3-21% of attending patients seek care for dermatological issues and among pediatric population it may be up to 31%.[5-7] So it is very crucial to understand the nature and extend of emergency dermatological situation which will ensure timely and appropriate identification of dangerous skin condition to take life saving measures.

Certain situations are really candidates for emergency intervention; Acute urticaria, angioedema, erythrodermic flares of preexisting dermatoses like psoriasis, atopic dermatitis etc, boils, cellulitis, staphylococcal scalded skin syndrome, septicemia, toxic shock syndrome, necrotizing fasciitis, erythema multiforme, drug reaction with eosinophilia and systemic symptoms (DRESS), Stevens-Johnson syndrome, toxic epidermal necrolysis (TEN), acute generalized exanthematous pustulosis (AGEP), anaphylactic drug reaction, vasculitis, etc. ,

Dermatological emergencies: Although there is no well-established definition of the word dermatological emergency, any disease presenting with generalized cutaneous and mucous membrane involvement which demands urgent life-saving interventions. Dermatological emergency can be defined as 'an acute or worsening dermatitis for <5 days'.[8]

Corresponding author
Mohammed Saiful Islam Bhuiyan, Associate Professor, Department of Dermatology & Venereology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, E-mail: drsaifulib@yahoo.com
Received: 15 November 2020 Accepted: 5 December 2020 Available Online: 000
Cite this Article:
Bhuiyan MSI Dermatological emergency and life threatening skin conditions. J. Ban. Acad. of Dermatol. 2021; 1 (1): 17-25

Available at: www.jbadbd.com
An official publication of Bangladesh Academy of Dermatology (B.A.D.)

Table I: Dermatological diseases need emergency care.[9-12]

Dermatological emergencies	
Group of diseases	**Cause**
Infectious skin diseases	Staphylococcal toxic shock syndrome, staphylococcal scalded skin syndrome, streptococcal toxic shock syndrome, necrotizing fasciitis, cellulitis, septicemia, cutaneous abscess/furuncle/carbuncle, meningococcemia, Lyme disease, viral exanthema, measles, chicken pox, herpes zoster, Rocky Mountain spotted fever, acute paronychia, disseminated candidiasis
Urticaria, angioedema and anaphylaxis	Viral infection, medications, foods, radiocontrast media, hair dye, arthropod and insect bite.
Drug reaction	Stevens-Johnson syndrome [SJS], toxic epidermal necrolysis (TEN) drug reaction with eosinophilia and systemic symptoms (DRESS), drug reaction with different hypersensitive syndrome, acute generalized exanthematous pustulosis (AGEP), urticaria, and erythema multiforme.
Inflammatory skin diseases	Eczema, contact dermatitis, pustular psoriasis, erythrodermic psoriasis.
Acute erythroderma	Psoriasis, atopic dermatitis, pityriasis rubra pilaris, seborrheic dermatitis, pemphigus foliaceus, mycosis fungoides, sezare syndrome.
Physical or agents	Burn, irritant contact dermatitis (acid, alkali, hair dye)
Auto immune bullous skin diseases	Pemphigus vulgaris, bullous pemphigoid
Connective tissue disease, vasculitis, superficial thrombosis/ thrombophlebitis	Acute SLE, Dermatomyositis, Leukocytoclastic vasculitis (LCV), Henoch-Schonleinpurpura, poly arteritis nodosum.
Benign or malignant tumor	Mycosis fungoides, sezare syndrome, leukemia cutis, melanoma, mastocytosis
Neonatal skin diseases	Harlequin ichthyosis, epidermolysis bullosa, acrodermatitis enteropathica
Other conditions	Acute graft-versus-host disease (aGVHD), calciphylaxis, purpura fulminans, Kawasaki disease, Sweet syndrome and its histiocytoid variant, pyoderma gangrenosum (PG), erythema nodosum, Lepra reaction, diaper dermatitis, Jarisch-Herxheimer etc.

Infectious skin diseases:

Different bacterial, viral, fungal infection of skin, subcutaneous or internal organ with wide array of severity can present to dermatology outpatient department (OPD) or emergency room for urgent care. This group of skin diseases were found as the leading (nearly half) cause of dermatology emergency care in many studies.[13-14] In an indian study by Priyanka et al.leprosy, STDs and Herpes zoster (21%) were the leading cutaneous infections those seek emergency care.[15] Infections which present with redness, warmth, pain, tenderness, edema, fever,

blister, scalding etc. make patients panic. Some of them are less serious initially like acute paronychia (pseudo dermatological emergency)and some are real candidate of urgent lifesaving intervention like necrotizing fasciitis (NF), staphylococcal toxic shock syndrome, staphylococcal scalded skin syndrome, streptococcal toxic shock syndrome, meningococcemia, septicemia, disseminated herpes simplex, disseminated chicken pox, herpes zoster ophthalmicus or disseminated herpes zoster. Many maculopapular viral infections especially mumps, measles, and rubella as well as other childhood viral infection like roseola and erythema infectiosum warrant patient and parents attend at emergency department.

Urticaria, angioedema and anaphylaxis:

Patients with urticaria with or without angioedema is very common in the population and concerning to seek urgent supports for the painful, severe itchy wheals to laryngeal edema, anaphylaxis and severe respiratory problems. Urticaria represents about 11.4 to 68.1% of dermatological emergency.[16-17] Approximately 40% of patients with urticaria also experience angioedema (swelling that occurs beneath the skin).[18] In USA each year 80,000 to 112,000 patients attend emergency department (ED) for angioedema and on average 4.0 persons for each 100,000 persons need hospital admission.[19] Vast majority of acute urticaria, angioedema and anaphylaxis are unknown and specific causes cannot be identified. Viral infection as well as drug, food, radio-contrast media, parasitic infestation, insect or arthropod bite are responsible for acute urticaria, angioedema or anaphylaxis. Anaphylaxis is a dramatic situation that can rapidly progress to death. Hereditary angioedema is an uncommon.[20]

Drug reaction: SJS, TEN and DRESS syndrome:

Adverse cutaneous drug reactions (ACDR) are very common entity that brings patients to dermatological emergency. It is the commonest acute drug reaction (ADR) and responsible for about 2% of hospital admissions.[21-22] Patients with history of taking different medications may present with different varieties drug-induced severe cutaneous adverse reactions (SCARs) include acute generalized exanthematous pustulosis (AGEP), drug reaction with eosinophilia and systemic symptoms (DRESS), and epidermal necrolysis (Stevens-Johnson syndrome [SJS], toxic epidermal necrolysis).[23]As each of these syndromes are distinct entities with different clinical, biological, and histological patterns and identify the particular syndrome and the culprit medicine is the prime job in managing drug reaction.[23]

Table II: Drugs commonly causes adverse drug reaction

Drugs
Anti-convulsants (Carbamazepine, Phenytoin, Phenobarbital)
NSAIDs (naproxen, ibuprofen, tramadol, indomethacin, ketoprofen, diclofenac)
Anti-microbial agents (Ciprofloxacin, Amoxicillin, Cotrimoxazol, tetracycline, Doxicycline, Metronidazole and Anti-TB drugs)
Allopurinol
Sulfasalazine
Dapsone
Antihypertensive

Acute erythroderma:

Acute erythroderma is another deadly skin condition develops due to generalized inflammation affecting skin. It may develop in normal skin due to underlying systemic inflammation or drug reaction (primary) or in pre-existing skin diseases (systemic). Very often it is misdiagnosed. Though the cause of a good number of erythroderma remain unsettled; erythrodermic flare of preexisting skin diseases including psoriasis, eczema, PRP, seborrheic dermatitis, pemphigus foliaceus, cutaneous lymphoma, drug reaction and internal malignancies are common in elderly.[24] Erythroderma in children is uncommon but challenging situation for its life threatening potentials. In infants and newborns infections, ichthyosiform erythroderma, atopic dermatitis, infantile seborrheic dermatitis are common cause.[25]In older children drug reaction is the commonest cause of erythroderma followed by psoriasis, genodermatoses, staphylococcal scalded skin syndrome.[25]Understanding the cause and the potential life threatening consequences is very important in the management erythroderma.

Bullous disease:

Bullous diseases are frightening conditions for patients bring them to emergency department. Some of autoimmune bullous diseases including bullous pemphigoid (BP), pemphigus vulgaris, pemphigus foliaceus and paraneoplastic pemphigus are really life threatening. These are mostly disease of elderly. Different types of hereditary epidermolysis

bullosa (EB) in children are very disabling and life threatening.

Mortality in dermatology:

It is common believe that skin diseases are not that fatal but those work in dermatology wards very often face of patients with different skin diseases. In an Indian study among admitted patients for dermatological problems yearly mortality rate was 3.58%. A prospective study on 309 patients of erythroderma in Brazil over 12 years 9.1% died due to complication of erythroderma. [27] Though overall mortality due to angioedema is very low (0.36 deaths per million population) it creates significant physical discomfort and psychological impact.[28]TEN is one of the most serious dermatological emergency 10%-70%patients of TEN died principally due to severe complications of multiple organ failure and disseminated infections.[29] Pemphigus vulgaris and TEN are the leading skin disease of death and most of the patients are elderly (61-70 years) involving large areas of skin, sepsis, pneumonia and fluid-electrolyte imbalance.[26] Mortality from pemphigus was dramatically reduced, from 75% to 30% after introduction of corticosteroids in the early 1950s and further use of adjuvant use of immunosuppressants in the 1980s probably contributed to the further decrease in mortality from the disease itself to below 5%.[30] Death rate for SSSS rate in children is 3% with timely appropriate treatment, more than 50% in elderly and nearly 100% in those with comorbidities, despite antibiotic treatment.[31] Mortality due to necrotizing fasciitis(NF) is alarmingly high, it is nearly 100% without surgical intervention.[32] Purpura fulminans is another grave condition with mortality rate up to 35% but recent advancement in the diagnosis and treatment have improved the survival.[33]

Pathogenesis:

Many serious skin diseases may impair structural and functional integrity of skin leads to different complications including infection, loss of fluid, electrolyte, protein and metabolic derangement. In TEN/SJS full-thickness epidermis of the skin and mucous membranes is sloughed. Involvement of eyes, gastrointestinal, genitourinary, and respiratory mucosa can cause grave situation like gastrointestinal bleeding, pulmonary embolism, myocardial infarction, pulmonary edema, and sepsis with multi-organ failure.[34] Like severe burn, diseases like SSSS, necrotizing fasciitis (NF), erythroderma, Stevens-Johnson syndrome or angioedema with dyspnea can be life-threatening. These situation can lead to a dangerous sequelae “Acute skin failure”.

The term “skin failure” is not much known like respiratory, cardiac or renal failure but in some situations skin fails to perform its function. Many dermatological conditions can disrupt the interconnecting structural and functional integrity of skin. This inability to maintain structural and functional integrity of skin to conserve core temperature, water, electrolyte and protein leading to fluid-electrolyte imbalance and failure of its barrier function to prevent entry of foreign substance.[35]

Staphylococcal scalded skin syndrome (SSSS) is initiated by the exfoliative (epidermolytic) toxins (ET-ETA and ETB) of Staphylococcus aureus. Both toxins act specifically in the stratum granulosum of the epidermis by attaching to the filaggrin which acts as intracellular anchors of desmosomes and ultimately causes epidermal splitting.[36]

In the deadly flesh-eating disease NF seeding of bacteria occurs into the deep tissue planes following penetrative injury or surgery and bacteria rapidly multiply within viable tissue. It may be either polymicrobial (mixture of aerobic and anaerobic organisms, Gram-positive organisms, such as Staphylococcus aureus, S pyogenes, and enterococci; Gram-negative aerobes, such as Escherichia coli and Pseudomonas species; and anaerobic organisms, such as Bacteroides or Clostridium species) or monomicrobial. Fibrous adherence between subcutaneous tissues and fasciae block extension of infection in the hands, feet, and scalp and absence of such attachments in the trunk, limbs, vessels favors spread of infection. Ultimately it causes widespread tissue destruction, edema, myositis, thrombosis, ischemia and gangrene.[32]

In purpura fulminans rapidly progressing cutaneous necrosis and disseminated intravascular coagulation occurs mostly in large vein vessels leading to widespread multiorgan failure.[33] Hereditary or acquired defect in protein C and /or protein S or other coagulation pathways, infection (Neisseria meningitides, Streptococcus pneumoniae, Group A and B streptococci, Haemophilus influenzae, Staphylococcus aureus, other bacteria, Plasmodium falciparum) and some unknown etiology are behind this disseminated intravascular coagulation.[33]

In erythroderma where most of the water conserving capacity of epidermis is hampered and transpeidermal water loss raised up to forty times than the normal. Body also loses protein, sodium, chloride

and potassium which leads to reduce intravascular volume, formation of hyperosmolar urine, low urinary output leads to renal failure. [37] Patients with toxic epidermal necrolysis and autoimmune bullous disorders have, in addition, extra loss of Na+, K+ and Cl- in the blister fluid. It also alters body metabolism enormously, cutaneous blood flow is raised and causes huge heat loss. Increased compensatory catabolic activity and basal metabolic rate lead to hypoalbuminemia and severe edema. Increased cutaneous blood flow nearby doubles the cardiac output and may contribute to high output cardiac failure.[37]

Suppression of insulin secretion and insulin resistance cause hyperglycemia and glycosuria, which cause amino acid breakdown leading to further worsening of hypercatabolic state and condition of the patient. Both external and internal environment favors the growth of different organism leads to bacteremia, sepsis and death. [37]

Patients with acute generalized pustular psoriasis may develop acute hypocalcemia secondary to severe hypoalbuminemia. The principal nutrients lost in acute skin failure are protein and iron. The main causes of hypoproteinemia are continuous loss through shed scales, increased BMR, decreased hepatic synthesis, dermatogenic enteropathy leading to protein loss (seen in fulminant psoriasis and other cases of chronic erythroderma), and dilution due to hypervolemia (which is not of much significance).[38] Aspiration pneumonitis, pulmonary edema (secondary to capillary leak syndrome) and adult respiratory distress syndrome (ARDS) are fatal respiratory complications.[39]

Evaluation of dermatological skin conditions: An emergency physician attending a patient with dermatological complain or work at dermatology ward should look for any feature suggesting life threatening condition that need emergency support. Prompt response is essential in such dangerous situation with abnormal pulse, pressure, temperature, respiration and level of consciousness. Suppose a patient with wheals may present with respiratory difficulties due to laryngeal edema and hypotension due to anaphylactic shock or a toxic looking patient presenting with petechiae, fever and disorientation deserve immediate vital rescue. One patient having history of taking medication like methotrexate and present with petechial rash warrant different line of intervention. So during evaluating an unknown skin condition search for some history, cutaneous and non-cutaneous signs are important. Important history and physical findings that can give a key sign for diagnosis of a skin disease needs emergency care (Table III and Table IV).

Table III: Important history and general examination features of dermatological emergency conditions.[40]

History and general findings	Diseases
Extreme age	Neonates or infants: Meningococcemia, Kawasaki disease, viral exanthema, Harlequin ichthyosis Old age: Pemphigus vulgaris, meningococcemia, toxic epidermal necrolysis, Stevens-Johnson syndrome, hypersensitivity syndrome, toxic shock syndrome
Toxic look	Necrotizing fasciitis, meningococcemia, toxic epidermal necrolysis, Stevens-Johnson syndrome, hypersensitivity syndrome, toxic shock syndrome, Rocky Mountain spotted fever
Altered mental status or confusion	Sepsis, hypo perfusion, and meningococcemia.
Severe itching	Urticaria, poison ivy, erythrodermic or pustular psoriasis, acute exacerbation of dermatitis
Rapidity of progression	Urticaria, poison ivy, erythrodermic or pustular psoriasis, acute exacerbation of dermatitis
Insect or bee infestation	
Recreational outdoor activity or travel history	travel history Dengue, malaria, hemorrhagic fever, Ebola, lyme disease, Rocky Mountain spotted fever

Past medical history	Patient of valvular heart disease or intravenous drug users may develop endocarditis which may present with cutaneous feature.
Drug	Table II (Mention in Table II)
Blood or blood product	Anaphylaxis, transfusion related acute graft versus host reaction.
Chemical	Hair dye and corrosive agents
ChemImmune statusical	Disseminated herpes zoster, meningococcemia, necrotizing fasciitis may develop in HIV cases, cancer chemo therapy, diabetic or other immune-compromised conditions.
Fever	Chicken pox, measles and other viral exanthem, sepsis, Rocky Mountain spotted fever, toxic shock syndrome, erythema multiforme, connective tissue disease, vasculitis, Kawasaki disease, Stevens-Johnson syndrome, toxic epidermal necrolysis
Lymphadenopathy	Sezare syndrome, drug reaction with different hypersensitive syndrome, leukemia cutis
Low blood pressure	Septicemia, toxic shock syndrome, meningococcemia, Rocky Mountain spotted fever, toxic epidermal necrolysis, Stevens-Johnson syndrome

Table IV: Skin presentations of life threatening skin diseases:[40]

Cutaneous signs	**Diseases**
Wheals	Urticaria, angioedema, anaphylaxis, Arthropod or insect bite, mastocytosis, drug reaction
Erythroderma	Pemphigus foliaceus, erythrodermic psoriasis, Atopic dermatitis, pityriasis rubra pilaris, Sézary syndrome
Pustules	Generalized pustular psoriasis, Acute generalized exanthematous pustulosis (AGEP), subcorneal pustular dermatosis of Sneddon and Wilkinson, Sweet syndrome, disseminated candidiasis, Herpes simplex virus, and Staphylococcus species.
Morbilliform eruption	Viral exanthems, drug reaction with eosinophilia and systemic symptoms (DRESS), Disseminated fungal infections Drug reactions Rickettsia Toxoplasmosis
Petechiae	Thrombocytopenia, leukemia, sepsis, meningococcemia, endocarditis, Malaria, Rocky Mountain spotted fever, Tick-borne illnesses, methotrexate poisoning
Vesicles	Pemphigus vulgaris, bullous pemphigoid, epidermolysis bullosa, neonatal herpes simplex virus, smallpox, vaccinia virus
Large denuded skin	Pemphigus vulgaris

Oral or mucosal or genital lesions	Erythema multiforme major, toxic epidermal necrolysis, Stevens-Johnson syndrome, pemphigus vulgaris
Hemorrhagic bullae	Meningococcemia
Violaceous, dusky discolorations, Ischemia of the digits and limb, Necrotizing and gangrenous area	Scleroderma, vasculitis (SLE, ANCA-related vasculitis, cryoglobulinemia, rheumatoid vasculitis, etc.), embolic diseases, necrotizing fasciitis.
Pain or tenderness of skin	Necrotizing fasciitis, cellulitis

Management:

This review is aimed to understand the burden of emergency situations in dermatology practice. It is crucial to timely diagnose the diseases which demands immediate appropriate intervention and seeking support from allied discipline or ICU. Continuous close monitoring of body temperature, heart rate, pulse rate, urine (volume, osmolarity, glucose), and input-output chart should be ensured. Arterial blood gas analysis (ABG), complete blood count (CBC), blood urea, creatinine, glucose, electrolytes, albumin, LFT, complete urine examination and chest radiograph are essential. In patients of severe bullous drug reactions, pemphigus vulgaris, erythroderma and acute skin failure loss of skin barrier function, metabolic and other organ functions are such grave that they need support like a patient of 100% burn patients. There are enough evidence that management of TEN-SJS patients in burn unit significantly improve the patient survival.[41]

Conclusion:

Many patients with dermatological conditions attend in emergency department or OPD for emergency care. Some are really need immediate lifesaving intervention. Many admitted patients in dermatology wards also sometimes progress to critical stage which can be prevented by timely assessment, management and appropriate referral. Certain acute conditions need management in intensive care unit. Though emergency situations in dermatology is less in dermatology comparing with other discipline but their existence is not negligible. Physicians working in emergency department must have some basic knowledge of this skin conditions and dermatologists should be well capable in managing such emergency cases both in OPD and wards. Dermatologists should be cautious and careful in diagnosis, management, timely intervention and referral in these emergency situations to prevent fatal consequences.

Conflicts of interest: No conflict of interest.

References:

1. Hay RJ, Johns NE, Williams HC et al. The global burden of skin disease in 2010: an analysis of the prevalence and impact of skin conditions. Invest Dermatol. 2014 Jun; 134(6):1527-1534.
2. Karimkhani C, Dellavalle RP, Coffeng LE et al. Global Skin Disease Morbidity and Mortality: An Update From the Global Burden of Disease Study 2013. JAMA Dermatol. 2017;153(5):406–412. doi:10.1001/jamadermatol.2016.5538
3. Nguyen SH, Nguyen LH, Vu GT et al. Health-Related Quality of Life Impairment among Patients with Different Skin Diseases in Vietnam: A Cross-Sectional Study Int. J. Environ. Res. Public Health 2019;16:305
4. Kini SP, DeLong LK, Veledar E et al. The impact of pruritus on quality of life: the skin equivalent of pain. Arch Dermatol 2011; 147(10): 1153–6.
5. Baibergenova A, Shear NH. Skin Conditions That Bring Patients to Emergency Departments. Arch Dermatol. 2011;147(1):118–120
6. Gupta S, Sandhu K, Kumar B. Evaluation of emergency dermatological consultations in a tertiary care centre in North India. J Eur Acad Dermatol Venereol. 2003;17:303-5.
7. Shivaram V, Christoph RA, Hayden GF. Skin disorders encountered in a pediatric emergency department. Pediatr Emerg Care. 1993;9(4):202-204.
8. Murr D, Bocquet H, Bachot N et al. Medical activity in a emergency outpatient department dermatology. Ann DermatolVenereol 2003; 130: 167–170,IndianJournal of Emergency Medicine 2018;4(3):147-153September2018
9. Isnard C, Ingen-Housz-Oro S, Fardet L et al. Dermato-

logical emergencies: evolution from 2008 to 2014 and perspectives. J Eur Acad Dermatol Venereol. 2017 Feb;31(2):274-279. doi: 10.1111/jdv.13860. Epub 2016 Sep 29. PMID: 27681584.
10. Ansorge C, Miocic JM, von Bubnoff D et al. Resources spent on dermatological emergency patients: A twelve-month prospective data collection from Germany. Journal of the German Society of Dermatology: JDDG. 2019 Oct;17(10):1018-1026. DOI: 10.1111/ddg.13922.
11. Lai-Kwon J, Weiland TJ, Chong AH et al. Which dermatological conditions present to an emergency department in australia? Emerg Med Int. 2014;2014:463026. doi: 10.1155/2014/463026.
12. Mitra D, Chopra A, Saraswat N et al. An Observational Study to Describe the Clinical Pattern of Dermatological Emergencies from Emergency Department and Intensive Care Unit: Our Experience from a Tertiary Care Hospital in Northern India. Indian Dermatol Online J. 2019;10(2):144-148. doi:10.4103/idoj.IDOJ_318_18
13. Baibergenova A, Shear N Skin Conditions That Bring Patients to Emergency Departments Archives of dermatology 147(1):118-20
14. Drago F, Gasparini G, Signori A et al. Dermatological consultations in an observation unit of an emergency department in Italy. J Eur Acad Dermatol Venereol 2015; 29: 973–980
15. Priyanka CP, Amit SM, Sejal HT et al. Dermatological emergencies: a prospective study in a tertiary care hospital, Gujarat, India . Int J Res Med. 2014; 3(4);90-95
16. Wang E, Lim BL, Than KY. Dermatological conditions presenting at an emergency department in Singapore. Singapore Med J. 2009 Sep;50(9):881-4. PMID: 19787176.
17. Kim J, Cho HH, Hong JS et al. Skin conditions presenting in emergency room in Korea: an eight-year retrospective analysis. J Eur Acad Dermatol Venereol.20132:49-8.
18. Powell RJ, Leech SC, Till S et al. British Society for Allergy and Clinical Immunology BSACI guideline for the management of chronic urticaria and angioedema. Clin Exp Allergy. 2015;45(3):547–565. doi: 10.1111/cea.12494.
19. Gaeta TJ, Clark S, Pelletier AJ et al. National study of US emergency department visits for acute allergic reactions, 1993 to 2004.Gaeta TJ, Clark S, Pelletier AJ, Camargo CA Ann Allergy Asthma Immunol. 2007 Apr; 98(4):360-5.
20. Pier J, Bingemann TA Urticaria, Angioedema, and Anaphylaxis. Pediatrics in Review Jun 2020, 41 (6) 283-292; DOI: 10.1542/pir.2019-0056
21. Nelson KM, Talbert RL. Drug-related hospital admissions. Pharmacotherapy. 1996;16:701–7.
22. Singh H, Kumar BN, Sinha T et al. The incidence and nature of drug-related hospital admission: A 6-month observational study in a tertiary health care hospital. J Pharmacol Pharmacother. 2011;2:17–20.
23. Sultana A, Bhuiyan MSI, Mahmud MM Pattern of Adverse Cutaneous Drug Reactions (ACDR) to Systemic Drugs. Urticaria, Angioedema, and Anaphylaxis 2019;47(3):32-36. https://doi.org/10.3329/bmj.v47i3.43496
24. Modi KR, Patel NM, Solanki A et al. Evaluation of Emergency Dermatological Conditions: A Prospective Study. Indian Journal of Emergency Medicine. 2018;4(3):147-152.
25. Sarkar R, Garg VK. Erythroderma in children. Indian J Dermatol Venereol Leprol. 2010 Jul-Aug;76(4):341-7. doi: 10.4103/0378-6323.66576. PMID: 20657113.
26. Nair PS, Moorthy PK, Yogiragan Y. A study of mortality in dermatology. Indian J Dermatol Venereol Leprol 2005;71:23-5.
27. Miyashiro, D., Sanches, J.A. Erythroderma: a prospective study of 309 patients followed for 12 years in a tertiary center. Sci Rep 10, 9774 (2020). https://doi.org/10.1038/s41598-020-66040-7
28. Crochet J, Lepelley M, Yahiaoui N et al. Bradykinin mechanism is the main responsible for death by isolated asphyxiating angioedema in France. Clin Exp Allergy. 2019; 49: 252-254.
29. Heng YK, Lee HY, Roujeau JC. Epidermal necrolysis: 60 years of errors and advances. Br J Dermatol. 2015;173:1250–1254
30. Carson PJ, Hameed A, Ahmed AR. Influence of treatment on the clinical course of pemphigus vulgaris. J Am Acad Dermatol 1996;34:645-52.
31. Gemell CG. Staphylococcal scalded skin syndrome. J Med Microbiol 1995;43:318–27
32. Puvanendran R, Huey JC, Pasupathy S. Necrotizing fasciitis. Can Fam Physician. 2009;55(10):981-987.
33. Urbaniak JR, O'Neil MT, Meyer LC. Purpura fulminans. J bone Joint Surg Am. 1973;55:69–77.
34. Abate MS, Battle LR, Emerson AN et al. Dermatologic Urgencies and Emergencies: What Every Pathologist Should Know. Arch Pathol Lab Med. 2019 Aug;143(8):919-942. doi: 10.5858/arpa.2018-0239-RA. Epub 2019 Feb 20. PMID: 30785787.
35. Irvine C. "Skin failure"- a real entity: discussion paper. J R Soc Med 1991;84:412-3.
36. Ladhani S, Evans RW Staphylococcal scalded skin syndrome. Arch Dis Child 1998;78:85–88
37. Sehgal VN, Srivastava G, Sardara K. Erythroderma/ Exfoliative dermatitis: a synopsis. Int J Dermatol. 2004 Jan;65(2):100–102.
38. Inamadar AC, Palit A. Acute skin failure: concept, causes, consequences and care. Indian J Dermatol

Venereol Leprol. 2005 Nov-Dec;71(6):379-85. doi: 10.4103/0378-6323.18007. PMID: 16394477.
39. Rothe MJ, Bialy TL, Grant-Kels JM. Erythroderma. Dermatol Clin 2000;18:405-15.
40. Nguyen T, Freedman J Dermatologic Emergencies: Diagnosing And Managing Life-Threatening Rashes. Emergency Medicine Practice. 2002;4(2):1-27.
41. Palmieri TL, Greenhalgh DG, Saffle JR et al. A multi-center review of toxic epidermal necrolysis treated in U.S. burn centers at the end of the twentieth century. J Burn Care Rehabil. 2002 Mar-Apr;23(2):87-96. doi: 10.1097/00004630-200203000-00004. PMID: 11882797.