Overview of exanthems: a case series in a tertiary care hospital

Ramesh A., Thamizhinian K.*

Department of Dermatology, Madras Medical College, Chennai, Tamil Nadu, India

Received: 21 February 2020
Revised: 11 June 2020
Accepted: 12 June 2020

*Correspondence:
Dr. Thamizhinian K.,
E-mail: kts.inian@gmail.com

ABSTRACT

Background: Generalized rashes are the most common conditions seen by primary care physician and the most common reason for new patient visit to dermatologists. There is often difficulty in diagnosing a generalized rash because many conditions produce similar rashes and a single condition can result in rashes with varied appearance. Accurate diagnosis is important because treatment varies depending on the cause. Hence, we decided to undertake a steady on the various presentations of exanthems in Madras medical college Chennai. To find out the incidence of exanthems in the OPD of Department of Dermatology, Venerology and Leprosy (DVL) in Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai to help in early diagnosis and treatment of the diseases.

Methods: The study included all the newly diagnosed cases attending to the OPD of DVL, Madras Medical College, Chennai for a period of three months. Diagnosis was done based on clinical grounds and lab investigations were done whenever required.

Results: An analytical study of the medical records of patients attending the OPD of DVL, Madras Medical College, Chennai shows that maculopapular rash is the most common presentation of exanthems followed by papules, vesiculobullous, pustular, nodules, verrucous lesions.

Conclusions: The present study includes exanthems as a whole on contrary to many such studies performed in other parts of India which included rashes caused by viral infections and drugs. Our study included generalized skin eruptions due to infections, drugs, specific dermatoses, allergy.

Keywords: Exanthems, Maculopapular rash, Papules, Nodules, Vesiculobullous

INTRODUCTION

Skin is the largest organ of the body. The pattern of skin diseases varies from one country to another country and within various regions of the same country.1 Most of the people with skin disorder will not visit a dermatologist unless they have symptoms like itching, pain or it is widespread.

An exanthem is a skin rash that may be associated with mucous membrane eruption, fever or other symptoms. Beside the ‘classical exanthems’ commonly occurring in childhood, other exanthems, defined as ‘atypical’ for the different morphology and causal agents, may occur. The atypical exanthem can be associated with fever or other constitutional symptoms and have an infectious or toxic or mixed etiology.2 We describe herein etiology and epidemiology of the exanthems caused by infectious agents, drugs, allergic skin eruptions, papulosquamous and vesiculobullous eruptions.

Generalized rashes are the most common condition seen by primary care physicians3 and the most common reason for new patient visit to dermatologists.4 Skin rashes in course varies ranging from infections, allergy, physical and chemical damage. It can range from simple insect
bite and scabies to various serious disorders like Steven Johnson syndrome. Distinguishing viral exanthems from other life-threatening diseases with similar cutaneous manifestations may be crucial. Hence early identification of skin disease is important for preventing life-threatening complications. The present study was planned to have an insight into the various presentations of skin rashes that appear in the outpatient department of a tertiary care hospital like Rajiv Gandhi Government General Hospital and Madras Medical College, Chennai to determine the prevalence of exanthems and to help in the early diagnosis and treatment of such conditions.

METHODS

This was an observational study carried out from June 1, 2019 to August 31, 2019 in the department of DVL, Madras Medical College, Chennai. All new patients with generalized skin eruptions who attended the OPD for skin problems during this period were included in the study. History and clinical examination were performed for each patient and diagnosis were made on clinical examination. Difficult cases were diagnosed by some basic investigations like KOH preparation for fungus, scabies, Tzank smear for bullous disorders, skin biopsy and histopathological examination. Individuals less than 18 years of age were considered as children while those above values were considered adults. The study was divided into four parts selection of the study population, history taking and data collection, clinical examination and relevant investigations and data analysis. Different patterns of skin rashes like maculopapular, papular, nodular, pustular, verrucous, vesiculobullous were noted and compared with data from different countries and different regions within the same country. Statistical analysis was conducted with SPSS Statistics 24.0 (IBM corporation, Armonk, NY).

RESULTS

For better visualization and understanding the results, the pattern of skin rashes has been shown in bar chart.

Sex distribution of exanthems

A total of 224 patients with exanthem who presented to the OPD of DVL, Madras medical college, Chennai. Out of those 38% were males, 49% were females and 13% were children (patients less than 18 years of age were included in children). This shows an increased incidence of exanthems in female patients compared to males with a difference of 11% (Figure 1).

Age distribution in exanthems

Out of the 224 patients studied, 24% of the patients belonged to age group 31-40 years followed by 21% in age group 21-30 years, 16% in age group 41-50 years, 14% in age group 11-20 years, 12% in age group 51-60 years, 8% in age group 61-70 years, 2% in age group 2-10 years, 2% in age group >70 years, 1% each in less than 2 months and 2 months to 2 years of age. This shows that most of the exanthematous eruptions occur in the age group 31-40 years (Figure 2).
disorder of childhood and other identified causes 10% like acrodermatitis enteropathica, dariers disease, hailey disease, grovers disease. Other un-identified causes included 4% of the patients studied. The pattern of skin rashes in the patients studied showed that nearly 60% of the patients had maculopapular rashes, 22% had papular eruptions, 11% had vesiculobullous eruptions, 3% had pustular eruptions, 2% had nodular eruptions, 2% had verrucous eruptions. Hence based on the distribution of exanthems infectious exanthems were the most common cause for generalized skin rashes and the most common presenting feature was maculopapular rashes (Figure 3).

**Figure 3: Diseases presenting as generalized rashes.**

**Figure 4: Most common causes for exanthems.**

**Figure 5: Most common presentation of exanthems.**

**DISCUSSION**

The word exanthem means a skin eruption that bursts forth or blooms. Exanthematous diseases are characterized by widespread, symmetric, erythematous, discrete or confluent macules and papules that initially do not form scales.\(^6\) It is one of the few diseases where maculopapular rash is an appropriate term. Diseases that begin with exanthems may be caused by bacteria, viruses or drugs. Atypical exanthem is an acute skin eruption that differs from classical viral exanthems like measles, rubella or erythema infectiosum. They are usually associated with nonspecific systemic symptoms like fever, arthralgia, malaise or upper respiratory tract infection or gastrointestinal tract infection. Most of the diseases have a number of characteristic features such as a common primary lesion, distribution, duration and systemic symptoms. Some are accompanied by oral lesions that are referred to as enanthems.\(^7\)

Viral exanthems present with generalized nonspecific rash characterized by the appearance of erythematous macules and papules described as maculopapular rash.\(^8\) They are caused by measles, rubella, rosetta infantum, erythema infectious, infectious mononucleosis, acute graft versus host disease, acute human immuno deficiency virus, echovirus, coxsackie virus, togavirus and others.\(^9\) Bacterial infections can also cause exanthems at times examples include meningococcemia, staphylococcal scalded skin syndrome, secondary syphilis etc. Infestations like scabies and other parasitic and helminthic infections can also cause widespread nonspecific skin eruptions. Fungal infections like tinea corporis can cause extensive dermatophytosis with erythematous papulosquamous eruptions that are often misdiagnosed and mistreated.\(^10\)

In our study the most common cause for exanthems were infectious exanthems due to bacterial, viral and fungal infections and infestations due to scabies which is in correlation with a study conducted by Kar et al based on pattern of skin diseases in a tertiary care institution in Kolkata followed by drug eruptions, allergic skin
eruptions due to insect bite allergy, urticaria etc., followed by specific dermatoses that include papulosquamous and vesiculobullous eruptions and other identified causes like grovers disease, hailey disease, dairers disease other unidentified causes that were included under miscellaneous eruptions as shown in Figure 4. The most common clinical presentation of exanthematos eruptions in our study was found to be maculopapular, papular, vesiculobullous, pustular, nodular, verrucous in decreasing order as shown in Figure 5.

**Infectious exanthems**

In our study the most common cause for exanthems were infectious exanthems contributing to 29% of all the exanthematos eruptions. The most common were maculopapular rash due to nonspecific viral exanthems, vesicular lesions due to chicken pox, verrucous lesions due to verruca vulgaris caused by HPV, maculopapular lesions due to HIV, papular lesions due to *Molluscum contagiosum* caused by *Poxvirus*, maculopapular eruptions due to secondary syphilis caused by *Treponema pallidum*, leprous caused by *M. leprae*, infestations like scabies caused by *Sarcoptes scabiei*. The most common cause for infectious exanthems were viral infections 64%, infestations 22%, bacterial infections 8% and fungal infections 6% which correlated with previous studies conducted in other parts of India. Infestation with scabies included a major bulk of patients in our study which was in correlation with study conducted by Kar et al and it indicates the economy, education and ignorance level of patients need to be improved as shown in Figure 6.

**Viral infections**

Viral exanthems both classic childhood and para-infectious exanthems occurring provoked by viral infections are described in both paediatric and adult population. Morbilliform rashes may signify causes due to both viral and drug induced rashes but the presence of petechiae and vesicles are highly suggestive of infection. The erythematous vesicular patterns are highly suggestive of viral infections whereas erythematopapular or pustular patterns are highly suggestive of drug reactions. The presence of exanthems on hands/feet, buttocks, face or a combination of these are more consistent with viral infection if drug reaction with eosinophilia and systemic symptoms is ruled out. Viral infections have five common clinical features which includes upper respiratory tract infection symptoms, infectious mononucleosis (fatigue, fever, lymphadenopathy, and pharyngitis), arthralgia/arthritis/myalgia, under immunized or unimmunized status; and acral/oral involvement.

Measles is characterized by a distinct prodromal phase with fever, rhinorrhea, cough, and conjunctival congestion. Koplik spots consisting of gray white sand-like lesions with surrounding erythema in the buccal mucosa opposite the lower second molar tooth are pathognomonic. Erythematous, confluent, maculopapular rash develops usually on the fourth day of fever, beginning behind the ears and forehead and progressing downward. The rash resolves in the same order with residual brownish discoloration and desquamation which fades over the next 10 days. The rash of rubella consists of minute, discrete macules, in contrast to the confluent rash of measles. The rash appears within 24 hours of onset prodromal symptoms, spreads rapidly from face to trunk and extremities and disappears altogether by the third day. Posterior cervical and postauricular lymphadenopathy, although not pathognomonic, is commonly seen. Roseola infantum is otherwise called as exanthema subitum. It usually begins with fever for 3-5 days initially which resolves around the time of onset of subitum, with the rash, a pink, short lived eruption. Adults have cervical lymphadenopathy, with variable rash and fever that may last for months. The rash usually starts on the trunk and spreads to the face and extremities. HHV 6 is the most frequent cause. Erythema infectiosum is otherwise called the fifth disease. Fever with characteristic slapped cheek appearance develops 2-4 days before the onset of generalized rash which begins on proximal extremities and spreads both centrally and peripherally. The disease is caused by parvovirus B19. HIV rash has an acute onset 1 to 6 weeks after infection and is usually accompanied by fever, malaise, virus seroconversion myalgias, arthralgias and lymphadenopathy. HIV seroconversion illness may be associated with a nonpruritic generalized maculopapular rash involving trunk, hands and feet sometimes associated with painful mucosal erosions. The characteristic exanthem of dengue fever is estimated to occur in 50% to 82% of patients with dengue fever. The initial rash involves a flushing erythema of the face, neck and chest that typically occurs within the first 24 to 48 hours of the onset of symptoms. The subsequent rash seen 3-5 days later is characterized by a generalized morbilliform eruption with petechiae and islands of sparing “white islands in a sea of red” and it’s thought to be an immune response to the virus. The most common exanthematos eruptions during childhood are caused by the enteroviruses echovirus and coxsackie virus. Lesions are erythematous maculopapules with areas of confluence, but they may be urticarial, vesicular or some items petechial. The palms and soles may be involved. Hand, foot and mouth disease is a contagious enteroviral infection occurring primarily in childhood and characterized by vesicular eruption and erosive stomatitis. It is often caused by coxsackievirus A16 and enterovirus 71. It can present with atypical perioral eruptions and skin manifestations that extend beyond the palmar and plantar surfaces. Pityriasis rosea is an acute self-limiting disorder primarily affecting children and young adults. HHV-6 and HHV-7 may play a part in some patients with PR, but other causative agents may exist. The exanthem in PR consists of discrete oval salmon colored papules and macules that may become
confluent. The eruption often begins with a single herald patch, a week or more before the other smaller lesions.  

**Bacterial infections**

Bacterial infections can sometimes cause widespread generalized rashes that can be difficult to differentiate from drug eruptions. Among bacterial infections, scarlet fever shows a typical systemic rash. Systemic rashes are also found in other bacterial infections, including leptospirosis, mycoplasma infection, secondary syphilis, disseminated gonococcal and meningococcal infections.  

Scarlet fever is caused by streptococcus beta hemolyticus and its exotoxins. With an incubation period of 1-5 days it presents with scarlet papules on the whole-body surface except inside of elbows and around mouth with hyperpigmentation in skin creases. Chills, fever, sore throat, strawberry tongue and desquamation after rash are other features.  

Toxic shock syndrome is a life-threatening illness caused by streptococcus pyogenes group A or staphylococcus aureus infection. The hallmarks of TSSs are high fever, myalgia, vomiting, diarrhea, headache and non-focal neurological abnormalities accompanying macular Erythroderma followed by desquamation, hypotension and multiple organ involvement. There will be erythema and Edema of palms and soles and scarlatiniform flexural accentuation of the rash with petechia haemorrhages, mucous membrane hyperaemia and strawberry tongue. They usually complicate the use of absorbent tampons, barrier contraceptives, surgical and postpartum wound infections, burns, cutaneous lesions, osteomyelitis and arthritis. Hematogenously disseminated gonococcal infection shows rapid progression resulting in papular rashes, petechiae, hemorrhagic folliculosis that appears mostly on the torso. Neisseria gonorrhea can be detected in the skin lesions. Rickettsioses are worldwide distributed zoonoses caused by obligate intracellular gram-negative bacteria which have marked tropism for endothelial cells of small vessels. After incubation period of 5-10 days patients complain of fever, chills, conjunctival injection, myalgia and headache followed 3 days later by a macular rash starting on the wrists and ankles as all not itchy pink lesions that become maculopapular with extension to extremities, buttocks, face and trunk. Eschars may be present. Case fatality is very high in untreated cases. In syphilis if the primary form is untreated, secondary syphilis may develop from 20-60 days after infection, resulting in an erythematous maculopapular rash with common palmoplantar involvement. There may be scarring alopecia, ulceration of mucous membranes and characteristic condyloma lata in the flexures. Systemic symptoms include fever, lethargy, myalgia and arthralgia. Lepromatous leprosy is characterized by multiple lepromatous macules that are smaller than those seen in tuberculoid leprosy. Lepromatous macules may have poorly defined borders and no loss of sensation. In addition to macules, nodules, papules or plaques can be seen.  

**Infestation**

In our study patients with scabies formed a major bulk contributing to 6.3% of all the exanthematous skin eruptions. Classical scabies in the adult presents as an intensely pruritic rash 3-4 weeks after infestation. In adults and older children, sites of predilection include the interdigital web spaces, wrists, anterior axillary folds, periumbilical skin, pelvic girdle including buttocks, ankles, the penis in males, and the periareolar region in females. In infants and small children, the palms, soles, face, neck, and scalp may also be involved. Patients typically complain that the pruritis is more intense at night. Two forms of skin eruption are typically observed that includes a erythematous papular or vesicular lesions that are associated with the burrows, and a more generalized papular pruritic eruption unrelated to obvious mite activity. In our study cimicosis was another major finding with 3.6% of patients of the total. Bedbug bites are known as cimicosis. Patient develops itch or a barely visible punctum. Other lesions are pruritic, usually painless, erythematous macules, papules, nodules, urticarial wheals, and blisters. Bullous rashes occurring days later may represent late-phase response of IgE-mediated hypersensitivity to salivary protein. Common sites are arms, shoulders, and legs.  

**Drug eruptions**

Drug eruptions account for 22% of all the exanthematous skin eruptions in our study becoming the second most common cause for exanthems next to infectious exanthems. This is in correlation with reports from previous studies. In everyday clinical practice, almost all physicians come across many instances of suspected adverse cutaneous drug reactions in different forms. Cutaneous reactions are the most common adverse effect of drugs. Adverse cutaneous reactions to drugs are frequent, affecting 2-3% of all hospitalized patients. Fortunately, only approximately 2% of adverse cutaneous reactions are severe and very few are fatal. The incidence of ACDR in developing countries such as India is found to be 2-5% of the in patients, however, there is a lack of comprehensive data amongst out-patients. The inadequacy of data could be attributed to reasons such as diagnostic dilemmas and lack of awareness to report. The most common cause of drug eruptions includes penicillins, cephalosporins, sulfonamides, allopurinol as well as anticonvulsant medications. Previous studies indicate that drug induced reactions are reported for nearly all prescription, usually at rates exceeding 10 cases per 1000 new users. Exanthematous drug eruptions, also known as maculopapular drug eruptions, are the most common cutaneous skin reactions and represent approximately 95% of all cutaneous drug eruptions. Exanthematous drug
eruptions usually begin within 1-2 weeks of starting a medication and gradually resolve 1-2 weeks following cessation. A study from North India also found maculopapular rash to be the most common type of ACDR which correlates with our study.29 The most common drugs related to adverse drug reactions are antibiotics like amoxicillin, chemotherapeutic drugs, antiplatelet drugs, diuretics, hydroxychloroquine, anticonvulsants, antidiabetic drugs, NSAIDs, Sulfone, radiographic contrast media, beta-2 agonists etc. the most common types of reactions are maculopapular eruptions, urticarial and fixed drug eruptions. Toxic epidermal necrolysis, erythema multiforme and fixed drug eruptions share similar pathologic features and are caused by many of the same drugs. Typical patient seen by a dermatologist is a hospitalized patient receiving several medications. Maculopapular rash usually occurs 7-10 days after the drug is first taken. They are generalized, symmetric and often pruritic. Erythema multiforme is caused by a hypersensitivity reaction due to sensitization by a drug (mostly sulfa drugs) and a source of infection (streptococcus, staphylococcus, mycoplasma, herpes simplex, and herpes zoster), and is accompanied by systemic symptoms, rashes with various patterns (including vesicular rashes), and fever. Mild forms of this disease result in rashes localized to the arms, hands, and feet, whereas severe forms (Stevens-Johnson syndrome) spread to the mouth, genitalia, and the mucocutaneous junction of the anus.

**Allergic skin eruptions**

In our study allergic skin eruptions contributed to 16% of all the exanthematous eruptions which are next to infectious and drug induced exanthems. The incidence of allergic skin eruptions in comparative to infections and drug induced eruptions has not been mentioned in any of the previous studies conducted in India. Allergic skin eruptions atopic dermatitis, contact dermatitis specifically to cement, insect bite allergy etc.

**Specific dermatoses**

Exanthematous eruptions due to specific dermatoses included papulosquamous and vesiculobullous eruptions. Papulosquamous eruptions included psoriasis, lichen planus, pityriasis rosea, pityriasis rubra pilaris.30 In our study specific dermatoses contributed to 16% of the total exanthematous eruptions only next to allergic skin eruptions. Out of that 16% papulosquamous eruptions included psoriasis 3.2%, PRP 0.5%, lichen planus 1.8%, extensive dermatophytosis 1.8%, mycosis fungoides 0.5%, guttate psoriasis 1.8% and vesiculobullous eruptions included Pemphigus vulgaris 3.2%, Bullous pemphigoid 2.3% and chronic bullous disorder of childhood 0.5%, grovers disease 0.5%. In psoriasis the lesions are distinctive that they begin as red scaling papules that coalesce to form round to oval plaques which can easily be distinguished from the surrounding normal skin. The scale is silvery white, adherent and reveals bleeding point when removed (Auspitz sign).31 Pityriasis rubra pilaris is a rare, chronic disease of unknown etiology. Classic adult PRP begins insidiously usually in the fifth or sixth decade of life with small, indolent, red scaling plaque on the face or upper body which slowly enlarges over days and weeks, palms and soles thicken and bright red orange follicular papules appear on the dorsum of proximal phalanges, elbows, knees and trunk.32 Lichen planus is a unique inflammatory cutaneous and mucous membrane reaction pattern of unknown etiology. The lesions are pruritic, planar, polygonal, purple papules. Close inspection of the surface shows a lacy, reticular pattern of crisscrossed whitish lines that can be accentuated by a drop of immersion oil called Wickhams striae. Rarely a line of papules may extend the length of the extremity. Vesicles or bullae may appear on preexisting lesions or on normal skin.33 The prototypic presentation of grover disease consists of a self-limited papulovesicular rash on the upper trunk. The rash begins as a sudden onset of small papules and fragile vesicles, which can quickly form crusts and keratotic erosions. The characteristic distribution of the lesions has them most commonly located along the trunk and proximal extremities. Some patients are asymptomatic, but most present with pruritis.34

The clinical presentation of *Mycosis fungoides* may be divided into classic, consistent, and atypical lesions. The classic morphology includes arcuate lesions, poikilodermatous patches, and plaques with atrophy; consistent lesions can present with erythema, papulosquamous lesions, alopecia, and hypopigmentation; atypical lesions include blisters, pustules, and digitate lesions. Classic locations include the face, buttocks, intertriginous areas, and breasts; consistent locations include the trunk and proximal extremities; atypical locations are the distal extremities, the palms or soles and a single lesion anywhere on the body. MF should be ruled out if a clinical eruption that is initially thought to be banal is refractory to treatment.35 Pemphigus vulgaris can manifest as a mucosal-dominant, mucocutaneous or, less frequently, solely cutaneous type. Lesions classically start in the oral mucosa and might then extend to the skin. Oral mucosa involvement consists of flaccid blisters that easily rupture, leaving painful erosions, especially in the buccal area. In addition to the oropharyngeal mucosa, other mucous membranes might be less frequently affected. Lesions of the skin, which frequently affect the head, upper trunk and groin, are characterized by flaccid blisters and partly crusted erosions on healthy-appearing or erythematous skin.36

In bullous pemphigoid the characteristic skin lesion is a large tense blister arising on erythematous base or on normal skin. These lesions are most common in the lower abdomen, inner or anterior thighs and flexor forearms. The bullae are usually filled with clear fluid but may be hemorrhagic. In some patients, blisters arise after persistent urticarial lesions, and in some, urticarial lesions

are the sole manifestations of the disease. Oral and ocular mucosal involvement rarely occurs. 37

Other identified diseases

Other identified conditions that presented with exanthematous skin eruptions in our study included Darier’s disease 0.5%, hailey disease 0.5%, Keratosis pilaris 0.5%, miliaria 6.4%, neurofibromatosis 0.9%, pigmented purpuric dermatosis 1.4% which contributed to approximately 10% of the total patients with exanthematous skin eruptions included in our study.

Other unidentified causes

Nearly 4% of the patients with exanthematous skin eruptions included in our study who did not fit in to any of the diagnostic criteria and treated symptomatically were included under miscellaneous or unidentified causes.

CONCLUSION

From our study it is evident that the most common cause for generalized exanthematous skin eruptions are due to infections out of which viral infections are the most common cause followed by bacterial infections, drugs, allergy, specific dermatoses and other identified and unidentified causes. The higher incidence of diseases like scabies indicate the economy and ignorance level of patients. It necessitates the importance of patient education in personal hygiene and preventive measures. The frequency of skin disorder is varying day by day and the pattern of skin rashes varies based on different factors. Hence it is necessary to have knowledge about the disease pattern and epidemiology for accurate diagnosis and earlier treatment and prevent life threatening complications.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee

Figure 7: (A) Generalized lichen planus, (B) atopic dermatitis, (C) psoriasis vulgaris, and (D) adverse drug reaction.

Figure 8: (A) Pityriasis rosea, (B) chronic bullous disorder of childhood, (C) scabies, and (D) miliaria pustulosa.

Figure 9: (A) Pemphigus vulgaris, (B) lepromatous leprosy, (C) molluscum contagiosum, (D) cutaneous amyloidosis, and (E) extensive dermatophytosis.

Figure 10: (A) Secondary syphilis, (B) acneiform eruptions, (C) verruca vulgaris, and (D) cimecosis.
REFERENCES
