A burst in the incidence of viral exanthsens

Carmen Maria Salavastru, Anca Mihaela Stanciu, Klaus Fritz, George Sorin Tiplica

ABSTRACT

Background: Vaccines have a major role in eradication programs of viral diseases. Vaccines against measles, rubella, and varicella are included in the vaccination schedules for children in most countries. Objective: A comparative analysis between 2011 and 2012 was performed to investigate if the number of patients with viral exanthems reported to our clinic in 2012 was increased. Materials and Methods: Patients were grouped in four categories: rubella, measles, varicella and other viral exanthems. Results: Between January and April 2011, there were registered 37 cases with viral exanthems: 69.5% presented with varicella and 30.5% with other viral exanthems. Between January and April 2012, there were 178 cases registered with viral eruption, of which 37% were of other viral exanthems, 35.4% rubella, 19.7% measles and 7.9% varicella. The highest incidence was seen in patients aged between 20 and 29 years (52.2%), with 21% having measles, 32.2% rubella, 9% varicella and 37.6% having other exanthems. In 2012, the number of cases of viral exanthems increased 5 times, with important outbreaks of new cases of measles and rubella. Conclusions: Although vaccines against measles and rubella were being used since 1979 and 1998 respectively, it was only in 2004, that these vaccines became part of the mandatory vaccination schedule. Although persons under 32 years should be protected against measles infection if they are previously vaccinated, more than 90% of the registered cases of measles occurred in such patients. The patients registered between January and April 2011 were mostly pediatric. Adults also were much more affected with measles, rubella, or varicella viruses in 2012 than in 2011.

Key words: Measles, Romania, rubella, vaccination, viral exanthems

INTRODUCTION

Viral exanthem is a widespread nonspecific rash usually characterized by a generalized eruption of erythematous papules and macules. In most of the cases, they are correlated with self-limited disease. However, in some cases, diagnosis of an exanthema may be crucial to preventing further spread of the disease.

Certain exanthems have distinct patterns of rashes and prodromal (prerash) symptoms which aid in incriminating the causative virus. In many cases, however, an accurate diagnosis cannot be made on the basis of clinical aspect alone. History may be helpful when evaluating these patients, specifically their disease contacts, immunization record, previous exanthematous illnesses and associated prodromal symptoms.

Some illnesses are seasonal, and this knowledge may be useful, too. Manifestation and morbidity of infections differ between the sexes and among different ages.

Measles or rubeola is a highly infectious disease with a worldwide distribution caused by an RNA paramyxovirus with a basic reproductive number of 15-20 (e.g. one case of measles will result in at least 15 new cases infection when introduced in a fully susceptible population).

Measles remains one of the leading causes of childhood mortality with more than 530,000 children worldwide dying from measles each year.

Vashishtha et al. show that in India, the median case fatality ratio of measles is 1.63% and cites a recent study that estimates that 80,000 Indian children die each year due to measles with it's complications amounting to 4% of under-five deaths.

Measles vaccine was used for the 1st time in 1963, in United States. First dose is administrated between 12 and 15 months, followed by the booster shot at the age of 7 years (first grade).

Live, attenuated measles vaccine are available either as monovalent vaccine or as
measles-containing vaccine (MCV) in combination with rubella or mumps vaccines.

In 1985 a routine MCV (MCV 1) was introduced in India’s Expanded Program on Immunization, with a recommended age for vaccination of 9-12 months. A second dose of measles vaccine (MCV 2) was recommended in the Indian states with >80% evaluated coverage for MCV 1. The MCV 2 was administered at the time of the DPT booster dose (at 16-24 months of age). For the Indian states with <80% evaluated coverage for MCV 1 a catch-up measles vaccination campaign was implemented for children aged 9 months to 10 years.[7]

Rubella, also called the German measles or 3 days measles, is an epidemic disease caused by an enveloped RNA togavirus.[10] The mechanism of infection is similar to measles.

Rubella vaccine was first introduced in 1969. At the moment, administration of the vaccine is the same as for measles vaccine as they are given in combination.

Varicella is caused by the varicella-zoster virus.[10] Varicella vaccine was developed in 1970, in Japan and started to be routinely used in Japan, Korea and afterwards, starting with 1995, in the United States. A tetravalent combination with measles, mumps, rubella (MMR) and varicella is available from 2005. First dose of the vaccine should be administrated between 12 and 15 months and the second dose between 4 and 6 years old, before kindergarten or first grade.

Adults and older children who have not had varicella can also be vaccinated, and the vaccine doses should be 4-8 weeks apart.

The effectiveness of the vaccine is 100% in prevention of moderate and severe disease and 85-90% in preventing varicella in general. The vaccine gives protection for at least 20 years. However, breakthrough infections can occur even in those who have been vaccinated.[11]

MATERIALS AND METHODS

At the beginning of 2012, an increased number of patients with viral exanthemas reported to our outpatient clinic; therefore, a comparative analysis between 2011 and 2012 was performed. The interval chosen was January to April, due to the higher incidence of the viral diseases during this period of the year. The search was made for all of the diagnosis of viral exanthemas. Patients were grouped in four categories: Rubella, measles, varicella, and viral exanthemas. The diagnosis for varicella, rubella and measles was made based on the presence of their clinical signs and evolution of the disease [Annex 1].[2,4,7,8,10,15] A clue for the diagnosis was the patient’s history of exposure to an infected contact. The generic name of viral exanthemas was used for all the other viral eruptions.

RESULTS

In 2011, between January and April, from the 3723 patient attending our clinic, 37 cases were registered with viral exanthemas (1%). Among them, 69.5% presented with varicella (26 cases) and 30.5% with miscellaneous types of viral exanthemas (11 cases). There were no cases of rubella or measles registered during this period. The patients were between 6 months and 64 years old, with an average age of 25.2 years. The patients suffering from varicella had an average age of 30.8 years (the youngest was 14 years old, and the oldest was 64 years old). Most of the varicella cases registered were aged between 10 and 19 years old (14 cases). For the other age groups, the distribution was even. Viral exanthemas patients were younger, having an average age of 12.5 years old [Figure 1a]. Viral exanthemas affected only patients aged between 6 months and 23 years old, each decade having an even distribution. Women outnumbered men in a ratio of 3:1. There were no significant difference between the rural and the urban area.

Between January and April 2012, of the 3402 patients who addressed our clinic, 178 were registered with viral eruption, of which 35.4% were diagnosed with rubella (63 cases), 19.7% with measles (35 cases), 7.9% with varicella (14 cases) and 37% being other types viral exanthemas (66 cases). Patients were aged between 4 months and 51 years old, with a mean age of 24.2 years, with no significant difference between the groups [Figure 1b]. The highest percentage of patients were aged between 20 and 29 years (52.2%). Of these, 21% were suffering from measles (20 cases), 32.2% from rubella (30 cases), 37.6% from other types of viral exanthemas (35 cases) and only 9% from varicella (eight cases). Other incidence peaks for rubella were registered between 10-19 years and 30-39 years: 13 and 17 cases respectively. The incidence of varicella was between 6 months and 64 years old, with an average age of 25.2 years. The patients suffering from varicella had an average age of 30.8 years (the youngest was 14 years old, and the oldest was 64 years old). Most of the varicella cases registered were aged between 10 and 19 years old (14 cases). For the other age groups, the distribution was even. Viral exanthemas patients were younger, having an average age of 12.5 years old [Figure 1a]. Viral exanthemas affected only patients aged between 6 months and 23 years old, each decade having an even distribution. Women outnumbered men in a ratio of 3:1. There were no significant difference between the rural and the urban area.

Between January and April 2012, of the 3402 patients who attended our clinic, 37 cases were registered with viral exanthemas (1%). Among them, 69.5% presented with varicella (26 cases) and 30.5% with miscellaneous types of viral exanthemas (11 cases). There were no cases of rubella or measles registered during this period. The patients were between 6 months and 64 years old, with an average age of 25.2 years. The patients suffering from varicella had an average age of 30.8 years (the youngest was 14 years old, and the oldest was 64 years old). Most of the varicella cases registered were aged between 10 and 19 years old (14 cases). For the other age groups, the distribution was even. Viral exanthemas patients were younger, having an average age of 12.5 years old [Figure 1a]. Viral exanthemas affected only patients aged between 6 months and 23 years old, each decade having an even distribution. Women outnumbered men in a ratio of 3:1. There were no significant difference between the rural and the urban area.

Figure 1: Number of cases registered between January and April 2011 (a) and 2012 (b) divided by age groups
a ratio of 2.5:1. The majority of the patients were coming from an urban area (82.7%).

**DISCUSSION**

Compared to 2011, in 2012, the number of cases of viral exanthemas was 5 times higher, especially due to the outbreak of new cases of measles and rubella.

In Romania, in 1979 anti-measles vaccination was first introduced, followed by the anti-rubella vaccination in 1998 (bivalent measles-rubella) that was administrated only to teenage girls. In 2004, anti-MMR vaccine was introduced in the mandatory vaccination schedule. Today, in Romania, children younger than 9 years should benefit from the immunization given by the vaccination against rubella. This aspect is reflected in the figures obtained; in 2012, wherein none of our patients affected by rubella infection was younger than 9 years. A potential risk of congenital rubella syndrome can occur if the infection affects pregnant women. In 2012, only a small number of women of childbearing age were registered (15 cases), with a male: female ratio of 3:1. The most recent rubella outbreak reported in Romania was at the end of 2011 in Salaj, in North-Western part of the country, with 1840 cases being registered. Among these, 98% were never vaccinated against rubella. The highest incidence was recorded in teenagers.

---

**Annex 1: Rubella, measles and varicella at a glance**

| Pathogenic agent | Rubella | Measles | Varicella |
|------------------|---------|---------|----------|
| At risk          | Togavirus | Preschool-age children who escaped vaccination; school-age children/adolescents in whom vaccination failed | Varicella-zoster virus, family *Herpesviridae* |
| Season           | Late winter/early spring | Late winter/spring | Young children, nonimmune individuals |
| Incubation period| 14-21 days | 8-12 days | Second attack rate within households is 80-95% |
| Infectious period| 5-7 days before rash to 3-5 days after the rash | 1-2 days before prodrome to 4 days after the onset of rash | Sporadic |
| Prodrome          | Children: absent to mild | Day 7-11 after exposure | 10-21 days |
|                  | Adolescents and adults: fever, malaise, sore throat, nausea, anorexia, painful occipital lymphadenopathy | Fever, cough, coryza, and conjunctivitis | Via respiratory droplets and vesicle fluid, 2 days before to 5 days after the onset of rash |
| Enanthem          | Forschheimer's spots=petechiae on the hard palate | Koplik’s spots appear 2 days before the rash, last 2 days into the rash | Ulcers may appear in the mouth, the top of the throat and the genital area |
| Exanthem          | Pinkred macules and papules on the face and spreads caudally over 24 h | Erythematous macules and papules appearing behind the ears and at the anterior hairline, coalescing, spreading over the neck and trunk distally, and finally affecting the upper and lower extremities including the hands and feet, with the entire body involved by day 3. The rash fades in order of appearance, and as it disappears, it becomes nonblanching and brownish-yellow | The rash begins as small red dots on the face, scalp, torso and upper arms and legs; progressing over 10-12 h to small bumps, blisters and pustules; followed by umbilication and the formation of scabs. Intense itch is usually present. Blisters may also occur on the palms and soles |
| Complications     | Arthralgias/arthritis in older patients | Otitis media | Secondary bacterial infection: 5-10% |
|                  | Peripheral neuritis, encephalitis, thrombocytopenic purpura – rare | Bronchopneumonia | Otitis media: 5% |
|                  | Congenital rubella syndrome | Encephalitis | Higher risk for adults, neonates, immunocomp |
|                  | Infection during the first trimester | Myocarditis | Pneumonitis |
|                  | IUGR, eye findings, deafness, cardiac defects, anemia, thrombocytopenia, skin nodules | Pericarditis | Encephalitis |
|                  | | Subacute sclerosing panencephalitis–late sequelae due to persistent infection of the CNS | Cerebellar ataxia |
|                  | | | Hepatitis |
| Treatment        | Supportive treatment | Supportive treatment | Other rare comps-Reye syndrome, Guillain-Barre, nephritis, carditis, arthritis, orchitis, uveitis |
|                  | | | Supportive treatment |
|                  | | | Oral acyclovir |
|                  | | | Immunoglobulin therapy |

IUGR: Intrauterine growth restriction, CNS: Central nervous system
Even if the vaccine against measles was first introduced in 1979, sporadic cases and minor epidemics still occur. Although persons under 32 years should be protected against measles infection due to the vaccine, more than 90% of the registered cases of measles occurred in patients that should have been immunized. This situation might have been caused by failure of parents to immunize their children and the failure of childhood immunization to protect some teenagers and adults.\[13,14\]

In addition, the introduction of measles vaccination in Europe in 1960s and 1970s fundamentally changed the epidemiology of the disease. The proportion of the population which must be immune in order for transmission to be stopped, called “critical proportion,” is not achieved because the vaccination coverage is low. As a consequence, population from countries where there is a sub-optimal vaccine uptake will experience outbreaks until, through catch-up vaccination campaigns; the number of immune people is kept above the “critical proportion.”\[5,13\]

Surveillance data report of measles monitoring in Europe, in 2011, mention Romania among the countries with the highest number of cases, next to Italy, German, Spain and France. In these five countries, more than 90% of all cases of measles from Europe were accounted for. In 2011, In 2011, Romania reported more than 4000 cases of measles.\[10\]

In Romania, like in most of the European countries, varicella vaccine is not on the mandatory vaccination list.

The patients affected by viral exanthemas between January and April 2011 are mostly pediatric patients. Most common causes of an erythematous viral exanthema in children are nonpolio Enteroviruses (coxackie viruses, echo viruses, Enteroviruses), respiratory viruses (adenoviruses, rhinoviruses, parainfluenza viruses, respiratory syncytial virus, influenza viruses), acute Epstein-Barr virus, human herpes viruses 6 and 7 and parvovirus B19.

In 2012, adults were more affected by exanthematous viral infections. Measles, rubella or varicella viruses were involved in 63% of the cases. In 37% of the cases, infective agents as parvovirus B19, Epstein-Barr virus, cytomegalovirus could be considered.

Measles and rubella elimination is a priority to World Health Organization/Europe. It is important that member states take appropriate action by sustaining high immunization coverage among children and to reduce susceptibility among older age groups. The regional goal is to eliminate measles and rubella by 2015.\[10\]

REFERENCES

1. Sarkar R, Mishra K, Garg VK. Fever with rash in a child in India. Indian J Dermatol Venereol Leprol 2012;78:251-62.
2. Scott LA, Stone MS. Viral exanthems. Dermatol Online J 2003;9:4.
3. Eshima N, Tokumaru O, Hara S, Bacal K, Koromatsu S, Karukaya S, et al. Age-specific sex-related differences in infections: A statistical analysis of national surveillance data in Japan. PLoS One 2012;7:e42261.
4. Belzarizian LT, Lorenzo ME, Pearlson AL, Sweeney SM, Wiss K. Chapter 192: Exanthematous Viral Diseases. In Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffell DJ, Wolff K, editors. Fitzpatrick’s Dermatology in General Medicine. 8th ed., Vol. 2. The McGraw Hill Co.; 2012. p. 2337-66.
5. European Centre for Disease Prevention and Control. European monthly measles monitoring (EMMO). Surveillance Report. Issue 8:21February, 2012. Available from: http://www.ecdc.europa.eu/en/publications/publications/sur_emmo_european-monthly-measles-monitoring-february-2012.pdf. [Last accessed on 2012 Dec 05].
6. Berggren KL, Tharp M, Boyer KM. Vaccine-associated “wild-type” measles. Pediatr Dermatol 2005;22:130-2.
7. Vashishtha VM, Choudhary P, Bansal CP, Gupta SG. Measles control strategies in India: Position paper of Indian Academy of Pediatrics. Indian Pediatr 2013;50:561-4.
8. Battagay R, Itin C, Itin P. Dermatological signs and symptoms of measles: A prospective case series and comparison with the literature. Dermatology 2012;224:1-4.
9. National Network of Immunization Information. Measles, Mumps, Rubella (MMR), 2012. Available from: http://www.immunizationinfo.org/vaccines/measles. [Last accessed on 2012 Dec 05].
10. Schmader KE, Oxman MN. Chapter 194: Varicella and Herpes Zoster. In Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffell DJ, Wolff K, editors. Fitzpatrick’s Dermatology in General Medicine. 8th ed., Vol. 2. The McGraw Hill Co.; 2012. p. 2383-401.
11. National Network of Immunization Information-Varicella, 2012. Available from: http://www.immunizationinfo.org/vaccines/varicella-chickenpox. [Last accessed on 2012 Dec 05].
12. Matei D. Vaccination program in Romania 2009. Rev Medica Rom 2009;56:303-8.
13. Janta D, Stanescu A, Lupulescu E, Molnar G, Pistol A. Ongoing rubella outbreak among adolescents in Salaj, Romania, September 2011–January 2012. Euro Surveill. 2012;17(7):pii=20089. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20089 [Last accessed on 2014 Feb 22].
14. Derrough T, Bacci S, Lopalco PL. Letter to the editor: Commitment needed for the prevention of congenital rubella syndrome in Europe. Euro Surveill. 2012;17(10):pii=20106. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20106 [Last accessed on 2014 Feb 22].
15. World Health Organization Regional Office for Europe. Eliminating measles and rubella and preventing congenital rubella infection, 2012. Available from: http://www.euro.who.int/en/what-we-do/health-topics/communicable-diseases/measles-and-rubella. [Last accessed on 2012 Dec 05].
16. Dhillion S, Curran MP. Live attenuated measles, mumps, rubella, and varicella zoster virus vaccine (Priorix-Tetra). Paediatr Drugs 2008;10:337-47.

Cite this article as: Salavastru CM, Staniciu AM, Fritz K, Tiplica GS. A burst in the incidence of viral exanthems. Indian Dermatol Online J 2014;5:144-7.

Source of Support: Nil, Conflict of Interest: None declared.