

SM Kadri¹*, Saleem-ur-Rehman², Kausar Rehana³ and Irini Gergianaki⁴

¹State Surveillance Officer, Communicable Diseases, Kashmir, India ²Director Health Services, Kashmir, India ³Epidemiologist in Department of Health Services, Kashmir, India ⁴University of Crete, Greece

*Corresponding Author: Kadri SM, State Surveillance officer, Communicable Diseases, Kashmir, India Division of epidemiology and public health, RFPTC Building, Barzulla, Srinagar 190005, Kashmir, India.

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Abstract

Backround: Varicella (chickenpox) is caused by varicella zoster virus (VZV). Epidemiological profile of chickenpox varies considerably across countries, healthcare systems and immunization policies. In India, chickenpox remains an important public health issue and outbreaks are not uncommon, since vaccination is not universal.

Aim: To examine the regional disease pattern of chicken pox infection in Kashmir region from 2013 to 2015, update the occurrence outbreak rates and compare for any alterations of epidemiological characteristics.

Methods: Surveillance data were collected weekly, as a part of the Integrated Disease Surveillance program, India. The clinical definition of cases was used for the surveillance rates and outbreaks. Chickenpox occurrence was analyzed in 12 districts for a period of 3 years (2013 - 2015) and trends were analyzed according to age, sex, residency and seasonality.

Results: Seven, six and seven Chickenpox outbreaks occurred in 2013, 2014 and 2015 in the Kashmir region each corresponding to 80, 97 and 129 total cases of varicella respectively. A hundred percent of outbreaks occurred in rural areas and there were no difference in occurrence among genders. A seasonal pattern was observed, with cases increasing during warm months. The average age of patients was ten (range 4-20) years. Notably all of the infected children were non immunized.

Conclusion: A programme of varicella vaccination can potentially change the epidemiology of varicella and limit its burden in childhood as well as its social and financial cost.

Keywords: Chickenpox; Surveillance; Outbreaks; India; Communicable Disease; India; Varicella Vaccine

Abbreviations

VZV: Varicella Zoster Virus; IDSP: Integrated Disease Surveillance Program

Introduction

Chicken pox (varicella) is the primary infection caused by Varicella Zoster Virus (VZV) and it predominantly affects children, with high-

est incidence in the 1-9 years old age group [1]. Varicella is a highly contagious disease with an attack rate of 62-100% [1]. In otherwise healthy children it is self-limiting, presenting with mild symptoms like a vesicular rash, fever and malaise [2]. Dangerous or even fatal complications like secondary bacterial infections can emerge (pneumonitis, arthritis, osteomyeltis, encephalitis, sepsis) [3,4] especially in neonates, immune compromised or elderly patients [1]. Varicella can be prevented by vaccination [1] which is safe and effective (in 80 - 85% against disease and in > 95% of cases in terms of preventing from serious complications) [2].

Although varicella occurs worldwide, there are differences in its epidemiology profile between various countries and especially between temperate and tropical regions. In pre-vaccination era, in temperate countries, like US and UK, more than 90% of people were affected before adolescence years [5]. On the contrary, in non developed tropical regions, chickenpox infection occurs at older ages [6,5]. Due to this later sero conversion in tropical countries more pregnant women are affected and this is of great concern because congenital varicella syndrome may occur. In addition, it is estimated that chickenpox is five times more likely to be fatal in pregnancy than in the nonpregnant adult [7]. Another difference is that temperate regions show predominance of varicella infection in the winter and early spring [5]. Less seasonality is reported in tropics. Outbreaks are periodic and usually represented by epidemic cycle of 2 - 5 years [8]. These differences are not fully explored. Among other factors the climate, the density of the population, rural vs urban [9], the existing risk of an individual to be infected and the characteristics of the virus can all play a role [5]. Nowadays, the main differences in epidemiology are due to the vaccination coverage system. In the countries that have adopted a universal vaccination system, the disease is rare in children [2,10], although mild breakthrough outbreaks [10] can occur.

In many parts of the world, Chicken pox can be better prevented. It is well established that although Varicella incidence rates are decreasing in countries that have implemented vaccination programs [11], this is not the case in the developing countries [12]. According to W.H.O, 4.2 million severe complications which require hospitalization and 4200 deaths attributed to varicella occur globally every year [5]. The age-standardized death ratio has declined from 3 per 100,000 in the pre vaccination era to 0,1 (CI 95% 0.0-0.7) in 100,000 in 2010, in high income countries [5] the remaining chicken pox burden should receive serious consideration because of health, social and economical costs [4]. In India, chicken Pox outbreaks are not uncommon [6]. The IDSP – Integrated Disease surveillance Program [13] compiles surveillance outbreak data from all states and Union Territories. Characteristically, 30% the outbreaks reported in last years Kashmir Region were Chicken Pox cases.

Our main objectives were

i) To describe the distribution and characteristics of Chicken pox infections in Kashmir region between 2013 -15 and compare it with other local and global trends, identifying any differences.

ii) To make specific recommendations for Chicken Pox prevention and control and discuss the policy issues related to the Varicella Vaccination for the region of Kashmir.

ii) To recognize areas of further in-depth studies that may emerge from this study.

Methods

Case Definition

For the purpose of this study, the clinical diagnosis was taken as the case definition a febrile illness with acute onset of diffuse-generalized maculo papulovesicular rash without other apparent cause [14]. Laboratory confirmation was not performed in consideration to the high cost and difficulty in access to appropriate tests. Outbreak was defined as \geq 5 varicella cases that are related in place and are epidemiologically linked [14].

Work Flow-Data Collection

The current data has been collected as weekly report in the continuous ongoing process as a part of Integrated disease surveillance

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181

program – India. It is collected by the surveillance program staff (PHC/ CHC / Doctor / ANM). Our surveillance programme can be characterized as active/passive. Each case was reported in a paper-specified format that includes basic demographic variables (age, gender, region), clinical details of the infected patient and vaccination status [14]. Data were entered in an electronic database that was designed for the surveillance purposes. Completeness of the data sets was high (> 97%). The surveillance system can be characterized adequate in terms of usability, providing the opportunity of quality-data (weekly/monthly/annually reports, incidence per region, demographic features) so that outbreaks were detected and controlled in time [15].

Statistical Analysis

The data were expressed as mean ± standard deviation (SD). Frequencies are expressed as percentages. All analysis was performed by using Statistical Package SPPS 22v.

Approval of the study

All patients and parents were fully informed for the scope of our investigation. The study was under the approval of the Directorate of Health Services, Kashmir, India.

Results

During a three-year period, from January, 2013 to December, 2015, in the Kashmir region we report an increasing rate of cases (eighty, ninty seven and a hundred twenty nine cases respectively in calendar years), corresponding to an increase rate of 24.1. The number of attacks were stable (seven, six and seven) as shown in Figure 1. Notably, during first months of 2016 (Jan-May) we had already 135 cases.

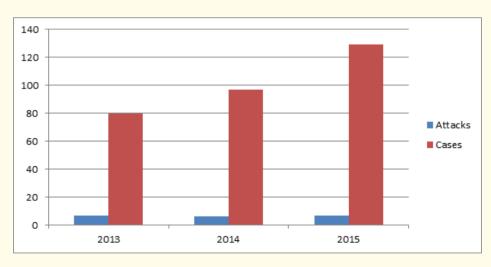
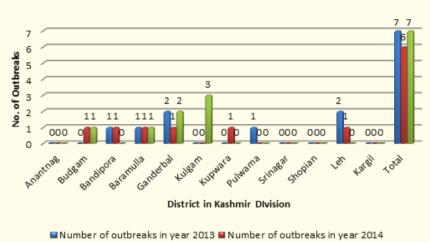


Figure 1: Total Number of Varicella Attacks and Cases during 2013-2015, Kashmir India.

Distribution of cases by age and residency

In 2013, the average age of people infected was 10 years old (range 4 - 20yrs). In 2014, the average age was 10 years old (range 4 - 20yrs) and in 2015 it was 15 years old (range 4-35yrs). All (100%) of outbreaks occurred in rural areas. Analyzing further the outbreak trends in relevance to the geographical area (Figure 2), we found that all outbreaks occurred in 8 out of the 12 districts under study. In

two of such areas (Baramulla and Ganderbal) there were one or more outbreaks every year during this three-year-period. The largest outbreak was reported in 2015 in Kulgam (69 cases out of 129 total in the whole study period) as shown in Figure 3.



Number of outbreaks in year 2015

Figure 2: Chicken Pox Oubreaks per geographical region in Kashmir, 2013-2015.

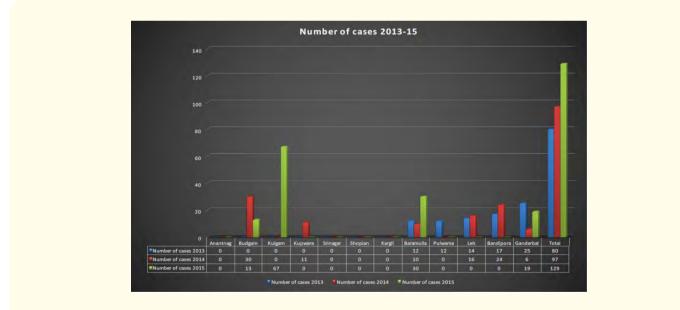


Figure 3: Number of VZV cases 2013-15 per region.

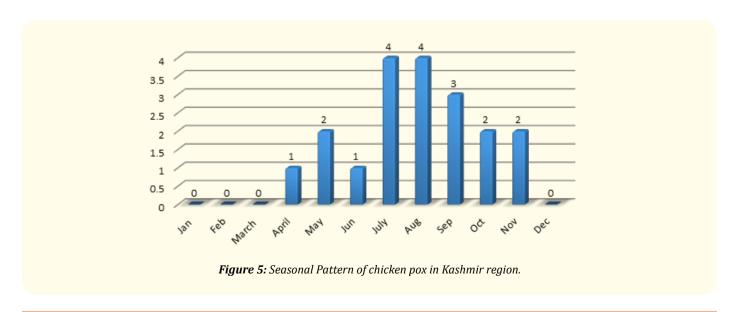
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District wise trends in Chicken pox District cases 2013-15 Anantnag Budgam Kulgam Kupwara Srinagar Shopian Kargil Baramulla Pulwama Leh Bandipora Ganderbal Total

As shown in Figure 4, we report that in one third of our study region there is an increasing trend in outbreaks.

Figure 4: VZV occurrence trends by region.

Interestingly, there is a clear seasonal pattern in VZV occurrence. In the year 2013, the peak months of outbreaks have been from May to July. In 2014, August and in 2015, it has been May, July and September. In total for the 3y-study period, there were no cases during the winter but a high peak in July and August and then plateaued during autumn months (Figure 5). Half of the total epidemics occurred during July-August-September.



184

Distribution Per Gender. No gender based difference is reported in 290 cases of the outbreaks (147 men vs 143 women) as shown in Figure 6. Only slight differences in various districts per calendar year.

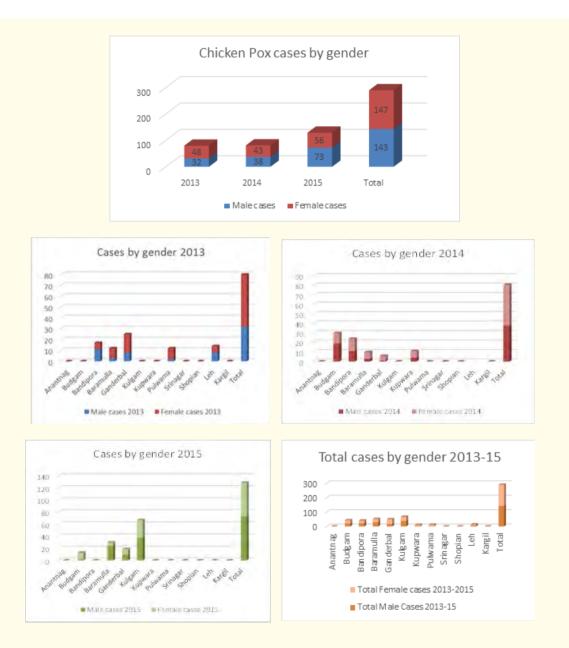


Figure 6: Male to Female ratio per year and per district in VZV patients.

Actions Taken

For every case of suspected varicella outbreak the Rapid Response Team visited school/village for further investigation (Figure 7). Upon confirmation, the patients were given treatment and the school was closed for a short period of about three days. Awareness was given to the people of affected village/ school regarding the way of transmission of VZV (Figure 8). Teachers and parents were educated

about the symptoms and were advised to isolate the affected cases in order to prevent clustering of cases and inhibit further transmission of disease and give the patients plenty of fluids and proper bed rest. Advice was given to follow proper cough etiquettes and hygienic hand washing to prevent spread of Chickenpox. There was a vigilance on the situation, camps were organised in the schools infected (Figure 1) and door-to-door education was performed, regarding the disease and its control.



Figure 7: Photos during the study of an outbreak in public school.



Figure 8: Educational Material (infographic) about Chickenpox Prevention.

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Discussion

In the present study, we report an increasing trend of chicken pox cases and ongoing outbreaks in Kashmir area, during a three year surveillance study period (2013-2015). The majority of the cases were otherwise healthy school-aged children from rural areas of the region. Both genders were equally affected and there was a seasonal pattern.

Chickenpox outbreaks in India are not uncommon [6,16]. In 2012, an outbreak was described in young trainee nurses (mean age 18.9) living in an institutional hostel who were vaccinated with a single dose [16]. Sinha et al reported chickenpox outbreaks which were observed every year from 1970 - 74 in a small West Bengal village and the cases occurred between March and June with a mean age of 23.4 years [39]. About twenty years later, in a varicella epidemic in rural southern India, an overall attack rate of 5.9% and 1% mortality was observed. In contrast to our study, the attack rate in susceptible children below eight years old was low, although families lived in small single room houses [40]. High infection rates in early adulthood show that population at these periods and regions had not encounter VZV during childhood. Comparing with these studies with our results we notice a slight shift to lower mean age in our region.

It appears that there is some seasonal variation in acute cases of varicella in India. In a number of studies, incidence was found to peak during the cooler times of the year while dropping off in the summer months. In a previous epidemic in Kerala White [41] it was found that most varicella cases are reported between January and February, the coolest months of the year [42]. A more recent outbreak in a rural community in North India highlights that epidemiological factors contributing could be ambient temperature in winter and people living in a naive community, in close proximity, which in turn leads to the rapid transmission of the virus. Other studies have found also a seasonality pattern but results are inconsistent among different districts regarding months that incidence peaks [17,6]. In addition, most studies describe no gender difference in sero positivity [1] and this agrees with our findings. Outbreaks with similar epidemiological profile was described in Iraq during the period 2007-2011 with > 65% of patients being in the age group of 5 - 14 [18].

As noted before all of the cases in the present studied were not immunized. In India, varicella vaccination has not yet been included in the national immunization schedule [19] and it is only available by private medical practitioners. The coverage percentage in our region is unknown. The crude herd rate for varicella [i.e the percentage of people in a population that is immune so that infection of susceptible people is prevented] is estimated to be 90% [20].

Although varicella vaccine is highly effective in reducing disease transmission and preventing the disease and its complications, vaccination policies and strategies regarding chickenpox vary considerably among countries [21,22]. USA was among the first to add varicella vaccine in the immunization schedule in 1996. This resulted in considerable decrease in mortality, especially in the age group 1 - 4 years and hospitalization rates [23,24,11]. Uruguay has also implemented the vaccine early in 1999 and after six years reported 81% decline in hospitalization due to varicella and more than 90% coverage percentage [11]. In Canada and Europe eight countries (Germany, Greece, Latvia and seven Italian regions are some of them) added the varicella immunization as a part of the national immunization schedule with high coverage [21,22]. Varicella vaccine is known to be effective and there is even more benefit from the second dose which gives lasting effect [25]. Parental refusal of vaccination sustains an emerging issue [26]. Discussion with a family doctor is associated with greater vaccination rates, indicating that specialist opinion influences the parental attitudes [27-29]. There is an ongoing research and discussion towards implementing the best strategy vaccination tailored to the needs of each county, with the trend towards universal, high sustained coverage as a cost-effective method [30-33]. Local monitor of coverage and robust disease surveillance is also highlighted in studies as an important issue as epidemiology of the virus can shift [34].

The US was also the first country also to adopt a universal routine two dose varicella vaccination program; other countries implemented universal 1-dose programs as a routine schedule. Several countries (e.g., China, Japan) have single dose recommendation for varicella vaccination, with vaccine available for private purchase. A characteristic comparison made by a recent study that report that of

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62% varicella vaccination coverage in Shandong area in China was higher than that of Bavaria, Germany (53% in 2008), where varicella immunization has been universally recommended and free of charge since 2004 [35]. In the same study urban children were more likely to have be vaccinated vs. rural children (72.1 vs. 59.6%, p < 0.001), as were those living within five kilometers of their designated immunization clinic (62.6 vs. 59.3%, p = 0.02). So there are many factors to play a role in the net result and any design of a health vaccination police should take into consideration [7,36,37].

A high proportion of unvaccinated case-patients suggest low vaccination coverage as a cause of the outbreak; a high proportion of vaccinated case-patients is suggestive of vaccine failure as a cause of the outbreak [38]. The varicella vaccine does not provide 100% protection; it is expected that cases will occur among vaccinated persons, although disease is generally milder than that in unvaccinated persons as has been observed in immunized case patients [43]. Immunization is probably of the most effective public health measures in childhood morbidity and mortality, caused by vaccine preventable diseases. However, outbreaks of vaccine preventable diseases continue to occur even in developed countries, and this may be attributed to unimmunized or under-immunized subpopulations despite high overall vaccination coverage. Several underlying factors for suboptimal vaccine uptake have been described, but are complex and present variablity among different countries, healthcare settings and individually groups. It is, therefore, essential to monitor vaccination coverage regularly and identify factors. in order to implement appropriate health policies.

As WHO concluded [44] before countries decide on the introduction of varicella vaccine into routine childhood immunization programmes, they should set up adequate disease surveillance to assess the varicella disease burden, with provision of continued surveillance after introduction of vaccination. SAGE recommended that routine childhood immunization against varicella could be considered in countries where the disease has an important public health impact and causes a substantial socio-economic burden. However, resources should be sufficient to ensure reaching and sustaining vaccine coverage $\geq 80\%$, as vaccine coverage of 20% – 80% would shift varicella to older ages with the risk of an associated increase of severe disease and mortality. Those countries deciding to introduce routine childhood varicella immunization, should administer vaccination at 12 – 18 months of age. The number of doses administered is dependent on the goal of the vaccination programme. One dose is sufficient to reduce mortality and severe morbidity from varicella. Two doses induce higher effectiveness and should therefore be recommended in countries where the programmatic goal is, in addition to decreasing severe disease, to further reduce the number of cases and outbreaks.

A programme of varicella vaccination can potentially change the epidemiology of varicella and limit its burden in childhood as well as its social and financial cost.

Conclusion

There are unmet needs regarding varicella prevention and control strategy in India. It is a high priority to identify unvaccinated individuals at risk and naive communities. Also, there is a need for regular training programmes of health workers so that highly contagious communicable diseases like varicella can be detected in time and such outbreaks can be prevented for further spread. Vaccination strategy should de revised in term of cost-effect and public health programs to support awareness of the disease and the immunization benefits.

Recommendations

Due to increasing in the number of cases of chicken pox it is recommended that:

- 1. Vaccination to be included in universal immunized programme.
- 2. Research is needed to further enlighten if any change in pattern of virus for which the affected population is not immunized.
- 3. Control of outbreaks of chicken pox among schools and education of the public, parents and students.

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Disclosures

No potential conflict of interest s disclosed.

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At District Level

- 1. Chief Medical Officers, Kashmir, India]
- 2. Medical Superintendents of all districts of Kashmir, India
- 3. District surveillance units [DSUs] of IDSP, Kashmir, India

At Divisional Level

- 1. Dr. Afshan Abdullah [State Epidemiologist IDSP]
- 2. Dr. Farooz Ahmad [State Microbiologist]
- 3. Mr. Imtiyaz Amin [State DM]
- 4. Ms Irfana Bhat [State DEO]

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