Epidemiologic and Clinical Features of Measles and Rubella in a Rural Area in China

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Background: Changes in the epidemiologic and clinical features of measles have resulted in diagnostic difficulties in distinguishing between measles and other rash and fever illnesses such as rubella. The objectives of this article are to report the true morbidity and epidemiologic and clinical features of measles and rubella, provide objective diagnostic indicators for distinguishing between the 2 diseases, and provide a time-efficient scientific basis for accurately evaluating the effectiveness of immunization with the measles vaccine and regulating the control strategies for measles in the rural areas of China in the cold chain era.

Methods: From 1992 to 2002, patients with measles and rubella were recorded and reported routinely in the rural disease surveillance spots of Jingzhou District, Hubei Province, by collecting their sera and testing for measles and rubella IgM and IgG antibodies.

Results: Over the 11-year study period, 146 cases of measles were reported in the disease surveillance spots. The annual incidence of measles was highest in 1999 (118.8/100,000 population). The incidence of measles in the 4–6 and 7–15 year old age groups were higher than in other age groups. During 5 outbreaks of measles, a total of 128 cases were reported, accounting for 87.7% of the total number of measles cases. A total of 566 rubella cases were reported, with 3 epidemic peaks (in 1992, 1997 and 2002). The incidence of rubella in the 4–6 and 7–15 year old age groups were higher than in other age groups. There were 13 outbreaks of rubella, with 547 cases being reported, accounting for 96.6% of the total number of rubella cases. Accuracy of the clinical diagnosis of measles was 40%, while it was 100% for rubella. The proportions of patients who had a moderate to high fever (≥ 38.6°C) in the measles group (89.5%) and the combined infection (both measles and rubella) group (90%) were significantly higher than that of the rubella group (30.6%). The proportions of patients whose prodromal stage lasted ≥ 3 days in the former 2 groups (68.4% and 95%, respectively) were significantly higher than that of the rubella group (16.7%). The proportions of patients whose exanthema lasted ≥ 4 days in the former 2 groups (78.9% and 75%, respectively) were significantly higher than that of the rubella group (26.9%).

Conclusion: Measles and rubella are 2 common communicable diseases in the children of Jingzhou District, with outbreaks being the main epidemic form. Some clinical features such as temperature, duration of the prodromal stage and exanthema are different in measles and rubella, and they can be useful in distinguishing between the 2 diseases. Accuracy in the clinical diagnosis of measles should be improved by enhancing serologic testing for measles and rubella, and by identifying patients' specific clinical characteristics. [*J Chin Med Assoc* 2005;68(12):571–577]

Key Words: clinical features, epidemiology, measles, rubella, surveillance

Introduction

Measles is one of the most common infectious diseases in children in developing countries. Before the measles vaccine was successfully introduced, nearly everyone worldwide contracted the disease by the age of 5 years,[1] with a fatality of 11–83.1% in children.[2]

An attenuated live measles vaccine was authorized for use in Jingzhou District, Hubei Province, China, in 1966. Between 1972 and 1978, the measles vaccine

was routinely used in children aged 8 months to 7 years in the winter or spring of each year. An expanded program of immunization was implemented in 1979, and a cold chain system was set up in 1984. Unpublished data show that the estimated coverage rate of the measles vaccine was only about 40% in 1-year-olds during the 1970s in Jingzhou District, but it rose gradually from 66% in 1984 to 68.6% in 1986, 66.4% in 1987 and 72.9% in 1990. The annual morbidity rate of measles in Jingzhou District was very high in the pre-vaccine era (3.4–1,429.6/100,000 population; mean, 498.1/100,000 population), but it decreased from a mean of 363.4/100,000 population (8.7–1,028.4/100,000 population) in 1972–1978 to 37.1/100,000 population (12.9–67/100,000 population) in the early phase (1979–1984) of the expanded program of immunization.[3] However, a large outbreak of measles, confirmed by serology, was reported in all the townships of Jingzhou District in the spring of 1991, with a high incidence of 254/100,000 population.[4] At the same time, the epidemiologic features and clinical symptoms of measles changed remarkably, resulting in diagnostic difficulty in distinguishing between measles and other rash and fever illnesses such as rubella.

We conducted a study, from 1992 to 2002, to investigate measles and rubella in the rural disease surveillance spots of Jingzhou District, Hubei Province, with the following objectives in mind: to study the true morbidity and epidemiologic and clinical features of measles and rubella in the cold chain era; to provide objective diagnostic indicators for distinguishing between the 2 diseases; and to provide a time-efficient scientific basis for accurately evaluating the effectiveness of immunization with the measles vaccine and regulating the control strategies for measles.

Methods

The surveillance of measles and rubella was conducted in the rural disease surveillance spots of Jingzhou District by the Hubei Center for Disease Prevention and Control. The surveillance was established in 1986, and includes 3 townships (59 villages) with an estimated population of 100,000. There are 3 township health centers and 56 village clinics in the surveillance spots, and about 80% of the village doctors have worked for more than 10 years. Evaluation of the quality of disease reporting is carried out in all 3 health centers and in 6–8 selected village clinics every year.

Data collection

From 1992 to 2002, in the rural disease surveillance spots, all clinically confirmed cases of measles and rubella were reported to the health centers and the anti-epidemic station of Jingzhou District by epidemiologic workers. The epidemiologic investigation for sporadic cases of measles or rubella was implemented by the health center doctors, while the survey of outbreak patients was commonly carried out by the epidemiologist of the anti-epidemic station and health center doctors. At the same time, a structured epidemiologic questionnaire was completed by the epidemiologic doctors, and patients' blood, collected in the acute and convalescent stages of the disease, was tested for measles and rubella IgM and IgG antibodies.

In this study, the case definitions of measles and rubella used were promulgated by the Ministry of Public Health, People's Republic of China.[5] Suspected measles was defined as fever (≥ 38°C) and cough or runny nose or red eyes (conjunctivitis), and a generalized red rash lasting ≥ 3 days, and a history of contact with a suspected measles case within 2 weeks before symptom onset. Clinical measles was defined as suspected measles and Koplik's spots found on physical examination. Confirmed measles was defined as suspected or clinical measles and a 4-fold or greater rise in IgG levels in the double blood test (or IgG titer ≥ 1:6,400 in single blood) and/or positive measles IgM antibody.

Suspected rubella was defined as fever (< 38°C), lymph node enlargement behind the ear and/or below the lower jaw, and a generalized or localized red rash appearing on the first or next day of illness and disappearing rapidly within 3 days. Clinical rubella was defined as suspected rubella and a history of contact with a suspected rubella case 2–3 weeks before symptom onset, and/or a history of immunization with measles vaccine, or a decrease in white blood cell count and an increase in lymphocyte count. Confirmed rubella was defined as suspected or clinical rubella and positive rubella IgM antibody.

An outbreak of measles or rubella was defined as the occurrence of ≥ 3 cases during an incubation period of 14 days in a village with obvious epidemiologic links to each other.

Serologic testing

Blood samples from patients with suspected measles were tested for IgM and IgG antibodies against the measles virus by enzyme immunoassay (EIA) in the anti-epidemic station (EIA test kits were provided by the Institute of Virology, Chinese Academy of Preventive Medicine). All sera, regardless of whether it was positive or negative for measles IgM and IgG,

were sent to the Institute of Virology, Hubei Academy of Medical Sciences to test for IgM against the rubella virus by EIA.

Patients who tested positive for measles IgM and/or had a 4-fold rise in IgG level in double blood were diagnosed as having measles. Patients who tested positive for rubella IgM were diagnosed as having rubella. Patients simultaneously positive for measles IgM and/or IgG antibodies and rubella IgM antibody were diagnosed as having a combined infection of measles and rubella.

Measles vaccine coverage rate

There were 7 investigations conducted on the coverage rate of the measles vaccine among children aged 12–24 months in the past 11 years by the anti-epidemic station of Jingzhou District. The probability proportional to size (PPS) method, recommended by the World Health Organization (WHO), was used.

Statistical analysis

The annual incidences of measles and rubella were calculated with the population of the surveillance spots (data from the Public Security Bureau, Jingzhou District) as the denominator. The populations used in calculating the age-specific incidences of measles and rubella for each age group over the whole observation period were estimated according to the proportions of specific age groups in the general population, which came from a population sampling survey of Jingzhou disease surveillance spots in 1991. The Chi-squared test was used to compare the incidence, ratio and clinical features of measles and rubella.

Results

Incidences of measles and rubella

From 1992 to 2002, a total of 146 measles cases (54 confirmed and 92 clinical measles cases) was reported in the surveillance spots. Measles cases were reported every year, except in 1998 and 2000 (Table 1). The annual incidences were significantly different ($\chi^2 = 11,772.64$; $p < 0.0001$). The incidence of measles was highest in 1999 (118.79/100,000 population), with lower incidences (1–10/100,000 population) in the other years.

A total of 566 rubella cases (88 confirmed and 478 clinical rubella cases) was reported. The annual incidences were also significantly different ($\chi^2 = 656.66$; $p < 0.0001$), and demonstrated approximately 3 epidemic peaks (65.8–107.7/100,000 population in 1992–1993; 94.8–173.7/100,000 population in 1997–1999; 71/100,000 population in 2002) at intervals of 2–3 years (Table 1).

Outbreak and sporadic cases

The surveillance results show that outbreaks were the main epidemic form of measles and rubella. Five outbreaks of measles (1 in 1995, 3 in 1999, 1 in 2001) comprising 128 cases were reported between 1992 and 2002, accounting for 87.7% of the total number of measles cases reported over this period. The measles outbreak in 1995 was the smallest one (4 cases), and the largest outbreak was in 1999 (79 cases). During the same period, 13 outbreaks of rubella comprising 547 cases were reported, accounting for 96.6% of the total number of rubella cases. The number of cases in

Table 1. Morbidity of measles and rubella and rate of measles vaccine coverage in the disease surveillance spots in 1992–2002

| Year | Population, n | Measles | | Rubella | | Immunization rate with measles vaccine, % |
		Cases, n*	Incidence (/100,000)	Cases, n*	Incidence (/100,000)	
1992	104,032	3	2.9	112	107.7	66.7
1993	104,849	2	1.9	69	65.8	–
1994	105,811	1	1.0	9	8.5	–
1995	103,510	7	6.8	10	9.7	–
1996	101,896	2	2.0	16	15.7	83.3
1997	101,341	1	1.0	176	173.7	83.3
1998	103,332	0	0.0	6	5.8	–
1999	100,176	119	118.8	95	94.8	87.1
2000	99,045	0	0.0	1	1.0	98.4
2001	100,545	10	10.0	2	2.0	85.7
2002	98,645	1	1.0	70	71.0	83.3

*The number of measles and rubella cases includes clinical and confirmed cases.

the smallest rubella outbreak was 4, while that in the largest outbreak was 133 (in 1997).

Two outbreaks were judged to be of combined infections of measles and rubella viruses, with a total of 195 cases. In these 2 combined outbreaks, it was roughly estimated, according to the positive rates of measles and rubella antibodies in the patients tested, that there were 112 measles patients and 96 rubella patients.

Seasonal distribution

The peak of the measles epidemic was May–July, that of rubella was April–June, and that of the combined infection was May–June, accounting for 67.7%, 87.1% and 86.2% of the total number of cases, respectively (Figure 1).
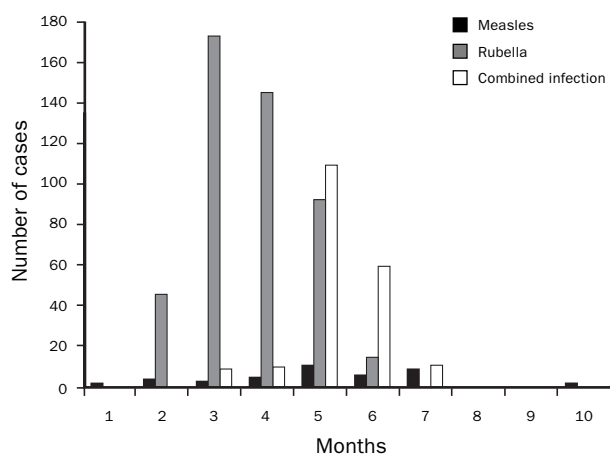
Figure 1. Distribution of measles, rubella and combined infection (measles and rubella) by month (1992–2002).

Age distribution

There was no obvious change in the age distribution of measles and rubella over the study period, and the annual incidences of the 2 diseases by age group were calculated by the accumulated cases in each age group divided by the accumulated population of the same age group. Table 2 shows that the incidences of measles among the age groups were significantly different ($\chi^2 = 419.12$; $p < 0.0001$), with peak incidences occurring in 3 age groups: < 8 months, 4–6 years and 7–15 years old. However, the ratio of measles cases in all age groups indicated that only the 4–6 and 7–15 year old age groups were the 2 peak age groups, accounting for 40.4% and 42.5% of the total number of cases, respectively. The number of measles patients in the ≥ 16 years old group was 20, accounting for 13.7% of the total number of cases.

The incidences of rubella among the age groups were also significantly different ($\chi^2 = 2,071.6$; $p < 0.0001$), with peak incidences occurring in 2 age groups: 4–6 years and 7–15 years old. The case ratios in these 2 groups were also higher than those of the other groups, accounting for 19.8% and 73.7% of the total number of cases, respectively (Table 2).

Measles attack rate and vaccine coverage rate

During 1992–2002, 7 investigations were conducted on the coverage rate of the measles vaccine among children aged 12–24 months. The coverage rate exceeded 83% except in 1992 when it was 66.7%. Except for the high incidence of measles in 1999 owing to a large measles outbreak, morbidities in the other years correlated with the coverage rate of the measles vaccine (Table 1).

Table 2. Incidence and ratio of measles and rubella among different age groups in 1992–2002

Age group	Accumulated population*	Measles			Rubella		
		Accumulated cases, $n^\dagger$	Annual incidence (/100,000)	Ratio (%)	Accumulated cases, $n^\dagger$	Annual incidence (/100,000)	Ratio (%)
< 8 mo	12,152	2	16.5	1.4	4	32.9	0.7
8 mo – 3 yr	58,798	3	5.1	2.1	20	34.0	3.5
4–6 yr	74,217	59	79.5	40.4	112	150.9	19.8
7–15 yr	151,047	62	41.1	42.5	417	276.1	73.7
16–20 yr	122,432	5	4.1	3.4	3	2.5	0.5
21–30 yr	257,929	10	3.9	6.9	10	3.9	1.8
≥ 31 yr	446,607	5	1.1	3.4	0	0.0	0.0
Total	1,123,182	146	13.0	100	566	50.4	100

*Accumulated population was estimated according to the proportion of population by age obtained from an investigation conducted in the disease surveillance spots in 1991; †accumulated number of measles and rubella cases includes clinical and confirmed cases.

Of the 75 measles cases investigated, 31 (41.3%) had received at least 1 dose of the measles vaccine, 40 (53.3%) did not have a clear history of vaccination, and 4 (5.3%) had not received vaccine.

Clinical features of measles and rubella

Analysis of the clinical features of 19 measles cases, 108 rubella cases, and 20 combined measles and rubella cases (all were students) showed that the proportions of patients who had a moderate to high fever (≥ 38.6°C) in the measles group (17, 89.5%) and the combined infection group (18, 90%) were significantly higher than that of the rubella group (33, 30.6%) (χ^2 = 30.86 and 32.51; all $p < 0.0001$). Upper respiratory tract symptoms were also more severe in the former 2 groups than in the rubella group.

The proportions of patients whose prodromal stage lasted ≥ 3 days in the measles and combined infection groups (13, 68.4% and 19, 95%, respectively) were significantly higher than that of the rubella group (18, 16.7%) (χ^2 = 23.46 and 50.39; all $p < 0.0001$), and that of the measles group was also higher than that of the combined infection group ($p = 0.035$).

The proportions of patients whose exanthema lasted ≥ 4 days in the measles (15, 78.9%) and combined infection (15, 75%) groups were significantly higher than that of the rubella group (29, 26.9%) (χ^2 = 19.37 and 17.3; all $p < 0.0001$).

The proportions of patients with pigmentation and branny or fine desquamation in the former 2 groups (12, 63.2% and 11, 55%, respectively) were also significantly higher than that of the rubella group (14, 13%) (χ^2 = 25.00 and 18.97; all $p < 0.0001$).

Clinical and laboratory diagnosis

A total of 8 measles outbreaks and 8 rubella outbreaks were reported during the study period; 5 and 2 outbreaks were tested for IgM and IgG antibodies of measles and rubella IgM, respectively, accounting for 43.8% of the total number of outbreaks.

Of the 5 suspected measles outbreaks tested, 2 were confirmed to be combined measles and rubella infections, and 3 were rubella infections; the clinical diagnostic accuracy rate for measles was 40%. The 2 rubella outbreaks tested were both confirmed to be rubella infections; the clinical diagnostic accuracy rate for rubella was 100%.

In the 2 outbreaks of combined infection, the blood samples of 99 patients were tested for measles IgM; the positive rate was 52.5% (52 patients). Of the 108 patients tested for rubella IgM, 49 tested positive – a positive rate of 45.4%. Of the 99 cases tested

simultaneously for measles and rubella IgM, 24 tested positive – a combined positive rate of 24.2%.

In 5 sporadic suspected measles cases with blood samples (1 patient had double samples), 1 tested positive for measles IgM, 1 had a 4-fold rise in measles IgG levels, 2 tested positive for rubella IgM, and 1 was negative. These results demonstrated a diagnostic accuracy rate for measles of 40% in the sporadic measles cases.

Discussion

From 1992 to 2002, we conducted 10 investigations into the reporting of all vested infectious diseases, including measles and rubella (unpublished data), and the results showed that in the health centers and clinics, the overall number of under-reported measles and rubella patients accounted for only 3.13% of the total number of cases found. This demonstrated that the number of cases is generally reported accurately, and reflects the incidence and the epidemic features of measles and rubella in the observed population.

At present, measles remains an important cause of death in children in developing countries, and the WHO estimated that there were 30–40 million measles cases and 777,000 deaths from measles worldwide in 2000, with similar numbers in 2001.[6,7] Our results also indicate that measles is still a common infectious disease in children younger than 15 years in Jingzhou District, with a high annual incidence. Measles accounted for 20.5% (146/712) of the total number of measles and rubella cases, which is significantly higher than the active surveillance results (2%) from Brazil in 1999.[7]

The following epidemiologic features of measles were demonstrated:

1. Annual mean incidence has significantly decreased by 71.8%, from 46.2/100,000 population in 1985–1991 to 13/100,000 population in 1992–2002.[2]

2. At present, outbreaks are the main epidemic pattern, accounting for 87.7% of cases. A significant reduction in incidence should be expected if the measles vaccine coverage rate is increased in rural areas.

3. There is a clear epidemic peak in spring and early summer, but it is later than in Henan and Sichuan provinces.[8,9]

4. Peak measles incidence occurs in children aged < 8 months and 4–15 years, similar to other reports.[8–10] A rise in incidence in children aged < 8 months indicates a declining trend of placental transmission of measles antibodies and should be watched closely.

In recent years, owing to the emphasis on enhancing basic immunization with measles vaccine and overlooking booster immunizations in 7-year-olds, students' immunity has gradually declined as a result of primary immune failure and natural disappearance of the antibody, and it could be an important cause of the high measles incidence during childhood.

5. Increased combined infection rate of measles and rubella. Similar incidents have also occurred in other provinces in China.[11] This could be related to the lack of specific measles and rubella antibodies in some students as a result of the abovementioned decline in measles immunity, a low vaccination rate (estimated 10%) with rubella vaccine, and the students being in close contact with each other in the school environment.

During the study period, serologic diagnosis was only performed in 7 of 16 measles and rubella outbreaks, and in 5 of 37 sporadic measles and rubella cases. The proportion of cases tested was very low, and that could have influenced the accuracy of disease diagnosis to a certain extent. The accuracy of clinical diagnosis was 40% and 100% for measles and rubella, respectively, indicating a high rate of wrong diagnosis for measles. Apart from the alleviation of the clinical symptoms of measles due to extensive injection of the measles vaccine, shortage of test reagents for measles in the health centers and a lack of clinical experience of the doctors were associated with a lower rate of accurate diagnosis for measles. This could have resulted in an overestimation of measles incidence and an underestimation of rubella incidence. However, there were only 29 undetected measles cases, including the outbreak (15 cases) and sporadic cases (14 cases), and about 17 measles cases could have been mistakenly diagnosed according to the wrong diagnosis rate of 60%. Thus, the corrected number of measles cases should be 129, and the actual annual incidence should be 11.5/100,000 population.

In recent years, a trend has emerged of measles symptoms being alleviated along with improvement in immunization with the measles vaccine, causing great difficulty in diagnosis and identification of measles and rubella. After analyzing the clinical data of some of the cases, we found that measles symptoms remain different from those of rubella (despite their severity having decreased) in the following 5 ways:

1. The respiratory tract manifestations of measles are more severe than those of rubella.
2. Most patients with measles have moderate to high fever ($\geq 38.6°C$), while most patients with rubella have low or no fever.
3. Most patients with measles have a prodromal stage that lasts ≥ 3 days, while the prodromal stage in most patients with rubella lasts only 1 day.
4. Exanthema in most measles patients lasts ≥ 4 days, while it lasts < 3 days in most rubella patients.
5. Pigmentation and branny or fine desquamation are found in 63% of measles cases, and in only 13% of rubella cases.

These clinical characteristics have also been reported by other authors.[12,13] A full understanding of these features will be beneficial for clinical diagnosis. With regard to the control and eradication of measles, strengthening serologic testing for measles, rubella and other viruses is very important for identifying rash and fever illnesses, as well as for understanding and analyzing the epidemic situation of measles so that precautionary measures can be improved.

Only a small number of children have undergone vaccination with the rubella vaccine since its introduction in 1999. These surveillance results demonstrate the epidemic characteristics of rubella in the rural population of Jingzhou District, and provide basic and important data for developing control strategies and evaluating the effectiveness of control measures for rubella in the future.

Acknowledgments

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