ORIGINAL ARTICLE

Retrospective Review of Serologic Rubella Activity in University Hospital Kuala Lumpur

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Summary

A retrospective review of rubella serological results carried out in the Virus Diagnostic Unit, University Hospital Kuala Lumpur (UHKL) from January 1993 to September 1999 showed the presence of rubella infection annually which appeared to increase periodically every two to three years. There was no statistical significant difference in the rubella positive rate between male and female population aged 14 to 48 years. Congenital rubella infections (CRI) occurred in babies delivered in UHKL yearly from 1993 to 1998 with an average incidence rate of 48 per 100,000 deliveries. Peaks of rubella cases appeared to be followed by an increase in incidence of CRI cases 6 to 9 months later.

The study showed that only 50.8% clinically diagnosed rubella was confirmed by laboratory finding. This study also showed an increase of rubella activity for the months of July, August and September 1999 and this may herald an increase of CRI cases in the coming millennium.

Key Words: Rubella, Congenital rubella infection

Introduction

Rubella, initially known as "German Measles", was recognised as a distinct disease by an International Congress of Medicine in London in 1881[1]. Its importance was not recognised until 1941 when it was noted to be an important cause of congenital defects by N. McAlister Gregg[2]. Subsequent retrospective studies in Australia as well as in other countries confirmed this finding[3,4] and these have been substantiated by many prospective and clinicopathological studies[5-12].

Live attenuated rubella virus vaccine was first available in 1969 and was first used in the United States of America under the Universal Rubella Vaccination Programme in an attempt to stop the transmission of virus and the occurrence of congenital rubella infection[1]. Five years after its introduction, the incidence of congenital infection had dropped dramatically[13] and there has been no report of endogenous congenital infection for the last 5 years in USA. The United Kingdom adopted the Selective Rubella Vaccination Programme since 1970 and despite its intensive vaccination programme, outbreaks of rubella infection with congenitally infected babies continued to occur[1]. By 1988, UK has switched over to the Universal Vaccination Programme as adopted by the U.S.A[1]. Similarly, Singapore started off with the Selective Rubella Vaccination Programme and subsequently switched over to the Universal Rubella Vaccination Programme by 1989 (personal communication).

In Malaysia, a study by Lam[14] in 1972 showed that the rubella antibody rate in the female population of childbearing age in Kuala Lumpur was about 50% which was lower than those reported from temperate

countries, though similar to rates found in other tropical countries excepting Singapore. Similar to vaccination practices in U.K., Malaysia adopted the Selective Rubella Vaccination Programme for primary six schoolgirls since early 1980s (personal communication). The incidence of rubella infection in Malaysia during the pre- and post-vaccination era was not known since it is not a notifiable disease. This retrospective study is an attempt to review the serologic rubella activity of patients suspected to be infected as well as babies born in the UHKL with congenital rubella infection.

Materials and Methods

The samples were from patients with the clinical diagnosis of rubella seen in the University Malaya Students' Health Clinic and University Hospital Outpatient Clinic and babies delivered in UHKL with the clinical features of intrauterine infection.

The clinical diagnosis of rubella was based on the provisional diagnosis of query rubella stated in the virological investigation request form. The definitive diagnosis of rubella infection was based on the laboratory evidence of specific anti-rubella IgM detected using a commercial ELISA kit (Radim, Italy). The procedure of carrying out the IgM-ELISA test on the clinical samples was based on the protocol provided with the commercial kit.

The diagnosis of congenital rubella infection was based on the detection of anti-rubella specific IgM from babies with the clinical diagnosis of intrauterine infection within 6 months of birth using the same commercial ELISA kit. The number of cases of congenital rubella infected babies for a particular month and year was taken as the month and year of birth of the infected babies and not on the month and year of the diagnosis made.

The statistical analysis of any significant association on the data set was based on Chi-square test and Student's t-test. The association between parameters was accepted as significant if the p-value was equal to or less than 0.05.

Results

A total of 132 patients (aged from 14 to 48 years) with provisional clinical diagnosis of rubella were submitted for serological confirmation from January 1993 to September 1999. Sixty-seven patients (50.8%) were confirmed to have rubella by the presence of anti-rubella specific IgM (Table I).

The data set in Table I was further analysed to determine whether the Selective Rubella Vaccination Programme introduced in 1980s had any effect on the positive rate of rubella between male and female populations aged 14 to 48 years old. The overall findings showed that there was no reduction in the number of positive rubella cases in the female population compared to that of male population (x^2=2.49, p=0.1). Analysis on a yearly basis also showed that there was no significant difference in the positive rate of rubella between the male and female as seen in 1993 (Fisher exact, p=1), 1994 (Fisher exact, P=1), 1995 (Fisher exact, p=1), 1996 (Fisher exact, p=0.68), 1997 (x^2=0.03, p=0.87), 1998 (Fisher exact, p=1) and 1999 (x^2=2.76, p=0.10).

Table I
Clinically Suspected and Serologically Confirmed Cases of Rubella Infection Aged 14 to 48 Years

Year	1993	1994	1995	1996	1997	1998	1999*	Total
Male	3 (1)#	9 (4)	6 (2)	11 (8)	13 (7)	5 (4)	16 (11)	63 (37)
Female	4 (1)	16 (6)	5 (2)	13 (8)	16 (8)	2 (1)	13 (4)	69 (30)
Total	7 (2)	25 (10)	11 (4)	24 (16)	29 (15)	7 (5)	29 (15)	132 (67)
% C.D.	28.6	40.0	36.4	66.7	51.7	71.4	51.7	50.8

* = *data only up to September*
\# = *bracket indicate cases with positive rubella IgM*
% C.D. = percentage of correct clinical diagnosis supported by positive serum IgM

Table II
Number of Serologically Confirmed Cases of Congenital Rubella Infection and Number of Deliveries per Year From 1993 to 1998, UHKL

Year	CRI	No. of Delivery	CRI per 100,000 Delivery
1993	2	6410	31
1994	6	6459	93
1995	4	6368	63
1996	2	6320	32
1997	3	6258	50
1998	1	5343	19
Total	18	37158	48

CRI = congenital rubella infected baby

During the study period, six females were serologically confirmed to have rubella in early pregnancies, one in 1993 (June), one in 1995 (October), two in 1996 (September, December), one in 1997 (October) and one in 1998 (December). The subsequent outcome of their pregnancies was unknown in this study.

Table II showed the number of babies delivered in UHKL with serologically confirmed congenital rubella infection (CRI) versus the annual total number of deliveries for each year from 1993 to 1998. There were cases of CRI noted annually over the study period though it fluctuated from as low as one per year to as high as six for the year 1994. Hence, the incidence rate of CRI in UHKL ranged from 19 to 93 per 100,000 deliveries with an average of 48 per 100,000 deliveries.

Figure 1 showed the monthly incidence of rubella cases and babies with CRI from January 1993 to September 1999. There appeared to be a periodic pattern of rubella activity with increased incidence of rubella cases at two and half to three year's interval. Peaks of rubella cases also appeared to be followed by increase occurrence of CRI cases 6 to 9 months later.

Discussion

In Malaysia, diagnosis of rubella infection is usually based on clinical features without laboratory

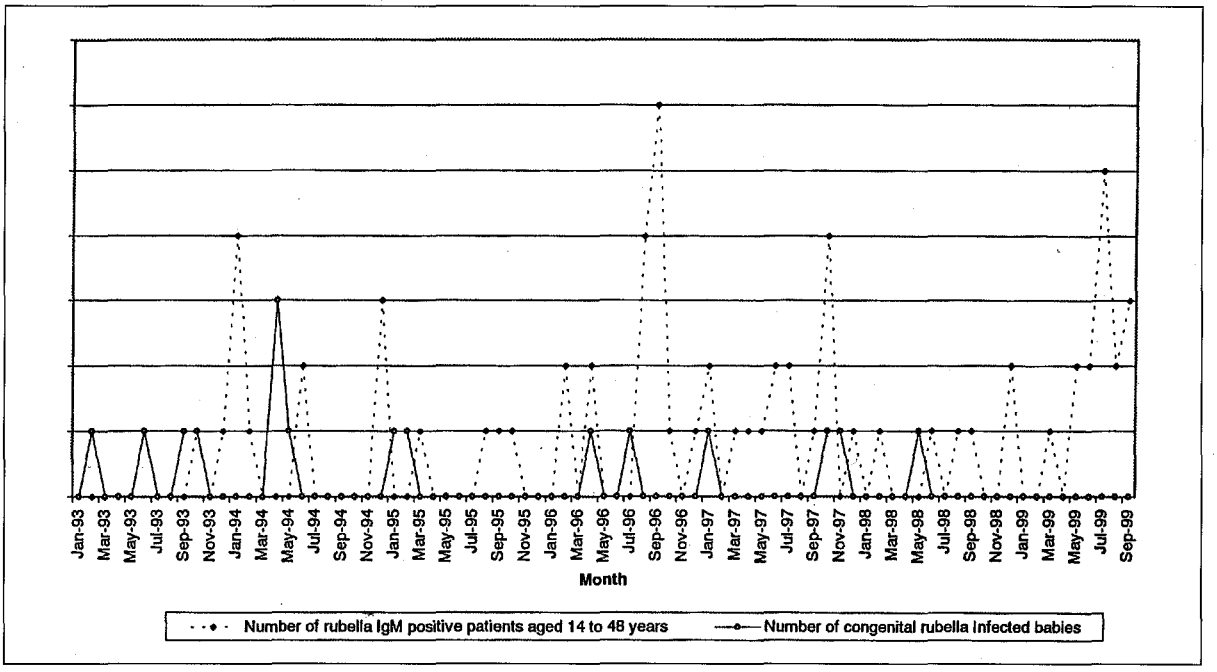

Fig. 1: Monthly incidence of rubella IgM positive cases and congenital rubella infected newborn babies from January 1993 to September 1999.

confirmation. From this limited study, it is evident that only about half of clinically diagnosed cases is supported by laboratory evidence and from 1993 to 1999, serologically confirmation ranged from a low of 28.6% in 1993 to 71.4% in 1998. It is therefore important that all clinically suspected cases of rubella should be submitted for laboratory confirmation.

Although this study is limited by the small sample size and the possibility of bias as it is based on the urban population, it does show that rubella is endemic in Malaysia and selective rubella vaccination programme did not seem to affect its transmission in the community. The vaccination programme also did not significantly reduce the positive rate of rubella in the female population, neither did it prevent the occurrence of congenital rubella infection. Moreover, the number of cases of CRI recorded in this study may be an underestimate of the actual problem as some cases of CRI may not be obvious enough to be detected during the neonatal period and infected pregnant mothers may have undergone termination of pregnancy. This study strongly suggests that the present selective rubella vaccination programme should be reviewed with a view to changing over to the universal programme as instituted in the U.S.A., U.K. and Singapore since it has been shown to be effective in breaking the transmission of rubella and prevent the occurrence of congenital rubella infection.

This retrospective study also indicates that there appeared to be an increase in rubella cases every two to three years followed by an increase number of cases of CRI 6 to 9 months later. However, as stated earlier, this study could also be biased by a sample size and a data set based on a single hospital. A proper prospective time series study based on both urban and rural populations needs to be carried out to ascertain the pattern of rubella activity and CRI in the country.

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