HK J Paediatr (new series) 2010;**15**:116-125

Hospitalisations for Varicella Among Children and Adolescents in a Tertiary Referral Hospital in Hong Kong, 2004 to 2008

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Abstract

Objective: To describe the epidemiology of varicella-associated morbidities in paediatric patients hospitalised at a tertiary referral hospital in Hong Kong from 2004 to 2008. ***Methods:*** The hospital discharge database and medical records of Princess Margaret Hospital were retrospectively analysed for admissions associated with varicella from 2004 to 2008. Patients aged less than 18 years were included in the study. ***Results:*** During the study period, 598 children (328 males, 270 females) were hospitalised for varicella or its complications. The mean age on admission was 57.6 months (range 1-204 months) and the mean duration of hospitalisation was 3.7 days (range 1-27 days). The overall complication rate was 47%. Skin and soft tissue infections were the most common complication (43.1%), followed by surgical scarlet fever (35.2%), neurological complications (18.1%) and pneumonia (8.2%). Compared to immunocompetent children, immunocompromised children were more likely to be older ($p < 0.001$) and hospitalised for longer periods ($p<0.001$), but had a lower complication rate (13.8% vs 48.7%) as a result of institution of specific antiviral therapy ($p<0.001$). Five patients required intensive care and two of them were immunocompromised. There was no mortality. ***Conclusion:*** Varicella can lead to serious complications and prolonged hospitalisation, even in previously healthy children. This study provides important information on the local epidemiology of children hospitalised for varicella in the era following the introduction of varicella vaccine.

Key words Chickenpox; Child; Complication; Epidemiology; Varicella

Introduction

Varicella, or chickenpox, accounts for significant morbidities despite the availability of a safe and efficacious live attenuated vaccine. Caused by the ubiquitous varicella-zoster virus (VZV), chickenpox used to be considered a relatively benign communicable disease of childhood.[1] However, serious complications including secondary bacterial skin and soft tissue infections, cerebellitis (acute cerebellar ataxia), encephalitis, pneumonia and coagulopathy can occur.[1,2] Hospitalisations due to chickenpox are considerable in developed countries, especially among children. An accurate estimate of chickenpox complications has not been clearly established, ranging from 40.7% to 83.3% of children hospitalised with the condition.[3-7] Furthermore, a mortality rate of 2-3 per 100,000 affected persons has been reported.[1] Therefore, varicella remains an important public health issue worldwide.

The epidemiology of varicella appears to vary among different geographic regions, climatic belts, population densities, and degrees of socioeconomic development.[8-10]

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Received October 20, 2009

In Hong Kong, detailed rates and characteristics of both complicated and uncomplicated chickenpox in children have not been clearly described.

A live attenuated varicella vaccine developed from the Oka strain of VZV was approved for administration to children in Japan in 1986.[11] A program of universal childhood vaccination against varicella has been introduced in the United States since 1995 with a resultant change of the epidemiology of varicella in the country.[12-15] However, in Hong Kong, there is no recommendation for universal vaccination against varicella in children, despite the availability of a safe and effective vaccine licensed since 1996.

The objective of our study was to investigate varicella-associated morbidities in hospitalised children in order to better inform the local epidemiology of varicella to facilitate consideration for varicella vaccination strategy in Hong Kong.

Methods

A retrospective study was conducted to analyse the clinical information of all children and adolescents aged below 18 years who were hospitalised for varicella at Princess Margaret Hospital, a tertiary referral hospital for paediatric infectious diseases, between 1 January 2004 and 31 December 2008. Since the clinical manifestation and course of illness of varicella is very typical, diagnosis was generally made clinically by experienced senior paediatricians in the infectious disease team during hospitalisation without the need for virological confirmation. Cases were identified by reviewing hospital discharge records retrieved using the relevant International Classification of Diseases 9th Edition (ICD-9) principal or secondary discharge diagnostic codes for varicella or chickenpox, as in other epidemiological studies.[2,3,16,17]

All medical records were reviewed by the lead investigator (YC Chan). When the recorded information appeared incomplete or dubious, further review of the written medical records was conducted by two senior investigators (YW Kwan and CW Leung) who were the senior paediatricians personally managing the patients throughout the years in the paediatric infectious disease team. Findings as recorded were clarified and differences in opinions, if any, were resolved by consensus. The whole medical record, including both the written and computerised components, was reviewed for every patient in the study. When formal reports of chest radiographs were not previously provided by radiologists in the records, the images were reviewed by at least 2 of the 3 investigators (YC Chan, YW Kwan and CW Leung) for cases with a discharge diagnosis of pneumonia. Agreement on the interpretation of radiological findings and final diagnosis of pneumonia were reached by consensus opinion.

The diagnosis of encephalitis was based on clinical features (decreased consciousness and seizure or focal neurologic deficit), cerebrospinal fluid (CSF) pleocytosis, electroencephalographic changes and neuroimaging findings.[18] Cerebellitis was diagnosed by clinical findings of ataxia and other cerebellar signs. Pneumonia was diagnosed if there was a combination of compatible clinical features (including fever, cough and increased work of breathing, with or without supplementary oxygen requirement) together with radiological evidence of pneumonia. It is well established that confirmation of the bacterial pathogen in childhood pneumonia is rather difficult and the specificity of a positive sputum culture is considered to be low for the diagnosis of bacterial pneumonia. In this study, probable bacterial pneumonia was defined as pneumonia with evidences suggestive of bacterial infection, including laboratory findings such as leukocytosis, neutrophila, markedly elevated C-reactive protein (CRP) or positive bacterial culture of one predominant organism from deep respiratory secretions (endotracheal aspirate or sputum collected by physiotherapists during chest physiotherapy); radiological evidence of bronchopneumonic infiltrates or lobar consolidation, without interstitial or reticulonodular pattern or residual calcifications or fibrosis on recovery which is in favour of primary varicella pneumonitis; as well as prompt clinical response to antibacterial therapy. Skin and soft tissue infections were diagnosed by clinical signs of focal infection of vesicular skin lesions, cellulitis, cutaneous or subcutaneous abscess, myositis or necrotising fasciitis. Surgical scarlet fever, a bacterial toxin syndrome clinically indistinguishable from classical scarlet fever, which is caused by exotoxin-producing streptococcal, and less commonly, staphylococcal, infection of the skin, soft tissues, wounds or burn, was diagnosed clinically by the detection of a generalised sandpaper-like scarlatiniform punctuate or macular erythema together with a strawberry tongue, Pastia's lines and evidence of focal infection of chickenpox skin lesions. Coagulopathy was diagnosed by clinical and laboratory evidence of disseminated intravascular coagulation or immune thrombocytopenic purpura.

Clinical information of immunocompromised patients

were collected and analysed separately in comparison to immunocompetent patients. The immunocompromising conditions included primary immunodeficiency, malignancy, treatment with chemotherapeutic or immunosuppressive agents, and organ transplantation.[3]

As chickenpox is a statutorily notifiable disease in Hong Kong, accurate notification figures for the year 2004 to 2008 were obtainable from the Surveillance and Epidemiology Branch, Centre for Health Protection (CHP) of the Department of Health to estimate the annual incidence rates for the general population and for children below 18 years of age. Mid-year population figures were obtained from the Census and Statistics Department of Hong Kong Government with the assistance of CHP. Hospitalisation figures for chickenpox were also requested from CHP in an attempt to estimate the annual hospitalisation rates. However, such figures were not available and only hospital attendance figures, including attendances to emergency departments and clinics of public and private hospitals could be provided. Hence, only annual hospital attendance rates for chickenpox could be ascertained, which were unlikely to approximate the actual annual hospitalisation rates as the number of individuals discharged after receiving treatment from emergency departments and hospital out-patient clinics could not be determined.

Statistical Analysis

Age of the patients (months) and length of hospitalisation (days) were expressed as means and ranges. Comparison among groups were performed using the chi-square or Fisher's exact test, where appropriate. Mann-Whitney test was used for non-normally distributed data. A p-value <0.05 was considered statistically significant. Data were analysed using SPSS software (version 16.0; SPSS Inc, Chicago, IL, USA).

Results

Annual incidence rates. The annual notification figures and estimated annual incidence rates of chickenpox in Hong Kong from 2004 to 2008 are shown in Table 1. Over the study period, 91.1% (59204/64999) of all chickenpox notifications belonged to the paediatric population aged below 18 years. The average annual chickenpox notification rate in individuals aged below 18 years was 981 per 100,000 paediatric population.

Annual hospital attendance rates. The annual notification figures and estimated hospital attendance rates (inclusive of public and private hospitals) for chickenpox in individuals aged below 18 years are shown in Table 2. The average annual hospital attendance rate in individuals aged below 18 years was 285.8 per 100,000 paediatric population. Therefore, an average of 29.1% of all notified paediatric cases of chickenpox had attended either public or private hospitals for treatment during the study period.

Hospitalisation figures for current study. 598 hospital records with discharge diagnostic coding for varicella or chickenpox were identified and analysed in this study. This accounted for 3.5% (598/17288) of all paediatric cases of chickenpox attending to either public or private hospital during the study period. The annual varicella-associated

Table 1 Chickenpox notification figures, mid-year population, and estimated annual incidence rates for chickenpox in Hong Kong, 2004-2008

Year	No. of chickenpox notification*		Mid-year population#		Estimated annual incidence rate for chickenpox (per 100,000 persons)	
	Individuals aged <18	All ages	Individuals aged <18	All ages	Individuals aged <18	All ages
2004	10742	11784	1264395	6783468	849.6	173.7
2005	10911	11933	1231952	6813191	885.7	175.1
2006	13299	14415	1204080	6857140	1104.5	210.2
2007	16382	17940	1180924	6925889	1387.2	259.0
2008	7870	8927	1160368	6977745	678.2	127.9

* Data source from Centre for Health Protection, Department of Health, Government of Hong Kong SAR

\# Data source from Census and Statistics Department, Government of Hong Kong SAR

Table 2 Chickenpox notification figures and estimated annual hospital attendance rates of chickenpox for individuals aged below 18 years in Hong Kong, 2004-2008

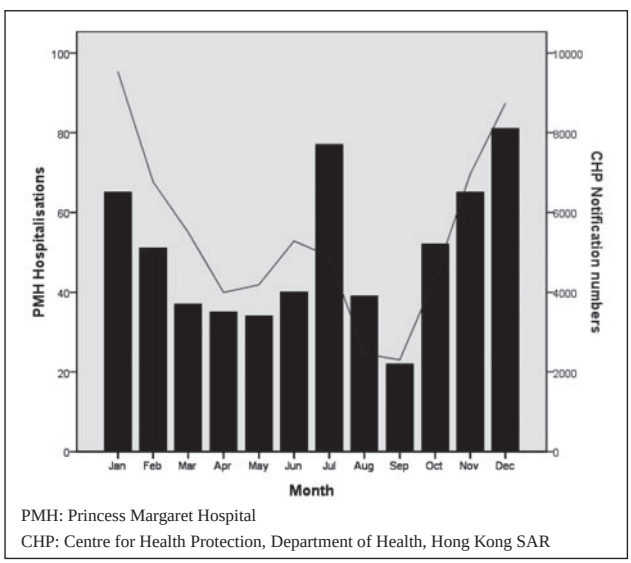
Year	No. of individuals <18 yr attending public and private hospitals for chickenpox* (%)	No. of chickenpox notification for individuals <18 yr#	Estimated annual hospital attendance rate for individuals <18 yr (per 100,000 persons)
2004	3598 (33.5%)	10742	284.6
2005	3522 (32.3%)	10911	285.9
2006	3600 (27.1%)	13299	299.0
2007	4198 (25.6%)	16382	355.5
2008	2370 (30.1%)	7870	204.2

* Reported by emergency departments and other units of public and private hospitals

Reported from all sources

hospitalisation figures from 2004 to 2008 were 83, 110, 135, 156 and 114, respectively. The monthly distribution of varicella-associated hospitalisations for our hospital and that for all cases notified in Hong Kong are shown in Figure 1. A bimodal distribution of cases was observed, with hospitalisations and disease incidences showing similar peaking in the winter months of December and January, and a lesser peak in the summer months of June and July.

Demographic features. For all years combined there were a total of 328 male (54.8%) and 270 female (45.2%) patients hospitalised for varicella, with a slight male predominance at a ratio of 1.2 to 1. Their mean age was 57.6 months (range 1-204 months). Sixty-four patients (10.7%) were aged 6 months or under, 335 (56.0%) were aged 7 months to 5 years, 126 (21.1%) were aged above 5 years to 10 years, and 73 (12.2%) were aged above 10 years. Immunocompromised patients were significantly older, with a mean age of 89.6 months (range 18-204 months) as compared to 56.1 months (range 1-204 months) for immunocompetent patients ($p<0.001$). They were hospitalised earlier in the course of their illness than those who were immunocompetent. The mean time from onset of fever to hospital admission was 1.2 days (range 0-5 days) and 2.1 days (range 0-9 days) for immuncompromised and immunocompetent patients, respectively ($p=0.003$). The mean time from onset of rash to hospital admission for immunocompromised and immunocompetent patients were 2.4 days (range 1-6 days) and 3.8 days (range 1-15 days), respectively ($p=0.001$).



PMH: Princess Margaret Hospital

CHP: Centre for Health Protection, Department of Health, Hong Kong SAR

Figure 1 Comparison of monthly distribution of chickenpox-associated paediatric hospitalisations at Princess Margaret Hospital and monthly chickenpox notifications for all ages in Hong Kong, 2004-2008.

Length of hospitalisation. The overall mean length of hospitalisation was 3.7 days (range 1-27 days). It was noted that the length of hospitalisation was significantly longer in patients with complicated varicella compared to those without complications, with a mean of 4.3 days (range 1-24 days) vs 3.1 days (range 1-27 days), respectively ($p<0.001$). The length of hospitalisation was also significantly longer in immunocompromised patients compared to those who are immunocompetent, with a mean of 6.6 days (range 1-18 days) vs 3.5 days (median 3 days, range 1-27 days), respectively ($p<0.001$). The duration of hospitalisation was relatively long for some uncomplicated cases because they required additional treatment for some other underlying chronic diseases or medical/surgical conditions coincidental with their chickenpox infection. Some cases also required

prolonged isolation as a means of prevention and control of institutional/hospital outbreaks of varicella.

Underlying conditions. Majority of the hospitalised patients were previously healthy. Only 29 out of 598 (4.8%) children were immunocompromised. They were receiving immunosuppressive therapy (including 11 patients with nephropathy, 2 patients with systemic lupus erythematosus, 1 patient with myasthenia gravis, 1 patient with pure red cell aplasia and 1 patient with liver transplant); or cancer chemotherapy (including 9 patients with acute lymphocytic leukaemia, 1 patient with chronic myeloid leukaemia and 2 patients with solid tumours); or suffering from primary immunodeficiency (including 1 patient with congenital asplenia). All immunocompromised children received intravenous acyclovir therapy for varicella right after admission.

Complications of varicella. 281 out of 598 (47%) patients developed complications of varicella (Table 3). Among all complications, skin and soft tissue infections were the most common and found in 121 (43.1%) patients who developed complicated varicella. Mild cases of skin and soft tissue infections were empirically treated with antibiotics targeting the two most likely causative organisms, *Staphylococcus aureus* and *Streptococcus pyogenes*, without the need for further laboratory evaluation to confirm the bacterial aetiology as they invariably responded readily to treatment. In severe cases, attempts were always made to recover the bacterial pathogens through appropriate microbiological investigations of pus, body fluids or tissues. Again, *Staphylococcus aureus* and *Streptococcus pyogenes* were the culprits identified. Ninety-nine patients (35.2%) had surgical scarlet fever which responded readily to empirical antibiotic treatment targeting *Staphylococcus aureus* and *Streptococcus pyogenes*. Neurological complications were observed in 51 patients (18.1%), including 1 case of encephalitis, 1 case of aseptic meningitis, 4 cases of cerebellitis, 5 cases of afebrile seizure and 40 cases of febrile seizure. The patient with encephalitis had electroencephalographic features suggestive of viral encephalitis but normal cranial computed tomography (CT) findings, while the CSF investigations were negative for both bacteria and viruses. The patient with aseptic meningitis had CSF pleocytosis and biochemistry suggestive of viral meningitis. VZV antibody titre of the CSF was elevated, while cranial CT examination was normal. Among the 4 patients with cerebellitis, only two had lumbar puncture performed and both CSF examinations were negative for bacteria and viruses. All of them had normal cranial CT findings. Probable bacterial pneumonia was identified in 23 patients based on suggestive findings

Table 3 Spectrum of complications in children hospitalised for chickenpox at Princess Margaret Hospital, 2004-2008

	No. (%)* **(n=281)**
Skin and soft tissue infections	**121 (43.1%)**
• focal infection of chickenpox lesions	99 (35.2%)
• cellulitis	11 (3.9%)
• abscess	10 (3.6%)
• necrotising fasciitis (with STSS)	1 (0.4%)
Surgical scarlet fever	**99 (35.2%)**
Neurological complications	**51 (18.1%)**
• febrile seizure	40 (14.2%)
• afebrile seizure	5 (1.8%)
• cerebellitis	4 (1.4%)
• encephalitis	1 (0.4%)
• aseptic meningitis	1 (0.4%)
Pneumonia	**23 (8.2%)**
Others#	**9 (3.2%)**

* Some children developed more than 1 complication hence total number of complications and percentages exceed 281 and 100%, respectively

3 clinical sepsis, 1 streptococcal septic shock, 3 immune thrombocytopenic purpura, 2 Henoch-Schonlein purpura

STSS = Streptococcal toxic shock syndrome

and opinions reached by consensus, and none showed features suggestive of primary varicella pneumonitis. All were treated with antibiotics and only 4 mild cases were empirically treated without blood investigations performed. The rest 19 cases had leukocytosis, neutrophilia or markedly elevated CRP. Due to the low specificity of sputum culture for diagnosis of bacterial pneumonia in children, sputum was not routinely saved for culture in patients with clinical and radiological evidences of pneumonia. *Streptococcus pneumoniae* was isolated from sputum culture in 2 patients, *Haemophilus influenzae* was isolated from sputum culture in 1 patient, and *Pseudomonas aerugionosa* was isolated from endotracheal aspirate culture in 1 patient who received mechanical ventilation and intensive care. All chest radiographs available for review showed either bronchopneumonic infiltrates or lobar consolidation, without interstitial or reticulonodular pattern, and no evidence of residual calcifications or fibrosis on recovery. All 23 cases showed prompt clinical response to antibacterial therapy and recovered completely without pulmonary sequelae. Although 4 patients had also received acyclovir therapy, the relatively benign clinical course did not support the possibility of primary varicella pneumonitis, which is well known for its aggressive clinical course with rapid deterioration and high mortality despite specific antiviral therapy and appropriate supportive care. The only severe case requiring mechanical ventilation and intensive care received both antibacterial and antiviral therapies but did not show residual radiological evidence or abnormal lung function suggestive of recovery from primary varicella pneumonitis on serial follow-up. *Pseudomonas aeruginosa* was isolated from the endotracheal aspirate culture of this patient. Nine patients (3.2%) developed other complications, including clinical sepsis, immune thrombocytopenic purpura and Henoch-Schonlein purpura in 4, 3 and 2 patients, respectively. For the 4 patients with clinical sepsis, only 1 had a positive blood culture yielding *group A streptococcus*, while others had clinical features of sepsis as well as laboratory evidence such as leukocytosis, neutrophilia, neutropenia or markedly elevated CRP. Prior antibiotic therapy before hospitalisation might explain the failure to recover the causative bacterial pathogens, at least in some of them. Among all cases, 285 patients (47.7%) received antibacterial therapy while 56 (9.4%) received antiviral (acyclovir) therapy. None of the patients included in the current study were treated with varicella-zoster immunoglobulin (VZIG). Probable bacterial complications (including skin and soft tissue infections, surgical scarlet fever, probable bacterial pneumonia, sepsis and streptococcal toxic shock syndrome) occurred in 85.1% (239/281) of all hospitalised children with complications in this study, accounting for 81.5% (247/303) of all complications identified.

Complications by age. The mean age of patients with complicated varicella was 51.6 months (range 1-204 months). Patients without complications appeared to be older and had a mean age of 62.9 months (range 1-204 months). However, the difference was not statistically significant (p=0.183).

Life-threatening complications. There were 5 patients with severe complicated varicella requiring intensive care but all survived without significant sequelae. Two of them were immunocompromised. A 12-year-old boy who had congenital asplenia and a history of surgical repair for complex cyanotic heart disease developed *Pseudomonas aeruginosa* pneumonia with acute respiratory failure and septic shock 1 week after the onset of rash. He required mechanical ventilation and inotropic support, in addition to antibacterial and antiviral therapies. A 6-year-old boy who was receiving maintenance chemotherapy for acute lymphoblastic leukemia developed neutropenic fever, clinical sepsis with thrombocytopenia and deranged liver function. He required blood products transfusion besides antibibacterial and antiviral therapies. Life-threatening complications occurred in three other immunocompetent children. A 4-year-old girl developed necrotising fasciitis of the right buttock and was complicated by streptococcal toxic shock syndrome with disseminated intravascular coagulopathy 1 day after the onset of vesicular eruption. She required repeated surgical debridement, split skin graft, inotropic support and blood products transfusion besides antibacterial therapy. A 2-year-old girl developed left anterolateral chest wall abscess, surgical scarlet fever and streptococcal septic shock 3 days after the onset of rash. She required incision and drainage of abscess, antibiotic therapy and fluid resuscitation. A 3-year-old girl developed generalised tonic-clonic convulsion and imparied consciousness 8 days after the onset of rash. She was found to have hyponatraemia and electroencephalographic abnormalities suggestive of encephalitis. She received antiviral and supportive therapy and recovered with no neurological sequelae.

Complications in immunocompromised patients. Four out of 29 (13.8%) immunocompromised patients developed complications, which was significantly less common as compared to immunocompetent patients (277 out of 569, or 48.7%). Apart from the two immunocompromised patients described above, one child with focal segmental

glomerulosclerosis and another one with myasthenia gravis who were both on immunosuppressive therapy developed probable bacterial pneumonia. None of the immunocompromised patients developed skin and soft tissue infections, surgical scarlet fever, neurological complications or coagulopathy.

Discussion

The disease burden of chickenpox in Hong Kong is substantial as reflected by the average annual notification rate of 981 per 100,000 children aged below 18 years during the study period, although a large proportion of cases are likely uncomplicated. The actual disease burden of complicated chickenpox could not be ascertained as accurate figures of chickenpox complications for the whole territory were not available for comparison. Furthermore, accurate hospitalisation figures for chickenpox were also difficult to ascertain. Nevertheless, an average annual hospital attendance rate of 285.8 per 100,000 children aged below 18 years during the study period suggests that a substantial 30% of all notified paediatric cases of chickenpox will require medical consultation and/or treatment at either public or private hospitals. Even though many of these children do not suffer from complicated disease, the significant burden to the health care system is obvious.

This is the only local study describing hospitalisations for chickenpox in children in recent years. As Princess Margaret Hospital is a territory-wide referral centre for paediatric infectious diseases, our data set and the spectrum of complications that we encountered in our practice are considerable and likely representative. All cases of varicella were diagnosed clinically by experienced paediatricians and virological confirmation was generally not required for proper clinical management.

Age-specific hospitalisation rates for varicella vary between studies and generally peak in children aged 1-4 years.[3,4,9,19-22] This highlights the importance of early childhood immunisation in order to prevent the occurrence of varicella and hence its complications. The range and severity of varicella complications in childhood have been described in various studies.[3,9,19,22-31] The complication rates reported in literature among children hospitalised for varicella range from 40.7% to 83.3%.[3-7] This may be due to variability in the methodology of data collection and analysis, geographical conditions, and hospital admission policies. In our study, the overall complication rate in hospitalised children was 47%. The distribution of complications in our study was similar to those reported in other paediatric series, with skin and soft tissue infections occurring most frequently.[4,5,16,22,32-34] A previous retrospective study from our centre reviewing the complications in 2839 children aged less than 16 years who were hospitalised for varicella from 1988 to 1995, before the licensure of varicella vaccines in Hong Kong, reported the same finding.[35]

Although immunocompromised children are known to be at risk of severe complications of chickenpox or even disseminated disease, complications occurring in immunocompetent children are highly unpredictable. There were 2 previously healthy children with life-threatening skin and soft tissue infections requiring intensive care in our current study. One had necrotising fasciitis and toxic shock syndrome, and the other had chest wall abscess and septic shock. Both were caused by Group A Streptococcus (*Streptococcus pyogenes*), underscoring the potential invasiveness of this bacteria which is commonly found in the resident flora of normal skin. Surgical scarlet fever was increasingly recognised as a complication of varicella especially in children under 5 years of age, and was the second commonest complication in our previous and current studies.[35] Both resident flora of the normal skin, *Staphylococcus aureus* and *Streptococcus pyogenes*, are the two major causative agents.

Of the 51 children with neurological complications, only 1 previously healthy 3-year-old girl required intensive care for encephalitis and recovered without neurological sequelae. The spectrum of neurological complications of chickenpox seen in children admitted to our hospital in recent years appeared to be relatively benign, with the majority being febrile seizures and all had spontaneous uneventful recovery. This is in contrast to our previous experience in the pre-varicella vaccine era when severe varicella encephalitis resulting in significant neurological deficits despite antiviral therapy appeared to be relatively more common (unpublished data). This apparent change in epidemiology remains to be explained.

A similar discrepancy was also observed regarding the change in incidence of primary varicella pneumonitis, which is a rare but devastating complication associated with significant morbidity and mortality despite specific antiviral therapy and good supportive care. No child in the current study suffered from this complication. In our previous study, we have managed 4 cases of primary varicella pneumonitis involving 1 neonate and 3 children aged 7 to 15 years, 2 of whom were immunocompromised.[35] The neonate made a

complete recovery while 1 previously healthy child died. Of the 2 immunocompromised children who recovered, one was left with severe hypoxic cerebral injury. The increasing number of children receiving varicella vaccination outside of the universal childhood immunisation programme of Hong Kong in recent years might have contributed to significant reduction in the overall incidence of varicella, and hence its associated rare complications, although the degree of herd protection provided by an unknown coverage rate of varicella vaccine among the local childhood population remains to be determined.

Overall, 85.1% of all hospitalised children in this study developed complications which were probably caused by bacterial pathogens, and 81.5% of all recorded episodes of complications were likely bacterial in origin. Clinicians should be mindful of the common occurrence of secondary bacterial infection in a child with chickenpox, Such should be carefully looked for, and properly investigated if severe. Apart from specific antiviral therapy which is indicated in selected cases, the importance of antibacterial therapy in many cases of complicated chickenpox cannot be overemphasized.

It has been reported that chickenpox can cause greater morbidity and mortality in immunocompromised children than in the general population.[18] In our study, all immunocompromised patients were treated with intravenous acyclovir and monitored closely right after admission. They were generally older (due to their specific underlying conditions) and hospitalised earlier in the course of their illness as compared to immunocompetent children. Only 2 immunocompromised patients developed severe complicated varicella requiring intensive care and none had skin and soft tissue infections, surgical scarlet fever, neurological complications or coagulopathy. The paradoxically lower complication rate and better prognosis observed in this group of patients is understandable. In view of their known underlying risks for severe complications of varicella, these patients were generally hospitalised at an early stage of their illness and prompt definitive antiviral therapy and close monitoring were instituted once they are clinically diagnosed. Furthermore, many of them had already received prior post-exposure prophylaxis with varicella-specific immunoglobulin which, despite apparent failure of immunoprophylaxis, they were likely to be partially protected from developing severe illness, leading to a more favourable outcome although their length of hospitalisation appeared to be longer. On the contrary, complications of varicella are highly unpredictable in immunocompetent patients and empirical or pre-emptive antiviral therapy is not generally recommended before any severe complications are evident. Besides, one of the main reasons for admitting immunocompetent children with varicella to hospital is because they already presented with complications which necessitate in-patient management, hence resulting in an apparently higher complication rate as observed in this study.

Our study may have some limitations. As it was a hospital-based study, children with mild disease and less severe complications might have been excluded due to the absence of hospitalisation. However, the more significant complications resulting from chickenpox should have been captured by our study. Using discharge diagnostic codes for data collection might result in ascertainment bias due to the possibility of miscoding. However, studies investigating the accuracy of ICD-9 codes for various diseases in different countries suggested that this is a useful tool for epidemiological studies.[4,36,37] In addition, chickenpox is considered an easily recognisable childhood disease due to the presence of a characteristic rash which is most often pathognomonic. Hence, it is rarely subject to misdiagnosis and miscoding.[2,38] Because of the retrospective nature of this study, some relevant data were not retrievable sine they were not solicited or incompletely documented during hospitalisation, and some laboratory investigations were inevitably incomplete. Cautious interpretation of the results of our study is necessary.

Universal immunisation against chickenpox, implemented in the United States since 1995, has resulted in significant decrease in morbidity and mortality due to VZV infection, as well as chickenpox-associated medical expenditures and indirect socioeconomic costs.[12,14,15] In Germany, routine varicella vaccination is recommended in healthy children.[12,39,40] In Taiwan, varicella vaccination has been included in the routine childhood vaccination program nationwide since 2004.[11] The post-licensure safety record of varicella vaccines has been excellent.[41,42] Cost-benefit analyses of varicella immunisation have been performed in different countries.[43-45] Several countries are currently in the process of developing or implementing universal varicella vaccination programmes for children.[46] Further reduction in the overall disease burden of varicella in developed countries will be expected.

The significant complication rate and length of hospitalisation, as well as the possible severe complications necessitating intensive care as observed in the current study all challenge the preconception of varicella as a benign childhood illness. More importantly, complications are unpredictable and are now more commonly encountered

in previously healthy children as they are considered not at risk and generally do not receive timely specific antiviral therapy until severe disease or serious complications arise. We believe that our previous and current studies provide important information on varicella-associated morbidities in paediatric patients requiring hospitalisation for varicella in Hong Kong. In order to have an accurate assessment of the epidemiology and overall disease burden of varicella in both the community and hospital settings, and the impact of varicella vaccination on the overall burden of VZV infection including herpes zoster in the long run, further large-scale study including both children and adults is needed to provide additional data to inform cost-effectiveness analysis upon which the decision of introducing universal varicella vaccination in Hong Kong could be based.

In conclusion, varicella is not always a mild childhood illness and complications are unpredictable in the untreated previously healthy children, which can result in significant morbidity and prolonged hospitalisation. Immunocompromised children, though traditionally considered to be at risk of serious disease with VZV infection, may not suffer from increased incidence of complications if timely specific antiviral therapy is instituted. An accurate assessment of the disease burden of varicella and the cost-effectiveness of implementing universal varicella vaccination in Hong Kong will require important information such as provided by this study.

Acknowledgements

We would like to thank Dr Christine Wong, Dr SK Chuang and Dr Thomas Tsang of the Centre for Health Protection, Department of Heath for their kind support and assistance with retrieval of notification and hospital attendance figures for chickenpox.

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