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Influenza-associated hospitalisation

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Key Message

The disease burden associated with influenza includes not only acute respiratory diseases but also cerebrovascular disease, ischaemic heart disease and diabetes mellitus.

Introduction

Influenza may result in hospitalisation, especially in young children and the elderly or in those with chronic diseases. Hospitalisation for influenza is under-reported owing to the non-specific symptoms of influenza and lack of laboratory tests. Excess hospitalisation and mortality associated with influenza have been used to measure the health impacts of influenza.[1-3] Excess hospitalisation was calculated as the difference in hospitalisation numbers between the epidemic and non-epidemic periods within a year, or between the epidemic years with apparent influenza peaks and the baseline years without any apparent increase of influenza activity. It is difficult to apply the same approach to tropical and subtropical regions such as Hong Kong, where there are no well-defined epidemic periods or even clear seasonal patterns of influenza activity. We used Poisson regression to estimate the disease burden related to influenza in the circumstance without a clear influenza seasonality.[4]

Aims and objectives

To evaluate influenza-associated hospitalisation for different age-groups in Hong Kong.

Methods

The weekly numbers of hospital discharge diagnoses from 14 acute hospitals in Hong Kong during the period 1996-2000 were obtained from the Hospital Authority. The disease categories included acute respiratory disease (ARD) [International Classification of Diseases version 9 (ICD9) codes 460-466, 480-487] and its sub-category pneumonia and influenza (P&I) [ICD9 480-487], cerebrovascular disease (CVD) [ICD9 430-438], ischaemic heart disease (IHD) [ICD9 410-414] and diabetes mellitus [ICD9 250]. The weekly proportion of specimens positive for influenza A and B (influenza A+B), and for respiratory syncytial virus (RSV) were obtained from the microbiology laboratory of Queen Mary Hospital and were adopted to represent influenza and RSV activity.

We used Poisson regression to model the weekly counts of hospitalisation for each disease category.[5] We built a core model to control for confounding factors including temperature, relative humidity, long-term trends and seasonality. This core model was accepted once the partial autocorrelation plots of its residuals did not have any discernible patterns. The variables influenza A+B and RSV were entered into the core model to assess the impacts of influenza activity with adjustment for RSV. The lag effects of influenza were assessed by entering the variable influenza A+B measured at 0-3 weeks before the admission week and selecting the one with the most significant effect (ie the smallest P value for the coefficient).

The percentage of excess hospitalisation attributable to influenza was calculated as the ratio of the difference between the total observed and expected hospitalisation under the assumption that influenza A+B was zero, to the total number of observed hospitalisation. This percentage of excess hospitalisation was then multiplied by the total hospitalisation per year to get the excess number, which was further divided by the population to obtain a rate of excess hospitalisation per 100 000 inhabitants.

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Table. Influenza-associated excess hospitalisation in Hong Kong from 1996 to 2000, after adjusting for co-variates including respiratory syncytial virus

Age-group (years)	Lag (weeks)	Excess hospitalisation per year		P value
		% (95% CI)	No. (95% CI) per 100 000 inhabitants	
Acute respiratory disease				
0-14	0	9.3 (7.7, 10.8)	163.3 (135.2, 189.7)	<0.001
15-39	0	7.2 (3.3, 10.8)	6.0 (2.7, 8.9)	0.001
40-64	1	11.0 (7.9, 13.9)	14.9 (10.7, 18.8)	<0.001
65-74	1	11.5 (8.4, 14.3)	83.8 (61.2, 104.2)	<0.001
75+	0	8.7 (6.5, 10.8)	266.0 (198.7, 330.2)	<0.001
All	0	10.9 (9.5, 12.1)	60.6 (52.8, 67.2)	<0.001
Pneumonia and influenza				
0-14	1	14.7 (11.8, 17.4)	70.4 (56.5, 83.3)	<0.001
15-39	1	10.5 (6.1, 14.4)	2.9 (1.7, 4.0)	<0.001
40-64	1	8.7 (5.0, 12.1)	6.8 (3.9, 9.4)	<0.001
65-74	1	11.0 (8.1, 13.8)	58.7 (43.3, 73.7)	<0.001
75+	0	7.1 (4.8, 9.3)	176.3 (119.2, 231.0)	<0.001
All	1	11.6 (10.2, 12.9)	29.3 (25.8, 32.6)	<0.001

Results

In all age-groups, influenza was significantly associated with 10.9% of total hospitalisation for ARD, 11.6% for P&I, 1.5% for CVD, 1.8% for IHD and 3.5% for diabetes (P<0.01) [Table]. In addition, ARD and P&I were significantly associated with influenza (P<0.001). Influenza accounted for 9.3% and 11.5% of hospitalisation for ARD in the 0-14 and 65-74 years age-groups, respectively. For both disease categories, the influenza-associated excess hospitalisation rates per 100 000 inhabitants were estimated to be lowest (6.0 for ARD and 2.9 for P&I) in the 15-39 years age-group, and highest (266.0 for ARD and 176.3 for P&I) in the 75+ years age-group (Table).

Influenza was significantly associated with hospitalisation for CVD (P=0.001) and IHD (P<0.01) only in the 75+ years age-group, with rates of 55.4 and 56.4 per 100 000 inhabitants. Influenza was also significantly associated with 2.0% of all hospitalisation for IHD in the 40-64 years age-group (P<0.05). In addition, influenza was significantly associated with hospitalisation for diabetes (P<0.01), with rates being 6.6, 23.9 and 53.3 per 100 000 inhabitants in the 40-64, 65-74 and 75+ years age-groups, respectively. For all these chronic diseases CVD, IHD and diabetes, the rates of influenza-associated excess hospitalisation were highest in the 75+ years age-group (Fig).

Discussion

In this study, influenza was significantly associated with cardiorespiratory hospitalisation in all age-groups in Hong Kong. According to our estimates, influenza accounted for 29.3 excess P&I hospitalisations per 100 000 inhabitants in all age-groups and 11.6% of total hospitalisations. These estimates were comparable with those reported by a study in the US using a similar Poisson regression approach. Annually there was a 36.8 influenza-associated excess P&I hospitalisations per 100 000 inhabitants for all ages, accounting for 8.6% of all hospitalisations for this diagnosis during the period 1979 to 2001.[6] Those aged 75+ years had the highest hospitalisation rates for all disease categories investigated. The influenza-associated hospitalisation for ARD was lowest in the 15-39 years age-group, a pattern echoed in the US study.[6]

Influenza was associated with excess hospitalisation for chronic diseases such as CVD and IHD, especially in those older than 65 years. Numerous studies have suggested that influenza infection may cause damage not only to the respiratory system, but also to the circulatory organs. Influenza might trigger alterations in circulating clotting factors, platelet aggregation and lysis, concentrations of inflammatory-response proteins and cytokine concentrations. These may enhance thrombotic tendencies, impair vasodilation, or even lead to endothelial injury. In addition, acute respiratory tract infection is associated with an increased risk of myocardial infarction and stroke.[7]

The association between influenza and hospitalisation for diabetes was significant. Our study was the first

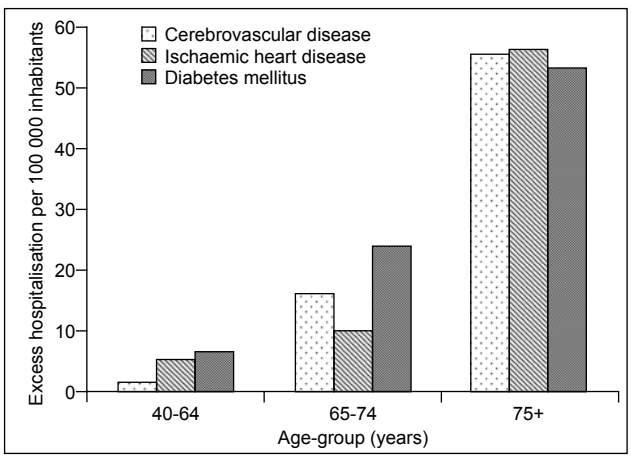

Fig. Excess hospitalisation per 100 000 inhabitants associated with influenza at different age-groups

showing that influenza was associated with hospitalisation for diabetes mellitus in persons older than 40 years. Although increased morbidity and mortality of diabetes during influenza epidemics has long been recognised, we were able to assess the excess hospitalisation rates due to year-round influenza virus activity rather than in epidemic periods alone. The increased hospitalisation of diabetic patients may be explained by their impaired immune responses, which probably leads to secondary bacterial infections and further increases morbidity and mortality. Moreover, influenza and its complications may increase the chance of diabetic patients suffering a range of diabetes-related complications that may or may not be directly related to influenza.

Young children and the elderly are high-risk groups in tropical and subtropical settings; they would most benefit from influenza vaccination. Influenza also significantly increased the risk of hospitalisation in patients with underlying chronic conditions such as CVD, IHD and diabetes. These results provide evidence to support the promotion of influenza vaccination in patients with these chronic diseases.

Poisson regression modelling is a valid approach to assess disease impacts of influenza in tropical and subtropical regions with uncertain seasonal patterns of virus activity. The estimates based on Poisson regression modelling have been proved to be robust to unobserved confounding factors such as smoking status and chronic co-morbidity.[8] However, this methodology has the limitation of over-controlling underlying seasonal variations of disease morbidity in the core model. It is possible that some of this seasonal variation may also be attributable to the seasonal activity of influenza, but this portion of the variation cannot be separated from others in this type of analysis. Therefore, our estimates are very likely to underestimate the true impact of influenza on hospitalisation. An approach that can also capture the seasonal variation of disease morbidity associated with influenza virus circulation is needed.

Conclusions

Our study demonstrated an association of influenza with hospitalisation, not only for ARD (including P&I), but also for chronic diseases such as CVD, IHD, and diabetes mellitus. The excess hospitalisation rates associated with influenza in Hong Kong were estimated to be close to the rates in the US.

Influenza vaccination in the tropics should be promoted to achieve a direct benefit of reducing influenza-associated hospitalisation. The Poisson regression approach is applicable in estimating disease burden associated with influenza in Hong Kong, and can be adapted to other subtropical/tropical regions.

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