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Influenza in Malaysia: A Systematic Review

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Abstract

This paper reviews the effects and burden of human influenza in Malaysia as documented in scientific publications and portrayed in the media. The burden of influenza is under appreciated and understudied in many developing countries, where there is often a perception that influenza is mainly a disease of temperate climates. The World Health Organisation (WHO) strongly recommends studies of influenza epidemiology, disease burden, and vaccine effectiveness in developing countries to encouraging further uptake of vaccine.

Keywords: Influenza, Malaysia, systematic review

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Introduction

Influenza is a respiratory tract infection (RTI) that causes disease ranging from mild upper RTI to severe pneumonia. Life- threatening complications such as secondary bacterial pneumonia, myocarditis and encephalopathy may occur. Influenza viruses are in the *Orthomyxoviridae* family and are divided into influenza A, B and C (1). Influenza viruses originally infect birds, but have evolved to also affect mammals, including humans (2).

Influenza generally seen year-round in Malaysia, with no clear seasonal trends. Influenza A usually detected more frequently than influenza B, although year-to-year variation may be considerable (3). The outbreak generated national interest as influenza causes millions of infections yearly and 250,000- 500,000 deaths globally. In Malaysia, of 1362 children, 51 (3.7%) died, 46 of whom were in an intensive care unit during the pandemic H1N1 2009 (4).

Generally, it is treated with antiviral, Oseltamivir (TAMIFLU®) which is available in Malaysian Drug Formulary. Oseltamivir is a neuraminidase inhibitor indicated for the treatment and prevention of influenza A and B. The most effective means of control is vaccination, however neuraminidase inhibitors started within 48 hour on onset of influenza symptoms shortens the duration of illness (5). Additional therapy with antibacterial agents should be prescribed at the discretion of the clinician if secondary bacterial pneumonia is suspected (5).

High risk groups are children less than 5 years old, elderly aged 65 years or older, pregnant women, adults and children who have chronic pulmonary, cardiovascular, hepatic, haematological, neurological, neuromuscular or metabolic disorders (5).

Methods

Searches of paper titles, abstracts and full text content performed in Google Scholar and PubMed. Search terms used were 'influenza' and Malaysia'. The types of studies included were epidemiology reviews and in-vivo studies which involved retrospective study design. Those study use Malaysia Influenza Surveillance System to collects data by disease-based and laboratory-based surveillance. Detection methods are using conventional methods which are the immunofluorescence or culture, RSV is the commonest respiratory virus detected in children with ARI, while influenza identified in 2.0-3.2% of cases while other non-conventional detection methods use is PCR. The study evaluated based on its design and findings.

Result and Discussion

Table 1: Summary of study characteristics:

Author & Date	Title of article	Location	Sample characteristics	Details
Muhammad Ismail et. al. 2011(4)	Characteristics of Children Hospitalized for Pandemic (H1N1) 2009, Malaysia	All over Malaysia	n = 1362 Children < 12 years old	Children <12 years old who hospitalised for influenza like illness (ILI) from June 18, 2009, through March 1, 2010, and for whom pandemic (H1N1) 2009 infection confirmed by real-time reverse transcription–PCR. Reviewed and approved by the Malaysian Research and Ethics Committee. Informed consent was provided for patients with confirmed diagnoses.
Sam et. al. 2009 (3)	Clinical features of Malaysian children hospitalised with community-acquired seasonal influenza	Universiti Malaya Medical Centre (UMMC)	n = 132 Children < 15 years old	Paediatric patients who admitted with laboratory- confirmed influenza from 2002 to 2007 data from the diagnostic virology laboratory. Laboratory confirmed influenza defined as the detection of influenza virus antigen by immunofluorescence or isolation of

				influenza virus, from a clinical specimen. Nosocomial infections, defined as onset of influenza more than 48 h after admission, were excluded.
Dhanoa et. al 2011(6)	Epidemiology and clinical characteristics of hospitalized patients with pandemic influenza A (H1N1) 2009 infections: the effects of bacterial coinfection.	Hospital Sultanah Aminah Johor Bahru (HSAJB)	n = 50	Retrospective study Involved hospitalised patients with laboratory-confirmed H1N1 infections (September 2009 to May 2010). Multiplex PCR used to determine coexisting other respiratory viruses. Comparison made between patients with and without bacterial coinfection.

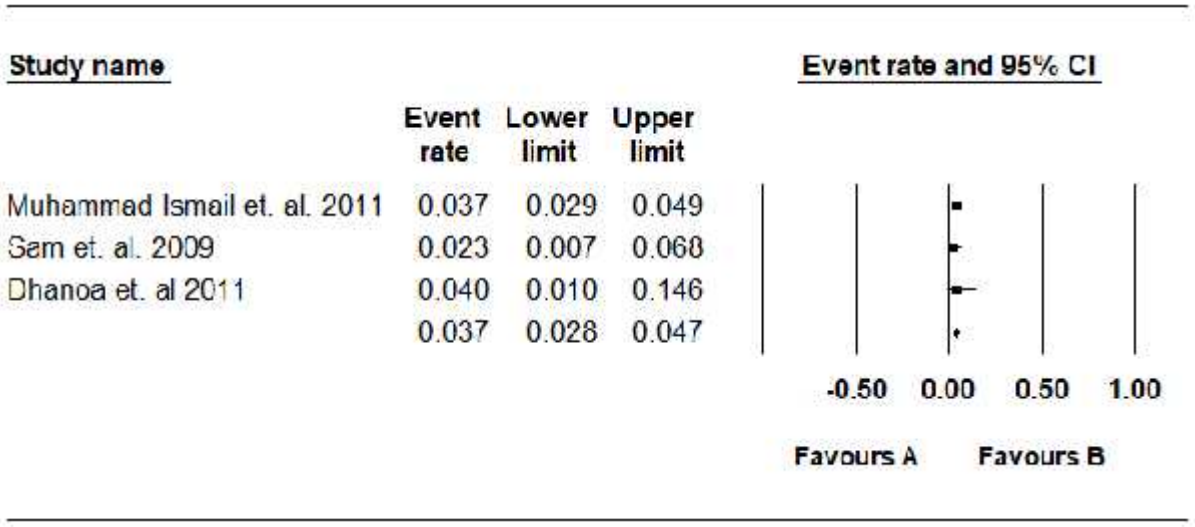
Table 2: Prediction intervals for prevalence

Number of studies	3
Degrees of freedom	2
Point estimate	-3.272
Standard error	0.136
Lower limit (logit unit)	-3.539
Upper limit (logit unit)	-3.005
Z-value	-24.033

Table 3: Heterogeneity

Q-value	0.750
df (Q)	2
P-value	< 0.001

Table 4: Influenza mortality prevalence



This analysis includes three studies where mortality among influenza patients is evaluated. Outcome was the number of influenza patients with death outcome. The effect size is the influenza mortality rate.

A quick view of the plot suggests the risk of influenza death varied slightly from study to study, ranging from 2.3% to 4.0%. Based on this analysis alone, it seems that much of this variation reflects differences in real proportions. The mean prevalence is 0.037 with a 95% confidence interval of 0.028 to 0.047.

The pooled estimate of prevalence is 0.037, which means that about 3.7% of influenza patients died. The confidence interval for the prevalence is 0.028 to 0.047, which tell us the mean prevalence in the universe of studies could fall anywhere in this range.

The observed effect size varies from study to study, but some of variation is expected due to sampling error. The Q-statistic provides a test of the null hypothesis that all studies in the analysis share a common effect size. If all studies shared the same effect size, the expected value of Q would be equal to the degrees of freedom. The Q-value is 0.750 with 2 degrees of freedom and $p < 0.001$. We can reject the null hypothesis the true effect size is the same in all these studies.

Limitation

Antivirals are restricted to selected cases and require specialist authorization which interferes with prompt treatment of influenza. However, indiscriminate use of oseltamivir leads to resistant strains. As resistance is easily acquired, the effectiveness of oseltamivir in a pandemic may soon be lost (7).

The use of influenza vaccine is extremely low despite the growing evidence that influenza is a significant health problem in developing countries. In Malaysia, no recommendations provided for influenza vaccination in children, and the unknown burden of influenza precludes cost-benefit analysis (8). The incidence and overall burden of influenza in Malaysia is not known, as surveillance data are limited.

There is also insufficient manufacturing capacity of the effective influenza vaccine for the whole world, and usually most of the new vaccines will be supplied to developed countries (9). Thus, poorer countries may have limited access to vaccines, even in the medium term.

Conclusion:

Although the data obtained from the three literatures showed the risk of influenza death varied slightly from study to study. However, obviously influenza causes a significant and under recognised burden of disease in Malaysia. This results derived from the three literature involves in this research highlights the need to raise awareness among the public health and clinical communities for the influenza burden and consequences of this important illness. This study highlight the importance of establishing ongoing disease surveillance programs which involve clinics and hospitals to effectively monitor influenza disease dynamics in Malaysia as well as to improve vaccination strategies in the country against Influenza infection.

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Reference

1. Lysholm F, Wetterbom A, Lindau C, Darban H, Bjerkner A, Fahlander K, et al. Characterization of the viral microbiome in patients with severe lower respiratory tract infections, using metagenomic sequencing. PloS one. 2012;7(2):e30875.
2. Wolfe ND, Dunavan CP, Diamond J. Origins of major human infectious diseases. Nature. 2007;447(7142):279-83.
3. Sam I-C, Abdul-Murad A, Karunakaran R, Rampal S, Chan Y-F, Nathan AM, et al. Clinical features of Malaysian children hospitalized with community-acquired seasonal influenza. International Journal of Infectious Diseases. 2010;14:e36-e40.
4. Ismail HIM, Tan KK, Lee YL, Pau WS, Razali KA, Mohamed T, et al. Characteristics of children hospitalized for pandemic (H1N1) 2009, Malaysia. Emerging infectious diseases. 2011;17(4):708.
5. Management guidelines for influenza A-H1N1 for paediatric patients: Ministry of Health Malaysia; 2009 26-August-2009.

6. Dhanoa A, Fang NC, Hassan SS, Kaniappan P, Rajasekaram G. Epidemiology and clinical characteristics of hospitalized patients with pandemic influenza A (H1N1) 2009 infections: the effects of bacterial coinfection. Virology journal. 2011;8(1):501.
7. De Jong MD, Thanh TT, Khanh TH, Hien VM, Smith GJ, Chau NV, et al. Oseltamivir resistance during treatment of influenza A (H5N1) infection. New England Journal of Medicine. 2005;353(25):2667-72.
8. Samad AH, Usul MH, Zakaria D, Ismail R, Tasset-Tisseau A, Baron-Papillon F, et al. Workplace vaccination against influenza in Malaysia: does the employer benefit? Journal of occupational health. 2006;48(1):1-10.
9. Oshitani H, Kamigaki T, Suzuki A. Major issues and challenges of influenza pandemic preparedness in developing countries. Emerging infectious diseases. 2008;14(6):875.