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The Epidemiology of the First Wave of H1N1 Influenza Pandemic in Australia: A Population-Based Study

Julie A. Pasco*[1,2], Geoff C. Nicholson[3], Sharon L. Brennan[1,2], Kathy E. Bennett[1], Amelia G. Dobbins[1] and Eugene Athan[4]

[1]*School of Medicine, Deakin University, Geelong, VIC 3220, Australia*

[2]*North West Academic Centre, Department of Medicine, The University of Melbourne, St Albans, VIC 3021, Australia*

[3]*Rural Clinical School, School of Medicine, The University of Queensland, Toowoomba, QLD 4350, Australia*

[4]*Department of Infectious Diseases, Barwon Health Geelong, VIC 3220, Australia*

Abstract: *Objectives*: Following the recent H1N1 influenza pandemic we were able to describe seropositivity in a representative sample of adults prior to the availability of a specific vaccine.

Methods: This cross-sectional serological study is set in the Barwon Statistical Division, Australia. Blood samples were collected from September 2009 through to May 2010, from 1184 individuals (569 men, 615 women; median age 61.7 years), randomly selected from electoral rolls. Serum was analysed for specific H1N1 immunity using a haemagglutination inhibition test. A self-report provided information about symptoms, demographics and healthcare. Associations between H1N1 infection, gender, households and occupation were determined using logistic regression, adjusting for age.

Results: Of 1184 individuals, 129 (58 men, 71 women) were seropositive. Gender-adjusted age-specific prevalence was: 8.3% 20-29 years, 13.5% 30-39, 10.4% 40-49, 6.5% 50-59, 9.7% 60-69, 10.3% 70-79, 18.8% 80+. Standardised prevalence was 10.3% (95%CI 9.6-11.0). No associations were detected between seropositivity and gender (OR=0.82, 95%CI 0.57-1.19) or being a healthcare worker (OR=1.43, 95%CI 0.62-3.29). Smokers (OR=1.86, 95%CI 1.09-3.15) and those socioeconomically disadvantaged (OR=2.52, 95%CI 1.24-5.13) were at increased risk. Among 129 seropositive individuals, 31 reported symptoms that were either mild (n = 13) or moderate (time off work, doctor visit, n = 18). For age <60, 39.6% of seropositive individuals reported symptoms, whereas the proportion was 13.2% for age 60+.

Conclusions: Following the pandemic, the proportion of seropositive adults was low, but significant subclinical infection was found. Social disadvantage increased the likelihood of infection. The low symptom rate for older ages may relate to pre-existing immunity.

Keywords: Epidemiology, H1N1, hospitalization, influenza A virus, pandemics, signs and symptoms, population-based study.

INTRODUCTION

Following early reports of a novel strain of H1N1 Influenza A in North America in March 2009 there was rapid widespread community transmission to all continents and the World Health Organisation (WHO) declared a global influenza pandemic (http://www.who.int/mediacentre/news/statements/2009/h1n1_pandemic_phase6_20090611/en/index.html). The influenza pandemic placed extraordinary demand on public health services around the world [1]. Eventually the clinical course and clinical features of the pandemic strain were found to be comparable to seasonal influenza [2]; however, there was an over representation of moderate to severe infection among pregnant women and obese patients [3-5]. No population-based serological surveys had been undertaken to estimate the true incidence of infection in our community. We therefore used the opportunity to describe the seropositivity of pandemic H1N1 influenza in a sample of adults prior to the availability of a specific vaccine. We wanted to measure seropositivity in an adult population and estimate potential risk factors such as occupational and childcare exposure and also to describe the spectrum of clinical disease and the level of subclinical infection

MATERIALS AND METHODOLOGY

This cross-sectional study is a sub-study of the Geelong Osteoporosis Study (GOS). Cohorts of men and women were selected at random from electoral rolls covering the Barwon Statistical Division in south-eastern Australia. In Australia voting is compulsory for all citizens 18 years of age or more. The electoral roll is a register of all eligible voters and provides the most comprehensive available list of adult Australian citizens. Age-stratified cohorts of 1494 women and 1540

*Address correspondence to this author at the Barwon Epidemiology and Biostatistics Unit, School of Medicine, Deakin University, PO Box 281, Geelong, Victoria 3220, Australia; Tel: +61 3 42153331;
Fax: +61 3 42153491; E-mail: juliep@barwonhealth.org.au

men were recruited in 1994-7 (77% response) and 2001-6 (67% response), respectively. At least 100 women and 100 men were recruited in each five-year age group from 20 to 69 years and 200 of each sex for both the 70-79 and 80+ year groups [6]. A further sample of 221 women listed as aged 20-29 years on the 2005 electoral roll was recruited 2006-8 (82% response) [6]. In 2009-10, subjects were invited to participate in this sub-study by providing a blood sample and completing a questionnaire. The study was approved by the Barwon Health Human Research Ethics Committee. All participants provided informed, written consent.

From a potential pool of 2075 GOS participants (973 men and 1102 women) who were alive, living in the region and able to be contacted, 1184 (569 men and 615 women) agreed to participate in this sub-study (57% response). Blood samples were collected between September 2009 and May 2010, predating the roll out of the Pandemic vaccine in the region. Serum was aliquoted and stored at -80C for random batch analysis. Serum was analysed for specific H1N1 immunity using a haemagglutination inhibition test, performed at the Commonwealth Scientific and Industrial Research Organisation's (CSIRO's) Australian Animal Health Laboratory (AAHL) in Geelong. Seropositivity was defined as a titre $\geq$ 1:40.

Height and weight were measured to the nearest 0.1 cm and 0.1 kg, respectively, and body mass index (BMI) was calculated in kg/m^2. Subjects were categorised as obese if BMI was $\geq$30.0 kg/m^2 [7].

A self-report questionnaire was designed to seek information concerning occupation, employment status, living arrangements (number and ages of other people living in household), pregnancy status, and lifestyle choices including medication use, smoking and alcohol consumption. Exposure to chronic respiratory disease (including chronic lung disease, asthma, chronic obstructive pulmonary disease and emphysema), chronic heart disease and diabetes were also documented by self-report. Details of influenza-like symptoms (fever $\geq$38C, cough and/or sore throat <72 hours duration), respiratory illness and vaccination history were also documented. Individuals who experienced an influenza-like illness during the study period responded to questions about diagnostic tests, treatment, hospital admissions and impact on normal activities. Symptom severity was classified as severe if the subject was hospitalised, moderate if the subject required time of work or visited a doctor; otherwise they were classified as mild.

Socioeconomic status (SES) was ascertained using the Australian Bureau of Statistic's (ABS) Index of Relative Socioeconomic Advantage and Disadvantage (IRSAD) [8]. The IRSAD scores reflect the overall level of advantage and disadvantage measured at the area-level, and captures a wide range of socioeconomic attributes including education, occupation, income, unemployment and household structure. For analyses, participants were categorised into quintiles of SES based on their IRSAD scores using cut-points for the Barwon Statistical Division as determined by the ABS. Quintile 1 denotes the most disadvantaged area, and quintile 5 the most advantaged.

Statistics

Prevalence data were standardised by age and gender to Australian population profiles (ABS Catalogue No. 2001.0). Associations between H1N1 seropositivity (outcome) and gender, occupation, employment status, household living arrangements, pregnancy status, medication use, smoking, alcohol consumption, chronic respiratory disease, chronic heart disease, diabetes and SES (exposures) were determined using multivariable regression analysis. Models were tested for confounders and effect modifiers. Statistical analyses were performed using Minitab (version 15; Minitab, State College, PA, USA).

RESULTS

Prevalence

Of 1184 individuals (569 men and 615 women), 129 (58 men and 71 women) were seropositive. Age- and gender-adjusted prevalence was 8.3% for age 20-29 years, 13.5% for 30-39 years, 10.4% for 40-49 years, 6.5% for 50-59 years, 9.7% for 60-69 years, 10.3% for 70-79 years and 18.8% for 80+ (Fig. **1**). Standardised prevalence for age 20+ was 10.3%. (95%CI 9.6-11.0).

Subject characteristics are shown, overall, and according to H1N1 infection status in Table **1**. A greater proportion of seropositive individuals were smokers, fewer than expected seropositive individuals were self-employed and more than expected were not employed and seropositive individuals tended to be over-represented in the lowest SES quintile and under-represented in the highest SES quintile. No differences in H1N1 seropositive status were detected between those with chronic respiratory disease, pregnancy, obesity or diabetes, while those with chronic heart disease tended to be over-represented in the seropositive group.

Risk Factors for H1N1 Seropositivity

Smokers were more likely to be seropositive (OR=1.86, 95%CI 1.09-3.15, p=0.02). Compared to those who were employed fulltime, there was a trend for those self-employed to be less likely to be seropositive (OR=0.31, 95%CI 0.07-1.35, p=0.1).

No associations were detected between H1N1 infection and gender (OR=0.82 95%CI 0.57-1.19, p=0.3), being a healthcare worker (OR=1.43, 95%CI 0.62-3.29, p=0.4), having chronic respiratory disease (OR=0.92, 95%CI 0.50-1.69, p=0.8) or chronic heart disease (OR=1.50, 95%CI 0.70-3.23, p=0.3), being obese (OR=0.98, 95%CI 0.65-1.46, p=0.9) or diabetic (OR=0.73, 95%CI 0.36-1.50, p=0.4); there was a trend for increased risk among childcare-workers/teachers (OR=1.93, 95%CI 0.87-4.30, p=0.1) and those living with children (OR=1.57, 95%CI 0.85-2.90, p=0.2). Individuals in the lowest SES quintile were 2.5-fold more likely to be seropositive than those who were least disadvantaged (OR=2.52, 95%CI 1.24-5.13, p=0.01). This association was not explained by smoking habits, employment, living with children or the number of people living in the household.

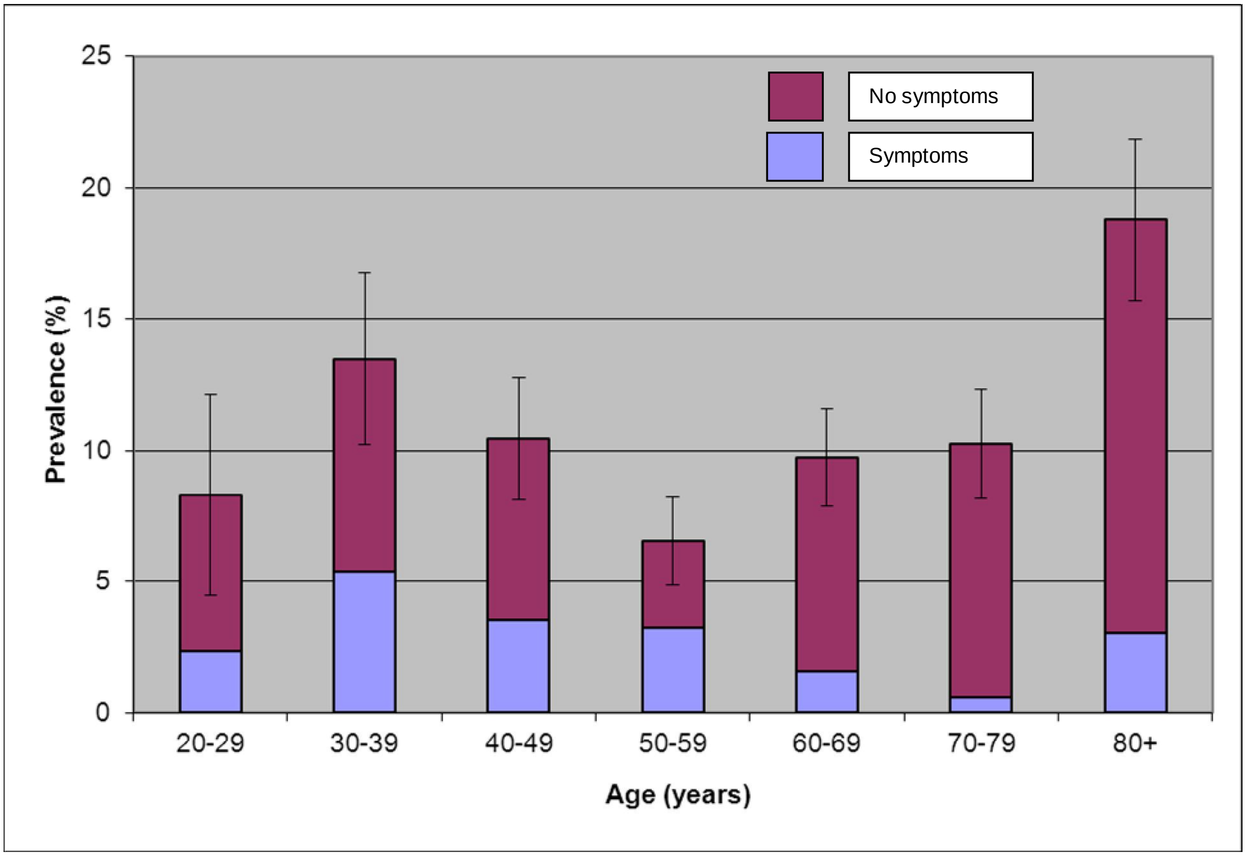

Fig. (1). The prevalence of seropositivity by age. The lower portion of bars represents those who reported influenza-like symptoms. The error bars represent the standard error.

Symptoms

Among 129 seropositive individuals, symptoms were reported by 24.0% (n=31): for 10.1% (n=13) symptoms were mild, 14.0% (n=18) moderate (6 time off work, 16 doctor visit) and none was severe (no hospitalisations). Two had diagnostic tests performed for H1N1 infection; none was prescribed treatment. Raw data showed that for age <60 years, 39.6% reported symptoms whereas the proportion was 13.2% for age 60+. The age- and gender-adjusted proportions of seropositive individuals who reported influenza-type symptoms are shown in Fig. (**1**).

Upper respiratory tract symptoms were reported in 26 symptomatic individuals (17 sore throat, 22 cough, 16 runny nose, 13 shortness of breath, 13 sinus congestion); two with gastrointestinal symptoms (1 diarrhoea, 2 vomiting); 25 with constitutional symptoms (18 headache, 19 fatigue, 12 chills, 16 body ache) and 18 with other symptoms (4 chest pain, 12 stiffness, 6 ear ache, 3 conjunctivitis).

DISCUSSION

Historically, a pandemic strain of influenza appears periodically every second generation, at times with devastating virulence. In this population-based study among adults during the first wave of pandemic H1N1 infection in Australia, we found an overall prevalence of 10.3%. The proportion of adults who were seropositive was relatively low in view of the susceptibility of the population. This was highest in young adults with the exception of the over 80 year cohort, possibly related to previous immunity from circulating H1N1 strains before 1957. This is also supported by the very low symptom rate for the older age group who were found to be seropositive.

Our study found a similar age pattern as that of a median of 21-22 years in symptomatic laboratory confirmed cases of pandemic influenza from sentinel surveillance sites in Victoria and Western Australia [9]. The low virulence of this pandemic strain was comparable to seasonal influenza with significant subclinical infection found. An opportunistic serological survey among children in Western Australia following the 2009 pandemic reported that 25% of preschool and 40% of school age children had evidence of recent infection [10]. Most were asymptomatic although this was not carefully assessed given the limits in methodology in this study. These results and our findings provide some support for the early public health response of pre-emptive school closures to delay community transmission rather than awaiting the onset of symptomatic infection to drive decision making pending the availability of an effective vaccine.

Overall there was substantial subclinical infection and we found low rates of clinical disease with mild and moderate symptoms requiring time off work or seeking medical attention and there were no hospitalisations.

We found that history of contact with children increased the likelihood of infection, and a recent transmission study during the seasonal influenza season found a five-fold in-

Table 1. Subject Characteristics for the Whole Group and According to Seropositivity. Data are Presented as Mean (±SD) or n (%).

	All n=1184	Seropositive		
		Yes n = 129	No n = 1055	p
Male	569 (48.1%)	58 (45.0%)	511 (48.4%)	0.46
Age (yr)	60.5 (±16.8)	62.9 (±19.6)	60.3 (±16.4)	0.16
BMI (kg/m^2)	28.1 (±5.3)	28.2 (±5.6)	28.1 (±5.2)	0.87
Obese (BMI>30.0 kg/m^2)	353 (29.8%)	38 (29.5%)	315 (29.9%)	0.93
Current smoker	123 (10.4%)	20 (15.5%)	103 (9.8%)	0.04
Healthcare worker	53 (4.5%)	7 (5.4%)	46 (4.4%)	0.59
Childcare worker/teacher	48 (4.1%)	8 (6.2%)	40 (3.8%)	0.19
Employment status				0.05
Full-time	284 (24.0%)	27 (20.9%)	257 (24.4%)	
Part-time	139 (11.7%)	10 (7.8%)	129 (12.2%)	
Casual	64 (5.4%)	7 (5.4%)	57 (5.4%)	
Self-employed	63 (5.3%)	2 (1.6%)	61 (5.8%)	
Not employed	634 (53.6%)	83 (64.3%)	551 (52.2%)	
Highest level of education				0.18
Primary	75 (6.3%)	11 (8.5%)	64 (6.1%)	
Some secondary	393 (33.2%)	52 (40.3%)	341 (32.3%)	
Completed secondary	276 (23.3%)	22 (17.1%)	254 (24.1%)	
Post-secondary	152 (12.8%)	14 (10.9%)	138 (13.1%)	
Tertiary	288 (24.3%)	30 (23.3%)	258 (24.5%)	
Lives alone	196 (16.6%)	27 (20.9%)	169 (16.0%)	0.16
Lives with children aged <12 yr	161 (13.6%)	19 (14.7%)	142 (13.5%)	0.69
Socioeconomic status				0.11
Quintile 1 (low)	234 (19.8%)	35 (27.1%)	199 (18.9%)	
Quintile 2	272 (23.0%)	30 (23.3%)	242 (22.9%)	
Quintile 3	280 (23.7%)	27 (20.9%)	253 (24.0%)	
Quintile 4	231 (19.5%)	26 (20.2%)	205 (19.4%)	
Quintile 5	167 (14.1%)	11 (8.5%)	156 (14.8%)	
Chronic respiratory disease	129 (10.9%)	13 (10.1%)	116 (11.0%)	0.75
Pregnancy	13 (1.1%)	1 (0.8%)	12 (1.1%)	1
Chronic heart disease	53 (4.5%)	9 (7.0%)	44 (4.2%)	0.15
Diabetes	99 (8.4%)	9 (7.0%)	90 (8.5%)	0.55

crease in secondary household cases following confirmed influenza in index child cases [11]. Among health workers we did not find an increased infection risk compared to background. Additional precautions and use of personal protective equipment were widely used across health services during the H1N1 pandemic and may have contributed to this risk reduction. We did not observe an increased risk associated with obesity; limited numbers restricted our ability to further explore the relationship with pregnancy.

We observed a clear inverse association with SES for infection and this relationship was not explained by smoking habits, employment, living with children or the number of people living in the household. Compliance with precautionary recommendations to control the spread of H1N1 has been associated with greater educational attainment in studies of adults from the USA [12] and Singapore [13]. Perception of a health threat, and compliance with preventive measures, are more likely to occur for those with greater health literacy [14] - a construct referring to the capacity of an individual to obtain and understand health information and employ specific health-related behaviours that are effective in reducing the risk of disease, and one which has been associated with higher education and income. In contrast, those with lower health literacy are, in theory, more likely to engage in risk-taking behaviour, more likely to be influenced by peers, and less likely to comply with recommended preventive measures.

It is a given that greater transmission intensity correlates with spatial concentrations of individuals [15]. Those of lower SES are more likely to experience spatial concentrations of populations, for instance on public transport such as buses and trains. Whilst we were unable to account for spatial concentrations and/or public transport use, a study of adult males and females from Singapore reported a higher seroconversion rate associated with use of local public transport [16]. Whilst a Canadian study found no association between public transport and H1N1 [17], this discrepancy may be explained by the study methodology whereby participants were primarily recruited from urban areas, thus potentially limiting the range of socioeconomic groups included for analysis. However, that same Canadian study reported that large social gatherings were associated with an increased likelihood of seroconversion [17]. Furthermore, individuals of greater social disadvantage are more likely to have smaller homes [18] and, whilst living with children or the number of people living in the household did not explain our findings, we were unable to examine population density relative to the size of the home. Although the precise implications of community-specific factors on seropositivity remain unknown, targeted educational and behavioural interventions to improve respiratory, and hand, hygiene practices to reduce disease transmission would be well directed toward those of greater social disadvantage using readily accessible avenues such as television.

The strength of this study is that it is population-based. Furthermore, serology was performed independently by laboratory technicians who were blinded to questionnaire data and clinical measures. However, we acknowledge several limitations. The study involved adults only. The accuracy of self-reported data concerning symptoms, employment and lifestyle practices may have been subject to recall bias. It also remains unknown how many influenza infections lead to seropositivity at convalescence. Unless this fraction is high, seropositivity may be a poor measure of cumulative incidence of infection. Given that subclinical infections are difficult to confirm virologically, while serologic response is correlated with disease severity, this fraction is likely to remain elusive.

CONCLUSION

This study provides some important evidence to inform key public health interventions, at the individual-behaviour level and at the level of population-wide health promotion messages, in an influenza pandemic response. These include protection of vulnerable populations such as the elderly and socially disadvantaged groups. The reasons predisposing these groups to H1N1 infection remain to be understood.

CONFLICT OF INTEREST

The authors declare that they do not have competing interests.

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