Outbreak of 2009 pandemic influenza A(H1N1) in a Finnish garrison - a serological survey

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In September 2009, an outbreak of 2009 pandemic influenza A(H1N1) took place in a Finnish garrison. In November 2009, we performed a serological survey among 984 recruits undergoing their military service at the garrison and related the results to self-reported upper respiratory tract infection (URTI) with or without fever. Of 346 volunteers who donated a blood sample, 169 (49%) had pandemic influenza A(H1N1) virus-specific antibodies. Of those, 84 (50%) reported no recent history of URTI, suggesting that a major part of those infected with pandemic influenza A(H1N1) virus may be asymptomatic.

Outbreak description

In September 2009, one of the earliest outbreaks of 2009 pandemic influenza A(H1N1) in Finland took place in a garrison of 984 military conscripts. Before this outbreak, most of the infections caused by the pandemic influenza A(H1N1) virus in Finland were sporadic and often related to prior travel abroad. The number of visits to the primary healthcare services (PHS) of the garrison due to upper respiratory tract infections (URTI) increased rapidly during week 36 starting on 31 August 2009.

During the preceding weekend leave, on 29-30 August, six conscripts had fallen ill with high fever and cough. Nasopharyngeal swabs were taken as part of a routine screening diagnostic test for respiratory viruses and tested positive for 2009 pandemic influenza A(H1N1) virus by polymerase chain reaction (PCR). In total, 335 conscripts (34% of the garrison population) visited the PHS due to URTI between 31 August and 30 September 2009. During the same time period nasopharyngeal swabs were collected from 52 of 335 (13%) of the conscripts and 28 of these 52 (54%) were pandemic influenza A(H1N1)-positive by PCR. The most common symptoms among the PCR-confirmed cases were fever (≥38°C) (27/28), lethargy (27/28), cough (22/28), sore throat (18/28) headache (15/28), rhinorrhoea (12/28 and myalgia or arthralgia (9/28). The mean duration of fever was three days (range, 0-5 days), and on average the conscripts returned to service after five days. None of them had severe complications or required intensive care. Seven conscripts with asthma were treated with antiviral agents during the outbreak, which waned by the end of September. In late October and in November new cases appeared when sustained community transmission of the pandemic began in Finland.

A serological and epidemiological survey was conducted in order to study the prevalence of pandemic influenza A(H1N1) virus infections in this defined population after the outbreak.

Methods

Nasopharyngeal swabs

Initially, during 1-14 September, one to five nasopharyngeal samples were taken per day from conscripts who presented with URTI and fever at the PHS to confirm the diagnosis. After 15 September, sampling was performed randomly from URTI patients. The samples were analysed at the national influenza center of the Finnish National Institute for Health and Welfare (THL) by PCR for pandemic influenza A(H1N1) virus [1], seasonal influenza A, influenza B, parainfluenza 1, 2 and 3, adeno- and respiratory syncytial viruses. Nasopharyngeal samples taken during September were analysed by PCR also for rhino- and enteroviruses at the THL enterovirus laboratory.

Serological and epidemiological survey

All conscripts who had been serving in the garrison during the outbreak (n=984) were invited to participate in the study. The study was approved by the coordinating ethics committee of the hospital districts of Helsinki and Uusimaa, and the volunteers gave informed consent before enrolment in the study. Serum samples were taken from volunteers between 6 November and 3 December 2009.The participants were instructed to fill out a questionnaire at the time of sampling about possible symptoms of URTI, fever and/or diarrhoea experienced during the observation period of July to November 2009. Specific antibodies to the pandemic influenza A(H1N1) virus were analysed by haemagglutination inhibition (HI) according to standard methods [2]. The virus strain used as antigen was A/Finland/554/2009(H1N1v) [3]. Serum samples were

tested in two-fold serial dilutions starting at an initial dilution of 1:10. The highest serum dilution was 1:640. Antibody titres ≥10 were regarded positive.

Clinical records from the PHS were examined according to the international classification of diseases (ICD-10) codes specific for influenza (J10 and J11). SPSS version 16 and Microsoft Excel were used for statistical analyses.

Results

Nasopharyngeal swabs

Altogether, 79 nasopharyngeal swabs were taken between 1 September and 3 December; 44% (35/79) of them were positive for 2009 pandemic influenza A(H1N1) virus by PCR. From a total of 52 nasopharyngeal samples taken during the outbreak in September 54% (28/52) were positive for 2009 pandemic influenza A(H1N1) virus, whereas 37% (19/52) tested positive for rhinovirus. Five samples were negative for all tested viruses. Three conscripts had a simultaneous infection with rhinovirus and 2009 pandemic influenza A(H1N1) virus.

The pandemic influenza A(H1N1) virus was found more frequently during the first half of September, but later the rhinovirus predominated (Figure). Other viruses were rarely present in the nasopharyngeal samples: seasonal influenza A was detected in samples from two conscripts and parainfluenza type 2 in one.

Serological and epidemiological survey

A total of 346 (35%) conscripts volunteered to donate a blood sample and filled out the questionnaire; 99% were male (mean age 21 years; range 20–28). In addition, 139 (14%) conscripts only filled out the questionnaire, making the total who responded to the questionnaire survey 485 (49%).

Nearly half of those who volunteered to give a blood sample (49%, 169/346) had detectable antibodies (titres ≥10) against the 2009 pandemic influenza A(H1N1) virus. In approximately half of these seropositive individuals (46%, 77/169) antibody titres ≥40 were detected.

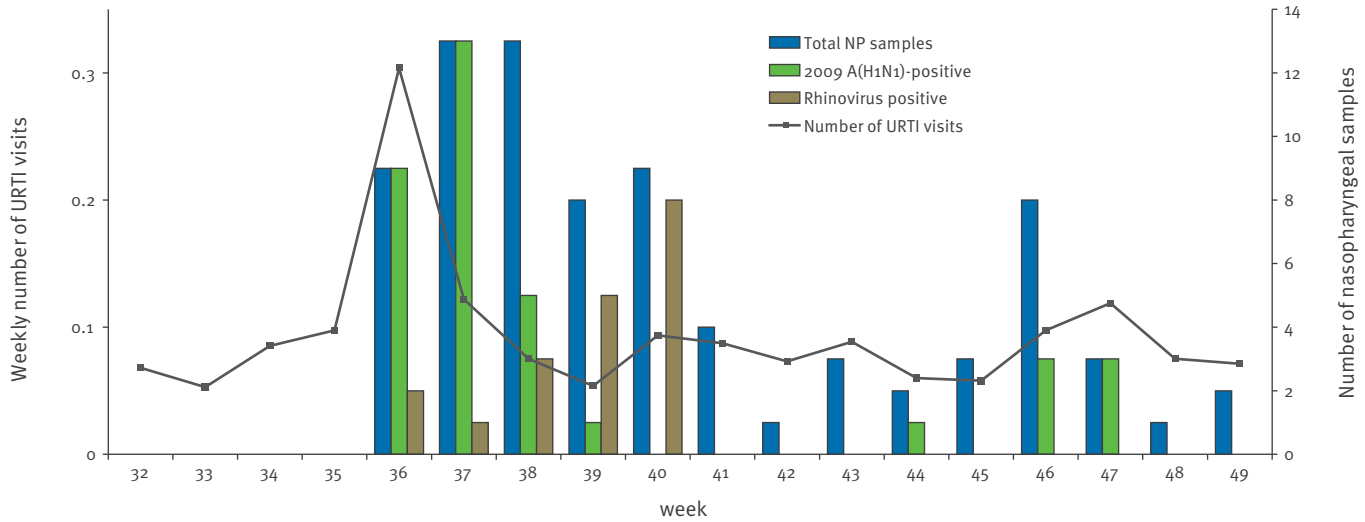
Eight of the participants had a preceding PCR-confirmed 2009 pandemic influenza A(H1N1) virus infection; seven of them were seropositive (median antibody titre 80, range 10-160) and in one individual no 2009 A(H1N1)-specific antibodies were detected two months after the PCR-confirmed 2009 pandemic influenza A(H1N1) virus infection.

Based on the responses to the questionnaire, 50% (84/169) of the seropositive participants did not report any history of URTI, 35% (59/169) reported having had a URTI with fever and 15% (26/169) a URTI without fever (Table). The proportion of seropositives among the participants without any history of URTI was 45% (84/186). The history of having had a URTI with fever was slightly more common among seropositive than among seronegative participants (35% versus 24%), but the difference was not statistically significant. Of the 139 conscripts who only filled out the questionnaire, 97 (70%) did not report any history of URTI, 25 (18%) reported having had a URTI without fever, and 17 (12%) a URTI with fever.

According to the PHS clinical records, a clinical diagnosis of influenza was made in 103 of the 984 conscripts (10%) between 31 August and 30 September, and in 123

FIGURE

Weekly number of URTI-associated visits of the conscript population (n=984), August – November 2009, Finland[a]



NP: nasopharyngeal; URTI: upper respiratory tract infection

[a] The number of NP samples collected during August-November 2009 and the samples positive for 2009 pandemic A(H1N1) virus and rhinovirus by PCR are presented as bars.

conscripts (13%) during the whole observation period covered by the questionnaire (July to November 2009). Of the 346 study participants who donated a blood sample the clinical diagnosis of influenza was made in 47 (14%), and 77% (36/47) of these were seropositive.

Discussion and conclusions

We combined PCR and serological laboratory results with clinical data from the PHS of a garrison as well as from questionnaires filled out by voluntary military recruits after the outbreak of 2009 pandemic influenza A(H1N1), which started before the sustained community transmission of the virus was ongoing in Finland. The epidemic in the general Finnish population began later, during weeks 41-42 in October 2009, and it peaked during weeks 43-45 and 45-48 in northern and southern Finland, respectively.

Military garrisons present a high risk environment for the spread of respiratory disease due to large numbers of conscripts living in close proximity [4]. This may partly explain the high proportion of infected subjects in our study population. A total of 346 conscripts (35%) donated a blood sample and nearly half (49%) of these individuals had antibodies against the 2009 pandemic influenza A(H1N1) virus. The true seroprevalence caused by the outbreak may have been lower than observed due to possible pre-existing cross-reactive immunity. Although some of the conscripts may have been infected during travel abroad or by contacts to travellers in spring and summer 2009 before entering the service in July, the majority of the recruit population was expected to lack immunity against the virus and the baseline prevalence of cross-reacting antibodies against the 2009 pandemic influenza A(H1N1) virus among the conscripts was assumed to be low. According to a recent serological study in Finland, the prevalence of cross-reacting antibodies (HI titre ≥1:10) against the 2009 A(H1N1) virus was less than 2.5% in the 20-39 age group.[3]. This study was based, however, on serum specimens collected during 2004 and 2005, and the seasonal A(H1N1) influenza epidemic in Europe during the winter 2007-8 may have elevated the prevalence of cross-reacting antibodies. In a recent cross-sectional serological study from England, a detectable level of cross-reacting antibodies (HI titre ≥1:8) was found as frequently as in 25% of serum samples obtained in 2008 from 15-24 year-olds [5].

Based on the questionnaire, a history of URTI was more common among the volunteers who donated a blood sample (46%) than among the conscripts who only filled out the questionnaire (30%). As the prevalence of antibodies specific to the 2009 pandemic influenza A(H1N1) virus was high (45%) also among the participants without symptoms of URTI, the proportion of infected individuals in the entire study population might be assumed to be approximately of the same magnitude. However, it is unlikely that this reflects high infection rates also in the general Finnish population. In fact, in England fewer infections were reported - one third of children were considered to have been infected during the 2009 pandemic wave in regions with a high incidence [5].

According to the responses to our questionnaire (n=485), half of the seropositive individuals did not have a history of a URTI or fever. Of the seropositives, 15% had experienced only URTI symptoms, and only one third of the seropositives reported to have had URTI with fever during the study period. Of note is that a proportion of the seropositive individuals may have had pre-existing cross-reactive immunity, and thus these subjects may have been misclassified as asymptomatic cases, which would tend to lower the true proportion of asymptomatic infections. On the other hand, the high frequency of symptoms reported by the seronegative participants was probably caused by the concurrent circulation of rhinovirus. Also, a proportion of the seropositives may have had URTI symptoms due to rhinovirus infection, but not because of A(H1N1) infection. Consequently, the proportion of asymptomatic 2009 A(H1N1) infections may have been higher than observed, after all.

Table

Serological status and history of upper respiratory tract infection with and without fever reported by 346 volunteers, July to November 2009, Finland

	Number of participants (%)						Total	
	Haemagglutination inhibition titre							
	Seronegative		Seropositive					
	< 10		10 - 20		≥40			
URTI with fever	42 (23.7)	(41.6)	32 (34.8)	(31.7)	27 (35.1)	(26.7)	101 (29.2)	(100)
URTI without fever	33 (18.6)	(55.9)	16 (17.4)	(27.1)	10 (13.0)	(16.9)	59 (17.1)	(100)
No reported symptoms of URTI	102 (57.6)	(54.8)	44 (47.8)	(23.7)	40 (51.9)	(21.5)	186 (53.8)	(100)
Total	177 (100)	(51.2)	92 (100)	(26.6)	77 (100)	(22.3)	346 (100)	(100)

URTI: upper respiratory tract infection

In this thoroughly monitored population of 984 conscripts, the clinical diagnosis of influenza was made by a healthcare professional in only 10% of these during the outbreak, suggesting at least five times higher than estimated incidence of infection as compared with clinical surveillance. Well in line with these findings, Miller *et al*. [5] suggested a ten times higher incidence of pandemic influenza A(H1N1) virus infection among English children than that based on the number of clinical diagnoses of influenza-like illness made in general practice. Furthermore, previously reported school outbreaks are similar to our findings of rapid and extensive spread of the infection [6]. The high proportion of asymptomatic and mild infections in our study may partly be explained by the characteristics of the study population, which consisted of young healthy adults. Remarkably, none of our subjects developed severe symptoms.

Timely implementation of strict control measures such as strict isolation and active case finding in other similar, perhaps even more closed, settings e.g. on board navy vessels, has been reported to be effective in limiting the spread of infection [7, 8]. In contrast to these earlier reports, extensive measures were not taken during our outbreak to reduce the spread of the disease in the garrison. The importance of hand hygiene was stressed and proper coughing and sneezing behaviour was advised and encouraged. Only patients with fever were kept hospitalised in the infirmary, and obviously this was not enough to prevent the spread of infection. Instead, strict isolation of the infected units might have limited or perhaps even stopped the transmission within the garrison. In order to reduce influenza morbidity in garrisons and the risk of transmission to the community, specific vaccinations could be the only effective preventive measure.

In conclusion, we report that approximately half of the military conscripts living in crowded garrison quarters may have been infected during an outbreak of pandemic influenza A(H1N1) virus in September 2009. Half of the infections may have been asymptomatic, only a minority of the infected individuals developed clinically typical influenza, and none severe illness. It has been suggested earlier that other respiratory virus infections may inhibit the spread of influenza [9] and *vice versa* [10]. Whether there was interference between rhinovirus and 2009 pandemic influenza A(H1N1) virus in our outbreak remains unsolved.

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