Is abdominal obesity associated with the 2009 influenza A (H1N1) pandemic in Korean school-aged children?

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Accepted 1 November 2011. Published online 8 December 2011.

Objective Given their medical vulnerabilities, we investigated the epidemiological factors related to H1N1 infection in school-aged children.

Methods This study analyzed data collected on 7448 school-aged children in South Korea between 18 November and 8 December 2009.

Results We found that H1N1 infection was associated with body mass index (BMI), waist circumference (WC), the use of facemasks, contact history with H1N1-infected persons, and overseas travel history ($P < 0.05$). In addition, WC quartiles were significantly associated with H1N1 infection after adjusting for BMI and other confounding variables [OR (95% CI); 1.00, 1.10 (0.72–1.43), 1.13 (0.76–1.67), and 2.71 (1.74–4.24), respectively].

Conclusions Abdominal obesity and the use of facemasks appear to be independently associated with H1N1 infection in school-aged children. We infer that providing education on wearing facemasks and specific planning for abdominally obese children and adolescents may be effective means of reducing the spread of the influenza pandemic in school-aged children.

Keywords Abdominal obesity, influenza A (H1N1).

Introduction Since April 2009, the novel influenza A virus strain (H1N1) has rapidly spread worldwide, and greatly affected school-aged children, a trend that differs from that of seasonal influenza. Therefore, understanding the infection-related characteristics of this group is important for planning for pandemic influenza.

Obesity, which has been proposed as a risk factor for poor outcomes in H1N1-infected individuals, has previously been evaluated using only body mass index (BMI) and excluding waist circumference (WC). Although several reports have investigated the association between children’s behavioral risk factors and seasonal influenza, studies on children’s behavioral risk factors and H1N1 infection are scarce. In this study, we investigated demographic and epidemiological factors, including anthropometric (BMI, WC) and behavioral patterns, related to H1N1 infection in school-aged children.

Methods Data collection

This study initially included all school-aged children ($n = 39,551$) in Seodaemun-gu, a district in Seoul, South Korea, between 18 November and 8 December 2009, prior to the initiation of the vaccination program against H1N1 (Figure 1). In this article, school-aged children refer to students between 7 and 18 years old. Among them, we excluded schools which principal refused consent to participate in this study ($n = 23,606$), students meeting the exclusion criteria for vaccination or disagreeing with our study ($n = 7,483$), those for whom data for WC, BMI, or H1N1 diagnosis information were missing ($n = 554$), and those who had been taking antiviral medication before H1N1 infection was confirmed ($n = 460$). Finally, a total of 7448 school-age children and adolescents were enrolled in our study. The data were collected by self-reported questionnaire. Before this study was conducted, nurse-teachers

Please cite this paper as: Kim et al. (2012) Is abdominal obesity associated with the 2009 influenza A (H1N1) pandemic in Korean school-aged children? Influenza and Other Respiratory Viruses 6(5), 313–317.
in each school educated students (or their parents) to measure their (or their children’s) WC according to World Health Organization protocol.6 After teaching, the nurse-teachers reaffirmed their measures, and made the measurement report form standardized. The height and weight of the students were matched to their school health records. Demographic information (age, gender, height, weight, WC), H1N1-related information (H1N1 infection history, antiviral medication history for seasonal influenza, overseas travel history, contact history with H1N1-infected persons, seasonal influenza vaccination history), behavioral information (hand washing, wearing facemasks, after-school study hours, use of public transportation), and information on underlying conditions were gathered. The presence of H1N1 was diagnosed using reverse transcriptase-polymerase chain reaction (RT-PCR) method, the influenza rapid antigen test, or viral cultures. This study was approved by the Yonsei University Severance Hospital Institutional Review Board.

Statistical analysis
Continuous variables are expressed as mean ± 1 SD. Categorical variables are expressed as a percentage. Student’s t-tests and chi-square tests were used to distinguish demographic and epidemiological differences between the H1N1 case group and the non-infected group. The odds ratio (OR) and 95% confidence intervals (CI) were calculated for each variable in relation to H1N1 infection. Independent associations with H1N1 infection were assessed using stepwise multivariate logistic regression analysis, using age, gender, WC, BMI, hand washing, wearing a facemask, after-school study hours, use of public transportation, regular exercise, underlying conditions, influenza A (H1N1) contact history, vaccination, and overseas trip. Variables associated with H1N1 at P value below 0.15 were included into a model. Only variables associated with H1N1 infection at P value below 0.05 were retained in the final model. In addition, BMI and WC were divided into quartiles, and the OR and 95% CI for H1N1 infection were calculated after adjusting for confounding variables using multivariate logistic regression analysis. A P value below 0.05 indicated statistical significance. All analyses were performed using SAS version 9.1 (SAS Institute, Cary, NC, USA).

Results
The demographic and epidemiological characteristics of the 7448 subjects (3149 males and 4299 females) are outlined in Table 1. The number of H1N1 cases was 417 (5.6%). The mean age of the subjects was 12.97 ± 3.03 years, and there was no significant age difference between the H1N1 case group and non-infected groups. There was a significantly higher proportion of male cases (P < 0.01), and 80 students (19.2%) with H1N1 infection had underlying diseases (asthma, 18; atopy, 60; cardiac disease, 2).

Students with H1N1 were more obese and had larger WC. The majority of students with H1N1 did not wear facemasks, and continuous use of facemasks exhibited a significant negative relationship with H1N1 infection (OR 0.51, 95% CI 0.30–0.88). A history of contact with H1N1-infected persons and overseas travel history were associated with H1N1 infection.

A stepwise logistic regression analysis revealed that WC, the use of facemasks, a history of contact with H1N1-infected persons, and overseas travel history were independent factors associated with H1N1 infection, and the ORs (95% CI) for H1N1 infection regarding these variables were 1.10 (1.10–1.12), 0.44 (0.23–0.49), 3.48 (2.79–4.33), and 1.73 (1.19–2.51) (data not shown).

Table 2 presents the relationship between H1N1 infection and BMI, WC quartiles. Although BMI was associated with H1N1 infection after adjusting for age and gender, this relationship disappeared after adjusting for WC. However, WC was significantly associated with H1N1 infection after additional adjustment for BMI. In model 4, the ORs (95% CI) for H1N1 infection across the WC quartiles were 1.00, 1.10 (0.72–1.45), 1.13 (0.76–1.67), and 2.71 (1.74–4.24), after adjusting for age, gender, BMI, hand washing, the use of facemasks, after-school study hours, the use of public transportation, regular exercise, underlying
**Table 1. Clinical characteristics of school-aged children infected with H1N1**

| Characteristics                        | Total no. or mean ± SD (n = 7448) | Cases* no.(%) or mean ± SD (n = 417) | Odds ratio (95% CI) | P value** |
|----------------------------------------|-----------------------------------|--------------------------------------|---------------------|-----------|
| Age (years)                            | 12.97 ± 3.03                      | 13.24 ± 2.92                        | 1.03 (1.00–1.07)    | 0.42      |
| Primary school                         | 3139                              | 165 (5.3)                           |                     |           |
| Middle school                          | 2555                              | 144 (5.6)                           |                     |           |
| High school                            | 1754                              | 108 (6.2)                           |                     |           |
| Male                                   | 3149                              | 225 (7.1)                           | 1.64 (1.35–2.01)    | <0.01     |
| Body mass index (kg/m²)                | 19.17 ± 2.77                      | 20.13 ± 3.23                        | 1.13 (1.10–1.17)    | <0.01     |
| <17.25                                 | 1868                              | 75 (4.0)                            |                     |           |
| 17.25–19.03                            | 1831                              | 94 (5.1)                            |                     |           |
| 19.04–20.93                            | 1886                              | 101 (5.4)                           |                     |           |
| >20.93                                 | 1863                              | 147 (7.9)                           |                     |           |
| Waist circumference (cm)               | 64.83 ± 7.47                      | 68.37 ± 8.54                        | 1.08 (1.06–1.10)    | <0.01     |
| <60.96                                 | 1668                              | 71 (4.3)                            |                     |           |
| 60.96–66.03                            | 1524                              | 72 (4.7)                            |                     |           |
| 66.04–71.11                            | 1972                              | 101 (5.1)                           |                     |           |
| >71.11                                 | 1867                              | 173 (9.3)                           |                     |           |
| Hand washing                           | 5.88 ± 3.37                       | 5.79 ± 3.58                         | 0.99 (0.96–1.02)    | 0.58      |
| Wearing a facemask                     |                                   |                                     |                     |           |
| Non-user                               | 4164                              | 239 (5.7)                           | 1 (reference)       | 0.04      |
| Irregular user                         | 2819                              | 164 (5.8)                           | 1.02 (0.83–1.25)    |           |
| Continuous user                        | 466                               | 14 (3.0)                            | 0.51 (0.30–0.88)    |           |
| After-school study hours               | 7.91 ± 7.87                       | 8.58 ± 7.97                         | 1.01 (1.00–1.02)    | 0.07      |
| Use of public transportation           | 1.84 ± 2.19                       | 0.81 ± 0.79                         | 0.98 (0.93–1.03)    | 0.43      |
| Regular exercise                       | 2728                              | 147 (5.4)                           | 0.94 (0.76–1.15)    | 0.91      |
| Underlying conditions                  |                                   |                                     |                     |           |
| Asthma                                 | 171                               | 18 (10.5)                           |                     |           |
| Atopy                                  | 891                               | 60 (6.7)                            |                     |           |
| Cardiac disease                        | 20                                | 2 (10.0)                            |                     |           |
| Renal disease                          | 12                                | 0 (0.0)                             |                     |           |
| Liver disease                          | 11                                | 0 (0.0)                             |                     |           |
| Diabetes                               | 6                                 | 0 (0.0)                             |                     |           |
| Influenza A (H1N1) contact history     | 1829                              | 216 (11.8)                          | 3.60 (2.95–4.40)    | <0.01     |
| Vaccination                            | 1719                              | 90 (5.2)                            | 0.92 (0.72–1.17)    | 0.49      |
| Overseas trip                          | 457 (6.1)                         | 40 (8.8)                            | 1.68 (1.19–2.36)    | <0.01     |

*Influenza A (H1N1) infection was defined as a positive by real-time RT-PCR, rapid influenza test, or viral culture result. Conversely, a negative result by RT-PCR indicated a lack of influenza A (H1N1) infection. **P values between cases and controls were calculated using the t-test (for continuous variables), or χ²-test (for categorical variables). Odds ratios (OR) and 95% confidence intervals (CI) were calculated for each variable for H1N1 infection.

Hand washing frequency was ascertained using a questionnaire with the question, ‘How many times do you wash your hands in a day?’ Facemask use was classified into three groups: nonusers, irregular users (including rare and usual users), or continuous users. Use of public transportation was defined as time spent riding the bus or subway in a week. Regular exercise was defined as exercise or physical work for more than 30 min three times a week. Vaccination was defined as receiving a seasonal vaccination history in 2008 or 2009. Overseas trip history was defined as having a history of taking a trip abroad in 2009.

**Discussion**

Because school-aged children are more susceptible to pandemic H1N1 infection than older persons, understanding the epidemiological predictors of infected and susceptible children is important for future planning for pandemic influenza. Here, we investigated the epidemiological characteristics of H1N1 infection in school-aged children including anthropometric and behavioral variables.

In previous studies, obesity has been proposed as a risk factor influencing poor outcomes in pandemic H1N1 influenza; however, its role remains controversial.
addition, there are no available data on WC, a surrogate marker for abdominal obesity, in relation to H1N1 infection.

Our study revealed that obese children, particularly abdominally obese children, are more vulnerable to H1N1 infection. Although abdominal obesity is a greater risk factor for the development of metabolic and cardiovascular disease than general adiposity, little is known about the effects of abdominal obesity on immune response and the development of infectious disease. Recent studies in humans and animal models have demonstrated that several obesity-associated changes, such as excessive inflammation, altered adipokine signaling, and metabolic changes, could affect immune response, as manifested by decreased cytokine production, decreased response to antigen/mitogen stimulation, reduced macrophage and dendritic cell function, and natural killer cell impairment. Additional studies are needed to understand the interactions between abdominal obesity and immune response and infectious disease.

As in previous studies, we observed the preventive effect of wearing facemasks. This suggests that the continuous use of facemasks is an easy and effective method to prevent the spread of H1N1 infection.

Our study has several limitations. First, its cross-sectional design precludes the confirmation of a causal relationship between the variables. Further studies of different populations are necessary to better understand the relationship between epidemiological factors and H1N1 infection. Although H1N1 infection was defined as a positive real-time RT-PCR, rapid influenza test, or viral culture, we considered the possibility of ascertainment bias that previous infection in the earlier wave or asymptomatic infection may have been missed and difference in access to H1N1 exam, along with prior diagnosis due to severity of infection existed. In addition, measurement bias in the self-reported questionnaire and WC measurements were unavoidable. However, to reduce the bias, the tutorial was provided to teach individuals the proper WC measurement technique including appropriate anatomic landmarks and proper tape placement. Finally, we cannot rule out the possibility that obese children might spend more time indoors and thus their H1N1 exposure increased. But our data showed no significant difference between obese and normal weight children in according to the after-school study hours, public transportation use, and exercise (data not shown).

In conclusion, abdominal obesity and the use of facemasks were independently associated with H1N1 infection in school-aged children. We infer that providing education on wearing facemasks and specific planning for abdominally obese students for pandemic influenza may be effective and also minimize health care costs.
Acknowledgements
We would like to express great appreciation to Gui Bin Kang, the director of the Seodaemun-gu Public Health Center, for her efforts in data collection.

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