



## Outbreak, Surveillance and Investigation Reports

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### Risk Factors for Community-acquired Pneumonia in Malaysian Pilgrims Attending the Hajj, 2012

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#### Abstract

Community-acquired pneumonia (CAP) is an important cause of morbidity and mortality in Malaysian pilgrims attending the Hajj every year. This study aimed to determine risk factors associated with CAP in Malaysians attending the Hajj. We conducted an unmatched case-control study at a Malaysian hospital in Mecca from September 2012 to January 2013, during the Hajj season. Individuals who met the definition of CAP were selected as cases. Controls were randomly selected among Malaysian pilgrims staying in the same accommodation as the cases, and followed up two weeks after returning to Malaysia. Information on risk factors was gathered using a structured questionnaire, and the strength of association was assessed using adjusted odds ratios (AOR) and 95% confidence intervals (CI) through a multiple logistic regression model. The study identified 108 cases and 673 unmatched controls. Among cases, 57.4% were males and 98.1% were aged more than 50 years. CAP was significantly associated with drinking over three liters of water daily (AOR = 0.2, 95% CI = 0.9-0.4), taking multivitamins (AOR = 0.2, 95% CI = 0.9-0.5), age 60 years or more (AOR = 20.2, 95% CI = 10.6-38.3), asthma/chronic obstructive airway disease (AOR = 5.9, 95% CI = 2.4-14.7) and congestive cardiac failure (AOR = 5.4, 95% CI = 2.0-14.7). Determining potentially preventable risk factors for CAP could help to inform public health programs for future Hajj pilgrims and might potentially reduce the associated morbidity and mortality.

**Keywords:** Hajj, pilgrims, community-acquired pneumonia, risk factors, multivitamin

#### Introduction

Every year, about 28,000 people or 0.1% of Malaysian population perform Hajj in Mecca, Saudi Arabia.<sup>1,2,3</sup> Hajj activities are physically very demanding<sup>4</sup> and expose pilgrims to excessive heat, extreme congestion and other hazards<sup>5</sup>. These activities increase the risk of developing health problems such as respiratory infectious diseases that are transmitted by droplets or aerosols.<sup>1,6,7</sup> Preventing outbreak-prone infectious diseases such as influenza<sup>8</sup>, community-acquired pneumonia (CAP), tuberculosis<sup>9</sup>, meningococcal meningitis and severe acute respiratory syndrome in pilgrims has thus presented significant challenges to Malaysian medical teams.<sup>2,3</sup>

In addition to wearing face masks and practicing proper personal hygiene, vaccination has been the mainstay of preventive measures for pilgrims.<sup>3</sup>

Following directives of Saudi Health Authority<sup>5,10,11,12</sup>, Malaysian policy requires vaccination against meningococcal meningitis at least two weeks prior to embarking on the Hajj<sup>13</sup>. Pilgrims aged over 59 years or with co-morbidities are also encouraged to take influenza vaccination<sup>10,12,14,15</sup> and pneumococcal vaccination<sup>1</sup>.

In 2003, infectious diseases and pneumonia accounted for 36.4% and 19.7% respectively for admissions to Saudi health facilities in Mecca during the Hajj<sup>6,10,11,16</sup>. In addition, high mortality of pneumonia (22%) were observed among pilgrims admitted to intensive care units during the Hajj period of 2004.<sup>16</sup> The objectives of this study were to determine risk factors associated with CAP among Malaysian pilgrims performing the Hajj in 2012, and identify potential preventive measures in the Hajj.

## Methods

An unmatched case-control study was designed to determine risk factors associated with CAP in Malaysian pilgrims. This study was conducted in Mecca, Saudi Arabia, during the Hajj season in October 2012.

The study defined CAP as acquiring fever (temperature  $>37.8^{\circ}\text{C}$ ), chest X-ray findings consistent with pneumonia, and one or more of the following signs and symptoms: cough, purulent sputum, change in sputum characteristics, dyspnea, tachypnea, cyanosis and auscultation evidence of pulmonary consolidation (dullness, crepitation, bronchial breathing) or changes in complete blood count, especially neutropenia. Cases were identified in Malaysian pilgrims admitted to Malaysian hospitals. Controls were those with no stated clinical symptoms and were drawn from Malaysian pilgrims staying in local accommodations.

The sample size was calculated based on a type I error set at 5% (95% confidence level), a power of 80%, and a case-to-control ratio of 1:4. The percentage of controls exposed to pneumonia was deemed, based on estimation from the previous episodes of pneumonia occurred among Malaysian pilgrims, to be 15% and odds ratio (OR) to be detected was two. By using Open Epi software version 7, the calculated sample size was 570. After considering a non-response rate of 20%, the required sample size was increased to 684 participants.

Cases were selected among those admitted and diagnosed to have CAP by systematic random sampling from the admission list in Malaysian hospitals. Controls were selected by simple random sampling from lists of Malaysian Hajj pilgrims staying in the same accommodation and at the same floor with the selected cases. Controls were then followed up by home visit or telephone call for two weeks after returning to Malaysia in order to exclude episodes of pneumonia infection<sup>5</sup>.

Identification of cases and controls was undertaken from September 2012 to January 2013. Demographic data were obtained from the Pilgrims Health Information System (PHIS), Tabung Haji, Malaysia, and data on risk factors were gathered through face-to-face interviews by attending physicians using structured questionnaires. A written informed consent was obtained from all participants prior to interview. Known risk factors and preventive measures for CAP, including prior vaccination, wearing a face mask and taking oral multivitamin, food and volume of water intake, were selected for analysis.

Collected data were entered into the PHIS system by the attending physicians. All data from the PHIS were

exported to statistical databases for analysis. Descriptive analyses were performed and univariate analysis conducted using binary logistic regression. Variables having a p-value less than 0.25 from the univariate analysis were included in the initial multivariate logistic regression model. Variables were then selected by a forward-and-stepwise method to arrive at the final model. Multicollinearity and interaction terms were checked, and the Hosmer-Lemeshow test, classification table and ROC curve were applied to check the model fitness. The strength of association for each risk factor was assessed using crude and adjusted odds ratios (AOR).

This study had been registered with the Malaysian National Medical Research Register (NMRR-11-1000-10694) and approved by the Medical Research Ethics Committee Malaysia.

## Results

### Descriptive Analysis

The study recruited 108 peoples with pneumonia and 673 unmatched controls among Malaysian pilgrims. Most of the cases (57.4%) were males. The mean age was 68.2 years for cases (range 50-85 years) and 51.3 years for controls (range 24-81 years). Most (81.1%) of the pilgrims lived at accommodations more than 700 m from the Great Mosque of Mecca (Masjid al Haram). Upper respiratory tract infection (URTI) was observed among most of the cases (79.6%) and the controls (69.2%). Pneumococcal vaccination was received in 27.8% of cases and 38.0% of controls. Most of the controls (83.8%) wore a clinical mask as a preventive measure while only 58.3% of cases used the mask. Low multivitamin (21.3%) and adequate water (20.4%) intakes were found among cases as compared to multivitamin (66.3%) and water (67.0%) intake among the controls (Table 1).

### Univariate Analysis

Statistically significant and positive associations were observed for increasing age (OR = 36.1, 95% CI = 20.5-63.4 for age 60 and above) and distance from the pilgrim's hotel to the Masjid al Haram mosque between 800-899 m (OR = 5.1, 95% CI = 1.8-14.7). Pre-existing medical conditions, including diabetes mellitus, tuberculosis, asthma/chronic obstructive airway disease (COAD), congestive cardiac failure (CCF), hypertension and end stage renal failure were also revealed as significant risk factors. Pneumococcal vaccination, wearing a facemask, intake of supplemental multivitamin and intake of extra food in addition to food served by Hajj organizers, and drinking more than three liters of water per day were significantly associated with reduced risk of CAP (Table 2).

**Table 1. Distribution of cases and controls among Malaysian pilgrims performing the Hajj in 2012**

Factor	Cases (n=108)		Controls (n=673)	
	Number	Percent	Number	Percent
<b>Gender</b>				
Male	62	57.4	333	49.5
Female	46	42.6	340	50.5
<b>Age group (year)</b>				
≤50	2	1.9	292	43.4
>50-60	24	22.2	321	47.7
>60-70	36	33.3	52	7.7
>70-80	38	35.2	7	1.0
>80	8	7.4	1	0.1
<b>State of residence</b>				
Johor	15	13.9	22	3.3
Kedah	11	10.2	79	11.7
Kelantan	8	7.4	80	11.9
Kuala Lumpur	6	5.6	43	6.4
Melaka	4	3.7	37	5.5
Negeri Sembilan	3	2.8	54	8.0
Pahang	10	9.3	42	6.2
Perak	13	12.0	74	11.0
Perlis	3	2.8	17	2.5
Pulau Pinang	3	2.8	35	5.2
Sabah	4	3.7	22	3.3
Sarawak	1	0.9	19	2.8
Selangor	21	19.4	80	11.9
Terengganu	6	5.6	69	10.3
<b>Distance from hotel to Masjid al Haram (meter)</b>				
Less than 600	5	6.3	89	12.3
600-699	4	5.1	50	7.4
700-799	38	48.1	300	44.6
800-899	18	22.8	58	8.6
900-999	10	12.7	125	18.6
≥1000	4	5.1	57	8.5
<b>Pre-existing medical conditions and risk related behavior</b>				
Diabetes mellitus	34	31.5	96	14.3
Tuberculosis	8	7.4	1	0.1
Asthma/Chronic obstructive airway disease	30	27.8	35	5.2
Congestive cardiac failure	20	18.5	16	2.4
Hypertension	63	58.3	146	21.7
End stage renal failure	4	3.7	2	0.3
Splenectomy	3	2.8	6	0.9
Upper respiratory tract infection	86	79.6	466	69.2
Smoking	10	9.3	45	6.7
<b>Preventive measures</b>				
Vaccination (pneumococcal)	30	27.8	25.6	38.0
Wearing mask	63	58.3	56.4	83.8
Multivitamin intake	23	21.3	44.6	66.3
Additional food intake	67	62.0	57.1	84.8
Water intake (>3 liters)	22	20.4	45.1	67.0

**Table 2. Univariate analysis of the risk factors associated with community-acquired pneumonia among Malaysian pilgrims performing the Hajj in 2012**

Factor	Odds ratio	95% CI	P-value	
Gender				
Male	1.4	0.9	2.1	0.1
Age group (year)				
≤50	Ref			
>50-60	10.9	2.6	46.6	0.001
>60-70	101.1	23.6	432.7	<0.001
>70-80	792.6	158.8	3954.8	<0.001
>80	1168.0	95.8	14244.9	<0.001
Distance from hotel to Masjid al Haram (meter)				
Less than 600	Ref			
600-699	1.3	0.3	5.2	>0.05
700-799	2.1	0.8	5.6	>0.05
800-899	5.1	1.8	14.7	0.002
900-999	1.3	0.4	4.0	>0.05
1000 and above	1.2	0.3	4.5	>0.05
Pre-existing medical conditions and risk related behavior				
Diabetes Mellitus	2.8	1.7	4.4	<0.001
Tuberculosis	53.8	6.7	434.4	<0.001
Asthma/Chronic obstructive airways disease	7.0	4.1	12.1	<0.001
Congestive cardiac failure	9.3	4.7	18.9	<0.001
Hypertension	5.1	3.3	7.7	<0.001
End stage renal failure	12.9	2.3	71.3	<0.001
Splenuctomy	3.2	0.8	13.0	>0.05
Upper respiratory tract infection	1.7	1.1	2.8	0.028
Smoking	1.4	0.7	2.9	>0.05
Preventive Measures				
Vaccination (pneumococcal)	0.6	0.4	0.9	0.040
Wearing mask	0.3	0.2	0.4	<0.001
Multivitamin intake	0.1	0.1	0.2	<0.001
Additional food intake	0.3	0.2	0.5	<0.001
Water intake (>3 liters)	0.1	0.1	0.3	<0.001

### Multivariate Analysis

The multivariate analysis showed significantly increased risk of CAP with age 60 years or more (AOR = 20.2, 95% CI = 10.6-38.3) and with asthma/COAD (AOR = 5.9, 95% CI = 2.4-14.7) and CCF (AOR = 5.4, 95% CI = 2.0-14.7). Intake of water more than three liters per day (AOR = 0.2, 95% CI = 0.9-0.4) and supplemental multivitamin (AOR = 0.2, 95% CI = 0.9-0.5) were independently associated with a significantly reduced risk of CAP (Table 3).

The final model was checked for multicollinearity using the correlation estimates and standard errors found to be relatively small for age, CCF and asthma/COAD. With ROC curve applied to check the model fitness, the area under the curve (AUC) was more than 80%, with AUC 0.93, p-value less than 0.05, cut-off point at age 58.5 years produced (1-specificity) 0.13 and sensitivity 0.84.

**Table 3. Adjusted odds ratios of factors associated with community-acquired pneumonia among Malaysian pilgrims performing the Hajj in 2012**

Risk factor	Adjusted odds ratio	95% CI
Age (≥60 years)	20.2	10.6-38.3
Water intake (≥3 liters)	0.2	0.9-0.4
Multivitamin intake	0.2	0.9-0.5
Asthma/chronic obstructive airway disease	5.9	2.4-14.7
Congestive cardiac failure	5.4	2.0-14.7

Remark: Odds ratio was adjusted for all variables.

### Discussion

In this study of Hajj pilgrims from Malaysia, we identified several risk factors for CAP, including age 60 years and above, and pre-existing conditions of asthma/COAD, CCF and hypertension. In addition, we

identified significant protective factors, including intake of water more than three liters per day and intake one tablet of supplemental multivitamin on daily basis. Education on importance of health screening, health examination, vaccination, daily water intake and nutritional supplements was provided to the pilgrims before leaving to Saudi Arabia. This played an important role in helping them to lessen the risk of getting CAP during the Hajj season.

In our study, the likelihood of acquiring CAP rose with increasing age, a result consistent with other studies of Hajj pilgrims<sup>12,17,18</sup>, and was especially high in pilgrims aged 60 years or more and with underlying cardiorespiratory illnesses such as asthma/COAD, CCF and hypertension. Most of the Malaysian Hajj pilgrims were aged more than 50 years and most of them had at least one pre-existing medical condition or chronic disease such as diabetes, hypertension or heart diseases. During the pilgrimage, pilgrims must be physically fit to do all related activities.<sup>5</sup> One of the physical activities is walking to the Masjid al Haram mosque. We noticed that pilgrim's accommodations were generally quite far away from the mosque (more than 700m). Some of the pilgrims might be exhausted after several trips to and from the mosque, and thus, might have increased the risk of acquiring CAP. The compulsory health screening and examinations for the Malaysian pilgrims evaluates their fitness to travel and participate in the Hajj activities. In addition, health information and vaccinations are given during their health examination<sup>19</sup>. Those diagnosed to have any illnesses are managed accordingly. If the process of management needs a longer time, they are advised to postpone the trip and reapply when their conditions were satisfactory, fit to travel and physically able to perform the Hajj activities in the future<sup>19</sup>.

Although the health status of pilgrims participating in the Hajj is typically satisfactory prior to departure, the sudden change of environment may increase the susceptibility of some pilgrims to acquire respiratory diseases.<sup>3,5,6,7</sup> The changing environment is related to overcrowding and congested conditions in the mosques where the situation creates the possibility of exposing them to diseases via the respiratory system.<sup>3,8,19</sup> Their situation worsens with some activities related to ongoing construction work and renovation of the mosque, indirectly contributing to the air pollution. These situations might also contribute to an increased risk of CAP among those who had history of asthma or COAD.<sup>20</sup> The risk could be higher when they are not taking any extra preventive measures such as wearing a protective face mask<sup>5,16</sup>. As we found, pilgrims were more prone to develop CAP if they had pre-existing

medical conditions. It is possible that these vulnerable individuals might have sustained CAP from the changing environment, depending on their daily activities or attitudes towards taking care of their own health<sup>21</sup>.

Prolonged exposure to sunlight and excessive heat may cause dehydration and increase vulnerability to infection,<sup>1,5</sup> including URTI and pneumonia, which if not treated promptly, can become severe<sup>7,17</sup>. We found that intake of three or more liter of water per day was associated with a reduced risk of CAP<sup>22</sup>. Another protective factor was intake of supplementary multivitamin. Medical screening of pilgrims prior to departure did not typically include evaluation of nutritional status, and/or presence of vitamin deficiencies and related conditions. Pilgrims were provided with two meals, namely lunch and dinner, and were given a choice to buy other foods which are readily accessible. The suggestion that multivitamin could play an important role in preventing pneumonia merits further research. Since multivitamins are proactively provided to all pilgrims, declining intake could be indirectly linked to other important health behaviors that could influence acquisition of CAP.

In this study, we assumed that all the pilgrims were physically well before departing for Saudi Arabia since they were declared medically fit to travel. We also observed that there were no cases of pneumonia or any pneumonia-related hospital admissions among those staying in Medina during eight days before moving to Mecca. Respiratory diseases have also been described as the most common cause for hospital admission during the Hajj.<sup>8,20,17,23</sup> Known organisms found in some studies included *Klebsiella pneumoniae*, *Hemophilus influenzae*, *Streptococcus pneumoniae*, and *Mycobacterium tuberculosis*.<sup>19,24,25</sup> Influenza<sup>5,6</sup> and pneumococcal vaccines are two alternative vaccines recommended for the pilgrims by the Ministry of Health, Malaysia.<sup>19,26,27</sup> Since neither of these vaccines are compulsory, there is no official documentation to confirm whether the pilgrims have received the vaccinations. In addition, the vaccines are only available at private health facilities.

### Limitations

One of the main limitations of our study was that no laboratory support was available to differentiate the organisms causing pneumonia. As eligible non-cases were all willing to respond to the study, data were collected from more controls than we had planned. Since people who needed further investigations were referred to Arab hospitals for further management, the treatment outcome of those people were not be able to retrieve.

## Public Health Action and Recommendations

Hajj is an example of a mass gathering and CAP is one of the important infectious diseases that are associated with mass gatherings. Though no death was identified among the respondents, reduction of mortality and morbidity associated with CAP was possible via appropriate preventive measures as suggested by results in this study. High risk groups included those who are aged 60 years or over, and those with comorbidities such as asthma, COAD and CCF. These groups were advised to strictly follow health management, perform merely the essential Hajj activities, drink the appropriate amount of water and take supplementary multivitamin.

## Conclusion

Association of CAP with the risk factors found in this study might be useful for implementing preventive measures during the Hajj pilgrimage. The risk of getting CAP could be reduced in pilgrims who were aged 60 years or more and those with co-morbidities if they supplemented their diet with multivitamin, kept well hydrated, and strictly followed advice by health authorities.

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