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Influenza Prevalence and Risk Factors: A Population-Based Cross-Sectional Study

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Abstract

Background: Influenza infection can lead to mortality and morbidity. In densely populated Kuala Lumpur, Malaysia, the transmission of influenza-like illness (ILI) is high. This study assessed the prevalence and epidemiology of influenza in the target population.

Methods: A cross-sectional convenience sample study was conducted in government clinics of Cheras, Malaysia, from November 1, 2022, to February 28, 2023. Consent was sought from patients older than 18 years with symptoms of ILI (fever, cough, and onset within 10 days). A nasopharyngeal swab preceded an influenza rapid test. Logistic regression was used in SPSS 22.0 to evaluate the data.

Results: Among 438 patients, 55 (12.6%) tested positive for influenza type B, 9 (2%) tested positive for type A, and 374 (85.4%) were negative. Patients in the group that was 10 years older than the younger group had 1.47 times the odds of having influenza. The odds of positive influenza rose 1.133 times per unit of body mass index (BMI). Patients with chronic lung illness were 6.7 times (95% confidence interval, 2.742–16.287) more likely to test positive for influenza. Sex and smoking history did not affect the rate of influenza infection ($p > 0.05$).

Conclusions: An association was found between age, BMI, and chronic lung disease with influenza infection but not with sex or smoking.

Keywords: influenza, prevalence, public health, respiratory infection

INTRODUCTION

Viral respiratory infection is recognized as a public health concern likely to result in an increase in morbidity and mortality. Seasonal influenza–associated respiratory infection accounts for an estimated 300,000 to 650,000 deaths worldwide. Sub-Saharan Africa has the highest estimated mortality rate (EMR) of 2.8 to 16.5 per 100,000 individuals, followed by Southeast Asia, which has the second highest EMR of 3.5 to 9.2 per 100,000 individuals. Age-specific EMR is highest among those >75 years old, in whom rates were found to be 51.3 to 99.4 per 100,000 individuals for the year 2018.[1,2] Common organisms causing respiratory infections are rhinovirus (34%), coronavirus (14%), influenza (9%), bacteria (8%), and respiratory syncytial virus (4%). Although influenza is the third most common organism, 37.9% of influenza patients with the illness require consultation, which is higher than among patients with rhinovirus (17.6%) or coronavirus (17.6%)[3]. Previous studies reported that 26% to 37.9% of patients with influenza presented with influenza-like illness (ILI) to outpatient clinics, and 6% to 14% were admitted due to pneumonia in Southeast Asian countries.[3–5] Environmental and host (nonenvironmental) factors contribute to the spread of infection among humans. Environmental factors that contribute to the increase in the spread of respiratory viral infections include rainfall, humidity, ground temperature, particulate matter, and airflow. Nonenvironmental (host) factors that lead to infectivity and complications after respiratory virus infection include patient age, sex, smoking history, body mass index (BMI), socioeconomic status, underlying comorbidities, and immunocompromise.[4,8,9]

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Malaysia is a country in Southeast Asia with a population of 32.6 million. It is a middle-income country with a gross national income per capita of USD 10,209 in 2020.[10] The second most common cause of death in Malaysia is lower respiratory tract infections, with total deaths of 23,477 and an age-standardized death rate of 90.22 in the year 2020. Worldwide, Malaysia ranked 33rd for death due to lower respiratory tract infections in 2020.[11] Studies conducted in Malaysia have shown that influenza A is more predominant, followed by influenza B.[9,12–14] In Malaysia, the H1N1 pandemic of 2009 and the COVID-19 pandemic of 2020–2022 raised awareness among the public and health care workers regarding the severity of respiratory viral illness and the importance of prevention. Kuala Lumpur, being the capital city of Malaysia, has a high population density and therefore higher risk of ILI spread. Unfortunately, only a few epidemiological studies have been conducted on influenza in Malaysia. An adult study was performed in Sarawak, Malaysia, in 2019 and a pediatric study in Sabah, Malaysia, in 2022. Obtaining the most up-to-date data on prevalence is essential for public health workers to carry out control and prevention programs. Thus, to address this gap, we conducted a study investigating the prevalence and epidemiology of influenza among the population of Cheras, Kuala Lumpur, using data from patients with ILI who presented to health clinics. The findings of this study will be useful and applicable to other countries and populations with similar distributions as Cheras.

METHODS

This study was approved by the Ministry of Health Medical Research Ethics Committee (NMRR ID-22-01287). We conducted a cross-sectional study in Cheras, Kuala Lumpur, Malaysia, which is under the administration of the Department of Health of Federal Territory Kuala Lumpur & Putrajaya. Cheras has a population density of 7,913/km^2, making it a suitable site.[10] The population of interest comprised adults who sought treatment for ILI in government clinics of Cheras Health District. The study was conducted for a period of 4 months beginning from November 1, 2022, until February 28, 2023. We calculated a sample size of 163 using a web-based sample size calculator (Statulator) estimating for a single proportion, with a 95% confidence level, precision of 0.05, and expected proportion of influenza of 11.9%.[14] With an add-on 20% drop rate to 163 samples, the sample size required was 196. We performed convenience sampling for patients who presented to these clinics. However, this leads to accessibility bias, as patients who did not present to the government clinics in Cheras were not included in this study.

The inclusion criteria were age greater than 18 years and a diagnosis of ILI by the treating physician. In Malaysia, the diagnosis of ILI is based on the guidelines of the World Health Organization, which include a fever of ≥ 38 °C, cough, and onset within the past 10 days.[11] This study focuses on only adult patients; pediatric patients were not included because their risk factors are different than that of adults. Patients who were not keen to participate in this study were excluded. The patient's influenza vaccination history was not explored in this study.

Informed consent was obtained from the identified patients before the clinical samples were collected. Participants were provided an explanation of the sample collection method (nasopharyngeal swabbing technique), informed of complications of the procedures, and advised how the collected information will be reported. Patients were subjected to nasopharyngeal swabbing, whereby the sample was taken by a health care professional. The sample was then subjected to an influenza rapid test, which was done on site. The kit used was the QuickVue Influenza A+B test, which had 94% sensitivity and 90% specificity for influenza A and 70% sensitivity and 97% specificity for influenza B.[15] For each patient, we gathered information such as age, sex, BMI, smoking history, and presence of an underlying chronic lung disease. The results of these clinical samples were recorded in an Excel spreadsheet.

We then analyzed these data to study the prevalence of influenza virus infection among patients with ILI based on their demographics. The prevalence in this study was defined as the number of patients diagnosed with ILI found to be influenza positive, divided by the total number of patients diagnosed with ILI. Categorical data were described by frequency (%) and continuous variables by mean and standard deviation.

We used the Statistical Package for Social Sciences 22.0 (IBM Corporation, Armonk, NY, USA) to analyze the data. We performed a binary logistic regression to estimate the relationship between variables age, sex, BMI, smoking history, and presence of chronic lung disease with the outcome variable (influenza or noninfluenza). Goodness-of-fit statistics were used to determine whether this model adequately described the data. First, the Omnibus test of model coefficients was used to test the model's fit. The Hosmer and Lemeshow test result of >0.05 indicated a good fit (i.e., no difference between the observed and predicted model). Regression estimates, p value, odds ratio (OR), and 95% confidence interval (CI) from large-sample Wald confidence intervals were calculated for each variable. A p value of 0.05 (two-sided) indicated statistical significance.

RESULTS

We collected a total of 438 samples from patients who presented with ILI to the government health clinic in Cheras district during the 4-month period from November 1, 2022, until February 28, 2023. Table 1 shows the demographic characteristics of the patients involved in this study. The mean age of these patients was 35.28 years, with a standard deviation of 12.94. There were 223 males, accounting for 50.9% of the total sample, and 215 females (49.1%). The mean BMI of the sampled patients was 25.67 kg/m^2 with a standard deviation of 4.68. Based on smoking history, 26 (5.9%) patients were active smokers, 86 (19.6%) were former smokers (patients who smoked any form of cigarettes in the past, irrespective of duration, and who had quit smoking at the time of this study), and 326 (74.4%) were nonsmokers. Patients were also asked if they had underlying chronic lung diseases such as asthma, chronic obstructive pulmonary disease (COPD), lung cancer, tuberculosis, lung fibrosis, or other lung conditions. Of the patients, 27 (6.2%) had underlying chronic lung disease, whereas 411 (93.8%) patients did not have any underlying lung conditions (Table 1).

Of the 438 patients, 9 (2%) tested positive for influenza type A, 55 (12.6%) tested positive for influenza type B, and 374 (85.4%) tested negative for influenza. The prevalence (95% CI) for influenza type A was 2% (binomial CI: 0.9%–3.8%; normal approximation CI: 0.7%–3.3%). On the other hand, the prevalence (95% CI) for influenza type B was 12.6% (binomial CI: 9.6%–16%; normal approximation CI: 9.5%–15.7%). The prevalence of no influenza was 85.4% (binomial CI: 81.7%–88.6%; normal approximation CI: 82.1%–88.7%). The mean age of patients with no influenza was 34 years as compared with 43 years for influenza-positive patients. The mean BMI of influenza-positive patients was 28.7 kg/m^2, whereas that of patients without influenza was 25.2 kg/m^2. Among the 64 patients who were influenza positive, 39 (60.9%) were male and 25 (39.1%) were female. Nonsmokers accounted for most of the influenza-positive patients (42 [65.6%]), followed by active smokers (16 [25%]) and former smokers (6 [9.4%]). We also found that 49 (76.6%) of the influenza-positive patients did not have an underlying chronic lung condition, whereas 15 (23.4%) of them did (Table 2).

We performed univariate logistic regression. Using SPSS, patients who tested positive for influenza were classified as 1, whereas patients who tested negative for influenza were classified as 0. The relationship between the predictors and the outcome is shown in the the logistic regression table with the variables in the equation. Age and BMI were kept as numerical variables, as the “linear in logit” assumption was satisfied. Based on the logistic regression table, we found that the variables that had significant value were age, BMI, and underlying chronic lung disease. Sex and smoking history were found to be nonsignificant (Table 3).

Subsequently, we performed multiple logistic regression using the variables age, BMI, and underlying chronic lung disease. The variables sex and smoking history were removed. The deviance of goodness-of-fit was 1.000 (a value >0.05), showing that this multiple logistic regression model was a good fit. Nagelkerke’s R^2 showed a value of 0.23, indicating that the 23% change in the criterion variable could be accounted for by the predictor variables in the model. The classification table showed that the specificity for this model was 98.1%. The overall accuracy rate was 86.3%. The model-fitting information then showed lower values of Akaike information criterion (AIC) and Bayesian information criterion (BIC) when the nonsignificant variables (sex and smoking history) were removed (AIC: 293.3, BIC: 309.6) as compared with when all five independent variables were included (AIC: 303.4, BIC: 331.9), which indicates a better fit of the model. We found all three variables to be significant and then calculated their adjusted ORs (Table 4). The group that was 10 years older than the younger group had 1.47 (1.039^{10} = 1.52) times the odds of having influenza. On the other hand, a unit rise in BMI increased the likelihood of having positive influenza 1.133 times. For patients with underlying chronic lung illness, the adjusted OR was 6.683, with a 95% CI of 2.742 to 16.287. A patient with an underlying chronic lung disease had a 6.7 times greater chance of testing positive for influenza than those without lung disease (Table 4).

TABLE 1. Demographic status of the patients

Variable	N	%
Number of patients	438	
Age, years		
Mean ± SD	35.28 ±12.94	
Median (Q1–Q3)	32 (25–42)	
Gender		
Male	223	50.9
Female	215	49.1
BMI		
Mean ± SD	25.67 ± 4.68	
Median (Q1–Q3)	25.5 (22.45–28)	
Smoking history		
Nonsmoker	326	74.4
Former smoker	26	5.9
Active smoker	86	19.6
Chronic lung disease		
Absent	411	93.8
Present	27	6.2

TABLE 2. Descriptive data of the patients with influenza

Variable	Influenza negative	Influenza positive
	N (%)	N (%)
Sample size	374 (85.4)	64 (14.6)
Gender		
Female	190 (50.8)	25 (39.1)
Male	184 (49.2)	39 (60.9)
Smoking history		
Nonsmoker	284 (75.9)	42 (65.6)
Former smoker	20 (5.3)	6 (9.4)
Active smoker	70 (18.7)	16 (25.0)
Chronic lung disease		
Absent	362 (96.8)	49 (76.6)
Present	12 (3.2)	15 (23.4)

TABLE 3. Univariate logistic regression: Variables in the equation

Variable	Wald statistic	Unadjusted OR	95% Confidence interval for unadjusted OR		*p*
			Lower bound	Upper bound	
Age	14.876	1.043	1.021	1.065	<0.001
Sex					
Female	*Ref*				
Male	3.145	1.894	0.935	3.837	0.076
BMI	16.014	1.133	1.066	1.204	<0.001
Lung disease					
No	*Ref*				
Yes	17.290	6.706	2.735	16.443	<0.001
Smoking history					
Nonsmoker	*Ref*				
Former smoker	0.119	1.226	0.384	3.915	0.731
Active smoker	0.070	1.112	0.508	2.435	0.791

TABLE 4. Multiple logistic regression: Parameter estimates

Variable	Wald statistic	Adjusted OR	95% Confidence interval for adjusted OR		*p*
			Lower bound	Upper bound	
Age	13.036	1.039	1.018	1.060	<0.001
BMI	16.328	1.133	1.067	1.204	<0.001
Lung disease					
No	*Ref*				
Yes	17.471	6.683	2.742	16.287	<0.001

Based on the tests performed in SPSS, the model-fitting information showed higher values of AIC and BIC when the interactions were done (AIC: 296.7, BIC: 325.2) as compared with when no interactions with variables were done (AIC: 293.3, BIC: 309.6). The deviance of goodness-of-fit was 1.000 (a value greater than 0.05), showing that this multiple logistic regression model had a good fit. We found that, when these variables interacted, all possible interactions were not statistically significant.

DISCUSSION

In this study, we found that age, BMI, and underlying chronic lung conditions were associated with influenza infection among adult patients. These findings are consistent with other studies, in which older persons were found to be at a higher risk of getting infected by respiratory infections and of ending up with complications and mortality. The age-specific EMR was highest among the population older than 75 years, whereby the rates were found to be 51.3 to 99.4 per 100,000 individuals for the year 2018.[1,2] In one study, the authors reported that influenza-associated hospitalization among patients older than 75 years was 47 times higher than that among patients who were aged 25 to 44 years.[16] Adults' immune systems deteriorate as they age, making them more vulnerable to illnesses such as influenza. This drop in immune function could be related to a decrease in immune cell generation or a decrease in the ability of immune cells to operate appropriately.[17] According to the Centers of Disease Control and Prevention, older people are more likely to develop complications, have severe and prolonged disease, and have a higher mortality rate.[8] However, we did not explore those outcomes in this study.

One of the key findings of this paper was that an increase in BMI causes an increase in the odds of having an influenza infection. Research has been conducted on the association between obesity and rate of respiratory infection. In a study conducted in Italy during the COVID-19 pandemic, the authors found that a BMI of >30 kg/m^2 was associated with a higher rate of severe illness. A BMI of >30 kg/m^2 was also associated with a higher rate of mortality following complications of COVID-19.[18] This finding was similar for other respiratory infections, whereby a BMI of >30 kg/m^2 was associated with higher morbidity and hospitalization following respiratory tract infections.[19] A systematic review and meta-analysis found that obese people had a considerably increased risk of influenza infection and hospitalization due to influenza.[20] In addition, according to another study, obese vaccinated persons also had an increased risk of influenza infection as compared with nonobese vaccinated persons.[21]

In this study, we found that the odds of a patient with an underlying chronic lung disease testing positive for influenza were 6.7 times higher than those without a lung disease. These findings were also similar to the results of other studies, which reported that certain medical conditions, such as asthma, COPD, and cystic fibrosis, had a higher association with influenza and that those patients might also develop complications.[8,9,14,22] In a recent study, it was found that, regardless of age or smoking status, patients with COPD had an elevated risk of respiratory illness–related hospitalization during influenza outbreaks.[23] Many studies have found exacerbations of COPD to be frequently caused by influenza. These exacerbations were linked to worsening airflow obstruction, hospitalization, decreased quality of life, progression of disease, death, and, ultimately, significant health care–related expenses.[24]

The statistical analysis for the present study did not support the hypothesis of previous studies, whereby many studies showed an association between smoking and influenza infection[25,26] and the influence of sex on influenza infection.[11,27] In this study, however, we found no link between sex or smoking and getting the flu. We found that more males (50.9%) were infected with influenza as compared with females (49.1%). However, after we performed logistic regression, we found no significant association between influenza infection rate and sex. On the other hand, based on other previous empirical studies, women of reproductive age have a greater incidence of influenza and influenza-related hospitalizations than men of the same age do, although this pattern reverses before puberty and at older ages.[11] The possible reason why smoking did not exhibit and an association with influenza is that patients self-reported their smoking status, and underreporting or misreporting of smoking behaviors might have occurred, which could lead to bias in these results. In addition, we did not study other confounding variables such as type of housing, income, and number of persons in a household. In addition, patients were not matched in terms of age, BMI, or underlying health conditions to study the effect of smoking and sex, respectively, on influenza infection rates.

This is the first study conducted in Kuala Lumpur, Malaysia, after the COVID-19 pandemic to examine the prevalence of influenza among patients with ILI and their demographics. It allows us to gain a deeper understanding of influenza and facilitates future research, particularly in the area of influenza prevention. This study is limited by the fact that smoking history was self-reported, resulting in bias, and uncontrolled confounding variables such as type of housing, income, and number of persons in a household were not studied here. Because we included only patients who presented themselves to the clinics, there is a potential accessibility bias, thus making it as one of our limitations. We also did not study the patients' other underlying chronic diseases (diabetes mellitus, stroke, and other medical conditions) or history of influenza vaccination. In addition, we selected only those patients who presented to government clinics in the Cheras Health District; patients attending private clinic were excluded. In light of the study's objectives, it is imperative to approach the interpretation of the results with caution, considering the limitations inherent in the convenience sampling method used and other risk factors (patients' underlying medical illness) not being explored. The findings of this study can be used to understand the prevalence of ILI in other countries/areas with a similar tropical climate and population with a similar distribution as Cheras.

CONCLUSIONS

The aim of this study was to determine the prevalence and epidemiological characteristics of influenza among the target population. We found that among this study population, 12.6% tested positive for influenza type B, 2% tested positive for influenza type A, and 85.4% tested negative for influenza. This study provides evidence that influenza contributes to ILI cases in the Cheras population, whereby there is an association between age, BMI, and underlying chronic lung condition with influenza infection; however, there was no significant association between sex or smoking with influenza infection. Findings of this study will also be useful for other countries and populations with similar population distributions as Cheras. Therefore, we recommend the use of rapid influenza testing kits in health care facilities and other private clinics. This will aid in the early detection of influenza and the reduction in morbidity and mortality following influenza infection, especially among those with risk factors. Future surveillance of influenza virus molecular characterization will provide a greater understanding of influenza within the community.

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CONFLICT OF INTEREST

None declared.

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