PUBLIC HEALTH RESEARCH

Factors Associated with Asymptomatic COVID-19 Patients in Petaling District, Selangor, Malaysia

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ABSTRACT

Introduction	The rapid spread of the Coronavirus disease 2019 (COVID-19) worldwide has led the World Health Organization to declare COVID-19 outbreak as a pandemic on March 11, 2020. As the local studies on factors leading to the absence or presence of clinical illness among the COVID-19 cases are sparse, the study aims to determine the factors associated with asymptomatic COVID-19 patients in Petaling District, Selangor, Malaysia.
Methods	Data on COVID-19 patients were extracted from the database of confirmed cases in Petaling District Health Office, Selangor, Malaysia from 3rd February 2020 to 30th April 2020. An asymptomatic laboratory-confirmed case is a person infected with COVID-19 who does not develop any symptoms. The study included socio-demographic variables, the detailed information on clinical manifestations and co-morbidity of the patients. Descriptive and multiple logistic regression analyses were conducted to determine the factors associated with asymptomatic patients.
Results	The overall COVID-19 patients in Petaling District were 434. Approximately 70% *(n= 292)* of the patients were symptomatic while 32.7% *(n= 142)* were asymptomatic. Multivple logistic regression analyses revealed that factors significantly associated with asymptomatic patients were age below 40 years old (aOR: 1.79, 95% CI 1.11, 2.86), non-Malaysians (aOR: 3.22, 95% CI 1.44, 7.19) and local cases (aOR: 2.51, 95% CI 1.42, 4.42). Gender, ethnicity, co-morbidity and township were not significantly associated with asymptomatic patients.
Conclusions	Approximately one-third of COVID-19 patients were asymptomatic and the risk factors identified were younger age, non-Malaysians and local cases. Rigorous epidemiological investigation is helpful in identifying COVID-19 cases among these group of people who are asymptomatic.
Keywords	COVID-19 - Asymptomatic - Pandemic – Malaysia.

INTRODUCTION

In late December 2019, a first case of unidentified pneumonia was reported in Wuhan, Hubei, China and thereafter, the number of reported cases with the same clinical characteristics had rapidly increased in Wuhan as well as other parts of the world.[1,2] The investigation revealed that this unidentified disease was caused by a member of the family of coronaviruses and the investigators had named this unidentified pneumonia disease as novel coronavirus pneumonia.[3] Later, the World Health Organization (WHO) renamed the disease as coronavirus disease 2019 or COVID-19.[4] As of March 3rd 2020, the WHO reported that a total of 67,217 and 13,087 confirmed cases have been detected in the Hubei Province and in other 34 provinces in China, respectively.[5] Thereafter, the positive cases and deaths increased rapidly with major outbreaks reported in South Korea, Italy, Iran, the United States and more than 50 other countries.[6] This phenomena had sparked a global alarm, leading an expert to postulate that the morbidity might infect 40-70% of the global population in the coming years.[7] The rapid spread of the disease unabated worldwide which may endanger the health of large number of people had lead the WHO to declare COVID-19 as a pandemic on March 11, 2020 and has urged all affected countries to take urgent and aggressive action to control this pandemic.[8]

In COVID-19, some people are more vulnerable to the virus than others, it is capable of putting people of any age into a critical condition. The most common symptoms of this highly contagious virus are fever, dry cough, and tiredness. Other less common symptoms include aches and pains, nasal congestion, headache, conjunctivitis, sore throat, diarrhea, loss of taste or smell. These symptoms are usually mild and the majority of this cases have spontaneously recovered.[9] However, a few people especially older people, and those with underlying medical problems like high blood pressure, heart and lung problems, diabetes, or cancer, are at a higher risk of developing serious illness such as severe pneumonia, pulmonary oedema, acute respiratory distress syndrome, or multiple organ failure.[10] According to Wu et al,[11] about 80% of the symptomatic COVID-19 cases will remain mild and relatively well, whereas about 15% will develop more severe disease and the remaining 5% may require critical care.

The spread of the virus by symptomatic cases is well documented.[8-11] However, the virus can also be asymptomatic, causing no noticeable illness in some people and this asymptomatic people are the potential sources of COVID-19 infection to other healthy population due to the viral loads in their respiratory secretions could be as high as those from symptomatic cases.[12,13] Normally, most asymptomatic infections do not seek medical assistance due to no obvious clinical signs and poor prevention awareness, which contribute to the rapid spread of disease.[14] There is mixed evidence on the proportion of people that are asymptomatic and a few studies revealed the asymptomatic cases can be as high as 80% and some of this asymptomatic patients will become symptomatic over the next few days or weeks.[15-18] Studies on factors leading to the absence or presence of clinical illness among the COVID-19 cases are sparse. In the absence of immunisation and proactive testing strategies, a large portion of the population may remain susceptible to COVID-19 infection.

In view of the above scenario, a comprehensive study is warranted to provide relevant information on the factors associated with asymptomatic COVID-19 cases. The findings of this study may assist the relevant health authorities in disease control and prevention measures. Thus, this study aims to determine the factors associated with asymptomatic COVID-19 patients in Petaling District, Selangor, Malaysia.

METHODS

This cross-sectional study was conducted from February 2020 to April 2020 in Petaling District Health Office, Selangor, Malaysia. The data was extracted from 3rd February 2020 to 30th April 2020 in the Petaling District Health Office database. A confirmed COVID-19 patient was defined as a positive result of naso-pharyngeal samples using laboratory-based Polymerase chain reaction (PCR) test. A symptomatic COVID-19 patient is a person who has developed symptoms compatible with COVID-19 virus infection. While, an asymptomatic laboratory confirmed patient is a person infected with COVID-19 but does not develop any symptoms.[5]

There were seven socio-demographic variables included in this study; sex (male, female), age (<40 years and ≥ 40 years old), ethnicity (Malays, non-Malay), citizenship (Malaysian, non-Malaysian), transmission (local,imported cases); township (Petaling, Sungai Buloh, Damansara, Bukit Raja). The local cases were defined as the patients who got the COVID-19 infection in the country. While, the imported cases were defined as the patients who contracted the COVID-19 from abroad. Presence of co-morbidity was defined as patients who answered "yes" to having two or more co-morbidities (i.e. diabetes mellitus, hypertension, heart disease, chronic lung disease or chronic kidney disease). In addition, the study also included detailed information on clinical manifestations (i.e. fever, cough, runny nose, sore throat and short of breath). Approval to conduct this study was obtained from the Medical Research and Ethics Committee, Ministry of Health Malaysia (NMRR-20-720-54598). Prior to the study, permission to undertake the study was obtained from the Petaling District Health Office, Selangor, Malaysia. All patient

information was kept confidential and specific identification code was given to each patient to ensure confidentiality and anonymity.

Data were analysed using SPSS version 23.0. The patients' profile data was summarized using descriptive statistics [frequency (*n*) and percentages (%)]. Bivariable analysis was done to examine associations between independent variables and symptomatic/asymptomatic COVID-19 cases. Crude odds ratios (cOR) were used to describe the strength of association between each dependent and independent variable. A multivariable logistic regression model was fitted to determine the factors associated with asymptomatic cases, adjusted for all other covariates. The adjusted OR (aOR) and its corresponding 95% Confidence Interval (CI), with a p-value of less than 0.05 was considered significant in the logistic regression model.

RESULTS

As of 30th April 2020, a total of 434 COVID-19 patients were reported in the Petaling District, Selangor, Malaysia. Of these, 292 (67.3%) were patients with symptoms and the remaining (n = 142, 32.7%) were asymptomatic. The township of Petaling reported the highest number of patients (n = 127, 29.3%), while the Bukit Raja reported the lowest number of patients (15.2%). The majority of the patients were Malaysians (87.8%), of Malay ethnicity (62.9%), males (54.1%), and aged <40 years old (51.6%). Three quarters of the cases were caused by local transmission (75.3%) and most of them had no co-morbidity (88.2%). Among the symptomatic patients, majority of the patients were Malaysians (94.5%), of Malay ethnicity (67.5%), aged ≥40 years old (53.4%), and from Petaling township (27.4%). In addition, more than 70% of the COVID-19 cases were caused by local transmission and most of them (86.3%) had no co-morbidity. Fever was the most common symptom among the patients (68.2%), followed by cough (46.9%) and sore throat (26.0%). Among asymptomatic patients, most of the patients were also Malaysians (73.9%), of Malay ethnicity (53.5%), aged <40 years old (62.0%), and also from Petaling township (33.1%). Furthermore, majority of the asymptomatic COVID-19 patients were infected through local transmission (85.9%) and most of them (92.3%) had no co-morbidity (Table 1).

Table 1 Characteristics of COVID-19 patients in Petaling District, Selangor, Malaysia.

Characteristics	COVID-19 patients					
	Symptomatic		Asymptomatic		Total	
	n	%	*n*	%	*n*	%
Age group (years)						
<40	136	46.6	88	62.0	224	51.6
≥40	156	53.4	54	38.0	210	48.4
Gender						
Male	146	50.0	89	62.7	235	54.1
Female	146	50.0	53	37.3	199	45.9
Ethnicity						
Malay	197	67.5	76	53.5	273	62.9
Non-Malay	95	32.5	66	46.5	161	37.1
Citizenship						
Malaysian	276	94.5	105	73.9	381	87.8
Non-Malaysian	16	5.5	37	26.1	53	12.2
Transmission						
Local	205	70.2	122	85.9	327	75.3
Imported cases	87	29.8	20	14.1	107	24.7
Co-morbidity						
No	252	86.3	131	92.3	383	88.2
Yes	40	13.7	11	7.7	51	11.8
Township						
Petaling	80	27.4	47	33.1	127	29.3
Sungai Buloh	97	33.2	27	19.0	124	28.6
Damansara	83	28.4	33	23.2	116	26.7
Bukit Raja	32	11.0	34	23.9	66	15.2
Symptom Status						
Fever	199	68.2	-	-	199	68.2
Cough	137	46.9	-	-	137	46.9
Sore throat	76	26.0	-	-	76	26.0
Runny nose	57	19.5	-	-	57	19.5
Overall	292	67.3	142	32.7	434	100.0

The bivariable analysis of independent variables and symptom status of the patients showed a significant association between asymptomatic status with patient's age, gender, ethnicity, citizenship, transmission and township. Asymptomatic cases were mostly among patients aged <40 years old (cOR 1.86, 95%CI 1.24, 2.81), males (cOR 1.67, 95%CI 1.11, 2.53), non-Malays (cOR 1.80, 95%CI 1.19, 2.71), non-Malaysians (cOR 6.07, 95%CI 3.24, 11.39), and local transmission cases (cOR 2.58, 95%CI 1.51, 4.42). Based on township status, patients from Sungai Buloh (cOR 0.47, 95%CI 0.27, 0.82) were less likely to be asymptomatic compared to other areas. However, there was no significant association between asymptomatic cases and co-morbidity status. The variables included in the multivariable logistic regression model were age group, gender, ethnicity, citizenship, transmission, co-morbidity and township. After adjusting for confounders, three variables were found to be statistically significant predictors for asymptomatic COVID-19 cases. Patients aged < 40 years old (aOR 1.79, 95%CI 1.11,2.86) were more likely to be asymptomatic compared with those aged ≥ 40 years old. COVID-19 patients who were non-Malaysians (aOR 3.22, 95%CI 1.44, 7.19) and local transmission cases (aOR 2.51, 95%CI 1.42, 4.42) COVID-19 were more likely to be asymptomatic compared to their respective counterparts. However, there was no significant association between asymptomatic cases and gender, ethnicity, co-morbidity and township (Table 2).

Table 2 Factors associated with asymptomatic COVID-19 patients

Variable	n	Simple LR		Multiple LR	
		Crude OR (95% CI)	p	Adjusted OR (95% CI)	p
Age group (years)					0.015*
<40	88	1.86 (1.24 – 2.81)	0.003*	1.79 (1.11 - 2.86)	
≥40	54	1		1	
Gender					0.227
Male	89	1.67 (1.11 - 2.53)	0.013*	1.32 (0.83 - 2.10)	
Female	53	1		1	
Ethnicity					0.396
Malay	76	1	0.005*	1	
Non-Malay	66	1.80 (1.19 - 2.71)		1.26 (0.73 - 2.16)	
Citizenship					0.004*
Malaysian	105	1	0.001*	1	
Non-Malaysian	37	6.07 (3.24 - 11.39)		3.22 (1.44 - 7.19)	
Transmission					0.001*
Local	122	2.58 (1.51 - 4.42)	0.001*	2.51 (1.42 - 4.42)	
Imported cases	20	1		1	
Co-morbidity					0.365
No	131	1.89 (0.93 - 3.80)	0.075	1.42 (0.66 - 3.06)	
Yes	11	1		1	
Township					
Petaling	47	1		1	
Sungai Buloh	27	0.47 (0.27 - 0.82)	0.009*	0.61 (0.33 - 1.11)	0.107
Damansara	33	0.67 (0.39 - 1.16)	0.157	0.91 (0.50 - 1.63)	0.757
Bukit Raja	34	1.80 (0.99 - 3.30)	0.054	1.81 (0.91 - 3.59)	0.086

Significant at p < 0.05.

DISCUSSION

WHO has recognized COVID-19 as an infectious disease caused by a newly discovered strain of coronavirus, a type of virus known to cause respiratory infections in humans and has been working closely with the Ministry of Health from the affected countries to control this pandemic.[19] Due to the novelty of this virus, several challenges are faced in controlling this infection such as the presence of asymptomatic infection which may lead to difficulty in diagnosing and controlling the infection.[20] Our findings from 434 patients in Petaling District, Selangor, Malaysia revealed that approximately one-third of the patients were asymptomatic and the factors associated with being asymptomatic were younger age group (< 40 years), nationality (non-Malaysian) and local transmission cases.

The study revealed that patients of younger age group were more likely to be asymptomatic

compared to older patients. Our findings coincide with few other studies which also demonstrated a significant association between age and asymptomatic cases.[21-23] A cross-sectional survey by Mei et al.[21] reported that the COVID-19 young-age group had a fewer number of symptoms and lower rate of fever than their older counterparts, they did not seem to be susceptible, or their symptoms were relatively mild or no symptoms at all. Similarly, a study among 81 young adults with COVID-19 infection admitted to King Abdullah University Hospital, Jordan revealed that about half of the patients (*n*= 37, 45.7%) were asymptomatic.[22] In a systematic review study on asymptomatic COVID-19 patients by Kronbichler[23] revealed that most of the asymptomatic patients were from younger age with the mean age of 31.0 (standard deviation: 23.8) years old. The above studies have shown that asymptomatic patients were more common in young and middle-aged individuals, suggesting that age and the status of health may play an important role in the severity of COVID-19, possibly related to different immune responses to the diseases.[12] Furthermore, the surface enzyme angiotensin-converting enzyme (ACE2) which has proven to promote internalization of COVID-19 into the human cells was lower in the younger age group compared to adult.[24]

The present findings also revealed that asymptomatic patients were mostly among non-Malaysians. Several studies have described varying degrees of illness (mild, severe, or critical) including of asymptomatic patients may be due to the strain of the COVID-19 virus, features of the population demographic and genetics.[25-28] In Petaling District, a total of 37 asymptomatic COVID-19 patients were non-Malaysians and approximately 81% (n= 30) of them were from Bangladesh. Thus, the demographic characteristics of the Bangladeshis may play an important role in determining the factors associated with asymptomatic cases in this study. The most possible reason identified was the inherent immunity among Bangladeshis.[26] Historically, they may experience repeated attacks of respiratory viruses which may keep their immune system primed and has probability of providing some forms of protection from COVID-19 virus.[26] Another possible reason is the individual genetic variation that may help to explain about different immune responses to a virus in different population and may become more resilient to conditions in those countries compared to other countries.[27,28] Furthermore, the virus may have mutated when it spreads from China to different part of the continents, which may explain why some COVID-19 patients from different countries showed no symptoms compared to other patients in other countries.[26]

In this study, it was noted that the likelihood of being asymptomatic was higher among local transmission cases than the imported cases whom had contracted the disease before returning to the country. The COVID-19 virus originated from China has been mutated to different groups worldwide during the pandemic and initially the virus can be divided into three types: A, B and C. The less contagious type B was the most common type in East Asia including in Malaysia, while the more contagious and lethal types A and C are normally found in Europeans and Americans.[26,29] In our study, all asymptomatic COVID-19 patients (n= 20) were found to be the citizen of Malaysia. Of these, 45% (n = 9) of them had been to United Kingdom before travelling back to the country while another 20% of the patients had been to European countries (n = 2) and United State of America (n = 2). This could be the one of the reason for the local transmission cases in Petaling District were more likely to be asymptomatic compared to the imported cases. In addition, this argument is consistent with the study by Cambridge University and Los Alamos National Laboratory Scientists which reported that the virus has mutated into contagious strain as it left East Asia while traveled to Europe and spreaded in the United States.[30]

This study has some limitations. First, only the COVID-19 confirmed patients resided in Petaling District were included in the study. Patients who were admitted to the hospital in this District, but not a resident of the district of Petaling, were not recorded into the database at the Petaling District Health Office. It would be better to include as many patients as possible from other districts or states to better generalization of the result. Second, the investigation of the patients was conducted through telephone interview by using a standardized investigation form, which is very brief and less informative. In addition, the information obtained from the telephone interview may be subjected to response bias. For instance, it is difficult for the patient to elaborate their responses clearly over phone. Nonetheless, face to face interview is not advisable as the risk of contracting COVID-19 is higher. Lastly, the medical records of the patients who were admitted to the hospital were not available from the database. The strength of the study is that the data collected was considered valid and reliable as the investigations were conducted by trained medical personnel and further verified by a qualified epidemiologist at the Petaling District Health Office.

CONCLUSION

Approximately one-third of COVID-19 patients in Petaling District were asymptomatic and these patients are easily spreading the virus to others without realizing they are infected. The risk factors identified were younger age, non-Malaysians and local transmission cases. Rigorous epidemiological investigation is helpful in identifying COVID-19 among these groups of people who are

asymptomatic. Appropriate strategies, such as social distancing, wearing face masks in public, frequent hand washing should be strongly implemented to prevent disease transmission from asymptomatic individuals. Lastly, this study provides a better understanding of various factors that might be contributing to the asymptomatic COVID-19 patients in Petaling District, which serves as baseline findings for future control and research.

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