<div style="text-align:center">**ORIGINAL ARTICLE**</div>

THE INCUBATION PERIOD OF CORONAVIRUS DISEASE 2019 (COVID-19) IN PETALING DISTRICT, MALAYSIA

Ainul Nadziha Mohd Hanafiah[1], Lee Soo Cheng [2], Lim Kuang Kuay [3], Waramlah Ramlan [4], Diana Raj [4], Shiehafiel Fieqri Hussin [4], Ridwan Sanaudi [3], Roslinda Abu Sapian [3], Nurul Syarbani Eliana Musa [3] and Mohamed Paid Yusoff [5].

[1] Institute for Health Systems Research, National Institutes of Health, Ministry of Health, No. 1 Jalan Setia Murni U13/52, Setia Alam, 40170 Shah Alam, Selangor, Malaysia.
[2] Petaling District Health Office, Selangor, Ministry of Health, Wisma SAHOCA, No. 1 Jalan SS6/3A, 47301 Petaling Jaya, Selangor, Malaysia.
[3] Institute for Public Health, National Institutes of Health, Ministry of Health, No. 1 Jalan Setia Murni U13/52, Setia Alam, 40170 Shah Alam, Selangor, Malaysia.
[4] Ministry of Health, Level 6, Menara Prisma, Precinct 3, 62675, Putrajaya, Malaysia.
[5] Petaling District Health Office, Selangor, Ministry of Health, Wisma SAHOCA, No. 1 Jalan SS6/3A, 47301 Petaling Jaya, Selangor, Malaysia

Corresponding author: Ainul Nadziha Mohd Hanafiah
Email: ainulnadziha@gmail.com

ABSTRACT

The outbreak of COVID-19 has affected the world with over two million cases globally. Malaysia has witnessed over 5,000 with almost 100 deaths as of 22 April 2020. Knowledge on the incubation period of COVID-19 is scarce due to the novelty of the virus. The aim of this study was to determine the incubation period of COVID-19 infection in the district of Petaling in Malaysia. A cross-sectional study was conducted using secondary data from the Petaling District Health Office. We analysed data of laboratory-confirmed COVID-19 cases notified to the Petaling District Health Office between 3 February 2020 and 13 April 2020. Our study included 219 cases. The median incubation period of COVID-19 among the cases was five days (interquartile range 3.0-8.0). Four main clusters were identified, with significant difference found between two of the clusters. Cluster A has a shorter incubation period 3.5 (3.0-6.8) compared to cluster B as most of the confirmed cases knew the source of infection. COVID-19 incubation period in Petaling, Malaysia fits within the range estimated by the World Health Organization. Based on the upper value of the incubation period interquartile range in our study, the length of quarantine and period of contact tracing should be at least 8 days. This finding is in accordance with our current practice to control the spread of COVID-19.

Keywords: incubation period; COVID-19; coronavirus; Petaling district.

INTRODUCTION

The world has been deeply affected by the pandemic of the novel coronavirus infection, better known as COVID-19, which started as an epidemic in the city of Wuhan, Hubei province, China in December 2019. COVID-19, which manifests like pneumonia with symptoms such as fever, dry cough, sore throat, myalgia and fatigue[1,2], is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Severe fatal complications such as organ failure, septic shock, pulmonary oedema, severe pneumonia, and acute respiratory distress syndrome have also been reported[3,4].

The World Health Organization declared that the outbreak constituted a Public Health Emergency of International Concern (PHEIC) on 30 January 2020[5]. The spread of COVID-19 from the epicenter of Wuhan, China has resulted in 2,471,136 confirmed cases and 169,006 deaths globally as of 22 April 2020[6]. Malaysia has reported 5,532 confirmed cases with 93 deaths[7], while in Petaling district confirmed cases were 371 with five deaths up until 22 April 2020[8].

The novelty of the coronavirus with unclear clinical spectrum and testing capacity has made it difficult for countries to establish the incubation period of the disease. Knowledge on COVID-19 incubation period is a key epidemiological parameter in establishing and evaluating public health activities such as monitoring, control, and surveillance of infectious diseases, as well as for modelling of epidemics. Incubation period is defined as the time interval between exposure and onset of symptomatic disease[9,10].

Only a few studies have been conducted to determine the incubation period of COVID-19. Findings were based on epidemiological data from a few countries, but mostly from China. Incubation period have been estimated to range between 3·6 and 6·4 days[11-18]. In Malaysia similar studies have yet to be found. Therefore, the aim of this study was to determine the incubation period of COVID-19 infection in the district of Petaling, Malaysia. Findings from this study will add to the body of knowledge on incubation period of COVID-19 and will assist epidemiologists and the public health fraternity globally in the

planning of necessary monitoring, control, and prevention measures.

METHODS

This was a cross-sectional study carried out using data obtained from the Petaling District Health Office, Selangor, Malaysia. Data extracted were those of confirmed cases notified to the Petaling District Health Office between 3 February 2020 and 13 April 2020. Data on symptomatic confirmed cases with known dates of exposure and onset of symptoms were included in this study. Information on socio-demographic characteristics, clinical manifestations, co-morbidities, travelling history and source of infection were included in the study.

Study Definitions

A confirmed COVID-19 case is defined as a person with a laboratory-confirmed positive result[19]. We defined incubation period as the time elapsed between exposure to a confirmed case and the date of onset of symptom(s).

Symptom onset date is defined as the date when the signs or symptoms suggestive of COVID-19 (i.e. cough, shortness of breath and sore throat, with or without fever) first appear[19], while the date of exposure is defined as the latest date of contact with a confirmed positive case

Statistical analysis

Statistical analyses were performed using SPSS software version 26 (IBM SPSS, Chicago, IL, USA). No imputation was made for missing data. Categorical variables were summarised as counts and percentages. All continuous variables were statistically tested for normality using the Shapiro-Wilk test before performing any further statistical analysis. Continuous variables such as age and incubation period were expressed as medians and interquartile ranges as both were not normally distributed. Non-parametric test (Kruskal-Wallis test) was performed to compare the differences of incubation periods between the clusters listed in this study. We then performed Dunn's nonparametric comparison for post-hoc testing following a significant Kruskal-Wallis test. The pairwise comparisons using the Dunn-Bonferroni method were produced where the level of significant for adjusted p-value is set at 0.05.

Ethics

Ethical approval was obtained from the Medical and Research Ethics Committee (MREC), Ministry of Health Malaysia (research registration number: NMRR-20-793-54770). Approval was also obtained from the Petaling Health District Office prior to the study and no findings which could identify any individual will be published.

RESULTS

A total of 219 cases were included in this study, with 52% female cases. By age groups, 54% were aged 40 years old and above; about 70% cases were Malay, and majority were Malaysians (96%). We identified four main clusters from the dataset: Cluster A (20.1%) consists of people from a corporate organisation, Cluster B (19.6%) consists of people who attended a religious event, Cluster C (33.8%) are imported cases from abroad, and Cluster D (26.5%) consists of other categories like individual home clusters or sporadic cases.

In terms of municipality, most were from Petaling Jaya, followed by Shah Alam and Subang Jaya. About 66% of the transmission cases were local transmission, three quarters of the cases had no travel history (72.1%) and 63% did not have co-morbidity (Table 1).

Significant differences were observed in the median incubation period of the clusters (p=0.002), whereas, no significant differences were found in age, gender, ethnicity, municipality, transmission, nationality, travelling history, healthcare worker and co-morbidity (Table 1).

Majority of the cases (70.8%) had fever, followed by respiratory symptoms (69.4%). Our study identified the top three co-morbidities of the cases as hypertension (19.2%), diabetes mellitus (12.3%) and heart disease (4.6%) (Table 1).

The median incubation period of COVID-19 among the cases is 5.0 days (interquartile range 3.0-8.0). The longest median incubation period was found for cluster B, which is 8.0 days (interquartile range 4.0-11.0), while the shortest median was for cluster A, which is 3.5 days (interquartile range 3.0-6.8). Significant difference was observed between clusters A and B (p=0.001), however, there was no significant difference between the other cluster combinations (Table 2).

Table 1: The sociodemographic characteristics, clusters, co-morbidity and clinical manifestations of COVID-19 cases

Characteristics	Incubation Period		
	n(%)	Median (IQR)	p
Age			
Below 40	101 (46.1)	6.0 (3.5-9.0)	
40 and above	118 (53·9)	5·0 (3·0-8·0)	0.197
Gender			
Male	105 (47.9)	6.0 (3.5-8.0)	
Female	114 (52.1)	5.0 (3.0-9.0)	0.639
Ethnicity			
Malay	153 (69.9)	5.0 (3.0-8.5)	
Chinese	41 (18.7)	5.0 (3.0-7.0)	
Indian	14 (6.4)	7.5 (5.0-9.5)	
Others	11 (5.0)	7.0 (6.0-12.0)	0.111
Nationality			
Malaysian	210 (95.9)	5.0 (3.0-8.0)	
Non-Malaysians	9 (4.1)	7.0 (6.0-12.5)	0.062
Cluster			
A	44 (20.1)	3.5 (3.0-6.8)	
B	43 (19.6)	8.0 (4.0-11.0)	
C	74 (33.8)	6·0 (3.8-8.0)	
D	58 (26.5)	5·0 (3.0-8.0)	0.002*
Municipality			
Petaling Jaya	88 (40.2)	5.0 (3.0-8.0)	
Shah Alam	71 (32.4)	5.0 (3.0-8.0)	
Subang Jaya	60 (27.4)	6.0 (4.0-10.8)	0·265
Transmission			
Local	145 (66.2)	5.0 (3.0-9.0)	
Import	74 (33.8)	6.0 (3.8-8.0)	0.788
Travelling history			
Yes	61 (27.9)	5.0 (3.0-8.5)	
No	158 (72.1)	6.0 (3.0-8.3)	0.555
Healthcare worker			
Yes	21 (9.6)	6.0 (3.0-9.0)	
No	198 (90.4)	4.0 (3.0-8.0)	0.431
Co-morbidity			
Yes	81 (37.0)	6.0 (3.0-9.0)	
No	138 (63.0)	5.0 (3.0-8.0)	0.736
Clinical manifestations			
Fever	155 (70.8)		
Respiratory symptoms	152 (69.4)		
Constitutional symptoms	39 (17.8)		
Musculoskeletal symptoms	14 (6.4)		
Gastrointestinal symptoms	10 (4.6)		
Loss of taste and smell	7 (3.2)		

Table 2: The median incubation period of COVID-19 by clusters

Cluster	n	Median	IQR	X2 statistic* (df)	p
A[a]	44	3.5	3.0-6.8		
B[b]	43	8.0	4.0-11.0		
C[c]	74	6.0	3.8-8.0	15.2 (3)	0.002
D[d]	58	5.0	3.0-8.0		
Total	219	5.0	3.0-8.0		

Kruskal-Wallis test
Post Hoc tests: [ab]p =0.001; [ac]p =0.153; [ad]p =0.478; [bc]p =0.203; [bd]p =0.100; [cd]p =1.00

DISCUSSION

From this study, we present data on 219 laboratory-confirmed positive COVID-19 cases in Petaling district. Approximately 70% of these cases were Malays, which can be explained by the two big clusters, i.e. cluster A and B, which are made up of almost all Malays.

The analysis of data yielded a median incubation period of 5 days, which is within the range of incubation period of 0 to 14 days estimated by the WHO, and 2 to 12 days estimated by the European Centre for Disease Prevention and Control (ECDC)[20,21]. Our findings are comparable to the median incubation period values for the severe acute respiratory syndrome (SARS) as well as the Middle East respiratory syndrome (MERS)[15,22]. However, a systematic review reported a shorter median incubation period of 4 days in SARS[23]. Our findings are also consistent with recent estimations of incubation period for COVID-19 in studies in China[13,16], but is longer than findings from Korea which reported a median incubation period of 3 days, and 5.2 days in a study based on 10 cases in China[12,14]. The variation that we identified in the incubation period distribution between studies could be associated with differences in the ascertainment or reporting of exposure dates and illness onset dates, differences in the source or mode of infection, or environmental differences[22].

When comparing the incubation periods between clusters in Petaling, we noted that the median incubation periods are significantly different between cluster B (religious gathering) and cluster A (corporate organisation). Cluster B has the longest median incubation period of 8 days (interquartile range 4.0-11.0) amongst all the clusters in Petaling. This is probably due to the continuous and repeated exposure amongst individuals within the religious cluster as they are a close-knit community. Hence, the exact dates of exposure are often unclear. Apart from Petaling, neighbouring countries like Singapore also reported cases from the same religious group, although no specific incubation period was reported[24]. On the other hand, cluster A has a shorter median incubation period of 3.5 days (interquartile range 3.0-6.8) which concurs with

findings of similar studies in Singapore, Korea and China[14,18,24]. Most of the cases in cluster A reported precise exposure dates and the onset of symptoms because majority of the cases were certain of their exposure source and dates by knowing the positive cases they were exposed to. A higher infecting dose or viral load due to direct transmission as well as higher virulence of the strain could possibly lead to a shorter incubation period as reported in SARS and MERS in previous study[22, 25].

In our analysis, both extreme values of incubation period in clusters A and B were 'averaged out' into a midpoint value, thus resulting in the incubation period of 5 days. A similar finding is demonstrated in a previous study comparing incubation periods of SARS between Hong Kong and Toronto[25].

Clinical manifestations that were commonly reported in our study were fever and respiratory symptoms like cough, sore throat, runny nose and shortness of breath, which concurs with other studies[2,18]. Our study also uncovered reports of neurological symptoms, specifically loss of taste and smell by 7 cases. Although it is not in the COVID-19 symptom list by World Health Organization[26], a study by Menni et al.[27] which studied the prevalence of loss of smell and taste among confirmed COVID-19 cases found this feature to be a strong predictor of COVID-19 infection.

Due to the novelty of this virus, several challenges had to be tackled when determining the onset of the disease as some of the confirmed cases presented with atypical clinical manifestations such as gastrointestinal (diarrhoea, abdominal pain), musculoskeletal (myalgia, arthralgia) and other constitutional symptoms (headache, lethargy), which is consistent with findings in other studies[2,12,28,29]. Our study also included the 'loss of taste and smell' manifestation when determining the date of clinical onset. A study reported that atypical presentations may have been missed and led to difficulty in diagnosing and controlling the infection[12]. Another challenge we faced was when confirmed positive cases in our study were asymptomatic (n=76; data not shown), which was also found in other studies[30-32]. This

made it impossible to determine the incubation period for these cases.

The strengths of our study are as follows; firstly, all COVID-19 cases were investigated by trained health personnel and further verified by qualified epidemiologists. Secondly, with the establishment of the clusters from our data, we were able to demonstrate the significant difference in the median incubation period between 2 clusters which dates of exposure were more precise (cluster A) versus less precise dates due to continuous and repeated exposure amongst individuals (cluster B). Thirdly, we included the atypical symptoms in ascertaining the date of onset of symptoms. This enabled us to determine the incubation period, which otherwise would not have been possible if we had followed strictly the list of typical clinical manifestations of COVID-19. The limitation we identified in this study is that data might have been subjected to recall bias, which could affect the accuracy of dates of symptom onset or exposure. This may have resulted in incubation periods which are either too long or too short. Nonetheless, we included all the outliers in the analysis and reported our findings as median.

In **conclusion**, the median incubation period of COVID-19 in Petaling district is 5 days, which fits within the range estimated by the World Health Organization. Cluster A has a shorter incubation period compared to cluster B as most of the confirmed cases knew the source of infection.

Recommendation

Currently, the quarantine period for persons exposed to confirmed positive COVID-19 cases is 14 days. Based on the highest median incubation period in our study, medical observation or quarantine period should be of a minimum of 8 days to halt the spread of disease. And we recommend to maintain the current practice of quarantine of 14 days. With the highest value of the incubation period interquartile range being 11, therefore, our recommendation is justified, and will suffice to curb the spread of disease.

Secondly, in view of the interest of the public health fraternity to improve their monitoring, control, and surveillance activities, further studies should be done to better understand the transmission of COVID-19 in asymptomatic cases.

Availability of data and materials
The dataset that support the findings of this article belongs to the study. At present, the data are not publicly available but can be obtained from the authors upon reasonable request and with the permission from the Director General of Health, Malaysia.

Authors' contributions
ANMH, LSC and MPY were responsible for the concept, development and supervision of the research. RS, LKK and WR analysed the data; ANMH, DR and SFH constructed the draft manuscript. All authors contributed to the writing of the manuscript, reviewing and approving the final manuscript.

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