Epidemiological Features of COVID-19 Patients in Terengganu State of Malaysia and the Predictors for SARS-CoV-2 Transmissibility

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ABSTRACT

Background: Terengganu state has experienced fifteen COVID-19 communal clusters throughout the year 2020. Knowing the predisposing factors of COVID-19 transmissibility can be helpful in planning the control and preventive measures. This study aimed to describe the socio-demographic and clinical characteristics of COVID-19 patients in Terengganu state, and to determine the predictors for SARS-CoV-2 transmissibility using RT-PCR cycle threshold (Ct) value as surrogate marker.

Materials and Methods: A cross-sectional study was conducted in Terengganu state including all COVID-19 cases from 1st March 2020 until 31st January 2021 based on retrospective record review. The inclusion criteria were individuals with laboratory RT-PCR confirmed positive test for COVID-19. Descriptive statistics, simple and multiple linear regression analyses were employed for statistical analysis.

Result: There were 2,142 COVID-19 cases in Terengganu during the studied period. The mean age of cases was 33 (±17) years. Majority of COVID-19 cases were male (60.6%), adult (70.0%) and from working group (49.2%). 3.9% of cases were healthcare workers. Among the common symptoms were fever (17.2%) and cough (14.0). The mean RT-PCR Ct value was 25.76 (±10.99). Multiple linear regression revealed older age, male gender, having fever and cough as the significant predictors for high SARS-CoV-2 transmissibility with β: -0.06 (95%CI: -0.09,-0.03); p=0.001; β: -3.80 (95%CI: -4.73,-2.86); p=0.001; β: -1.31 (95%CI: -2.54,-0.08); p=0.037; β: -1.86 (95%CI: -3.51,-0.20); p=0.026, respectively.

Conclusion: Early detection and isolation of vulnerable cases based on pinpointed risk factors in centralized quarantine station or hospital is recommended to reduce the risk of transmission and to ensure optimal care is given.

Keywords: COVID-19, SARS-CoV-2, RT-PCR, Ct value, transmissibility, Malaysia

I. INTRODUCTION

Coronavirus Disease (COVID-19) which is caused by severe acute respiratory syndrome coronavirus (SARS-CoV-2) spreads rapidly from person to person; and the virus is transmitted by asymptomatic infected individuals and symptomatic individuals via oral fluid droplets, mainly airborne via coughing or sneezing [1]. In Malaysia, the first case of COVID-19 was detected on 25th January 2020 among three individuals who previously had close contact with an infected person in Singapore [1]. One year later, the disease had spread nationwide and there were more than 214,000 cases reported at the end of January 2021 with 760 deaths related to COVID-19. Malaysia also has identified around 817 COVID-19 clusters as of 31st January 2021 which affected all states and federal territories in Malaysia [2]. One of the Malaysian states which had substantial number of COVID-19 cases due to clustering through community transmission is Terengganu state. Terengganu state of Malaysia has experienced fifteen COVID-19 communal clusters throughout the year 2020 which had affected all eight districts [3], [4]. As of 31st January 2021, the total number of COVID-19 cases in Terengganu were 2,142 with 4 deaths related to COVID-19 [2].

Currently, the gold standard for COVID-19 diagnosis is by using real-time reverse-transcription polymerase chain reaction (RT-PCR) test, and cycle threshold (Ct) value provides a measure of the SARS-CoV-2 viral load in the sample for RT-PCR testing for COVID-19. The Ct value is inversely related to the viral load in which lower Ct values correspond to higher viral ribonucleic acid (RNA) concentrations [3], [5]. Higher level of viral RNA indicates high infectivity and directly contributes to high transmissibility of the virus [6], [7].

To the best of our knowledge, there is yet no well-published study on the factors related to high transmissibility of SARS-CoV-2 in Malaysian setting. As
Terengganu state had experienced surge of COVID-19 cases from the very beginning of the pandemic, timely control measures by modulating the pinpointed risk factors are critical to attenuate SARS-CoV-2 transmission in the community. Therefore, this study is aimed to describe the socio-demographic and clinical characteristics of COVID-19 patients, and to determine the predictors of high transmissibility of SARS-CoV-2 based on RT-PCR Ct values in Terengganu state of Malaysia.

II. MATERIAL AND METHODS

We conducted a state-wide cross-sectional study in Terengganu state of Malaysia based on retrospective record review involving all COVID-19 confirmed case. The study samples were all COVID-19 confirmed cases notified to Terengganu State Health Department between 1st March 2020 until 31st January 2021 who fulfilled study criteria. The inclusion criterion were individuals with laboratory confirmed positive test result for COVID-19 using reverse transcription polymerase chain reaction (RT-PCR) [8].

The required sample size was calculated using G*Power calculation for multiple linear regression test [9]. The estimated minimal sample size needed was 1175 samples using effect size, \( f^2 \) of 0.02, 5% type 1 error, 80% power and additional 30% of samples with incomplete data.

Data were collected from Terengganu state’s CDCIS e-Notifikasi online registry (an online database for infectious diseases under the governance of Ministry of Health Malaysia) and SIMKA Outbreak system (a Malaysian public health laboratory online database for COVID-19 test results reporting). The retrieved information for independent variables included socio-demographic characteristics such as age, gender, occupation, and symptoms (fever, cough, sore throat, coryza, myalgia, headache, anosmia, ageusia, diarrhoea, dyspnoea). The dependent variable was the RT-PCR Ct values as surrogate marker for transmissibility level. Only clinically important variables (age, gender, clinical symptoms) were included for determining the predictors for high transmissibility of SARS-CoV-2.

III. STATISTICAL METHODS

Data entry and analysis were done by using SPSS Statistics (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.). Descriptive statistics with mean and standard deviation (SD), frequency and percentages were calculated. Simple and multiple linear regression analysis were used to determine factors related with high transmissibility of SARS-CoV-2. All significant variables with a \( p \)-value <0.25 from univariable analysis and clinically important variables were chosen for multiple linear regression analysis. A \( p \)-value<0.05 was considered statistically significant.

IV. RESULTS

From 1st March 2020 until 31st January 2021, there were 2,142 COVID-19 cases notified to Terengganu State Health Department. The mean age of cases was 33 (±17). Majority of COVID-19 cases were male (60.6%), adult (70.0%), and from working group (49.2%). 3.9% of cases were healthcare workers (Table 1).

**TABLE I: SOCIO-DEMOGRAPHIC CHARACTERISTICS OF COVID-19 CASES IN TERENGGANU STATE OF MALAYSIA (N=2142)**

| Characteristics | Frequency, n (%) |
|-----------------|-----------------|
| Age in years*   | 33 (±17)        |
| Age groups      |                 |
| Child (<10)     | 176 (8.2)       |
| Adolescent (10-19) | 290 (13.5)   |
| Adult (>19 - <60) | 1499 (70.0)  |
| Elderly (≥60)   | 177 (8.3)       |
| Gender          |                 |
| Female          | 844 (39.4)      |
| Male            | 1298 (60.6)     |
| Occupation      |                 |
| Not working     | 382 (17.8)      |
| Working (HCW)   | 83 (3.9)        |
| Working (non-HCW) | 971 (45.3)    |
| Student         | 464 (21.7)      |
| Prison inmate   | 242 (11.3)      |

*Mean (±SD); HCW: Healthcare worker

**TABLE II: CLINICAL CHARACTERISTICS AMONG COVID-19 CASES IN TERENGGANU STATE OF MALAYSIA (N=2142)**

| Characteristics | Frequency, n (%) |
|-----------------|-----------------|
| Ct value*       | 25.76 (±10.99)  |
| Fever           |                 |
| No              | 1774 (82.8)     |
| Yes             | 368 (17.2)      |
| Cough           |                 |
| No              | 1842 (86.0)     |
| Yes             | 300 (14.0)      |
| Sore throat     |                 |
| No              | 1960 (91.7)     |
| Yes             | 178 (8.3)       |
| Coryza          |                 |
| No              | 2012 (93.9)     |
| Yes             | 130 (6.1)       |
| Myalgia         |                 |
| No              | 2114 (98.7)     |
| Yes             | 28 (1.3)        |
| Headache        |                 |
| No              | 2094 (97.8)     |
| Yes             | 48 (2.2)        |
| Anosmia         |                 |
| No              | 2054 (95.9)     |
| Yes             | 88 (4.1)        |
| Ageusia         |                 |
| No              | 2097 (97.9)     |
| Yes             | 45 (2.1)        |
| Diarrhoea       |                 |
| No              | 2127 (99.3)     |
| Yes             | 15 (0.7)        |
| Dyspnea         |                 |
| No              | 2120 (99.0)     |
| Yes             | 22 (1.0)        |

*Mean (±SD)
The mean RT-PCR Ct value reported for patients in Terengganu was 25.76 (±10.99). Among the reported symptoms were fever (17.2%), cough (14.0%), sore throat (8.3%), coryza (6.1%), anosmia (4.1%), headache (2.2%), ageusia (2.1%), myalgia (1.3%), dyspnea (1.0%) and diarrhea (0.7%) (Table II).

In the univariable analysis, age, gender, fever, cough and ageusia were selected for multivariable analysis as their p-values were less than 0.25. Multiple linear regression revealed older age, male gender, having fever and cough as the significant predictors for high SARS-CoV-2 transmissibility with β: -0.06 (95%CI: -0.09, -0.03); p<0.001; β: -3.80 (95%CI: -4.73, -2.86); p<0.001; β: -1.31 (95%CI: -2.54, -0.08); p=0.037; β: -1.86 (95%CI: -3.51, -0.20); p=0.028, respectively (Table III).

V. DISCUSSION

In our study, the socio-demographic features of COVID-19 patients in Terengganu are in line with findings from previous Malaysian studies [4], [10], of which we share similar findings on the mean age, gender, and age group among our COVID-19 cases. The proportion of healthcare workers infected with COVID-19 (3.9%) in Terengganu is slightly higher than the national proportion (3.57%) reported in December 2020 [11]. Meanwhile, our mean Ct value is slightly lower than the reported mean Ct value (26.15) during the Dang Mutiar and Makekar COVID-19 clusters in Dungun district of Terengganu [3], but they are still within the same range of infectivity level. As for the clinical characteristics, there is similarity on the common COVID-19 symptoms between our study with the previous local nationwide study [10]. However, ours reported fever as the most common symptom, while [10] demonstrated cough as the predominant one.

Theoretically, the initial dose of virus and the amount of virus an individual has at any one time might worsen the severity of COVID-19 disease. Studies had shown higher SARS-CoV-2 viral loads might worsen outcomes and increase disease severity and mortality risk [12], [13]. Data from previous study suggested the viral load is higher in patients with more severe disease [14]. Each index case with high viral load is capable to transmit COVID-19 to an average of 6.25 secondary cases [7]. Therefore,

### TABLE III: PREDICTORS FOR SARS-COV-2 TRANSMISSIBILITY AMONG COVID-19 CASES IN TERENGGANU BY SIMPLE AND MULTIPLE LINEAR REGRESSION (N=2142)

| Variables | Simple linear regression | Multiple linear regression |
|-----------|--------------------------|--------------------------|
|           | Crude β (95%CI) | p-value | Adjusted β (95%CI) | t-stat | p-value |
| Age       | -0.06 (-0.09, -0.03) | <0.001* | -0.06 (-0.09, -0.04) | -4.73 | <0.001* |
| Gender    | 1.00                   | 1.00                   |
| Female    | 1.00                   | 1.00                   |
| Male      | -3.58 (-4.52, -2.64)  | <0.001* | -3.79 (-4.73, -2.86) | -7.96 | <0.001* |
| Fever     | 1.00                   | 1.00                   |
| No        | 1.00                   | 1.00                   |
| Yes       | -1.55 (-2.78, -0.32)  | 0.014* | -1.31 (-2.54, -0.08) | -2.08 | 0.037* |
| Cough     | 1.00                   | 1.00                   |
| No        | 1.00                   | 1.00                   |
| Yes       | -2.54 (-3.88, -1.20)  | <0.001* | -1.86 (-3.51, -0.20) | -2.20 | 0.028* |
| Sore throat| 1.00                   | 1.00                   |
| No        | 1.00                   | 1.00                   |
| Yes       | -2.18 (-3.87, -0.49)  | 0.011* | -0.83 (-2.75, 1.09) | -0.84 | 0.40   |
| Coryza    | 1.00                   | 1.00                   |
| No        | 1.00                   | 1.00                   |
| Yes       | 0.50 (-1.45, 2.45)    | 0.616 | -                  | -     | -      |
| Myalgia   | 1.00                   | 1.00                   |
| No        | 1.00                   | 1.00                   |
| Yes       | -3.29 (-7.39, 0.81)   | 0.116 | -2.59 (-6.69, 1.51) | -1.24 | 0.216  |
| Headache  | 1.00                   | 1.00                   |
| No        | 1.00                   | 1.00                   |
| Yes       | -0.16 (-3.31, 2.99)   | 0.919 | -                  | -     | -      |
| Anosmia   | 1.00                   | 1.00                   |
| No        | 1.00                   | 1.00                   |
| Yes       | -0.63 (-2.97, 1.72)   | 0.601 | -                  | -     | -      |
| Ageusia   | 1.00                   | 1.00                   |
| No        | 1.00                   | 1.00                   |
| Yes       | 2.88 (-0.37, 6.13)    | 0.082 | 3.01 (-0.41, 6.02) | 1.74  | 0.075  |
| Diarrhea  | 1.00                   | 1.00                   |
| No        | 1.00                   | 1.00                   |
| Yes       | 0.933 (-4.66, 6.52)   | 0.744 | -                  | -     | -      |
| Dyspnoea  | 1.00                   | 1.00                   |
| No        | 1.00                   | 1.00                   |
| Yes       | 2.03 (-2.60, 6.65)    | 0.390 | -                  | -     | -      |

R²=71.6%; Stepwise/backward/forward multiple linear regression applied; Model assumptions are fulfilled; No interactions among independent variables; No multicollinearity detected. *p-value <0.05
hypothesetically, high viral load (or low Ct value) particularly in severe COVID-19 cases would correlate with high transmissibility of SARS-CoV-2.

Our study reported cases with advanced age tend to have lower Ct value which could be linked to high possibility of elderly to acquire severe form of COVID-19 as reported in previous Malaysian study [10]. Similarly, a Chinese study reported patients with advanced age were more likely to have severe COVID-19 (adjusted odds ratio (aOR) 1.03; p<0.05) [15]. Possible explanation for tendency of elderly to acquire severe COVID-19 is due to immunosenessence and comorbidities which are commonly associated with elderly which subsequently posed higher risk for SARS-CoV-2 transmissibility [16].

Our study also reported male cases were more likely to have lower Ct value (higher transmissibility) which could be linked to high proportion of men (71.5%) to acquire severe form of COVID-19 as reported in previous local study [10]. Study had demonstrated that biological sex does influence COVID-19 outcomes. SARS-CoV-2 binds to angiotensin-converting enzyme 2 (ACE-2) receptor with high affinity, of which ACE-2 protein is expressed higher in male which could explain high susceptibility of male to COVID-19. Besides, estrogens are postulated to play role some roles in protecting women from COVID-19 by reducing the expression levels of the receptor for the SARS-CoV-2 virus [17]. Therefore, women pose less risk in acquiring and transmitting SARS-CoV-2 as compared to men due to these biological constructs.

Various clinical symptoms had been reported to be associated with COVID-19 [10], [18]. In our study, fever and cough were the commonest symptoms reported among COVID-19 cases and those presented with fever and cough were more likely to have lower Ct value (higher viral load). Presence of symptoms played an important role in the transmission dynamics of COVID-19 as there was different transmission risk at different exposure window periods before and after symptoms onset. Reference [19] reported that there is a relatively short infectious period of COVID-19 and a higher transmission risk around the time of symptom onset of the index case, followed by a lower transmission risk at the later stage of disease. Previous study also demonstrated highest viral load in throat swabs were demonstrated in samples which were collected at the time of symptom onset, hence postulating that infectiousness peaked on or before symptom onset [20]. As previous study suggested the viral load is higher in patients with more severe form of COVID [14], then it is less surprising when a Chinese study showed the most common symptoms present in severe COVID-19 were fever and cough [21], implying patients with these symptoms were more likely to transmit SARS-CoV-2 to other secondary cases.

Due to the limitation of secondary data, our study did not include some known confounders such as duration from last exposure to diagnosis and type of exposure to index cases. Nevertheless, this study had enough sample size. Future researches may employ other study designs such as cohort study for better understanding of risk factors for SARS-CoV-2 transmissibility.

VI. CONCLUSION

In conclusion, advanced age, male, having symptoms of fever and cough were the significant determinants for high SARS-CoV-2 transmissibility. Therefore, early screening and prompt isolation for infected individuals from the vulnerable group based on the studied factors is necessary to reduce transmission to close contacts. Moreover, proper isolation of symptomatic elderly cases in centralized quarantine station or even better in hospital is recommended as compared to home quarantine to reduce the risk of transmission and to ensure optimal care is given. Although case detection and isolation are widely practiced nowadays, the measures alone may not be sufficient to contain the pandemic due to high transmissibility of COVID-19 before and immediately after symptom onset. Therefore, more generalized measures may be required to effectively contain the transmission such as social distancing and avoiding crowded places.

AUTHORS’ CONTRIBUTION

Awang H, Abd Rahman MA and Embong K conceptualized the study; Awang H, E.L. Yaacob, M.S. Abd Majid and Wahab A conducted the data collection; Awang H analyzed the data and drafted the manuscript. All the authors read and approved the final manuscript.

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CONFLICT OF INTEREST

Authors declared that they do not have any conflict of interest.

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