

ORIGINAL ARTICLE

CHARACTERISTICS AND COVID-19 INFECTION OUTCOME AMONG RURAL POPULATION IN NEGERI SEMBILAN, MALAYSIA

Rahmat Dapari^{1*}, Mohd Hafizuddin Mahfot^{1,5}, Mohd Safrin Bin Mohamad Bashaabidin^{1,6}, Nazri Che Dom², Mohd Rohaizat Hassan³ and Syed Sharizman Syed Abdul Rahim⁴

¹Department of Community Health, Faculty of Medicine and Health Sciences, 43400 Universiti Putra Malaysia Serdang, Selangor, Malaysia.

²Faculty of Health Sciences, Universiti Teknologi MARA, 42300 Puncak Alam, Selangor, Malaysia.

³Department of Community Health, Faculty of Medicine, National University of Malaysia, 56000 Cheras, Kuala Lumpur, Malaysia.

⁴Public Health Medicine Department, Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, 88400 Kota Kinabalu, Sabah, Malaysia.

⁵Disease Control Division, Ministry of Health Malaysia.

⁶Institute for Medical Research, Malaysia

*Corresponding author: Rahmat Dapari

Email: drrahmat@upm.edu.my

ABSTRACT

Coronavirus Disease 2019 (COVID-19) pandemic has still affected many countries around the world. While several studies have been published substantially regarding the risk factors of severe COVID-19 infection, less is known about the factors associated with COVID-19 infection among rural populations. This study aims to determine the characteristics and COVID-19 infection outcome in the rural population in Negeri Sembilan, Malaysia. Cross-sectional study was conducted in year 2021 among 3004 Laboratory-Confirmed COVID-19 cases in rural areas in Negeri Sembilan, Malaysia. The data was collected using proforma from list of COVID-19 cases in district health office and has been analyzed using SPSS version 25. Analysis shows that 884 (29.4%) out of 3004 Laboratory-Confirmed COVID-19 cases are classified as moderate-severe. The significant characteristics for moderate-severe COVID-19 infections were age (age 60 and above: aOR 2.00, 95% CI 1.474 - 2.715), gender (female: aOR 1.20, 95% CI 1.014-1.430), ethnicity (Chinese: aOR 3.09, 95% CI 1.746-5.454), employment status (employed: aOR 1.40, 95% CI 1.115-1.714), and chronic diseases (having chronic diseases: aOR 1.70, 95% CI 1.350-2.133). Early recognition of these characteristics among COVID-19 patients and prompt management of these cases might help to reduce COVID-19 severity in future.

Keywords: COVID-19, Outcomes, Rural, Chronic diseases

INTRODUCTION

The novel coronavirus disease 2019 (COVID-19) pandemic reached over 262 million confirmed infections and claimed the lives of more than five million people worldwide¹. Since COVID-19 was first identified in Malaysia in 25 January 2020, the number of infected persons has been propagating tremendously². Until December 2021, more than 2.6 million cases and 30 thousand deaths were reported in Malaysia³. Due to the overwhelming influx of COVID-19 patients in gazette hospitals, it has

significantly strained the Malaysia health care system.

The COVID-19 virus spreads primarily through droplets of saliva or discharge from the nose when an infected person coughs or sneezes. COVID-19 is not just a pulmonary disease primarily, but the emerging data suggest severe COVID-19 also affects extrapulmonary system such as cardiac, neurological, renal, hepatic, haematologic systems⁴⁻¹⁰. Most people infected with the COVID-19 virus will experience mild to moderate respiratory illness and recover without requiring special treatment. However, various

factors such as gender, age, and those with underlying medical problems like cardiovascular disease, diabetes, chronic respiratory disease, and cancer are more likely to develop serious illness¹¹⁻¹⁷.

All of these factors may influence the COVID-19 infection outcome in general population. While several studies have been published substantially regarding the factors associated with severity of COVID-19 infection, less is known about the factors associated with COVID-19 infection among rural population. Rural population may expose to risk of severe infection as they may have poor knowledge and access to healthcare facilities. Nevertheless, early recognition of the severe Covid-19 cases had allowed appropriate admission, prompt management and best treatment options provided to the affected patients at the right time and reducing mortality¹⁸. It is crucial to identify the characteristics of associated factors of COVID-19 infection outcome especially among rural population. Thus, this study aims to determine the characteristic and COVID-19 infection outcome in rural population in Negeri Sembilan, Malaysia.

METHODS

Study Location

This cross-sectional study was performed from October to December 2021 in rural areas in, Jempul district, Negeri Sembilan, Malaysia. Negeri Sembilan has estimated population 1,129,100 in year 2021. Male account 578,100 (51.2%) and female 551,000 (48.8%). Majority are Malays (59.8) followed by Chinese (20.3%), Indian (13.6%) and others (6.3%)¹⁹.

Sample-Size Calculation

We estimated the required sample size for each potentially associated factor and used the highest estimated number. The sample size for this study was calculated using the two proportions formula as the outcome measure is two categorical data which is (1) mild and (2) moderate-severe. The required sample size for this study with 95% precision and

80% power, was estimated to be 3080 based on study "COVID-19 patients with hypertension have more severe disease: a multicenter retrospective observational study"²⁰. The samples of this study were from all laboratory-confirmed COVID-19 infection. For secondary data collection, no additional dropout rate was added as the data is readily available.

Sampling procedure and Study Instruments

Based on sample size calculation, 3080 sample is needed for data analysis to identify the risk factors of COVID-19 infection severity. A simple random sampling procedure was used to choose 3080 laboratory-confirmed COVID-19 infection patients diagnosed from January to October 2021 from district health office. A study proforma was used in this study to collect the independent and dependent variable. Out of 3080, 76 (2.5%) of the sample variables were incomplete and were removed from the data analysis. The final sample size fulfils the inclusion and exclusion criteria were 3004.

Study variables

The dependent variable in this study was the COVID-19 outcome based on COVID-19 criteria for hospital referral and admission. Ministry of Health Malaysia, as per Annex 2e, Clinical Management of Confirmed Covid-19 Case in Adult and Paediatric has adopted the recommendation by clinically dividing the Covid-19 positive cases into five categories. In the Annex 2E, the Covid-19 severity increases as per ascending categorical number²¹. In this study, patients with COVID-19 category 1 and 2A were categorise as Mild as only require home Monitoring. Meanwhile, patients with COVID-19 category 2B, 3, 4 and 5 were categorise as Moderate-Severe as require referral to the Treatment and Quarantine Centre (PKRC) or hospital depend on the clinical stage. Thus, the COVID-19 infection outcome in this study was divided into two categories: (1) mild and (2) moderate-severe. The status of

the COVID-19 outcome is based on the District Health Office COVID-19 records.

There were three components of independent variable: 1) sociodemographic factors such as age (base on birthday and categories into four group), gender (male, and female), ethnicity (Malay, Chinese, Indian, aboriginal, and others), nationality (Malaysian, and Foreigner), and occupational status (employed, and unemployed), and residency status (Taman, Village, Felcra/ Felda/ Ladang), 2) medical condition such as chronic diseases, diabetes mellitus, hypertension, bronchial asthma, cardiovascular diseases, thyroid disease, chronic kidney disease, cancer, and pregnancy. Chronic disease defines as one or any combination of medical illness (diabetes mellitus, hypertension, cardiovascular diseases, cerebrovascular disease, chronic kidney disease, bronchial asthma, and cancer). 3) Case classification either local case or import cases.

Data collection and processing Analysis

Data was collected using proforma for specific variables by trained field researchers. The data was collected from Surveillance Unit in District Health Office. All variable was transformed into excel before converted into SPSS. The collected data were analysed using SPSS software (IBM SPSS Version 25.0). The data was coded, cleaned and recoded before analysing. All hypothesis testing in this study used a two-directional test with the significance level (α) set at 0.05. The Chi-square test was used to determine the association between the dependent variable and all the independent variables with categorical data. To control for possible confounding, all variables in the bivariate logistic regression model with a p-value <0.25 were added to the multivariable logistic regression model, and variables in the multiple logistic regression model with a p-value ≤ 0.05

were considered statistically significant to find the significant adjusted odds ratio at 95% confidence intervals.

Ethical Approval

Ethical approval for this study was obtained from the Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia. Study was registered in the National Medical Research Register (NMRR) (ID-22-00125-ZAO). Ethical approval was also obtained from the Ethics Committee of Universiti Putra Malaysia (JKEUPM - 2021 - 911). This study does not involve human subjects either through intervention or interactions with the individual. All data were collected from the existing Laboratory-confirmed COVID-19 infection data registry and all data were analyzed anonymously, and hence; informed consent was not required.

RESULTS

A total of 3004 data was obtained after data cleaning and checking for completeness. The results from the descriptive analysis and factors association with COVID-19 severity are presented in Table 1a, Table 2b and Figure 1.

Characteristic and COVID-19 infection outcome

Multiple Logistic Regression was performed to identify the significant characteristic of COVID-19 infection outcome. As shown in figure 2, only five of the factors made a statistically significant contribution to the final model namely age, gender, ethnicity, employment status, and chronic diseases status using "Forward and Backward Stepwise Likelihood Ratio" method. The full model had a good fit, indicating that the model was able to distinguish between respondents who have Moderate-severe and mild COVID-19 Infection.

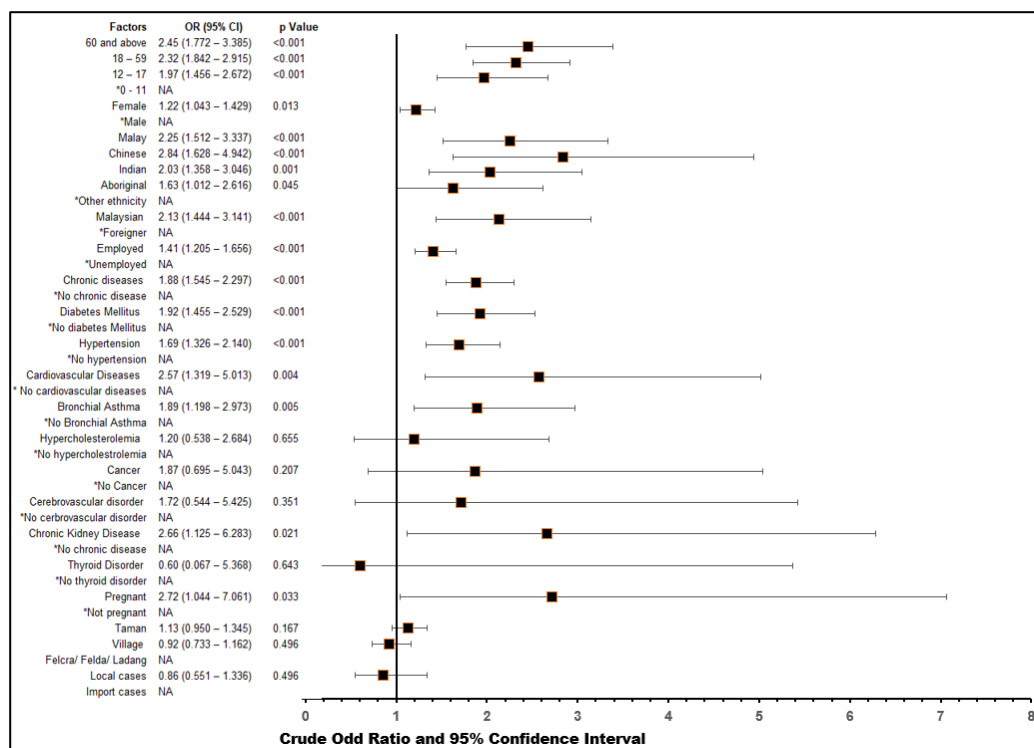


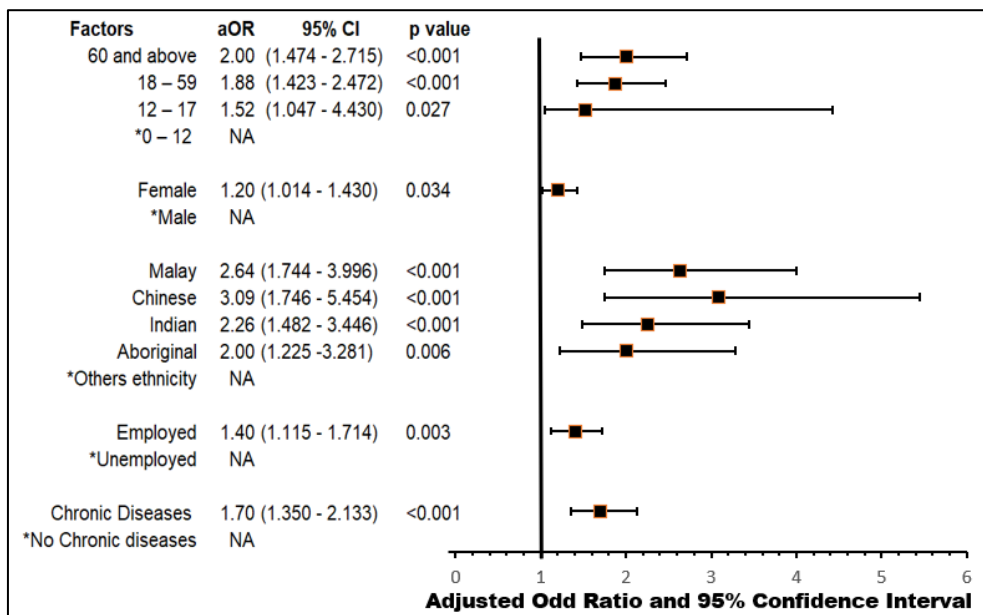
Figure 1: Characteristic and COVID-19 infection outcome

Table 1a. Respondent’s characteristic (sociodemographic and case classification

Variable	Total n = 3004 (%)	Moderate-Severe n = 884 (%)	Mild n = 2120 (%)
Age			
60 and above	275 (9.2)	94 (34.2)	181 (65.8)
18 - 59	1733 (57.7)	571 (32.9)	1162 (67.1)
12 - 17	373 (12.4)	110 (29.5)	263 (70.5)
0 - 11	623 (20.7)	109 (17.5)	514 (82.5)
Gender			
Female	1427 (47.5)	451 (31.6)	976 (68.4)
Male	1577 (52.5)	433 (27.5)	1144 (72.5)
Ethnicity			
Malay	1468 (48.9)	461 (31.4)	1007 (68.6)
Chinese	101 (3.4)	37 (36.6)	64 (63.4)
Indian	993 (33.1)	291 (29.3)	702 (70.7)
Aboriginal	253 (8.4)	63 (24.9)	190 (75.1)
Others	189 (6.3)	32 (16.9)	157 (83.1)
Nationality			
Malaysian	2815 (93.7)	852 (30.3)	1963 (69.7)
Foreigner	189 (6.3)	32 (16.9)	157 (83.1)
Employment status			
Employed	1202 (40.0)	406 (33.8)	796 (66.2)
Unemployed	1802 (60.0)	478 (26.5)	1324 (73.5)
Residency Status			
Taman	1356 (45.1)	422 (31.1)	934 (68.9)
Village	538 (17.9)	145 (27.0)	393 (73.0)
Felcra/ Felda/ Ladang	1110 (37.0)	317 (28.6)	793 (71.4)
Case Classification			
Local case	2912 (96.9)	854 (29.3)	2058 (70.7)
Imported case	92 (3.1)	30 (32.6)	62 (67.4)

Table 1b. Respondent's characteristic (Chronic disease and pregnancy status)

Variable	Total n = 3004 (%)	Moderate-Severe n = 884 (%)	Mild n = 2120 (%)
Chronic disease			
Yes	503 (16.7)	207 (41.2)	296 (58.8)
No	2501 (83.3)	677 (27.1)	1824 (72.9)
Diabetes Mellitus			
Yes	225 (7.5)	97 (43.1)	128 (56.9)
No	2779 (92.5)	787 (28.3)	1992 (71.7)
Hypertension			
Yes	319 (10.6)	127 (39.8)	192 (60.2)
No	2685 (89.4)	757 (28.2)	1928 (71.8)
Cardiovascular Diseases			
Yes	35 (1.2)	18 (51.4)	17 (48.6)
No	2969 (98.8)	866 (29.2)	2103 (70.8)
Bronchial Asthma			
Yes	78 (2.6)	34 (43.6)	44 (56.4)
No	2926 (97.4)	850 (29.0)	2076 (71.0)
Hypercholesterolemia			
Yes	27 (0.9)	9 (33.3)	18 (66.7)
No	2977 (99.1)	875 (29.4)	2102 (70.6)
Cancer			
Yes	16 (0.5)	7 (43.8)	9 (56.3)
No	2988 (99.5)	877 (29.4)	2111 (70.6)
Cerebrovascular disorder			
Yes	12 (0.4)	5 (41.7)	7 (58.3)
No	2992 (99.6)	879 (29.4)	2113 (70.6)
Chronic Kidney Disease			
Yes	21 (0.7)	11 (52.4)	10 (47.6)
No	2983 (99.3)	873 (29.3)	2110 (70.7)
Thyroid Disorder			
Yes	5 (0.2)	1 (20.0)	4 (80.0)
No	2999 (99.8)	883 (29.4)	2116 (70.6)
Pregnant			
Yes	17 (0.6)	9 (52.9)	8 (47.1)
No	2987 (99.4)	875 (29.3)	2112 (70.7)



Note: p-value < 0.05 is significant

Hosmer and Lemeshow test, Chi-square = 2.776, df = 8, p = 0.948

Cox and Snell R² = 0.040, Nagelkerke R² = 0.057, Overall accuracy 70.6%

Figure 2: Multiple Logistic Regression of patient characteristic and COVID-19 infection outcome

DISCUSSION

COVID-19, unlike SARS-CoV and MERS-CoV has spread worldwide tremendously. While several studies have been published substantially regarding the predictors of severe COVID-19 infection in general population, less is known about the factors associated with COVID-19 infection among rural population. Using multivariable analysis, we found age, gender, ethnicity, employment status, and chronic diseases were the significant characteristic associated with COVID-19 infection outcome.

Age

COVID-19 causes infection in any age group but may have different outcome depend on the age categories. The data analysis of this study among rural population shows that age is significantly associated with Covid-19 outcome with those of age 60 and above are more likely to have moderate to severe infection outcome followed by age of 18-59 and age 12-17, compared to paediatrics patient age 0-12. Generally, aging

populations with health conditions and immunosenescence are prone to have severe infection in viral disease²². As evidence, our study has showed that patient’s age is a consistent biological risk factor associated with the severity of COVID-19. The finding is consistent with the other study that demonstrate age as predictor for severe COVID-19 infection²³. Older COVID-19 patients are more prone to develop severe COVID-19 infection as they are at a greater risk of developing acute respiratory depressed syndrome (ARDS). Besides, the proportion of COVID-19 patients who required mechanical ventilation increase with age, whereby, the infected individual aged 60 and above is 4 times higher as compared to younger age²⁴. The previous study in China also proved that older age is significantly associated with severe COVID-19 and death due to COVID-19²⁵⁻²⁸. Thus, the risk of severe infection based on age characteristics shows similar results between rural and general population. Other studies that look into age-related factor also observed that paediatrics and young

adolescent age group are less likely to suffer from a severe form of Covid-19 infection²⁹⁻³⁰. The reason of such relative resistant towards severe Covid-19 infection among children and young adolescent remains unclear. Among possible explanation could be due to reason that children and young adolescent are less likely to have risk factors such as co-morbidities, smoking, and obesity and have better innate immune response and recovery ability compared to adults²⁹.

Gender

Our study found that female has a greater risk to suffer moderate-severe COVID-19 infection as compared to male. The result of this finding is contradicted with other study which observed that male is more likely to suffer from a severe Covid-19 infection and these finding may be explained as male are more likely associated with smoking³¹⁻³⁴. In Malaysia, the prevalence of smoking is higher in male than female³⁵. Besides that, male also more likely to be involve with outdoor activities and occupation that could insidiously and readily insulted their lung prior worsened by Covid-19 infection. However, this finding is not consistent with a nationwide study in Malaysia, whereby, gender is not associated with the severity of COVID-19 infection³⁶. Recent study in Selangor also indicates gender has no role to predict intubation among positive COVID-19 cases³⁷.

The reason why female is more likely to suffer from moderate-severe Covid-19 infection in this rural population remain unclear. Some plausible explanation to this phenomenon is the female group in this study are older and suffered from chronic diseases more than male counterparts. However, further evaluation is required to claim the argument.

Ethnicity

The association of ethnicity on the severity of COVID-19 infection remains unclear³⁸. In this study, ethnicity found to be significantly associated with the

severity of Covid-19 infection. Based on the analysis, Chinese are more likely to have moderate to severe Covid-19 infection outcome followed by Malay, Indian, and aboriginal, compared to other ethnicities. This finding is similar with another nationwide observational study on clinical characteristics and risk factors for severe COVID-19 infections done locally, in Malaysia³⁹. Despite of limited published literature on the ethnicity data of COVID-19 patients, emerging data from a systematic review that look into the impact of ethnicity on clinical outcomes in Covid-19, found out that being Black, Asian, and Minority Ethnic (BAME) individual had reported worse clinical outcome³⁹. Other study also demonstrate that individuals of Black and Asian ancestry have a higher chance of contracting COVID-19 than White people, and Asians is at higher risk of severe COVID-19 infection and death⁴⁰. Moreover, recent cohort study in United Kingdom reported risk of hospitalization, ICU admission and death due to COVID-19 infection were higher in the South Asian group than White group, but were lower in Black group⁴¹. Ethnicity is a complex issue and the disproportion could be linked to social, economic and health inequalities as well as genetic predisposition, biological or pathophysiological differences across the ethnicities in response to infection⁴².

Employment status

The data analysis in this study shows that employment status is a significant risk factor for COVID-19 infection outcome among rural population. Those who are employed are more likely to have moderate-severe infection outcome as compared to unemployed. More than half of the rural population in this study was unemployed with a third of this group came from the children and young adolescent group. Employment status directly affect income and draw the structural inequities that subsequently contribute to individual health status and ability to assess medical access⁴³. This could explain why employment status is a significant risk factor associated with the severity of Covid-19 infection in this

study. However, why those who were employed are more likely to suffer from moderate-severe Covid-19 infection in this study is unclear. Possible explanation includes, those who are employed were required to leave their home more and have themselves exposed to a more virulent Covid-19 variant.

Chronic diseases

Our study reveals that patients with comorbidities have higher risk of getting moderate-severe COVID-19 infection, whereby, we reported patients with chronic diseases, if they get infected with COVID-19, the risk to get moderate-severe COVID-19 is increase by 70%. Chronic diseases have also been found to be significantly associated with infection outcome in other studies. A study on risk factors for severe and critically ill Covid-19 patients in China shows that chronic diseases such as hypertension, diabetes, obesity, chronic lung diseases, heart, liver, kidney diseases, and immunodeficiencies associated with progression of COVID-19 into a severe and critical stage⁴⁴. Another study on predictors of Covid-19 severity in United States also shows that those with cardiovascular disease, chronic kidney disease, chronic lung diseases, diabetes mellitus, hypertension, immunosuppression, obesity, and sickle cell disease, predispose patients to an unfavourable clinical course and increased risk of intubation and death⁴⁵.

Strength

This strength of this study is large sample size and using complete secondary data set.

Limitations

Our study has the following limitations. First, the variables were limited based on screening form by the district health office, thus limit the exploration of other factors that may associated with COVID-19 infection severity. Second, the diagnosis of medical illness was based on patient history during the screening, there may be a very small number of patients with medical condition which may not have been accurately recorded.

Third, clinical staging for COVID-19 severity was done on the day of screening and laboratory investigation. Thus, patients that may experience worsening clinical condition were not recorded as the outcome of the study. However, these limitations will not affect the reliability of our overall results. For future research, primary data collection using standard set of questionnaires can be used to avoid these limitations.

CONCLUSION

The significant characteristics for moderate-severe COVID-19 infections were age, gender, ethnicity, employment status, and chronic diseases. Early recognition and prompt management of these cases might help to reduce COVID-19 severity in future.

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Conflict of Interest

The authors declare that there is no competing interest.

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