Malaysian Journal of Pharmaceutical Sciences
Vol. 20, No. 2, 105–120 (2022)

CLINICAL CHARACTERISTICS OF INDIVIDUALS DIED WITH COVID-19 IN MALAYSIA

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Published online: 16 Nov 2022
To cite this article: DANIAL, M., ARULAPPEN, A. L., SOELAR, S. A., CH'NG, A. S. H. & LOOI I. (2022) Clinical characteristics of individuals died with COVID-19 in Malaysia, *Malaysian Journal of Pharmaceutical Sciences*, 20(2): 105–120, https://doi.org/10.21315/mjps2022.20.2.9
To link to this article: https://doi.org/10.21315/mjps2022.20.2.9

ABSTRACT

Battling the COVID-19 pandemic still is the main agenda of many countries in the world today. This study aims to describe the clinical characteristics of COVID-19-related deaths in Malaysia in 2020. Data was obtained from the daily press conference on the COVID-19 situation in Malaysia. Only information on daily deaths were collected for the purpose of this study. A total of 471 COVID-19 deaths reported in Malaysia in 2020. Number of deaths reported for the age categories < 65 years old and ≥ 65 years old were almost equal. Majority of deaths were reported among male (66.2%), Malaysian (82.8%), from the state of Sabah (56.3%) and with comorbidities (75.4%). Commonly reported comorbidities were hypertension (53.1%), diabetes mellitus (37.6%) and heart disease (17.4%). Gout was more prevalent and attributed to significant rate of mortality in individuals ≥ 65 years old (6.1%; p = 0.011), whereas obesity (5.8%; p = 0.003) and asthma (4.5%; p = 0.040) were more prevalent and attributed to significant rate of mortality in individuals < 65 years old. Heart disease was more prevalent among males (n = 64, 20.5%; p = 0.013) and obesity was more prevalent among women (n = 11, 6.9%; p = 0.003). Furthermore, presence of comorbidities was significantly higher in Malaysians (p < 0.001) with two and more comorbidities (p = 0.007). Early detection of risk factors for critical conditions is urgently required to provide adequate supportive treatment.

***Keywords*:** Comorbidities, COVID-19, Died, Malaysia, Public data

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INTRODUCTION

All countries worldwide have been working primarily to reduce coronavirus disease 2019 (COVID-19) infection and its physiological, sociological and economic impacts in their respective countries since 2020. The epicentre of the outbreak was reported to originate from a wet market in Hubei Province, Wuhan, China in December 2019, where a pneumonia-like outbreak was reported to have a high infection rate and mortality (Jin *et al.* 2020). Subsequently, the outbreak was reported to cause by a coronavirus and it was classified as 2019 novel coronavirus (2019-nCoV), and the disease was named COVID-19 (Pradhan and Olsson 2020). Coronaviruses have been found in a large number of domestic and wild mammals and birds, with some studies suggesting that birds and bats are the natural reservoirs of the virus (Anand *et al*. 2020). Genetic analysis reveals that viral strains of COVID-19 indicated a recent shift to humans from animal reservoirs (Anand *et al*. 2020).

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is primarily transmitted by respiratory droplets from person to person and the clinical characteristics of COVID-19 vary from asymptomatic respiratory infections to serious pneumonia (Kai and Kai 2020). Clinical classifications of severity as defined by the National Health Committee of China are (a) mild with the imaging shows no signs of pneumonia; (b) moderate associated with the presence of fever, respiratory tract symptoms and imaging shows signs of pneumonia; (c) severe associated with the presence of any of these signs such as respiratory distress with a respiratory rate of 30 beats/min or in the resting state, the finger oxygen saturation is 93% with arterial blood oxygen partial pressure (PaO_2/oxygen concentration [FiO_2] of 300 mmHg); (d) critical is associated with one of the following conditions such as respiratory failure which requires mechanical ventilation, shock and intensive care unit (ICU) admission (Jin *et al*. 2020). Clinical staging of syndrome associated with COVID-19 in Malaysia are categorised into five stages. Stage 1: asymptomatic (absence of flu-like symptoms such as fever, dry cough, and shortness of breath or difficulty breathing and other related symptoms such as chills and repeated shaking, muscle pain, headache, sore throat and loss of sense of taste or smell); stage 2: symptomatic, no pneumonia (with symptoms and without pneumonia); stage 3: symptomatic with pneumonia (with symptoms and with pneumonia); stage 4: symptomatic with pneumonia that requires supplemental oxygen and stage 5: critically ill with multi-organ involvement (Ministry of Health Malaysia 2020a).

In Malaysia, about 1 in 2 COVID-19 individuals exhibit no symptoms at the time they tested positive (Timbuong 2020). Furthermore, a study conducted by the Institute for Clinical Research (ICR) Malaysia involving 5,889 COVID-19 individuals reported 31.6% individuals have symptoms but no lung involvement, 13.6% individuals have lung infection without shortness of breath, 3.5% individuals have lung infection with shortness of breath, 1.1% individuals were very sick and 50.2% individuals exhibits no symptoms at all. Additionally, commonest symptoms among Malaysians upon admission are cough, fever and sore throat (Institute for Clinical Research 2020).

In 2020, there were 83,943,230 COVID-19 cases and 1,826,917 COVID-19 related deaths reported worldwide (Worldometers.info 2020). As of 31 December 2020, there was a total of 113,010 cases reported in Malaysia, with the total number of recoveries at 88,941 cases (78.7% of the total cases) and 471 deaths (0.42% of the total cases) (Ministry of Health Malaysia 2020d).The death toll for every 1 million people in the United States of America was 741, United Kingdom 732, Indonesia 54 and the Philippines 70, while deaths in Malaysia were still at a low level of 9 deaths per 1 million population (Worldometers.info 2020). Data reported from Malaysia indicated about 85.4% of the total mortality due to COVID-19 were among individuals aged ≥ 50 years old with high blood pressure, diabetes and heart disease (Ministry of Health Malaysia 2020e).

Therefore, the present study aims to describe the clinical characteristics of COVID-19-related deaths and the association between demographic factors and comorbidities in individuals died with COVID-19 in Malaysia.

METHODS

Data Collection from the COVID-19 Publicly Available Data in Malaysia

Public data that was presented by the Director-General of the Ministry of Health (MOH) Malaysia during the daily press conference on the COVID-19 situation in Malaysia in year 2020 were collected retrospectively for the purpose of this study. The duration of the data collected for this study was from the time the first case of COVID-19 positive case reported in Malaysia which was on 25 January 2020 until 31 December 2020. Only information on daily deaths were collected for the purpose of this study which includes the death number, state of origin, gender, age, place where the death was recorded and presence of comorbidities. Data from all the 471 deaths reported among COVID-19 positive individuals in Malaysia in the year 2020 were included in the study and none was excluded.

At the onset of the COVID-19 outbreak in Wuhan, China, the MOH responded with the preparedness to contain the infection in Malaysia. MOH activated the National Crisis Preparedness and Response Centre (CPRC) to monitor current developments on COVID-19 in the country and to prepare for the pandemic (Ministry of Communication and Multimedia Malaysia 2020).

Daily COVID-19 positive cases for SARS-CoV-2 from all the 13 states and 3 federal territories (Kuala Lumpur, Putrajaya and Labuan) in Malaysia will be identified through positive reverse transcription-polymerase chain reaction (RT-PCR) results that were conducted at various government and non-government health facilities which must be uploaded into the Public Health Laboratory Information System (SIMKA), which is monitored by the MOH through the District Health Office (PKD), the State Health Department and the National Public Health Laboratory to ensure the appropriateness of the results (CPRC Kebangsaan-Kementerian Kesihatan Malaysia 2020). Daily COVID-19 positive cases for the completed data which consist of cases in each state, number of recovered and new cases, new clusters information, number of individuals in the ICU, number of individuals requiring oxygen support and number of daily deaths. Only the death number, state of origin, gender, age, place where the death was recorded and presence of comorbidities will be briefly described for COVID-19 positive individuals who died daily. This information will be sent from PKDs of all the states and federal territories to the CPRC by 12 noon daily. These data together with the advice on cubing the COVID-19 infections will be presented by the Director-General of the MOH Malaysia during the daily press conference on the COVID-19 situation in Malaysia (Ministry of Health Malaysia 2020d) and thereafter the contents of the press statement are made available on the website (Bernama 2021).

COVID-19-related deaths were defined as those occurring in individuals who tested positive through RT-PCR, independently from pre-existing diseases that may have caused or contributed to death. The system was unable to collect detailed clinical data (CPRC Kebangsaan-Kementerian Kesihatan Malaysia 2020).

Ethical Approval

The study was carried out after obtaining the approval from the Medical Research & Ethics Committee (MREC), Ministry of Health Malaysia (MOH). Study approval number: KKM/ NIHSEC/ P20-1920 (4) dated 10 September 2020.

The need to obtain consent from study participants was waived as there is no direct interaction with the study participants in accordance with the Medical Research and Ethics Committee (MREC), MOH Malaysia regulations.

Statistical Analysis

Data were expressed as mean ± SD, median (interquartile range [IQR]) or percentages, as appropriate. Continuously distributed variables were analysed using either *t*-test or Mann-Whitney U test depending on skewness of data, whereas for categorical variables analysis was performed using the Pearson's chi-squared (X^2) test. All statistical analysis was performed using IBM SPSS version 22.0, SPSS, Inc., Chicago, IL) statistical software. Two-sided *p*-values of less than 0.05 were considered statistically significant.

RESULTS

Demographic Characteristics

In Malaysia, 2020 was the first year of our nation's battle against the COVID-19 pandemic, with a total of 471 deaths reported among COVID-19 positive individuals. The mean age of individuals who died with COVID-19 infection was 63 (SD = 15.99) years old (Table 1), with those below 65 years old makes up to about 52% of the total. The minimum age reported was 1 year old Malaysian and, the maximum age was 130 years old non-Malaysian, both deaths were reported from the state of Sabah (Ministry of Health 2020b; 2020c). Males constitute over 66% and more than 80% of deaths were reported among Malaysians. Over 75% of these individuals were reported with at least one pre-existing comorbidities. Majority of the individuals were reported with comorbidities such as hypertension (*n* = 250, 53.1%), diabetes mellitus (*n* = 177, 37.6%), heart disease (*n* = 82, 17.4%), kidney disease (*n* = 68, 14.4%) and dyslipidaemia (*n* = 56, 11.9%). From the top 5 hospitals that reported the most deaths in 2020, the top 3 hospitals were the Hospital Duchess of Kent (*n* = 81, 17.2%), Hospital Queen Elizabeth (*n* = 73, 15.5%) and Hospital Tawau (*n* = 56, 11.9%) which are all located in the state of Sabah, East Malaysia. The remainder two hospitals are located in West Malaysia: Hospital Sungai Buloh, Selangor (*n* = 38, 8.1%) and Hospital Enche' Besar Hajjah Khalsom, Johor (*n* = 25, 5.3%), respectively. This resulted in more than 50% of deaths was reported from the state of Sabah compared to other states in Malaysia.

Table 1: Demographic characteristics of COVID-19 positive individuals who died in Malaysia in year 2020 (*n* = 471).

Characteristics	Overall (*n* = 471)	
	Mean (SD)	***n* (%)**
Age (years old)	63.0 (15.99)	
< 65		243 (51.6)
≥ 65		228 (48.4)
Gender		
Male		312 (66.2)
Female		159 (33.8)
Nationality		
Malaysian		390 (82.8)
Non-Malaysian		81 (17.2)
State reported		
Sabah		265 (56.3)
Selangor		38 (8.1)
Johor		36 (7.6)
Kuala Lumpur		30 (6.4)
Sarawak		18 (3.8)
Others		84 (17.8)
Comorbidities		
Hypertension		250 (53.1)
Diabetes mellitus		177 (37.6)
Heart disease		82 (17.4)
Kidney disease		68 (14.4)
Dyslipidaemia		56 (11.9)
Stroke		49(10.4)
Gout		18 (3.8)
Lung disease		17 (3.6)
Cancer		16 (3.4)
Obesity		16 (3.4)
Asthma		14 (3.0)
Others		51 (10.8)
Number of comorbidities		
0		116 (24.6)
1		111 (23.6)
2		92 (19.5)
3		106 (22.5)
4 or more		46 (9.8)

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Table 1: (*continued*)

Characteristics	Overall (*n* = 471)	
	Mean (SD)	***n* (%)**
Hospital where death reported		
Hospital Duchess of Kent		81 (17.2)
Hospital Queen Elizabeth		73 (15.5)
Hospital Tawau		56 (11.9)
Hospital Sungai Buloh		38 (8.1)
Hospital Enche' Besar Hajjah Khalsom		25 (5.3)
Others		198 (41.9)

Note: SD = standard deviation.

Second and Third COVID-19 Infection Wave in Malaysia

COVID-19 infection waves show a progressive increase in daily reported positive cases and mortality over time. When these figures are graphed over time, they form a wave pattern, indicating that the incidence of infection peaked during a specific time frame, followed by a valley. A wave is the crest-trough pattern of an epidemic's or pandemic's spread (Dutta 2021).

Three infection waves of COVID-19 pandemic have been reported in Malaysia by the end of 2020. There have been no deaths reported in the first infection wave which begun in 25 January 2020 and ended in 16 February 2020. In the second infection wave which begun on 27 February 2020 until 30 June 2020, about 141 deaths were reported (Ahmad and Pfordten 2020). Simultaneously, the third infection wave which begun on 8 October 2020 and which is still activate at the end of 2020, have been reported with 330 deaths (New Straits Times 2020a). Majority of the deaths reported from the second wave were primarily from Hospital Kuala Lumpur (*n* = 17) and from Wilayah Persekutuan Kuala Lumpur (*n* = 26) (Figure 1) and majority of the deaths reported from the third wave were from the Hospital Duchess of Kent (*n* = 80) and state of Sabah (*n* = 247) (Figure 2). The association between COVID-19 infection waves and demographic parameters aids in the localisation of higher incidence of positive cases and mortality throughout the respective wave time frame in different states in Malaysia. As a comparison the number of deaths reported in the third infection rate was alarmingly high compared to the first two infection waves.

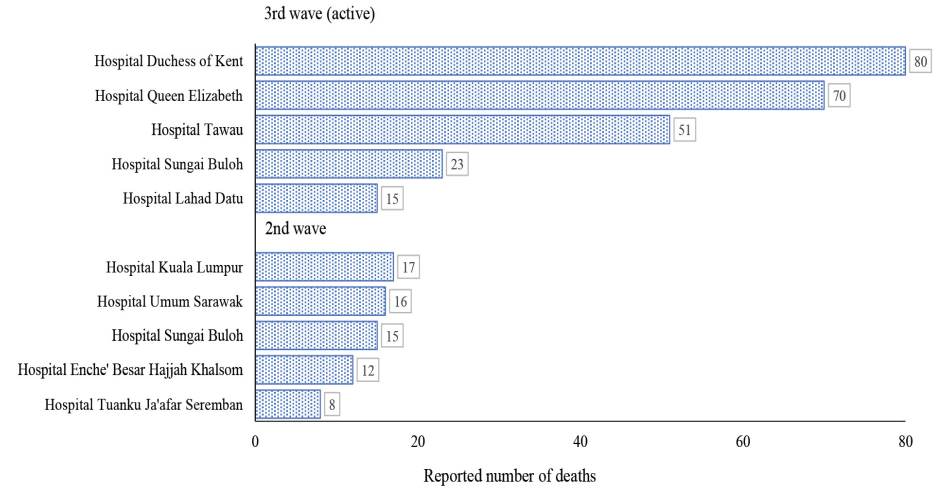

Figure 1: Hospitals that reported highest number of COVID-19 related mortalities in Malaysia for year 2020 based on infection wave.

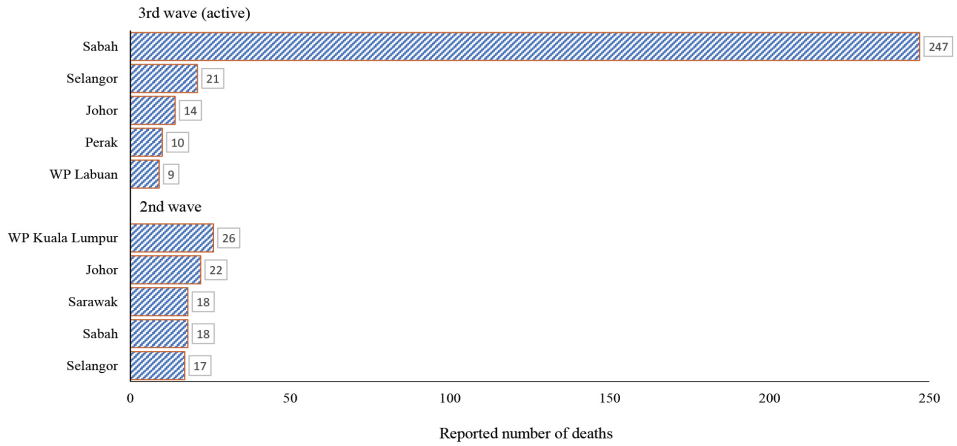

Figure 2: States that reported highest number of COVID-19 related mortalities in Malaysia for year 2020 based on infection wave.

Association between Demographic Factors and Comorbidities

To access the demographic association between the reported comorbidities, an analysis was performed based on the categories of age, gender, nationality and state reports. Individuals who died with COVID-19 in Malaysia had a high prevalence of comorbidities, with hypertension and diabetes mellitus accounting for more than 40% of all reported comorbidities (Table 2).

Table 2: Association between demographic factors and comorbidities among COVID-19 positive individuals who died in Malaysia in year 2020 (*n* = 471).

Characteristics	Age groups			Gender			Nationality			State reported		
	< 65 years old (*n* = 243)	≥ 65 years old (*n* = 228)	*p*-value[a]	Male (*n* = 312)	Female (*n* = 159)	*p*-value[a]	Malaysian (*n* = 390)	Non-Malaysian (*n* = 81)	*p*-value[a]	Sabah (*n* = 265)	Non-Sabah (*n* = 206)	*p*-value[a]
	n (%)	*n* (%)		*n* (%)	*n* (%)		*n* (%)	*n* (%)		*n* (%)	*n* (%)	
Comorbidities												
Hypertension	122 (50.2)	128 (56.1)	0.197	161 (51.6)	89 (56.0)	0.369	229 (58.7)	21 (25.9)	< 0.001*	132 (49.8)	118 (57.3)	0.107
Diabetes mellitus	100 (41.2)	77 (33.8)	0.098	118 (37.8)	59 (37.1)	0.880	158 (40.5)	19 (23.5)	0.004*	82 (30.9)	95 (46.1)	0.001*
Heart disease	37 (15.2)	45 (19.7)	0.197	64 (20.5)	18 (11.3)	0.013*	72 (18.5)	10 (12.3)	0.187	44 (16.6)	38 (18.4)	0.601
Kidney disease	41 (16.9)	27 (11.8)	0.121	50 (16.0)	18 (11.3)	0.169	65 (16.7)	3 (3.7)	0.003*	23 (8.7)	45 (21.8)	< 0.001*
Dyslipidaemia	27 (11.1)	29 (12.7)	0.590	34 (10.9)	22 (13.8)	0.351	53 (13.6)	3 (3.7)	0.012*	35 (13.2)	21 (10.2)	0.316
Stroke	22 (9.1)	27 (11.8)	0.322	37 (11.9)	12 (7.5)	0.147	42 (10.8)	7 (8.6)	0.568	28 (10.6)	21 (10.2)	0.896
Gout	4 (1.6)	14 (6.1)	0.011*	14 (4.5)	4 (2.5)	0.291	15 (3.8)	3 (3.7)	0.951	11 (4.2)	7 (3.4)	0.672
Lung disease	5 (2.1)	12 (5.3)	0.062	13 (4.2)	4 (2.5)	0.364	16 (4.1)	1 (1.2)	0.208	12 (4.5)	5 (2.4)	0.225
Cancer	6 (2.5)	10 (4.4)	0.251	8 (2.6)	8 (5.0)	0.162	15 (3.8)	1 (1.2)	0.238	8 (3.0)	8 (3.9)	0.607
Obesity	14 (5.8)	2 (0.9)	0.003*	5 (1.6)	11 (6.9)	0.003*	15 (3.8)	1 (1.2)	0.238	7 (2.6)	9 (4.4)	0.305
Asthma	11 (4.5)	3 (1.3)	0.040*	7 (2.2)	7 (4.4)	0.192	12 (3.1)	2 (2.5)	0.769	9 (3.4)	5 (2.4)	0.539
Others	21 (8.6)	30 (13.2)	0.115	30 (9.6)	21 (13.2)	0.235	45 (11.5)	6 (7.4)	0.276	31 (11.7)	20 (9.7)	0.491
Number of comorbidities			0.511			0.770						0.109
0	65 (26.7)	51 (22.4)		76 (24.4)	40 (25.2)		79 (20.3)	37 (45.7)		71 (26.8)	45 (21.8)	
1	59 (24.3)	52 (22.8)		73 (23.4)	38 (23.9)		88 (22.6)	23 (28.4)		70 (26.4)	41 (19.9)	
2	42 (17.3)	50 (21.9)		65 (20.8)	27 (17.0)		81 (20.8)	11 (13.6)		47 (17.7)	45 (21.8)	
3	51 (21.0)	55 (24.1)		66 (21.2)	40 (25.2)		98 (25.1)	8 (9.9)		57 (21.5)	49 (23.8)	
4 or more	26 (10.7)	20 (8.8)		32 (10.3)	14 (8.8)		44 (11.3)	2 (2.5)		20 (7.5)	26 (12.6)	

Notes: [a]Pearson's chi-squared test for independence; **p*-value < 0.05.

In terms of age category-based comparison, gout was most prevalent among individuals ≥ 65 years old (n =14, 6.1%) with higher rate of mortality (p = 0.011). On contrary, comorbidities obesity (n = 14, 5.8%; p = 0.003) and asthma (n = 11, 4.5%; p = 0.040) were more prevalent among individuals who were < 65 years old with significant mortality rates. Heart disease was more prevalent among males (n = 64, 20.5%; p = 0.013) and obesity was more prevalent among women (n = 11, 6.9%; p = 0.003) in gender-based comparison among individuals who died with COVID-19. Furthermore, a nationality-based comparison of individuals who died with COVID-19 shows that Malaysians had a higher prevalence of comorbidities such as hypertension (n = 229, 58.7%; p < 0.001), diabetes mellitus (n = 158, 40.5%; p = 0.004), kidney disease (n = 65, 16.7%; p = 0.003) and dyslipidaemia (n = 53, 13.6%; p = 0.012).

The state-based comparison was made using Sabah and non-Sabah states as many positive cases emerged from the state of Sabah that spread to the other states in Malaysia following the Sabah state by-elections (New Straits Times 2020b). By the end of 2020, non-Sabah states recorded a higher number and a more significant prevalence of individuals who died with COVID-19 with comorbidities such as diabetes mellitus (n = 95, 46.1%; p = 0.001) and kidney disease (n = 45, 21.8%; p < 0.001).

Malaysians reported having more comorbidities than non-Malaysians, indicating a significant difference in the association between the number of comorbidities and the demographic factor (p < 0.001).

The presence or absence of comorbidities was compared to demographic factors. There were about 335 individuals with comorbidities and 116 individuals without comorbidities. Categories that had higher rates of mortality among individuals who died with COVID-19 were individuals who were ≥ 65 years old (OR: 1.13; 95% CI: 0.73, 1.75), female (OR: 1.05; 95% CI: 0.66, 1.66), Malaysian (OR: 3.27; 95% CI: 1.93, 5.54) and from the non-Sabah state (OR: 1.00; 95% CI: 0.63, 1.58). Malaysians with comorbidities had higher mortality rate when compared between the presence or absence of comorbidities (p < 0.001) (Table 3).

Similarly, when comparison was made between the presence of 1 (n = 111) and ≥ 2 (n = 244) comorbidities, categories that had higher rates of mortality among individuals who died with COVID-19 were individuals who were ≥ 65 years old (OR: 1.09; 95% CI: 0.69, 1.73), female (OR: 1.01; 95% CI: 0.62, 1.64), Malaysian (OR: 2.47; 95% CI: 1.28, 4.77) and from non-Sabah state (OR: 1.44; 95% CI: 0.90, 2.32). Malaysians with ≥ 2 comorbidities had higher mortality rate (p = 0.007) (Table 4).

Table 3: Comparison of demographic factors between without and with any comorbidities.

Characteristics	Without (n = 116)	With (n = 355)	Simple logistic regression		Multiple logistic regression	
	n (%)	n (%)	Crude OR (95% CI)	p-value	Adj. OR (95% CI)	p-value
Age (years old)						
< 65	65 (56.0)	178 (50.1)	1.00 (ref.)		1.00 (ref.)	
≥ 65	51 (44.0)	177 (49.9)	1.27 (0.83, 1.93)	0.271	1.13 (0.73, 1.75)	0.570
Gender						
Male	76 (65.5)	236 (66.5)	1.00 (ref.)		1.00 (ref.)	
Female	40 (34.5)	119 (33.5)	0.96 (0.62, 1.49)	0.849	1.05 (0.66, 1.66)	0.840

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Table 3: (*continued*)

Characteristics	Without (*n* = 116)	With (*n* = 355)	Simple logistic regression		Multiple logistic regression	
	n (%)	*n* (%)	Crude OR (95% CI)	*p*-value	Adj. OR (95% CI)	*p*-value
Nationality						
Non-Malaysian	37 (31.9)	44 (12.4)	1.00 (ref.)		1.00 (ref.)	
Malaysian	79 (68.1)	311 (87.6)	3.31 (2.00, 5.47)	< 0.001*	3.27 (1.93, 5.54)	< 0.001*
State reported						
Sabah	71 (61.2)	194 (54.6)	1.00 (ref.)		1.00 (ref.)	
Non-Sabah	45 (38.8)	161 (45.4)	1.31 (0.85, 2.01)	0.217	1.00 (0.63, 1.58)	0.999

Notes: Adj. OR (95% CI) = adjusted odds ratio (95% confidence interval); *p-value < 0.05.

Table 4: Comparison of demographic factors between 1 comorbidity and ≥ 2 comorbidities.

Characteristics	1 (*n* = 111)	≥ 2 (*n* = 244)	Simple logistic regression		Multiple logistic regression	
	n (%)	*n* (%)	Crude OR (95% CI)	*p*-value	Adj. OR (95% CI)	*p*-value
Age (years old)						
< 65	59 (53.2)	119 (48.8)	1.00 (ref.)		1.00 (ref.)	
≥ 65	52 (46.8)	125 (51.2)	1.19 (0.76, 1.87)	0.444	1.09 (0.69, 1.73)	0.718
Gender						
Male	73 (65.8)	163 (66.8)	1.00 (ref.)		1.00 (ref.)	
Female	38 (34.2)	81 (33.2)	0.96 (0.59, 1.53)	0.848	1.01 (0.62, 1.64)	0.969
Nationality						
Non-Malaysian	23 (20.7)	21 (8.6)	1.00 (ref.)		1.00 (ref.)	
Malaysian	88 (79.3)	223 (91.4)	2.78 (1.46, 5.27)	0.002*	2.47 (1.28, 4.77)	0.007*
*State reported						
Sabah	70 (63.1)	124 (50.8)	1.00 (ref.)		1.00 (ref.)	
Non-Sabah	41 (36.9)	120 (49.2)	1.65 (1.04, 2.62)	0.032*	1.44 (0.90, 2.32)	0.132

Notes: Adj. OR (95% CI) = adjusted odds ratio (95% confidence interval); *p-value < 0.05.

DISCUSSION

Public data categorisation to access the demographic association between the reported comorbidities in this study provides more comprehensive details of the COVID-19 related mortality from public domains in Malaysia.

From our study, two thirds of individuals who died in 2020 due to COVID-19 were Malaysian men. Similarly, studies conducted in China and Italy reported deaths occurred in primarily in COVID-19 positive males compared to females (Di Stadio *et al*. 2020). Gender is a risk factor for increased severity and mortality in individuals with COVID-19, regardless of age and susceptibility due to composition of sex chromosomes which plays an important role disease outcome (Jin *et al*. 2020). Shorter life expectancy in men (72.2 years old)

compared to women (77.3 years old) in Malaysia and worldwide (DOSM, 2020) would correlate to a higher prevalence of mortality in men as disease outcomes.

Males and females show a distinct difference in immune system responses, with females developing better immune responses to pathogens due to the presence of two copies of X chromosomes instead of one copy in males. Females have better strategy to overcome the early attack of the SARS-CoV-2 virus due to two copies of X chromosomes compared to males (Pradhan and Olsson 2020). In addition, sex hormone oestrogen, which is more prevalent in females, enhances protection from severe acute respiratory syndrome (SARS) infections (Channappanavar *et al*. 2017).

Furthermore, the differences in immune system responses between males and females can be a significant contributor to viral load, disease severity and mortality (Heron 2019). Similar to our study findings, males are associated with higher mortality due to heart disease, diabetes, liver disease, kidney disease and cancer, as these diseases are primarily gender-related and thus may be attributed to gender-specific mortality among positive COVID-19 individuals (Wakabayashi 2017). A recent study stated that coronavirus can be present in male testis with viral RNA analysis revealed that males display delayed viral clearance of SARS-CoV-2 RNA compared to females (Zheng *et al*. 2020).

The state of Sabah, East Malaysia, had the highest number of COVID-19 deaths in Malaysia in 2020. Coronavirus infections have been on the rise in Sabah since a state-wide election in September 2020 (New Straits Times 2020b). Thus, the higher prevalence of mortality among in the state of Sabah could be attributed to delay in seeking treatment even after falling ill that are likely leading to more severe COVID-19 infections and the state's higher death rate. Furthermore, other possible factors were many communities live far in the interior or on remote islands rendering contact tracing or transporting individuals to health facilities quickly (Rozanna 2020).

Finding from our study indicates that, a minor proportion of the individual who were < 65 years old who died with COVID-19 had lesser or no comorbidities compared with individuals who were ≥ 65 years old who had higher number of comorbidities. This indicates that, healthy individuals can potentially develop clinically significant respiratory and non-respiratory complications from COVID-19, which can be life-threatening. In contrast, older individuals are more vulnerable to mortality due to their pre-existing comorbidities condition (Palmieri *et al.* 2020). Moreover, some of the positive COVID-19 individuals identified in the public domain in Malaysia were listed as brought in dead (BID) suggesting that the person had died before they could be admitted to hospital, and therefore no comorbidities had been reported (Salim 2020).

Gout was prevalent and increased the mortality rate in individuals aged ≥ 65 years old. Individuals with gout are usually present with elevated amounts of auto-inflammatory interleukin-1β (Topless *et al*. 2020). It has been reported that the overexpression of interleukin-1β by the body's innate immune response could potentially lead to increased immune response to SARS-CoV-2, resulting in people with gout will be at risk of poor COVID-19 outcomes (Del Valle *et al.* 2020).

This study's results coincides with previously reported studies, which reported that severe symptoms and higher mortality were observed when comorbidities such as diabetes, hypertension, cardiovascular disease and kidney disease are present in both young and older individuals (Di Stadio *et al*. 2020). The elevated protein furin levels in the blood plasma act as an independent predictor for disease onset, progression and premature mortality in individuals with diabetes, heart disease and kidney disease (Fernandez *et al.* 2018). Weak immune system in the body enables furin-mediated entry of the SARS-CoV-2 virus into target cells thereby increasing the viral load (Critchley *et al.* 2018). Severely impacted organs by SARS-CoV-2 infection, were the lungs, liver and kidney that exhibits high

expressions of furin (Ganesan *et al.* 2020). Additionally, SARS-CoV-2 infection can cause direct primary myocardial injury or worsen original myocardial injury (Oudit *et al.* 2009). It was further confirmed with the detection of ribose nucleic acid (RNA) of SARS-CoV from the heart tissues of the dead COVID-19 individuals (Li *et al.* 2020).

Obesity is a risk factor for COVID-19-related mortality in both men and women. This finding is consistent with recent research indicating that obesity is a risk factor (Huang *et al*. 2020). The adipose tissues of obese individuals could serve as a potential reservoir for the deposition of SARS-CoV-2 before they spread to other organs in the body. This is achieved by the alteration of immune response which directly weakens the host defence and leads to cytokine storm in case of infection with SARS-CoV-2 in obese individuals (Sattar, McInnes and McMurray 2020). Obesity diminishes the role of the lungs through increased resistance in the airways and increased difficulty in expanding the lungs. When obese individuals are to be admitted to ICU, it is difficult to raise their oxygen saturation levels and ventilate them (Sattar, McInnes and McMurray 2020), which ultimately leads to death.

The majority of individuals who died with COVID-19 in Malaysia in year 2020, had at least of two or more comorbidities. Similarly, previously reported studies corelated presence of multiple comorbidities with elevated risk of mortality and adverse outcomes in COVID-19 positive individuals (Fernandez *et al.* 2018). Also, it was reported that the major comorbidities such as hypertension and diabetes were more common in older individuals, in contrast with comorbidities such as obesity, HIV and chronic liver disease which were more prevalent in younger individuals (Palmieri *et al*. 2020). In case of an individual with many comorbidities, COVID-19 infection could be attributed as cause of death, but there is no confirmation can be made on this. This is because it is difficult to establish the cause of death in persons with multiple comorbidities and infected with SARS-CoV-2. Therefore, it is important to establish internationally agreed criteria to classify deaths as attributable to COVID- 19 infection as to ease reporting and global comparison (Palmieri *et al*. 2020). Thus, to over this problem, the WHO has issued international guidelines for the certification and coding of SARS-CoV-2 infections as a cause of death, which will help to standardise and compare mortality outcomes across countries (World Health Organization 2020).

Study Limitation

In this study, only the brief information described for COVID-19 positive individuals who died daily in Malaysia that was presented by the Director-General of MOH Malaysia during his daily press conference on the COVID-19 situation in Malaysia was included in this study. The limited data sharing was done to avoid misinterpretations by the public (Razak 2020). Secondly, there could be underreporting for some pre-existing conditions. Lastly, generalisability of our findings may be limited, as we provide data only on COVID-19 deaths reported in Malaysia in 2020.

CONCLUSION

Majority of individuals who died with COVID-19 in Malaysia in year 2020 were present with multiple comorbidities such as hypertension, diabetes mellitus, gout, obesity, asthma and heart disease. Additionally, small proportion of deaths occurred in individuals with COVID-19 who did not have pre-existing comorbidities. Early detection of risk factors for critical conditions is urgently required, not only to define more specifically the underlying clinical and epidemiological characteristics, but also to promote adequate supportive treatment and prompt access to the ICU. Though the data for the research is localised, the

comorbidities that were associated with the mortality among the COVID-19 individuals were the comorbidities that were profoundly found and reported in our region. For future research, it is recommended an online system is adopted to automatically capture the COVID-19 data in real-time which could provide more detailed information for more in-depth research and analysis. These data could also aid in prediction research, in predicting possible infection waves in the future, which will enable the deployment of resources and manpower where ever it is most needed.

ACKNOWLEDGEMENTS

We would like to thank the Director General of Health Malaysia for the permission to publish this article. The data set of this study are publicly available from the daily press statement by the Ministry of Health Malaysia on updates on the COVID-19 situation in Malaysia.

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