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Original Article

Risk Factors of Covid-19 Confirmed Died Patients in Dr. Kariadi Hospital: A Retrospective Study

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ABSTRACT

Covid-19 is a communicable disease causing global pandemic. Some factors inflict worse infection. This study aims to investigate risk factors of Covid-19 confirmed died patients at Dr. Kariadi Hospital Semarang. It is a retrospective study with a total sample of all Covid-19 confirmed patients involving died and healed patients from March to June 2020. Data was gathered from screening forms and analysed with Chi Square (confidence interval of 95%). This study found sixteen risk factors of Covid-19 confirmed died patients involving age (p= 0.000; OR= 8.803; 95% CI 3.982-19.462), entrepreneur (p= 0.041; OR= 14.894; 95% CI 1.12-198.65), farmer/trader (p= 0.029; OR= 25.625; 95% CI 1.40-469.25), contact history (p= 0.000; OR= 12.923; 95% CI 6.163-27.097), fever (p= 0.000; OR= 4.877; 95% CI 2.647-8.984), dyspnea (p=0.000; OR= 17.018; 95% CI 8.523-33.977), cough (p= 0.009; OR= 2.178; 95% CI 1.205-3.935), lethargic (p=0.010; OR= 2.282; 95% CI 1.205-4.323), cold (p= 0.002; OR= 0.180; 95% CI 0.054-0.600), diabetes (p=0.000; OR= 9.767; 95% CI 3.932-24.263), COPD (p= 0.001; OR= 6.360; 95% CI 2.164-18.690), hypertension (p= 0.043; OR= 2.436; 95% CI 1.008-5.887), cancer (p=0.001; OR= 9.647; 95% CI 2.413-38.579), heart disease (p= 0.000; OR= 12.226; 95% CI 2.4-62.294), neurological disorders (p=0.008; OR= 6.057; 95% CI 1.650-22.232), and immune disorders (p=0.031; OR= 1.625; 95% CI 1.186-113.899). Adequate handling is needed to prevent death. in patients with confirmed Covid-19 who have risk factors.

Keywords: *Risk factor; Confirmed patients; Covid 19*; *Died; Retrospective*

ABSTRAK

Covid-19 merupakan penyakit yang cepat menular sehingga menyebabkan pandemi di seluruh negara. Ada beberapa faktor risiko yang menjadikan Covid-19 menginfeksi seseorang menjadi lebih parah. Penelitian ini bertujuan untuk mengetahui faktor risiko pasien terkonfirmasi Covid-19 yang meninggal dunia di RSUP Dr. Kariadi. Penelitian ini merupakan retrospective study. Populasi adalah seluruh pasien terkonfirmasi Covid-19 di RSUP Dr. Kariadi. Sampel penelitian adalah seluruh pasien terkonfirmasi Covid-19 yang terdiri dari pasien meninggal dan sembuh tercatat sejak bulan Maret sampai Juni 2020. Data diperoleh dari formulir screeening dan dianalisis menggunakan uji Chi Square dengan tingkat kepercayaan 95%. Hasil peneltian menemukan enam belas faktor risiko pasien terkonfirmasi Covid-19 meninggal, yaitu umur (p= 0,000; OR= 8,803; 95% CI 3,982-19,462), wiraswasta (p= 0,041; OR= 14,894; 95% CI 1,12-198,65), petani/pedagang (p= 0,029; OR= 25,625; 95% CI 1,40-469,25), riwayat kontak (p= 0,000; OR= 12,923; 95% CI 6,163-27,097), demam (p= 0,000; OR= 4,877; 95% CI 2,647-8,984), sesak napas (p=0,000; OR= 17,018; 95% CI 8,523-33,977), batuk (p= 0,009; OR= 2,178; 95% CI 1,205-3,935), lemah lesu (p=0,010; OR= 2,282; 95% CI 1,205-4,323), pilek (p= 0,002; OR= 0,180; 95% CI 0,054-0,600), diabetes (p=0,000; OR= 9,767; 95% CI 3,932-24,263), gangguan paru kronik (p= 0,001; OR= 6,360; 95% CI 2,164-18,690), hipertensi (p= 0,043; OR= 2,436; 95% CI 1,008-5,887), keganasan (p=0,001; OR= 9,647; 95% CI 2,413-38,579), penyakit jantung (p= 0,000; OR= 12,226; 95% CI 2,4-62,294), gangguan neurologis (p=0,008; OR= 6,057; 95% CI 1,650-22,232), and gangguan imunitas (p=0,031; OR= 1,625; 95% CI 1,186-113,899). Dibutuhkan penanganan yang adekuat untuk mencegah kematian pada pasien terkonfirmasi Covid-19 yang memiliki faktor risiko.

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***Kata kunci**: Faktor resiko*; *pasien terkonfirmasi; Covid-19; meninggal; retrospektif*

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INTRODUCTION

Covid-19 is a communicable disease first reported in Wuhan, China in December 2019. Covid-19 known as Novel Coronavirus caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). The first spread to other countries occured from 2020.[1] In comparison with SARS and MERS, Covid 19 is more contagious resulting in global pandemic.[2,3] Cases of pneumonia with unknown aetiology was announced as a Public Health Emergency of International Concern (PHEIC) in the end of January 2020 and declared as pandemic on 11 March 2020.[4]

Covid-19 was predicted to have mortality rate lower than SARS and MERS, in fact its mortality rate is 2%[2] - 2.3% or 20 times greater than common influenza.[4] Covid-19 cases is more prevalent among older people having comorbidities such as cardiovascular disease, diabetes, hypertension[2], chronic respiratory disease and cancer.[4,5,6]

Transmission of Covid-19 can occur between people with or without symptoms. Virus can survive for more than 72 hours resulting is fast contagion.3 So far, Covid-19 spreads through air when performing aerosol-generating medical procedures where virus can survive for 3-16 hours. In this case, health practitioners such as laboratory technicians have greater risk for Covid-19 exposure. Outside medical facilities, Covid-19 is found in the group of people in the crowded rooms such as restaurant and fitness centre without adequate ventilation.[7]

The fast spread of the virus results in fast growing of new cases. Worldwide, it was confirmed 172.558 positive cases and 3.921 death on 30 June 2020.[8] In Indonesia, the first case was reported on 3 March 2020. It was then found 56.385 cases involving 24.806 healed cases and 2.876 death cases on 30 June 2020. In Central Java, it was confirmed 3.836 cases involving 1.159 healed cases and 150 death cases.[9] It suggests the mortality rate of Covid-19 in Indonesia and Central Java is about 5.1% and 3.9% respectively. It is significantly greater than global mortality rate (Case Fatality Rate 2.3%) and South East Asian mortality rate (CFR 2.1%).[8]

The high confirmed cases and mortality rate are a result of host and virus factors. The virus ability to defeat host immune systems serve as determinant of infection severity. Inadequate host immune response results in virus mutation and more severe host tissue destruction. It is compounded with the virus ability to evade from host immune and replicate thus unrecognised by host immune.[6] Data indicate Covid-19 is more prevalence among elderly and those with comorbidities. The mortality rate is higher among older people.[10]

The presence or absence of symptoms is not the sole hint as a study from China found 12.6% infection occurs pre-symptomatic and some cases confirmed without symptom (asymptomatic).[11] Covid-19 patients without symptom may transmit viruses to other people. People in group in certain environment are at high risk for infection such as dormitory, prison, other closed environment, and public facilities such as bus stop, bus station, airport and shopping centre.[7]

People having close contact with Covid-19 patients or taking care of Covid-19 patients have heightened risk for Covid-19 exposure.[12] Besides, smoking is associated with heightened disease severity and Covid-19 related mortality.[13,14] Other factors such as vitamin D availability is considered playing important role for decreasing virus infection risk. It is known

that Covid-19 cases are increasing during winter where 25-hidroxyvitamin D concentration is low in human body.[15] Conversely, countries in the south hemisphere with dry season tend to have low case numbers. Race is also considered having relationship with percentage of Covid-19 related cases and death cases.[16]

Nutritional status data were secondary data based on *Kartu Menuju Sehat*/ Children Growth Chart (KMS/CGC) obtained from Kokar Health Center. Nutritional status data based on anthropometric measurements of body weight (kg) for age (month). Subjects recruited in four categories nutritional status, in line with the proportion in the population, i.e. 7.7% severely underweight, 19.2% underweight, 70.5% normal and 2.6% overweight.

Dr. Kariadi Hospital is a referral hospital in Central Java having role and responsibilities for handling Covid-19 patients involving those who are suspected, having history of close physical contact with patients, confirmed Covid-19 patients and healed patients. The number of Covid-19 patients is predicted to keep increasing and end in uncertain time. The higher death cases may occur as more cases are found, particularly when several risk factors present. Covid-19 can impact significantly human life sustainability as supported by a study by Trias-Llimós dan Bilal found Covid-19 lowers life expectancy 1.9 and 1.6 years for male and female respectively in Madrid, Spain.[17] It encourages authors to investigate risk factors of Covid-19 confirmed dead patients in Dr. Kariadi Hospital.

MATERIALS AND METHODS

It is a retrospective study. The population involves all Covid-19 confirmed patients at Dr. Kariadi Hospital. Research samples involve all Covid-19 confirmed patients both healed and died patients from March to June 2020. The inclusion criteria involved Covid-19 confirmed patients both died and healed patients confirmed based on swab test. The exclusion criteria involved patients both in inpatient and outpatient settings still waiting for swab test results. Data was gathered from screening forms filled by patients or health practitioners interviewing patients on arrival (secondary data). Data was analysed with Chi-square with confidence interval of 95% using SPSS version 25. This research has gone through the review stage and has received approval from the Health Research Ethics Committee Dr. Kariadi Hospital No. 561 / EC / KEPK-RSDK / 2020.

RESULTS AND DISCUSSION

Covid-19 confirmed patients are 277 patients involving 59 died and 218 healed cases from March to June 2020. Research findings are shown at Table 1.

Bivariate test shows sixteen risk factors of Covid-19 confirmed died patients involving age (p= 0.000; OR= 8.803; 95% CI 3.982-19.462), entrepreneur (p= 0.041; OR=14.894; 95% CI 1.12-198.65), farmer/trader (p= 0.029; OR= 25.625; 95% CI 1.40-469.25), contact history (p= 0.000; OR= 12.923; 95% CI 6.163-27.097), fever (p= 0.000; OR=4.877; 95% CI 2.647-8.984), dyspnea (p=0.000; OR= 17.018; 95% CI 8.523-33.977), cough (p= 0.009; OR= 2.178; 95% CI 1.205-3.935), lethargic (p=0.010; OR= 2.282; 95% CI 1.205-4.323), cold (p= 0.002; OR= 0.180; 95% CI 0.054-0.600), diabetes (p=0.000; OR= 9.767; 95% CI 3.932-24.263), COPD (p= 0.001; OR= 6.360; 95% CI 2.164-18.690), hypertension (p= 0.043; OR= 2.436; 95% CI 1.008-5.887), cancer (p=0.001; OR= 9.647; 95% CI 2.413-38.579), heart disease (p= 0.000; OR= 12.226; 95% CI 2.4-62.294), neurological disorders (p=0.008; OR= 6.057; 95% CI 1.650-22.232), and immune disorders (p=0.031; OR= 1.625; 95% CI 1.186-113.899).

In confirmed died patients we found that the cause of death was mostly caused by respirato ry failure 40 cases (67.80%) and the rest caused by cardiovascular / MOD 19 cases (32.20%). Furthermore, the days to develop critical all for deadly patient are 6-7 days with the shortest

day 0 days and the longest day 28 days. Treatment given to Covid-19 confirmed patients consists of non-pharmacological and pharmacological therapy. Non-pharmacological therapy includes chest X-ray examination, monitoring for signs such as tachypnea, oxygen saturation, lymphopenia, progressive CRP and progressive lactic acidosis, and management of critical cases, respiratory failure, hypoxemia and ARDS. Pharmacological therapy are giving vitamin C, vitamin B1, zinc, azithromycin, antiniotics according to clinical conditions, chloroquine sulfate, hydroxycortisone injection, and antivirals (Favipiravir, umifenovir, remdesivir, and oseltamivir).

Table 1. Risk factors of Covid-19 confirmed death and healed patients

Risk factors	Total (n=277)	Number of death cases (n=59)	Number of healed cases (n=218)	p- value	OR (95% CI)
Age	38.99±14.954	53.27±13.249	35.12±12.925		
≥ 60	32 (11.6)	20 (33.9)	12 (5.5)	0.000	8.803 (3.982-19.462)
≤ 59	245 (88.4)	39 (66.1)	206 (94.5)		
Gender					
Male	145 (52.3)	36 (61.0)	109 (50.0)	0.133	-
Female	132 (47.7)	23 (39.0)	109 (50.0)		
Occupation					
Civil servant	169 (61.7)	11 (19.0)	158 (73.1)	0.922	-
Private sectors	30 (10.9)	7 (12.1)	23 (10.6)	0.265	-
Entrepreneur	23 (8.4)	12 (20.7)	11 (5.1)	0.041	14.894 (1.12-198.65)
Farmer/trader	8 (2.9)	7 (12.1)	1 (0.5)	0.029	25.625 (1.40-469.25)
Labour/driver/odd jobs	6 (2.2)	5 (8.6)	1 (0.5)	0.199	-
Unemployed/house wife/student	38 (13.9)	16 (27.6)	22 (10.2)	0.126	-
N/A	3	1	2		
Traveling history					
Yes	30 (11.5)	7 (13.2)	23 (11.0)	0.813	-
No	232 (88.5)	46 (86.8)	186 (89.0)		
N/A	15	6	9		
Contact history					
Yes	180 (70.6)	12 (25.0)	168 (81.2)	0.000	12.923
No	75 (29.4)	36 (75.0)	39 (18.8)		(6.163-27.097)
N/A	22	11	11		
Symptoms					
Fever	97 (35.0)	38 (64.4)	59 (27.1)	0.000	4.877 (2.647-8.984)
dyspnea	64 (23.1)	40 (67.8)	24 (11.0)	0.000	17.018 (8.523-33.977)
Cough	132 (47.7)	37 (62.7)	95 (43.6)	0.009	2.178 (1.205-3.935)
Lethargic	60 (21.7)	20 (33.9)	40 (18.3)	0.010	2.282 (1.205-4.323)
Nauseous vomit	28 (10.1)	9 (15.3)	19 (8.7)	0.139	-
Diarrhea	22 (7.9)	8 (13.6)	14 (6.4)	0.072	-
Shore throat	58 (20.9)	7 (11.9)	51 (23.4)	0.053	-
Headache	39 (14.1)	6 (10.2)	33 (15.2)	0.330	-
Cold	53 (19.1)	3 (5.1)	50 (22.9)	0.002	0.180 (0.054-0.600)
Loss of consciousness	3 (1.1)	2 (3.4)	1 (0.5)	0.054	-
Symptom duration (days)	5.82 ± 6.899	5.63 ± 5.622	5.91 ± 7.502		
≥ 6	55 (34.2)	17 (29.3)	38 (36.9)	0.330	-
≤ 5	106 (65.8)	41 (70.7)	65 (63.1)		
comorbidities					
Diabetes	24 (8.7)	16 (27.1)	8 (3.7)	0.000	9.767 (3.932-24.263)
COPD	15 (5.4)	9 (15.3)	6 (2.8)	0.001	6.360 (2.164-18.690)
Hypertension	24 (8.7)	9 (15.3)	15 (6.9)	0.043	2.436 (1.008-5.887)
Cancer	10 (3.6)	7 (11.9)	3 (1.4)	0.001	9.647 (2.413-38.579)
Heart disease	8 (2.9)	6 (10.2)	2 (0.9)	0.000	12.226 (2.4-62.294)
Neurological disorders	10 (3.6)	6 (10.2)	4 (1.8)	0.008	6.057 (1.650-22.232)
Immune disorders	4 (1.4)	3 (1.1)	1 (0.5)	0.031	11.625 (1.186-113.899)
Pregnancy/childbirth	6 (2.2)	1 (1.7)	5 (2.3)	0.779	-
Chronic kidney disease	1 (0.4)	0 (0.0)	1 (0.5)	0.602	-
Chronic liver disease	2 (0.7)	0 (0.0)	2 (0.9)	0.460	-
Others	6 (2.2)	1 (1.7)	5 (2.3)	0.779	-

DISCUSSION

The research results are showed sixteen risk factors of Covid-19 confirmed died patients involving age, occupation (entrepreneur, farmer/trader), contact history, symptoms (fever, dyspnea, cough, lethargic, cold), comorbidities (diabetes, COPD, hypertension, cancer, heart disease, neurological disorders and immune disorders) ($p<0.05$). Meanwhile, gender, traveling history and duration of symptoms were not risk factors for death in Covid-19 confirmed patients ($p>0.05$).

Age is one of the death-contributing factors among Covid-19 confirmed patients especially in the older age group. Onder et al.[18] found a higher case fatality rate in the age group over 80 years in Italy and China (20.2% and 14%) compared to other age groups. Nearly all studies have found a different mean age in patients with confirmed Covid-19. Zhou et al.[19] found mean death ages of Covid-19 patients is 69 years (63-76 years) and heightened along with age progression (p= 0.0043; OR= 1.10; 95 % CI 1.03-1.17). Harlem[20] found most Covid-19 positive cases in the age group of 25-44 years (28% and 31% respectively) and 45-64 years (26% and 27% respectively) in the high case country group (n= 178.469) and in the medium case country group (n= 178.196). Nie et al.[21] Found mean ages of Covid-19 confirmed patients is 43$\pm$15.09 years. They also found a relationship between ages and Covid-19 severity (p= 0.003; OR=:1.026; 95% CI 1.009-1.043). Lai et al.[22] state characteristic of the first 100 Covid-19 cases in Hong Kong with the greatest proportions are among those aged 45 years (76%) and is increasing along with age progression ($p<0.001$). Gemes et al.[23] predicted one out of five people in Sweden are at risk of severe Covid-19 known from prognostic factors aged older than 70 years (14.1%).

This study found most Covid-19 confirmed patients are male, but it does not affect the numbers of death cases. These findings are similar with a study by Nie et al. stating that most Covid-19 patients are male accounting for 377 people (56.2%) and this result is not statistically significant ($p>0.05$).[21] It is also in line with WHO that the percentage infection distribution in male is greater than female (51% vs 47%). WHO states the caused by different female against viruses and infections.[24] Alobuia et al. found female respondents were at least 85% more likely to have high practice scores compared to males ($p < 0.001$) in action against Covid-19.[25]

The risky occupation during this study is farmer/trader and entrepreneur. In many cases, farmers are traders too. These findings are similar with that found in Henan, China showing that the greatest cases occurred among farmers (21.2%) and labours (15.2%). Death cases among farmers are around 0.3%.[21] Mutambudzi et al. categorize the entrepreneur as other essential workers that had a higher risk of severe Covid-19 (RR= 1.60; 95% CI 1.05-2.45).[26] Furthermore, National Statistics state that occupations demanding direct interaction with many people is very risky. Farmers/traders and entrepreneur are types of occupations demanding direct interaction with many people without knowing whether they are infected by Covid-19 or not.[27]

Contact history in this study is defined as direct contact with a suspected, probable or confirmed Covid-19 patients. Findings show great number of died patients without any contact history. Conversely, healed patients are found to have greater contact history. Centers for Disease Control and Prevention (CDC) stipulates close contact as a risk factor mainly among people living in the same house with a confirmed case without physical distancing.[28] A study by Nie et al. found a relationship between direct contact with infected patients and Covid-19 severity (p= 0.039; OR= 0.456; 95% CI 0.213-0.976). In addition, Nie et al. found visitation to crowded places such as hospitals and traditional markets augment positive cases. However, the sources of contagion of some Covid-19 positive cases are still unknown.[21]

This study found the presence of symptoms serves as risk factors of Covid-19. Confirmed death cases show more symptoms than healed cases. From ten symptoms, seven symptoms show a higher percentage in death cases than healed that is fever (64.4 vs 27.1), dyspnea (67.8 vs 11.0), cough (62.7 vs 43.6), lethargic (33.9 vs 18.3), nauseous vomit (15.3 vs 8.7), diarrhea (13.6 vs 6.4), and loss of consciousness (3.4 vs 0.5). Sanyaolu et al.

showed the percentage of common symptoms similar with this study, that is fever (88.8%), dry cough (68%) and fatigue (33%), productive cough (28.5%), SOB (17%), muscle pain (14.4%), sore throat (11.4%), headache (10.2%), diarrhea (4.4%), nausea and vomiting (4.1%), rhinorrhea (3.2%), abdominal pain (0.16%), and chest pain (0.11%).[29] The high case of patients with symptoms is tightly related with ages and comorbidities. The risk for diseases severity increases along with age progression resulting in paediatrics tend to show no symptom (asymptomatic) compared with adults.[24] Although Byambasuren et al. found 6-41% asymptomatic cases,[30] but Qu et al. found some symptoms such dyspnea ($p<0.001$), shortness of breath ($p<0.01$) and chest distress ($p<0.05$) were correlated with death.[31]

This study found no difference in symptom duration between death cases and healed cases. This indicates that the duration of symptoms is not a risk factor for death in confirmed Covid-19 patients. However, the duration of symptom in this study was about 6 days, both in death cases (0 to 12 days) and healed cases (2 to 13 days). This study similar with Sanyaolu et al. found symptoms of Covid-19 appear 5 days (2 to 14 days).[29]

The presence of comorbidities can worsen patient conditions particularly those indicated for Covid-19. Zhou et al. found 91 patients (48%) have comorbidities and significantly correlated to Covid-19 related death ($p<0.5$). The comorbidities in death cases and healed cases are hypertension (48% vs 23%; $p=0.0008$), diabetes (31% vs 14%; $p=0.0051$), coronary heart disease (24% vs 1%; $p=<0.0001$), chronic obstructive lung disease (7% vs 1%; $p=0.047$), chronic kidney disease (4% vs 0%; $p=0.024$), and other (20% vs 8%; $p=0.016$).[19] Harlem found three most common chronic diseases involving hypertension (33% and 25 % respectively), obesity (28% and 15% respectively) and diabetes (15% and 8% respectively).[20] Not only adults, comorbidities also can be fatal among paediatrics. Oualha et al. found 19 paediatrics (70%) aged between 1 month and 18 years with comorbidities (neurological, respiratory, and sickle cell disease). Of five died paediatrics, two were died as a result of comorbidities.[32] A meta-analysis by Patel found 21% paediatrics has comorbidities such as asthma, immunosuppression and cardiovascular disease. The mortality rate of children that were hospitalized with Covid-19 was 0.18%.[33]

There are so many risk factors that are likely to contribute to the occurrence of death in confirmed Covid-19 patients while the risk factors examined in this study were only a small part. This is a limitation of this study. Apart from the risk factors in this study, other risk factors such as education level, smoking behavior, nutritional intake, physical activity, socioeconomic, body mass index (BMI) category, lifestyle-related factors (alcohol consumption) and other factors needs to be researched. Almost no confirmed cause of death for Covid-19 patients who died was caused by only one factor. This is the same as that found by Sanyaolu et al. that older patients with Covid-19, especially those 65 years old and above, who have comorbidities, are more likely to develop a more severe course and increased admission rate into the intensive care unit (ICU) and mortality from the COVID-19 disease.[29]

CONCLUSION

Age, occupation (entrepreneur and farmer/trader), contact history, symptoms (fever, dypsnea, cough, lethargic and cold), and comorbidities (diabetes, COPD, hypertension, cancer, heart disease, neurological disorders, and immune disorders) were risk factors of Covid-19 confirmed died patients in Dr. Kariadi Hospital. Meanwhile, gender, traveling history and duration of symptoms were not risk factors for death in Covid-19 confirmed patients in Dr. Kariadi Hospital. Adequate handling is needed to prevent death in patients with confirmed Covid-19 who have risk factors.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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