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Pneumonia-related deaths in sleman based on verbal autopsy: an observational study

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ABSTRACT

Pneumonia has long been and remains one of the leading causes of death, especially among children and the elderly. Until this study was released, only the Jakarta province fulfilled the national target of pneumonia case findings. Thus, it is important to determine the characteristics and prevalence of pneumonia-related deaths in Sleman District based on verbal autopsy. This cross-sectional study used secondary data from Sleman HDSS cycles 1 to 7. The subject of this study was a person aged over 28 days who passed away due to pneumonia between 2015 and 2022 and met the criteria for sample inclusion. Fisher's exact and Pearson's chi-square tests were used to analyze the data. The number of subjects who died due to pneumonia was 65 subjects (33,3%), and the number of subjects who died due to other causes was 130 (66,7%). The prevalence of those who died due to pneumonia was lower than non-pneumonia death for all of the predetermined risk factors, including elderly age, male sex, low education level, high occupational risk, smoking history, alcohol consumption, asthma history, COPD history, stroke history, tuberculosis history, hospitalization history, and very thin or malnourished body with sex, occupational status & type, and nutritional status being statistically significant. The prevalence of pneumonia-related deaths in the Sleman HDSS VA population is 33,3%, with some risk factors that may affect it.

Keywords: pneumonia; pneumonia mortality; risk factors; verbal autopsy.
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INTRODUCTION

Two and a half million people died due to pneumonia in 2019.[1] Pneumonia has one of the highest mortality rates for children globally.[2] It has received attention from numerous countries globally due to the large number of children infected. Each year, more than 1400 patients per 100.000 children suffer from pneumonia, which was reported to mostly happen in South Asia (2500 cases/100.000 children) and West and Central Africa (1620 cases/100.000 children).[3] The World Health Organization also stated that pneumonia accounted for 808.694 children mortality in 2017, with fifteen percent of all mortality occurring to children under five years old.

Acute respiratory infections have been listed among the top ten causes of death, particularly among children under five, for more than a decade now.[4] Pneumonia, classified as an Acute Respiratory Infection (ARI), can be attributed to viruses, fungi, or bacteria.[5] It is prevalent in underdeveloped and impoverished nations that lack reliable healthcare systems. Prevention of pneumonia can be achieved through immunization, proper nutrition, and maintaining a clean environment. Early detection of pneumonia symptoms is crucial for effective prevention of fatalities. In 2018, the target set by the government for identifying cases of pneumonia was 80%. However, according to the Ministry of Health of the Republic of Indonesia's report, only Jakarta, out of 34 provinces, had met the national target.[6] Due to the differing conditions amongst the provinces of Indonesia, each district has the autonomy to decide the target based on the situation there. The Daerah Istimewa Yogyakarta (DIY) province has five districts, including the Sleman district, which struggles with pneumonia cases, especially in children. The coverage for pneumonia case findings in Sleman was 42,6%, below the targeted province target of 46,4% and district target of 60% in 2018.[6] Based on these data, assessing pneumonia cases more thoroughly is crucial to bring light to the pneumonia situation in Sleman.

Pneumonia may spread from air-borne droplets and blood, especially during and shortly after birth.[5] Additionally, indoor air pollution caused by cooking and heating with biomass fuels such as wood or animal dung may increase the susceptibility to pneumonia.[7] This is still commonly seen in some areas of Sleman, especially the low socioeconomic areas where cooking with firewood is the norm. Smoking, both passive and active, is a major risk factor for pneumonia. According to the data obtained in 2021, 33,8% of Indonesian adults use tobacco, including nearly two-thirds of men (men 62.9% and women 4.8%), which increases the risk of these smokers contracting pneumonia.[8]

Pneumonia is a multifactorial disease affected by, but not limited to age, sex, education level, occupational status and type, smoking, alcohol consumption, asthma, HIV/AIDS, COPD, stroke, tuberculosis, hospitalization history,

nutritional status, diabetes mellitus, hypertension, and vaccination status. It is necessary to study the association between some of these variables and deaths due to pneumonia to understand further which risk factors are related to pneumonia mortality in Sleman.

The reasoning behind verbal autopsy usage is that not all pneumonia-related deaths are recorded in the medical records of medical facilities. Verbal autopsy is a valid option for pneumonia-related deaths, which may be overlooked due to the location of the deceased person's death (out of hospital settings). To this day, there has not yet been a comprehensive study of pneumonia mortality cases in Sleman. Therefore, there is still a lot to be studied regarding pneumonia-related deaths to understand the pneumonia situation in Sleman better. By comprehensively analyzing the data on pneumonia-related deaths, we may better understand the characteristics of pneumonia mortality, especially those not recorded in medical records in Sleman. Exploring risk factors of pneumonia-related mortality is valuable in the community health approach, including promotion, prevention, and early case findings. The objective of this research is to utilize verbal autopsy to identify the prevalence and characteristics of deaths related to pneumonia in the Sleman District.

METHOD

Types and study design

The study was a cross sectional study based on the Health and Demographic Surveillance System's (HDSS) longitudinal study data in cycles 1-7 in the Sleman District of Yogyakarta, Indonesia. Exploring pneumonia-related mortality in the community through verbal autopsy is very important since not all deaths are witnessed by health workers. This study was observational, in which the researcher(s) observed the effects of a risk factor, diagnostic test, or treatments without intervention.

Time and study setting

This study used secondary data from the verbal autopsy reports from the Sleman Health and Demographic Surveillance System (HDSS). The Sleman HDSS is a surveillance system that collects population transitional data, health status, and social transitional data regularly over a set period (cycles). The Sleman HDSS team conducted verbal autopsy at numerous households in the Sleman District from 2015 to 2022, and this study used the data from 2015 to 2022. The secondary data procurement occurred in the Sleman HDSS office in two months between September and October 2022. After obtaining secondary data, the univariate and bivariate analysis was carried out.

Study population and subjects

The study population was the Sleman District residents, recorded in the Sleman HDSS questionnaire. The deceased people listed in the Sleman HDSS verbal autopsy report are the study subjects. The study individuals aged above 4 weeks (28 days) who passed away from pneumonia between 2015 and 2022 due to pneumonia and/or experienced respiratory problems before death met the criteria for sample inclusion. Any Sleman District HDSS samples with insufficient data were excluded. The sample size for the study was decided based on the accessibility of the gathered data and its adherence to the inclusion and exclusion criteria.

Study variables

The study variables are divided into independent and dependent variables. In the study context, the independent variable was assumed to be the cause, and the dependent variable was assumed to be the effect. Pneumonia-related mortality was the study's outcome and the dependent variable. The independent variables, on the other hand, included age, sex, education level, occupational status and type, smoking, alcohol consumption, asthma, HIV/AIDS, COPD, stroke, tuberculosis, hospitalization history, and nutritional status. There were no confounding variables in this study. A total of 14 questions from the verbal autopsy questionnaire were used.

Study material

This study utilized the Sleman Regency HDSS Verbal Autopsy (VA) Questionnaire from 2015 until 2022. Verbal autopsy is a research method to determine the probable cause of death using the WHO standardized questionnaires by obtaining information about the circumstances of the deceased person from their family or close ones. The verbal autopsy interview was done after the primary data collection results are obtained and analyzed using the interVA software. The questionnaires used in this study are attached in the appendix below.

Study plans

As the first step of the study, the research topic was decided and modified according to the Sleman HDSS available while ensuring the study's authenticity. After the application was approved, the Sleman HDSS dataset was sorted with the corresponding variables. Data processing starts with data retrieval; then, datasets are combined according to the studied variables, analyzed for accuracy, cleaned up for the missing data, coded and entered into the statistical analysis program. The data will then be presented in various tables, analyzed, and compared with the results of previous studies.

Data analysis

The first stage in data analysis was to explain the information obtained during the study. This was done by utilizing figures to provide the data with a visual representation and statistics to give it a numerical explanation. The frequency of the independent factors in pneumonia-related mortality and non-pneumonia-related mortality was determined using a univariate analysis. The dataset was analyzed using the SPSS software, and a bivariate analysis was carried out.

Data analysis was carried out using Pearson's chi-square and Fisher's exact test to determine the statistical significance of the variables. Fisher's exact test was used when there were small sample sizes (expected count less than 5). For the alcohol consumption variable, because there were cells with zero as an observed value, the prevalence ratio was counted manually using the Haldane-Anscombe correction. Comparisons were done using cross-tabulations and prevalence ratio with a 95% confidence interval.

Ethical consideration

The main study titled "*Manfaat Verbal Autopsy dalam Memperkirakan Sebab Kematian di Luar Fasilitas Pelayanan Kesehatan Sebelum dan Semasa Pandemi Covid-19*" was approved by The Medical and Health Research Ethics Committee (MHREC) Faculty of Medicine Public Health and Nursing Universitas Gadjah Mada on 21st of April 2022. The approval reference number is KE/FK/0475/EC/2022. Since the author is not included in the initial study protocol, an amendment was done before this study began.

RESULT

There was a total of 996 subjects who were included in all cycles (1-7) of the verbal autopsy of HDSS Sleman. The data are then selected according to the exclusion criteria and included for analysis in this study. The subject disposition is shown in Figure 1.

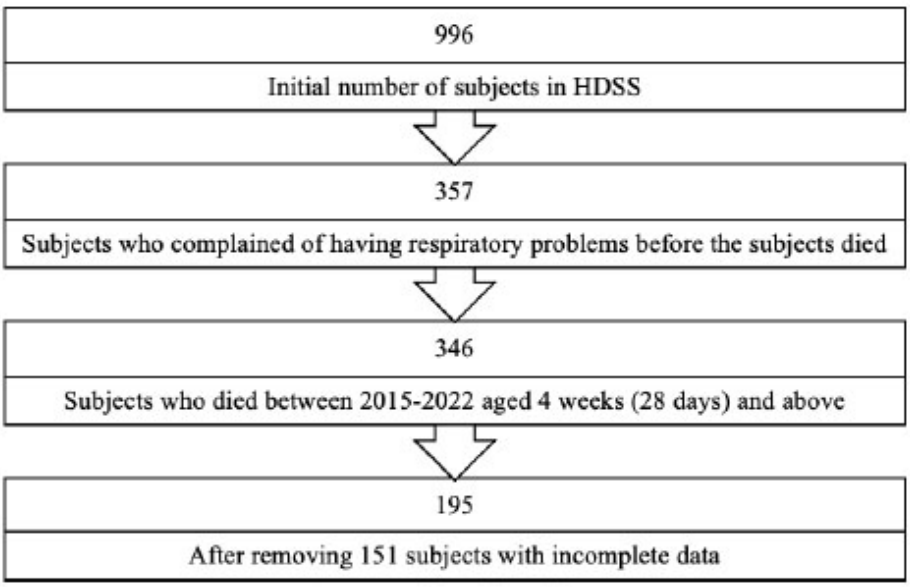

Figure 1. Subject disposition.

According to this study, most of the subjects are elderly male with a lower education level, a lower occupational risk, has never smoked, does not consume alcohol, has no history of asthma, HIV/AIDS, COPD, stroke, tuberculosis, had been hospitalized before, and a normal weight. The demographic characteristics of the subjects can be seen in the table below:

The mean age of this study's subject is 67 years old, whereas the median age is 68 years old, and the mode is 65 years old. The occupational status data collected are as follows in order of highest percentage to lowest: working a job (43%), housewife (32,3%), unemployed (20,6%), pensioner (2,2%), and student (0,5%). Additionally, some subjects worked before they died, including farming with the highest proportion, selling merchandise and food, and being a parking attendant. Most job types they worked on before death were left blank or unknown.

The proportion of pneumonia mortality is smaller than that of non-pneumonia mortality (33,3%). Furthermore, the number of pneumonia and non-pneumonia-related deaths by year of death can be seen in Figure 2.

From the figure, we can see that the highest proportion of pneumonia deaths was observed during 2021, with 25 pneumonia-related deaths and 22 non-pneumonia-related deaths. The COVID-19 pandemic can contribute to this finding, although many organs failure caused by COVID-19 can lead to patient death. The lowest proportion of pneumonia deaths was observed during 2016, in which 4 pneumonia-related deaths were found, with 32 deaths by other causes. Table 2 shows the potential factors which are linked to pneumonia-related mortality. There were no subjects who had an HIV/AIDS history in this study. Most of the subjects who died due to pneumonia were elderly females with a low education level, a low occupational risk, did not smoke, did not drink alcohol, and did not have a history of asthma, COPD, HIV/AIDS, stroke, or tuberculosis, has had hospitalization history, and has a normal nutritional status.

The prevalence ratio of pneumonia was lower in the elderly, male sex, high occupational risk, smoking history, alcohol consumption, asthma history, COPD history, stroke history, tuberculosis history, hospitalization history, and very thin or malnourished variables. There was no correlation between low educational level and pneumonia mortality. All segments in the community had similar risks of pneumonia-related mortality.

DISCUSSION

his study found none of the variables to be significant risk factors for pneumonia-related deaths in Sleman. Contrary to the theory provided in the bibliographical review, the risk factors found in the previous study contributed to a lower likelihood of the subjects dying due to pneumonia, which can be observed in all the variable prevalence ratios of less than one (table 3). Only three variables have a statistically significant ($p < 0,005$) value: age, occupational status & type, and nutritional status. However, all three variables and the rest have contradicting results with previous findings.

The first variable in this study is age. This study's prevalence ratio of pneumonia mortality is lower in the elderly group, with a non-statistically significant value. This study finds that people in the elderly age group category are 0,879 less likely to die due to pneumonia than the elderly age group, but the result is not statistically significant. Since the result is statistically insignificant, it is safe to assume that old age is a risk factor for pneumonia deaths based on previous findings.

Severe pneumonia in the elderly has been known to be difficult to treat and often involves multiple organs.[9] Old age has been closely correlated with slowing down the immune system and respiratory defense function, thus increasing the

Table 1. Demographic characteristics

Variables	Descriptive (N=195)	
	n	%
Age		
Children (0-17)	0	0
Young adult (18-25)	0	0
Adult (26-64)	77	39,5
Elderly (65 and over)	118	60,5
Sex		
Male	105	53,8
Female	90	46,2
Education level		
Lower education level	171	87,7
Higher education level	24	12,3
Occupational status & type		
Higher occupational risk	41	21
Lower occupational risk	154	79
Smoking		
Has smoked	71	36,4
Never smoked	124	63,6
Alcohol consumption		
Yes	2	1
No	193	99
Asthma		
Yes	19	9,7
No	176	90,3
HIV/AIDS infection		
Yes	0	0
No	195	100
COPD history		
Yes	18	9,2
No	177	90,8
Stroke history		
Yes	19	9,7
No	176	90,3
Tuberculosis history		
Yes	10	5,1
No	185	94,9
Hospitalization history		
Yes	193	99
No	2	1
Nutritional status		
Very thin or malnourished	63	32,3
Normal weight	132	67,7

incidence rate of pneumonia, especially severe pneumonia.[10] Pneumonia is also prevalent in young children (especially under 5 years old) whose immune system has not fully developed yet. However, the prognosis is good for most children compared to older age.[11] Since this study has no data regarding children, no comparison can be made regarding children and older age in pneumonia mortality.

Moreover, there may be a delay in pneumonia diagnosis, which is contributed by negative chest radiographs commonly found in the elderly with pneumonia (p=0,0003), making chest radiographs unreliable for patients with advanced frailty.[12] The elderly also often have more drug-resistant bacteria than younger patients, especially those with comorbidities or those who live in chronic care facilities.[13]

The next variable in this study is sex. This study found the male sex to be 0,649 less likely to die due to pneumonia than females, and the value is statistically significant. According to an 8-year-long previous study in the United States with 92.332 subjects, patients admitted to pediatric hospitals have consistently more male than female patients across nearly all disease categories (61% vs 53%; p=0,008; respectively), including 26% of diseases which affect the respiratory system.[14] Males are also more susceptible to acute viral infections, tuberculosis, and pneumonia; with a worse prognosis.[15]

One possible explanation for the difference in findings between this study and the previous studies is the inclusion criteria. This study compared pneumonia mortality with people who suffered respiratory problems, some of which died due to lung-related problems such as pulmonary tuberculosis and COPD. Since pneumonia is an umbrella term and is often mistaken for other diseases, there may be subjects who should have been in the pneumonia category but are included in the non-pneumonia category, thus affecting the result. Even though the result of this study for the sex variable is statistically significant, there is yet to be a previous study backing up this finding. However, we can account for the geographic factors and differences in sample sizes to attribute to these differences.

The reasoning behind the male sex predominance in pneumonia and pneumonia-related mortality is not exactly known. A possible explanation for this is that inflammatory reactions may be driven by hormonal status. Another hypothesis suggested that a gene locus on the X chromosome in humans involved immunoglobulin synthesis, thus suppressing inflammation.[16] Another study by Yang et al. found that estrogen, the main female sex hormone, improves the ability of macrophages to kill bacteria in the lungs. Estrogen works by increasing proteins produced from the NOS3 gene.[17]

Some socioeconomic and behavioral factors may play a role in developing pneumonia in both sexes. Many women in Indonesia work for low salaries, have part-time jobs, or are housewives. Since the percentage of women who was a housewife before they died (32,3%) in this study is relatively high, some of them may be left without a source of income if their husband were deceased, causing them to have poor quality medical care, thus

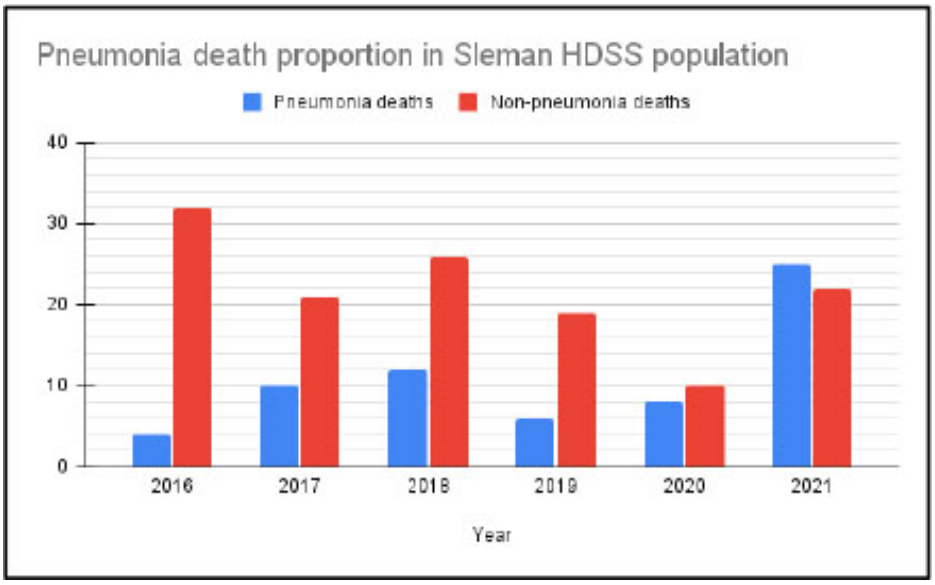

Figure 2. Pneumonia deaths by year.

affecting the results of this study.

The next variable in this study is education level. This study finds no correlation between education level and pneumonia mortality with no statistical significance. Previous studies have shown a correlation between pneumonia occurrence and education level. The education level is closely linked with socioeconomic status and are both social determinants of health. In a study located in Colombia, it was found that the risk of dying was significantly higher among the lower-educated adults aged 25 and above for both men and women, with a relative risk of 2,34 (95% CI 2,32 – 2,36) for primary education.[18] Another study in Brazil found that the proportion of hospital pneumonia admissions relative to the overall admissions is greater in cities with higher levels of social inequality ($p < 0,05$).[19] However, the slight difference in lower education definition may contribute to the difference in findings.

Although this study found no correlation between education level and pneumonia deaths, there are several reasons why low education level may be correlated to pneumonia deaths in Sleman District. One of them may be due to late diagnosis; patients with low education levels might not recognize the signs of the disease before it is too late or recognize the disease but choose to go to alternative healers such as *dukun* instead of the hospital or clinic.[20] Additionally, places with lower socioeconomic levels (one of the main causes of lower education level), especially in Indonesia, have poor access to the healthcare system, thus making the disease progress further, causing it to have a worse prognosis and often leading to death.[21]

The result of this study suggested the high occupational risk group to be 0,413 times less likely to die due to pneumonia compared to the low-risk group and is statistically significant. The author does the grouping and the high occupational risk, including subjects who were working a job and being a housewife. This grouping was done based on the assumption that some jobs involve pneumonia occupational risk and the housewives had increased exposure to smoke caused by burning firewood. In retrospect, the results of this study for this variable may be affected by how broad the term "working a job" is and the lack of answers regarding the type of work they do. Some of those who filled the type of work the deceased in this study answered farming, which was not included in previous studies' high occupational risk. This might explain the contradictory result with previous studies' findings.

A previous study done in Denmark has found professions which typically include working with children (IRR 1,20; 95%CI 1,12 – 1,28), are closely related to public transportation (IRR 1,21; 95%CI 1,09 – 1,34) and nursing home care (IRR 1,10; 95%CI 1,03 – 1,18) had an increased rate of hospitalization with pneumonia compared to people working in public administration. This study also found a portion of people whose occupation is a housewife and/or is mostly cooking in their daily activities or is being a parking attendant.[22] This may be a risk for pneumonia and pneumonia-related mortality due to the inhalation trauma from using firewood or other biomass fuels that produce smoke to cook and transport.[23] However, we must also account that modernization has greatly reduced the need to burn firewood to cook.

In this study, most of the subjects' occupations before they passed away are unknown, making it difficult to infer the occupational hazards they may pose. Of the few who answered, the parking attendant who is closely related to public transport and is most likely often exposed to smoke has an increased risk of developing pneumonia. No conclusive data may group a specific occupational group as having high pneumonia and pneumonia mortality risk in Sleman from this study.

This study finds that the smoking group is 0,846 times less likely to die due to pneumonia. However, this study does not include the possibility of them being passive smoker, which is not included in the questionnaire. The verbal autopsy questionnaire only asked whether the subject smoked within a set period before the subject's death; thus, it did not differentiate whether the subject was a smoker but stopped or had only started smoking before their end. Ex-smokers have been known to have an increased risk of developing pneumonia compared to non-smokers, a meta-analysis showed (pooled OR 1.49, 95% CI 1.26–1.75, n = 8). This might explain the contradictory result of this study regarding the smoking group.[24]

Smoking has long been known as a significant risk factor for developing community-acquired pneumonia. At the same time, passive tobacco smoke exposure has a significant effect on the elderly (65 years old and above).[24] Passive smoking, especially in elderly and young children, is a known risk factor for severe pneumonia and increased risk of

Table 2. Association of pneumonia deaths

Variables	Pneumonia deaths (n=65)	Non-pneumonia deaths (n=130)	Total	p-value
Age				
Children (0-17)	0	0	0	
Young adults (18-25)	0	0	0	0,679†
Adult (26-64)	27	50	77	
Elderly (65 and over)	38	80	118	
Sex				
Male	28	77	105	*0,033†
Female	37	53	90	
Education level				
Lower education level	57	114	171	1,000†
Higher education level	8	16	24	
Occupational status & type				
Higher occupational risk	8	33	41	*0,035†
Lower occupational risk	57	97	154	
Smoking				
Has smoked	22	49	71	0,599†
Never smoked	43	81	124	
Alcohol consumption				
Yes	0	2	2	0,443‡
No	65	128	193	
Asthma				
Yes	6	13	19	0,864†
No	59	117	176	
HIV/AIDS infection				
Yes	0	0	0	-
No	65	130	195	
COPD history				
Yes	3	15	18	0,091‡
No	62	115	177	
Stroke history				
Yes	4	15	19	0,175‡
No	61	115	176	
Tuberculosis history				
Yes	1	9	10	0,098‡
No	64	121	185	
Hospitalization history				
Yes	64	129	193	0,557‡
No	1	1	2	
Nutritional status				
Very thin or malnourished	10	53	63	*0,0006†
Normal weight	55	77	132	

*Pearson's Chi-Square†; Fisher's Exact Test‡; *Significant value (p<0,005)*

pneumonia occurrence (p < 0,05).[25] A systematic review has also found a linear relationship between the amount of smoking and respiratory health, including the risks of COPD (RR 4,01; 95% CI 3,18 – 5,05), asthma (RR 1,61; 95% CI 1,07 – 2,42), and tuberculosis (RR 1,57; 95% CI 1,18 – 2,10); all of which were previously known pneumonia risk factors.[26]

Smoking impairs polymorphonuclear leukocyte function, which plays an important role in the host's defense against bacterial infection due to decreased neutrophil migration and leukocyte chemotaxis.[27] Smoking also decreases the $CD4^+$ T cell number, which then causes the reduction of antibody-secreting B cells and lowers serum immunoglobulin levels.[28]

Cigarette smoke and its components cause peribronchiolar inflammation and fibrosis, increased mucosal permeability, impairment of mucociliary clearance, changes in pathogen adherence, and disruption of the respiratory epithelium, which predisposes the host to upper and lower respiratory tract infections, including pneumonia.[29] Smoking also increases the risk of invasive pneumococcal pneumonia, which is associated with a high mortality rate, by 2-fold (OR 1,88; 95%CI 1,11 – 3,19).[30]

Similarly to smoking, alcohol consumption is a risk factor for community-acquired pneumonia (CAP) and poorer prognosis of CAP by impairing the defensive mechanisms of the respiratory tract.[31] Although the group who had a history of alcohol consumption

Table 3. Prevalence ratio of pneumonia mortality and its risk factors

Variables	Prevalence Ratio	95% Confidence Interval
Elderly	0,879	0,479 – 1,612
Male sex	0,520	0,285 – 0,951
Low education level	1,000	0,404 – 2,475
High occupational risk	0,413	0,178 – 0,954
Smoking history	0,846	0,453 – 1,579
Alcohol consumption	0,392	0,018 – 1,802
Asthma history	0,915	0,331 – 2,529
COPD history	0,371	0,103 – 1,330
Stroke history	0,503	0,159 – 1,581
Tuberculosis history	0,210	0,026 – 1,695
Hospitalization history	0,496	0,030 – 1,014
Very thin or malnourished	0,264	0,123 – 0,564

has a 0,392 likelihood of dying due to pneumonia, the result is not statistically significant. The drinking culture is not well-established in Indonesia; thus, it may affect the data gained in this study. Only a very small portion of subjects were known to have alcohol consumption habits. Additionally, stores which sell alcohol are not very common in Indonesia, especially in rural areas. *Badan Pusat Statistik (BPS)* recorded a decreasing trend of alcoholic drinks consumption in Indonesia since 2017-2021. In 2021, the amount of alcohol consumed is 0,6 L per person.[32]

Chronic alcohol intake or people with alcohol use disorder (AUD) is closely related to bacterial pneumonia, especially pneumococcal pneumonia. Prolonged alcohol consumption impairs the cell's phagocytic capacity, cytokine and chemokines release, and neutrophil chemoattractant, thus altering the neutrophil-driven lung immunity in response to *S. pneumonia* infection.[33] Patients with alcohol use disorder (AUD) often have a severe presentation of the disease, often with bilateral or multilobar pneumonia, which requires mechanical ventilation.

Moreover, alcohol also contributes to malnutrition, causing immune suppression and disrupting the interface between innate and adaptive pulmonary immunity, which further prevents the host's ability to eliminate pathogens.[34] Patients with a history of chronic alcohol use are also more prone to comorbidities, such as liver, kidney, and cardiac disorders, which cause worse prognosis, more complications, and more likelihood of developing resistant pathogens.[35]

The use of inhaled corticosteroids, commonly used for COPD, is also a risk factor associated with CAP (OR 3,09; 95% CI 2,14 – 4,46; p = 0,001). Inhaler use, especially with a spacer, is also identified as an independent risk factor for community-acquired pneumonia, which might be attributed to inhaler contamination, or the inhalation of pressurized aerosols might aid the entrance of microorganisms into the bronchial tree.[36] Between patients with underlying lung diseases, COPD patients were found to have a higher risk of pneumococcal pneumonia than those with asthma, regardless of age.[37]

In this study, the asthma and COPD groups had a decreased prevalence of pneumonia with a non-statistically significant value. Both groups should have had an increased risk of contracting pneumonia, specifically community-acquired pneumonia, and poorer outcomes due to it. COPD and asthma cause airway inflammation, increasing mucus production and leaving the respiratory system more susceptible to pneumococcal pneumonia.[38] The American Lung Association reported a 7.7x increased risk of contracting pneumococcal pneumonia for the elderly with COPD than those with no comorbidities and a 5.9x increased risk for the elderly with asthma.[39]

The Human Immunodeficiency Virus (HIV) infection is known to be a disease correlated with cell-mediated immunity. However, it is also a considerable contributor to humoral immunity dysfunction.[40] It makes its hosts more susceptible to bacterial infections, especially to *S. pneumoniae* and *H. influenzae*. This is due to a variety of reasons: polyclonal hypergammaglobulinemia, impaired activation of B-cells, and impaired pulmonary defenses.[40,41] CD4 regulates B-cell differentiation and is also indirectly involved in producing antibodies and phagocytosis.

HIV-positive patients, particularly those with less than 200 CD4 lymphocytes per cubic millimeter, have a highly increased rate of bacterial pneumonia, with HIV-positive patients with 500 CD4 lymphocytes per cubic millimeter also having significantly increased rates of bacterial pneumonia (p<0,022).[42] Bacterial pneumonia is also more commonly found in patients who were injection users amongst HIV-positive patients. In a cohort study of 5 years, upper respiratory infections, especially pneumonia, were the most common infection and occurred twice as frequently in HIV-positive patients than in HIV-negative patients (8,5 cases per 100 person-years, compared to 0,7 cases per 100 person-years; p < 0,001).[43] Since this study had no subjects with a history of HIV/AIDS, no analysis or inference can be made.

The most common form of pneumonia in stroke patients is aspiration pneumonia.[44] This study finds a decreased prevalence of pneumonia mortality by 0,503 in the group of patients with a history of stroke compared to the non-stroke patients. There is a disparity in the findings of this study, which was previously known. However, the value is statistically insignificant, and we can still assume the previous study findings to stay true.

Aspiration pneumonia may be caused by the less virulent bacteria and microbes that normally inhabit the upper airway tract and stomach. Furthermore, stroke-induced immunodeficiency has been linked with aspiration pneumonia, and Prass et al. concluded immunodeficiency to be necessary for the progression of bacterial aspiration into pneumonia.[45] The development of infection after stroke is also associated with poor prognosis and high mortality (OR 5,58; 95% CI 4,76 – 6,55).[46]

Pulmonary tuberculosis classically presents as chronic pneumonia, and acutely presenting tuberculosis is identical to community-acquired pneumonia.[47] As a matter of fact, *Mycobacterium*

tuberculosis is one of the etiological agents for community-acquired pneumonia in several countries.[48] As such, some community-acquired pneumonia shares the same pathogen as pulmonary tuberculosis. This study finds 0,21 less likelihood in the group with tuberculosis history, and the result is not statistically significant. This finding may be attributed to confounders not attributed in this study or other factors, and we can refer to previous studies regarding tuberculosis as pneumonia and pneumonia mortality risk factors.

Pulmonary tuberculosis (PTB) is the most common form of tuberculosis, which typically presents as a chronic disease but can also present as acute pneumonia.[49] Acute tuberculous pneumonia usually has the same clinical manifestations as community-acquired pneumonia but is caused by *Mycobacterium tuberculosis.* One systematic review found that over 10% of patients in Asia who have community-acquired pneumonia caused by *Mycobacterium tuberculosis.*[50]

Most of the study subjects have a history of hospitalization, which presents as an independent risk factor for pneumonia, especially nosocomial pneumonia or hospital-acquired pneumonia (HAP). However, the results of this study suggested that the group with a hospitalization history is 0,496x less likely to die due to pneumonia than those without, with a statistically non-significant value. Over 90% of pneumonia cases occur in patients who are intubated and mechanically ventilated, which were not questioned in the verbal autopsy questionnaire.[51]

Additionally, HAP is associated with an increased mortality rate, ranging from 20% to 50%, which may increase depending on the severity of the illness during admission to the hospital and underlying comorbidities.[52] The presence of chronic underlying diseases increases the risk of pneumonia and negatively impacts the outcome and severity of it. Hospitalization history was included as a variable in the study because there were no specific questions in the VA questionnaire regarding the well-known risk factors for hospital-acquired pneumonia, including tube feeding, use of mechanical ventilation, and intensive care unit (ICU) admission. As previously mentioned, using a feeding tube increases the risk of aspiration pneumonia.[53] Patients in the ICU are usually more vulnerable to nosocomial infection and often require mechanical ventilation.[54]

A very thin or malnourished body was found to have 0,264 less likelihood of dying due to pneumonia. This result has a statistically significant value and contradicts what was previously known. One study compared 10 cohort studies regarding cause of death and weight-for-age and found that patients with moderate and severe malnutrition have a higher risk of pneumonia-related mortality, especially in children (RR 8,09; 95% CI 4,36 – 15,01 in <3 SDs weight-for-age subjects).[55] Malnutrition in all age groups is associated with many adverse outcomes, including increased mortality and morbidity, longer hospital stays, and increased hospital costs due to it.[56]

Since most of the previous studies have attributed malnutrition to a high risk of pneumonia and pneumonia deaths in children and the elderly, the presence of adults with malnutrition might cause differing results. Additionally, the very thin or malnourished variable was subjectively decided by the family member who filled the VA questionnaire, not by a standardized measurement, some of whom may have differing opinions on the "very thin" or "malnourished" body.

According to the research, there is no significant difference in the risk of pneumonia-related mortality among different sectors of society. Therefore, promoting prevention and early identification of pneumonia cases throughout the community is crucial.

CONCLUSION

The prevalence of pneumonia-related mortality in comparison to non-pneumonia-related mortality in Sleman District based on verbal autopsy is 33,3%. There are no risk factors related to pneumonia deaths compared to other causes of death in this study. The highest prevalence of pneumonia-related mortality in 2021 can be related to the Covid-19 pandemic.

Most of the subjects are elderly male with lower education level, low occupational risk, does not smoke, does not drink alcohol, and does not have a history of asthma, COPD, HIV/AIDS, stroke, or tuberculosis, has had hospitalization history, and has a normal nutritional status. The majority of those who died of pneumonia were elderly females having a low education level, a low occupational risk, do not smoke, do not drink alcohol, and do not have a history of asthma, COPD, HIV/AIDS, stroke, or tuberculosis, has had hospitalization history, and has a normal nutritional status.

The study findings suggest no substantial variation in the risk of pneumonia-related mortality across different segments of society. As a result, promoting preventive measures and early detection of pneumonia cases within the community is essential.

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CONFLICT OF INTEREST

We have received research funding related to the topic of this study from the Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada. I also serve as a researcher for the Sleman Health and Demographic Surveillance System.

We confirm that these potential conflicts of interest have been disclosed in the interest of full transparency. We assure readers that these conflicts have not influenced the design, implementation, or interpretation of the research findings presented in this manuscript. We have conducted this study objectively and taken appropriate measures to minimize potential bias.

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AUTHOR CONTRIBUTION

Stephanie Audrey Handrianto conceptualized the research study,

designed, defined intellectual content, literature search, data acquisition, data analysis, manuscript preparation, and manuscript editing.

Beta Ahlam Gizela conceptualized the research study, designed, defined intellectual content, literature search, data acquisition, data analysis, manuscript preparation, manuscript editing, revising the manuscript, and supervised the overall project.

Djayanti Sari contributed to the research design and defined intellectual content, literature search, data acquisition, data analysis, and manuscript preparation.

Lukman Ade Chandra contributed to data analysis and manuscript preparation.

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