Original Article

Nosocomial COVID-19 Infection in Acute Neurological Diseases at the Indonesian National Referral Hospital

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ABSTRACT

Introduction: Neurological diseases elevate the susceptibility to respiratory tract ailments. This study aims to evaluate the incidence of nosocomial coronavirus disease 2019 (COVID-19) among non-COVID neurology inpatients and identify associated risk factors.

Objective: To assess nosocomial COVID-19 infection in non-COVID neurology inpatients and identify associated risk factors.

Material and Methods: A prospective cohort study was conducted during the initial wave of the COVID-19 pandemic, encompassing all non-COVID neurology inpatients at Dr. Cipto Mangunkusumo Hospital from May to September 2020. Clinical data were collected, and bivariate and multivariate analyses were employed to examine risk factors.

Result and Discussion: Among 308 subjects, 31 (10.6%) experienced nosocomial COVID-19 infection. Suspect cases constituted 77.4%, probable cases 16.1%, and confirmed cases 6%. Predominant neurological diseases included cerebrovascular disease (36.7%), CNS neoplasm (18.8%), and traumatic brain injury (15.6%). Comorbid diseases increased the infection risk by 6.53 times (95% CI 1.52-28.0), particularly non-CNS malignancy (12.37, 3.7-41.00), chronic pulmonary TB (12.29, 2.7-55.89), and hypertension (3.8, 1.3-11.4). Loss of consciousness and nasogastric tube (NGT) usage elevated the risk by 2.92 (1.37-6.21) and 4.68 (1.95-11.24) times. This study reinforces existing evidence that hospitalized patients with neurological diseases are more susceptible to COVID-19, particularly due to loss of consciousness and NGT usage. The risk is amplified with comorbidities such as non-CNS malignancy, chronic pulmonary TB, and hypertension.

Conclusion: Individual neurological diseases alone did not heighten the risk of COVID-19 infection. Notably, factors like loss of consciousness, NGT usage, and comorbid diseases significantly correlate with nosocomial COVID-19 infection in non-COVID neurology inpatients.

Keywords: covid-19; nosocomial infection; neurological diseases

INTRODUCTION

Coronavirus disease 2019 (COVID-19) was declared a global pandemic in March 2020, initially registering 706,837 cases with a case fatality rate of 2.97%.[1,2] Jakarta, Indonesia, bore the highest proportion of cases, witnessing a surge from 3,524 cases per month in April-June 2020 to a substantial 34,271 cases within five months.[2,3]

In response to the escalating COVID-19 threat, hospitals rapidly adjusted their services. As a developing country, we encountered numerous challenges in establishing optimal protocols during the early stages of the first wave.[4-7] Nevertheless, the imperative to sustain inpatient services for non-COVID patients persisted, leading to an overwhelming influx of patients at Dr. Cipto Mangunkusumo Hospital, the national referral center.

Additionally, individuals with neurological diseases faced heightened susceptibility to respiratory infections, including COVID-19, because of their underlying conditions. Previous studies have highlighted the increased risk, severity, and mortality associated with pre-existing neurological diseases in COVID-19. However, none have explored the vulnerability to new COVID-19 infections during the acute phase of neurological diseases upon hospital admission. Furthermore, nosocomial COVID-19 infections were prevalent in the early outbreak. Therefore, as part of our hospital's protocol evaluation, we aim to investigate whether non-COVID neurology inpatients exhibit greater susceptibility to COVID-19 during hospitalization and to identify factors associated with COVID-19 disease.

MATERIAL AND METHODS

This prospective cohort study, conducted from May to September 2020 during the initial wave of the COVID-19 pandemic in Indonesia, focused on neurology patients admitted to Dr. Cipto Mangunkusumo Hospital, all of whom initially tested negative for COVID-19. Participants were monitored until discharge or a subsequent COVID-19 diagnosis. Clinical data collected encompassed demographic information, such as age and sex, as well as specific neurological diseases (e.g., neoplasms of the CNS, traumatic brain injury, autoimmune disorders, CNS infections, cerebral vascular diseases, and other neurological conditions). Additionally, comorbidities, including diabetes mellitus, hypertension, non-CNS malignancy, chronic pulmonary tuberculosis, immunocompromised conditions, and cerebrocardiovascular diseases, were documented. Furthermore, pote

risk factors for COVID-19 infection were explored, including loss of consciousness, length of hospital stay, duration of bed rest, and the use of a nasogastric tube.

COVID-19 infection was diagnosed per the World Health Organization (WHO) criteria, including Suspected, Probable, and Confirmed cases. Nosocomial infections were defined as those acquired during hospitalization unrelated to the admission reason, with specific criteria for Nosocomial COVID, involving a positive SARS-CoV-2 reverse transcriptase polymerase chain reaction (RT-PCR) result on the third day or later of hospitalization or within 14 days of discharge.[8]

Ethical approval was granted by the Health Research Ethics Committee, Faculty of Medicine, Universitas Indonesia, under approval number KET-466/UN.2F1/ETIK/PPM.00.02/2020.

Statistical Analysis

Using SPSS version 25, the normality of numerical data was assessed through the Kolmogorov–Smirnov test. Normally distributed data are presented as mean (±standard deviation), while non-normally distributed data are displayed as median (minimum-maximum). Analysis employed either an unpaired T-test or Mann–Whitney test based on distribution. Categorical data are expressed as frequencies and percentages, and group comparisons were conducted using chi-square and Fisher's exact test. Statistical significance was considered when $p \leq 0.05$. Further analysis involved logistic regression to identify variables independently associated with nosocomial COVID-19 infection.

RESULT

This study enrolled 308 non-COVID-19 neurology inpatients, with a median age of 48 years and a slight male predominance (55.8%). The most prevalent neurological diseases were cerebrovascular disease (36.7%), followed by CNS neoplasm (18.8%), traumatic brain injury (15.6%), and brain infection (14.3%). Comorbidities were present in most subjects (71.4%), with one-third having more than one comorbid condition; hypertension (38.6%) and cardiovascular disease (16.9%) were the most common. Decrea

consciousness was observed in only 29.22% of subjects, and 16.6% were bedridden for over 14 days. Notably, nearly half of the subjects used a nasogastric tube (NGT) (Table 1).

Table 1. Demographic Characteristics of the non-covid neurology inpatient (n=308)

	n	%
Age, years; median (min–max)	48 (15–83)	
Sex		
Male	172	55.8
Female	136	44.2
Neurological diseases		
CNS autoimmune	30	9.7
CNS infection	44	14.3
CNS neoplasm	58	18.8
Traumatic brain injury	48	15.6
Cerebrovascular disease	113	36.7
Other	15	4.8
Comorbid disease	**220**	**71.4**
Diabetes mellitus	50	16.2
Hypertension	119	38.6
Non-CNS malignancy	40	13.0
Chronic pulmonary TB	25	8.1
Immunocompromised	8	2.6
HIV	18	5.8
Cardiovascular disease	52	16.9
Other	25	8.1
Loss of consciousness	90	29.22
Duration of bed rest		
≤14 days	257	83.4
>14 days	61	16.6
Use of NGT	141	45.8
Length of hospital stay	221	71.8
≤14 days	87	28.2
>14 days		

CNS, central nervous system; NGT, nasogastric tube

During hospitalization, 31 subjects (10%) were diagnosed with COVID-19, as depicted in Figure 1. The majority (77.4%) were classified as suspected COVID-19, 16.1% as probable COVID-19, and 6.4% as confirmed COVID-19.

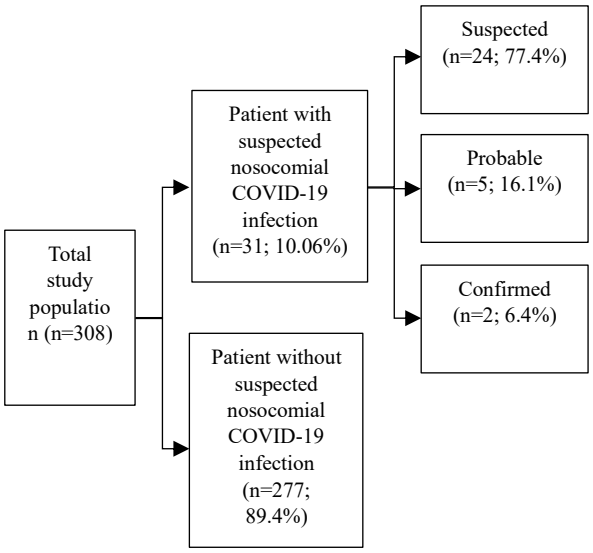

Figure 1. Nosocomial COVID-19 infection in the Study Population

In Table 2, all potential risk factors considered for bivariate analysis are listed. Subjects infected with COVID-19 were notably older (56 (20-81) vs 48 (15-83); p 0.034). Approximately 20% of subjects with pre-existing

cerebrovascular disease and CNS malignancy were infected by COVID-19, although this association did not reach statistical significance. In contrast, subjects with comorbid diseases were more susceptible to infection (6.53, 95% CI 1.52-28: p 0.004). Non-CNS malignancies (4.70, 95% CI 2.05-10.78; p 0.001) and chronic pulmonary TB (3.25, 95% CI 1.19-8.90; p 0.028) posed a higher risk of COVID-19 infection. Additionally, factors such as loss of consciousness (2.92, 95% CI 1.37-6.21; p 0.004), duration of bedrest less than 14 days (0.31, 95% CI 0.14-0.69; p 0.003), and the use of nasogastric tube (NGT) (4.68, 95% CI 1.95-11.24; p <0.001) were also significantly associated with COVID-19 infection.

The multivariate analysis using logistic regression aimed to identify independent and significant variables as risk factors for COVID-19 infection. The stepwise method was employed in this study, resulting in the selection of the following variables: age (p 0.034), infectious neurological disease (p 0.099), CNS neoplasms (p 0.044), patients with comorbid diseases (p 0.004), comorbid hypertension (p 0.118), comorbid non-CNS malignancy (p 0.001), comorbid chronic pulmonary TB (p 0.028), loss of consciousness (p 0.004), longer hospital stay (p 0.074), longer duration of bed rest (p 0.003), and the use of NGT (p<0.001).

Non-CNS malignancy and chronic pulmonary TB demonstrated a significant association, with almost 13 times the risk (12.37, 95% CI 3.7–41.00; p <0.001), (12.29, 95% CI 2.7–55.89; p 0.001). Interestingly, hypertension was also found to be associated with an increased risk of COVID-19 infection (3.8, 95% CI 1.3-11.4: p 0.016).

Table 2. Factors related to COVID-19 infection during hospitalization (n=308)

	COVID-19 Infection				**p**	**Odds ratio (95% CI)**
	Yes (n=31)		**No (n=277)**			
	n	**%**	**n**	**%**		
Age, years; median (min–max)	56 (20–81)		48 (15-83)		**0.034**	
Sex						
Male	18	10.5	154	89.5	0.793	1.10 (0.52–2.34)

Female	13	9.4	123	90.4		
Neurological diseases						
Autoimmune	2	6.7	28	93.3	0.752	1.63 (0.36-7.20)
Infection	1	2.3	43	39.6	0.099	5.51 (0.73-41.50)
CNS malignancy	10	17.2	48	82.8	0.044	0.44 (0.19-0.99)
Trauma	5	10.4	43	89.6	1.000	0.95 (0.34-2.62)
Cerebrovascular disease	12	10.6	101	89.4	0.805	0.90 (0.42-1.94)
Other	1	6.7	14	93.3	1.000	0.62 (0.08-4.93)
Comorbid disease	29	13.2	191	86.8	0.004	6.53 (1.52-28.0)
Diabetes mellitus	5	10	45	90	0.987	0.99 (0.36–2.71)
Hypertension	16	13.4	103	86.6	0.118	1.80 (0.85–3.79)
Non-CNS malignancy	11	27.5	29	72.5	0.001	4.70 (2.05–10.78)
Chronic pulmonary TB	6	24	19	76	0.028	3.25 (1.19–8.90)
Immunocompromised	1	12.5	7	87.5	0.576	1.28 (0.15–10.80)
HIV	1	5.6	16	94.4	1.00	0.51 (0.06–3.96)
Cardiovascular disease	4	7.7	48	92.3	0.533	0.70 (0.23–2.11)
Other	1	4.2	23	95.8	0.490	0.35 (0.04–2.69)
Loss of consciousness	15	6.8	203	93.2	0.004	2.92 (1.37–6.21)
Length of hospital stay					0.074	0.51 (0.24–1.09)
≤14 days	18	8.1	203	91.9		
>14 days	13	14.9	74	85.1		
Duration of bed rest					0.003	0.31 (0.14–0.69)
≤14 days	20	7.8	237	92.2		
>14 days	11	21.6	40	78.4		
Use of NGT	24	17	117	83	<0.001	4.68 (1.95–11.24)

Note: CI=confidence interval

Table 3. Multivariate analysis of factors related to COVID-19 infection during hospitalization

Subvariable	B	Wald	P	OR (95% CI)
Non-CNS malignancy as comorbidity	2.515	16.922	<0.001	12.37 (3.7–41.00)
Chronic pulmonary TB as comorbidity	2.509	10.536	0.001	12.29 (2.7–55.89)
Hypertension as comorbidity	1.346	5.851	0.016	3.8 (1.3-11.4)
Constant	-4.454	47.456	<0.001	0.01

DISCUSSION

Patients with neurological diseases, in general, were found to be susceptible to COVID-19 infections. Our study revealed that 10.1% of non-COVID neurology ward inpatients became infected with COVID-19 during their hospitalization.[6-7] The first case of COVID-19 in our hospital was identified in early March 2020. Since then, the number of cases has increased rapidly as our hospital implemented and accelerated the COVID-19 protocol. Our study, conducted since May 2020, was integral to evaluating the effectiveness of the protocol.

During the early outbreak in Wuhan, the incidence of nosocomial COVID-19 infection was 41%, which is understandable given that it was the very first outbreak. Conversely, a study at the US Academic Medical Centre, conducted from March to May 2020, reported a very low incidence of nosocomial COVID-19 infection (1.7%).[9,10] It is noteworthy that each study encompassed all hospitalized patients, not solely those in the neurology ward. However, recognizing the higher risk of COVID-19 infection among patients with neurological diseases, our study specifically focused on neurology patients admitted to the hospital with negative PCR test results.

Most studies have consistently reported an association between pre-existing and subsequent neurological diseases and an increased risk of COVID-19 infection. Among COVID-19 patients with neurological comorbidities, 22.4% of cases were identified, with the most common conditions being cerebrovascular disease and cognitive impairment.[11,12] In our study, all neurological diseases leading to hospital admission were documented. Cerebrovascular disease accounted for one-third of all

etiologies, yet only 10.6% of these cases resulted in COVID-19 infection. On the other hand, CNS neoplasms, comprising 18.8%, exhibited a higher incidence, especially when metastases from non-CNS neoplasms were present, indicating the highest risk (17.2%). The multi-organ damage caused by CNS neoplasm metastases can trigger an inflammatory reaction leading to systemic immunosuppression, rendering individuals more susceptible to secondary infections, including COVID-19.[13-16] However, our study found that none of the neurological diseases in the acute phase alone increased the risk of COVID-19 infection.

On the contrary, the impact of certain neurological disease-related factors specifically, loss of consciousness, the use of nasogastric tubes (NGT), and the duration of bed rest contributed significantly to the risk of COVID-19 infection.[17-20] Approximately 30% of our patients presented with loss of consciousness, resulting in a 2.92 times increased risk of COVID-19 infection (95% CI 1.37-6.21; p 0.004). However, our findings indicate that if patients regained consciousness and were mobile before 14 days, the risk of COVID-19 infection was reduced. This observation aligns with Wake *et al.*'s study, where out of 45 hospital-acquired COVID-19 cases, 17% developed between days 8 to 14, with the rest occurring after day 14.[20]

Patient experiencing unconsciousness often require more extended immobilization and supportive therapy, including the use of NGT.[21] Studies by Said *et al.* revealed that among 94 cases, 60.5% of patients with nasogastric intubation developed nosocomial pneumonia infections, while Huang *et al.* noted that nasogastric tube intervention contributed to the development of stroke-associated pneumonia (SAP).[22,23] While other studies have demonstrated that NGT use is associated with an increased risk of pneumonia, no specific studies have established a direct link between NGT use and the risk of developing COVID-19.[21, 24] Our study found a substantial fivefold increase in the risk of COVID-19 infection with the use of NGT. Hence, the management of patients with neurological diseases warrants careful attention to three

crucial factors: loss of consciousness, prolonged bed rest, and the use of nasogastric tubes (NGT).

Comorbidities such as hypertension, diabetes mellitus, non-CNS malignancies, immunocompromised conditions, and chronic pulmonary tuberculosis (TB) increase the risk of COVID-19.[25-29] In our study, we found an association between overall comorbid diseases and the risk of COVID-19 infection (6.53, 95% CI 1.52-28; p 0.004). Chronic pulmonary TB, aside from non-CNS malignancy, showed a similar risk of COVID-19 infection, potentially due to compromised T-cell immunity and weakened innate immune responses.[26] Our study highlighted an even higher risk of COVID-19 in neurological patients with TB as a comorbid disease (12.29, 95% CI 2.7–55.89), emphasizing the need for careful observation in this population.

Surprisingly, hypertension was also associated with COVID-19 infection. A systematic review by DiCarlo *et al.* reported hypertension as a common comorbidity (31.1%) in COVID-19 patients with neurological diseases.[12] However, Schiffrin *et al.* noted that the presence of hypertension in COVID-19 patients does not necessarily imply a causal relationship, given its prevalence in the elderly, who are at a higher risk of COVID-19 infection.[18] Further studies are required to clarify the relationship between pre-existing hypertension in patients with neurological diseases and susceptibility to COVID-19.

CONCLUSION

This study, conducted during the early stages of the first COVID-19 wave, provides insights into the incidence and risk factors of COVID-19 among non-COVID neurology inpatients. In the acute phase of neurological diseases, the heightened risk of COVID-19 infection is influenced by the combined effects of the disease and comorbidities, with factors such as loss of consciousness, nasogastric tube use, non-CNS malignancy, chronic pulmonary tuberculosis, and hypertension being notable contributors—essential considerations when evaluating vulnerability. The study highlights early mobilization as a significant preventive measure against respiratory diseases, including COVID-19. Importantly, our findings

challenge the notion that neurological diseases alone inherently increase the risk of COVID-19 infection during the acute phase. However, it is crucial to acknowledge study limitations, including the reliance on limited diagnostic tools during the initial pandemic wave, heavily relying on clinical judgment for COVID-19 diagnosis, and the study's constrained duration due to dynamic changes in hospital policies. These limitations underscore the importance of considering them when interpreting the results and emphasize the need for further research in different phases of the pandemic with improved diagnostic capabilities.

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