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Short Running Title: COVID-19 treatment audit Brunei

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### ABSTRACT:

Older people with COVID-19 infections are at high risk of adverse outcomes, such as hospitalization and death. Initially, all patients with COVID-19 infections were admitted into a designated isolation hospital. After the second wave, these patients could be admitted to any hospital in specific COVID-19 wards, thus all clinicians had to be familiar with the COVID-19 treatment guidelines. This was a retrospective review of electronic medical records for patients admitted under Geriatric Medicine in RIPAS Hospital with COVID-19 infections between 1<sup>st</sup> April 2022 and 30<sup>th</sup> September 2022. The local guidelines recommended intravenous remdesivir for patients with risk factors for complications if they presented within a week of symptom onset, as well as dexamethasone and venous thromboembolism prophylaxis. Compliance to these guidelines were audited. Among the 41 patients, approximately two-thirds were wheelchair or bedbound, while more than 40% were fully dependent. Almost one in five passed away in hospital. The compliance rate of treatment with remdesivir was 82.9%, while among the oxygen dependent patients, treatment with dexamethasone and fondaparinux were 88.2% and 70.9% respectively. While there appears to be a relatively high rate of compliance with COVID-19 management guidelines in older people admitted to RIPAS Hospital, there is still some room for improvement, given that older people are at high risk of poor outcomes with COVID-19 infections.

**Keywords:** COVID-19, dexamethasone, geriatrics, remdesivir, treatment

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### INTRODUCTION:

As of 28<sup>th</sup> February 2023, there were 278698 confirmed cases and 150 deaths due to COVID-19 infections in Brunei Darussalam [1]. In older people, COVID-19 infections are associated with

adverse outcomes, such as hospitalization and death. Older people also tend to present atypically with delirium or neurological symptoms and without fever, contributing to a delay in diagnosis and treatment [2].

When the first local case in Brunei was reported on 9<sup>th</sup> March 2020, all COVID-19 infections were admitted into the designated isolation hospital and community isolation centres [3]. After the second wave started on 7<sup>th</sup> August 2021, it became clear that it was not possible to maintain a zero-COVID strategy with the newer transmissible COVID-19 variants such as Delta and Omicron strains. Those with mild symptoms were required to self-isolate at home. However, patients with COVID-19 infections requiring hospital admission (for COVID or non-COVID related indications) would be admitted to the nearest hospital and isolated in designated COVID-19 wards [4]. This meant that clinicians in all hospitals had to be able to assess and manage COVID-19 infections and the associated complications. This was particularly relevant for the Geriatric Medicine team, as older people had a higher risk of contracting COVID-19 and develop complications [2].

The COVID-19 treatment algorithm developed by the national COVID-19 clinical management team was an important reference [5]. In the clinical pathway, patients are categorized based on disease severity: Category 1 (C 1) are asymptomatic, Category 2 (C 2) are symptomatic but do not have clinical or radiological evidence of pneumonia, Category 3 (C 3) have COVID-19 associated pneumonia but do not require oxygen,

Category 4 (C 4) are oxygen dependent, while Category 5 (C 5) require intubation and ventilatory support [4,5]. Risk factors for complications included unvaccinated or incompletely vaccinated patients, age 60 years and older, immunocompromised due to diseases or treatment, cancer, obesity, and presence of chronic diseases such as heart failure, respiratory disease, liver disease, renal disease and diabetes mellitus [5].

Based on the guidelines, C 1 to C 3 severity cases presenting within 7 days of symptom onset and have risk factors for complications should be treated with intravenous remdesivir for 3 days. Patients with C 4 or deteriorated and required oxygen during the admission should receive dexamethasone and prophylactic anticoagulation in addition to intravenous remdesivir [5]. Given the concerns regarding potential poor outcomes of older people with COVID-19 infections, the compliance to the treatment guidelines were audited.

#### **METHODS:**

All patients admitted under Geriatric Medicine in RIPAS Hospital with confirmed COVID-19 infections (positive reverse transcription polymerase chain reaction RT-PCR for the SARS-CoV-2 virus) between 1<sup>st</sup> April 2022 and 30<sup>th</sup> September 2022 were included. The electronic

health records for these patients were retrospectively reviewed for the following: patient demographics including age and gender, mobility and function in activities of daily living, comorbidities, COVID-19 vaccination status, severity category on admission, whether they were administered remdesivir, dexamethasone or fondaparinux, and outcomes including length of stay and inpatient mortality.

## RESULTS:

There were 41 patients identified. Median age was 80 years (range 77 to 94 years). Approximately two-thirds were wheelchair or bedbound, while more than 40% were fully dependent on activities of daily living. Table 1 summarises the baseline characteristics of the patients.

Table 1: Baseline characteristics of patients

<b>Demographic</b>	<b>N (%)</b>
<b>Gender:</b>	
Male	19 (46.3%)
Female	22 (53.7%)
<b>Mobility:</b>	
Independent	10 (24.3%)
Walking Aid	5 (12.2%)
Wheelchair-Bound	13 (31.7%)
Bed-bound	13 (31.7%)
<b>Activities of Daily Living:</b>	
Independent	9 (21.9%)
Semi-Independent / Requires Assistance	14 (34.1%)
Fully dependent	18 (43.9%)
<b>Co-morbidities:</b>	
Hypertension	39 (95.1%)
Dementia	20 (48.8%)
Diabetes Mellitus	20 (48.8%)
Stroke	12 (29.3%)
Pulmonary Disease	11 (26.8%)
Renal Failure	10 (24.4%)
<b>Vaccination Status:</b>	
Unvaccinated	4 (9.8%)
1 dose	0 (0%)
2 doses	23 (56.1%)
3 doses	14 (34.1%)

Table 2 shows the treatment administered stratified by severity staging at the time of presentation. As all patients admitted under Geriatric Medicine were considered high risk (at least one risk factor of age 60 years and older), they should be administered intravenous

remdesivir. This was given in 34 (82.9%) of patients. For those who are oxygen dependent (C4), they should also be administered dexamethasone and fondaparinux. This was done in 15 (88.2%) and 12 (70.9%) of the 17 Category 4 patients respectively.

Table 2: Treatment administered stratified by severity at the time of presentation

Treatment Modality	Administered to patient?	C 1 (n=2)	C 2 (n=13)	C 3 (n=9)	C 4 (n=17)	Total (n= 41)
Remdesivir	Yes	1 (50%)	10 (76.9%)	8 (88.8%)	15 (88.2%)	34 (82.9%)
	No	1 (50%)	3 (23.1%)	1 (11.1%)	2 (11.8%)	7 (17.1%)
Dexamethasone	Yes	1 (50%)	1 (7.7%)	2 (22.2%)	15 (88.2%)	19 (46.3%)
	No	1 (50%)	12 (92.3%)	7 (77.8%)	2 (11.8%)	22 (53.7%)
Fondaparinux	Yes	0 (0%)	5 (38.5%)	7 (77.8%)	12 (70.6%)	24 (58.5%)
	No	2 (100%)	8 (61.5%)	2 (22.2%)	5 (29.4%)	17 (41.5%)

Table 3: Number of patients classified according to number of vaccine doses and severity of COVID-19 infection and outcomes in terms of mortality and length of stay

	C 1	C 2	C 3	C 4	Mortality, n(%)	Mean LOS (days)
Unvaccinated (n = 4)	0	0	1	3	3 (75%)	13
1 dose (n = 0)	0	0	0	0	0	0
2 doses (n = 23)	2	0	12	9	5 (21.7%)	15.5
3 doses (n = 14)	0	8	1	5	1 (7.1%)	14

LOS – length of stay

The median length of stay was 16 days, ranging from 5 to 57 days. There were 9 (22.0%) patients who passed away in hospital. Table 3 shows the number of patients and COVID-19 vaccine doses

received for each severity category, and the mortality rate and length of stay outcomes based on vaccination doses and severity of infections.

**DISCUSSION:**

This was a retrospective audit of COVID-19 patients admitted under Geriatric Medicine to review the compliance with the local COVID-19 management guidelines. A significant proportion of the patients were relatively immobile and dependent on activities of daily living. This was similar to a descriptive study of geriatric medicine patients admitted to the hospital prior to the pandemic [6].

In this audit, just over 80% of patients received intravenous remdesivir, while among the oxygen dependent patients (C4), almost 90% of the COVID-19 patients received dexamethasone. A Spanish retrospective review of patients older than 80 years old hospitalized with COVID-19 infections showed that treatment with remdesivir had a lower 30-day all-cause mortality rate [7].

The RECOVERY Trial randomized patients to receive dexamethasone compared to usual care showed a reduction in 28-day mortality for patients on oxygen at randomization or those receiving mechanical ventilation [8]. In addition, a retrospective case-control study from 36 hospitals in France and Luxembourg showed that for patients aged 80 years and older and required oxygen had a reduced 14-day mortality among those treated with corticosteroids [9]. While the compliance rates for treatment with remdesivir

and dexamethasone were both above 80%, this should be improved further given the high risk of complications and mortality for older patients with COVID-19 infections.

The main medication used for venous thromboembolism (VTE) prophylaxis in RIPAS hospital is fondaparinux. A prospective cohort study from the United States showed that hospitalized patients with COVID-19 infections not on anticoagulation therapy had a 2.26 times increased risk of mortality [10]. A meta-analysis showed that incidence of VTE was up to 26% in hospitalized COVID-19 patients [11]. Thus, VTE prevention should be considered for high risk COVID-19 patients, which according to the local guideline is recommended for all oxygen dependent patients. This was only prescribed for about 70% of the patients. While this is a slight improvement from a 50% rate of VTE prophylaxis in a previous audit [12], there remains further room for improvement in this aspect.

Finally, despite the small numbers in the audit, there was an observable association between COVID-19 vaccination doses and reduced mortality. This supports the overall recommendations that older people should receive COVID-19 vaccinations to reduce the risk of severe infections and mortality [13].

**CONCLUSION:**

While there appears to be a relatively high rate of compliance with COVID-19 management guidelines in older people admitted to RIPAS Hospital, there is still some room for improvement, given that older people are at high risk of poor outcomes with COVID-19 infections.

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