

**PROPORTION AND FACTORS ASSOCIATED
WITH COVID-19 REINFECTION AMONG
UNIVERSITI SAINS MALAYSIA
HEALTH CAMPUS RESIDENTS**

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UNIVERSITI SAINS MALAYSIA

2023

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by

IJLAL SYAMIM BIN MOHD BASRI

**Thesis submitted in fulfilment of the requirements
for the degree of
Master of Public Health**

June 2023

ACKNOWLEDGEMENT

I would like to express my gratitude to Allah SWT for giving me opportunity and help endlessly in finishing the thesis. First and foremost, I would like to express my sincerest gratitude to my supervisor, Dr Noor Aman A Hamid, for his invaluable guidance, support, and encouragement throughout my research. Dr Noor Aman's expertise in the field has been instrumental in shaping my research direction and helped me to navigate through various challenges. I am immensely grateful for the time and effort he has invested in my research project. I would also like to extend my gratitude to my co-supervisor, Associate Professor Nor Azwany Yaakob, for her valuable inputs and guidance, which have been instrumental in shaping my research direction. Her dedication and support have been indispensable throughout my research project. Furthermore, I would like to acknowledge the contribution of my co-researcher, Dr Ahmad Mu'az Bin Kamalul Sahar, who has been an invaluable collaborator and has provided essential insights into my research project. I would also like to express my heartfelt appreciation to my wife, Ira Atika binti Mohd Nizam, for her unwavering support, love, and encouragement. Her support has been an essential factor in enabling me to complete this research project successfully. Moreover, I would like to give a special mention to my parents, Norzilah binti Hussain and Mohd Basri bin Basir. Their unwavering support, love, and belief in my abilities have been the cornerstone of my academic journey. I am forever grateful for their sacrifices and continuous encouragement. Finally, I would like to express my gratitude to all individuals who have played a role in my academic journey, including my lecturers, classmates, family, and friends. Without their support and encouragement, this research project would not have been possible.

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LIST OF SYMBOLS

| | |
|----------|--------------------------|
| α | Alpha |
| & | And |
| β | Beta |
| = | Equal to |
| < | Less than |
| > | More than |
| \geq | More than or equal to |
| n | Number of subjects |
| % | Percentage |
| P | Population's proportion |
| Δ | Precision of estimation |
| m | Ratio between two groups |
| Z | Z-score |

LIST OF ABBREVIATIONS

| | |
|-----------|---|
| ACE2 | angiotensin-converting enzyme 2 |
| aIRR | adjusted incidence rate ratio |
| adjOR | Adjusted Odds Ratio |
| B.1.1.7 | Alpha variant |
| B.1.351 | Beta variant |
| B.1.1.529 | Omicron variant |
| B.1.617.2 | Delta variant |
| BNT162b2 | Pfizer BioNTech Vaccine |
| ChAdOx1 | Oxford-AstraZeneca Vaccine |
| CoV | Coronavirus |
| COVID-19 | Coronavirus Disease |
| CDC | Centers for Disease Control and Prevention |
| CI | Confidence Interval |
| df | degree of freedom |
| HCW | Healthcare worker |
| HIV | human immunodeficiency virus |
| HR | Hazard Ratio |
| IBM | International Business Machines Corporation |
| IPC | Infection prevention and control |
| IQR | Interquartile Range |
| JEPeM | Jawatankuasa Etika Penyelidikan (Manusia) Universiti Sains Malaysia |
| MERS-CoV | Middle East respiratory syndrome coronavirus |

| | |
|------------|---|
| NAAT | nucleic acid amplification test |
| P.1 | Gamma variant |
| PCR | Polymerase Chain Reaction |
| PPE | Personal Protective Equipment |
| RNA | Ribonucleic acid |
| ROC | receiver operating characteristic |
| RR | Relative Risk |
| RTK-Ag | Rapid Antigen Test Kit |
| RT-PCR | Reverse Transcription – Polymerase Chain Reaction |
| SARS-CoV-2 | Severe Acute Respiratory Syndrome CoronaVirus 2 |
| SD | Standard Deviation |
| SPSS | Statistical Package for the Social Sciences |
| USM | Universiti Sains Malaysia |
| VIF | Variance Inflation Factor |
| WHO | World Health Organization |

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Appendix A: Study Proforma

Appendix B: Jawatankuasa Etika Penyelidikan (Manusia) Universiti
Sains Malaysia (JEPeM) Approval Letter

**PERKADARAN DAN FAKTOR YANG BERKAITAN DENGAN
JANGKITAN SEMULA COVID-19 DALAM KALANGAN WARGA
KAMPUS KESIHATAN UNIVERSITI SAINS MALAYSIA**

ABSTRAK

Latar Belakang: COVID-19 akan terus menjadi penyakit endemik di seluruh dunia, dan jangkitan semula mungkin boleh berlaku. Fenomena ini disebabkan oleh sifat COVID-19, yang menghasilkan varian baru yang menyebabkan peningkatan penularan dan pengelakan imuniti. Kampus Kesihatan Universiti Sains Malaysia (USM) adalah populasi yang unik kerana kampus ini mempunyai populasi berisiko tinggi disebabkan kewujudan pusat kesihatan di mana risiko pendedahan COVID-19 adalah tinggi dalam kalangan staf klinikal. Risiko ini juga dikongsi pelajar kesihatan klinikal yang tinggal di asrama pelajar dan berisiko menjangkiti penghuni lain. Mengenal pasti individu yang berisiko akan membantu kita dalam pencegahan dan kawalan penyakit yang lebih baik.

Objektif: Kajian ini bertujuan untuk menghuraikan peratusan jangkitan semula COVID-19 dalam kalangan warga Kampus Kesihatan USM dan untuk menentukan faktor-faktor yang berkaitan dengan jangkitan semula COVID-19 di kalangan warga Kampus Kesihatan USM bagi tahun 2021 dan 2022.

Metodologi: Ini adalah semakan rekod retrospektif menggunakan data sekunder tahun 2021 dan 2022 dari data wabak dan pengurusan penyakit COVID-19 di Kampus Kesihatan USM. Kajian ini dilakukan dari November 2022 hingga April 2023. Data yang relevan diekstrak dari lembaran EXCEL. Data dikumpulkan menggunakan proforma dan dianalisis menggunakan SPSS versi 26. Data dianalisis menggunakan analisis deskriptif, serta *simple* dan *multiple logistic regression*.

Keputusan: Sejumlah 137 kes daripada 3469 kes positif COVID-19 telah dimasukkan di dalam kajian ini di mana peratusan kes penularan semula COVID-19 adalah 3.95%. Faktor-faktor yang berkaitan dengan penularan semula COVID-19 yang didapati signifikan ialah kumpulan umur >40 tahun, adjOR = 0.265 (95% CI: 0.15,0.47, p-value <0.001), status vaksinasi, adjOR = 0.254 (95% CI: 0.15,0.43, p-value <0.001), dan penularan di tempat kerja, adjOR = 1.815 (95% CI: 1.06,3.10, p-value = 0.003).

Kesimpulan: Penularan semula COVID-19 adalah jarang berlaku di Kampus Kesihatan USM. Kumpulan umur >40 tahun, status vaksinasi, dan penularan di tempat kerja adalah faktor-faktor yang berkaitan dengan penularan semula COVID-19 di kalangan warga Kampus Kesihatan USM. Saringan yang ditargetkan kepada kumpulan umur muda perlu ditingkatkan dan penekanan yang lebih besar terhadap promosi kesihatan dan kesedaran di tempat kerja perlu untuk pencegahan dan kawalan jangkitan semula COVID-19.

KATA KUNCI: COVID-19, jangkitan berulang, prevalen, faktor berkaitan

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ABSTRACT

Background: COVID-19 will remain an endemic disease worldwide, and reinfection is possible. This phenomenon can be attributed to the highly mutable nature of COVID-19, which gives rise to new variants that exhibit increased transmission and immune evasion. Universiti Sains Malaysia (USM) Health Campus is a unique population as the campus has a higher-risk population due to the presence of a health center where the risk of COVID-19 exposure is the highest among the clinical staff. The risk is also shared among clinical health students who reside in student residences and risk exposing other residences. Identifying people at risk will help us in better prevention and control of the disease.

Objective: This study aimed to describe the proportion of COVID-19 reinfection among USM Health Campus residents and to determine the factors associated with COVID-19 reinfection among USM Health Campus residents for the years 2021 and 2022.

Methodology: This was a retrospective record review using secondary data year 2021 and 2022 from COVID-19 diseases outbreak and management data in USM Health Campus. The study was conducted from November 2022 till April 2023. Relevant data were extracted from the secured EXCEL sheet. The data were collected using proforma and were analyzed using SPSS version 26. The data were analyzed using descriptive analysis, as well as simple and multiple logistic regression.

Result: A total of 137 cases out of 3469 COVID-19 positive cases were included in this study in which the proportion of COVID-19 reinfection cases were 3.95%. The associated factors for COVID-19 reinfection that were found to be significant were age group >40 years old, adjOR = 0.265 (95% CI: 0.15,0.47, p-value <0.001), vaccination status, adjOR = 0.254 (95% CI: 0.15,0.43, p-value <0.001), and workplace transmission adjOR = 1.815 (95% CI: 1.06,3.10, p-value = 0.003).

Conclusions: COVID-19 reinfections were uncommon on USM Health Campus. Age group >40 years old, vaccination status and workplace transmission were the factors associated with COVID-19 reinfection among USM Health Campus residents. Screening targeted young age group should be enhanced and greater emphasis on health promotion and awareness in workplace for prevention and control of COVID-19 reinfection.

KEYWORD: COVID-19, reinfection, prevalence, associated factors

CHAPTER 1

INTRODUCTION

1.1 Background

The outbreak of the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) began in December 2019 in Wuhan City, Hubei Province, China, and rapidly spread across the globe (Guo et al., 2020). On January 30, 2020, the World Health Organization (WHO) officially declared the Coronavirus disease (COVID-19) outbreak a public health emergency of international concern, which was later escalated to a pandemic on March 11, 2020, impacting countries worldwide (WHO, 2020). Since then, COVID-19 has claimed numerous lives and caused significant disruptions to families, societies, and economies worldwide (Yu et al., 2021). However, it has also triggered an unprecedented and swift global response to address this health emergency (Balkhair, 2020). As of April 2023, the number of confirmed COVID-19 cases worldwide exceeded 700 million, with approximately 6.8 million deaths (WHO, 2023). In Malaysia, there have been approximately 5 million confirmed cases and 36,000 deaths recorded by the Ministry of Health Malaysia (Kementerian Kesihatan Malaysia, 2023). This current trend in Malaysia showed a rise in the daily incidence of the disease compared to the last few months.

1.1.1 COVID-19 Reinfection

COVID-19 is expected to persist as an endemic disease worldwide, allowing for the possibility of reinfection (Antia and Halloran, 2021). The initial form of the SARS-CoV-2 virus underwent rapid mutations, resulting in a variant with four genetic mutations (Hou et al., 2020; Korber et al., 2020). Over time, subsequent waves of SARS-CoV-2 variants have emerged, often exhibiting increased transmissibility and the ability to evade antibodies (Barouch, 2022). The alpha (B.1.1.7), beta (B.1.351),

and gamma (P.1) variants were first identified in late 2020 in the United Kingdom, South Africa, and Brazil, respectively. In the summer of 2021, the delta (B.1.617.2) variant, which originated in India, became the dominant variant globally, surpassing the earlier variants (Sanches et al., 2021). The highly contagious omicron (B.1.1.529) strain emerged as the most prevalent variant worldwide in late 2021 (Viana et al., 2022). Unlike the delta variant, which had only four mutations, the omicron variant carries over 50 mutations, including more than 30 in the spike protein. Consequently, it exhibits significantly greater resistance to neutralizing antibodies generated by vaccination or previous infection with non-omicron variants (Iketani et al., 2022).

Reinfection refers to testing positive for COVID-19, either through antigen or viral nucleic acid amplification tests (NAAT), after a 90-day period following the initial infection (O. Murchu E et al., 2022). The first documented case of reinfection was reported in Hong Kong in August 2020 (Parry, 2020). Over a 9-month period preceding the widespread circulation of variants, reinfections were infrequent among individuals previously infected (Akinbami *et al.*, 2021). This has been supported by several large-scale studies conducted in the United Kingdom, the United States, France, long-term care facilities in England, and South Africa. These studies have demonstrated a reduction in reinfection rates of up to 90% over a 6 to 10-month period among individuals who had tested positive for antibodies (Cohen *et al.*, 2021; Dimeglio *et al.*, 2021; Hall *et al.*, 2021; Harvey *et al.*, 2021; Krutikov *et al.*, 2021; Lumley *et al.*, 2021). Among the cases of reinfection, 2.0% resulted in death according to a study (Arslan et al., 2022). The emergence of new variants may increase the rates of reinfection and mortality (El-Shabasy et al., 2022). A meta-analysis revealed that the healthcare workers exhibited a greater susceptibility to reinfection in comparison to the community as a whole, with rates of 1.20% and 0.90%, respectively (Flacco et

al., 2022a). Thus, the consequences for health systems would be more significant if public health measures had not been appropriately implemented.

Universiti Sains Malaysia (USM) Health Campus comprised of Hospital USM, three academic schools and a research institution with nine campus residential blocks for both undergraduate and postgraduate students (Universiti Sains Malaysia, 2023). In response to the COVID-19 pandemic, The Response and Preparedness Plan for COVID-19 Pandemic and Other Infectious Disease Outbreaks was launched in March 2020 (Universiti Sains Malaysia, 2020). On November 26th, 2020, the Health Campus COVID-19 Operation Room was established in response to the 'Cluster Hilir' outbreak among healthcare workers at USM Hospital. The index case, who had a history of travel, was initially detected through symptomatic screening, which led to the identification of 21 subsequent positive COVID-19 cases at USM Hospital. The Ministry of Health Malaysia declared this as an outbreak (Ministry of Health, 2020). This Operation Room was led by the public health medical team. The main role is to ensure the continuity of patient care and academic activities via enhanced prevention and control measures. These include contact tracing, management of close contact and notification of cases and close contacts to the Kota Bharu District Health Office. The USM Health Campus COVID-19 database was created and designed as a surveillance database to facilitate public health actions.

The USM Health Campus population consists of two groups: health workers who travel from their homes and students who live on campus which is isolated from the general population. The first group includes health workers who commute daily to their workplaces, providing essential medical services. They interact with various risks of contracting COVID-19 during working and commuting. The second group consists of students residing on campus, creating a separate population segment that is isolated

from the general population outside the campus. Health workers face a higher risk of exposure due to their travel and interactions, requiring strict safety measures. Students on campus benefit from a controlled environment but still need safety protocols to maintain their well-being. Nevertheless, the absence of adequate measures presents an elevated vulnerability for healthcare workers and students to contract the disease through direct interactions. Hence, the purpose of this research was to determine the proportion of COVID-19 reinfections among residents of the USM Health Campus and to identify the associated factors.

1.2 Problem Statement

Despite implementing the best control and containment measures, the current surveillance for COVID-19 may not be entirely effective in preventing the spread of infection among USM residents. Over time, both staff members and family members continue to be infected, particularly among healthcare workers and students practicing at USM Hospital.

The COVID-19 reinfection rates are increasing in number due to the evolution of its variants. Despite that, there are no known factors associated with COVID-19 reinfection in USM Health Campus. Universiti Sains Malaysia Health Campus consists of a hospital that provides care for patients and a health campus that serves as a learning environment for students. Even though it was not a designated COVID-19 hospital (hospital which receive and treat covid cases), patients still come to get treatment without knowing their COVID-19 status and thus, putting healthcare workers at higher risk of getting COVID-19 reinfection. Healthcare workers, whether frontliners or non-frontliners, are at risk due to workplace and social exposure. As such, the population in USM Health Campus is a unique population to be studied as

the campus has a higher-risk population due to the presence of a health centre where the risk of COVID-19 exposure is the highest among the clinical staff. The risk is also shared among clinical health students who reside in student residences and risk exposing other residences.

1.3 Rationale

Researching COVID-19 reinfections among residents of the USM Health Campus can offer crucial insights into various essential aspects of the pandemic, public health, and how viral infections work. This study can provide a deeper understanding of immunity, how the virus spreads, and how well different interventions work. These insights can greatly contribute to making smarter decisions about public health strategies during the ongoing pandemic and potential future outbreaks. Moreover, since data on COVID-19 reinfections within the USM Health Campus population is accessible, it presents an opportunity to pinpoint individuals at risk. By uncovering the factors linked to reinfection, we can enhance health education efforts, promote better prevention practices, and implement effective control measures. This collective approach aims to minimize the strain on the healthcare system through well-organized public health actions.

1.4 Research Questions

- 1) What is the proportion of COVID-19 reinfection in USM Health Campus?
- 2) What are the factors associated with reinfection among USM Health Campus Residents?

1.5 Objectives of Study

1.5.1 General Objective

To study the proportion and factors associated with COVID-19 reinfection in USM Health Campus for the years 2021 and 2022.

1.5.2 Specific Objective

- 1) to describe the proportion of COVID-19 reinfection among USM Health Campus residents.
- 2) to determine factors associated with COVID-19 reinfection among USM Health Campus residents.

1.6 Research hypothesis

Sociodemographic, vaccination status, and occupation status are significantly associated with COVID-19 reinfection in USM Health Campus.

CHAPTER 2

LITERATURE REVIEW

A comprehensive literature search was conducted using several prominent online databases and search engines, including PubMed, Scopus, Google Scholar, Science Direct, Web of Science, and Springer Link. The search strategies employed involved the utilization of Boolean operators (AND, OR, NOT) to refine the results. The keywords used in the search included SARS-CoV-2, COVID-19, reinfection, associated factors, and risk factors.

2.1 The Infectious Agent: SARS-CoV-2 and its origin

SARS-CoV-2 belongs to the subgenus sarbecovirus, which is a β -coronavirus in the Orthocoronavirinae subfamily. It is an enveloped virus with a non-segmented positive-sense RNA genome (Zhu *et al.*, 2020). The taxonomic classification of coronaviruses (CoV) comprises four discrete genera, namely alpha, beta, gamma, and delta CoV.. Mammals can get infected with alpha and beta CoV and birds are more likely to contract gamma and delta CoV. Four different CoVs have been found to be infectious to humans with the low pathogenicity resulting in common cold symptoms. Other coronaviruses, such as SARS-CoV and MERS-CoV, have been identified as causative agents of grave respiratory ailments that may result in fatal outcomes (Yin and Wunderink, 2018). Through genetic analysis, it has been determined that SARS-CoV-2 shares approximately 96.2% similarity with a bat coronavirus known as RaTG13, while exhibiting around 79.5% similarity with SARS-CoV. This suggests a possible origin of SARS-CoV-2 from bats, with transmission to humans occurring through intermediate hosts that are yet to be identified. It has been established that SARS-CoV-2, like SARS-CoV, utilizes the angiotensin-converting enzyme 2 (ACE2)