Retrospective Study of COVID-19 Impact on Medication Use

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Article Info	ABSTRACT
	The coronavirus disease 2019 (COVID-19) pandemic shifted the medicine utilization landscape in hospitals globally. The purpose of this study was to assess changes in medication utilization throughout the course of the COVID-19 pandemic. A retrospective, descriptive study on medication use was conducted at a tertiary referral hospital in Malaysia. The study covered two periods: from 1 January 2018, to 31 December 2019 (pre-pandemic phase), and from 1 January 2020 to 31 December 2021 (pandemic phase). The analysis included 266 medicines, and the results indicated that most of the medications (n=142, 53.4%) experienced a decline in purchasing trends during the pandemic period (2020-2021). Notably, parenteral medications such as muscle relaxant cisatracurium besylate 2 mg/ml injection (1583.3%), vasopressin 20IU/mL injection (796%), vitamin B and C injection (672.9%,) and oral antipsychotic olanzapine 5mg (534.4%) witnessed an exponential increase in purchases. Conversely, several classes of medicines exhibited a decline in purchasing trends ranging from -45.7% to -73.7%. Notable decreases were observed in peptic ulcer medication, diuretics, and nasal decongestants. This study provides valuable insights into medication utilization trends during the pandemic and serves as a reference to the management of future global health emergencies. **Keywords:** COVID-19; drug utilization; pandemic, pharmacists

INTRODUCTION

The coronavirus disease 2019 (COVID-19) outbreak caused by novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in Wuhan, China, in December 2019, and has since taken the world by storm, eliciting a pandemic (Al-Qahtani, 2020). The second wave, which began on February 27, 2020, resulted in a total of 3,375 infections and 17 sub-clusters, with more than 30 reported deaths (Ahmad. & Pfordten., 2020). After battling to achieve a record of below 100 cases daily, from July to September 2020, Malaysia entered its third wave of the pandemic by 8 September 2020 (Hashim et al., 2021). Less than a year later on 25 July 2021, Malaysia had surpassed the 1 million mark for total cumulative cases with approximately 8000 lives lost (Anand, 2021). Amid the pandemic, obtaining medicines was challenging and lead to extra measures being taken primarily due to travel restrictions that hindered the importation and logistics of medications and medical supplies (Pharmaceutical Services Programme MOH Malaysia, 2020). Despite being an ongoing issue for decades, this worldwide pandemic has also compounded medicine shortage concerns. Medicine shortages at this critical time could lead to detrimental effects on patient outcome. One such example was seen in the economic challenges faced by Sudan, compounded by the effects of the pandemic, have given rise to a deficit in foreign currency, hindering the importation of essential raw materials required for pharmaceutical production. Insufficient domestic manufacturing capabilities were also significant barriers to the procurement of medications in Sudan and other Sub-Saharan African nations (Lucero-Prisno et al., 2020). Wealthier nations such as the United States were not spared from medicine shortages due to increased demand for medications due to COVID-19 and export restrictions by countries such as India and certain European Union member states (Piatek et al., 2020).

It is estimated that almost one third of the hospital's annual budget is allocated to purchasing materials and supplies, including medicines (Kant et al., 1996). The impact of COVID-19 on Spain's

public health budget, particularly during the 86-day peak of the pandemic, was evaluated by considering direct medical costs. The assessment revealed an estimated impact surpassing €9.4 billion, accounting for 12.3% of the total public health expenditure. Remarkably, this figure surpasses the economic burden of several other major health conditions in Spain, including cancer (€4.8 billion) and diabetes (€5.8 billion) (Carrera-Hueso et al., 2021). Given that pharmacy is one of the most critical support services in hospitals, efficient drug management is therefore essential (Goyal et al., 2016). Procurement of pharmaceuticals is a complex process that involves several processsses, agencies and manufacturers (Goyal et al., 2016). A well-designed procurement process assures that the right medicines are available in the right quantities at the right prices and of recognized quality at the right time (Goyal et al., 2016).

The World Health Organization (WHO) defines medicine utilization as "marketing, distribution, prescription, and use of drugs in society, with special emphasis on the resulting medical, social, and economic consequences" (World Health Organization., 2003). Medicine utilization studies quantify drug usage, including current patterns, trends, and the duration of use at various levels, such as national, regional, local, or institutional (Gama, 2008). In in-patient settings medication utilization provides valuable insight for assessing prescribing patterns, efficiency, and cost-effectiveness of hospital formularies (Kaur et al., 2014). Monitoring the real-world utilization of medications yields crucial insights into drug safety and the potential for adverse effects. Recognizing patterns of overuse, misuse, or underuse serves as a foundation for implementing interventions aimed at improving patient safety and mitigating the risks associated with specific drugs. This proactive approach allows for the refinement of healthcare practices and the development of strategies to ensure the optimal and safe use of medications in clinical settings.

In the event of COVID-19, medication utilization was seen to change significantly as hospitals were used to manage all COVID-19 patients, with other chronic conditions sidelined. In a retrospective study of admissions to four NYU Langone Health system hospitals during the peak COVID-19 period, the number of non-COVID-19 hospitalizations decreased significantly across a variety of diagnoses, compared to the same period in 2018 and 2019 (Blecker et al., 2021). There were decreases in exacerbations of chronic conditions (heart failure, chronic obstructive pulmonary disease), acute medical events requiring hospitalization (myocardial infarction, appendicitis), and injuries. The late COVID-19 period saw a gradual recovery in the number of hospitalizations for acute events; however, chronic disease hospitalizations did not (Blecker et al., 2021). Likewise, a narrative review by Kendzerska et al (2021) observed that the COVID-19 pandemic significantly reduced hospital admissions and emergency department visits for patients with acute myocardial infarction, stroke, heart failure, and other chronic cardiovascular conditions by 40% as compared to baseline (Kendzerska et al., 2021).

Data on medication use during the pandemic is limited globally but potentially helpful for future public health emergencies. This study aimed to assess changes in medication usage throughout the pandemic

MATERIALS AND METHODS
Study design

A retrospective, descriptive medication use study was conducted at a multi-specialty public hospital in Malaysia. The 1200-bed government-funded hospital is Johor's largest and serves as the primary referral and tertiary health center for the state. In the pre-pandemic period, the hospital had an estimated in-patient occupancy rate of 90% and this soared to a peak of 97%, during the delta surge of the pandemic. COVID-positive patients were accommodated in the normal wards, and operating theatres were converted to intensive care units. Additionally, clinics and elective surgeries were suspended to devote more personnel resources to manage COVID-19 patients. Medication use in this study was collected from the year 2018 to 2021. Two study periods were determined: A - from 1st January 2018 until 31st December 2019 (pre-pandemic phase) and B - from 1st January 2020 to 31st December 2021 (covers the 1st, 2nd and 3rd wave of the pandemic).

Ethics approval

This study has been registered with the National Medical Research Registry (Ref: NMRR ID-22-00573-6IH (IIR)) and ethical approval was granted by the Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia (MOH) and the Universiti Kebangsaan Malaysia Research Ethics Committee (Ref: JEP–2022-766). Permission from the Hospital Director and Head of Pharmacy Department was obtained prior to the study.

Study criteria

Historical medication purchase data was extracted using an electronic inventory system known as Pharmacy Information System (PhIS), which is implemented in all government health facilities nationwide. Information obtained from PhIS pertaining to this study include the active ingredients, strength of medication, dosage form, packaging unit and purchased quantity. The medications included in this study were those purchased by the Logistics Pharmacy Unit, utilized in-patient in the COVID-19 designated wards and fit the following criteria: i) COVID-19-specific medications that is defined as drugs approved for the treatment of COVID-19 and drugs under investigation or reported to have antiviral activity against COVID-19 and ii) medications that may be used for supportive treatment in COVID-19 positive patients including medicines to treat underlying co-morbidities. These medications were either proven to be effective in the treatment of COVID-19 or were suggested to offer potential benefits, and were therefore selected for inclusion. This selection was made in accordance with recommendations from the infectious disease team managing COVID-19 patients. Vaccines, intravenous drips solutions, topical preparations, syrup preparations and galenical preparations were excluded from this study.

Study instrument

The primary variables of interest in this study were all medications purchased for in-patient COVID-19 treatment and management and defined in the inclusion and exclusion criteria. A study form was developed to include the following data: drug name and Anatomical Therapeutic Class (ATC) classification, dosage form, packaging unit and number of units purchased for each medication and year drugs were purchased.

Data analysis

A spreadsheet with data on the frequencies, percentages, and charts was created using MS Excel (Microsoft Corporation, Redmond, WA). Statistical analysis was carried out using SPSS software (IBM Corp., Armonk, NY). Descriptive statistics and Kruskall-Wallis test were performed. P-value of less than 0.05 were defined as significant in this study. Normality tests conducted prior to data analysis showed that the total number of units purchased deviated from a normal distribution. The Kruskal-Wallis test was used to evaluate the relationship between the total units purchased and the year of purchase with "units" referring to the packaging unit (boxes) of medication.

RESULTS AND DISCUSSION

A total of 400 types of medication were used in the in-patient setting during the pre-pandemic years 2018-2019 (Figure 1). It was observed that majority of the medicine purchase during this phase belonged to the class J01 antibacterial for systemic use (53, 13%), followed by N05 psycholeptics (39, 10%), R03 drugs for obstructive airway diseases (24, 6%), B01 antithrombotic agents (21, 5%) and N03 antiepileptics (21, 5%). The top 10 ATC level 2 drug classes accounted for 58% of the medicines used in the in-patient setting. J01 antibacterial for systemic use (38, 14%) and N05 psycholeptics (26, 10%) dominated the medicine purchase during the pandemic phase. This is followed by the classes C01 cardiac therapy (17, 7%), B01 antithrombotic therapy (13, 5%) and both A10 drugs used in diabetes and N03 antiepileptics (11, 4%). Similarly, the top 10 ATC level 2 drug classes made up 58 % of the medicines used in the in-patient setting from 2020 to 2021 out of the 266 types of medicines purchased (Figure 2).

Overall, the total units of purchased medicines have been increasing over the years where n= 979,217 in 2018; n= 1,252,509 in 2019 followed by a sharp decline in the year 2020 where n= 1,085,857 and a surge in 2021 where n=1,332,820. A Kruskal-Wallis test showed that there was no significant association between the year of purchase and the number of units, $H(3) =1.9$, $P=0.593$.

Of the 266 medicines included in this study, more than half (n=142, 53.4%) experienced a decline in their purchasing trend during the pandemic period (2020-2021) when compared to the pre-pandemic period from 2018-2019 whilst the remaining 124 types (46.6%) displayed no change or showed an increase in purchase. A similar observation was made in a study by Mahuela et al (2023) which reported a decline in new diagnoses of chronic comorbidities during the pandemic, with fewer new cases identified in the periods following the lockdown compared to before the pandemic. Additionally, the number of medications dispensed decreased slightly over time, with women receiving fewer medications despite having a higher number of chronic disease diagnoses (Mahuela et al., 2023).
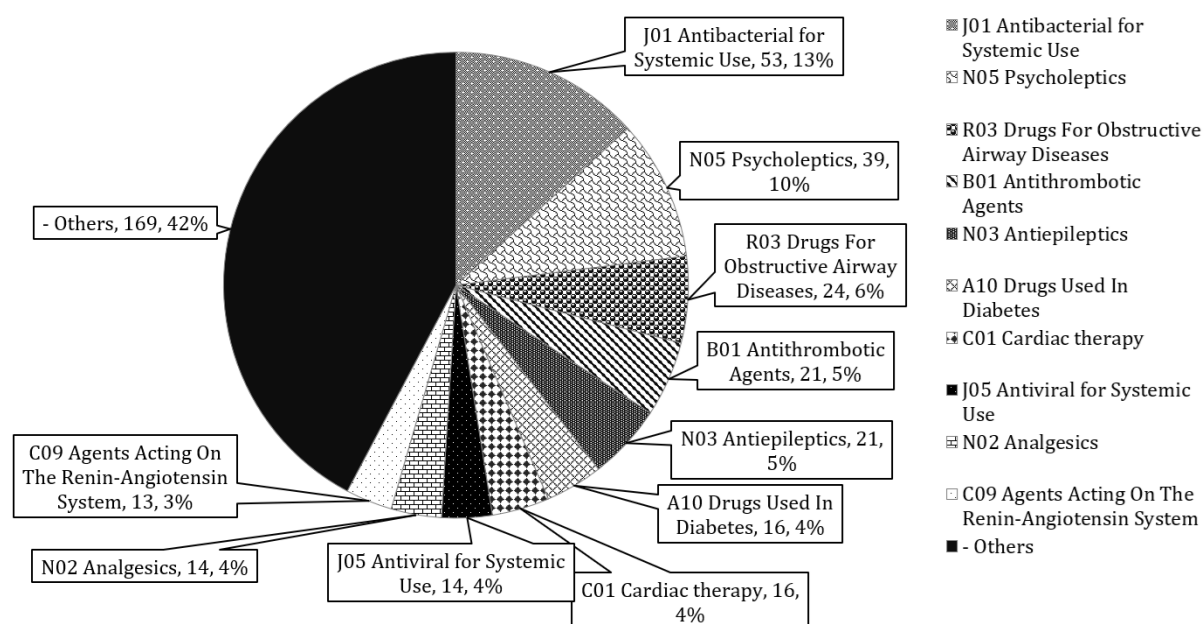
Figure 1. Medication distribution by ATC level 2 class based on the usage during pre-pandemic years (2018-2019)
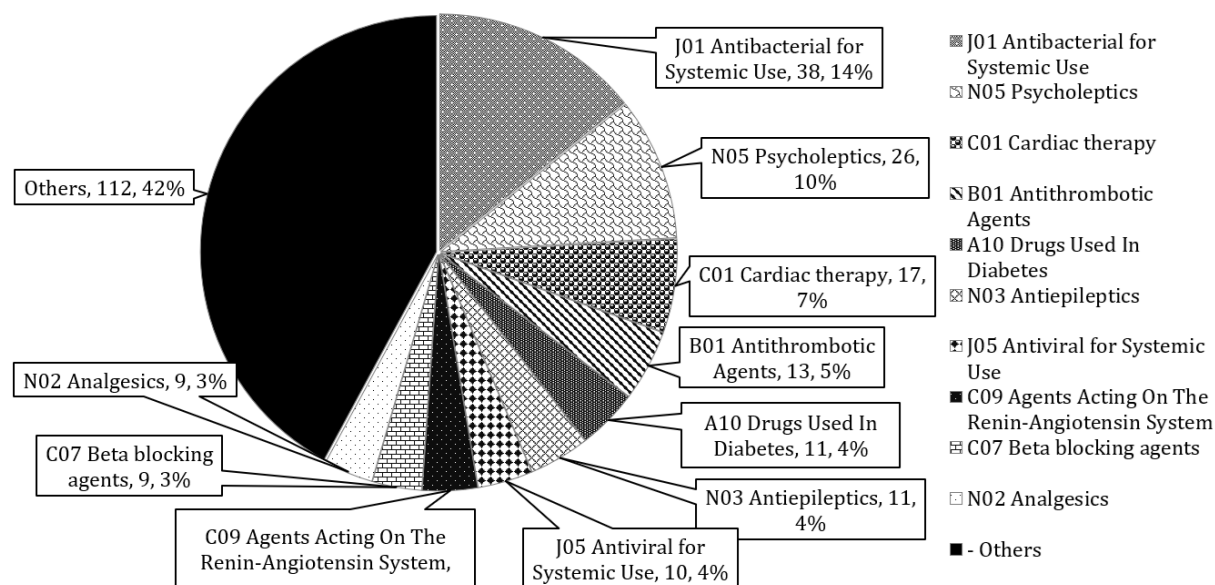

Figure 2. Medication distribution by ATC level 2 class based on the usage during the pandemic years (2020-2021)

The top 20 most purchased medicines between the two periods are shown (Table I). The most significant surge in medicine purchases during the pandemic was observed in the following categories: muscle relaxant cisatracurium besylate 2 mg/ml injection (1583.3%), followed by vasopressin 20IU/ml injection (796%), multivitamin injection (672.9%), and oral antipsychotic olanzapine 5mg (534.4%).

Table I. Medications most purchased over the pre-pandemic and pandemic years (2018-2021)

Medication	ATC CODE	Average 2018-2019 (pre-pandemic)	Average 2020-2021 (pandemic)	% Difference pre- and pandemic
Albendazole 200mg, Tablet	P02CA03	24	68	183.3
Atracurium 10mg/ml, Injection	M03AC04	373.5	1325	254.8
Cisatracurium 2mg/ml, Injection	M03AC11	15	252.5	1583.3
Cefepime 1gm, Injection	J01DE01	1685	4170	147.5
Dexamethasone Sodium Phosphate 4mg /ml, Injection	H02AB02	2962.5	9322.5	214.7
Dexmedetomidine 100mcg/ml, Injection (2ml/vial)	N05CM18	138	422.5	206.2
Enoxaparin 60mg, Injection	B01AB05	4837.5	13650	182.2
Esomeprazole 40mg, Injection	A02BC05	2927.5	7645	161.1
Fluconazole 100mg/50ml, Injection	J02AC01	161	492.5	205.9
Insulin Synthetic Human Intermediate-Acting 100 IU/ml, Vial	A10AC01	428.5	1092.5	155.0
Isosorbide Dinitrate 10mg, Tablet	C01DA08	35	104	197.1
Ketamine HCL 10mg/ml 20ml, Injection	N01AX03	280	700	150.0
Loperamide 2mg, Tablet	A07DA03	166	500	201.2
Methylprednisolone 500mg, Injection	H02AB04	242.5	680	180.4
Metoclopramide 5mg/ml, Injection (2ml)	A03FA01	607.5	1640	170.0
Midazolam 15mg/3ml, Injection (3ml)	N05CD08	2940	7700	161.9
Olanzapine 5mg Tablet	N05AH03	80	507.5	534.4
Potassium Dihydrogen Phosphate, Injection	B05XA06	190	535	181.6
Vasopressin 20IU/ml, Injection	H01BA01	12.5	112	796.0
Vitamin B and C 10mL, Injection	A11EB	66.5	514	672.9

ATC Code, Anatomical Therapeutic Chemical (ATC) Level 5, Total unit, total units of medicine purchased

Several medicines experienced a drastic decline in purchases during the pandemic period (Table II). The drop was seen especially in the purchase of oral diuretics hydrochlorothiazide 50mg (-73.7%), followed by oral antihistamine triprolidine 2.5mg & pseudoephedrine 60mg (-72.1%), ranitidine 25mg/ml injection (-71.2), analgesic diclofenac 50mg tablet (-66.5%) and antiepileptics phenobarbitone 200mg injection (-65.4%).

To the authors' knowledge, this is the first study to evaluate medication use pre and during the COVID-19 pandemic in Malaysia. Similar ATC classes such as antibiotics, psycholeptics and antithrombotic agents remained in the top category over the four years providing insight into the prescribing pattern and consumption of these classes of medication in this hospital. It is noteworthy that the consumption of antibiotics did not change drastically over the study period. In comparison a study in India demonstrated a significant increase in the overall monthly antibiotic usage in 2020 when compared to 2019 particularly through March and April 2020 (Padhan et al., 2021). A single-center antibiotic consumption study in Turkey showed that the total antibiotic consumptions during the pandemic period (811.4 DDD/1000 inpatient days) was significantly higher compared to the pre-pandemic period (725.8 DDD/1000 inpatient days) (Hamidi & Yılmaz, 2021). Findings of a systemic review and meta-analysis suggests that the pandemic may have accelerated the emergence and transmission of antimicrobial resistance, particularly for Gram-negative bacteria in hospital settings (Langford et al., 2023). Notably, the overall prevalence of bacterial co-infection in hospitalized COVID-19 patients from another systemic review and meta-analysis was found to be 11%, with a lower prevalence of 4% when considering only confirmed bacterial coinfections (Calderon et al., 2023).

Table II. Medications least purchased over the years (2018-2021)

Medication	ATC CODE	Average 2018-2019 (pre-pandemic)	Average 2020-2021 (pandemic)	% Difference pre- and pandemic
Alfacalcidol 1mcg Capsule	A11CC03	515	245	-52.4
Amoxycillin 500mg Capsule	J01CA04	1965	900	-54.2
Benzyl Penicillin 1MU (600mg) Injection	J01CE01	1755.5	775	-55.9
Benzylpenicillin 5MIU (3g) Injection	J01CE01	552.5	300	-45.7
Budesonide 1 mg/2 ml Nebulising Solution	R03BA02	277.5	134	-51.7
Captopril 25mg Tab	C09AA01	162	82.5	-49.1
Ciprofloxacin 250mg Tab	J01MA02	862.5	460	-46.7
Clindamycin 300mg/2ml Injection	J01FF01	2830	1150	-59.4
Cloxacillin 500gm Capsule	J01CF02	591	285	-51.8
Diclofenac Sodium 50mg Tab	M01AB05	337.5	113	-66.5
Digoxin 62.5mcg Tab	C01AA0	53	25.5	-51.9
Dihydrocodeine Tartrate 30mg Tablet	N02AA08	255.5	92	-64.0
Hydrochlorothiazide 50mg Tab	C03AA03	9.5	2.5	-73.7
Phenobarbitone Sodium 200 mg/ml Injection	N03AA02	40.5	14	-65.4
Ranitidine HCl 25mg/ml Injection	A02BA02	2575	742.5	-71.2
Telmisartan 40mg Tab	C09CA07	1192.5	585	-50.9
Terbinafine 250mg Tablet	D01BA02	257	99	-61.5
Trimetazidine 20mg Tab	C01EB15	857.5	420	-51.0
Triprolidine 2.5mg & Pseudoephedrine 60mg Tablet	R01BA52	21.5	6	-72.1
Zolpidem 10mg Tablet	N05CF02	150.5	69	-54.2

ATC Code, Anatomical Therapeutic Chemical (ATC) Level 5, Total unit, total units of medicine purchased

A comprehensive look into this revealed certain gaps present within antimicrobial stewardship programs as highlighted by Kubin et al (2021) such as challenges in diagnosis of co-infections, influx of critically ill patients coupled with the lack of trained staff in stewardship programs (Kubin et al., 2021). These insights underscore the need for enhanced stewardship efforts and strategic planning to mitigate the risks associated with increased antimicrobial resistance during global health emergencies. The present study showed that the purchase of certain psycholeptics such as dexmedetomidine and midazolam increased over the two study periods. However, previous work in Colombia showed an overall increase in dexmedetomidine (110%) consumption but a drop in midazolam consumption (-58%) in the year 2020 (Machado-Duque et al., 2022).

The four-year purchase analysis remained similar throughout the pre and as well as during the pandemic period, with a slight reduction in the year 2020. Patient admissions due to other diseases as well as surgical procedures were limited during the peak of the pandemic in 2020 as hospitals were mainly used for COVID-19 patient management, which could have contributed to the drop in medication purchase of other medicines (Kalanj et al., 2021; Nourazari et al., 2021; Santi et al., 2021). In addition to this, in spite of the high demand for COVID-19 treatment that year, the reduction in medicine purchase can be further attributed to the centralised procurement of COVID-19 related medicines (Pharmaceutical Services Programme MOH Malaysia, 2020) including favipiravir, tocilizumab, remdesivir and baricitinib by the Ministry of Health Malaysia to accelerate the availability of medicines. These medicines were then distributed nationwide to the designated COVID-19 treatment facilities. An additional budget of RM35.4 million was allocated for this purpose (Pharmaceutical Services Programme MOH Malaysia, 2020). The travel restrictions imposed during the pandemic affected the importation and logistics of medicines and medical supplies which further challenged the procurement

of medicines. Other countries were also observed to perform centralize purchasing of COVID-19 related essential equipment such as the National Unified Procurement Company for Medical Supplies (NUPCO) in Saudi Arabia for COVID-19 testing kits (Kalanj et al., 2021) and the European Union's Joint Procurement Agreement (JPA) in delivering necessary supplies and tools to member states while eliminating price gouging and drug and supply hoarding (McEvoy & Ferri, 2020). The Pharmaceutical Services Programme in Malaysia also played a crucial role in expediting the WHO Solidarity Trial by swiftly approving investigational products (IPs), including remdesivir, for use in clinical trials (Pharmaceutical Services Programme MOH Malaysia, 2020). All IPs underwent thorough evaluation within four working days, ensuring compliance with international regulatory standards without compromising quality (Pharmaceutical Services Programme MOH Malaysia, 2020). This further ensured the quality and safety of both procured and donated foreign and local products by verifying their registration status through drugs and cosmetics Notifications (Pharmaceutical Services Programme MOH Malaysia, 2020). Despite the thorough due diligence carried out prior to the approval of off-label use of medicines and investigational products in COVID-19 treatment by the relevant authorities, ethical considerations remain paramount. Patient autonomy, equity, transparency, and safety must remain at the forefront of these considerations. Clear and accurate information, supported by evidence, should be provided to mitigate therapeutic misconceptions and balance patient expectations before obtaining informed consent. Additionally, there is an obligation to comprehensively monitor patients, promptly report adverse events, and contribute to ongoing research efforts. This requires collaboration among healthcare professionals, regulatory agencies, policymakers, and patient advocacy groups to expand knowledge about the safety and effectiveness of this group of medicines.

COVID-19 is managed primarily through supportive measures. Data from purchasing history over the study period demonstrated that the unprecedented surge in medicine utilization occurred mostly in medicines used as supportive therapy in critically ill patients. A global time series study observed that analgesics recorded highest purchasing rates, followed by anticoagulants and sedatives. NMBAs, inotropes, and vasopressors increased significantly in developed countries in March 2020, while purchases for these categories increased in developing countries from April through August 2020 (Callaway Kim et al., 2021). Developing countries also significantly increased purchases for first-choice anticoagulants and sedatives during that period. The same study observed that no clear trends were observed between country-specific purchasing and available health system variables, except for a few countries such as Australia, Sweden, and Kazakhstan (Callaway Kim et al., 2021). Despite the global surge in demand for these medications in the care of COVID-19 patients, which led to supply chain shortages, our hospital has successfully maintained an uninterrupted supply. This ensured the delivery of optimal patient care without the need to resort to third-line therapeutic alternatives. This is in-line with the practice of other nations, which imply the selection of less optimal care choices did not occur, potentially mitigating the risk of increased adverse outcome rates and compromising patient safety (Callaway Kim et al., 2021). This underscores the salience for the implementation of conservation strategies and the exploration of alternative therapies for sedation, analgesia, and paralysis in patients affected by COVID-19 (Ammar et al., 2021; Siow et al., 2020).

The exponential increase in demand for cisatracurium during the pandemic can be attributed to several factors. The disruption in the supply of atracurium during the pandemic years led physicians to turn to cisatracurium as an alternative for a neuromuscular blocking agent (NMBA)(Bohand et al., 2021). Furthermore, cisatracurium is the only NMBA that has been studied in randomized controlled trials (ACURASYS and ROSE) for use in early, moderate-to-severe acute respiratory distress syndrome (ARDS) (PaO2/FiO2 < 150 mm Hg) (Ammar et al., 2021). Propofol is a commonly used sedative for patients requiring light sedation. However, in view of shortages, a judicious approach to reserve propofol use for cases requiring deep sedation has been suggested(Ammar et al., 2021). This aligns with the observed increase in dexmedetomidine usage over the pandemic period. Dexmedetomidine has been established as preferred alternative to propofol for critically ill patients regardless of their COVID-19 status provided there are no contraindications, such as bradyarrhythmia (Ammar et al., 2021). Apart from its potential in reducing delirium incidence, dexmedetomidine has showcased opioid-sparing effects, offering a potential avenue

to conserve the limited supply of analgesic agents (Ammar et al., 2021).

Intravenous multivitamin supplementation comprising a combination of B vitamins, vitamin C and dextrose was heavily used during the pandemic period. In hindsight, the anti-inflammatory and immunomodulatory effects of vitamin C supplementation, may have protective effects against severe form of the disease and Long COVID (Vollbracht & Kraft, 2022). Research on high-dose intravenous vitamin C in COVID-19 cases indicates improved oxygenation, and reduced inflammation, which are often seen in severe COVID-19 patients (Pedrosa et al., 2022). Early administration of high-dose intravenous vitamin C may decrease the likelihood of severe outcomes, including pneumonia and mortality. Long COVID, on the other hand, is characterized by persistent inflammation, thrombosis, and immune dysregulation (Vollbracht & Kraft, 2022). Studies in oncological diseases, viral infections, and autoimmune conditions demonstrate that high-dose intravenous vitamin C can significantly alleviate fatigue, cognitive disorders, pain, and depression; similar symptoms are observed in Long COVID (Vollbracht & Kraft, 2022). Besides that, the incorporation of thiamine as an adjunctive therapy exhibited a noteworthy association with reduced in-hospital mortality and 30-day mortality rates among critically ill COVID-19 patients (Al Sulaiman et al., 2021). Additionally, those who received thiamine as part of adjunctive therapy exhibited a lower incidence of thrombosis during their ICU stay (Al Sulaiman et al., 2021). A drug modelling study demonstrated that neutral forms of vitamins B1 and B6 can bind to essential residues of human ACE-2 (HssACE-2), a protein crucial for the cellular invasion of SARS-CoV-2 (Aghamohammadi et al., 2022). This discovery suggests the potential of these vitamins as promising candidates for the creation of novel and more effective inhibitors against COVID-19 (Aghamohammadi et al., 2022).

Dexamethasone quickly became the standard therapy in the treatment of severe cases of COVID-19 resulting in the drastic rise in its utilization during the pandemic. Dexamethasone garnered attention based on findings from the RECOVERY (Randomized Evaluation of COVID-19 Therapy) trial. The trial demonstrated that the use of dexamethasone was associated with a lower death rate among patients receiving either invasive mechanical ventilation or oxygen alone (Recovery Collaborative Group, 2021). Following the positive results from the RECOVERY trial, various health organizations, including the World Health Organization (WHO) and the National Institutes of Health (NIH), incorporated dexamethasone into their treatment guidelines for severe COVID-19 (Johns et al., 2022). The use of corticosteroids in the treatment of COVID-19 can be justified based on previous evidence from studies on Acute Respiratory Distress Syndrome (ARDS) and acute fibrinous and organizing pneumonia (AFOP) (Johns et al., 2022). As an exclusive glucocorticoid, dexamethasone has the potential to deliver beneficial anti-inflammatory effects without the accompanying mineralocorticoid stimulation. This characteristic helps prevent sodium and fluid retention, which, if present, could worsen lung injury (Johns et al., 2022).

This present study also unraveled a growing concern in the consumption of antipsychotics particularly oral olanzapine, which showed a 534% increase between the two study periods. The association between psychosis and COVID-19 has been an area of research interest, and while not as commonly discussed as other COVID-19 symptoms, it has been recognized in some cases (Chaudhary et al., 2022; Smith et al., 2021). Several studies and case reports have documented instances of new-onset psychosis or exacerbation of pre-existing psychotic disorders in individuals with COVID-19 (Chaudhary et al., 2022; Smith et al., 2021). In 92% of patients, delusions were observed, and the duration of psychiatric symptoms ranged from 2 to 90 days. Concurrently, nonpsychiatric symptoms persisted for an approximate duration of 0 to 35 days. Among the patient cohort, 69% necessitated medical hospitalization, while 33% required psychiatric hospitalization. Almost all patients received antipsychotic medications as part of their treatment regimen (Smith et al., 2021). Although the findings of this current study do not imply a cause-and-effect relationship, they provide valuable insight into the mental health challenges among the Malaysian population and underscore the necessity for integrated care models and a universal approach moving forward in the post-pandemic era. Integrated mental health interventions commonly incorporate multidisciplinary teams, shared treatment planning, and workforce training to deliver coordinated and effective care (McHugh et al., 2024). This integration can occur across various levels of healthcare, including primary, secondary, and tertiary care, ensuring a seamless continuum of services for individuals (McHugh et al., 2024).

Moreover, universal interventions that emphasize lifestyle modifications such as adequate sleep, a healthy diet, exercise, and mindfulness practices can mitigate the overall burden of the impending mental health crisis affecting numerous countries (Vadivel et al., 2021).

A 206% increase in consumption of fluconazole injection was noted during the pandemic period in this study. This may be attributed to the heightened occurrence of candidemia during the COVID-19 pandemic (Kayaaslan et al., 2021; Routsi et al., 2022; Tsai et al., 2023). Additionally, there was a notable rise in non-albicans Candida species emerging as the predominant strain (Routsi et al., 2022; Tsai et al., 2023). Concurrently, there was a significant surge in fluconazole resistance, reaching rates of 37.7% and 48.4% in the pre-pandemic periods (Routsi et al., 2022). Hence, early detection and vigilant monitoring for the occurrence of multidrug-resistant infections among COVID-19 patients is crucial, given the limited treatment options and the potential risk of compromised clinical outcomes with inappropriate treatment. In addition, a significant increase in the use of injectable anticoagulants was noted in this study. The recommendations for the prevention of thrombotic complications related to COVID-19 favored the prescription of enoxaparin (low molecular weight heparin) or fondaparinux, which led to a sharp increase in their use (Hernandez et al., 2021). The results of the current study are consistent with the increased medication sales observed during the pandemic period from March to August 2020 in Australia (55%), Russia (42%) and Mexico (34%) (Hernandez et al., 2021).

We observed a decline in purchasing trends, ranging from -45.7% to -73.7%, in several medication classes, with the steepest declines seen in peptic ulcer medications, diuretics, and nasal decongestant. This shift in priorities may have led to reduced attention toward the management of other diseases and their associated medication. Physicians may have been more cautious in prescribing certain medications or may have opted for alternative treatments because of concerns about potential interactions or adverse effects associated with COVID -19. Likewise in Canada, three commonly used acute drugs-antibiotics, non-steroidal anti-inflammatory drugs (NSAIDs), and opioids also experienced a significant decline in both incident and prevalent use following the implementation of COVID-19 mitigation measures (Aboulatta et al., 2022). The lack of diuretics being prescribed also reflects the lack of patients admitted for chronic diseases. Previous studies showed that the most affected classes of drugs for chronic diseases were cardiovascular medications, antidiabetics, and respiratory medications. The incident use of the latter classes of medications showed a significant decrease of 23.05% in the first quarter of 2020; nevertheless, there was no significant change in the slope among incident users (Aboulatta et al., 2022).

The recent revision to the Poisons Act 1952 in Malaysia to incorporate electronic prescriptions played a significant role in the endorsement of telehealth services in community pharmacies (Loo et al., 2023) may have been a contributing factor to the decrease or unchanged utilization of chronic medicines. A moderate correlation was identified between the monthly growth rate of unique users and the number of active COVID-19 cases in the country, applicable to both assisted and direct consultations (Loo et al., 2023). Despite a decline in active COVID-19 cases and the removal of movement restrictions, the number of monthly users for both types of consultations remained consistently high (Loo et al., 2023). Comparatively, during the COVID-19 pandemic, 39% of the total general practice visits in Australia were conducted via telemedicine. An increase in telemedicine claims with mental health-related diagnoses was also observed (Wabe et al., 2022). Telemedicine utilization was also linked to fewer COVID-19 cases per capita, indicating that early adoption of telemedicine contributed to containing the virus's spread in certain regions (Vogt et al., 2022). A study by Zeltzer et al (2023) indicate that access to telemedicine post the COVID-19 lockdown resulted in a modest increase in primary care visits while reducing overall healthcare expenditures. The visits were characterized by a decrease in prescription rates despite an increase in follow-up consultations (Zeltzer et al., 2023). The positive experiences and benefits realized from previous studies suggest that telehealth has the potential to transform the healthcare delivery system permanently without jeopardizing its quality, increasing costs or raising medicine utilization (Zeltzer et al., 2023).

One of the salient takeaway messages from this study is that centralized purchasing can significantly enhance the resilience and sustainability of medication supply chains during global health emergencies. Key strategies include diversifying suppliers to reduce dependency and ensuring timely and transparent sharing of

information about supply chain disruptions, production capacities, and demand forecasts to coordinate efforts to maintain medication availability. Additionally, conducting comprehensive mapping of the entire supply chain to identify vulnerabilities and potential points of failure is crucial. Regulatory agencies can contribute by adopting flexible policies to expedite medication approvals and streamline import/export processes, thereby facilitating the establishment of strategic stockpiles of essential medications and medical supplies to ensure rapid access during emergencies.

Although this study provides valuable insights, it is important to recognize its limitations as a single-center study. Potential biases, such as selection bias and information bias, may have occurred during the data collection process. Consequently, the results should be interpreted with caution, as they may be selective and have limited generalizability to broader populations or settings. To enhance the generalizability of the findings and strengthen the evidence base, future research efforts should expand to include patient outcome information such as recovery rates, mortality, and length of stay.

CONCLUSION

Ultimately, this study sheds light on the shifts in drug purchasing trends, reflecting COVID-19's profound impact on healthcare practices. The dominance of antibacterial agents, psycholeptics, and antithrombotic therapies persisted, with notable increases in supportive medications like dexmedetomidine, cisatracurium, and dexamethasone for critically ill COVID-19 patients. Concurrently, a decline in certain medications underscores shifting priorities and challenges in managing chronic conditions during the pandemic. Centralized procurement played a crucial role in maintaining medication availability by ensuring the efficient distribution of essential drugs, mitigating supply chain disruptions, and preventing price gouging. Meanwhile, the rapid adoption of telemedicine facilitated continued patient care and chronic disease management, reducing the need for in-person visits and minimizing the risk of virus transmission. These strategies were pivotal in sustaining healthcare delivery during the pandemic and offer valuable lessons for future global health emergencies.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

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