

Differences in the Use of Covid-19 Comorbid Drugs in Before and Early Of Pandemic

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ABSTRACT

Comorbid patients with Covid 19 affect the severity of the infection. This study aims to examine the utilization of generic medications in the treatment of comorbid Covid-19. Data were retrieved retrospectively from Al Ihsan Hospital's medical records. The data summarize the use of generic medicines for comorbid Covid-19 in the year preceding and in the first year of the pandemic. Metformin is the most commonly recommended medication for type 2 diabetes management. In contrast, Acarbose was the most extensively used medicine before the epidemic. Pioglitazone is the least prescribed diabetes medication. Before the pandemic, Amlodipine 10 mg was the most commonly prescribed medication for cardiovascular disease management. This is distinct from the pre-pandemic period when Ramipril was the most frequently used medication. Verapamil was the least prescribed medication prior to and throughout the epidemic. Three of the eleven medicine names analyzed in the Diabetes Comorbid group indicated that there was a significant variation in use between before and during the pandemic. Thirteen of the twenty-one medicine names analyzed in the Cardiovascular Comorbid group showed a substantial variation in usage between before and during a pandemic.

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INTRODUCTION

The COVID-19 pandemic, caused by the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), is still a global health concern as of March 11, 2020, when the World Health Organization (WHO) proclaimed it a pandemic (B.P.O.M., 2021). Comorbidity is a factor in the high mortality rate of COVID-19-infected patients and contributes to the mortality rate of COVID-19-infected patients (Kemenkes RI, 2020). Comorbidity correlates more closely with illness severity than COVID-19. The three most prevalent comorbidities among COVID-19 patients in Indonesia

are diabetes (10–20%), hypertension (10–15%), and heart and other blood vessel disease (7–40%) (Karyono & Wicaksana, 2020).

The COVID-19 outbreak is an opportunity to promote pharmaceutical production in Indonesia. In 2020, the Chemical Industry group, Pharmacy, and Traditional Medicine achieved a growth rate of 9.39% (YoY), which is not only an increase from the growth rate of 8.48% (YoY) in 2019 but also the highest growth rate of all industry groups. However, due to a reliance on imported raw materials, approximately 60 percent of it is imported from China, so the Covid-19 pandemic has reduced Indonesian pharmaceutical industry output by up to 60 percent in May 2020 (Kementerian Perindustrian RI, 2021). Over the last few years, the number of drug shortages has increased. Several factors exacerbate the problem in this pandemic, including factory lockdowns due to quarantine, logistical issues caused by border closures, export bans, lockdowns in third-country suppliers of medicines to the EU, increased demand due to the treatment of COVID-19 patients, stockpiling in specific hospitals, as well as individual stockpiling by citizens and at the Member State level. (European Medicines Agency, 2020). The shortage of drugs necessary to treat COVID-19 is another significant issue; it is anticipated that the problem will worsen over time. It not only directly impacts the COVID-19 patient but also poses a risk to the health and safety of patients who are suffering from other disorders (Choo & Rajkumar, 2020)

Hospitals require reliable stock information and anticipated supply chain bottlenecks to prepare for the medicine shortage adequately. Consumption rates should be thoroughly analyzed and routinely audited by users (hospital pharmacies) (Deana et al., 2020). Hospital pharmacies in outbreak-affected and unaffected areas play a crucial role in ensuring enough storage and supply of required medications and other medical items and devices to fulfill demand, including masks, thermometers, goggles, and other needed equipment (Federation International Pharmaceutical, 2020).

Based on this background and study, this research aims to compare the consumption of the principal covid-19 comorbid drugs at Al Ihsan Hospital before and during the pandemic because it can be used as a reference for hospitals planning the procurement of covid-19 comorbid drugs.

RESEARCH METHOD

The research was conducted in R.S.U.D. Al Ihsan Kabupaten Bandung, Jawa Barat, Indonesia. The ethics and law committee, R.S.U.D, approved the study. Al-Ihsan, Indonesia, with Nomor : 070/6780/KEPK-RSUD.Al.Ihsan/2021. This study is a descriptive study through a quantitative approach by comparing data on the use of comorbid drugs before and during the covid-19 pandemic at Al Ihsan Hospital Bandung. The population of this study is all data on the use of generic drugs in the period April 2019 - September 2019 and April 2020 - September 2020. Inclusion criteria include the sample used in the study must meet the inclusion criteria, namely sales data for the first year of the pandemic period, namely March 2020 - March 2021, and 1 year before the pandemic period March 2019 - February 2020 Drugs that are taken data are generic drugs comorbid with COVID-19.

The data were compared between comorbid Covid-19 generic drugs before and after the pandemic. A statistical test was conducted using the Mann-Whitney *test* to see if there was a statistically significant difference between drug use before and during a pandemic.

RESULTS AND DISCUSSIONS

Diabetes is one of the most common comorbidities among COVID-19 patients (Chen et al., 2020; Li et al., 2021), and diabetes increases the COVID-19 mortality rate and predisposes to a very severe disease course (Kun'ain et al., 2020). In this research, during the pre-pandemic period, the most widely used diabetes drug was Acarbose 50 mg with 29,9831 tablets, followed by Glimepiride 2 with

26,2156 tablets and Metformin 500 mg with 27,9649 tablets. Meanwhile, the drug used the least was Pioglitazone 15; no drugs were used before the pandemic. For diabetes medication, the drug most used during the pandemic was Metformin 500 with 29,7059 tablets, followed by Glimepiride 2 mg with 26,7623 tablets and Acarbose 50 mg with 18,7491 tablets, while the drug that was least used was Pioglitazone 15, no drug was used during the pandemic. The drug with the greatest percentage increase was Acarbose 100, and the drug with the greatest decrease was Pioglitazone 30. This data is consistent with Varghese et al., (2021), who stated that various glucose-lowering agents, such as insulin and Metformin, are frequently used in diabetic patients for blood glucose management in COVID-19 patients. Metformin, often known as "Glucophage," is one of the most commonly given prescriptions for type 2 diabetes management, in contrast to pre-pandemic days when Acarbose 50 mg was the most commonly used treatment.

CVD was a frequent comorbidity in C.O.-VID-19 ancestors of SARS and MERS patients (Chan et al., 2003). Diabetes mellitus and cardiovascular disease were prevalent in SARS at 11% and 8%, respectively, and the presence of either comorbidity increased the risk of mortality by 12 times. COVID-19 interacts with the cardiovascular system on several levels, increasing morbidity in those who have cardiovascular disease and producing myocardial damage and dysfunction. (Clerkin et al., 2020). The precise mechanism of COVID-19's cardiac involvement is still under investigation. One proposed pathway is ACE2-mediated direct myocardial involvement. A mouse model indicated that SARS-CoV lung infection also induced an ACE2-dependent myocardial infection (Oudit et al., 2009; Shibata et al., 2020). During the pre-pandemic period, there were 72,540 tablets of Propranolol 10 mg, 63,3784 Amlodipine tablets, and 45,7388 tablets of Candesartan 16 mg. Meanwhile, Amlodipine 10 was the most widely used drug for the cardiovascular drug category during the pandemic, followed by Propranolol 10 mg and Candesartan 16 mg. Verapamil was the least prescribed drug before and during the pandemic. Lisinopril 10 mg was the drug whose usage percentage increased by 1461% followed by Diltiazem and Ramipril 2.5 mg. Meanwhile, the highest percentage reduction in drug use was Ramipril 10 mg. This is consistent with studies Peng et al., (2021), in which 1,078 COVID-19 patients with hypertension (74.40%) had Calcium Channel Blockers (C.C.B.), while 371 patients (25.60%) did not have C.C.B. (non-CCB group). Three hundred fifty-nine patients from the C.C.B. group were matched with 359 patients from the non-CCB group using propensity score matching. Meanwhile, according to Peng et al., 2021, angiotensin-converting enzyme inhibitors (A.C.E.I.) and angiotensin II receptor blockers (A.R.B.s) were the most commonly used pharmaceutical treatments (26.78%), followed by beta-blockers (16.80%), statins (16.52%), and antiplatelet medicines (13.39%). Theoretical research into the relationship between antihypertensive medicines and SARS-CoV-2 is still being conducted. Verapamil, a C.C.B., has been recognized to prevent influenza A virus infection since 1984 (Whelton et al., 2018). Furthermore, C.C.B. is effective against a variety of new viruses, including dengue, Zika, and dengue arenavirus infection (Lavanya & Cueva, 2012).

According to the normalcy test's calculation, the significance value for each test for each drug is less than 0.05. Consequently, the Mann-Whitney Test was performed on each medicine to see whether or not there was a significant difference before and during the pandemic. The Mann-Whitney test was performed on the groups of Diabetic Comorbid and Cardiovascular Comorbid. There are eleven medications in the Diabetes Comorbid category and twenty-one medications in the Cardiovascular Comorbid group. The Mann-Whitney test was conducted by comparing the significant value to the conditional value (0.5).

Table 1. Comparison of January to March 2019 and January to March 2020 Diabetic Drug Consumption and Mann Whitney Test

Drug	Mar 2019 - Feb 2020	Mar 2020 - Feb 2021	Δ (%)	Mann-Whitney Sig.
Acarbose 50	299831	187491	63%	0,059
Acarbose 100	106735	143430	134%	0,008
Glibeclamide	3138	1002	32%	0,409
Glimepirid 1	37467	45650	122%	0,068
Glimepirid 2	262156	267623	102%	0,034
Glimepirid 3	20887	19741	95%	0,214
Glimepirid 4	45173	25783	57%	0,000
Gliquidone 30	1250	60	5%	0,738
Metformin 500	279649	297059	106%	0,463
Pioglitazone 15	46	0	0%	-
Pioglitazone 30	3707	23	1%	0,522

Acarbose 100 mg, Glimepiride 2 mg, and Glimepiride 4 mg, three of the eleven medication names investigated in the Comorbid Diabetes category, reported a substantial change in sales between before and during the pandemic. This is stated because the obtained significance value is less than 0.05. Seven other medicines, including Acarbose 50 mg, Glibenclamide, Glimepiride 1 mg, Glimepiride 3 mg, Gliquidone 30 mg, Metformin 500 mg, and Pioglitazone 30 mg, did not have a substantial change in use from before the pandemic to during the pandemic. Pioglitazone 15 mg could not be evaluated as the data did not meet the requirements of the test.

Table 2. Comparison of January to March 2019 and January to March 2020 Cardiovascular Drug Consumption and Mann Whitney Test

Drug	Mar 2019 - Feb 2020	Mar 2020 - Feb 2021	Δ (%)	Mann-Whitney Sig.
Amiodaron inj	538	575	107%	0,811
Amlodipin 5	368378	331034	90%	0,000
Amlodipin 10	633784	722746	114%	0,000
Candesartan 16	457388	459041	100%	0,602
Captopril 12,5	28302	15386	54%	0,041
Captopril 25	96497	51500	53%	0,723
Captopril 50	28315	22807	81%	0,000
Clonidin 0,15	87627	83780	96%	0,000
Digoxin 0,25	35845	27781	78%	0,488
Diltiazem 30	1301	3381	260%	0,108
ISDN	497905	346251	70%	0,000
Lisinopril 5	1105	16148	1461%	0,000
Lisinopril 10	31654	50217	159%	0,000
Nifedipin 10	14252	12600	88%	0,010
Propanolol 10	72540	49887	69%	0,936
Ramipril 2,5	23273	41721	179%	0,001
Ramipril 5	69819	102232	146%	0,000
Ramipril 10	28357	11076	39%	0,067
Valsartan 80	2359	2315	98%	0,243
Valsartan 160	829	336	41%	0,000
Verapamil 80	170	105	62%	0,038

According to table 2, of the 21 drug names studied in the Cardiovascular Comorbid group, 13 drugs reported a significant difference in use between before and during the pandemic. These drugs include Amlodipine 5 mg, Amlodipine 10 mg, Captopril 12.5 mg, Captopril 50 mg, Clonidine 0.15 mg, Isdn, Lisinopril 5 mg, Lisinopril 10 mg, Nifedipine 10 mg, and Ramipril, and they have significant value less than 0.05. During the pandemic, there was no substantial change in the sales of eight additional medications, including Amiodarone injection, Candesartan 16 mg,

Captopril 25 mg, Digoxin 0.25 mg, Diltiazem 30 mg, Propanolol 10 mg, Ramipril 10 mg, and Valsartan 80 mg.

CONCLUSION

Metformin is the most often suggested treatment for type 2 diabetes. Before the outbreak, Acarbose was the most often used medication. Pioglitazone is the least prescribed medicine for diabetes. Prior to the pandemic, the most often recommended medicine for cardiovascular disease treatment was Amlodipine 10 mg. This is in contrast to the time before the pandemic when Ramipril was the most widely prescribed drug. Before and during the outbreak, Verapamil was the least prescribed medicine. Three of the eleven medication names assessed in the Diabetes Comorbid group suggested a significant difference in use before and during the pandemic. Thirteen of the twenty-one drug names studied in the Cardiovascular Comorbid group showed a significant change in utilization between before and during a pandemic.

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