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Assessment of Risk Factors and Drug Usage Pattern in Coronary Artery Disease among COVID-19 Patients in a Tertiary Care Hospital

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Abstract

Background: Coronary artery disease (CAD) continues to be one of the leading causes of morbidity and mortality. Previous studies have shown a high incidence of CAD in patients with risk factors such as diabetes mellitus, hypertension, dyslipidaemia, smoking, alcohol consumption, etc in COVID-19. Assessing the risk factors and drug usage patterns in CAD among COVID-19 patients to analyse the extent of judiciousness in drug usage is the objective of this study.

Methodology: A retrospective cross-sectional study for six months was carried out and data were collected from the medical records of patients who were admitted with CAD and COVID-positive in the Department of General Medicine satisfying the inclusion and exclusion criteria. Patient demographics with risk factors, associated comorbidities, and drug usage patterns were also recorded. The association between the risk factors and gender was analysed using a chi-square test with a significance of $p<0.05$. The drug usage pattern was analysed by using descriptive analysis.

Results: Among 73 subjects, the incidence of CAD was predominant in males (60.3%). Most of them were seen in the age group of (70-90 years). Among the risk factors, smoking (21.9%), alcohol consumption (15.1%), pneumonia (19.2%), hypertension (76.7%) and diabetes mellitus (78.0%) were found to be highly associated with gender. Aspirin, clopidogrel and esomeprazole were prescribed to all patients. The average number of drugs prescribed was found to be between 05-30 drugs.

Conclusion: The present study helped to evaluate various risk factors of CAD and detect the drug usage pattern in the treatment.

Keywords: Coronary artery disease, COVID-19, Drug usage, Anti-platelets, Antibiotics.

1. Introduction

Coronary artery disease (CAD) is a leading cause of illness and death worldwide. The World Health Organization estimates that 1.7% of the global population is affected by CAD. In India, 11% of individuals without diabetes and 21.4% of those with diabetes suffer from CAD(1). Atherosclerosis is a significant risk factor for CAD(2).

The COVID-19 pandemic has impacted over 245 million people and caused 5 million deaths globally(3). Patients with COVID-19 often experience respiratory symptoms, but other complications such as thrombosis, myocardial damage, kidney injury, and arrhythmias have been observed. Acute Coronary Syndrome (ACS) during COVID-19 may result from atherosclerotic plaque rupture due to endothelial damage, inflammatory responses, and cytokine storms(4).

Risk factors for CAD include both genetic and lifestyle elements, categorized into non-modifiable (age, gender, heredity, ethnicity) and modifiable (smoking, obesity, hypertension, high cholesterol, inactivity, diabetes, alcohol intake, diet) factors(5,6).

Treating ACS in COVID-19 patients is challenging due to limited data on clinical features, management, and risk factors. Safe medication practices are crucial for quality healthcare. There is a significant variation in the pharmacotherapy of CAD patients, highlighting the importance of rational drug use for safety and effectiveness. Polypharmacy can lead to irrational treatment, so prescribing indicators have been established to evaluate primary care performance(7).

Conducting drug utilization studies in CAD patients with COVID-19 can positively influence future prescription patterns and drug use. Therefore, we aim to analyze drug utilization by evaluating the prescribing practices at a tertiary care hospital in central Kerala, India.

2. Objectives

2.1. To assess the risk factors associated with CAD patients.

2.2. To study the drug usage pattern among CAD-affected COVID-19 patients.

3. Materials and Methods

Institutional ethics committee-approved retrospective cross-sectional study was carried out over the duration of 6 months between May 2023 and October 2023 in a tertiary care hospital in central Kerala, India. (IEC/16/78/23). Adult patients diagnosed with CAD and have undergone either PTCA or CABG among COVID-19 patients were included in the study. Outpatients and those who were discharged against medical advice and had critical illness were not included in the study. Data were collected from the medical record department using a suitable data collection form and were analyzed. Descriptive analysis was done with the help of a Microsoft Excel spreadsheet 2013 and was expressed in mean, frequency, and percentages, and a Chi-Square test was used to compare the categorical variables by using IBM SPSS version 21.

4. Results

A total of 73 patients were recruited in the study based on inclusion and exclusion criteria in which, the majority (60.3%) were found to be males as compared to their female counterparts. Most of the patients had a past medical history of 97.3% and only 2.7% of the patients had not. Around 91.8% followed a mixed diet and 16.1% were alcoholics which were males. The socio-demographic details are shown in Table 1.

Table 1: Socio-demographics

Demographics	**Number of Cases (N=73)**	**Percentage (%)**
Gender		
Female	29	39.7
Male	44	60.3
Age **Mean Age=68.78±11.56**		
30-50	7	9.6
50-70	33	45.2
70-90	33	45.2
Past Medical History		
Yes	71	97.3
No	2	2.7
Occupation		
Yes	4	5.5
No	69	94.5
Diet		
Veg	4	5.5
Nonveg	2	2.7
Both	67	91.8
Alcoholic		
Yes	11	16.1
No	62	84.9
Smoking		
Yes	16	21.9
No	57	78.1

Risk Factors

The table depicts the association between the risk factors and gender by applying the chi-square test with a 95% confidence interval, among all the risk factors, it is found that smoking, (0.001), alcohol consumption (0.002), hypertension (0.030), dyslipidaemia (0.027), and pneumonia (0.009) is found to be highly significant among all the risk factors assessed.

Table 2:Inferential analysis of Risk Factors with Gender

Risk Factors		**No of Cases (N=73) (%)**	**Males (N=44) (%)**	**Females (N=29) (%)**	**p Value (<0.05)**
Smoking	Yes	16 (21.9)	15(34.1)	1(3.4)	0.001
	No	57(78.1)	29(65.9)	28(96.5)	
Alcohol	Yes	11(15.1)	11(15.1)	0(0)	0.002

	No	62(84.9)	33(75)	29(100)	
DM	Yes	57(78)	32(72.7)	25(86.2)	0.141
	No	16(21.9)	12(27.2)	4(13.7)	
HTN	Yes	56(76.7)	30(68.1)	26(89.6)	0.030
	No	17(23.3)	14(31.8)	3(10.3)	
DLP	Yes	34(46.5)	25(56.8)	9(31)	0.027
	No	39(53.6	19(43.1)	20(69)	
Pneumonia	Yes	14(19.2)	4(9.1)	10(34.5)	0.009
	No	59(80.8	40(90.9)	19(65.5)	
Hypo Thyroidism	Yes	9(12.3)	6(13.6)	3(10.3)	0.486
	No	64(87.7)	38(86.3)	26(89.6)	
LRTI	Yes	8(11)	4(9.1)	4(13.8)	0.396
	No	65(89)	40(90.9)	25(86.2)	
COPD	Yes	8(11)	4(9.1)	4(13.8)	0.396
	No	65(89)	40(90.9)	25(86.2)	
CKD	Yes	8(11)	4(9.1)	4(13.8)	0.396
	No	65(89)	40(90.9)	25(86.2)	
CCF	Yes	5(6.8)	2(4.5)	3(10.3)	0.308
	No	68(93.2)	42(95.5)	26(89.7)	
AKD	Yes	4(5.5)	3(6.8)	1(3.4)	0.478
	No	69(94.5)	41(93.2)	28(96.6)	
Asthma	Yes	1(1.4)	0(0)	1(3.4)	0.397
	No	72(98.6)	44(100)	28(96.6)	

Figure 1:Number of Patients along with their Number of Risk Factors

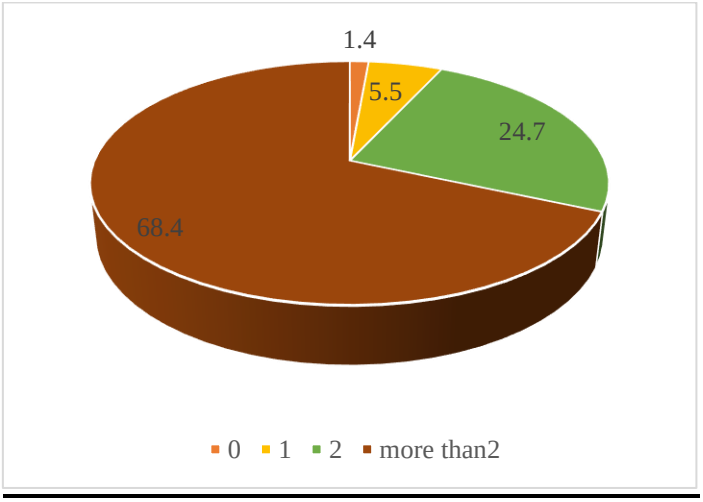


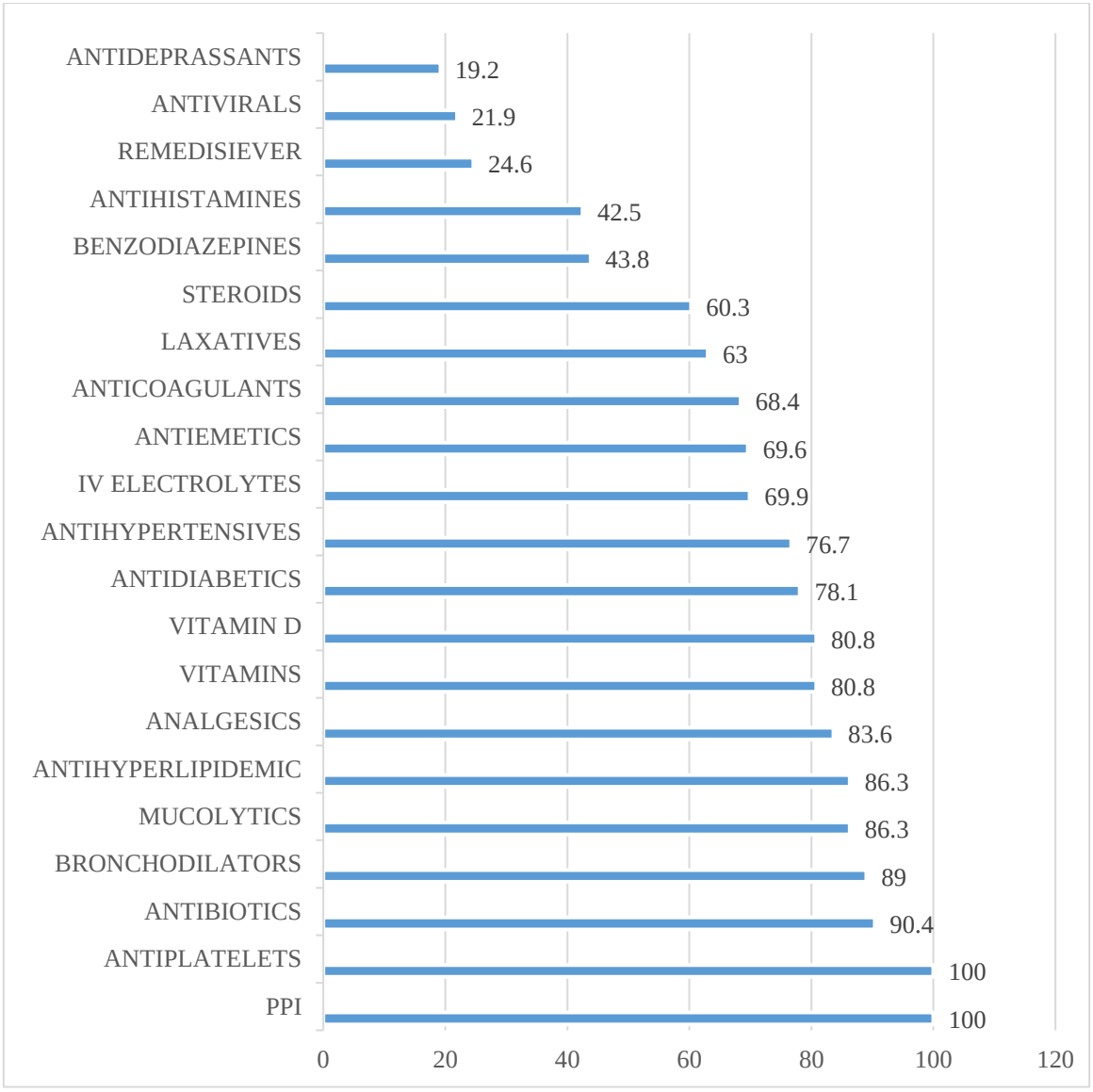
Figure 1 depicts the number of patients based on number of risk factors and it is found that among the total 73 patients, 68.4% of patients have more than 2 risk factors, and only 1.4% of patients and no risk factors.

Prescribed Drugs

Different categories of drugs were prescribed to the patients. Among them, antiplatelets were the most pr-

escribed (100%), along with these were also prescribed to all the patients (100%). antibiotics were the second most prescribed category of the drugs (90.3%) followed by bronchodilators (89%), mucolytics (86.3%) and anti-hyperlipidaemic agents (86.3%), analgesics (83.6The least prescribed antidepressants (19.2%). The data is depicted in the graph below.

Figure 2:Categories of Drugs Prescribed



PPI-Proton pump Inbitors.

Drug Usage Pattern of Common Cardiovascular Drugs in CAD

The utilization pattern of common cardiovascular drug classes used in the treatment of CAD among COVID-19 patients is shown in Table: 3

Table 3: Drug usage pattern of cardiac specific drugs

Drugs (Cardiac-Specific)	No: of Patients (N=73)	Percentage (%)
Antiplatelets		
Aspirin	45	61.6
Clopidogrel	24	32.9
Anticoagulants		
Rivaroxaban	34	46.6
Heparin (LMWH&UH)	40	54.7
Enoxaparin	10	13.7
Anti Hyperlipidaemic		
Statins	63	86.3
Other Than Statins	3	4.1
Antihypertensives		
Calcium Channel Blockers	27	36.9
ACE Inhibitors	20	27.3
Beta Blockers	27	36.9
ARBs	6	8.2
Anti-Anginal		
Nitrates	10	13.7
Nicorandil	6	8.2
Diuretics		
Furosemide	29	39.7
Spironolactone	7	9.6

COVID-19 Management in CAD Patients

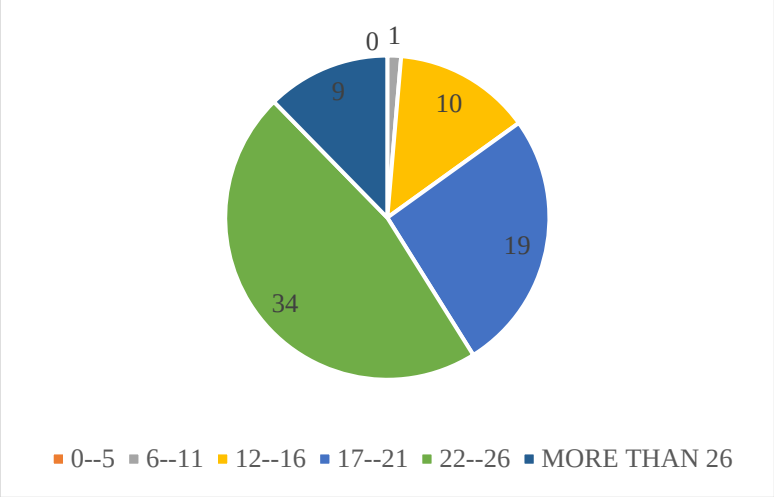
Table 4:Drug usage pattern of drugs in the management of COVID-19 infection

Drugs (COVID-19 Specific)	No: of Patients (N=73)	Percentage (%)
Antibiotics		
Azithromycin	27	37
Cefoperazone+sulbactam	23	31.5
Pipracillin+tazobactam	22	30.1
Cefixime	10	13.7
Antivirals		
Remdesivir	18	24.7
Favipiravir	17	23.2
Vitamins		
Vitamin D	59	80.8

Vitamins (except Vit D)	59	80.8
Bronchodilators	56	89
Mucolytics	63	86.3
Steroids	44	60.3
Antihistamines	31	42.5
Nebulization	49	67.1
Inhalers	9	12.3

Number of Cases Based on The Number of Drugs

Figure 3: Number of cases based on number of drugs.



5. Discussion

Coronary artery disease (CAD) is a leading cause of morbidity and mortality worldwide. The COVID-19 pandemic has garnered global attention, and recent research has highlighted an association between COVID-19 and CAD(8).

Our study included 73 patients, with men constituting the majority. Similar findings were reported by Kong et al. (2019) in South Korea and Roy (2019) in India. The higher prevalence of CAD in men can be attributed to differences in etiology and risk factors, including smoking and alcohol consumption(9).

Furthermore, our study revealed that individuals aged 50 and above had a higher incidence of CAD. This aligns with the results of Kong et al. (2019), who observed a similar trend in South Korea. The key risk factors for CAD are predominantly observed in older age groups, particularly those over 70 years old(10).

Regarding gender-specific risk factors, hypertension was the most prevalent. Escobar et al. (2002) from the Netherlands demonstrated that isolated systolic hypertension increases with age in both men and women, indicating arterial elasticity loss(11). Hypertension serves as a significant marker for high-risk patients, given the tendency for risk factors to cluster in the context of elevated blood pressure.

Smoking and alcohol use emerged as the most critical risk factors for coronary artery disease (CAD). Our study revealed a higher prevalence of smokers (21%) compared to drinkers (11%). Krishnan et al. (2012) from India reported that men were more prone to smoking addiction (30%) than women(8). Notably, our study found no significant variations in the association between dyslipidaemia and CAD.

Age and sex represent non-modifiable risk factors, while hypertension, dyslipidaemia, diabetes mellitus, alcohol use, and smoking fall under modifiable risk variables. Remarkably, over 65% of our patients exhibited at least two of these risk factors, underscoring the escalating CAD incidence with an increasing number of risk factors.

Furthermore, our analysis identified pneumonia (34%) as a significant risk factor among CAD patients for developing COVID-19 infections. Interestingly, pneumonia was more prevalent in females. Gunay et al. (2020) from Turkey highlighted pneumonia's relevance to COVID-19, particularly in male groups(12). COVID-19 outcomes have been linked to underlying comorbidities, especially cardiovascular disorders. CAD, by compromising myocardial oxygen flow, may exacerbate oxygen delivery insufficiency due to respiratory infections or pneumonia. Previous research suggests that CAD worsens the course of COVID-19 by aggravating hypoxemia and leading to severe disease.

Regarding medications, our study revealed a predominant use of antiplatelet agents (100%), followed by antihyperlipidemic (86%), antihypertensives (76%), and anticoagulants (68%). Most patients received multiple medications. George et al. (2013) from India similarly observed that CAD patients were commonly prescribed five classes of medications: antiplatelets (88%), statins (76%), ACE inhibitors / ARBs (72%), beta-blockers (58%), and anticoagulants (57%)(13).

In our study, 71% of patients exhibited polypharmacy (using more than five medications). When considering antiplatelet therapy for coronary artery disease (CAD), aspirin and clopidogrel were the most commonly recommended medications. Jneid et al. (2003) from China also found that these two drugs were frequently utilized among CAD patients. Aspirin, known for its efficacy in primary and secondary CAD prevention, synergizes well with clopidogrel, an alternative antiplatelet agent used in patients intolerant to aspirin(14).

Anticoagulants play a crucial role in managing valvular heart disease, venous thromboembolism, and atrial fibrillation (AF). In our study, rivaroxaban was the most frequently prescribed anticoagulant, followed by low-molecular-weight heparin (LMWH), unfractionated heparin (UH), and enoxaparin. Naliganti (2019) reported that over 53% of patients received LMWH and enoxaparin, while UH was administered to 4% of patients(15). These anticoagulants are beneficial in treating conditions such as pulmonary embolism, venous thrombosis, and unstable angina.

For individuals with CAD, antihyperlipidemic medications are essential for lipid management. Atorvastatin was the primary choice in our study, followed by rosuvastatin. Some patients received combinations of these drugs. Naliganti (2019) observed that atorvastatin was frequently prescribed in 80% of cases. This preference stems from atorvastatin's ability to reduce the risk of composite outcomes, including death, myocardial infarction (MI), cardiac arrest, and recurrent ischemia(16)

In our study, we investigated the risks associated with coronary artery disease (CAD). Here are the key findings related to medications and their implications:

1. Diabetes Management:

- Metformin was the most commonly prescribed medication (45%) for patients with CAD. Glimepiride followed closely at 30%. These anti-diabetic drugs play a crucial role in managing diabetes.
- Kaduskar (2017) from India highlighted that lipid-lowering medications can increase the risk of developing diabetes. As a result, metformin is recommended as a monotherapy for diabetes treatment.

2. Hypertension (HTN):

- HTN emerged as a significant risk factor in our study. Therefore, antihypertensive drugs like cilnidipine and telmisartan were frequently prescribed for CAD patients.

- Adejumo (2017) from Nigeria reported that calcium channel blockers (CCBs), ACE inhibitors (ACEs), and diuretics are effective in reducing blood pressure in CAD patients(17).Interestingly, the proportion of participants in monotherapy and those with tertiary education did not show statistically significant differences.

3. Anti-Anginal Medications:

- Nitrates were predominantly used as anti-anginal drugs in our patient cohort. These medications are considered safe and effective for managing ischemic symptoms related to coronary artery diseases.

4. Loop Diuretics:

- Furosemide, a loop diuretic, was commonly prescribed to most patients. Hansen S (2015) from Norway emphasized the importance of loop diuretics in treating systolic heart failure, and they hold strong recommendations in current guidelines(18).

5. Antibiotics and Antivirals:

- Patients received a combination of antibiotic, antiviral, and other generic medications as part of their treatment.
- Azithromycin was the most frequently prescribed antibiotic, followed by combination medications like cefixime.
- For COVID-19 patients, remdesivir and favipiravir, both antiviral medications, were commonly used. Mustafa Z (2021) from Pakistan reported that 45% received remdesivir, 93% received corticosteroids (dexamethasone), 84% received antibiotics, and 60% received antithrombotic(19). It's important to note that these medications may have cardiotoxic and proarrhythmic effects, especially in patients with pre-existing cardiovascular disease.

Dexamethasone has demonstrated clinical efficacy in treating severe COVID-19 cases. Specifically, it reduced 28-day mortality among hospitalized patients receiving invasive mechanical ventilation. However, our study had certain limitations:

1. Single-Centric Study: Our research was conducted at a single center, limiting the generalizability of results.
2. Hospital-Based Sample: The patient population may not fully represent the broader community due to the hospital-based nature of the study.
3. Causality Challenges: As with any cross-sectional study, drawing firm conclusions about causality is difficult.
4. Risk of Misclassification: Information on risk factors and treatment patterns relied on previous medical reports.

Future studies in different hospital settings could yield similar results

6. Conclusion

The present study aimed to identify copious risk factors and prerequisites for the early and satisfactory management of CAD among COVID-19 patients to prevent future complications. As the CAD patients were more with controllable risk factors (smoking, alcoholism) than uncontrollable risk factors (HTN, DLP, Pneumonia) proper counselling and early management of the risk factors for mostly under 65 years could somehow decrease the incidence of CAD to some extent. The study also showed various medications prescribed in CAD among COVID-19 patients were anti-platelets, anticoagulants, antihypertensive, statins, and anti-diabetics. GI protectants were additionally added to reduce gastric bleeding. According to WHO, prescribing in a generic name is advised in terms of rationality. In our study,

the usage of generic drugs was very low which points to the rational use of drugs. AHA guidelines are to be adopted in every hospital to provide a rational therapy for each CAD patient.

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