Factors Affecting the Prescription Pattern of Generic Cardiovascular Medicines: A Cross-Sectional Study in Dhaka City

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ABSTRACT: A growing trend of cardiovascular disease is a threat to national health. The objectives of the research are to analyze the association between prescribed generics with doctors' gender, academic degrees, location of practice and categories of generic medicines. A descriptive cross-sectional Dhaka-based study design was used to assess the prescriptions data. As a primary source of data, 403 prescriptions were collected for twelve months from six different locations of the cardiologists' practice chamber in Dhaka. A two-stage cluster sampling technique was used to collect prescriptions at a 95% confidence level with a 5% margin of error. For proportional to population size (PPS) sampling, cluster weight of specific areas was determined from a secondary source of data. Chi-Square (χ^2) goodness fit test revealed that gender, academic degrees, location of practice, therapeutic class of cardiovascular generics are statistically significant in association with prescribed generic medicine at a 5% level of significance (p-values <0.01).

Key words: Cardiologists, Prescription pattern, Therapeutic class, Generic cardiovascular medicine, Cluster sampling, Chi-square test.

INTRODUCTION

Cardiovascular diseases (CVDs) are the leading cause of death globally. An estimated 17.9 million people died from CVDs in 2019, representing 32% of all global deaths.[1] Over three-quarters of CVD deaths take place in low- and middle-income countries like Bangladesh.[1] CVDs can be categorized by the indications related to heart and blood circular networks which can be categorized as hypertension, dyslipidemia, stroke, atherosclerosis, thrombosis, myocardial infarction, congestive heart failure, disease of coronary artery and stroke. Cardiovascular disease is the number one cause of death in Bangladesh.[2] The current prevalence of hypertension, coronary artery disease, rheumatic heart disease and stroke is 20-25%, 4-6% and 0.3-1%, respectively.[3] The global cardiovascular drugs market is expected to grow from $87.79 billion by 2020 to $92.41 billion in 2021.[4] The market size of cardiovascular medicines in Bangladesh was BDT 658 Cr in 2011 and has been increased to BDT 3071 Cr in 2020 growing at 23.8% rate.[5] Different types of cardiovascular generic medicines available in the Bangladesh pharmaceutical market are angiotensin, calcium channel blocker (CCB), beta blocker (BB), antiarrhythmic, diuretics, angiotensin-converting enzyme inhibitors (ACEI), alpha adrenergic blocker and vasodilators.[5] The prescribed generic wise

branded cardiovascular medicines of different pharmaceutical companies are being used in the treatment of cardiac diseases in Dhaka city. Cardiac diseases are chronic illnesses thus the medications are often continued for a lifetime as preventive measures. The cardiac market is growing with significant potential where cardiologists are the customers and cardiac patients are the consumers of the pharmaceutical health care sector. The increasing sale trend of cardiovascular medicines indicates the rising of cardiac patients that need to be investigated.

Many factors affect doctors' prescriptions patterns. Previous studies have shown that factors such as gender, age, educational qualification, experience, specialty influence doctors' prescribing patterns.[6] The cardiologist is the decision-maker who diagnoses the patients and accordingly, identifies the medicines category to select a specific brand among a vast array of alternatives of generic medicines in the pharmaceutical market. The patients who have to take the selected medicines are responsible for paying for it.[7] The benefit of prescribing a specific cardiac medicine may be through the improvement of patients' health over time. But there are many factors other than scientific knowledge that affect the prescribing trend. Doctors' level of education, doctors' gender, doctor's demographic characteristics, patient's profile, the behavior of the peer physicians, patient's request on medication, number of patients examined per day are some of those factors.[8-10] Assessment of prescription patterns based on WHO prescribing indicators help to improve the quality of prescription.[11] Physicians' preferences in drug prescription are influenced by the quality of medicines, company reputation, communication relationship with the company, availability of medicines and price respectively.[12] Pharmaceutical marketing strategies have an important impact on physicians' prescribing patterns.[13] The effect of doctors' academic qualifications on prescription has been observed in the research.[14]

However, there were limitations of the existing study, only four factors were considered among many. Those factors that were not explored may have confounding effects on cardiologists' prescription patterns. Moreover, there was no study concerning the relationship of prescribed generic cardiovascular medicine with factors like doctors' gender, academic degrees, location of practice and categories of generic cardiovascular medicines in Dhaka city. In the present study, researchers carried out surveys on cardiologists' prescription patterns during their practice from the period of August 2020 to July 2021. The areas covered by the survey were Mirpur, Mohammadpur, Dhanmondi, Ramna, Uttara and Savar.

Research hypotheses development. As mentioned above, this study examined the factors affecting prescribed generic of cardiovascular medicines of cardiologists' prescriptions. Moreover, this research tested whether the factors like gender, academic qualifications, location of practice and types of generic medicines influence the prescribed generic of cardiovascular medicines or not.

For this purpose, the researchers addressed some questions-

(i) Is there any relationship between the gender of cardiologists and prescribed generic cardiovascular medicines?

(ii) Is there any association between the number of academic qualifications and prescribed generic of cardiovascular medicines?

(iii) Is there any relationship between the location of cardiologists' practice and prescribed generic of cardiovascular medicines?

(iv) Is there any relationship between the therapeutic class of cardiovascular medicines and prescribed generic of cardiovascular medicine?

(v) Is there any modification effect of gender and location of cardiologists' practice in the relation between the number of academic degrees and the number of prescribed generic medicines?

The research hypotheses to be tested in this study is given below:

No. of Hypotheses	Research Hypotheses
H_1	There is a relationship between the gender of cardiologists and prescribed generic cardiovascular medicines.
H_2	There is an association between the number of academic qualifications and prescribed generic of cardiovascular medicines.
H_3	There is a relationship between the location of cardiologists' practice and prescribed generic of cardiovascular medicines.
H_4	There is a relationship between the therapeutic class of cardiovascular medicines and prescribed generic cardiovascular medicines.
H_5	There is a modification effect of gender and location of cardiologists' practice in the relation between the number of academic degrees and the number of prescribed generic medicines.

METHODS

Sampling design. Data was collected by Two-stage cluster (area) sampling proportional to population size (PPS). The cluster size of 18 thanas was collected from the secondary data source- 4P Pharmaceutical Marketing Research & Consultancy's database. Then one-third (6 thanas) were selected in the first stage with PPS and in the second stage, 403 prescriptions were collected from these thana proportional to their size. The total sample size (approximately 385) was determined by Cochran's formula with a 5% margin of error and 5% level of significance.[15] The sample size was increased to 400 and the final sample size was 403 prescriptions. The whole sampling procedure is described in Table 1.

Statistical analysis. Chi-square goodness of fit test was used to evaluate whether the proportion of prescribed generic varies or depends on the cardiologists' gender, the number of degrees, location and the therapeutic class of the drugs.[16] In addition, the Pearson correlation coefficient was also used to investigate the relationship between quantitative variables. Statistical analysis was carried out using R programming language and MS Excel was used for data visualization.[17]

Table 1. Two-stage proportional to population size (PPS) cluster sampling.

Thana	Cluster size	Proportion	Sample size proportional to cluster size	Final sample size
Mirpur	401	0.44	176.85	177
Mohammadpur	141	0.16	62.18	63
Uttara	119	0.13	52.48	53
Savar	115	0.13	50.72	51
Dhanmondi	92	0.10	40.57	41
Ramna	39	0.04	17.20	18
Total	907	1.00	400.00	403

RESULTS AND DISCUSSION

In this study, 403 prescriptions were surveyed; from these prescriptions total number of generics prescribed by cardiologists was found 1278. Only the generics prescribed for chronic indications like hypertension, diabetes, respiratory and central nervous system disorders were taken for analysis. Table 2 shows the proportion of prescribed generic drugs according to physicians' gender. Out of 1278 prescribed generics, 91.39% generic was prescribed by male physicians. Consequently, the proportion of prescribed generic differ significantly from male to

female physician, χ^2 (1) $= 1748.4, p < 0.05$. The distribution of prescribed generic by gender of the Physicians is presented in Figure 1 (A).

Table 2. Association between prescribed generic and gender of the physicians.

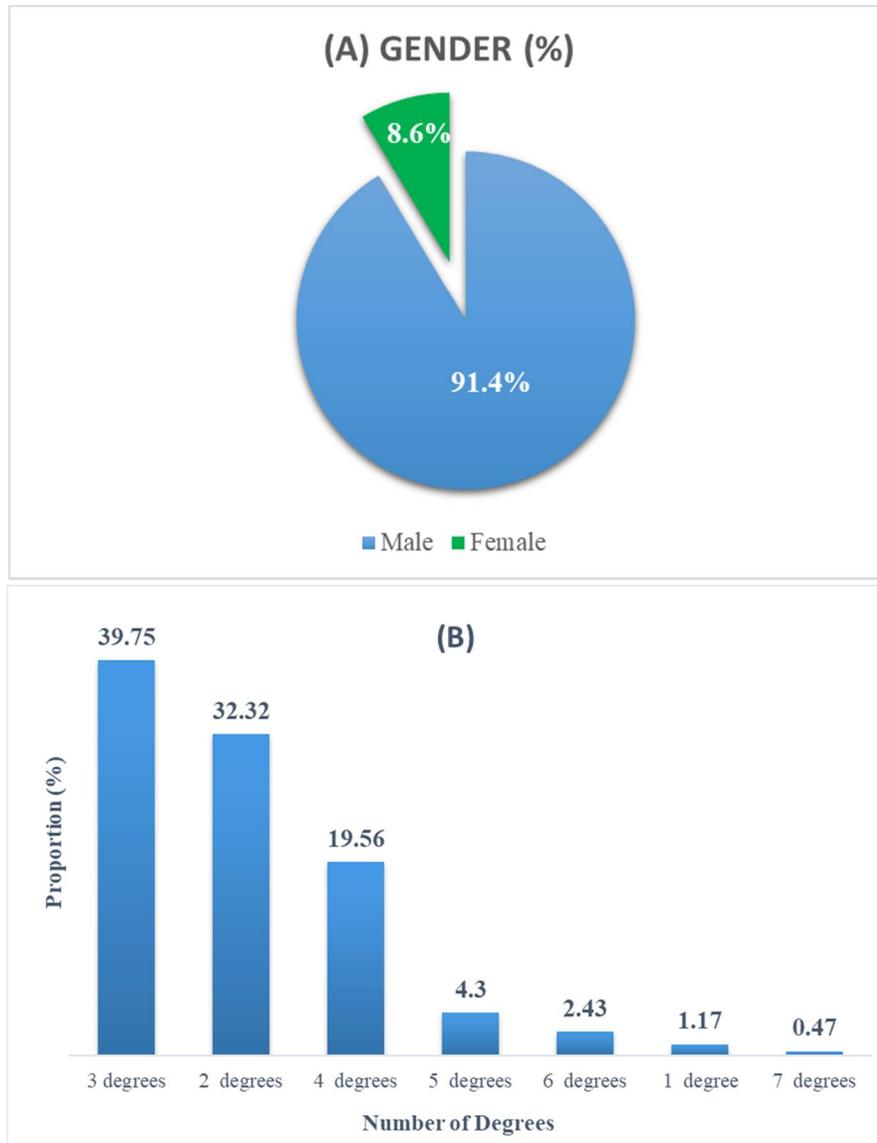| Gender	No. of generic prescribed	Percentage	χ^2 value	p-value (Difference in proportions)
Male	1168	91.39	1748.4	0.000
Female	110	8.61		

Figure 1. Distribution of prescribed generic (A) by gender and (B) number of degrees.

A total of thirty-two different degrees were found which can be categorized as a bachelor, master, post-graduate training, doctorate, diploma, fellowship and membership. The highest number of degree of cardiologists was found seven (07) and the lowest was one (01). All the cardiologists had an

MBBS degree. Cardiologists who had two degrees either had an MD (74%) or a D-CARD (16%). Cardiologists with three degrees had both MD and D-Card along with MBBS (15%). Another group of cardiologists with three degrees had an FCPS (30%) or FACC (7%) or CCD (6%) with an MBBS and MD. Cardiologists who have further degrees (*i.e.* four, five and more) had variations in the type of degrees they obtained. It was a different mix of FACP, FCCP, FSCAI, FACC, MRCP, PGT, CCD, DTCD etc. Table 3 shows that the majority of generic (39.75%) was prescribed by the cardiologists who had 3 degrees and the lowest generic (0.47%) was prescribed by the physicians who had 7 degrees. The proportion of prescribed generic differs significantly among cardiologists in terms of their number of degrees, $\chi^2(6) = 1674.6, p < 0.05$. The distribution of prescribed generic by the number of degrees is

presented in Figure 1(B). However, the Pearson correlation coefficient between the number of degrees and the number of prescribed generics was found positive but very weak ($r=0.018$, $p>0.05$) and insignificant.

Table 4 implies that the majority of the prescribed generic was from Mirpur (42.33%) and the lowest was from Ramna (5.87%). The proportion of prescribed generic also vary significantly across the area, $\chi^2(5) = 835.23, p < 0.05$. The distribution of prescribed generic by area is presented in Figure 2(A) from highest to lowest proportion. The high prescription flow from Mirpur and Mohammadpur is due to the country's two major cardiovascular institutions National Heart Foundation (NHF) & the National Institute of Cardiovascular Diseases (NICVD) are located in Mirpur & Mohammadpur Thana, respectively.

Table 3. Association between prescribed generic and number of degree of the physicians.

No. of degree	No. of generic prescribed	Percentage	χ^2 value	p-value (Difference in proportions)
1	15	1.17		
2	413	32.32		
3	508	39.75		
4	250	19.56	1674.6	0.000
5	55	4.30		
6	31	2.43		
7	6	0.47		

Table 4. Association between prescribed generic and area.

Area	No. of generic prescribed	Percentage	χ^2 value	p-value (Difference in proportions)
Dhanmondi	115	9.00		
Mirpur	541	42.33		
Mohammadpur	258	20.19		
Ramna	75	5.87	835.23	0.000
Savar	127	9.94		
Uttara	162	12.68		

Table 5 indicates that most of the prescribed generic came from the Antihypertensive class (27.93%). A significant proportion (14.79%) of Central Nervous System (CNS) generics has been

prescribed by cardiologists. It is because the prevalence of depression and anxiety disorders is strongly associated with cardiovascular disease (CVD) among adults.[18] On the other hand, the

respiratory class had the lowest proportion (0.78%). Proportion test reveals that the number of prescribed generics differs significantly across therapeutic classes, $\chi^2(6) = 437.48, p < 0.05$. The distribution of prescribed generic by therapeutic class is presented in Figure 2(B) from highest to lowest proportion.

Top 80% prescribed generic: In the sampled prescription, a total of forty-six (46) generics were found. But, only 12 generics (Nitroglycerin,

Clonazepam, Rosuvastatin, Bisoprolol, Atorvastatin, Clopidogrel+Acetylsalicylic Acid, Trimetazidine, Clopidogrel, Spironolactone+Furosemide, Escitalopram, Amlodipine+Olmesartan, Losartan) account top 80% generic prescribed by physicians. The result is shown in Figure 3.

The top 12 prescribed generic can be categorized as anti-anginal, CNS, Lipid-lowering agents, anticoagulant & antihypertensives (Table 6)

Table 5. Association between prescribed generic and therapeutic class.

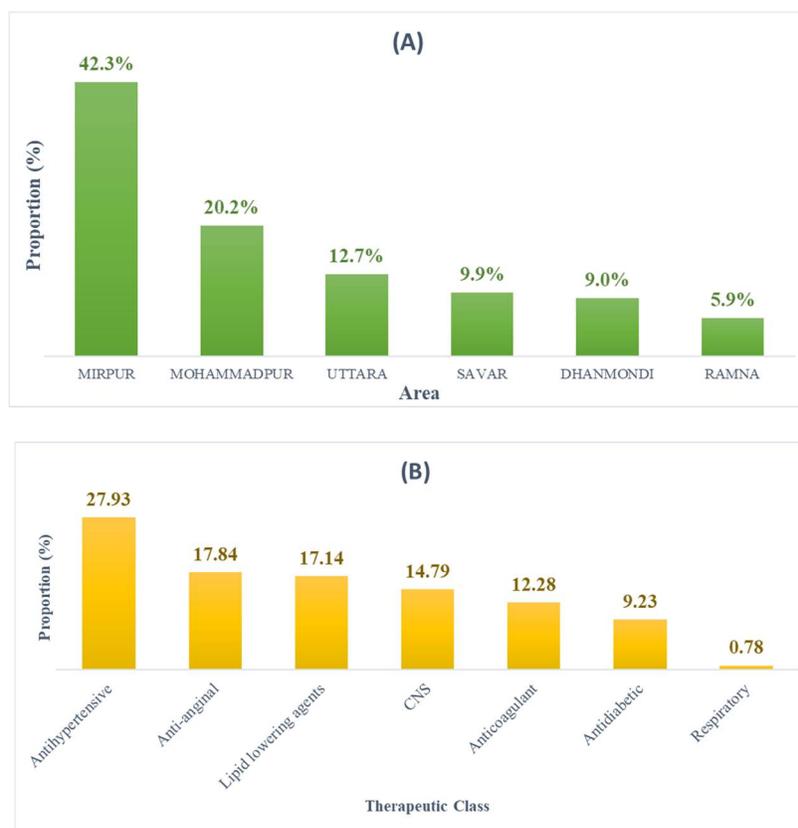| Therapeutic class	No. of generic prescribed	Percentage	χ^2 value	p-value (Difference in proportions)
Anti-anginal	228	17.84		
Anticoagulant	157	12.28		
Antidiabetic	118	9.23		
Antihypertensive	357	27.93	437.48	0.000
CNS	189	14.79		
Lipid-Lowering Agent	219	17.14		
Respiratory	10	0.78		

Figure 2. Distribution of prescribed generic by area and a therapeutic class of drugs.
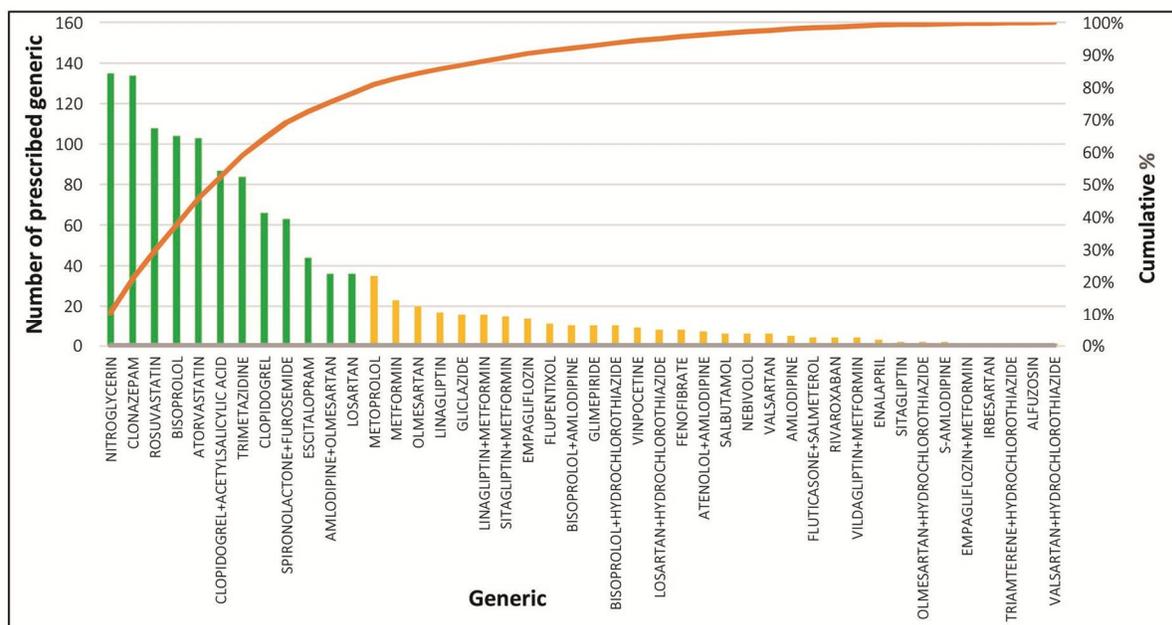
Figure 3. Pareto chart of the number of prescribed generics.

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Table 6. Category of the top 80% prescribed generics.

Category	Generic	No of prescription	% prescription (n/N) N=403
Anti-anginal	Nitroglycerin	135	33.5
	Trimetazidine	84	20.8
CNS	Clonazepam	134	33.3
	Escitalopram	44	10.9
Anticoagulant	Clopidogrel+ Acetyl Salicylic Acid	87	21.6
	Clopidogrel	66	16.4
Lipid-Lowering Agent	Rosuvastatin	108	26.8
	Atorvastatin	103	25.6
	Bisoprolol	104	25.8
Antihypertensive	Spironolactone+Furosemaide	63	15.6
	Amlodipine+ Olmesartan	36	8.9
	Losartan	36	8.9

Nitroglycerin (33.5%), clonazepam (33.3%) & rosuvastatin (26.8%) are the top three most prescribed generics. They are present in most of the prescriptions. For managing angina in CVD patients, nitroglycerin is the first-line treatment option as a vasodilator. It is prescribed in both sublingual spray and sustained release tablet form to manage the emergency and prevent future risk as well.[19] Trimetazidine (20.8%) is another generic that has been also prescribed frequently for angina pectoris.

As for clonazepam, it is widely prescribed as an anxiolytic medicine because roughly 11%-14% of CVD patients suffer from anxiety disorders and more than 40% of patients with chronic heart disease may have developed elevated anxiety symptoms.[18,20] Another top generic from the Pareto chart (Figure 3) is escitalopram (10.9%), an anti-depressant as depression is also associated with CVD.[18]

Rosuvastatin, the third most prescribed generic belongs to the lipid-lowering agent's sub-category.

Atorvastatin (25.6%) is another statin that has been prescribed almost at the same frequency. Statins are prescribed to CVD patients with a risk for atherosclerotic coronary disease to prevent or delay any ischemic events.[21] It is also beneficial to the patients who have a history of myocardial infarction (MI) and/or coronary revascularization.[22]

The next category of generic prescribed is the anticoagulant like Clopidogrel combination (21.6%) or Clopidogrel alone (16.4%). These generics are prescribed to reduce serious vascular events like MI, stroke and the risk of cardiovascular death.[23]

In the category of antihypertensive generics, prescribers have many options to choose from. Hence upon analysis, no single generics from the antihypertensive category were in the top three. Antihypertensives are prescribed in combination or alone based on the patient's profile, doctors' preference and available generics in the market.[8,10] In this current study, bisoprolol (25.8%), a beta-blocker is the most prescribed antihypertensive followed by combination generics like spironolactone-

hydrochlorothiazide (15.6%) a diuretics and amlodipine-olmesartan (8.9%), a calcium channel and angiotensin II receptor blocker combination.

Effect of gender and area in the relation between the number of degrees and number of prescribed generic. As mentioned earlier there was no significant relationship between the number of degrees of cardiologists and the number of prescribed generics. The exploratory scatter plot in Figure 4(A) also reveals that fact. But it is also notable that, female physicians were more likely to prescribe proportional to their number of degrees and among male physicians, there is no visual trend, Figure 4(B). In the same fashion, it is seen that physicians of Mohammadpur and Dhanmondi tended to prescribe more with respect to their number of degrees, Figure 4(C). This explores the fact that both gender and location of practice somehow affected the relationship between the number of degrees and the number of prescribed generics. Further study can be conducted to make a conclusive decision about this fact.
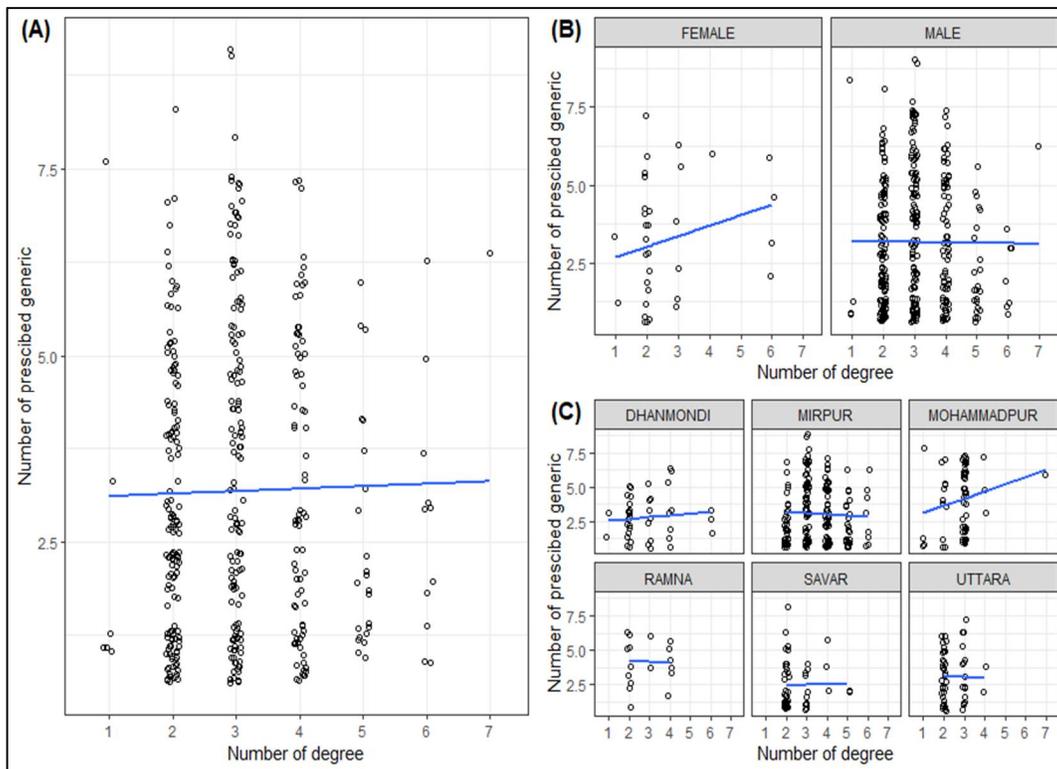

Figure 4. Relation between number of degrees and number of prescribed generic controlling for gender and area.

CONCLUSION AND RECOMMENDATION

In this current study gender, location of practice, academic qualification of the prescribers and therapeutic class are found significant with the prescribed generics. The study also revealed that a high number of CVD medicines along with other chronic medicines (CNS, antidiabetic & respiratory) were prescribed by the doctors with no warning of the possible side effects of long-term use of these chronic care medicines. To ensure rationale prescription pattern and patient's benefit, a few recommendations can be suggested based on the findings. First, the prescriber should follow the latest treatment guideline instructed by the recognized authority like the WHO, the ACC /AHA or the ESC. Secondly, the hospital and chamber should appoint a hospital pharmacist for comprehensive counseling to the patients about the potential adverse effect in long-term use and how to manage that. Third, CVD medicines cause an economic burden to the patients as they are usually expensive and patients need to continue it for life. Thus government should create mass level awareness programs on how to prevent cardiovascular disease along with other non-communicable diseases. Fourth, Large pharmaceuticals should join in this awareness program with the government as part of their CSR activity. Fifth, a pharmaceutical marketing manager can take this analysis into account to tailor their promotional focus of the CVD generics as per the location, academic qualification and gender of the prescribers.

LIMITATIONS

The study was conducted based on a few selected areas of Dhaka city. To get the national pictures more cities should be included in future. The current study was based on the doctor's profile and how it affected the prescription trend of cardiac generics. In the future, similar analysis can be done based on the patient's profile which will reveal how it affects the prescription trends as well. Overall, the process of prescription collection was time-consuming. Due to COVID-19, only 403 prescriptions were collected over one year upon primary survey. More prescriptions would have helped us to understand the whole scenario more accurately.

ABBREVIATIONS

ACC: American College of Cardiology
ACEI: Angiotensin-Converting Enzyme Inhibitors
AHA: American Heart Association
BB: Beta Blocker
CCB: Calcium Channel Blocker
CCD: Certificate Course on cardiovascular disease
CNS: Central Nervous system
CVDs: Cardiovascular diseases
D-CARD: Diploma in Cardiology
DTCD: Post Graduate Diploma in Tuberculosis and Chest Diseases
ESC: uropean Society of Cardiology
FACC: Fellow of American College of Cardiology
FACP: Fellow of the American College of Physicians
FCCP: Fellow of the American College of Chest Physicians
FSCAI: Fellow of the Society for Cardiovascular Angiography and Interventions
MBBS: Bachelor of Medicine, Bachelor of Surgery
MD: Doctor of Medicine
MI: Myocardial Infarction
MRCP: Member of the Royal College of Physicians
PGT: Postgraduate Training
PPS: Proportional to Population Size
WHO : World Health Organization

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