

# Study on Polypharmacy in Patients with Cardiovascular Diseases

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## ABSTRACT

We analyzed the prevalence of polypharmacy among cardiac patients in the National Institute of Cardiovascular Diseases of Dhaka, Bangladesh. Polypharmacy was defined as consumption of six or more drugs at the same time. We entered the drugs that were prescribed into the Drug Interaction Checker provided by MedScape online edition. Almost 85% of cardiac patients met criteria for three types of polypharmacy (minor, moderate and serious). However, serious and moderate types of polypharmacy were not influenced by the increase in number of disorders (polymorbidity) as well as by the total number of drugs taken. The most frequent cause and threat that is associated with polypharmacy comes primarily from the quality of drug-drug interactions and not the total number of drugs prescribed. Most of the dangerous consequences of polypharmacy came from the interaction of Clopidogrel with either Aspirin or PPIs. Our study emphasizes the need of informing doctors more about the problem of polypharmacy. Careful and thoughtful drug prescription strategy seems to be able to eliminate most of the cases of polypharmacy even in patients who are suffering from a multiple disorders simultaneously. The results also provide support for development of new drugs that take into account compatibility with other medication, especially in elderly people.

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## INTRODUCTION

Cardiovascular disease is one of the leading causes of death worldwide. About one third of deaths in the world (ca.17.3 million) are caused by cardiovascular dysfunctions each year (Mendis S, 2011). By 2020, cardiac disease and stroke will become the leading cause of both death and disability worldwide, with the number of fatalities projected to increase to over 20 million a year and by 2030 to over 24 million a year (Mackay, 2004). Eighty percent of all global cardiovascular disease related deaths occurs in a low and middle income countries (Murray, 1996). The scenario in the developing countries is epidemic because of social and economic burden that cardiac diseases carry

(Gaziano. 2007). There are many types of cardiovascular diseases which are interlinked with each other. For example high bad cholesterol causes atherosclerosis, hypertension is linked with stroke, myocardial infarction, heart failure and peripheral arterial disease (Rocha E et al. 2003; Yang X. et al. 2007; Rakugi H et al. 1996). Non-cardiovascular diseases are also strongly interconnected with the cardiac complications. Obesity (Luc et al., 2006), diabetes (Vaccaro et al., 1998; Howard et al., 2006; Wang et al., 2010), periodontal infections (Armitage GC et al. 2000; Beck JD et al. 1999) and depression (Barth J et al. 2004; Van der Kooy K et al. 2007) promotes the development of cardiovascular risk factors. In result, cardiovascular drugs alone are not sufficient to cure the cardiac patients. Thereby multiple disease states create the demand for multiple drug therapy. In this case combination drugs are used in the USA and have been permitted for use in parts of Europe, Asia and Latin America (Ellison et al., 2008; Blank, 2006). Many studies were conducted over the years about 'a single pill containing multiple drugs for the cardiac disease'

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(Blank *et al.*, 2007; Cowie, 2005; Hobbs *et al.*, 2006; Erdine *et al.*, 2009; Curran, 2010; Grimm *et al.*, 2010). Thus, multiple drug therapy is widely used for the treatment of problems including hypertension, ischemic heart disease (IHD) and heart failure together. Consequently, multiple drug therapy creates the concept of 'polypharmacy'.

### **Polypharmacy and its outcome**

Definitions of polypharmacy vary. It is described as a simultaneous prescription of two or more drugs (Veehof *et al.*, 2000; Bjerrum *et al.*, 1997; Brager and Sloand, 2005; Faries *et al.*, 2005), four or more drugs (Bikowski *et al.*, 2001), five or more drugs (Faries *et al.*, 2005; Linjakumpu *et al.*, 2002; Jorgensen *et al.*, 2001; Junius-Walker *et al.*, 2007). In a cross sectional study on 466 patients in Germany it has been shown that 26.7% of patients meet criteria for polypharmacy - using five or more drugs at the same time (Junius-Walker *et al.*, 2007). We have not found the fixed definition of 'polypharmacy' in the literature search. In our current research work we consider that the consistent and simultaneous use of multiple drugs (five and more) could be termed as 'polypharmacy'.

Being sometimes inevitable, polypharmacy is not always efficacious and safe. It is associated with increased mortality, morbidity and other costs. The use of multiple medications often leads to inappropriate drug use under prescription, low adherence and side effects (Volpe *et al.*, 2010). Polypharmacy with more than four pills taken daily leads to a lower compliance (Rottlaender *et al.*, 2007). More generally polypharmacy may result in: high rates of side effects, as a regular outcome of drug-drug interactions, errors in drugs use, reduced patient compliance due to drug-associated side effects and medication errors (Queneau, 2006).

Adverse effects management requires a hospital stay and, moreover, has a negative economic impact. Therefore, it is an important issue for improving health care quality by improving patient compliance and reducing the prescription costs. The United States and European Union have recently emphasized the assessment of prescription quality from the view point of efficacy and safety (Hoven *et al.*, 2005).

### **Polymorbidity and Polypharmacy in Cardiovascular disease**

One of the largest proportions of patients with cardiac disease is elderly people. This population group has a variety of life-lasting habits (e.g., smoking, physical inactivity, fat consumption, etc.) that are considered to be a risk factor for cardiovascular disease. These factors influence the development of many other possible dysfunctions, resulting in a complex treatment and polypharmacy (Vaccaro *et al.*, 1998). Moreover, the proportion of aged population is increasing nowadays. Elderly people are affected by severe and chronic diseases, often treated in primary care and show one of the highest rates of drug prescription (Jorgensen *et al.*, 2001). Studies indicated that there is an increased level of drug-drug interactions (DDIs) and polypharmacy among the elderly part of the population (Haider *et al.*, 2007). The most common diseases that are complimentary to the cardiovascular

disease are chronic obstructive pulmonary disease, diabetes, cognitive disorders, arthritis, gout, renal failure, osteoporosis and cancer. These dysfunctions require multiple drugs for adequate treatment (Gurwitz, 2004). Therefore, patients are bound to take multiple medications due to the polymorbidity. Steinman and colleagues evaluated inappropriate prescription and usage of medication among 196 elderly patients taking 5 or more drugs and displaying a high prevalence of hypertension, diabetes and ischemic heart disease (Steinman *et al.*, 2006). A longitudinal study showed that polypharmacy arises mainly in elderly patients who already use several drugs, suffering from cardiovascular diseases, diabetes, taking sedatives/hypnotics without a clear indication and those who develop hypertension or atrial fibrillation over time (Veehof *et al.*, 2000). Moreover, non prescription medication usage by the patient (Veehof *et al.*, 2000; Nobili *et al.*, 1997) is an additive factor as it accumulates more unwanted side effects which are completely unknown to the physicians. A cross-sectional analysis of 4,023 nursing home residents in Europe showed that polypharmacy (49.7%) and excessive polypharmacy (24.3%) are a common practice for many nursing home residents (Onder *et al.*, 2012).

### **AIMS OF THE STUDY**

Large number of cardiovascular patients is released from National Institute of Cardiovascular Disease in Bangladesh every year. However, there has been not a single review about the pattern of prescriptions and level of polypharmacy done so far.

The aim of the present study is to analyze the prescription pattern and polypharmacy in a comprehensive manner, including the evaluation of the factors increasing the likelihood of concurrent use of several medications by cardiac patient. More specifically we wanted to investigate the following point of interest: most frequently prescribed pharmacological classes and molecules, assess the prescribed combinations, check for gender difference in prescription, and find the prevalence of polypharmacy (taking  $\pm 6$  drugs) among cardiac patients. Furthermore, we were aiming at investigating the level of drug interactions; drugs that interact the most to produce the health hazard and to identify the risk factors that predisposed the patient to polypharmacy. Hence, the analysis and evaluation of prescription patterns might provide the basic answer of the present points of investigations.

### **HYPOTHESIS**

Cardiovascular disease is a complicated disorder which leads to many other diseases (e.g.: diabetes) in the long run. Age is the major risk factor for cardiac disease (Lakatta, 2002; Ramirez-Lassepas, 1998). It has been shown that the risk of stroke doubles every decade after age 55 (Ramirez-Lassepas, 1998; Bahle, 1998). We hypothesized that since number of disorders increases with age, elderly patients with cardiac dysfunctions may as well suffer from a number of other simultaneous diseases and show polypharmacy.

We also hypothesized that the lipid lowering agent and the antihypertensive drugs are the most frequently prescribed complementary medication in cardiac patients. There are two possible reasons for this assumption. First of all, food habits are being changed over the years due to the fatty and high cholesterol containing food consumption. Secondly, elderly people lead sedentary life style, therefore they might have higher cholesterol level (Jousilahti *et al.*, 1999).

We assumed that males are more prone to cardiac diseases than female. It has been shown that among middle-aged people, coronary heart disease is 2 to 5 times more common in male than in female population (Jousilahti *et al.*, 1999). One of possible reasons of this fact is that generally male smoke more than female. It was also shown that male population has a greater risk of heart disease than pre-menopausal women.

We also thought that polypharmacy might be bound to occur due to the polymorbidity of patients. Polymorbidity ultimately influences physicians (cardiologists) to prescribe multiple drugs in a single prescription. As a result of life threatening drug interactions caused by polypharmacy, longer hospital stay may require. The duration of hospital stay for drug interaction monitoring is not feasible for a densely populated country like Bangladesh. Finally, we also hypothesized that risk factors associated with the polypharmacy are polymorbidity, age, possibly gender and some other factors.

## MATERIALS AND METHOD

### Patient sample

Patients were enrolled in the period from 20<sup>th</sup> of April 2012 to 2<sup>nd</sup> of July 2012 in the National Institute of Cardiovascular Diseases (NICVD) in Sher-e-Bangla Nagar, Dhaka, Bangladesh. NICVD is the most renowned 400-bed health care institution (Banglapedia, 2012). We collected data of the patients ( $n = 182$ ) who were admitted to this institution from the hospital pharmacy-shop. The basic demographic information of each patient: age and gender; hospital admission and discharge dates, drugs prescribed and disease identified were also fixated. Disease types were evaluated in compliance with the 10th Revision of the International Classification of Diseases (ICD-10) (WHO, 2012a). The patient who had four or more diseases was considered as polymorbid (Wawruch *et al.*, 2008).

### Polypharmacy assessment

The number of medications prescribed by the physician was recorded and compared for each patient. There were many combinations of active substances, present in the prescription. Therefore, each drug was evaluated separately. Polypharmacy was assessed on the basis of individual age categories. Patient were grouped into 10-year age brackets (Below 30 years; 31–40; 41–50; 51–60; 61–70; 71– 80; Above 80 years). We considered polypharmacy when each patient takes six or more medications per day (Suchopar and Prokes, 2011). We followed the Anatomical Therapeutic Chemical classification (ATC) for

determining drug classes (WHO, 2012b). We investigated risk factors that predisposed the patient to polypharmacy. In order to identify combinations of drugs that can lead to dangerous outcomes we entered the drugs that were prescribed into the Drug Interaction Checker provided by MedScape online edition. The drug interaction could have either been minor, moderate and serious. Minor drug interaction does not require an ambulatory placement of the patient; both moderate and serious interactions required an ambulatory treatment.

### Statistical analysis

Continuous variables were characterized as mean  $\pm$  standard deviation (SD). Categorical variables were expressed by frequencies and percentages. All statistical tests were performed at a significance level of  $\alpha = 0.05$ . SPSS for Windows, version 19, was used. Differences in the distribution of categorical variables between patients with and without polypharmacy were compared using the  $\chi^2$  test. The Mann-Whitney U test was used to compare continuous variables in two groups. The normality was tested using the Kolmogorov-Smirnov test and a multivariate analysis, namely, binary logistic regression model was applied in order to identify the most important patient-related characteristics associated with polypharmacy. Only dichotomous variables which had a significant influence on the presence of polypharmacy in the univariate analysis (performed by the  $\chi^2$  test) were entered into the model.

## RESULTS AND DISCUSSION

In the group of 182 cardiac patients 72% were males that is in line with the fact that men are more prone to heart disease compared to women of a similar age (Jousilahti *et al.*, 1999). The average age  $\pm$  SD in all of the patients studied was  $49.2 \pm 16.48$  years (there were single cases of patients aged 3 month, 3, 4, 6 and 12 years old, as well as single cases of patients 80, 82 and 90 years old). Both groups of male and female patients were of approximately similar mean age (49.9 and 47.4 respectively). The mean number of different drugs taken by the patients was 7.34. Interestingly enough there was no sex difference in mean average number of drugs prescribed by doctors (7.32 for males and 7.39 for females). Majority of patients (84.6 %,  $n = 152$ ) met the criteria for polypharmacy (concurrent use of  $\pm 6$  drugs). Once again we did not observe mean polypharmacy difference in sex of the patients according to Mann-Whitney U test (85% of male and 84% of female patients met criteria for polypharmacy,  $F < 1$ ). The prevalence of polypharmacy on written prescriptions in individual age groups is created by dividing the patients into 10-year age brackets (7 subgroups). The highest proportion of persons taking  $\pm 6$  drugs was observed in the categories of 41–50, 51–60 and 61–70 age subgroups in males and females. Males had the highest polypharmacy level in between 51 to 60 years of age while female had 41 to 50. Therefore, female patient had highest polypharmacy at earlier stage of life than male patients. The results from the univariate analysis of variance indicated that age of patients

influenced the number of drugs taken. It seems that the older a person becomes more drugs he or she will have to take, ( $F(1,151)=3.25, p<0.05$ ). At the age group of 51 to 60 years old the number of drugs taken reaches its peak and stabilizes; then it shows a tendency to decrease until the age of 80. This however might be the result of our sample distribution with only few representatives of above 80- years' old population who all take 7 drugs and above. The Univariate analysis showed that there is also a significant influence of age on the overall level of polypharmacy of patients ( $(F(151)=4.12, p < 0.05)$ ). This showed that the chances of being a subject to polypharmacy increases with age. The main effect of gender was not significant ( $F<1$ ) meaning that both male and female patients had equal chances to face polypharmacy at anytime throughout their lives (gender\*polypharmacy interaction was also not significant  $F<1$ ).

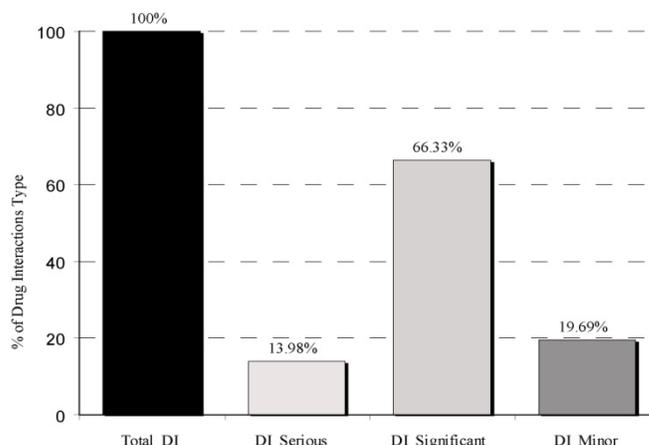
**Table 1** Univariate analysis for 3 types of polypharmacy

Serious polypharmacy			
Factors:	F values	p significance	
Age	2.208	<b>.003</b>	
Gender	3.598	.064	
Polymorbidity	.517	.723	
Gender*polymorbidity	.698	.558	
Age*polymorbidity	.841	.685	
Moderate polypharmacy			
Age	1.109	.357	
Gender	2.542	.117	
Polymorbidity	.335	.853	
Gender*polymorbidity	.994	.403	
Age*polymorbidity	.900	.610	
Minor polypharmacy			
Age	10.687	<b>.002</b>	
Gender	3.259	<b>.000</b>	
Polymorbidity	1.622	.183	
Gender*polymorbidity	7.556	<b>.000</b>	
Age*polymorbidity	1.894	<b>.024</b>	

We found that cardiac drugs predominates 48.04% of all prescribed class which is the highest percentage. Alimentary tract and metabolism drug class (24.02%) was the second shared prescribed class and the third shared class was Nervous system drugs (18.1%). Prescription pattern analysis reveals that Antithrombotic drugs (20.03%) were the most commonly prescribed class. Lipid lowering agents (17.09%), Beta blockers (15.75%) and Vasodilators are prescribed at almost the same percentages. Atorvastatin (16.29%), Clopidogrel+Aspirin (15.09%), Nitroglycerin (11.75%), Ramipril (9.21%), Metoprolol (8.54%) and Furosemide+ Spironolactone (8.01%) were the leading prescribed molecules. Most commonly preferred and prescribed cardiovascular combination drugs were Clopidogrel+Aspirin and Furosemide+ Spironolactone.

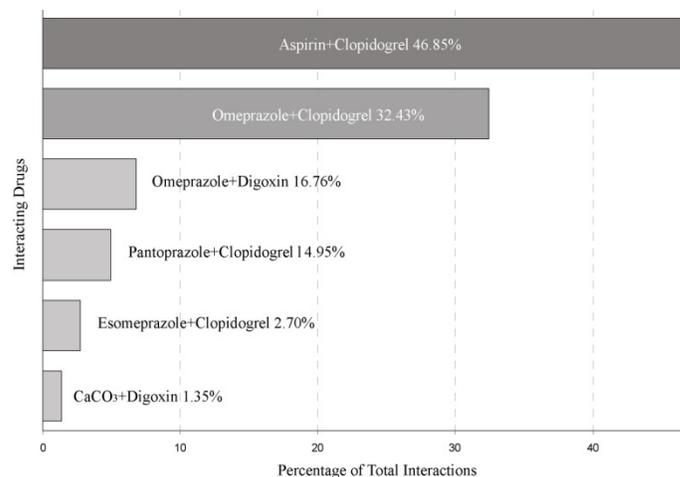
In order to have a closer look at factors that might influence polypharmacy we decided to split it into 3 groups: serious (13.98 % of the whole polypharmacy population), moderate (66.33%) and minor (19.69%). Serious and moderate types of polypharmacy require patients to be hospitalized and receive prescribed drugs under supervision of doctors. Minor type of polypharmacy is less conservative and allows patients to stay

and take medicaments at home (Kenngott *et al.*, 2010). The Univariate analysis on influence of various factors on the each type of polypharmacy is shown in table 1.



**Fig. 1:** Drug-Drug Interaction type in cardiac patients. Horizontal axis represents the Drug Interaction type and vertical axis represents percentage of interaction.

According to Mann-Whitney U test the number of cases of polypharmacy was significantly higher in cases with polymorbidity ( $p < 0.01$ ). This is understandable since polymorbidity creates the demand to take more drugs and it in turn increases the chances of polypharmacy. Interestingly, the increased number of disorders that the patient had (3, 4, 5 etc.) did not influence the polypharmacy in Univariate analysis of variance ( $p > 0.5$ ). It means that as soon as person was considered polymorbid (having more than 1 or 2 diseases) he or she had higher rates of polypharmacy. However, the exact number of diseases did not influence the level of polypharmacy. In other words, polypharmacy did not increase as a function of exact number of diseases a patient had. The Pearson's correlation analysis showed weak ( $r = 0.247; n = 182$ ) but significant ( $p < 0.01$ ) correlation of polypharmacy and polymorbidity.



**Fig. 2:** Severe drug-drug interactions. Horizontal axis represents percentage of drug-drug interactions and vertical axis represents the interacting drugs.

Then we investigated the drugs which are mostly responsible for these severe drug-drug interactions. We found that Aspirin + Clopidogrel (46.85%) and Omeprazole + Clopidogrel (32.43%) drugs in the same prescription produces the most severe drug interaction. We also showed that PPI (Proton Pump Inhibitor) and Clopidogrel combined in a single prescription can produce severe drug interactions (figure 2)

The goal of this study was to analyze the effects and precedence of polypharmacy in the discharge patients with cardiovascular disease in the cardiac hospital in the capital of Bangladesh, Dhaka. Since polypharmacy is the result of taking several different drugs as a result of one, two or more diseases present at the same time, we hypothesized that the level of polypharmacy would increase with age and we would be able to observe a significant correlation between factors of age and polypharmacy as well as polymorbidity and polypharmacy.

One of the important decisions is what to consider a polypharmacy. It was suggested before that 2+ drugs taken daily is considered to be polypharmacy (Veehof *et al.*, 2000). However, several previous studies used the criteria of  $\pm 6$  drugs in order to consider the case as polypharmacy (Linjakumpu *et al.*, 2002; Williamson and Chopin, 1980; Jyrkka *et al.*, 2006; Vinks *et al.*, 2006). We decided to use the stricter criteria and consider 6 or more drugs taken simultaneously as a defining feature of polypharmacy.

Consistent with previous findings that male population has a higher risk of cardiac diseases (Jousilahti *et al.*, 1999) 72% of observed population were males. However, among all the patients who were admitted to the hospital, there was no gender difference in number of drugs taken. Both male and female patients were on average prescribed the same number of drugs. It means that although men were more likely to get a cardiovascular disease, drugs prescribed the patients were logically similar in both males and females.

Similar with our expectations majority of patients (84.6 %) were taking  $\pm 6$  drugs and, therefore, their cases were classified as polypharmacy. It was also interesting not to observe any gender difference in number of drugs taken. It shows once again that there was no gender specific effect that predisposed one of the groups to be taking more drugs. In order to take a closer look at the effect of polypharmacy we subdivided it into 3 groups: serious, moderate and minor polypharmacy. Serious and moderate types of polypharmacy required constant attention of the doctor and stationary treatment. The minor type of polypharmacy, although could possibly cause some problems, did not require special attention from the doctor and allowed patients to take drugs at home.

The factor of age was significant in serious type of polypharmacy. It means that with an increase in age, people are more likely to have serious type of polypharmacy because of increasing number of diseases and other health problems that they have. This result is in line with previous research (Mackay *et al.* 2004). There were no other factors (gender, polymorbidity etc.) that would influence the polypharmacy in both serious and

moderate types of polypharmacy. This is very unusual situation, since the higher the polymorbidity, the higher the number of drugs that are taken by the patients and logically the higher the risk of polypharmacy. Nevertheless, in two most dangerous types of polypharmacy that required a stationary treatment at the hospital, there was no effect of polymorbidity. This fact might indicate that in some cases increased number of disorders is not the only cause of dangerous effect of polypharmacy. It seems that doctors can prescribe dangerous combination of drugs even when the number of disorders that the person possesses is relatively low.

A more typical picture is observed with minor type of polypharmacy. Here the analysis showed that the chances of polypharmacy are increasing with age as well age\*polymorbidity interaction was significant. Elderly people get sick more often, take more drugs and hence prone to polypharmacy. Another important aspect is significant effect of gender – here we observe an established fact that male subjects have higher rates of polypharmacy. This goes in line with significant gender\*polymorbidity interaction. Male subjects tend to have more diseases with increased age and therefore take more drugs and logically have higher rates of polypharmacy of minor type. Nevertheless, the mere fact of polypharmacy does not automatically mean dangerous consequences for the patient. As we can see here, there are no significant main effects (except for age) and interactions in the serious and moderate type of polypharmacy. However, there are the main effect of age, gender as well as gender\*polymorbidity and age\*polymorbidity interactions in minor case of polypharmacy. These results imply that doctors should pay more attention to the fact of polypharmacy and to hazard effect that it can induce in patients.

When combining all three types of polypharmacy together, we observed that polymorbidity significantly increased the chances of polypharmacy. However, increasing the number of disorders in patients did not influence the level of polypharmacy. It seems like the mere existence of polymorbidity influences polypharmacy, however increasing the exact number of disorders (2, 4, 7 etc.) does not increase the level of polypharmacy significantly.

We found that clopidogrel is a drug which creates most of the burden. It interacts mainly with aspirin and the proton pump inhibitors (PPIs).

Clopidogrel+Aspirin combination causes 46.85% drug interactions in cardiovascular patient. Pharmacological study report that Clopidogrel (inhibits ADP-induced platelet activation and aggregation by blocking the CYP2Y-12 receptor on the platelet membrane) and Aspirin (irreversibly acetylating the cyclooxygenase-1 enzyme, thus suppressing the production of thromboxane A2 and inhibiting platelet activation and aggregation) shows antithrombotic action by completely separate mechanism (Tourmousoglou and Rokkas, 2008) but their interaction increases effects of clopidogrel by pharmacodynamic synergism. Despite their antithrombotic efficacy, patients on these medications continue to suffer complications (Wang *et al.*, 2006). In spite of this complications, Clopidogrel has been used in

combination with aspirin to get the additional benefit at high risk cardiac patients (Squizzato *et al.*, 2011). This combination showed beneficial in acute non-ST coronary syndrome (Squizzato *et al.*, 2011) found reasonable and harmless option for “prevention of graft failure in radial artery grafts” (Sun *et al.*, 2010) and showed the reduction of ischemic complication (Sabatine *et al.*, 2005). Interestingly, no beneficial effect was found on the uses of clopidogrel alone or in association with aspirin on medical outcomes after CABG (Patel *et al.*, 2009; Gao *et al.*, 2009). Bhatt *et al.* in 2006 also have not found any significant effect on the uses of clopidogrel plus aspirin than aspirin alone in reducing the rate of myocardial infarction, stroke, or death from cardiac disease (Bhatt *et al.*, 2006). Therefore, it might be necessary to take both of this medications under strict control and observation of physicians.

We found that **Clopidogrel+PPIs** (Proton pump inhibitors) are the mostly responsible for drug interaction. Despite these interactions PPIs have been suggested for reducing the danger of gastrointestinal hemorrhage related with dual antiplatelet therapy (clopidogrel plus aspirin). However, studies showed that decreased efficacy of clopidogrel was observed when concurrently administered with a PPI (Gilard *et al.*, 2008). In a review study (MEDLINE database search from 1966-September 2009) it was concluded that cautious risk benefit estimation is necessary prior to prescribing PPIs for dual antiplatelet therapy taking patients (Liu and Jackevicius, 2010). Further studies are needed to clarify this drug interaction (Liu and Jackevicius, 2010; Norgard *et al.*, 2009). Another study did not report a significant interaction have not shown between the proton pump inhibitors and clopidogrel (Harmsze *et al.*, 2011). Alternative treatment strategies were suggested for recurrent myocardial infarction (Lau and Gurbel, 2009). It was also suggested not to add the PPI with the antiplatelet dual therapy without formal indication (Gilard *et al.*, 2008). The US Food and Drug Administration (FDA) discourages the concomitant use of drugs which diminish CYP2C19 (e.g., omeprazole) and suggests to separate intake of PPI and Clopidogrel (Laine and Hennekens, 2010). Separate intake (e.g., morning and night) of PPI and Clopidogrel might reduces the chance of interaction (Chow *et al.*, 2009) (However, see Kenngott *et al.*, for different results). We also suggest taking PPIs separately in order to avoid interactions.

Omeprazole + Digoxin interactions are also found in cardiac patients. During the coadministration of these medications level of digoxin is enhanced by omeprazole. The interaction may cause a spike in the concentration of the heart medication, which could lead to complications. So, the concomitant use of Clopidogrel plus aspirin or Clopidogrel plus PPIs or all together is still a dilemma. Therefore, it is necessary to assess the gastrointestinal risk of the patient, selectively choosing of PPIs which have the lowest interaction with clopidogrel, create a large gap between the intakes and conduct a post prescription monitoring of those drugs. Post prescription monitoring could reduce the risk of above mentioned problems associated with polypharmacy, specifically in the inpatient group. In case of

hospitalized patient, it is necessary to trained up the nurses about polypharmacy and drug interactions as its consequences. They can administer the mostly responsible interacting drugs with a minimal logical time gap. It is necessary to systematically monitor the drug consumption procedure in people whose drug prescription meets criteria for polypharmacy. But monitoring is not strictly possible for the ambulatory care patient. Therefore, in order to minimize the risk of polypharmacy and to ensure the safety of patients, doctors should pay a special attention while writing prescriptions and consistently review the lists of available medications and monitor the prescription outcomes (Ballentine, 2008). Popypill, might be another possible way to solve the issues. Advanced dosage form containing multiple medications with different release pattern could be a biggest solution for this case.

## CONCLUSION

We analyzed the prevalence of polypharmacy among cardiac patients in the Institute of Cardiology of Dhaka, Bangladesh. The purpose of the research was to identify whether the problem of polypharmacy exists in Bangladesh capital and what are the possible factors that influence this phenomenon. We observed that that the biggest proportion of patients met criteria for serious and moderate types of polypharmacy, which require stationary treatment in the hospital and closer attention from the doctor. Nevertheless, patients were released from the hospital and had to take medication at home, thus endangered by the side effect of polypharmacy. Interestingly serious and moderate type of polypharmacy were not caused by the mere increase in number of disorders in a single patient (polymorbidity) as well as by the total number of drugs taken. The danger that is associated with polypharmacy is coming primarily from the quality of drug-drug interactions, and not the overall amount of drugs overall. Most of the danger comes from the interaction of Clopidogrel with either Aspirin or with PPIs. Our study emphasizes the need to inform doctors about the problem of polypharmacy as well as provides support for development of new drugs that take into account compatibility with other medication, especially in elderly people.

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