ISSN: 2279 - 0594

Available Online at www.jbpr.in

Journal of Biomedical and Pharmaceutical Research 2 (3) 2013, 77-84

RESEARCH ARTICLE

EVALUATION OF PRESCRIBED CARDIOVASCULAR DRUGS MARKETED BY VARIOUS PHARMACEUTICAL COMPANIES OF BANGLADESH

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Received 28/04/2013; Revised 01 May 2013; Accepted 06 May 2013

ABSTRACT

Cardiovascular drugs encompass a large number of prescription medications that are used to control heart disease. It is a complicated group of drugs with many being used for multiple heart conditions. The main objective of this survey was to analyze the prescribed cardiovascular drugs with their brand name marketed by different local and international companies of Bangladesh. This was a descriptive cross-sectional survey involving patients, physicians and pharmacy in-charge based on a structured questionnaire format with answer sets and followed up by prescription monitoring. This study carried out at the outdoor of National Heart Foundation (Mirpur, Dhaka) and the Dhaka medical college hospital Pharmacy (Dhaka, Bangladesh) from January'12 to August'12. From total 700 prescriptions, 99% prescriptions were prescribed by the specialist but only 1% by general physicians. Out of the total patients with a male, female ratio of 57.14: 42.86, all patients were over 30 years and approximately 64.285 % the patients were demographically from urban area whereas 35.714% patients came from rural area. Individual patients got different classes of drugs including Beta-blockers, Organic nitrates, anticoagulant, anti-platelet and thrombolytic agents, Calcium channel blockers, Diuretics, ACE inhibitors, Lipid lowering agents and Miscellaneous agents were respectively 25.00, 19.57, 22.00,8.42,10.42,10.40 and 2.85 percent. This study may be guidelines for optimizing rational use of cardiovascular drugs and also a new statistical approach for effective cardiovascular disease management in Bangladesh.

KEYWORDS: Pharmaceutical Company, Chi-square test, Confidence interval at 95% confidence level, cardiovascular drugs (brand name)

INTRODUCTION:

Cardiovascular disease is not properly curable. According to World Health Organization (WHO), cardiovascular disease (CVD) is a common cause of premature morbidity and mortality. An estimated 17.3 million people died from CVDs in 2008, representing 30% of all global deaths. Of these deaths, an estimated 7.3 million were due to coronary heart disease and 6.2 million were due to stroke. By 2030, almost 25 million people will die from CVDs, mainly from heart disease and stroke. Over 80% of CVD deaths take place in low- and middle-income countries and occur almost equally in men and women. At the same time they often do not have the benefit of prevention programs compared to people in high-income countries. A study in Bangladesh revealed that 27.93%, 21.08% and 13.41% stroke patients with lipid disorder had high cholesterol, low density lipoprotein (LDL) and triglycerides (TG) level respectively. 42.67% patients had low high density lipoprotein (HDL) level showed in the same study. Trend of cardiovascular disease management and drug use are changing day by day. . In recent days, the approach of cardiovascular disease management is more preventive than cure. For example antioxidant, antilipidemic agents are used to reduce the factors. During this study, it was marked that cardiovascular drugs are effectively lifesaving one. These are projected to remain the single leading cause of death. The most prescribed drugs for the management of CVD's in Bangladesh are Beta-adrenoceptor blocker, Organic nitrates, Anticoagulant, anti-platelet and thrombolytic drug, Calcium channel blocker, Diuretics, Renin-angiotensin system drugs, Lipid lowering drugs, Miscellaneous drugs etc. This study was conducted to compare various cardiovascular drugs prescribed by physicians in Bangladesh. The aim of this study was to compile data on prescribed marketed cardiovascular drugs by their brand names of various local and multinational companies of Bangladesh for assessment on effective cardiovascular disease management. (Md. Abdul Muhit et. al., 2012, Badiuzzaman M et. al., 2009 & Shaila A et. al., 2007)[1, 7, 8]

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METHODOLOGY OF THE SURVEY:

STUDY DESIGN:

To perform this part of research protocol, the methodology, involved for the under taking of a number of steps. A randomized representative sample was determined before the required date was collected. Some confidential information was collected orally and some was collected in written form. Besides some information was collected by observation.

STUDY POPULATION:

The study populations include adults (age above 30 years) that are able to talk clearly. All the respondents who fulfilled the inclusion criteria were selected. This study period was from January '12 to August'12.

INCLUSION CRITERIA:

Adults of more than thirty years of age, who are cooperative and very cordial, use to take drugs from the pharmacy with prescription.

EXCLUSION CRITERIA:

Patients who are non-cooperative and feel disturb to talk with the respondents are excluding from this survey. Patients who are less than thirty years technically avoid those prescriptions.

Two sources were basically used to collect the data. Primary data was collected from the representative drug house, hospital and direct interview of patient. Secondary data was collected from several books, literature, other publication and internet.

RESULTS:

Seven hundred prescriptions were surveyed under this protocol. The doctor prescribed these prescriptions. Analyzing the prescription the findings that were obtained presented in this chapter in both tabular and graphical form.

Table 1: List of all types of prescribed cardiovascular drugs (n=700)

Therapeutic class	prescriptions	Percentage (%)	CI*%
Organic nitrates	137	19.57	16.25 % to 22.65 %
Beta-adrenoceptor blocker	175	25.00	21.79 % to 28.21 %
Anticoagulant, antiplatelet and thrombolytic drug	154	22.00	18.93 % to 25.07 %
Calcium channel blocker	59	8.42	6.36 % to 10.47 %
Diuretics	73	10.42	8.16 % to 12.69 %
Renin-angiotensin system drugs	73	10.40	1.62 % to 4.08 %
Lipid lowering drugs	20	2.85	0.44 % to 2.11 %
Miscellaneous	9	1.28	

CI*= Confidence interval calculated by standard statistical method at 95% confidence level

Figure 1: Comprehensive list of different cardiovascular drugs with their classes

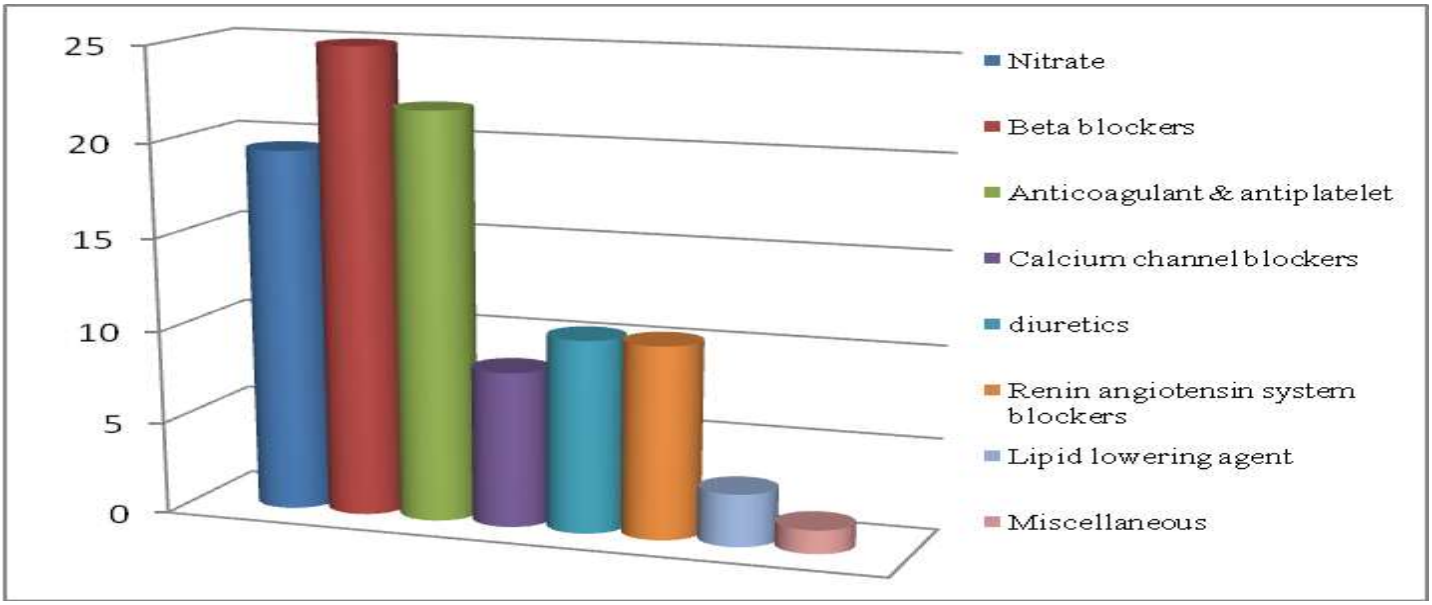

Table 2: All therapeutic class according to their brand name: (n=700):

Therapeutics class with their brand name	**%Percentage of therapeutics class n=700**	**No. of prescriptions individual brand**	**% of no of prescriptions individual brand**	***CI%**	**Therapeutics class with their brand name**	**%Percentage of therapeutics class n=700)**	**No. of prescriptions individual brand**	**% of no. of prescriptions individual brand**	***CI%**
List of organic nitrates (n=137) Nitroglycerine	60	82	59.85	35.55-45.56	**Various diuretic groups according to their class: (n=73)**				
Iso-Sorbidemononitrate	40	55	40.145	34.56-56.77	Thiazide	40.81	30	41.09	22.77-44.56
					Loop diuretic	28.57	21	28.76	23.78-34.67
					K^+- Sparing diuretics	30.62	22	30.13	21.67-56-56
Various brand name of Nitroglycerine: (n=60) Nitromint (Egis)	60	37	61.66	55.66-71.44	**Available Thiazide diuretics:** (n=30)				
					Hydrochlorothiazide	62	19	63.33	34.67-56.89
Nitrine (Healthcare)	2	1	1.66		Indapamide	38	11	36.66	23.55-56.99
Angised (GlaxoSmithKline)	4	2	3.33	0-22.45					
Nitrocard (Aristopharma)	12	6	10	5.89-32.89					
Nidocard (Drug International)	22	14	23.33	22.45-34.87					
Various brand of Isosorbidemononitrate: (n=40)					**Various brand name of Hydrochlorothiazide (n=19)**				
A-card(Acme P harma)	5.26	2	5	3.45-23.87					
Monocard (Drug International)	71	27	67.5	56.78-88.60	HTZ (Unihealth)	11.12	3	15.78	11.89-45.89
ISM (Aristo pharma)	10.52	4	10	3.89-23.89	Dezide (SK&F)	44.44	8	42.10	45.89-56.78
					Amizide (Aventis Pharma)	44.44	8	42.10	22.56-56.67
Monit (Opsonin Pharma)	2.70	1	2.5	0-34.65					
Esmo (Beximco)	5.26	3	7.5	2.78-34.45	**Available K^+-sparing diuretics. (n=22)**				

Monotrate (Sun Pharma	5.26	3	7.5	2.22-4545	Spironolactone	46.66	10	45.454	22.66-39.99
Various Generics of Beta blocker: (n=175)					Triamterene	26.67	6	27.272	22.66-44.89
Atenolol	36.7	64	36.57	22.34.44	Amiloride	26.67	6	27.272	11.45-33.88
Metoprolol	25.5	44	25.14	28.34-44.34	**Various brand name of Spironolactone: (n=10)**				
Propranolol	21.7	39	22.28	11.23-34.34	Frulac (Orion)	65.71	7	70	55.88-88.99
Carvedilol	16	28	22.28	21.34-34.67	Fruselac (Aristopharma)	14.29	1	10	2.56-45.78
Various brand name of atenolol: (n=64)					Fusid plus (Square)	20.00	2	20	3.88-21.76
Tenoloc (Acme)	25.64	16	25	28.34-44.34	**Available loop diuretics: (n=21)**				
Betanol (Aventis)	38.46	25	39	11.23-34.34	Frusemide	55.42	12	57.142	22.78-33.90
Tenocard (Aristo Pharma)	15.38	10	15.62	21.34-34.67	Torsemide	44.58	9	42.857	23.67-67.21
Tenoren (ACI	20.52	13	20.31	28.34-44.34	**Various brand name of furosemide: (n=12)**				
					Lasix (Aventis)	64.28	8	66.666	39.89-65.99
Various brand name of propranolol: (n=39)					Frulac (Orion)	28.58	3	25	9.99-38.98
					Edeloss (Incepta)	7.14	1	8.333	2.89-21.44
Propanol (Opsonin)	86.96	33	84.61	35.55--45.56	**Renin-angiotensin system drugs**: (n=73)				
Indever (ACI	13.04	6	15.38	34.56-56.77	Captopril	12.5	9	12.328	1.78-34.77
Various brand name of carvedilol; (n=28)					Lisinopril	3.12	2	2.739	0-23.66
Cervista (Incepta) Durol (Square)	41.18 5.88	11 2	39.28 7.1453	23.44-44.45	Ramipril	81.25	60	82.191	55.90-67.99
Ucardol (Unihealth)	52.94	15	53.57	34.56-56.56	Enalapril	3.125	2	2.739	0-23.20
					Various brand name				

					of Ramipril: (n=59)				
Various generics of Anticoagulant, antiplatelet and Fibrinolytic: (n=154)					Tritace (Aentis)	70.23	41	69.49	33.77-55.88
Aspirin	80.00	123	79.87	56.67-76.45	Ramicard (Drugint)	10.54	6	10.16	0-34.77
Clopidogrel	19.00	29	18.83	12.23-34.20	Ramoril (Incepta	19.23	12	20.338	4.77-21.99
Warfarin	1.00	2	1.29	0-23.45	**Various brand of captopril(n=9)**				
Various brand name of Aspirin: (n=123)					Cardopril (Beximco)	75	7	77.777	44.88-66.99
Ecosprin (Acme)	47.62	59	47.96	44.73-48.67	Acetor (Drugint	25	2	22.222	3.56-45.99
Carva (Square)	24.46	30	24.39	28.34-44.34	**Various generics of angiotensin-II receptor antagonist (Miscellaneous): (n=9)**				
Solrin (Opsonin)	19.52	24	19.512	11.23-34.34	Losartan-K	70.00	6	66.66	43.89-56.89
Aciprin (ACI)	2.23	3	2.439	21.34-34.67	Irbesartan	16.34	2	22.22	12.67-56.90
					Valsartan	13.66	1	11.11	1.67-34.78
					Various brands of losartan-K.(n=6)				
Eras (Unihealth)	6.17	7	5.691	1.34-34.45	Angilok (Square)	44.44	2	33.33	11.45-44.67
Various brand of clopidogrel(n=29)					Lok-50 (Globe Pharma)	11.11	1	16.66	12.78-34.78
Clopid (DrugInternational)	41.66	12	41.379	22.34-45.67	Asartil (Incepta)	33.34	2	33.33	23.56-44.56
Anclog (Square)	8.33	2	6.896	2.45-40.56	Losan (Orion)	11.11	1	16.66	2.78-32.88
					Various generics of Lipid lowering drugs(n=20)				
Pladex	16.67	5	17.241	6.67-	Fluvastatin	32.02	6	30	23.67-45.89

(Unihealth)				34.45					
					Atorvastatin	45.38	9	45	32.89
Clognil (Orion)	16.67	5	17.241	11.45-34.55	Simvastatin	7.7	2	10	2.55-23.66
Odrel (Beximco)	4.17	1	3.448	0-34.66	Fenofibrate	7.7	2	10	2.55-23.66
Lopirel (Incepta) Plagrin (Renata	8.33 4.17	3 1	10.344 3.448	2.55-34.44 0-23.45	Gemfibrozil	7.2	1	5	1.44-23.66
Various generics of calcium channel blocker: (n=59)					**Various brand of Atorvastati(n =9)**				
Amlodipine	50.00	30	50.84	22.34.44					
					Atova (Beximco)	40.00	3	33.333	22.89-45.88
Diltiazem	40.00	24	40.67	28.34-44.34					
Verapamil Nifedipine	4.00 6.00	2 4	3.38 6.77	11.23-34.34 0-22.45					
					Lipicon (SK+F)	20.00	2	22.222	12.56-34.89
Various brand name of amlodipine: (n=30)									
Amdocal (Beximco)	13.33	4	13.333	2.55-34-44	Avas (Opsonin)	20.00	2	22.222	12.56-34.89
Amlocard (Drug international)	53.33	16	53.333	34.89-56.88	Taven (Renata	20.00	2	22.222	12.56-34.89
Amlopin (Acme)	13.33	4	13.333	2.55-34.44					
Camlodin (Square) Locard (Jayson	13.34 6.67	4 2	13.333 6.666	2.55-34.44 0-33.70					
Various brand name of diltiazem: (n=24)									
Cardizem (Drug International)	31.58	8	33.333	22.44-34.78					
Diltizem (Square)	15.79	4	16.666	1.45-34.78					
Neocard (Beximco)	47.37	11	45.833	23.67-67.78					
Evascon (Reneta)	5.26	1	4.166	0.45-34.78					

CI*= Confidence interval calculated by standard statistical method at 95% confidence level

DISCUSSION:

The aim of this survey protocol has undertaken for assessing variable types of cardiovascular drugs and matter relating to about near future prospects of other new cardiovascular agents in Bangladesh. To fruitful cardiovascular disease management and to know the most widely used cardiovascular drugs in Bangladesh this study will be helpful. After completion the survey we discuss with prescribed doctors and showed them in Table-2 they completely comply with results. Prescriber informed us that aforementioned table class of drugs they use to prescribe for less side effect, prompt onset of action, minimum amount of drugs are require, cost effective, easily available in the market and patient compliance. In most of the classes in cardiovascular therapy combination therapy is applied so there is no sharp rise of a particular class. Beta blocker and anticoagulant, antiplatelet and thrombolytic class possess the approximate value indicate till they have high application in therapy. (Epstein M et. al.1992, Heaton PMJ et. al.2004)[4, 5]

PRESCRIBED THERAPEUTIC DRUGS IN VARIOUS DISORDERS:

Almost all prescriptions represent total therapeutic class of cardiovascular drugs. Confidence Interval for different therapeutic classes were estimated by standard statistical method which indicate the closeness of practical results with true results. (Esposti LD et. al.2004)[3]From data analysis, physicians prescribed organic nitrates 19.57% (95%CI*:16.25 % to 22.65 %) and Beta-blockers 25.0% (95%CI*:21.79 % to 28.21 %). Other antihypertensive drugs include Calcium channel blocker 8.42%(95%CI*:6.36 % to 10.47 %), Diuretics 10.42%(95%CI*:8.16 % to 12.69 %), Renin-angiotensin system drugs 10.40%(95%CI*:1.62 % to 4.08 %), Lipid lowering drugs 2.85%(95%CI*:0.44 % to 2.11 %), Anticoagulant, antiplatelet and thrombolytic drug 22.0%(95%CI*:21.79 % to 28.21 %) and Miscellaneous 1.28%(95%CI*:21.79 % to 28.21 %) in prescription (Table. 1 & Figure 1).

In the nitrate and nitrite class nitroglycerine is widely used and few local companies marketed this drug. So there is a prospect in local market to launch this product. Nitromint (n-60; **61.66 %Egis pharmaceuticals,CI*: 55.66-71.44%**) is a brand leader in this group of the inorganic nitrate where Isosorbidemononitrate is the main generic agent. Here the brand leader is Monocard (n=40.145; **27% Drug International pharmaceutical;CI*:56.78-88.60%).**

Till now beta blocker is a prime choice in maintaining blood pressure in elder person. Atenolol is the popular antihypertensive among the beta blocker. Because atenolol is more selective and less side effects than other beta blockers[2,6]. Atenolol preparations are more available and cheaper than other beta blockers. Betanol (n=64; **38.46%Aventis pharma; CI*11.23-34.34 %**) is the brand leader in this class. In non-selective class Propanol (n=39; **86.96%opsonin pharma; CI*:28.34-44.34%**) is the brand leader. In case of carvedilol the mixed (alpha, beta receptor) action drug Ucardol (**52.94% unihealth pharma)** is the brand leader and carvista (**41.18I% Incepta pharma**) near to it**.**

Now-a-day many companies are promoting Aspirin the famous NSAID as a cardiovascular agent and of course the dose is 75 mg as prophylactic. Aspirin takes 80% and clopidogrel is homeostasis affecting agent 19%. Aspirin is widely used because of their effectiveness, availability and low cost. In the Aspirin class Ecospirin **(n=59; 47.96% Acme; CI*:**44.73-48.67**%**) is the brand leader. In the clopidogrel class clopid (n=12; 41.38**% Drug international pharmaceutical; CI*:** 22.34-45.67**%)** Place in first position and pladex (n=5; 17**.24 %unihealth pharma;CI*: 6.67-34.45%**),Clognil (n=5;**16.67%Orionpharma;CI*: 11.45-34.55%**) possess the equal place.

In calcium channel blocker amlodipine occur as 50% and diltiazem 40%. Amlodipine preparations are more available and more clinically effective than other calcium channel blockers.Amlodipine brands amlocard **(n=30;** 53.333**% Drug international,CI*:**34.89-56.88**%**) was the brand leader.In the diltiazem brand, Neocard **(n=11;45.83.% Beximco pharmaceutical;CI*:**23.67-67.78**%**)is the brandleader, cardizem **(n=-8;33.33%Drug international;CI*:**22.44-34.78**%**) is the second position..Single use of diuretic produce various side effects like electrolyte imbalance, nephrotoxicity,hypovolaemia impotency etc. To reduce the side effects, diuretics are combinedly used. Commonly the thiazide diuretics are combined with k+ sparing diuretics. In markets combined diuretics are more available so the individual market share detection is very difficult task. Among the diuretics class thiazide is used in high quantity (n=73; 40.81%), brand of hydrochlorothiazide, dezide,SK&F and Amizide,Aventis pharma (n=19;44.44%;CI*:22.56-56.67%)was the brand leader and potassium sparing takes (n=73;30.62%) indapamide possess 38% and hydrochlorothiazide 62%. In potassium-sparing class spironolactone possesses 46.66% and triamterene and amiloride possess 26.67%.

Loop diuretic frusemide found in 55.42% quantity. In the frusemide class Lasix **(n=12; 64.28% Aventis pharma,CI*:**22.78-33.90%) having the 64.28% count among the brands. In ACE generic class ramipril from the 81.25% market and then captopril 12.50%. Ramipril preparations are more available in market. Among ramipril brand tritace (n=59; **70.23%Aventis**

pharmaceuticals;CI*;33.77-55.88%) possess the highest place the second place is for ramoril (n=59; 19.23%**Incepta pharma**;CI*:4.77-21.99%). In Angiotensin-II receptor antagonist class losartan consists of 70% of the market. Losartan is more effective than angiotensin-ii receptor antagonist. Losartan preparations are more available in the market. Losartan group angilok **(n-6; 44.44%Square pharmaceuticals;CI*:11.45-44.67%)** is the brand leader and Asartil (n=6;33.3% Incepta **pharmaceuticals** ;CI*:23.56-44.56) is in second position.

In Lipid lowering class atorvastatin is used in high quantity (n=20; 45.38%; CI* :) and then Fluvastatin takes (n=20;32.02%;CI*:23.67-45.89).Atorvastatins are more effective more available than other lipid lowering drugs. In Atorvastatin brand Atova **(n=9; 40%Beximco; CI*:22.89-45.88%**) is the brand leader. (Table 2)

From the above discussion, it is clear that though the potency and API are same but all the brands are not prescribed in the same percentage. There is a rationale that all the brands are not equally effective due to their formulation difference. Their stabilities in market are not same. Their sources of materials are not same. Their color and packaging have also impact on customer perception. Doctor's satisfaction on the product has immense effect on their prescription percentage. Brand image of manufacturer and availability of drug have created a vital factor in this regard. Pricing also has great impact in some cases. Besides these, this Survey has many drawbacks such as many times it was not possible to collect latest information about the drugs due to demand a charge for the new journals, medical representatives of different companies do such type presentation survey almost every time so drug housekeeper feels disturb in this events. Hence sometimes prescription goes in irregular fashion, Patient feels disturb to collect prescription; Professor level doctor's interview was very difficult.

CONCLUSION:

Data analysis shows that Beta-blockers and Anticoagulants of both local and multinational companies are prescribed mostly than other class of drugs in Bangladesh. Organic nitrates, anti-platelet and thrombolytic drug, Calcium channel blocker, Diuretics, Renin-angiotensin system drugs, Lipid lowering drugs are prescribed commonly. There is a bad trend that when patient feels good, they stop taking medication. However, this study based on demographic and statistical analysis were surveyed from National Heart Foundation & Dhaka Medical College Hospital, Dhaka, Bangladesh which are tertiary level hospitals, may not comply with the data to other generalized hospitals of Bangladesh. This study protocol will also help in further estimation of prescribed marketed cardiovascular drugs in Bangladesh.

ACKNOWLEDGEMENT:

The authors are thankful to National Heart Foundation & Dhaka Medical College Hospital, Dhaka Bangladesh and Patients for their cooperative conduct to run this survey properly.

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