“Prescription survey on cardiovascular disease and its treatment pattern in Dhaka division”

[In the partial fulfillment of the requirements for the degree of Bachelor of Pharmacy]

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APPROVAL

This Project paper, a survey on **"Prescription survey on cardiovascular disease and its treatment pattern in Dhaka division"** submitted to the Department of Pharmacy, Faculty of Allied Health Science, Daffodil International University, has been accepted as satisfactory for the partial fulfillment of the requirements for the degree of Bachelor of Pharmacy and approved as to its style and contents.

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Declaration

I, sahitto Biswas, hereby declare that this project is done by me under the guidance of Md. A.k. Azad, Assistant Professor & Coordinator M,pharm, Department of Pharmacy, Daffodil International University, in the partial fulfillment of the requirements for the degree of Bachelor of Pharmacy. The result embodied in this project has not been submitted to any other university or institute for the award of any degree.

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Certificate

This is to certify that the results of the investigation that are embodied in this thesis works are original and have not been submitted before in substance for any degree or diploma of this university. The entire work was submitted as a thesis work for the partial fulfillment of the degree of Bachelor of Pharmacy.

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– Sahitto Biswas

Dedication

My Parents,

The persons who always encourage me in every sphere of my life.

My teacher,

The persons who guided me in this process and the committee who kept me on track.

Abstract

Cardiovascular medications refer to a wide variety of prescription drugs utilized to manage heart disease. This is a complex category of drugs, as many of them can be used to treat multiple heart conditions. This study is driven across the Dhaka division, at different hospitals. It has taken almost 4 months (Jan 15- April 20, 2023). This survey mainly shows the causes of cardiovascular diseases on the basis of drugs are using to treat these diseases. Out of 700 prescriptions, 673 are exactly for cardiovascular disease and the remaining 27 are slightly related to these. Mainly male patients are more in number than females and the ratio is 60:40. Among cardiovascular diseases the maximum number of patients who have been suffering from Ischemic stroke (Recent & Pre) which is (34%). On the other hand, only (1%) of people have been suffering from Acute myeloid leukemia. Mainly 40-59 ages of people are suffering the most from cardiovascular diseases. In this segment, a maximum of 364 prescriptions were identified, representing the most commonly used drugs or percentages for treating different diseases. The drugs used in descending order of frequency were: lipid-lowering drugs, organic nitrates, beta-blockers, antiplatelets, ACE inhibitors, calcium channel blockers, antihypertensive drugs, angiotensin II receptor enzyme inhibitors, vinpocetine, and diuretics. The number of prescriptions for each drug was 225, 63, 170, 163, 4, 2, 27, 140, 10, 168, 17, and 35, respectively. The predominant use of these drugs indicates a high prevalence of cardiovascular disease caused by high cholesterol. Despite belonging to different generic groups, these therapeutic agents are commonly used in various prescriptions. For instance, clopidogrel is the most widely used antiplatelet drug (53%), bisoprolol is the most commonly used beta-blocker (38%), amlodipine is the most widely used calcium channel blocker (53%), atorvastatin is the most widely used lipid-lowering drug (82%), and spironolactone and frusemide are commonly used as loop and potassium-sparing diuretics, with utilization rates of (89%) and (94%), respectively. Telmisartan is the most commonly used angiotensin II receptor enzyme antagonist, with a utilization rate of (51%.) The study could offer recommendations for enhancing the appropriate usage of cardiovascular medications, as well as introduce a novel statistical technique to efficiently manage cardiovascular diseases in Bangladesh

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Introduction

1. Introduction:

The treatment of cardiovascular disease is ineffective, despite being a major cause of premature death and illness, according to the World Health Organization (WHO). In 2008, CVDs accounted for 30% of all deaths worldwide, resulting in 17.3 million fatalities. Of these, 6.2 million were caused by stroke and 7.3 million by coronary heart disease. By 2030, it is estimated that nearly 25 million people will die from CVDs, with heart disease and stroke being the leading causes of death. These deaths disproportionately affect middle- and low-income countries, with over 80% of CVD-related deaths occurring in these regions. Preventative efforts are often not available to those in these countries, unlike in high-income countries. A study in Bangladesh found that individuals with lipid disorders and stroke had high levels of LDL and triglycerides, while those with low levels of HDL were found to be 42.67%. The use of drugs in treating CVDs is constantly evolving, with a greater emphasis on prevention. Antioxidants and antilipidemic medicines are commonly used to reduce risk factors. Cardiovascular drugs have been shown to save lives and remain the primary cause of death. Beta-adrenoceptor blockers, organic nitrates, anticoagulants, antiplatelet and thrombolytics, calcium channel blockers, diuretics, medications for the renin-angiotensin system, lipid-lowering medications, and other medications are commonly prescribed in Bangladesh for the treatment of CVDs (Labu 2013).

1.1 Cardiovascular Disease:

Cardiovascular disease remains the leading cause of death for both men and women globally, although significant progress has been made in reducing acute cardiovascular mortality. However, there has been a considerable increase in the number of people suffering from cardiovascular disease. Without regular access to healthcare, these individuals may experience recurring acute care incidents, premature death, and multiple chronic cardiovascular disease issues due to both formal and informal prevention programs, such as cardiac rehabilitation. Cardiovascular disease encompasses a range of heart disorders including myocardial infarction and high blood pressure. The primary cause of coronary heart disease is the narrowing of blood vessels, which can lead to reduced blood and oxygen flow to the heart. Symptoms of CHD include angina pectoris or chest pain and myocardial infarction. A heart attack occurs when a blood clot suddenly blocks a blood vessel, which can cause damage to the heart muscle and lead to pain. Another type of heart disease is cardiac rhythm abnormalities, which can cause

rapid heartbeat, heart disturbances, and other unidentified disorders. The last stage of heart disease, heart failure with symptoms (CHF), is frequently a different type of heart condition. In summary, while there has been progress in reducing acute cardiovascular mortality, the increasing number of people suffering from cardiovascular disease highlights the importance of regular access to healthcare and prevention programs to avoid recurring acute care incidents, premature death, and multiple chronic cardiovascular disease issues (Mytton 2018).

1.2 Different types of cardiovascular diseases:

- Myocardial Infarction
    - ❖ Non-STEMI
    - ❖ STEMI
- Left Ventricular Failure
- Chronic Rheumatic Heart Disease
- Angina [Stable & Unstable]
- Diastolic Murmur
- Hypertension
- Ischemic heart disease
- Acute myeloid leukaemia
- Ischemic Stroke

1.3 Myocardial Infraction:

When a coronary channel becomes blocked by a blood clot, it can lead to a sudden death of heart muscle cells, known as an ischemic myocardial infarction. This happens because the blockage causes a lack of blood flow and oxygen to the affected area, which can result in severe disruptions to the heart's ionic and metabolic processes. The heart's ability to regenerate is limited, so the damaged tissue is replaced with scar tissue. This article explores the genetic mutations and cellular mechanisms that contribute to the damage healing and remodel the heart after an ischemic event, as well as common complications and current treatments (Thygesen 2007).

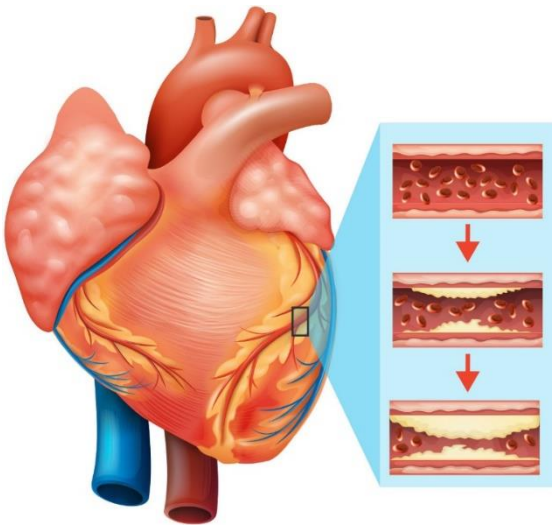

Fig 1: Myocardial Infarction.

1.3.1 Myocardial infarction's pathophysiology:

Intracellular acidosis, the production of inorganic phosphate due to the breakdown of creatine phosphate stores, and the inhibition of contractile proteins are responsible for ischemic systolic dysfunction. While motor function impairment can be regained, prolonged myocardial ischemia can lead to persistent dysfunction even after the restoration of blood flow. Myocardial stunning usually lasts less than 24 hours after the return of coronary flow (Frangogiannis 2011).

1.3.2 Types:

- **NSTEMI:**

  NSTEMI typically results from the full blockage of such a minor coronary artery or perhaps the partial blockage of a big coronary artery, which causes tissue loss damage to the cardiac muscle. The inner 13 to 23 of the left ventricular border is all that has a heart muscle injury in this instance. Hence, it is also known as a subendocardial infarction. The partial thickness injury to the heart muscle prevents ST-segment elevation from developing in this myocardial infarction. An increase in cardiac biomarkers (CK-MB or Troponin) inside the plasma in this instance serves as evidence of a muscle injury.

- **STEMI:**

  STEMI happens when a major coronary artery is completely blocked, causing the heart muscle to be damaged throughout its whole thickness. Because of its inclusion of the entire thickness, STEMI is also known as a transmural infarction. An ECG is produced as a result of the whole-thickness thickness injury to the cardiac muscle. According to the location of the myocardial infarction in relation to the left and right ventricles, it can be further defined as anterior, posterior, inferior, lateral, high medial, or anterolateral myocardial infarction.

1.3.3 What is responsible for myocardial infarction:

The main causes of the conditions studied in various research are usually chronic stress and lifestyle factors such as smoking and diet. Moreover, most individuals commonly report multiple factors in these studies. The patients surveyed typically agreed that there were several factors contributing to their condition, with an average of 7.3 causes identified. Among the most strongly supported variables were stress, high lipid levels, and consumption of fatty foods (French 2005).

1.3.4 Signs & symptoms of myocardial infarction:

Chest pain: The main symptom of a sudden heart attack is chest discomfort. Typically, this feeling is described as tightness, choking, squeezing, or heaviness in the middle of the chest that can spread to other parts of the body such as the neck, chin, shoulders, back, and arms, especially the left arm. Sometimes, the pain may only be felt in these other areas without any chest pain. Elderly individuals or those with diabetes mellitus are at risk of experiencing painless heart attacks, also called silent myocardial infarctions. This is because, with age and diabetes, the nerve fiber responsible for transmitting pain signals tends to weaken.

Wheezing: This could arise from progressive rheumatic heart disease or ischemia in left ventricular function.

Syncope: Sometimes, patients can experience syncope, a sudden and temporary loss of consciousness, which is commonly caused by either heart arrhythmia or a severe lack of oxygen

Tachycardia: Sympathetic nerve activity increases the heartbeat.

Bradycardia: Due to vagus nerve activity, persons with superior myocardial infarction may experience bradycardia (low pulse rate).

Carcinogenic shock: Some individuals may experience cancer-related shock as a result of weakened heart function.

1.3.5 Treatment of MI:

Left ventricular restraints: Ventricular restraint is a surgical technique used to treat heart failure that involves wrapping the entire outer surface of the heart with a man-made material. The purpose of this technique is to provide support to the heart during relaxation and prevent further damage to the heart muscle. Although there are currently no approved devices for this procedure, studies in animals and humans have shown promising results. The exact way that ventricular restraint works are not yet known, but it appears to reduce stress on the heart muscle and promote reverse remodeling. The degree of improvement in heart function and oxygen consumption is dependent on the amount of restraint applied, indicating that the level of restraint is a critical factor in determining the success of the treatment (Lee 2010). Following a myocardial infarction (MI), the left ventricle (LV) has been immobilized using bio-ink supports. Kelley et al.'s research indicates that limiting the growth of the infarct can prevent heart rhythm deterioration**.**

Stem cell therapy: Stem cell treatment is a hopeful approach for repairing damaged cardiac and vascular tissue following an acute myocardial infarction (AMI). Multiple randomized controlled-trials (RCTs) have been conducted worldwide to explore this strategy (Clifford 2012).

Pain relief: Usually, narcotic analgesics are employed for alleviating pain during an acute myocardial infarction, but there are alternate choices available. Other pain-relieving medications consist of beta-blockers, glyceryl trinitrate, streptokinase, and drugs that decrease ischemic damage (Herlitz 1989). Nitrate and opiate analgesics are effective in reducing pain. Nitrate works by expanding blood vessels and can be administered through a sublingual spray or buccal administration. If the pain persists after three doses spaced five minutes apart, intravenous therapy should be given, as long as the systolic blood pressure remains above 100 mm of mercury. Glyceryl trinitrate or isosorbide dinitrate can be given continuously at a dose of 0.6-1.2 mg/hour and 1-2 mg/hour, respectively. For severe pain, an intravenous opiate analgesic like morphine 10 mg or diamorphine 5 mg is typically used.

Re-perfusion therapy: The heart muscle is not instantly destroyed when a coronary artery is blocked. Most of the cardiac muscle in the afflicted area will not be damaged if blood flow is

resumed in just a few hours. There are two treatments that really can reopen a blocked blood vessel:

- **PCI:** Within 120 minutes of STEMI symptoms, Thrombolytic treatment is preferred unless primary PCI is available. If primary PCI is unavailable or cannot be completed within the time frame, thrombolytic treatment should be used. For individuals with non-ST segment elevation myocardial infarction who are medium to high-risk, early coronary angiography and revascularization using PCI or cardiac catheterization should be considered. Low-risk patients should receive early medical intervention, while clinical examination and revascularization are recommended only for those who do not respond to medical therapy.
- **Thrombolytic Therapy:** Just ST-segment elevation myocardial infarction is the indication. It is also known as fibrin medication. Streptokinase, the transmission of data and replaces are clot-busting medications that are on the market. These medications open the coronary artery's lumen and dissolve the blood clot. It must be delivered quickly. Yet, it may be given to individuals who arrive after 12 hours after the start of their chest symptoms after three hours. Thrombolytic therapy provides only a slight advantage and carries a risk within a 720-minute window. It is entirely unsafe for NSTEMI and should be steered clear of.
- **Antiplatelet:** The most effective drugs for preventing platelet aggregation during percutaneous coronary intervention are aspirin, clopidogrel and glycoprotein receptor inhibitors.

  Patients who undergo coronary artery bypass graft with stents need a combination of two antiplatelet agents, including clopidogrel and aspirin. The combination of two Antiplatelet agents showed that patients who received dual antiplatelet medication for 2.5 years instead of 1 year had lower rates of thrombosis and heart attack but higher rates of moderate or severe bleeding. Patients with acute myocardial infarction (MI) may get a good result from extended the combination of antiplatelet agents due to the higher risk of future MI and stent thrombosis. For patients who receive PCI for MI, prolonged dual antiplatelet medication beyond 1 year may be more beneficial than for those with more stable presentations (Yeh 2015).

Anticoagulant: For individuals who are not receiving reperfusion therapy, it is recommended that they start drug treatment to decrease the chance of thromboembolic complications and to prevent the reoccurrence of a heart attack. The prevention of blood clotting can be achieved

through the use of heparin, which is not in a fraction and has a low molecular mass, or penta saccharine or fractionated heparin. Low molecular weight heparin is more effective and safer than unfractionated. Low molecular weight heparin is also more effective and safer than penta saccharide.

Beta Blocker: Beta-blockers have a minor impact on short-term results, but they significantly reduce the risk of long-term all-cause mortality, cardiovascular mortality, and short-term reoccurrence of a heart attack (afi 2019). Beta-blockers reduce the need for oxygen in the heart muscle by lowering heart rate, blood pressure, and myocardial contractility, which also helps alleviate chest discomfort and ventricular arrhythmias. They can also increase blood flow to the heart muscle by extending the heart's diastolic period. When taken early, beta-blockers can decrease the size of a heart attack and the risk of death in patients who are not receiving thrombolytic treatment. However, recent studies on patients who are receiving thrombolytic treatment did not find a decrease in mortality rates, but did observe a decrease in the rates of recurrent ischemia and re-infarction. Taking an oral beta-blocker like atenolol 25-50 mg twice a day and metoprolol 25-50 mg daily is typically enough. However, if you have MI, heart block, hypotension, or bradycardia, beta-blockers should be avoided.

Angiotensin Converting enzyme: After a heart attack, it is recommended to initiate treatment with an Angiotensin Converting Enzyme inhibitor (ramipril, enalapril, captopril, lisinopril) within one or two days. The use of ACE inhibitors has been found to reduce ventricular remodel, delay the onset of cardiac muscle failure, and decrease the likelihood of another heart attack. In cases where an individual cannot tolerate ACE inhibitors, ARB such as an angiotensin II receptor antagonist agent or a combination of several factors can serve as a suitable alternative.

1.4 Left ventricular failure:

The circulatory system in the body, apart from the lungs' circulation, receives oxygenated blood from the lungs through the left side of the heart. If the left side of the heart fails, it can cause a backup of blood into the lungs, leading to insufficient blood and oxygen supply, resulting in breathing difficulties and tiredness. Typical respiratory symptoms such as an increase in respiratory rate and difficulty in breathing can occur due to this condition, which can also cause crackling sounds in the lungs, starting in the base and then spreading throughout the lungs, indicating the onset of fluid build-up in the alveoli. Cyanosis, a late sign of severe swelling to the hand or leg, is an indicator of inadequate oxygen levels in circulation (Adeyinka and

Kondamudi 2022). Dyspnea, exhaustion, and indications of volume overload describe heart failure, a common clinical condition. It has significant rates of morbidity and mortality, particularly in older people. A history and physical examination, chest radiography, electrocardiography, and laboratory analysis are all included in the first evaluation. The diagnostic gold standard for systolic or diastolic heart failure is echocardiography. It is necessary to be examined for ischemic heart disease (King 2012).

1.4.1 Causes of left ventricular failure:

- AMI (Heart Attack).
- Cardiac muscle rupture.
- Valve rupture.
- Valve destruction.
- Irregular heartbeat.
- Leakage in the aorta.
- Myocarditis.

1.4.2 Signs & Symptoms of left ventricular heart failure:

Initial symptoms may be minor, leading you to believe you have a cold or an allergy. They might even go unnoticed by you. But, when heart function deteriorates, you might notice:

- Coughing continuously.
- Breathing difficulty when walking or leaning over.
- Problems arise at the time of flat rest.
- Swelling in different parts of the body
- Losing of strength in a short time.

Over time, the heart may need to work harder to carry out its duties, which can lead to issues such as:

- shock to the heart.
- Arrythmias.

1.4.3 Treatments:

- Cardiac resynchronization therapy (CRT), also known as a biventricular pacemaker, is a treatment method that involves using a gentle electrical current to stimulate the heart's

pumping action and correct irregular heartbeat patterns (arrhythmia). This injectable tool is designed to improve the heart's function.

- Electrical cardioversion is the technique that aids in re-establishing a regular rhythm.
- ICD: An implantable device that detects arrhythmias and administers a mild electrical current to return the heartbeat to normal.
- An implantable pump that assists the heart to pump blood is known as a left ventricular assist device (LVAD).
- Transplanting a healthy heart from a donor to replace a damaged one is known as a heart transplant. Individuals who have the most severe types of left-sided heart failure should receive this therapy. (Chahine J 2020).

1.5 Angina:

Angina pectoris refers to the feeling of chest pressure, pain, or discomfort that arises due to an imbalance between the heart's oxygen demand and supply. This condition affects around 10 million people in the United States, with an annual incidence of 5,00,000 new cases. The primary reason behind angina is coronary artery disease, which narrows the lumen of the blood vessels that supply oxygen and nutrients to the heart muscle cells due to the build-up of atherosclerotic plaque. Additionally, angina can be exacerbated by vasospasms. Coronary artery disease typically affects the large epicardial coronary arteries that run along the surface of the heart. Angina can also be caused by aortic stenosis, hypertrophic cardiomyopathy, and valve disease. Elderly individuals are more susceptible to angina since they often have more severe coronary artery disease and less tolerance for conventional antianginal agent. Angina symptoms can observe earlier in men than women. (Kloner, Angina and its management 2007). Various studies have shown that females with coronary artery disease have a higher mortality rate from cardiovascular causes compared to their male counterparts. Although the symptoms of a heart attack and angina attack share similarities, they are not the same. Factors such as intense emotional states like anger, consuming large meals or eating too quickly, excessive physical activity, exposure to extreme temperatures, and smoking can all cause angina attacks. Overexertion-induced angina can usually be alleviated by stopping physical activity. However, seeking medical help immediately is vital regardless of the cause of chest pain or discomfort.

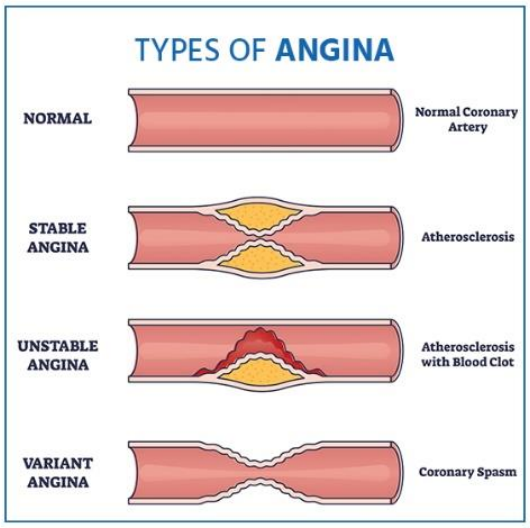

Fig 2: Angina

1.5.1 Type of angina:

There are five main types of angina:

Stable angina: As the artery disease doubles the risk of serious cardiovascular events, chronic angina pectoris is a typical symptom. Advanced age, severe types of angina, comorbid disorders, poor heart function, and the inability to undergo a stress test are all factors that raise risk (Ohman 2016). When the heart is forced to function more forcefully than usual, such as during exercise, stable angina develops. If you are aware that you have stable angina, you can anticipate the pattern because it follows a predictable pattern. After you quit working out or taking a drug often the pain normally disappears within a few minutes after taking nitroglycerin.

Unstable angina: Unstable angina is a common condition, with 6-8 percent of patients having a serious disease by which they can fall to death but not for cardiovascular disease. Scientists have developed a method that categorizes angina based on its severity, clinical context, and electrocardiographic irregularities. The varied clinical presentations of this condition make the prognosis unpredictable (Yeghiazarians 2000). Exercise- or rest-related episodes of unstable angina are dangerous conditions that require emergency care.

Prinzmetal,s angina: Variant angina, also known as Prinzmetal's angina. Moreover, it is characterized by a temporary increase in the STEMI on the ECG during an episode of chest pain, which is a form of angina pectoris. During midnight and early morning, when people are at rest or doing light exercise, ischemic events are common. Severe arrhythmias are the cause

of syncope, while the heart artery spasm is the cause of ischemic events. The coronary spasm can be avoided with the help of calcium channel blockers, long-acting nitrate, and Rho-kinase inhibitors. Early intervention is crucial, and drugs to stop uncontrollable coronary artery spasms must be created (Kusama 2011).

Microvascular angina: CMD, or dysfunction of the tiny blood vessels in the heart, is a predictor of poor outcomes in patients with or without blockages in their larger coronary arteries. Many people experience chest pain even when there is no blockage in these larger arteries. This type of chest pain called microvascular angina (MVA), is often difficult to distinguish from chest pain caused by blockages in these larger arteries. However, new non-invasive methods such as stress positron-emission tomography (PET) and cardiovascular magnetic resonance (CMR) myocardial perfusion imaging can now help doctors identify MVA more accurately (L{\"o}ffler, Coronary microvascular dysfunction, microvascular angina, and management 2016).

Atypical angina: Symptoms that may suggest the presence of atypical angina include a general discomfort in the chest area, difficulty breathing, tiredness, feeling sick, digestive problems, and experiencing pain in the neck or back. Atypical angina is not always painful, though. The likelihood of having a generalized discomfort in the chest is higher in women than in males. Realizing a little bit about the working of your heart may be important in order to comprehend what causes angina.

1.5.2 Angina can be predicted as CVD:

Among the risk factor of CVE (Cardiovascular events) and MI, angina is at the top of this. Severe angina showed a greater 1-year death rate than moderate angina, according to Spertus et al. Also, Heart and Soul Research says that people who have faced angina on a daily or weekly basis have more chances to get administration in the hospital for further fetal disease treatment. Angina increased the chance of serious adverse cardiac events over a ten-year period, according to research by Hlatky et al. Individuals who experience angina reported a lower quality of life compared to those who don't have angina. The current clinical evaluations indicate that the existence of angina deteriorates the quality of life in patients with ischemic cardiomyopathy, but it does not seem to have an impact on all-cause mortality. Secondary factors such as anemia, tachycardia, hyperthyroidism, infections accompanied by fever and chills, hypoglycemia, poorly managed hypertension, large meals, and infections can exacerbate angina symptoms (Kloner, Angina and its management 2017).

1.5.3 What causes angina:

The main reason for angina is a reduction in the blood supply to the heart muscle, which requires oxygen to survive and relies on blood to transport it. Insufficient oxygen delivery leads to a condition called ischemia. The most common cause of reduced blood flow to the heart muscle is coronary artery disease (CAD), where the coronary arteries that supply blood to the heart become narrow due to fatty deposits known as plaques, a condition called atherosclerosis. A blood clot or plaque rupture in a constricted artery can rapidly restrict or completely stop blood flow, causing a sudden and significant drop in blood supply to the heart muscle. When the oxygen demand is low, such as during rest, the heart muscle can cope with less blood flow without experiencing angina symptoms. However, when the need for oxygen increases during activities like exercise, angina can occur.

1.5.4 Risk factors:

- Angina is most prevalent in adults,
- If disease exists from parents.
- Tobacco inhalation.
- High level of sugar in the blood.
- If the blood pressure level is high.
- high lipid in the blood.
- Anxiety.
- As well as other medical conditions,
    - insufficient exercise
    - obesity
    - emotional stress
    - exposure to cold temperatures

1.5.6 Treatment of angina:

Antianginal Agent:

- **Nitrates agent:** Medications like sublingual nitroglycerin tablets and sprays can be effective in treating acute angina episodes by reducing systemic arterial pressure, oxygen demand, and widening coronary arteries. Patients may experience tingling or stinging under their tongue, but this is a positive sign that the medication is improving oxygen transport to the brain by dilating cerebral arteries. Nitroglycerin also improves

exercise tolerance and reduces the gradual angina attacks in a short time during exercise stress tests. However, individuals using PDE 5 inhibitors should not take nitroglycerin due to the risk of severe hypotension. Nitroglycerin can also be used as a preventative measure for angina.

- **B-Blockers:** B-blockers are effective medications for treating angina that works by decreasing oxygen consumption and improving exercise tolerance. The FDA has approved them for the treatment of hypertension and hypertrophic obstructive cardiomyopathy. However, they can cause various side effects such as bradycardia, aberrant conduction, fatigue, lethargy, depression, nightmares, erectile dysfunction, gastrointestinal distress, aggravation of insulin-induced hypoglycemia, and cold extremities due to peripheral vasoconstriction. Using b-blockers in combination with other antianginal agents should be approached with caution.
- **Calcium channel blockers:** Calcium channel blockers like Nifedipine, Amlodipine, Felodipine, and Nitrendipine prevent calcium from entering L-type calcium channels in the cardiac and smooth muscles of blood vessels. These blockers use various strategies to treat angina, including calming smooth muscle cells in the coronary arteries, reducing the narrow shape of the artery and resistance in the circulatory system, and lowering heart rate. Diltiazem and verapamil can cause negative side effects such as slow heart rate, electrical signal problems of the heart, stool movement down, swelling of the leg, worsening of heart failure, flushing, hypotension, headache, dizziness, and gastrointestinal issues. It is not advisable to use short-acting nifedipine to treat acute coronary syndromes. (Graboys 2003).
- **Ranolazine:** In ischemic heart disease, Ranolazine is a drug that lowers calcium excess and increases microvascular perfusion. It has been shown that ranolazine extends the duration of exercise, decreases the frequency of angina, and reduces recurrent ischemia in people with non-ST-segment elevation acute coronary syndromes. During the first week of hospitalization, Holter monitoring revealed that ranolazine reduces arrhythmias. People with chronic angina may benefit from its antiarrhythmic effects. In the RIVER-PCI study, there was no difference in hospitalization without revascularization or independence from ischemia-driven revascularization. However, in the CARISA Diabetes substudy, the agent used to reduce HbA1c levels is Ranolazine, likely due to improved insulin sensitivity or increased physical activity. (Wilson 2009).

1.6 Diastolic murmur:

A diastolic heart murmur is an abnormal noise that happens when your heart is at rest between beats, or during diastole, The lower number in a reading of blood pressure is the diastolic pressure. The noise of a murmur can resemble a "swish" or "whoosh." Blood passing through your heart's valves causes it to happen. Cardiac murmurs are frequently not harmful. Symptoms can, however, occasionally indicate heart problems. Your healthcare professional might do testing on you if you have a diastolic murmur to look for any additional heart issues.

1.6.1 Causes of diastolic murmur:

Diastolic murmurs can result from a variety of heart valve issues, including:

- **Aortic regurgitation:** When the aortic valve, which permits the blood to pass from the heart in the aorta, fails to shut entirely, it results in defects.
- **Pulmonic regurgitation:** Leaks resulting from the pulmonary valve, which joins your heart and lungs, failing to seal completely.
- **Mitral stenosis:** A constricted mitral valve, which connects the upper chamber of the left atrium to the lower chamber of the left ventricle..
- **Tricuspid stenosis:** The constriction of the tricuspid valve, which connects the upper right atrium and the lower right ventricle of the heart.

1.6.2 Treatment for the diastolic murmur:

Deeper cause determines the course of treatment. If a valve issue is the cause of the murmur, your doctor can suggest taking medication, having the valve fixed, or having the valve replaced.

Medicines might consist of:

- The use of ACE inhibitors like captopril and benazepril. These decrease the blood pressure.
- Beta-blockers lower your blood pressure and heart rate, such as succinate and metoprolol.
- Blood thinning medications, such as aspirin and warfarin reduce the likelihood that blood clots will form in blood vessels or organs.
- Body can flush out extra fluid with the aid of diuretics, sometimes known as water pills like torsemide or furosemide.

1.7 Ischemic heart disease:

Ischemic heart infection alludes to the degeneration of the heart due to a diminish in the bloodstream to the organ. The most guilty party for this diminishment in circulation is coronary course illness, where the courses providing blood to the heart contract. This condition may moreover be alluded to as cardiac ischemia or ischemic cardiomyopathy. As the heart becomes weaker, it must work harder to pump blood to the rest of the body, driving it to the next chance of blood clots, unpredictable heartbeats, heart disappointment, and other complications. Plaque buildup in any supply route within the body can cause ischemia and diminish blood supply, leading to a group of disorders called ischemic vascular disease (IVD). In case, the stream of oxygen-rich blood to the heart muscle is discouraged, angina or a heart assault may happen, coming about in extreme results and indeed passing (M. R. Thomas O'Connor 2014).

1.7.1 Signs and symptoms of ischemic heart disease:

Ischemic heart disease usually does not exhibit any indications or symptoms until an artery becomes significantly limited or totally obstructed. Many people are oblivious to the disease before experiencing a medical emergency, such as a stroke or heart attack. However, certain individuals may exhibit symptoms and demonstrate evidence of the illness. The symptoms and signs of affected arteries may differ.

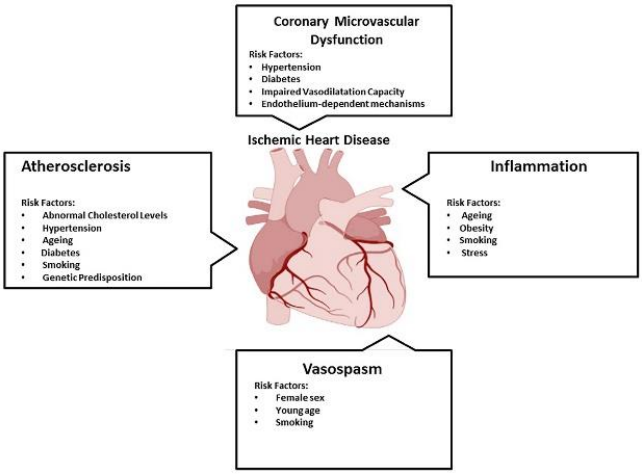

Fig 3: ischemic heart disease

1.7.2 Treatment of ischemic heart disease:

To effectively manage any ischemic heart condition, it is recommended to cease smoking, take medication to lower blood pressure and cholesterol levels, and stop drinking alcohol.

Additionally, certain individuals may need medication to prevent the formation of blood clots Prevention of medical problems, complications, and impairment also depends on keeping a healthy weight, exercising regularly, adhering to a balanced diet, controlling stress, and stopping or minimizing plaque build-up. If you suffer from severe atherosclerosis, consult your doctor. May also suggest undergoing surgery or a medical procedure. Restoring blood flow and lowering the risk of a heart attack are often the main goals of ischemic heart disease treatment (M. R. Thomas O'Connor 2014).

1.8 Hypertension:

Blacks and Latinos in particular are at risk for cardiovascular disease because of hypertension. Large-scale epidemiologic and clinical research have proven high rates of hypertension-related morbidity and mortality in minorities, especially blacks, and Hispanics. All patient populations experience non-compliance with pharmacological therapy and high dropout rates, but these rates are worse in inner-city populations due to factors such as chemical dependency, homelessness, poverty, and illiteracy. Clinics should select a condensed pharmacological regimen and steer clear of medications that cause intolerable side effects. Antihypertensive medications can be used to address increased vascular resistance, the root cause of hypertension. The origin of secondary hypertension is frequently a disease state, but primary hypertension is frequently unknown.

1.8.1 The difference of hypertension according to blood pressure:

Table (1):

Stage	Systolic BP mm Hg	Diastolic BP mm Hg	Comment
Natural	Less than120	Less than 80	Normal
Hypertension			
Stage 1	120 to 129	~ 80	Near about normal
Stage 2	130 to 139	90 to 99	Need for check up
Stage 3	>140	>80	Hospitalized
Stage 4	Less than 210	Less than 120	Emergency

1.8.2 Basic Physiology to control blood pressure:

The peripheral resistance and cardiac output must both be continuously adjusted in order to control blood pressure. The volume of blood that the heart circulates is determined by various factors such as the filling pressure of the ventricles, which is influenced by the pressure in the atria, the strength of the ventricles' contractions, heart rate, and the resistance of the blood vessels. The resistance is regulated by the small arterioles and large capacitance venules in the circulatory system. Additionally, the electrolyte balance and angiotensin II play a role in controlling the total amount of blood in circulation. The advancements in our understanding of autonomic cardiovascular control mechanisms from research in genetically altered mice are included in this review, along with measurement techniques for fundamental hemodynamic function and the function of autonomic nerves in blood pressure regulation (Janssen 2002).

BP = CO * SVR

CO = HR * SV

SVR = Total resistance of artery blood

SV = Amount of blood pumped by the heart each cycle

1.8.3 Agents that are used to treat hypertension:

Diuretics: Thiazide diuretics and loop diuretics can speed up the processes of natriuresis and diuresis. Despite belonging to distinct pharmacological categories, they are both considered the primary therapeutic class of antihypertensive drugs. Each drug has its own specific mechanisms of action and adverse effects, which have been thoroughly described. Additionally, there exists a different class of drugs known as potassium-sparing diuretics.

Angiotensin-converting enzyme inhibitors: In the early 1980s, Captopril became the first ACE inhibitor available for hypertension treatment. After that, scientists included other ACE inhibitors such as Enalapril, Perindopril, Lisinopril, Ramipril, Quinapril, Benazepril, Cilazapril, Trandolapril, and Zofenopril.

Angiotensin II receptor enzyme: In the late 1990s, Losartan became the initial angiotensin II receptor blocker (ARB) that was made available for the management of hypertension. Subsequently, scientists included other medications including Candesartan, Irbesartan, Valsartan, and Telmisartan.

Calcium channel blocker: A range of drugs called calcium-channel blockers (CCBs) consists of Verapamil, a Benzothiazepine, Diltiazem, a phenylethylamine, Nifedipine, and Amlodipine, which are classified as Dihydropyridines.

Renin-inhibitors: A group of medications referred to as calcium-channel blockers (CCBs) includes Verapamil, which is a type of Benzothiazepine, and Diltiazem, which is a type of Phenylethylamine, Nifedipine, and amlodipine, which are classified as Dihydropyridines (Laurent 2017).

1.9 Smoking and cardiovascular disease:

According to survey data on prescriptions, most of the patients a doctor sees are addicted to tobacco. The ways in which tobacco smoke is believed to cause cardiovascular disease, as well as the occurrence of smoking-induced heart disease, are discussed, including a biomarker-based approach. The aim is to determine how smoking causes CVD and how it can be treated. Smoking raises the risk of coronary heart disease by 2-4 times, sudden death by 700%, and is the leading preventable cause of cardiovascular disease and death. Smoking has also been linked to other health problems such as coronary artery disease, cerebral vascular disease, vehicle pulmonale, Nicotine, and carbon monoxide toxicity. Quitting smoking has been shown to reduce the risk of death from coronary heart disease and stroke. To help less educated individuals quit smoking, future efforts should focus on providing access to appropriate education and cessation methods. (Lakier 1992).

Chapter 2:

Purpose of my survey

2. Purpose:

The main purpose of my study is to observe the rational use of cardiovascular drugs in local people.

It also highlights:

- People's awareness about the cardiovascular drug.
- Food habit is the main cause of cardiovascular diseases.

Chapter 3:

Literature review

Title: Neurodevelopmental Outcome in Children with congenital heart disease.

Objective: The purpose of this review is to examine various aspects related to neurological injuries in newborns who have congenital heart disease. The review will focus on the extent of the neurological damage, as well as the mechanisms that cause the injury, which include pre-natal, pre-operative, intra-operative, and post-operative factors. Additionally, the review will explore the long-term developmental outcomes of these neurological injuries and identify possible therapeutic strategies that can be used to prevent or intervene in a timely manner. The review aims to provide a comprehensive understanding of the scope and nature of neurological injuries in newborns with congenital heart diseases to highlight the importance of addressing these injuries through appropriate interventions. This review will be useful for healthcare professionals, researchers, and families of affected newborns, as it provides valuable insights into the potential causes, outcomes, and strategies for managing neurological injuries in this population.

Introduction: The meaning of congenital heart disease differs significantly among various reports on the disease's epidemiology. Some reports exclude specific abnormalities such as persistent left superior vena cava or inferior vena cava-azygos continuity, as well as anomalies of systemic artery branches like a combined innominate-left-carotid arterial trunk. Other reports also exclude bicuspid aortic valves, mitral valve prolapse, Marfan syndrome, cardiomyopathies, and congenital arrhythmias. It can be debated whether the definition should be more comprehensive and include some of the mentioned anomalies. Nonetheless, Mitchell's definition identifies a clinically significant group that has substantially benefited from recent advances and, as a result, is undergoing the most rapid change in epidemiology (Van Der Bom 2011).

The movement of venous blood from the body to the arterial circulation generates low amounts of oxygen in the arteries in people with congenital heart disease, which results in bluish skin coloring. The quantity of blood flow shunting affects how much oxygen is depleted. Children with cyanotic heart disease frequently need surgical therapy because many do not live to adulthood. Eisenmenger's syndrome and tetralogy of Fallot are the two most typical causes of cyanotic congenital heart disease in adulthood (Wernovsky 2016).

Etiology: The cause of congenital heart disease is largely unknown, with only about 15% of cases having a known cause. Some chromosomal abnormalities, such as Down syndrome, are known to cause congenital heart disease, accounting for about 8-10% of cases. Defects in single genes account for about 3-5% of cases, often with associated non-cardiac malformations.

Environmental factors, such as maternal diabetes and phenylketonuria, account for about 2% of cases. Over 40 different genes have been implicated in non-syndromic congenital heart disease, with mutations in genes like GATA4 and NKX2-5 being known to cause the condition (Van Der Bom, The changing epidemiology of congenital heart disease 2021).

Effects on different stages:

Prematurity and low birth weight can worsen the health outcomes of infants with CHD by exacerbating certain negative effects. Preterm infants are vulnerable to various complications including pulmonary, hemodynamic, gastrointestinal, and developmental issues, which are also common risks for infants with CHD. Additionally, low birth weight, defined as less than 2.5 kg, may present a challenge for surgical repair and is often cited as a significant reason for postponing cardiac surgical procedures that require cardiopulmonary bypass (CPB).

The transition from fetal to neonatal life in full-term infants involves complex physiological processes, including the reduction of pulmonary vascular resistance and closure of various shunts. Infants with congenital heart disease (CHD) are at increased risk of cerebral hypoxic-ischemic injury due to altered cerebral blood flow. Delayed brain maturation and abnormal neurobehavioral patterns have been observed in these infants. Appropriate prenatal diagnosis of CHD and reducing the time to surgery can improve outcomes. Longer time to surgery is associated with an increased risk of adverse outcomes, including neurologic outcomes and increased cost. Early-term infants born at 37-38 weeks also have poorer long-term neurodevelopmental outcomes compared to those born beyond 39 weeks (Howell 2019).

Fetal Cardiovascular Physiology and Oxygen Delivery:

Structural heart disease in fetuses can lead to alterations in cerebral vascular resistance, which may affect neurological development and the transition from fetal to neonatal circulation. The circulation patterns of highly oxygenated blood to the brain and desaturated blood to the placenta may also be disrupted in fetuses with heart disease. Newborns with complex congenital heart disease often have neurological abnormalities prior to open heart surgery, including poor coordination of sucking swallowing, and breathing. Low cerebral blood flow, hypoxemia, and genetic syndromes may also contribute to developmental delays and brain abnormalities. Patients with a right to left shunt are at risk for air or particulate embolism reaching the brain from intravenous catheters (Wernovsky, Neurodevelopmental outcomes in children with congenital heart disease--what can we impact? 2016).

Decreases CNS Stability:

Researchers have been studying fetal brain development due to microcephaly, incomplete development of the white matter, and delayed cortical folding and white matter myelination. Dr. Limperopoulos conducted a groundbreaking study where she used fetal brain MRIs on 50 fetuses with CHD and 55 without. The study's cross-sectional data indicated significant differences in brain growth between the CHD and non-CHD fetuses, with the former starting to diverge from the latter in the first or third trimester of development. Fetuses with aortic arch anomalies had the poorest brain growth. Additionally, measurements of fetal cortical complexity also showed a similar divergence from normal development starting at the same time.

Conclusion:

Children with complex CHD are at risk for adverse neurodevelopmental outcomes. Although mild types of CHD do not affect CNS and neurodevelopmental outcomes, preschool and school-aged children with complex CHD exhibit cognitive and motor dysfunction, impaired visual-spatial and visual-motor skills, attention and academic difficulties, and a high incidence of learning disabilities. The factors that result in CNS injury and developmental dysfunction in these children are multiple and incompletely understood. Current investigations aim to understand the developing brain in the fetus with complex CHD, identify modifiable risk factors in the operating room and intensive care unit, and develop strategies to improve family psychosocial health, childhood development, and health-related quality of life after hospital discharge. An early post-operative surrogate variable with good predictive validity for long-term outcomes is needed, and MRI shows promise in this area. Identifying an appropriate surrogate variable can lead to reliable clinical trials to improve current outcomes.

Chapter 4:

Methodology

Methodology:

This survey has taken several steps and times to complete. As my survey is prescription based, I have collected 700 prescriptions. From there, I have got huge information and have created a vast report on the rational use of cardiovascular drugs.

Locations of my survey area:

I have resided in the Dhaka division, and I have chosen to conduct the survey in districts nearby. As prominent hospitals are predominantly found in urban settings, I have focused on visiting hospitals situated in the city areas.

Some of the hospitals I visited:

- National Institute of Cardiovascular Disease.
- Shaheed Tajuddin Ahmed Medical College, Gazipur.
- BIRDEM
- Pacchor Islamia hospital and diagnosis center.
- Upazila health complex, Razoir.
- Dhaka Medical College Hospital.
- DIABETIC ASSOCIATION MEDICAL COLLEGE & HOSPITAL.
- BSMMC, Hospital, Faridpur.
- 250 bedded General Hospital, Gopalgonj.

Duration and number of prescription collections:

I have visited hospitals for approximately 4 months and collected 700 prescriptions. Out of these prescriptions, almost 99% were prescribed by specialists, and less than 1% were prescribed by physicians.

Information collections:

Initially, the prescriptions were sorted based on the gender and age of patients. Later, I have categorized these cardiovascular drugs based on their therapeutic effect and have recorded them in a datasheet. Additionally, I have created charts and graphs to illustrate the quantity and percentage of these drugs.

Chapter 5:

Result and Discussion

Result:

Out of the 700 prescriptions, the majority of patients who visited different hospitals for cardiovascular disease are from urban areas. Among these patients, 80% are male and the remaining 20% are female. From these 700 prescriptions, 673 were prescribed specifically for cardiovascular disease, while the remaining 27 were prescribed for other diseases that were somewhat related to cardiovascular disease.

So, the no. of prescriptions for cardiovascular disease is mainly 673

Table (2): Comprehensive list of prescriptions according to their age:

Age	No. of prescriptions
<20	2
20-39	147
40-59	364
60-79	138
>80	22

Most patients affected by CVD are typically above the age of 30.

Table (3): Different cardiovascular disorders to these patients (In 673 prescriptions):

Cardiac disorders	Total prescriptions	Percentage %
Myocardial Infarction (STEMI & NSTEMI)	110	16
Left ventricular failure	65	10
Angina (Stable & Unstable)	148	22
Diastolic murmur	17	3
Hypertension	75	11
Acute myeloid leukemia	8	1
Chronic Rheumatic Heart Disease	23	3
Ischemic stroke (Recent & Pre)	227	34

Ischemic stroke is more causing cardiac disease. Which is 34%.

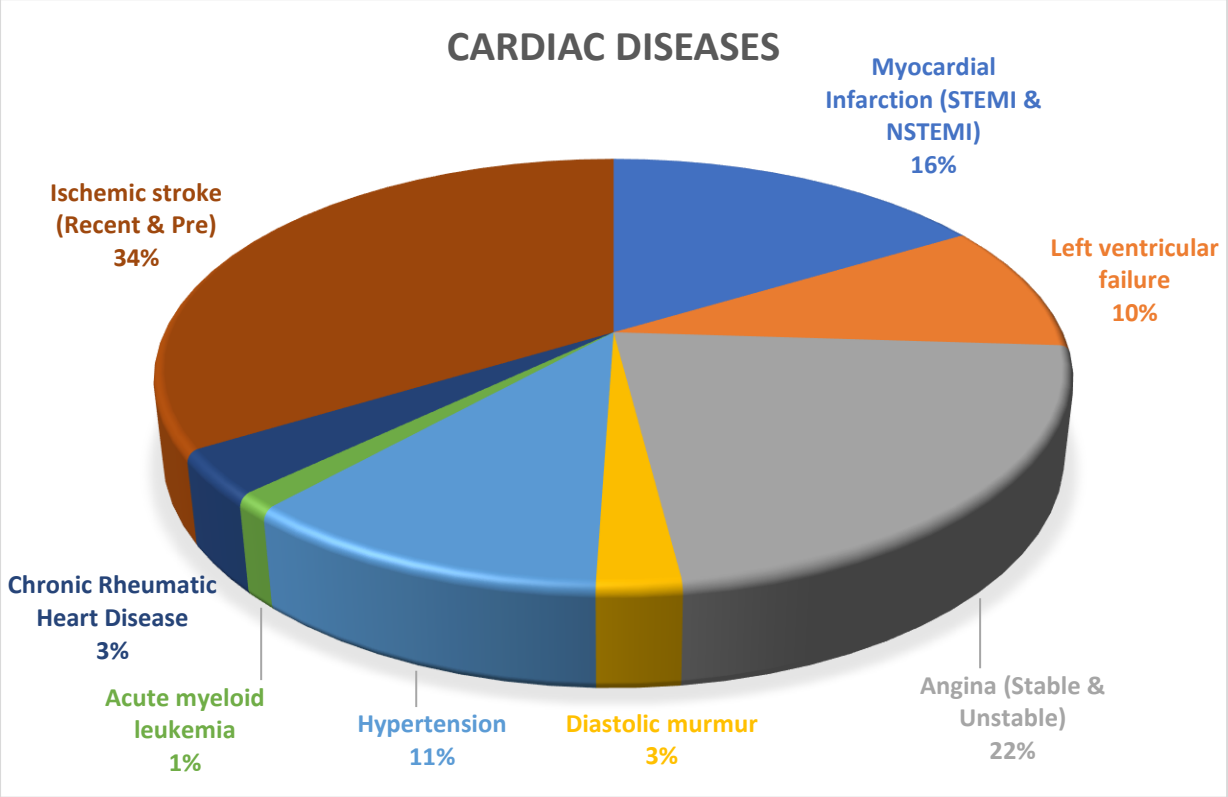

Fig 4: Different cardiovascular disorders in the patients

Table (4): Types of drugs used for cardiac diseases:

Therapeutic classes	Total prescriptions	Percentage %
Lipid-lowering drug	225	33
Organic nitrates	63	9
B-blockers	170	25
Antiplatelet	166	25
Anticoagulant	4	0.6
Thrombolytic	2	0.3
ACE inhibitor	27	4
Calcium channel blocker	140	21
Antihypertensive	10	1.5
Angiotensin II receptor Enzyme inhibitor	168	25
Vinpocetine	17	2.5
Diuretics	35	5

Here the result shows that the majority of people are suffering from CVD disease due to Cholesterol related problems. For this reason, Lipid-lowering drug is highly used. Food habit is the main cause of this problem.

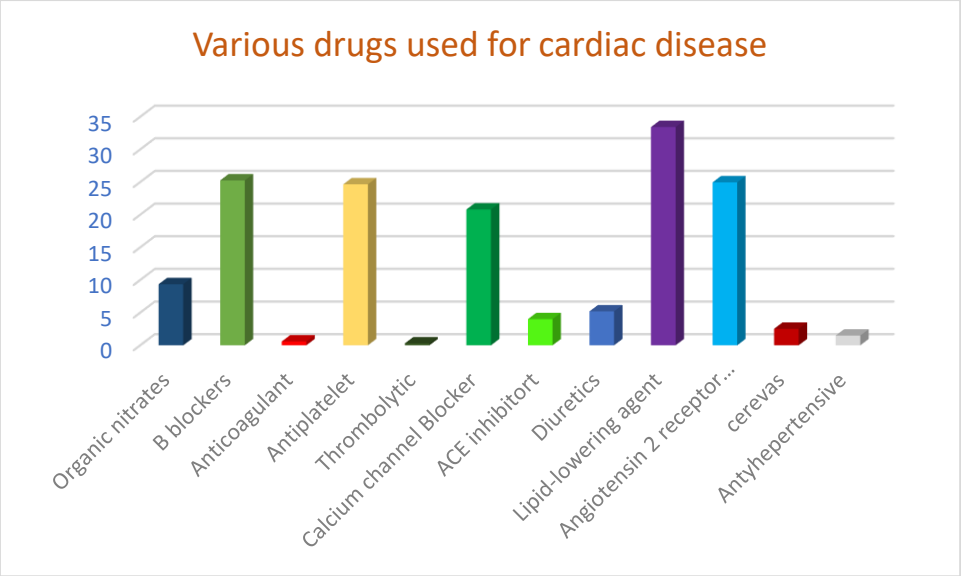

Fig 5: Various drugs used for cardiac disease

Table (5): Comparison among antiplatelet, thrombolytic and anticoagulants prescribed drugs:

Drugs Name	Total prescriptions	Percentage%
Warfarin	4	2
Aspirin	77	45.5
Clopidogrel	89	53
Streptokinase	1	0.6
Alteplase	1	0.6

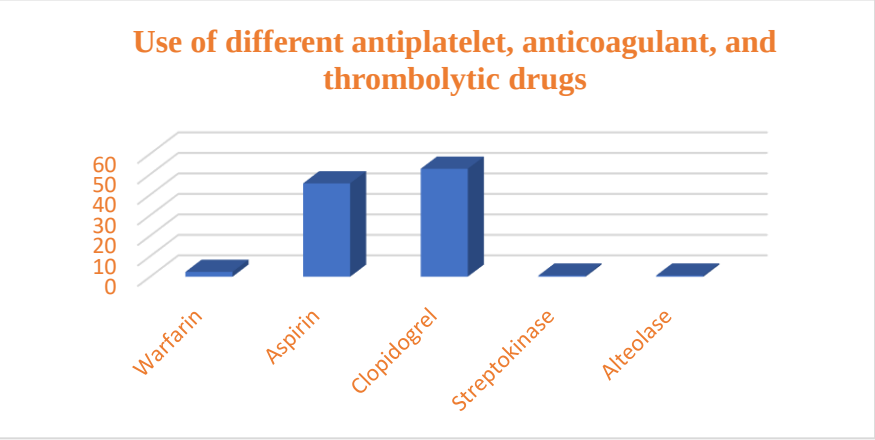

Fig 6: Use of different antiplatelet, anticoagulant, and thrombolytic drugs

Table (6): Use of various B-blockers:

Drug name	Total Prescriptions	Percentage %
Metoprolol	14	8
Carvedilol	2	1
Bisoprolol	65	38
Atenolol	35	20.5
Nebivolol	4	2
Propranolol	50	30

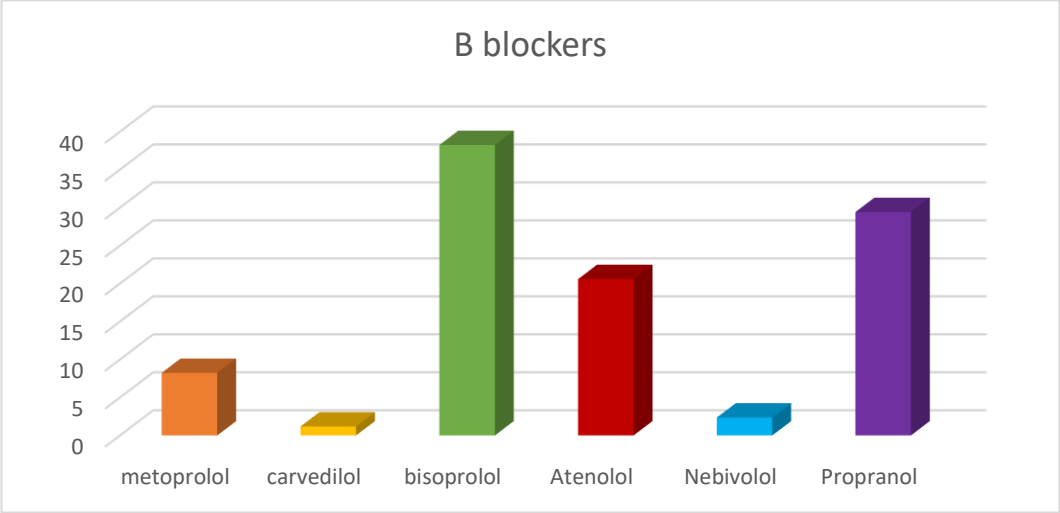

Fig 7: Use of various B-blockers

Table (7): Comparison among various types of calcium channel blockers prescribed drugs:

Drug name	No. of prescriptions	Percentage%
Amlodipine	74	53
Vinpocetine	17	12
trimetazidine	40	28.5
Nifedipine	4	3
Diltiazem	3	2
Verapamil	1	1
Cilnidipine	1	1

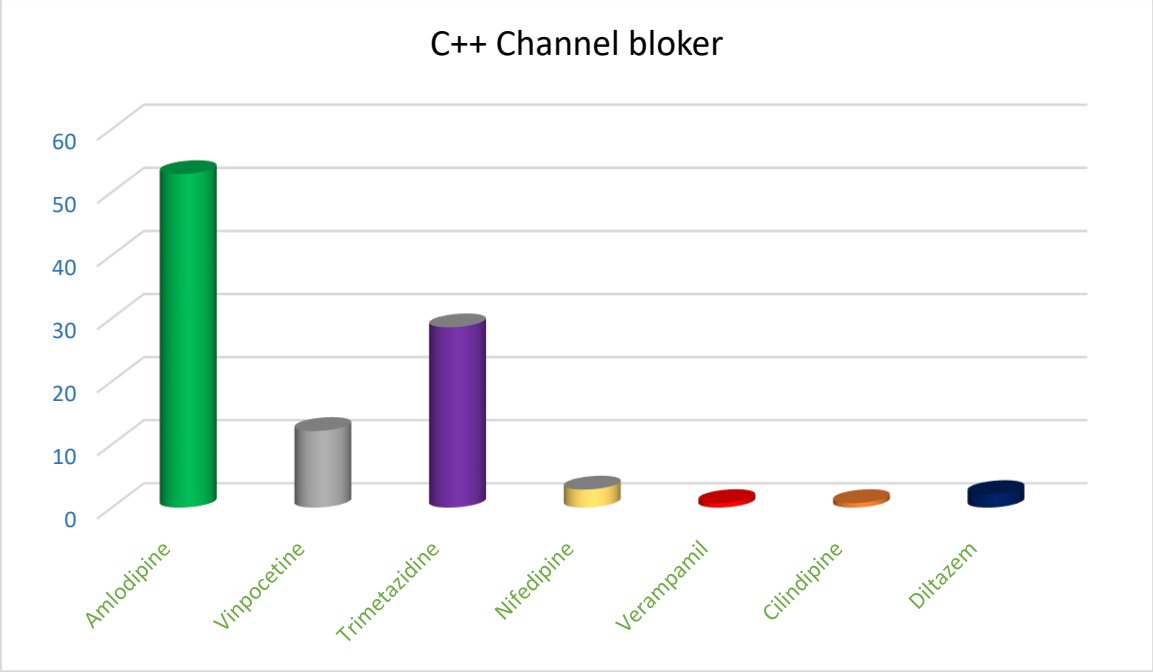

Fig 8: Comparison among various types of calcium channel blockers is using

Table (8): Comparison among lipid-lowering drugs:

Drug name	No. of prescriptions	Percentage %
Rosuvastatin	183	18
Atorvastatin	41	81
Fluvastatin	1	0.5

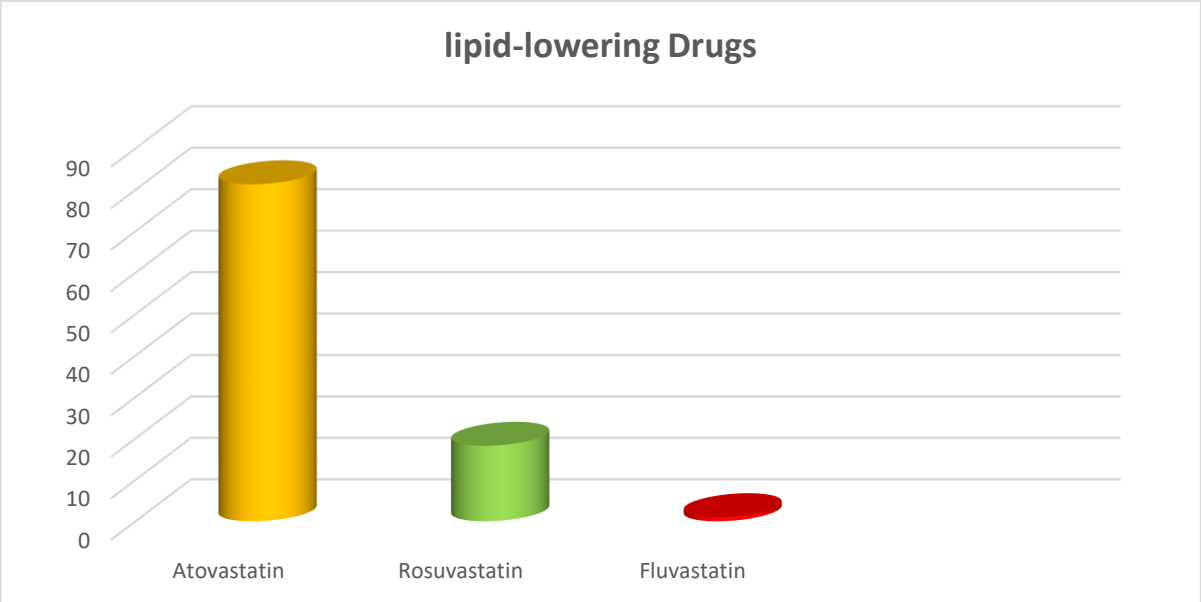

Fig 9: Comparison among lipid-lowering prescribed drug

Table (9): Comparison among loop diuretics prescribed drugs:

Drug name	No. of prescriptions	Percentage %
Frusemide	16	94
torsemide	1	6

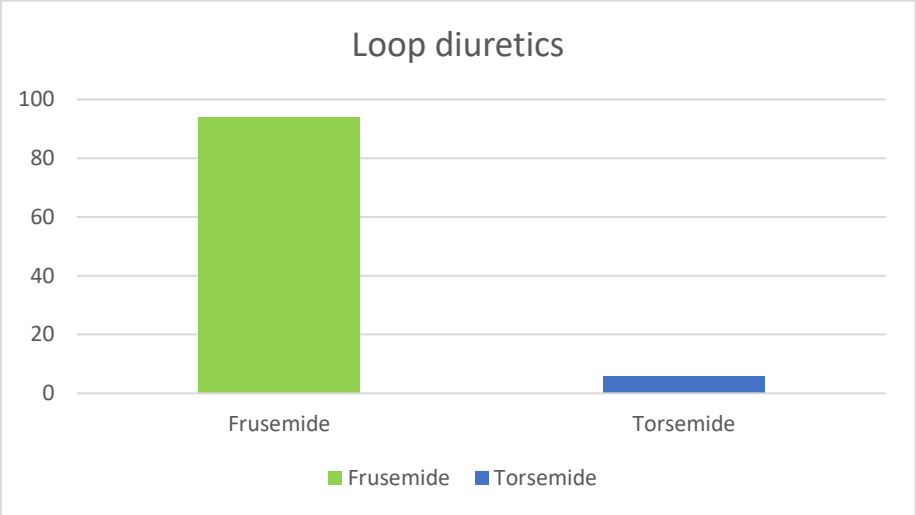

Fig 10: Comparison among loop diuretics prescribed drugs

Table (10): Comparison among k+ sparing diuretic prescribed drugs:

Drug name	No. of prescriptions	Percentage %
Spironolactone	17	89
Amiloride	1	11

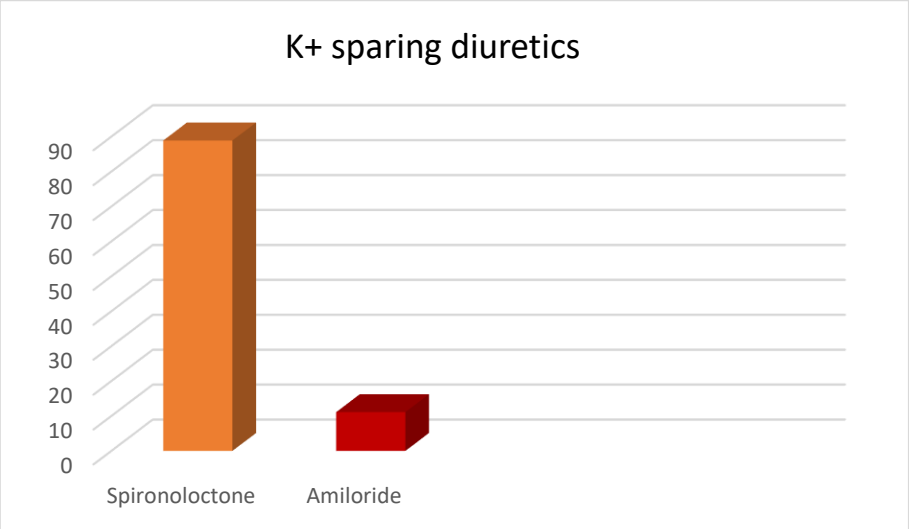

Fig 11: Comparison among k+ sparing diuretic prescribed drugs

Table (11): Comparison among Angiotensin 2 receptor enzyme antagonists:

Drug name	NO. of prescriptions	Percentage %
Olmesartan	35	21
Telmisartan	86	51
Losartan	47	28

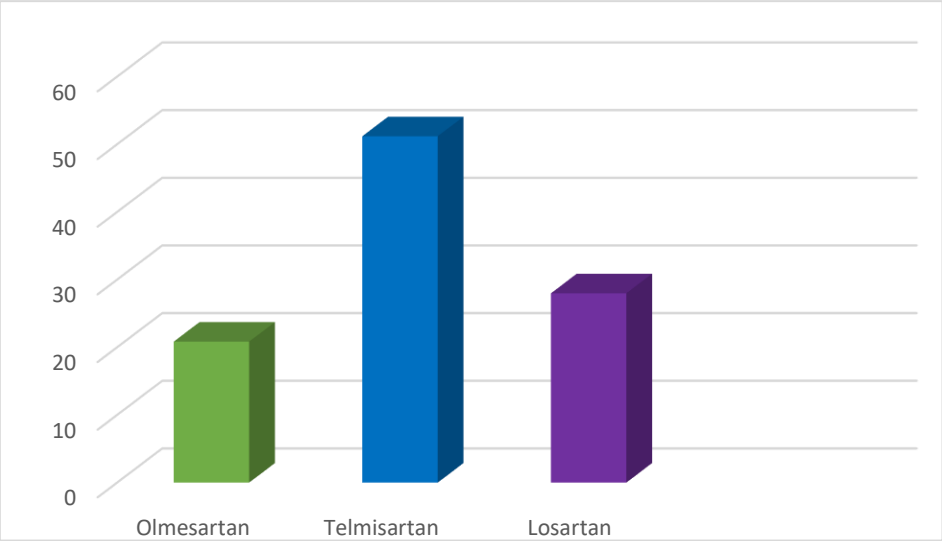

Fig 12: Comparison among Angiotensin 2 receptor enzyme antagonists

Table (12): Comparison among antihypertensive drugs:

Drug name	No. of prescriptions	Percentage %
Cilnidipine	4	40
prazosin	6	60

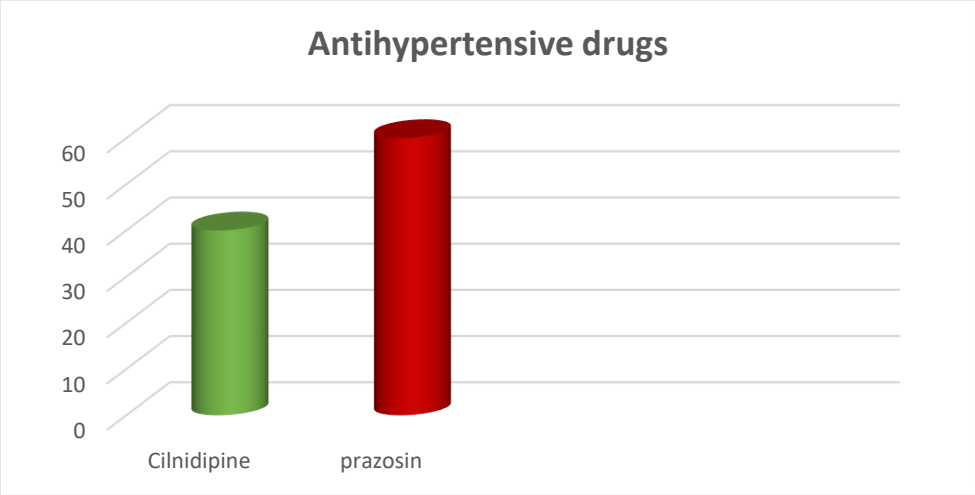

Fig 13: Comparison among antihypertensive drugs

Chapter: 6

Conclusion

6. Conclusion:

This study is driven across the Dhaka division, at different hospitals. It has taken almost 4 months (Jan 15- April 20). This survey mainly shows the causes of cardiovascular diseases on the basis of drugs are using to treat these diseases. Mainly male patients are more in number than females and the ratio is 60:40. The analysis shows that Ischemic stroke is a major cardiovascular disease. Lipid-lowering drugs are mostly used drugs. Organic nitrates, B blockers, ca++ channel blockers, and diuretics are also used.

There are some drawbacks to the survey. There is some lack of information. Types of diseases are always changing. The collection of prescriptions is more difficult. In hospitals, representatives from different companies treat in a bad manner. Shopkeepers are getting angry about more disturbance. On the other hand, Professor level doctor's interview is so much tough.

Chapter: 7

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