In-hospital Outcome of Diabetes Patients with Chronic Kidney Disease

By

Sabrina Kabir
Student ID: 14376002

A thesis submitted to the Department of Biotechnology in partial fulfillment of the requirements for the degree of
Master of Science

Biotechnology
Brac University
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Declaration

It is hereby declared that

1. The thesis submitted is my own original work while completing degree at Brac University.
2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
3. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.
4. I have acknowledged all main sources of help.

Student's Full Name & Signature:

_____

Sabrina Kabir
14376002

Approval

The thesis/project titled “In-hospital Outcome of Diabetes Patients with Chronic Kidney Disease” submitted by

1. Sabrina Kabir (14376002)

of final year has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Master of Science in Biotechnology on 11 March, 2021.

Examining Committee:

Supervisor:
(Member)

_____

Mohammad Rafiqul Islam, PhD
Associate Professor
Department of Mathematics and Natural Sciences

Program Coordinator:
(Member)

_____

Iftekhar Bin Naser, PhD
Assistant Professor
Department of Mathematics and Natural Sciences

Departmental Head:
(Chair)

_____

A F M Yusuf Haider, PhD
Professor and Chairperson
Department of Mathematics and Natural Sciences

Ethics Statement

I hereby humbly declare that this thesis entitled "**In-hospital Outcome of Diabetes Patients with Chronic Kidney Disease**" is based on work carried out by me and that no part of it has been presented previously for any higher degree.

The research work was carried out in the Department of Cardiology, National Institute of Cardiovascular Diseases, Dhaka.

Sabrina Kabir

Student ID: 14376002

Abstract/ Executive Summary

Chronic Kidney Disease is a risk factor for cardiovascular event- Angina, Myocardial Infarction, Arrhythmia, Diabetes and In-hospital complication. Several studies have been done to find out association of Chronic Kidney Disease with Diabetes with varying result. Few studies however, have investigated effect of Chronic Kidney Disease with Diabetes. The purpose of this study was to assess the In-hospital outcome of Diabetes with Chronic Kidney Disease in the department of Cardiology, National Institute of Cardiovascular Diseases. This was a prospective longitudinal study.

Acknowledgement

All praises to Almighty Allah, who has bestowed his kindness upon me by giving me the opportunity, courage, patience and providing me enough energy to carry out and complete the thesis successfully.

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I put my highest regards to all my study subjects, who consented without any hesitation for all examinations and investigations.

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Sabrina Kabir

Student ID: 14376002

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List of Acronyms

ACEI	Angiotensin converting enzyme inhibitor
ACS	Acute coronary syndrome
AKI	Acute kidney injury
ARF	Acute renal failure
ATN	Acute tubular necrosis
BNP	B-type natriuretic peptide
BUN	Blood urea nitrogen
CAD	Coronary Artery Disease
CCF	Congestive cardiac failure
CI	Confidence interval
CKD	Chronic kidney disease
CrCl	Creatinine clearance
CVD	Cardiovascular Disease
DM	Diabetes Mellitus
ESRD	End stage renal disease
(e)GFR	(estimated) Glomerular filtration rate
HD	Hemodialysis
HR	Hazard ratio

ICM	Diabetes
LVEF	Left ventricular ejection fraction
MACE	Major adverse cardiac event
NICE	National Institute for Health and Care Excellence
NICVD	National Institute of Cardiovascular Diseases
NSTEMI	Non-ST elevation MI
NT-proBNP	N-terminal pro b-type natriuretic peptide
NYHA	New York Heart Association
OR	Odds ratio
PCI	Percutaneous coronary intervention
RCT	Randomized controlled trial
RIFLE	Risk, Injury, Failure, Loss, End stage renal disease
RR	Relative risk
SD	Standard deviation
STEMI	ST elevation myocardial infarction

Chapter 1

Introduction

1.1 Introduction

According to the World Health Organization (WHO), almost 23.6 million deaths are going to be attributed to cardiovascular diseases (CVD), mainly stroke and heart diseases by the year 2030. CVDs include coronary heart disease (CHD), cerebrovascular diseases, peripheral arterial disease, rheumatic heart disease, congenital heart diseases, deep vein thrombosis and pulmonary embolism. The behavioral risk factors of CVD are smoking, physical inactivity and harmful use of alcohol. The metabolic risk factors are high blood pressure, raised blood glucose, raised blood lipids, overweight and obesity. Underlying factors include social, economic and cultural change manifested by globalization, urbanization, and population ageing. Other determinants include poverty, stress and hereditary factors (WHO 2011). CHD is among the leading causes of death in industrialized countries, with higher rates in men than in women; although as women age, CHD related mortality increases. Nutrition factors have been shown to play a major role in the etiology and management of CHD (Valentin F. et al. 2017).

The cardiovascular system is closely related to function of the kidneys. Renal insufficiency can affect cardiac performance leading to its failure which consequently worsens renal function. The fact, that impairment of one component of the cardiorenal system aggravates dysfunction of the other is clinically very important (Lisowska A. et al. 2004).

Heart failure (HF) is a specific term used to define the clinical syndrome when the heart is unable to pump enough blood to supply the metabolic needs of the body (Braunwald E.2019). Subjects with myocardial failure can have symptomatic HF or asymptomatic ventricular dysfunction. Symptoms of exercise intolerance are typically assessed by the New York Heart Association (NYHA) functional classification.

About half of all deaths in end-stage renal disease (ESRD) patients are attributable to cardiac causes (Murphy S, 2003). Heart failure and coronary heart disease (CHD) are highly prevalent in this population.

Chronic kidney disease (CKD) arises as a worldwide disease, affecting patients of different ages of ethnicities becoming an independent cardiovascular risk factor. Several studies suggested that mild-to-moderate elevations in serum creatinine levels are associated with increased rates of death from any cause and also, from cardiovascular causes (Levey AS, et al. 2017).

Composed of multiple adverse pathophysiological causes leading to the increased morbidity and mortality in CKD in general, an association with traditional risk factors configures an additional cause for worse outcome of CKD patients (Ritz E. 2003)

Diabetes is a growing public health problem (Hauptman PJ, Schwart PJ, Gold MR, et al. 2012) worldwide, and the incidence and prevalence of Diabetes continue to increase. ICM is also associated with high comorbidities (Schocken dd, et al.1992). Many variables have been assessed for their prognostic potential in ICM patients. A large number of clinical and hemodynamic variables have been identified as markers of prognosis in ICM. Important determinants of prognosis include the clinical severity of the disease [New York Heart Association (NYHA) functional class], the degree of left-ventricular ejection fraction (LVEF), (Gradman A. et al 1989,) residual ischemia and multivessel disease after myocardial infarction, myocardial viability, hemodynamic abnormalities, serum sodium, urea, creatinine, neurohormones and anemia, iron (Parameshwar J. et al. 1992).

The coexistence of Chronic Kidney Disease in Ishchemic cardiomyopathy patients is often defined as cardiorenal syndrome. Renal dysfunction is a common complication of Diabetes patients. Renal function is a prognostic risk marker for longterm mortality in Diabetes patients. The impaired hemodynamic status has probably the most negative effect on the renal function

in advanced CHF (Smilde TD. et al.2006). We have investigated the effect of renal dysfunction on cardiovascular mortality in patients with Diabetes.

There are several possible reasons for the association between kidney dysfunction and outcome in ICM patients. The prognosis becomes worse when patients have higher age, diabetes, hypertension. Impaired kidney function causes increased mortality results from decreased GFR.

Kidney dysfunction may be secondary to venous congestion, forward failure, renin-angiotensin-aldosterone system (RAAS) stimulation and sympathetic activation in heart failure (Di lullo L. et al. 2015).

Our aim was investigating the relationship between Chronic Kidney Diseases with outcome of Diabetes patients with coronary artery disease (CAD).

1.2 Rationale of the study

Renal dysfunction is a strong predictor of mortality in congestive heart failure patients. The precise mechanisms underlying renal dysfunction in congestive heart failure patients remain unclear. It has been reported that this might be due to vascular atherosclerosis or impaired hemodynamic status. Acute heart failure or congestive heart failure frequently leads to a reduction in cardiac output. The reduction in cardiac output can decrease blood pressure. Reduced blood pressure can decrease renal perfusion. Activation of the reninangiotensin-aldosterone (RAA) system rapidly influence heart failure, due to decreased renal perfusion.

Major risk factors including diabetes, increasing age, hypertension can also affect the renal function. Congestive heart failure is characterized by systemic inflammation, as evidenced by circulating levels of several inflammatory cytokines. Inflammation may facilitate renal function deterioration in congestive heart failure patients.

In this study, we investigate the effects of renal dysfunction with Diabetes patients to observe the hospital readmission, arrhythmia, cardiogenic shock and patient's mortality. But no such study was previously done in NICVD regarding this issue. So, the present study will be quite rational and time worthy.

1.3 Hypothesis

Chronic Kidney Disease has an adverse effect on In-hospital outcome in patient with Diabetes.

1.4 Objectives

General Objectives:

To observe in-hospital outcome of Diabetes patients with the Chronic Kidney Disease.

Specific Objectives:

- To determine the in-hospital outcome of Diabetes patients with normal renal function.
- To determine the in-hospital outcome of Diabetes patients with Chronic Kidney Disease.
- To compare outcome between two groups.

Chapter 2

Literature Review

2.1 Diabetes

Diabetes mellitus is recognized as being a syndrome, a collection of disorders that have hyperglycaemia and glucose intolerance as their hallmark, due either to insulin deficiency or to the impaired effectiveness of insulin's action, or to a combination of these. In order to understand diabetes, it is necessary to understand the normal physiological process occurring during and after a meal. Food passes through the digestive system, where nutrients, including proteins, fat and carbohydrates are absorbed into the bloodstream. The presence of sugar, a carbohydrate, signals to the endocrine pancreas to secrete the hormone insulin. Insulin causes the uptake and storage of sugar by almost all tissue types in the body, especially the liver, musculature and fat tissues (Roussel, 1998).

Unfortunately, there is no cure for diabetes yet but by controlling blood sugar levels through a healthy diet, exercise and medication the risk of long-term diabetes complications can be decreased. Long-term complications that can be experienced are:

- eyes – cataracts and retinopathy (gradual damaging of the eye) that may lead to blindness
- kidneys – kidney disease and kidney failure
- nerves – neuropathy (gradual damaging of nerves)
- feet – ulcers, infections, gangrene, etc.
- cardiovascular system – hardening of arteries, heart disease and stroke (Heart foundation, 2003).

The progressive nature of the disease necessitates constant reassessment of glycemic control in people with diabetes and appropriate adjustment of therapeutic regimens. When glycemic control is no longer maintained with a single agent, the addition of a second or third drug is usually more effective than switching to another single agent.

Medicinal plants which have showed anti-diabetic activity during earlier investigations include Panax species, Phyllanthus species, Acacia arabica, Aloe vera, Aloe barbadensis, Artemisia pallens, Momordica charantia, Alium cepa, Trigonella foenum-graecum etc (Soumyanath, 2006). Very few South-African plants have been scientifically analyzed for their anti-diabetic characteristics. The most recent work was done by Van Huyssteen (2007) and Van de Venter et al. (2008).

2.2 Classification of Diabetes Mellitus

A major requirement for orderly epidemiologic and clinical research on and for the management of diabetes mellitus is an appropriate classification. Furthermore, the process of understanding the etiology of a disease and studying its natural history involves the ability to identify and differentiate between its various forms and place them into a rational etiopathologic framework (Harris and Zimmet, 1997).

The contemporary classification of diabetes and other categories of glucose intolerance, based on research on this heterogeneous syndrome, was developed in 1979 by the National Diabetes Data Group. Two major forms of diabetes are recognized in Western countries; insulin dependent diabetes mellitus (IDDM, type I diabetes) and non-insulin dependent diabetes (NIDDM, type II diabetes). The evidence of this heterogeneity is overwhelming and includes the following:

a) there are many distinct disorders, most of which are individually rare, in which glucose intolerance is a feature;

b) there are large differences in the prevalence of the major forms of diabetes among various racial or ethnic groups world-wide;

c) glucose tolerance presents variable clinical features, for example, the differences between thin ketosis-prone, insulin dependent diabetes and obese, non-ketotic insulin resistant diabetes;

d) genetic, immunologic and clinical studies show that in Western countries, the forms of diabetes with their onset primarily in youth or in adulthood are distinct entities;

e) the type of non-insulin requiring diabetes in young people, which is inherited in an autosomal dominant fashion is clearly different from the classic acute diabetes of juveniles; and

f) in tropical countries, several clinical presentations occur, including fibrocalcific pancreatitis and malnutrition-related diabetes.

This and other collective evidence have been used to divide diabetes mellitus into four distinct types namely:

- insulin dependent diabetes,
- non-insulin dependent diabetes,
- malnutrition-related diabetes,
- other types of diabetes.

The classification highlights the marked heterogeneity of the diabetic syndrome. Such heterogeneity has important implications not only for clinical management of diabetes but also for biomedical research (Harris and Zimmet, 1997). In this study the focus was mainly on type II diabetes while type I diabetes was discussed briefly to point out the differences between the two types of diabetes.

2.2.1 Insulin dependent diabetes mellitus (IDDM)

The subclass of diabetes, type I diabetes, is generally characterized by the abrupt onset of severe symptoms, dependence on exogenous insulin to sustain life and proneness to ketosis even in the basal state, all of which is caused by absolute insulin deficiency. IDDM is the most prevalent type of diabetes among children and young adults in developing countries, and was formally termed juvenile diabetes (Harris and Zimmet, 1997). It is a catabolic disorder in which circulating insulin is virtually absent, plasma glucagon is elevated, and the pancreatic B cells fail to respond to all insulinogenic stimuli (Nolte and Karam, 2001).

Type I diabetes is thought to result from an infectious or toxic environmental contingency in people whose immune systems are genetically predisposed to develop a vigorous autoimmune response against pancreatic B cell antigens. Extrinsic factors that might affect B cell functioning include damage caused by viruses such as the mumps virus and coxsackie virus B4, by chemical agents, or by destructive cytotoxins and antibodies released from sensitized immunocytes. An underlying genetic defect relating to pancreatic B cell replication or function may predispose a person to the development of B cell failure after viral infections. In addition, specific HLA genes may increase susceptibility to a diabetogenic virus or may be linked to certain immune response genes that predispose patients to a destructive autoimmune response against their own islet cells (auto-aggression). Observations that pancreatic B cell damage appears to be lessened when immunosuppressive drugs such as cyclosporine or azathioprine are given at the initial manifestation of type I diabetes support the importance of auto-aggression by the immune system as a major factor in the pathogenesis of this type of diabetes (Nolte and Karam, 2001).

2.2.2 Non-insulin dependent diabetes mellitus (NIDDM)

Type II diabetes greatly out numbers all other forms of diabetes. Patients with NIDDM are not dependent on exogenous insulin for prevention of ketonuria and are not prone to ketosis. However, they may require insulin for the correction of fasting hyperglycaemia if this cannot be achieved with the use of diet or oral agents, and they may develop ketosis under special circumstances such as severe stress precipitated by infections or trauma (Harris and Zimmet, 1997).

The pathogenesis in type II diabetes is that the pancreas produces insulin but the body does not utilize the insulin correctly. This is primarily due to peripheral tissue insulin resistance where insulin-receptors or other intermediates in the insulin signaling pathways within body cells are insensitive to insulin and consequently glucose does not readily enter the tissue leading to hyperglycaemia or elevated blood glucose concentrations (Albright, 1997). Obesity, which generally results in impaired insulin action, is a common risk factor for this type of diabetes, and most patients with type II diabetes are obese (Nolte and Karan, 2001) and will ultimately require multiple anti-diabetic agents to maintain adequate glycaemic control (Gerich, 2001).

2.3 Chronic Kidney Disease

Chronic Kidney Disease dramatically increases the risk of developing Cardiovascular Diseases (CVD) (3-30 times depending on CKD stage and study). Nearly half of all deaths in Chronic Kidney Disease patients are from cardiovascular events, and Chronic Kidney Disease patients are more likely to die from CVD than progress to ESRD during their lifetime.

Risk factors for the development of CVD in patients with Chronic Kidney Disease can be divided into traditional and nontraditional factors. Traditional factors include hyperlipidemia, hypertension, diabetes, and smoking and are important risk factors for cardiovascular disease also among patients without Chronic Kidney Disease. These risk factors are also risk factors for Chronic Kidney Disease, and their prevalence has been reported to be twice as high among Chronic Kidney Disease patients compared to non-Chronic Kidney Disease patients. Nontraditional risk factors refer to the effects of chronic renal dysfunction on cardiac health.

Autonomic function is impaired in Chronic Kidney Disease patients, with a relative dominance of sympathetic over parasympathetic activity. The autonomic nervous system constitutes the efferent arm of the baro- and chemoreceptor reflex arcs. These reflexes are impaired in Chronic Kidney Disease.

Chronic Kidney Disease exacerbates atherosclerotic processes. Chronic Kidney Disease patients have more severe arterial hypertrophy and calcification and have stiffer arteries compared to non-Chronic Kidney Disease patients.

The mechanisms leading to arterial pathology and endothelial dysfunction in Chronic Kidney Disease are incompletely understood, but increased oxidative stress, low-grade inflammation, uremic toxins, increased wall stress (associated with arterial hypertension), and impaired calcium/phosphorous homeostasis likely contribute.

Left ventricular hypertrophy is present in 40% of Chronic Kidney Disease patients (mostly to the eccentric type), and the prevalence increases with declining GRF; for ESRD patients on hemodialysis, it is over 75%. Left ventricular hypertrophy is likely promoted by chronic hypertension (increased after load), anemia (reduced oxygen delivery), sympathetic and RAAS hyperactivity (increased cardiac fibrosis), and volume overload.

The frequent association of cardiovascular disease (CVD) with chronic kidney disease (CKD) is important because individuals with CKD are more likely to die of CVD than to develop kidney failure, CKD is treatable, and CKD appears to be a risk factor for CKD (Sarnak et al. 2003).

2.4 Aspect of cardiovascular disease in Bangladesh

CAD is an increasingly important medical and public problem, and is the leading cause of mortality in Bangladesh. The exact prevalence of CAD in Bangladesh is not known. Only a limited number of small-scale epidemiological studies are available. Probably the prevalence of IHD was first reported in 1976. A recent study indicated that, the prevalence of CAD among Bangladeshi population was between 1.85% and 3.4% in rural and 19.6% in an urban sample of working professionals (Islam and Majumder, 2013).

In 1998, the National Kidney Foundation (NKF) Task Force on Cardiovascular Disease in Chronic Renal Disease issued a report emphasizing the high risk of CVD in CKD. This report showed that there was a high prevalence of CVD in CKD patients and that mortality due to CVD was 10 to 30 times higher in dialysis patients than in general population. The task force recommended that patients with CKD be considered the “highest risk group” for subsequent CVD events and that treatment recommendations based on CVD risk stratification should take into account the highest-risk status of patients with CKD (Sarnak et al. 2003).

Reduced GRF

Reduced GFR is associated with a high prevalence of CVD risk factors and higher prevalence of CVD surrogates and clinical CVD. For example, several studies across a broad spectrum of population, such as the HOPE study, the Cardiovascular Health Study (CHS), the Hypertension

Optimal Treatment (HOT) study, the Framingham and Framingham Offspring studies, and the Atherosclerosis Risk In Communities (ARIC) study, have shown that levels of systolic blood pressure and total cholesterol and the percentage of subjects with low HDL are greater in subjects with decreased GFR. In addition, the percentage of subjects with diabetes, electrocardiographic LVH, IHD, and heart failure Diabetes are higher in those with decreased GFR (Sarnak et al. 2003).

Diabetes patients has previous history of Myocardial Infarction (MI) or non-ST elevation MI. This patients has reduced left ventricular Ejection fraction 35%. The myocardium of this patients has irreversible changed and ventricular remodeling. Renal hypo perfusion has done and renal function also decline. We investigated Chronic Kidney Disease on Diabetes to see the In-hospital outcome like Arrhythmia, Cardiogenic Shock, Death which causes recurrent hospital admission.

2.5 Relevant Studies

Hueb et al. (2019) studied on "Effect of chronic kidney disease in Diabetes". A strong association exists between renal impairment (CKD) and Diabetes (CAD). The role of renal impairment in the long-term prognosis of Diabetes patients with versus those without Diabetes patients is unknown. This study investigated whether renal impairment affects ventricular function.

In patients with preserved renal function (n=405), 73 events (18%) occurred, but 108 events (21.1%) occurred among those with Diabetes (n=513) (p<.001). Regarding left ventricular ejection fraction (LVEF) <50%, they found 84 events (21.5%) in Diabetes patients and 12(11.8%) in those with preserved renal function (P<.001). The presence of LVEF <50% brought about a modification effect. Death occurred in 22 (5.4%) patients with preserved renal function and in 73 (14.2%) with Diabetes (P<.001). In subjects with LVEF <50%, 66 deaths (16.9%) occurred in Diabetes patients and 7 (6.9%) in those with preserved renal function (p=.001). No differences were found in Diabetes strata regarding events or overall death among

those with preserved LVEF. In a multivariate model, GFR remained an independent predictor of death (P<.001).

They found no deleterious effects of Diabetes in patients with CAD when ventricular function was preserved. However, there was a worse prognosis in patients with Diabetes and ventricular dysfunction.

Ertas et al. (2012) studied to Renal function has an effect on cardiovascular mortality in patients with Diabetes. They found Data about renal function and glomerular filtration rate Baseline characteristics of the study group. Six hundred and thirty-seven patients with ICM were evaluated between January 2003 and January 2011. All individuals in the study population were admitted to the cardiology clinic because of decompensated heart failure. In this prospective observational study, a total of 637 patients (409 men, 228 women, 18-94 years old, mean age 63±13 years; New York Heart Association (NYHA) functional class II-IV) with diagnoses of Diabetes (402).

By the end of the study, 228 patients had died due to cardiovascular reasons. Renal dysfunction had an effect on cardiovascular mortality in patients with Diabetes.

Lofman et al. (2016) studied to Prevalence and prognostic impact of kidney disease on heart failure patients. They studied 47716 patients in the Swedish Heart Failure Registry. Patients were divided into five renal function strata based on estimated glomerular filtration rate using the Chronic Kidney Disease Epidemiology Collaboration equation. The adjusted association between kidney function and outcome was examined by Cox regression.

51% of the patients had eGFR <60 mL/min/1.73m^2 and 11% had eGFR<30. There was increasing mortality with decreasing kidney function regardless of age, presence of diabetes, New York Heart Association HYHA class, duration of heart failure and haemoglobin level. The risk HR (95% CI) persisted after adjusting for differences in baseline characteristics, severity of heart disease, and medical treatment.

Kidney dysfunction is common and strongly associated with short-term and long-term outcomes in patients with heart failure.

Lisowska et al. (2004) studied to "Heart failure in the patients with chronic kidney disease". Heart failure is highly prevalent in the population with chronic kidney disease. Upon starting dialysis, 37% of patients will have had a previous episode of heart failure, doubling the risk of death. Both systolic and/or diastolic function may be impaired. 15% of patients starting dialysis therapy have systolic dysfunction of the left ventricle. The prevalence of diastolic dysfunction at dialysis inception is unknown, but is likely to be high. Either systolic or diastolic dysfunction can lead to clinically evident congestive heart failure.

Chapter 3

Methods

3.1 Study design:

Prospective longitudinal study.

3.2 Place of study:

Department of cardiology, National Institute of Cardiovascular Diseases & Hospital Dhaka.

3.3 Period of study:

January 2020 to December 2020.

3.4 Study population:

Patient admitted in cardiology department both in CCU and wards.

3.5 Sampling Technique:

Convenient purposive sampling.

3.6 Sampling population:

All the patients with Diabetes admitted in NICVD with in the study period.

3.7 Sample size:

Total 120 cases will be the sample size for the study.

3.8 Sample size calculation:

As the sampling population was confined within patients of Diabetes in the Department of Cardiology, NICVD; the sample size calculation to test hypothesis in case of cross-sectional study was:

Estimation of sample size:

$$n = \left[\frac{z_\alpha \sqrt{2p(100-p)} + z_\beta \sqrt{p_1(100-p_1) + p_2(100-p_2)}}{p_1 - p_2} \right]^2$$

p_1 = proportion in one group = 50

p_2 = Proportion in other group = 70

p = $(p_1+p_2) \div 2 = 60$

z_α = z-value of SND at a 5% level of significance = 1.96

z_β = z-value of SND at a 80% power = 0.85

$$n = \left[\frac{z_\alpha \sqrt{2p(100-p)} + z_\beta \sqrt{p_1(100-p_1) + p_2(100-p_2)}}{p_1 - p_2} \right]^2$$

$$= \left[\frac{1.96\sqrt{120(100-60)} + 0.85\sqrt{50(100-50) + 70(100-70)}}{-20} \right]^2$$

$$= \left[\frac{1.96\sqrt{120(40)} + 0.85\sqrt{50(50) + 70(30)}}{-20} \right]^2$$

$$= \left[\frac{1.96\sqrt{4800} + 0.85\sqrt{2500 + 2100}}{-20} \right]^2$$

$$= \left[\frac{1.96\sqrt{4800} + 0.85\sqrt{4600}}{-20} \right]^2$$

$$= \left[\frac{1.96x69.28 + 0.85x67.82}{-20} \right]^2$$

$$= \left[\frac{135.79 + 57.65}{-20} \right]^2$$

$$= \left[\frac{193.44}{-20} \right]^2 = (9.67)^2 = 93.51$$

= 94

The estimated sample size is 120. As the study was done in a single centre within a limited period of time, so all the available sample within the study period fulfilling the inclusion and exclusion criteria were included in the study.

3.9 Ethical Consideration

The researcher is concerned about the ethical issues related to the study. In this study the following criteria will be followed to ensure maintaining the ethical values.

Formal ethical clearance will be taken from the ethical review committee of the NICVD conducting the study.

Confidentiality of the person and the information will be maintained, observed and unauthorized persons won't have any access to the data.

Informed written consent will be taken from the subject.

The content of the consent requirements will be such:

1. Explanation of the nature & purpose of the study,
2. Explanation of the procedure of study
3. Explanation that they have the right to refuse, accept & withdraw to participate in the study.

The participants don't gain financial benefit from this study.

3.10 Enrollment of the subjects:

A) Inclusion Criteria:

- Age > 18 years ≤ 75 years
- Presence of Q wave in ECG suggesting previous MI
- On Echocardiography
  - LVIDD more than 55
  - Ejection fraction less than 35% in Echocardiography.
  - Regional Wall motion abnormality, Scar tissue.

B) Exclusion criteria:

- Concomitant presence of any predominant severe systemic illness
- Patients with the symptoms of acute heart failure due to other concomitant diseases.

3.11 Variables:

a. **Demographic variables**:
    - Age
    - Sex
    - Height
    - Weight

b. **Risk factor variables:**
    - Hypertension
    - Lipid abnormalities (increased level of total and LDL cholesterol, Decreased-level of HDL cholesterol, increased TG)
    - Diabetes
    - Smoking

c. **Investigation variables**:
    - On Echocardiography
        - LVIDD more than 55
        - Ejection fraction less than 35% in Echocardiography.
        - Regional Wall motion abnormality, Scar tissue.
    - Serum creatinine
    - e GFR
    - Troponine I

d. Outcome and complications variables:

- Heart failure according to NYHA,
- Arrhythmia
- Cardiogenic shock
- Death
- Repetitive Hospital admission

3.12 Methodology

Procedure for data collection:

All patients admitted in the department of cardiology, NICVD, fulfilling the inclusion and exclusion criteria will be considered for the study.

- Informed written consent will be taken from each patient before enrollment.
- Meticulous history will be taken and detailed clinical examination will be done and recorded in pre designed structured form.
- Demographic data: Age, sex.
- Blood sample for Blood glucose, Serum creatinine.
- GRF from patient history
- All the above information was recorded in a data collection form consisting of relevant questioners, which was approved by an institutional review before beginning the study.
- Patients were followed up throughout their hospital stay and development of complications or occurrence of death were noted and recorded in the data collection form.
- Following parameters studied:
  - Heart failure
  - Cardiogenic shock

- Significant arrhythmias
- Unstable angina
- Death

Renal function

The primary indicator of renal function is the glomerular filtration rate (GFR). GFR is estimated from serum creatinine using online GFR calculator.

Patient follow-up

Clinical follow-up was done in CCU and WARD by periodic examination of patients. Index Hospital admission duration, the period of hospital staying the patient was examined by History taking, like shortness of breathing, number of readmission, any history of palpitation, syncope, vertigo, pedal edema etc taken. Clinical examination like pulse, BP, pericardium, JVP, Liver tenderness, Ascitis, cold clammy skin, urine output, height, weight etc was examined.

Then serum creatinine, blood sugar, serum electrolytes, Hb% etc was done.

Form serum creatitine e-GFR is measured from online calculator.

3.13 Data Collection

Data collected by using pre-designed data sheet.

3.14 Statistical methods

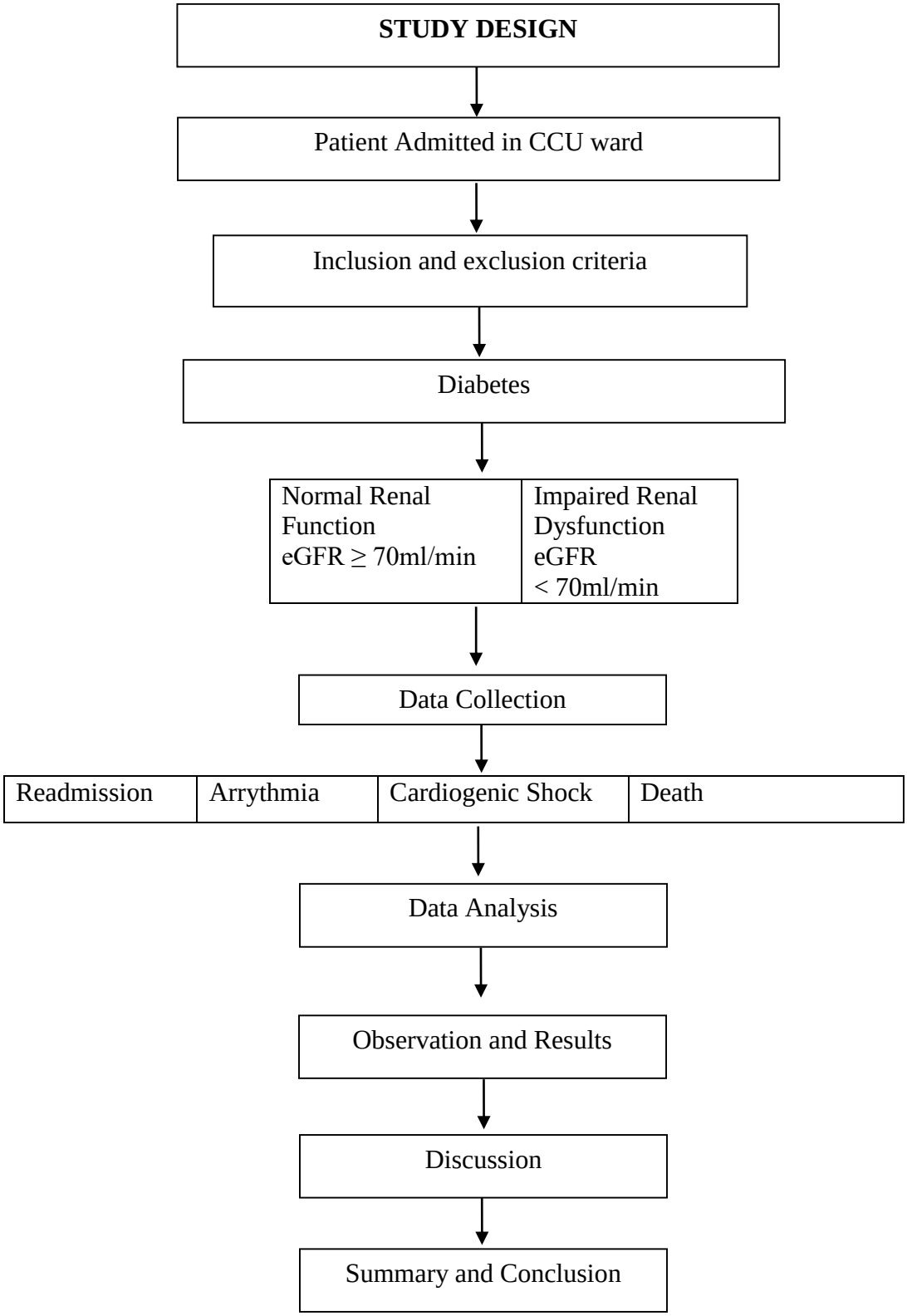
The numerical data obtained from this study will be analyzed and significance of difference will be estimated by using statistical methods. Continuous variable (quantitative data) will be estimated by using statistical methods. Continuous variable will be expressed as mean value ± standard deviation and compared using unpaired t- test, categorical variables (qualitative data) will be expressed as frequencies with percentages and compared using chi-squared (x^2) test. A

probability (p) value < 0.05 will be considered as statistical significant, but p > 0.05 will be considered as insignificant.

Statistical analysis will be carried out by using SPSS Version 23.0 (Statistical Package for the Social Science by SPSS inc. Chicago, IL, USA, 2015)

3.15 Grouping of the Study Patients

Study population was grouped initially as normal and Chronic Kidney Disease, on the basis of estimated serum GFR (ml/min/1.73 m^2) by GFR:
Group 1 patient having GFR ≥ 70 ml/min – Control group
Group 2 patient having GFR < 70 ml/min – Case group


STUDY DESIGN
Patient Admitted in CCU ward
Inclusion and exclusion criteria
Diabetes
Normal Renal Function eGFR ≥ 70ml/min
Impaired Renal Dysfunction eGFR < 70ml/min
Data Collection
Readmission
Arrythmia
Cardiogenic Shock
Death
Data Analysis
Observation and Results
Discussion
Summary and Conclusion

3.16 Operational Definition

Working Definition:

Diabetes:

Cardiomyopathy in the presence of prior extensive myocardial infarction, hibernating myocardium, or severe coronary artery disease. Diabetes accounts for almost half of the case of systolic HF (Brian P.Griffin, Manual of Cardiovascular Medicine, 5th addition, 2018).

In Diabetes, patients have Q Wave in ECG, in ECHO Cardiography bright hypo-echoeic area, Left ventricular ejection fraction <35%, in coronary angiogram 70% narrowing of Epicardial coronary artery present.

Chronic Kidney Disease

Chronic kidney disease (CKD) is defined as the presence of persistent (>3 months) functional or structural kidney abnormalities. A urine albumin-to-creatinine (ACR) ratio > 30 μg/mg from the first voided urine specimen and acquired under resting conditions is considered abnormal and an indicator of renal damage.

Stage	Assessments	
1	Kidney damage with normal GFR	≥90
2	Kidney damage with mild decrease in GFR	60-89
3A	Mild to moderate decrease in GFR	45-59
3B	Moderate to severe decrease in GFR	30-44
4	Severe decrease in GFR	15-29
5	End-stage renal disease	< 15

In-hospital outcome: In-hospital outcome means Index Hospital Admission, after the patient was admitted in CCU or in Ward, total duration of Hospital staying and patient follow up.

In-hospital outcome include Heart Failure, Arrhythmia, Cardiogenic Shock, Death, Cerebrovascular disease.

Estimation of eGFR by online calculator:

- Creatinine
- Age
- Sex
- Race

Impaired Renal Function: (Suwaidi et al 2002; Shilpak et al 2002)

Patients with eGFR of <70 ml/min and serum creatinine level≥ 1.5mg/dl. Impaired Renal Function include AKI and CKD, but in our study only **CKD should be considered**.

Grading of LV Function by Ejection Fraction (Lang, et al., 2006)

Normal ≥ 55%

Mildly abnormal 45-54%

Moderately abnormal 30-44%

Severely abnormal < 30%

Congestive heart failure (KILLIP CLASS): (Cannon et al. 2001).

Class 1: Absence of rales over the lung fields and absence of S_3.

Class 2: Rales over 50% or less of the lung fields or the presence of an S_3.

Class 3: Rales over more than 50% of the lung fields.

Class 4: Cardiogenic shock.

Heart Failure according to the EF:

I	HFrEF	≤ 40
II	HFpEF	≥ 50
	a. HFpEF, borderline	41-49
	b. HFpEF, improved	> 40
III	Chronic stable HF	Any
Acute decompensated		Any

Cardiogenic shock: (Cannon et al. 2001).

Clinical criteria of Cardiogenic shock are-

- Hypotension (systolic BP < 90 mmHg for at least 30 minutes or the need for supportive measures to maintain a systolic BP of ≥ 90 mmHg).
- End-organ hypo perfusion (cool extremities or a urine output of < 30 ml/hour.
- A heart rate of ≥ 100 bpm.

Arrhythmias: (Cannon et al. 2001).

a) Atrial arrhythmias- a new episode or acute recurrence of atrial arrhythmia documented by one of the following:

   i) atrial fibrillation/flutter.

   ii) supraventricular tachycardia that requires cardioversion, drug therapy, or is sustained for greater than 1 minute.

b) Ventricular arrhythmias- ventricular tachycardia or ventricular fibrillation requiring cardioversion and/or intravenous anti arrhythmic drugs.

c) High-degree atriventricular block- defined as third degree A-V block or second-degree A-V block with requiring pacing bradycardia.

Cardiorenal Syndrome: The term "Cardiorenal Syndrome" (CRS) describe the entity in which concomitant cardiac and renal dysfunction is present in the same patient. In this study type II should be considered (Chronic HF resulting in CKD).

Chapter 4

Observation and Results

4.1 Observation and Results

This was a prospective longitudinal study conducted in the National Institute of Cardiovascular Disease (NICVD), Dhaka for a period of one year starting from January, 2020 to December, 2020. The Main objective of the study was to assess the in-hospital outcome of the patients admitted with Diabetes and its relationship with on admission renal function.

Table I : **Age Distribution of the Study Population**

Age Group (Years)	Group I (n=50)		Group II (n=70)		Total (n=120)		p-value
	Number	%	Number	%	Number	%	
<40	2	4	5	7.1	7	5.83	
40-49	16	32	17	24.28	33	30	
50-59	18	36	28	40	46	40	
≥60	14	28	20	28.57	34	24.17	
Mean±SD	53.3±8.72		53.5±9.03		53.4±8.87		<0.001**

Unpaired t-test was done.

** means significant (P<0.005).

Group 1 = normal renal function

Group 2 = Chronic Kidney Disease

Minimum age of the patients was 18 years and maximum was 75 years. Age of all the patients were categorized into four classes. Major proportion of the patients (40%) were in 50-59 years age group; whereas few patients (5.83%) belonged to age less than 40 years. The mean age of the study population of group I was (53.3±8.72) years. The patients with group II were older than patients with Group I (53.3±8.72 vs. 53.5±9.03). Analysis revealed statistically significant (p<0.001) mean age difference between the study group.

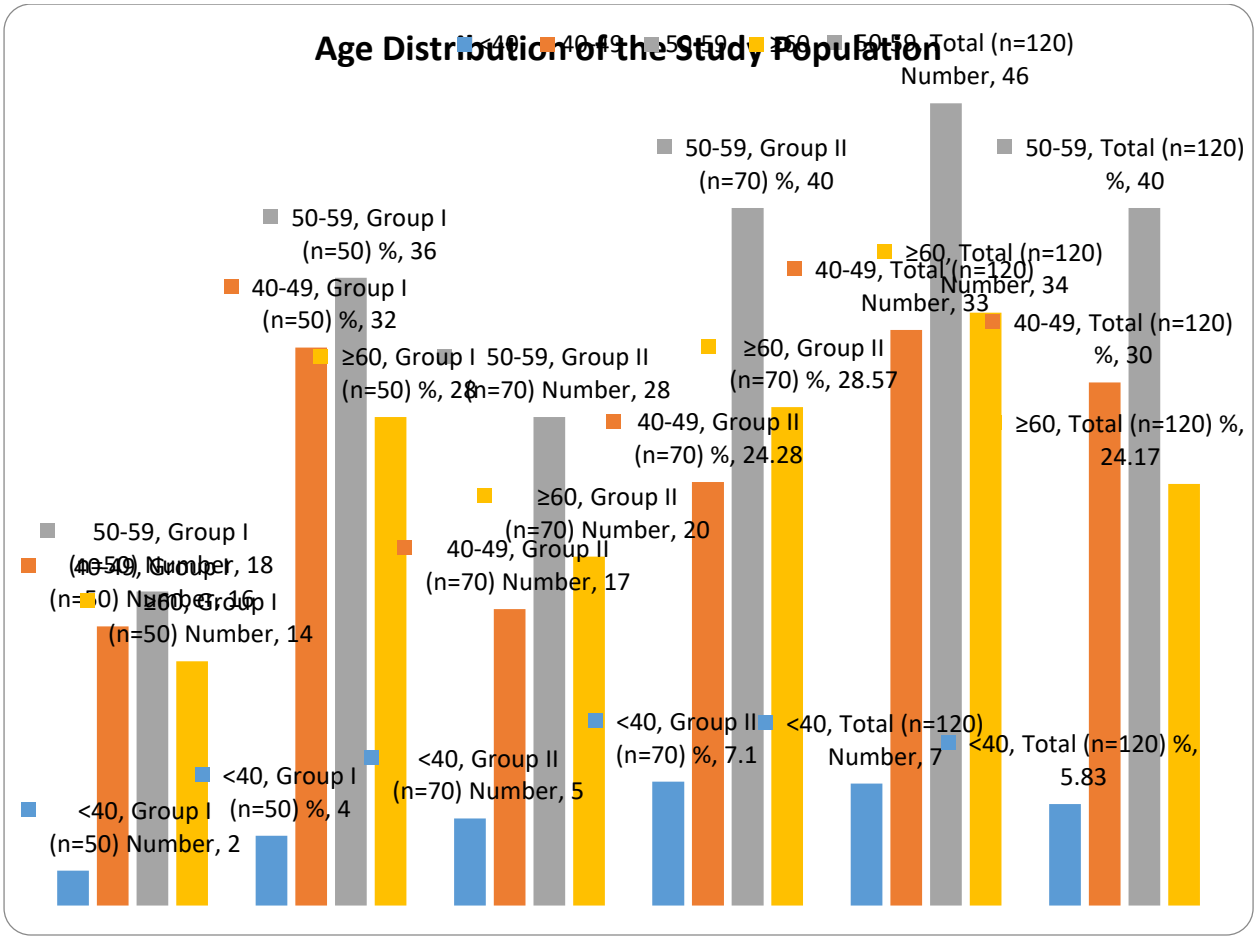


Figure I : **Age Distribution of the Study Population**

TableII: Sex distribution according to age group:

Age Group (Years)	Male (n=95)		Female (n=25)		Total (n=120)	
	Number	%	Number	%	Number	%
<40	10	10.52	3	12	13	10.83
40-49	15	15.78	6	24	21	17.5
50-59	40	42.11	9	36	49	40.83
≥60	30	31.57	7	28	37	30.83

Group 1 = Male Patient (n=95)

Group 2 = Female Patient (n=25)

According to the table II we found the total number of male patients was 95 and 42% of 50-59 age group is highest in the table. On the other hand 36% of female patients of 50-59 age group is also highest in the table.

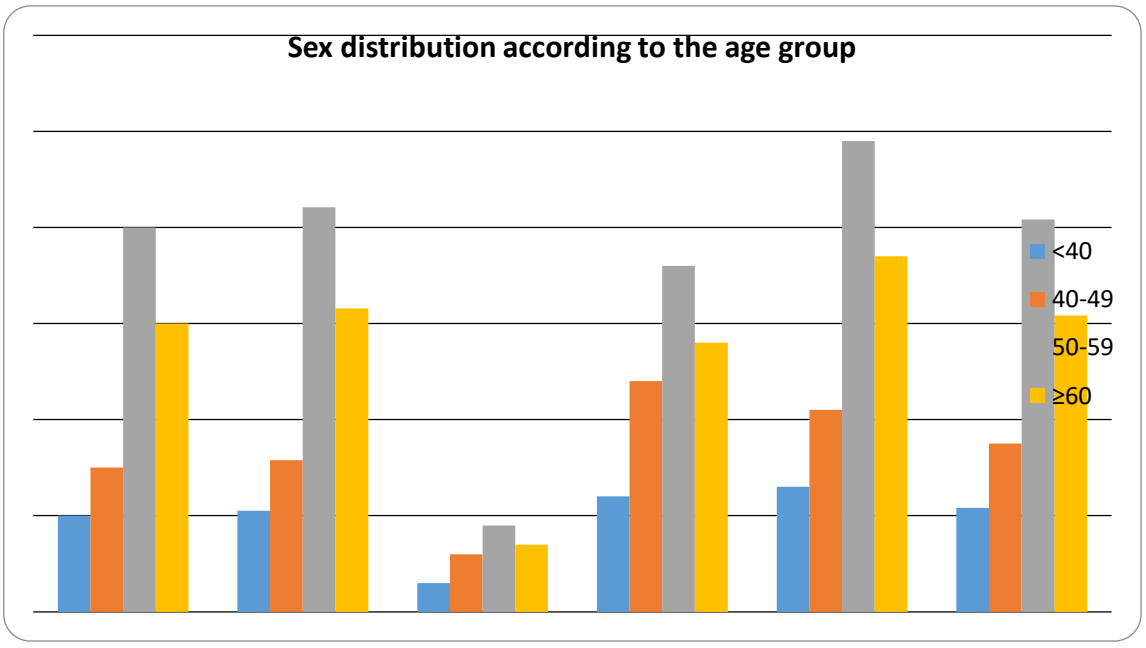


Figure II : **Sex distribution according to the age group**

Table III : **Sex Distribution of the Study Population according to the renal function**

Sex	Group I (n=50)		Group II (n=70)		Total (n=120)		p=value
	Number	%	Number	%	Number	%	
Male	40	80	55	78.57	95	79.17	0.003**
Female	10	20	15	21.43	25	20.83	
Mean±SD	53.3±9.40		53.78±8.90		53.54±9.15		

Chi-square test was done.

** means significant (p<0.05)

Group 1 = normal renal function

Group 2 = Chronic Kidney Disease

The above table shows sex distribution among the study population. In Group I 80% were male and 20% were female. In Group II 78.57% were male and 21.43% were female. Statistically significant association was seen in term of sex among the study groups (p<0.003). Male: Female ratio 4:1. Male patients were predominant in the study.

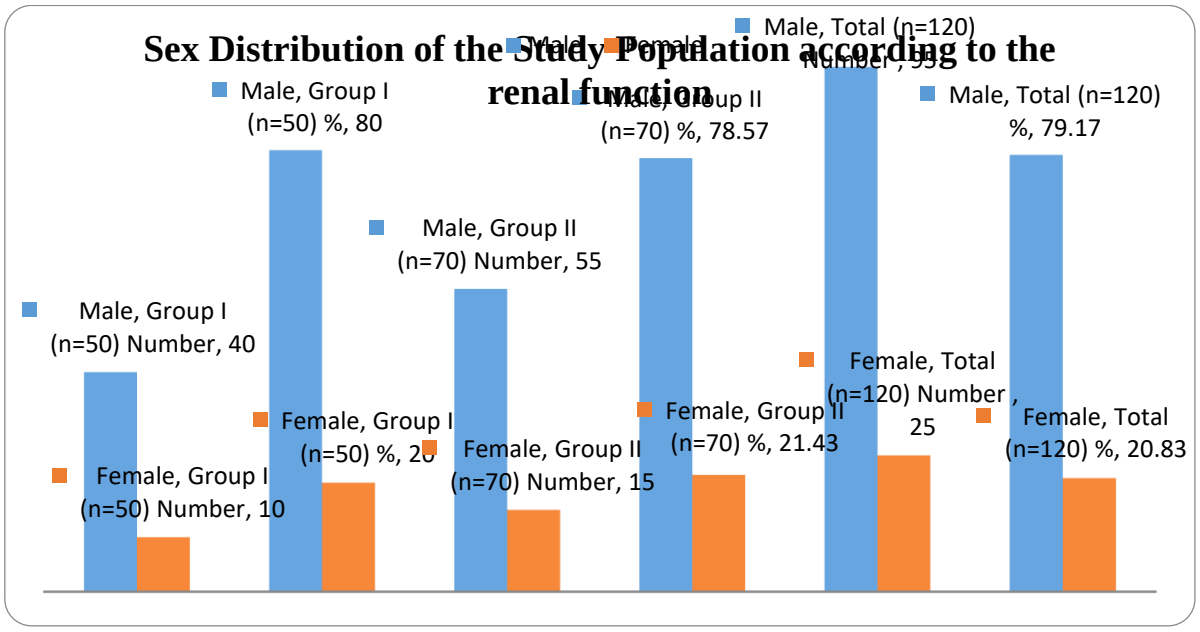


Figure III : **Sex Distribution of the Study Population according to the renal function**

Table IV : Distribution of the Study Population According to Cardiovascular Risk Factor

Risk Factors	Group I Normal GFR>70ml/min (n=50)		Group II Impaired GFR<70ml/min (n=70)		Total (n=120)		p-value
	No.	(%)	No.	(%)	No.	(%)	
Smoking	38	76	53	75.71	81	67.5	<0.001**
Hypertension	32	64	54	77.14	86	71.67	0.14*
Diabetes Mellitus	35	70	59	84.28	94	78.33	0.002**
Dyslipidaemia	30	60	45	64.28	75	62.5	0.29*

Chi Square test was done

** means significant ($p<0.05$)

* means not significant ($p>0.05$)

Group 1 = normal renal function

Group 2 = Chronic Kidney Disease

The presence of some established risk factors were collected by asking close ended questions and observing previous medical records. Patients with history of smoking and diabetes mellitus were significantly higher in Group II compared to Group I with p-value <0.001 and 0.002 respectively. Patients with hypertension and dyslipidaemia had higher percentage but did not show any significant association.

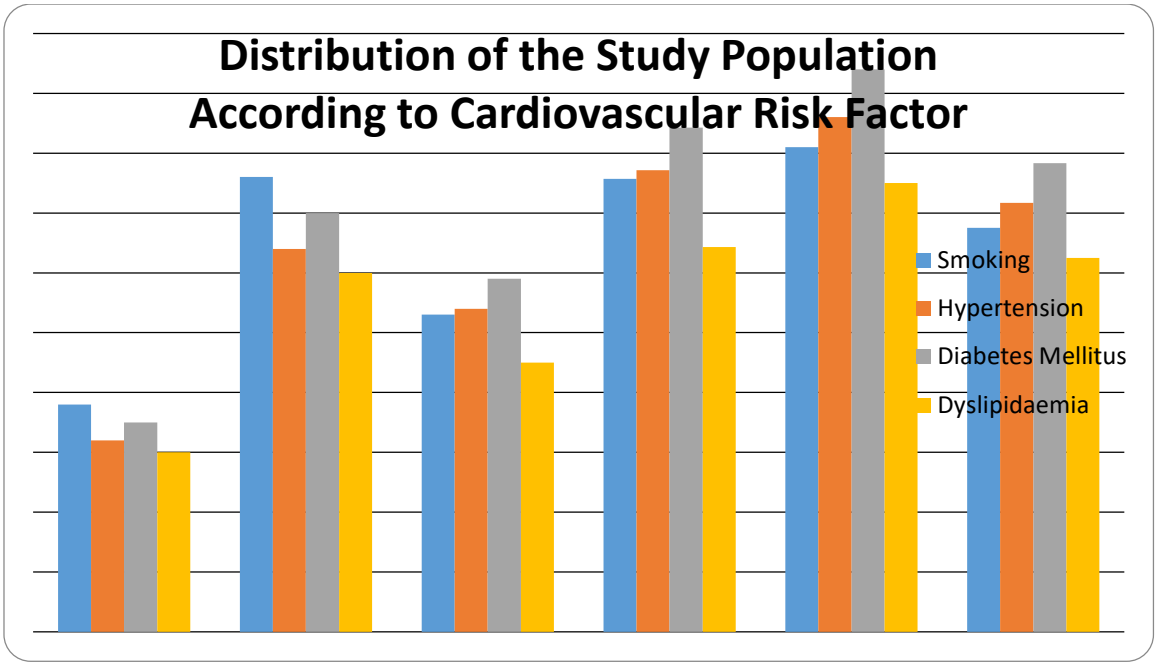


Table IV : Distribution of the Study Population According to Cardiovascular Risk Factor

Table V : Mean percent of ejection fraction of patients with normal and impaired GFR

Ejection Fraction (Percent)	GFR ml/min						p-value
	Normal GFR >70 (n=50)		Impaired GFR <70 (n=70)		Total (n=120)		
	No.	%	No.	%	No.	%	
36-39	20	40	22	31.43	42	35	
<35	30	60	48	68.57	78	65	
Mean±SD	31.7±4.98		31.78±4.67		31±4.79		0.001**

P value reached from chi square analysis

** p<0.01

Table V and figure V shows that the mean percent of ejection fraction was 31±4.79. It was 31.7±4.98 for the patients with normal GFR and 31.78±4.67 for the patients with impaired GFR and the mean difference was statistically significant (p<0.01).

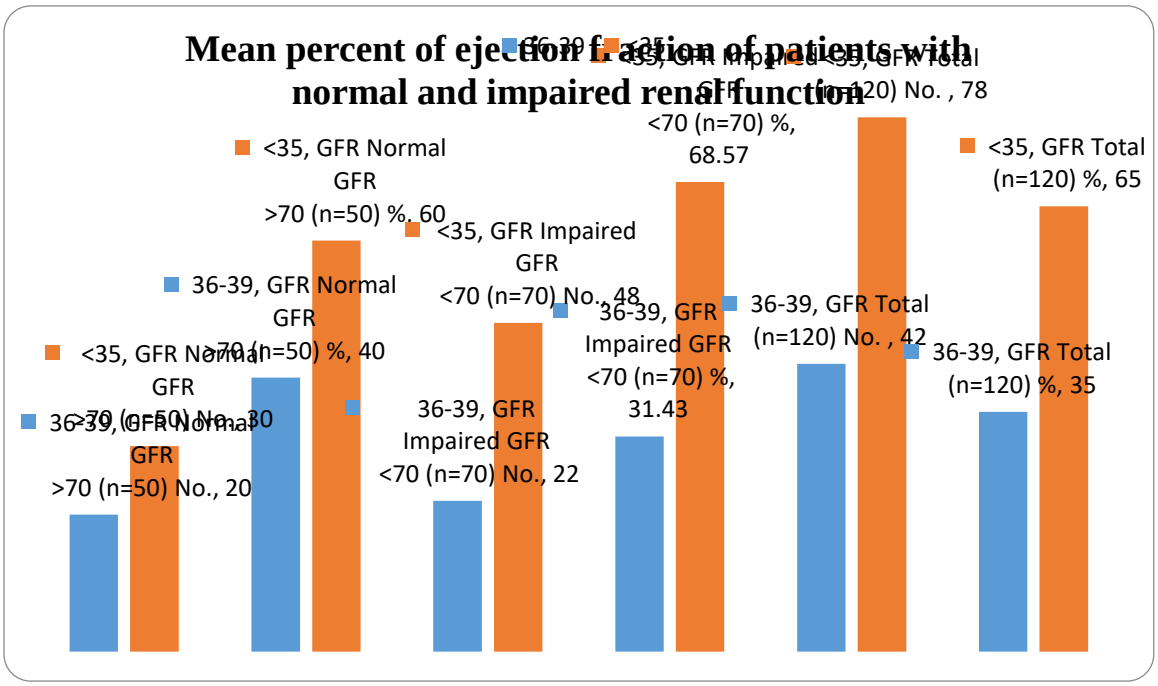


Figure V : Mean percent of ejection fraction of patients with normal and impaired GFR

Table VI : **Distribution of Patients by Heart Failure (Killip Class)**

Heart Failure	Sex						p-value
	Male Heart Failure (70 out of 95)		Female Heart Failure (20 out of 25)		Total (n=120)		
	No.	%	No.	%	No.	%	
Class I	8	7.3	3	12	11	9.16	<0.001**
Class II	15	15.7	4	16	19	15.83	
Class III	29	30.52	8	32	37	30.83	
Class IV	18	18.96	5	20	23	19.17	

Figure in parenthesis indicate range

P value reached from chi square analysis

** means significant (p<0.001).

According to Table VI, 30.52% of the studied male patients had Killip class III and 18.96% had Killip class IV heart failure whereas among the female patients 32% had Killip class III and 20% had Killip class IV heart failure. Analysis found statistically significant difference regarding the occurrence of heart failure between male and female patients (p<0.001).

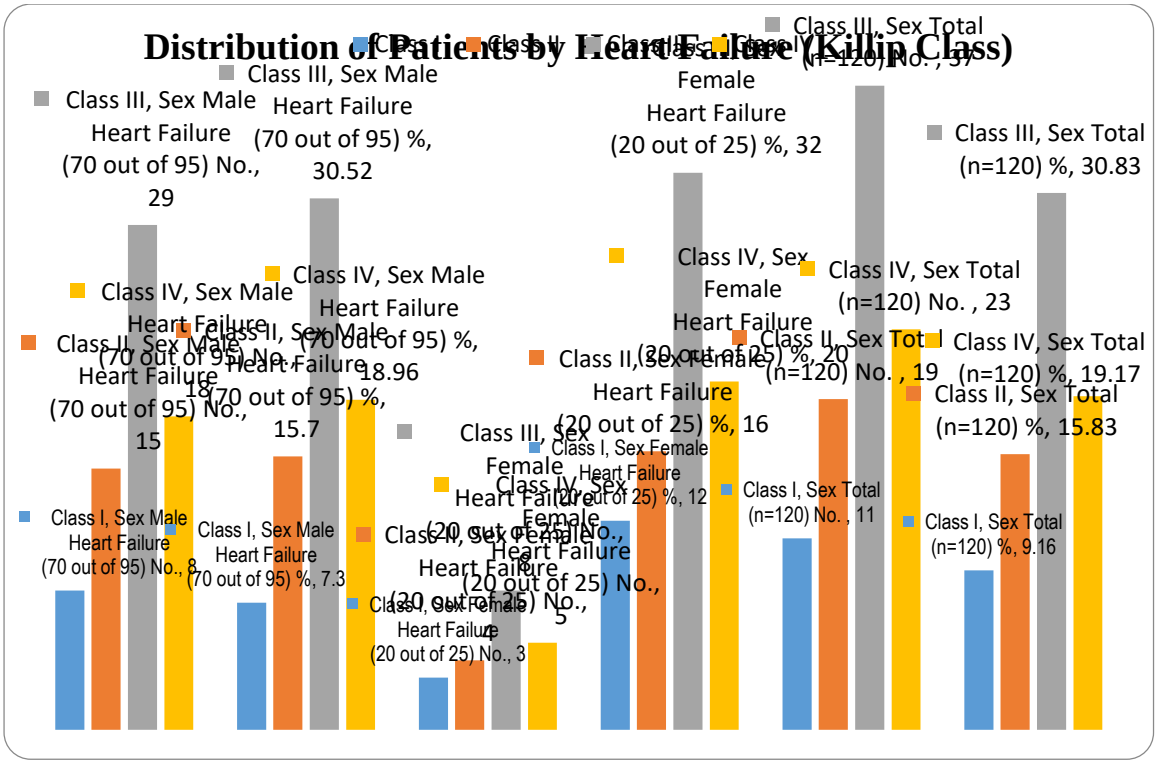


Figure VI : **Distribution of Patients by Heart Failure (Killip Class)**

Table VII : Pattern of Cardiac Complication of Patients with Normal and Impaired renal function

Complications	GFR ml/min						p-value
	Normal Renal Function GFR >70ml/min (n=50)		Impaired Renal Function GFR <70ml/min (n=70)		Total (n=120)		
	No.	%	No.	%	No.	%	
Heart Failure (Killip I-IV)	35	70	55	78.57	90	75	0.001***
Atrial Fibrillation	2	4	6	8.57	8	6.67	0.214NS
Ventricular Tachycardia	2	4	5	7.14	7	5.83	0.001***
Ventricular Fibrillation	2	4	4	5.71	6	5	0.052NS
Heart Block (1°,2°, 3°)	2	4	10	14.3	12	10	0.001***
Cardiogenic Shock	15	30	25	35	40	33.33	0.214NS

P value reached from chi square analysis

NS= Not significant ($p>0.05$)

***$p<0.001$

Table VII shows the pattern of in-hospital complications of the study patients in relation with GFR. It was observed that heart failure, ventricular tachycardia and Heart Block were significantly higher among the patients with Chronic Kidney Disease ($p<0.001$) compared to those with normal GFR. The other complications like atrial fibrillation,ventricular fibrillation, Cardiogenic Shock were also high among the patients with Chronic Kidney Disease than those with normal renal function, but the difference was not statistically significant ($p>0.05$).

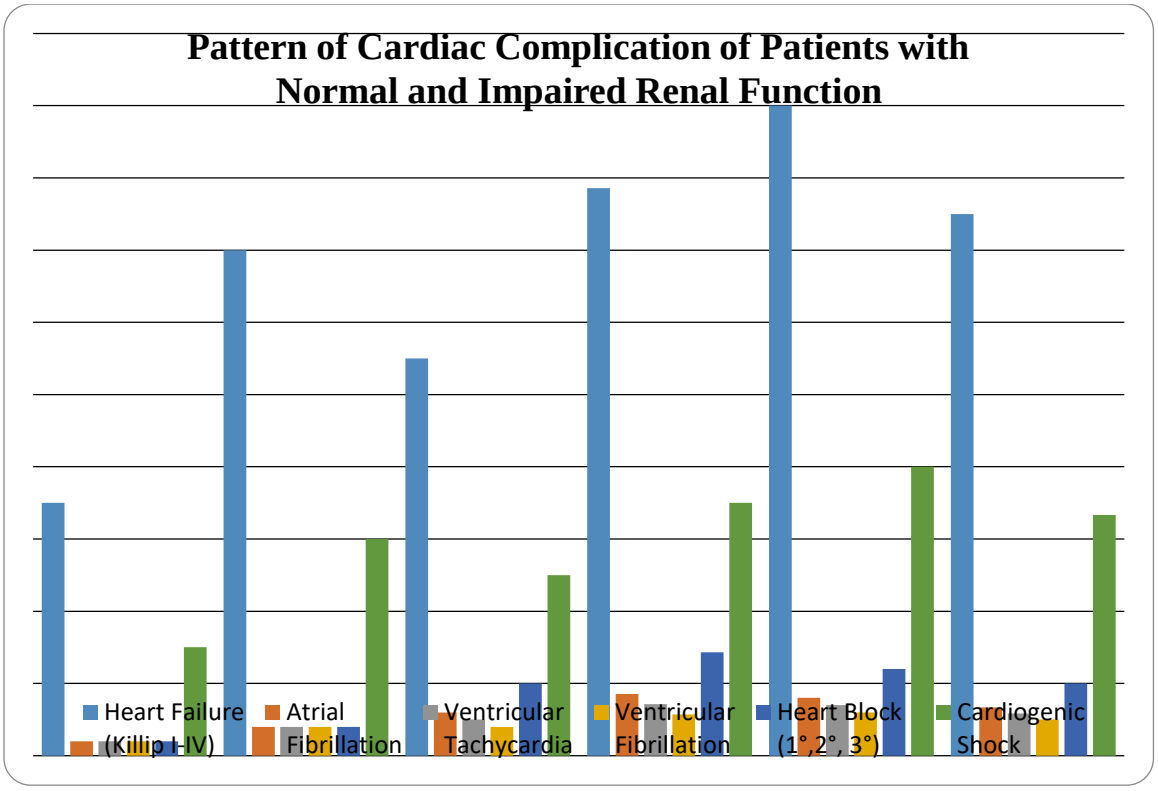


Figure VII : Pattern of Cardiac Complication of Patients with Normal and Impaired GFR

Table VIII : In-hospital Mobility of Patients with Normal and Impaired GFR

Morbidity	Study Patients						p-value
	Normal GFR >70ml/min (n=50)		Impaired Renal Function GFR <70ml/min (n=70)		Total (n=120)		
	No.	%	No.	%	No.	%	
Yes	24	48	40	57.14	64	53.33	
No	26	52	30	42.86	56	46.77	0.001***

P value reached from chi square analysis

*** p<0.001

Table VIII and Figure VIII shows that in-hospital morbidity was significantly higher in patients with Impaired GFR (57.14%) compared with that of normal GFR (48%) and the difference was statically significant (p<0.001). This indicated that risk of in-hospital complication higher in patients with impaired GFR compared to those with normal GFR.

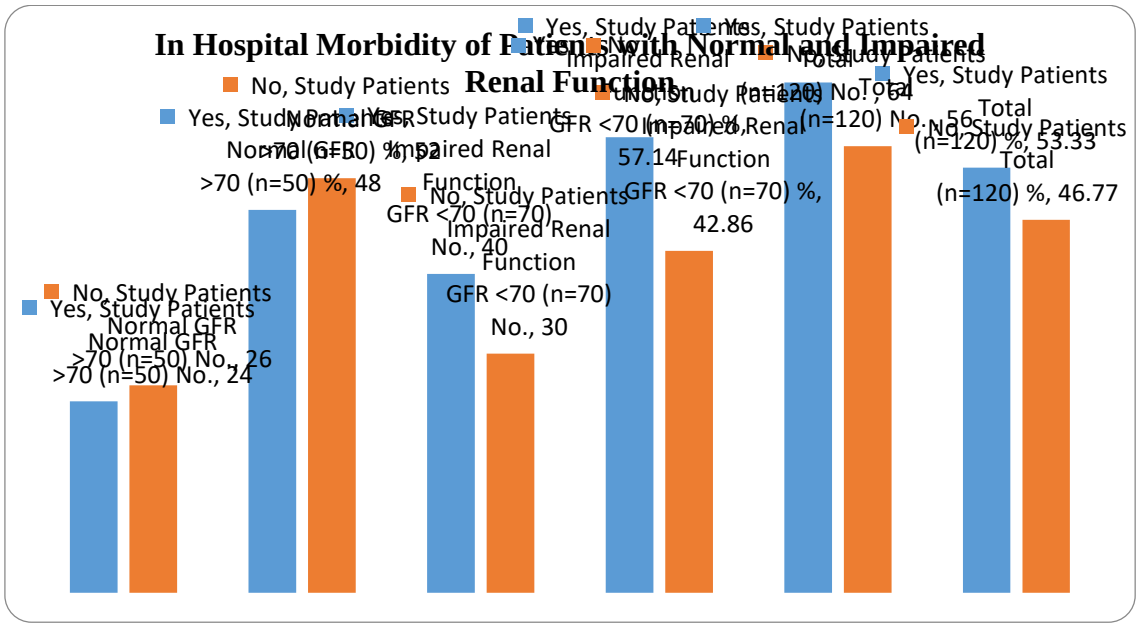


Figure VIII : In-hospital Mobility of Patients with Normal and Impaired GFR

Table IX : In-Hospital Mortality of Patients with Normal and Chronic Kidney Disease

	GFR						
	Normal Renal Function GFR >70ml/min (n=50)		Impaired Renal Function GFR <70mi/min (n=70)		Total (n=120)		
Mortality	No.	%	No.	%	No.	%	p-value
Yes	5	10	12	17.14	17	14.17	
No	45	90	58	82.86	103	85.83	0.173NS

P value reached from chi square analysis

P<0.005

Table IX shows that among the patients with Impaired GFR, 17.14% died during their hospital stay, whereas with normal GFR, 10% died despite proper treatment. So, statistically significant difference in terms of mortality was found between two groups of patients (p<0.005).

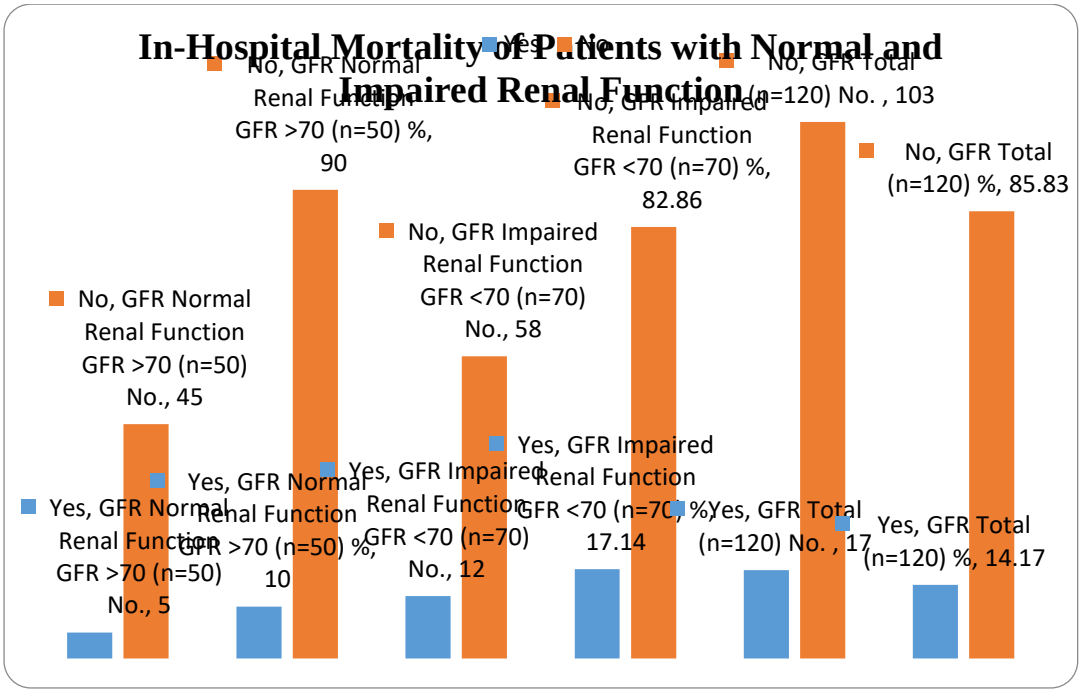


Figure IX : In-Hospital Mortality of Patients with Normal and Chronic Kidney Disease

Table X: **Comparison of the study population according to hospital stay**

Age	GFR ML/MIN				p value
	Group I >70ML/MIN (n=50)		Group II <70ML/MIN (n=70)		
	Days	%	Days	%	
<40	3	6	5	7.14	<0.001**
40-49	4	8	6	8.58	
50-59	6	12	9	12.86	
≥60	4	8	7	10	
Mean±SD	4.25±1.29		6.75±1.71		

Unpaired t-test was done.

** means significant ($p<0.05$)

Group I = normal renal function

Group II = Impaired Renal Function

The above table shows the hospital stay of the study subjects. Mean hospital stay was found higher in Group II compared to Group I (6.75±1.71 vs. 4.25±1.29) and the mean difference was statistically significant ($p<0.001$). The average hospital stay was 5.5±1.5 days of the study patients.

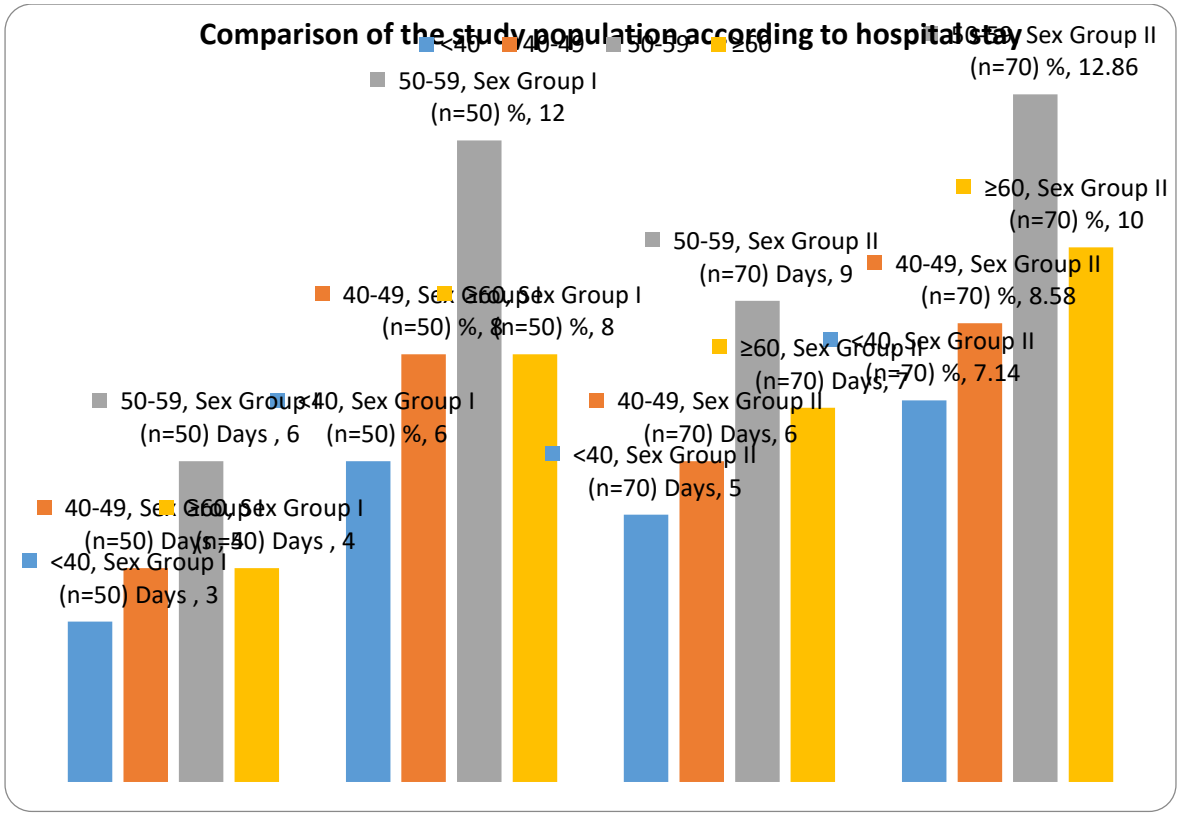


Figure X : **Comparison of the study population according to hospital stay**

Table-XI**: Multivariate logistic regression of ischemic cardiomyopathy patients with chronic kidney disease**

Variables	Standardized coefficient	Odds Radio (OR)	95% CI of OR	p-value
Age > 50 yrs	1.748	2.364	2.365-4.452	0.004*
Male gender	0.136	0.397	0.412-0.687	0.327
Smoking	1.023	2.734	2.413-6.214	0.039*
Diabetes mellitus	1.039	3.789	1.986-3.671	0.014*
Hypertension	0.367	0.927	0.215-0.369	0.431
EF (%)	0.239	0.874	0.583-0.691	0.648
Arrhythmia	0.345	0.239	0.157-0.693	0.415
Cardiogenic shock	0.014	0.417	0.225-0.744	0.587

*indicate significant

Multivariate logistic regression model was constructed with age (>50yrs), gender, smoking, diabetes mellitus, hypertension, EF as independent factor, arrhythmia and cardiogenic shock as dependent variables of ischemic cardiomyopathy patients with chronic kidney disease. After adjusting multivariate logistic regression age (>50yrs), smoking and diabetes mellitus was found significant risk factors for in hospital adverse outcome with ORs 2.364, 2.734 and 3.789 respectively.

Chapter 5

5.1 Discussion

This was a prospective longitudinal study conducted in the National Institute of Cardiovascular Disease (NICVD), Dhaka for a period of one year starting from January, 2020 to December, 2020. The Main objective of the study was to assess the In-hospital outcome of the patients admitted with Diabetes and its relationship with on admission renal function. A total 120 patients with Diabetes were included in this study. All patients were 18-75 years age and presented with shortness of breathing, ascities, paedal edama, tender hepatomegaly, raised JVP. On admission renal function of the study patients were assess using both serum creatinine (ml/dl) and serum GFR (ml/min). Later was calculated using online calculator.

5.2 Age of the study patient:

Age is an unmodifiable strong risk factor for Diabetes, which increases with the increases of age (Falk et al. 2001).

In the present study, mean age of the male and female patients was 53.4±8.87. The highest number of patients (40%) was in the age group of 50-59 years (Table I).

The age range of the study patients was 18-75 years. When age of patients with normal renal function was compared with that of patients with renal impairment, it was found that the mean age of patients with normal GFR was 53.3±8.72 years and mean age of patients with impaired GFR was 53.5±9.03 Years (Table I).

It was found that among patients with normal renal function, the highest percentage of patients were in the age range of 50-59 years (36%), whereas among patients with renal impairment, the highest percentage of patients (40%) were in the age group of 50-59 years (Table I). Analysis revealed that the mean age was significantly higher patients with renal impairment ($p<0.001$).

5.3 Risk Factors

Out of total 120 patients, proportion of male (79.17%) was higher than the female (20.83). The above table shows sex distribution among the study population. In Group I 80% were male and 20% were female. In Group II 78.57% were male and 21.43% were female. Statistically significant association was seen in term of sex among the study groups ($p<0.003$). Male: Female ratio 4:1. Male patients were predominant in the study. On an average, female patients had lower. It was statistically significant ($p<0.001$).

According to table IV with normal renal function group I smoking 76%, hypertension 64%, DM 70%, dyslipidemia 60%. With renal impairment (CKD), group II smoking 75.71%, hypertension 77.14%, DM 84.28%, Dyslipidemia 64.28% which is more than normal renal function patients. Here smoking, DM statistically significant ($p<0.001$), Hypertension, dyslipidemia is not statistically not significant ($p>0.001$)

5.4 Pattern of in-hospital Cardiac Complication of Patients with Normal and Impaired Renal Function

Table VII shows the pattern of in-hospital complications of the study patients in relation with GFR. It was observed that heart failure, ventricular tachycardia and heart block were significantly higher among the patients with Chronic Kidney Disease clearance ($p<0.001$) compared to those with normal GFR. The other complications like atrial fibrillation, ventricular fibrillation were also high among the patients with Chronic Kidney Disease clearance than those with normal GFR, but the difference was not statistically significant ($p>0.05$).

According to Table VI, 30.52% of the studied male patients had Killip class III and 18.96% had Killip class IV heart failure whereas among the female patients 32% had Killip class III and 20% had Killip class IV heart failure. Analysis found statistically significant difference regarding the occurrence of heart failure between male and female patients ($p<0.001$).

Freeman et al., in their study regarding renal dysfunction with Diabetes, 16% and 37% patients with heart failure had normal and Chronic Kidney Disease respectively (Freeman et al. 2003). All these findings are consistent with our findings in that heart failure was more in patients with renal impairment than those without and the incidence and severity both increases with increasing degree of renal impairment.

5.5 Pattern of in-hospital cardiac complications (morbidity) in relation with the serum GFR

In-hospital morbidity was significantly higher in patients with Impaired renal function (57.14%) compared with that of normal normal renal function (48%) and the difference was statically significant ($p<0.001$). This indicated that risk of in-hospital complication higher in patients with impaired GFR compared to those with normal GFR.

The development of heart failure, ventricular tachycardia was significantly higher among patients with Chronic Kidney Disease who were admitted with Diabetes, compared to those with Diabetes patients having normal renal function ($p<0.001$).

In their study regarding renal dysfunction in coronary care unit, McCullough et al. found that there was graded increase in the adjusted risk for atrial fibrillation, accelerated idioventricular rhythm, sustained ventricaular tachycardia and ventricular fibrillation with increasing degree of renal impairment. Development of heart failure after admission was also more in those with renal dysfunction than those without (McCullough et al. 2000).

Wilson et al. found increased incidence of ventricular fibrillation among Diabetes patients with renal impairment than those without. They also found increased incidence of left ventricular failure in patients with renal impairment.

5.6 In-hospital mortality of the studied patients.

Among patients with impaired renal impairment, 17.14% (n=12) died during their hospital stay, despite all necessary treatments. On the other hand, 10% (n=5) died with normal GFR during their hospital stay. However, statistically significant difference in terms of mortality was found between the two groups of patients ($p<0.05$).

Wilson et al. demonstrated in his study that baseline renal function in patients with Diabetes was an independent determinant of in-hospital death (Wilson et al. 2003).

Wright et al. demonstrated that, for in-hospital death patients with Diabetes, end-stage renal disease, severe renal dysfunction, and moderate renal dysfunction, increase congestive heart failure during hospitalization of patients those has increased age, DM (Wright et al. 2002).

5.7 Relation between renal function and mean ejection fraction of the study patients

The mean percent of ejection fraction was 31±4.79. It was 31.7±4.98 for the patients with normal renal function and 31.78±4.67 for the patients with impaired renal function and the mean difference was statistically significant ($p<0.01$).

Table V shows the mean distribution of mean percentage of ejection fraction according to the degree of renal impairment. The mean percent of ejection fraction was 31.7±4.98 among patients with normal serum GFR. Chi square test revealed that the mean percent of ejection fraction decreased with increasing severity of renal impairment ($p<0.001$).

McCullough et al. also found reduced LV ejection fraction among patients with Chronic Kidney Disease than those with normal renal function in their study. They also found evidence of LV dysfunction (measured by echocardiography) to be increasingly common with increasing

degree of renal impairment (McCullough et al. 2000). Freeman et al. in his study regarding Diabetes and renal dysfunction found LVEF of 50% and 44% among patients with normal and Chronic Kidney Disease ($p<0.001$). So, their findings are consistent with the findings of our study in that, patients with renal impairment have reduced LVEF, then those with normal renal function.

Chapter 6

Study Limitation

Although the result of this study supports the hypothesis, there are some facts to be considered which might have affected the result of the current study.

- The number of study population was relatively small.
- Sampling method was non-randomized, so there was risk of selection bias.
- It was a single center study.
- Renal insufficiency was defined utilizing the estimated GFR at the time of presentation. Duration and aetiology of renal insufficiency was not recorded. Therefore, acute changes in renal function just before admission or as a consequence of the acute event were not known.
- Serum creatinine concentration is only a crude measure of glomerular filtration rate.
- There were differences in baseline clinical characteristics between study groups. Some adverse outcomes in patients with renal impairment may be secondary to these baseline abnormalities.

Chapter 7

Summary

This is a prospective longitudinal study was carried out in the department of Cardiology, National Institute of Cardiovascular Diseases (NICVD), Dhaka during a period of one year from January, 2020 to December, 2020. The study was undertaken to find out the 'In-hospital Prognostic Outcome of Diabetes Patients with Chronic Kidney Disease'.

A total 120 patients with Diabetes was included in this study. All patients are above 18 years has a history of STEMI/NSTEMI before.

Patients were classified according to renal function using both the admission serum creatitine level and the estimated GFR. GFR was estimated by using the online GFR calculator. Study Procedure was followed as per protocol. Out of 120 study patients, 80 were male and 40 were female.

The age range the study patients was 18-75 years, with mean age of the male 53.97±9.49 and female 52.5±10 years. But majority of patients were in the age group of 50-59 years. Among the patients with normal renal function, highest percentage of patient was in the age range 50-59 years (36%). Where are among the patient was renal impairments highest percentage was in the age group of 50-59 (40%).

Mean age of this group I patients 53.3±8.72 years and mean age of group II patient is 53.5±9.03. Mean difference between groups was statistically significant.

Smoking was found to be common risk factors of the study patients with normal and impaired renal function. According to table IV with normal renal function (group I) smoking 76%, hypertension 64%, DM 70%, dyslipidemia 60%. With renal impairment (CKD) (group II), smoking75.71%, hypertension 77.14%, DM 84.28%, Dyslipidemia 64.28% which is more than normal renal function patients.

Among the studied patient 9.16% killip class I, 15.83% killip class II, 30.83% killip class III and 19.17% killip class IV.

Mean percentage of ejection fraction of the study patients was 31±4.79. EF 31.7±4.98 for patients with normal renal function and 31.78±4.67 for patient with Chronic Kidney Disease and mean difference was statistically significant. Mean percent of ejection fraction decreased with increasing of renal Impairment.

It was observed that development of heart failure, Ventricular tachycardia and carcinogenic shock were significantly higher among patients with Chronic Kidney Disease.
Total in-hospital complications were significantly higher among patients with Chronic Kidney Disease. In case of normal renal function Heart Failure (Killip I-IV) 70%, Atrial Fibrillation 4%, Ventricular Tachycardia 4%, Ventricular Fibrillation 4%, Heart Block (1°,2°, 3°) 4%, Cardiogenic Shock 30%.

In case of Chronic Kidney Disease Heart Failure (Killip I-IV) 78.57%, Atrial Fibrillation 8.57%, Ventricular Tachycardia 7.14%, Ventricular Fibrillation 5.71%, Heart Block (1°,2°, 3°) 14.3%, Cardiogenic Shock 35%.

Among patients with Chronic Kidney Disease, 12 patients (17.14%) died during their hospital stay. With normal renal function 5 patients (10%) died. So, statistically significant difference was present regarding in-hospital mortality between patients with normal and Chronic Kidney Disease.

With normal renal function Diabetes patients mean Hospital staying was 4.25 days but with CKD patients 6.75days so CKD patients had more Hospital staying. It was statistically significant.

Chapter 8

Recommendation

The present study concluded that chronic kidney disease evidence by e GFR <70ml/min was significantly associated with adverse in-hospital out come in patients with Diabetes, however this deleterious effect was seen among those with older age, male sex, reduced LVEF, DM. So chronic kidney disease as evidence by e GFR <70 ml/min may be considered as a prediction of adverse in-hospital outcome in patients with Diabetes.

Presence of chronic kidney disease can be used as a predictor of adverse in-hospital outcome.

Proper assessment, early detection and management, timely interventional strategy can be taken to reduce in-hospital outcome, disease burden, morbidity and mortality.

Larger number of patients and multiple center study can be taken for prevention of complication of Diabetes patients.

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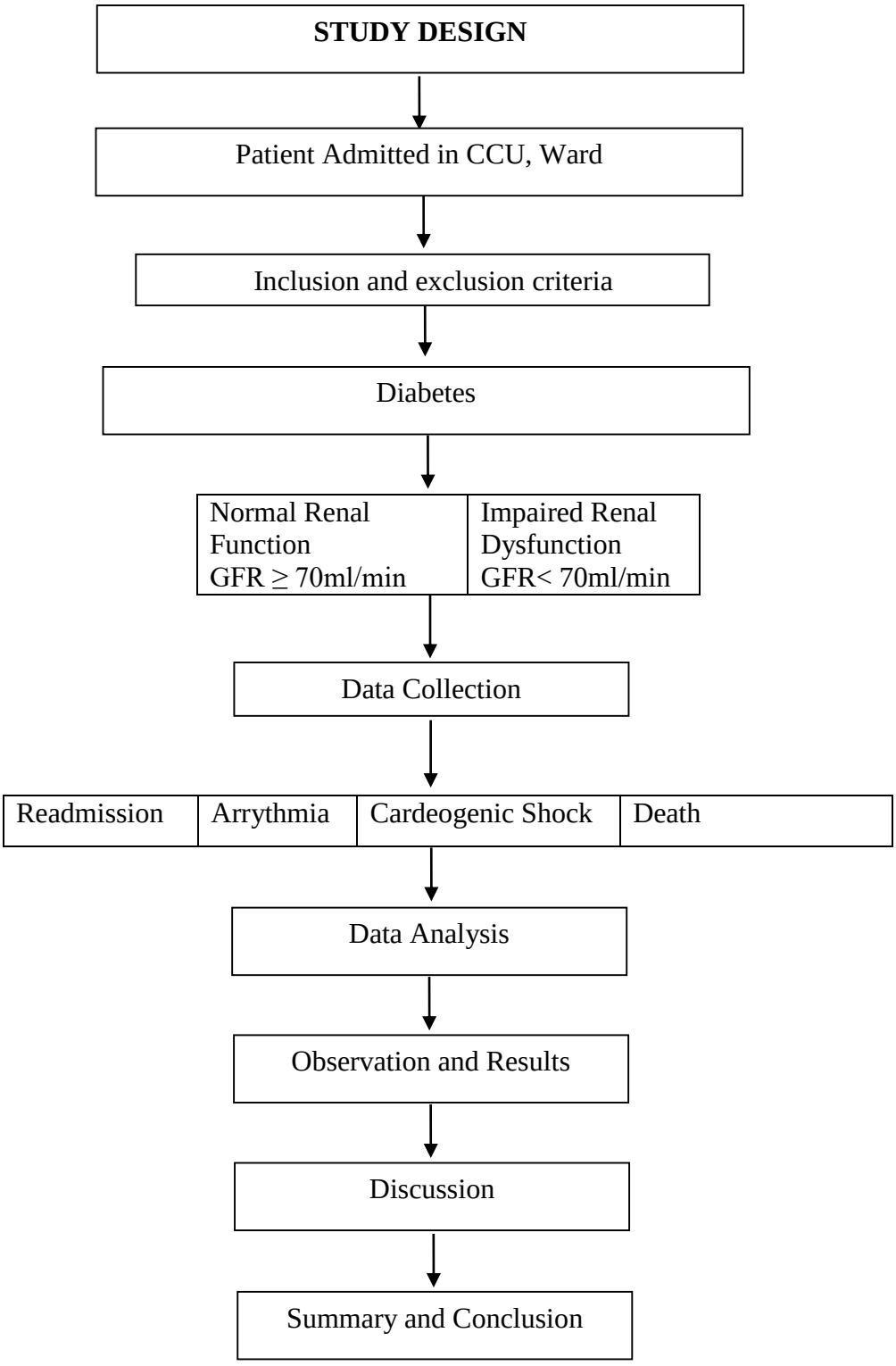
Appendix A

Study Design



Appendix B

Data Collection Form

Data Collection Sheet

In-hospital outcome of Diabetes patients with

Chronic Kidney Disease.

Serial No: .....

General characteristics

1. Patient's name	:			
2. Address	:			
3. Age in years	:			☐
4. Sex	:	1 = Male	2 = Female	☐
5. Date of admission	:	_____/_____/20		☐
6. Date of discharge	:	_____/_____/20		☐

Clinical Parameters

7. Heart Failure (Killip	:	1 = Class I, 2 = Class II, 3 = Class III, 4 = Class IV Class)		

Risk factors ☐

8. Smoking	:	1 = Yes	2 = No	☐
9. Hypertension	:	1 = Yes	2 = No	☐
10. Family history of CAD	:	1 = Yes	2 = No	☐
11. Diabetes mellitus	:	1 = Yes	2 = No	☐
12. Dislipidaemia	:	1 = Yes	2 = No	☐

Investigations

13. GFR : ☐

In-hospital Outcome :

1.1 Heart failure (Killip I-IV) : ☐

1.2 Atrial fibrillation : ☐

1.3 Ventricular tachycardia : ☐

1.4 Ventricular fibrillation: ☐

1.5 Heart Block :1st ,2nd,3rd degree ☐

1.6 Re-infarction : ☐

1.7 Cardiogenic shock : ☐

1.8 Death ☐

Signature and date

Appendix C

CONSENT FORM (English)

After being fully informed about the objectives, consequence of the study and my right to withdraw myself from the study at any time for any purpose, what so ever, I am ……. hereby giving consent to participate in the study conducted by Sabrina Kabir, Brac University, Dhaka.

I fully recognized that my participation in this study will generate valuable medical information that might be used for the interest of patients in future.

Hospital authority, doctors or any other staff will not be responsible for any adverse consequences during the study.

I shall try my best to comply with the instructions given by throughout the whole period of study.

Signature……

Thumb impression…….

Date……

Appendix D

অবহিত সম্মতি পত্র

(CONSENT FORM)

রোগীর নাম ঃ

বয়স ঃ

ঠিকানা ঃ

আমি স্বজ্ঞানে, স্বেচ্ছায় এবং সুস্থ মনে এই গবেষণামূলক কার্যক্রমে স্বেচ্ছায় অংশগ্রহণ করতে সম্মত হয়েছি। আমাকে জানানো হয়েছে যে, এই গবেষণা ফলদায়ক হবে এবং ভবিষ্যতে আমাদের দেশে এই ধরনের রোগিরা যথেষ্ট উপকৃত হবে। আমি এই গবেষণা কার্যক্রম হতে নিজেকে প্রত্যাহার করার অধিকার রাখি। আমি এই গবেষণার জন্য কোন আর্থিক সুবিধা গ্রহণ করবো না। আমার ব্যক্তিগত গোপনীয়তা রক্ষা করা হবে। আমি স্বেচ্ছায়, স্বজ্ঞানে ও সানন্দে এই সম্মতি পত্রে স্বাক্ষর করলাম।

রোগীর স্বাক্ষর/টিপ সই

নাম ঃ

তারিখ ঃ.....