## **Review Article**



# Diabetes and Myocardial Infarction: Epidemiology, Pathological Mechanism, Preventive Measures and Future Directions - A Mini Review

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#### ABSTRACT

Diabetes is a chronic metabolic disorder. Long term diabetes mellitus leads to diabetic ketoacidosis, hyperosmolar hyperglycemic state, diabetic retinopathy, diabetic nephropathy, diabetic foot and myocardial infarction. Myocardial infarction is the most important complications of diabetes mellitus affects large number of people. In this article we reviewed the Complications of diabetes mellitus and also discussed the epidemiology, pathophysiology, preventive measures of myocardial infarction and future research in the treatment of diabetes mellitus. Diabetes mellitus is significantly associated with acute myocardial infarction. The common risk factors of myocardial infarction are smoking, alcohol consumption, diabetes mellitus, hypertension, obesity andstress. Preventive measures include reducing blood pressure, correcting dyslipidemia, reducing obesity, smoking cessation, exercise and reducing cholesterol and also include drug therapy like beta blockers, aspirin and Angiotensin converting enzyme (ACE)- inhibitors.

Keywords: Diabetes mellitus, Myocardial infarction, Epidemiology, Pathophysiology, Preventive measures.

#### **INTRODUCTION**

iabetes mellitus is a chronic metabolic disorder. It is characterized by severe hyperglycemia which is mainly due to defective insulin secretion, insulin action or both. Low insulin level or insulin resistance of target tissues is the reasons for metabolic deformity. In other words, diabetes mellitus refers to a group of metabolic diseases that affects how the body uses blood sugar (glucose). Glucose is important for health because it is a vital source of energy for the cells that make up muscles and tissues <sup>1</sup>. Intensity of the disease depends upon the type and period of diabetes. Most of the type 2 diabetes mellitus patients may be asymptomatic during early years of diabetes mellitus. But some people from severe symptoms like polyuria, polydypsia, polyphagia, weight loss, increased appetite, tiredness, dry skin. The category of diabetes mellitus is based on its etiology and symptoms, there are four types of diabetes mellitus; Type 1 diabetes mellitus, Type 2 diabetes mellitus, gestational diabetes mellitus and maturity onset diabetes of the young (MODY) <sup>2</sup>.

In most of the countries 85-95% of the people were diagnosed with type 2 diabetes than type 1 diabetes. In worldwide, the incidence of diabetes is increasing considerably. Over the past 30 years the global burden of diabetes mellitus has increased from 30 million in 1985 to 382 million in 2014. In future these rates will further increase<sup>3</sup>. Prevalence of diabetes mellitus in adults worldwide was found to be 4.0% in 1995 and it will be increased to 5.4 % in the year 2023. Diabetes mellitus is higher in developed countries compared to developing countries. By the year of 2025, greater than 75% of people with diabetes will reside in developing countries as

compared with 62% in 1995. India, China and US will be a major country with large number of people suffering from diabetes. Majority of the people suffering from diabetes are in the age of 45-65 years  $^4$ .

The most important complications of diabetes mellitus are diabetic retinopathy, diabetic ketoacidosis, diabetic foot ulcer, diabetic nephropathy, hyperosmolar hyperglycemic state and myocardial infarction. The most leading cause of vision loss is diabetic retinopathy which affected 2.6 Million people in 2015 and caused a visual impairment and which will rise up to 3.2 million in 2020 which was estimated in many populations based studies<sup>5</sup>. The mortality rate of diabetic ketoacidosis is very low i.e. <1% in Scotland <sup>6</sup> and USA <sup>7</sup>. This will vary according to health care setting. In India, 30% of Inpatient death occurs due to diabetic ketoacidosis<sup>8</sup>. Diabetic foot ulcer is one of the important complications of diabetes. Diabetic foot ulcer will be developing in up to 25% of patient with diabetes, according to Singh et al <sup>9</sup>. In 2005, diabetic nephropathy was developed in 33,000 type I diabetic patients and 405,000 type 2 diabetic patients in Spain<sup>10</sup>. In 2013, in Catalonia, Spain showed a decrease from 6456 per million population in 2002 to 600 per million population in end stage renal disease <sup>11</sup>. Diabetes mellitus is the first cause of end stage renal disease in Spain<sup>12</sup>. Hyperosmolar hyperglycemic state mostly occurs in the patients older than 65 years of age<sup>13,14</sup>. 10 to 20% mortality rate for patients with hyperosmolar hyperglycemic state which is 10 times higher approximately than diabetic ketoacidosis<sup>15</sup>. The mortality rate was deceased in between 1980 and 2009<sup>16</sup>. In the United states, there are approximately 600,000 to 800,000 persons suffer from myocardial infarction <sup>17</sup>. In recent years, because of greater



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improvement in diagnosis and therapy, it has been reduced to 5% or less,  $^{18}$  the overall mortality is 200,000  $^{17}$ .

Myocardial infarction is the cardiovascular disease, which is the most important cause of morbidity and mortality in diabetes patients. So the main role of diabetic treatment is to improve the cardiovascular risk of diabetes patients. Cardiovascular risk factors including obesity, hypertension, dyslipidemia is common in patients with diabetes mellitus. Hence, we reviewed the epidemiology, risk factors, preventive measures of myocardial infarction to provide better treatment for myocardial infarcted patients.

## **COMPLICATIONS OF DIABETES MELLITUS**

#### **Diabetic Ketoacidosis (DKA)**

Diabetic ketoacidosis (DKA) is a metabolic derangement distinguished by hyperglycemia, metabolic acidosis and ketoacidosis. It mostly occur in patients with diabetes who have lack of insulin, such as in type 2 diabetes mellitus or absolute depletion of insulin, such as in type 1 diabetes mellitus in the presence of increased counter regulatory hormones (cortisol, growth hormone, epinephrine and glucagon). Dehydration, increase in insulin counterregulatory hormones and worsening of peripheral insulin resistance can contribute to a the development of diabetic ketoacidosis which is mainly caused by infections, acute medical illness involving the cardiovascular system (CVS) and gastrointestinal tract (GIT), diseases of the endocrine axis like acromegaly, cushing syndrome.

#### Hyperosmolar Hyperglycemic State (HHS)

Hyperosmolar hyperglycemic state (HHS) is the lifethreatening endocrine disease and it commonly affect people with type two diabetes. The incidence is increased by 52.4% among children from 1997-2009<sup>19</sup>. It occurs in patient with type 2 diabetes who can still produce insulin. Prefound dehydration, marked hyperglycemia, neurological impairment and mild or no ketosis are the hallmarks of hyperosmolar hyperglycemic state.

Hyperosmolar hyperglycemic state is mostly seen in elderly type 2 diabetic patients; however, it also occurs in children and young adults. Its mortality rate (20%) is 10 times higher than mortality rate of patients with diabetic ketoacidosis<sup>20,21,22</sup>. The prognosis is determined by severity of dehydration, presence of co-morbidities and older age. Replacing volume deficit and correcting hyperosmolality, hyperglycemia and electrolyte imbalance are the main treatment of hyperosmolar hyperglycemic state.

## **Diabetic Retinopathy (DR)**

The most common diabetic micro vascular complication is diabetic retinopathy (DR). Some report suggested that due to development in systemic control, the incidence of visual impairment from diabetic retinopathy has been decreased in recent years in the US greatly<sup>23</sup>. The diabetic retinopathy is the expanding problem globally. It currently affects almost 100 million people worldwide and it is an increase in health burden. Diabetic retinopathy related visual

impairment and blindness has been increased by 27% and 64% respectively in the year of 1990 and 2010 <sup>24</sup>.

Duration of diabetes, poor glycemic control and hypertension are the major risk factor for the rapid progression of diabetic retinopathy. Rapid lowering of glucose level and hypoglycemia may aggravate preproliferative diabetic retinopathy and also precipitate vitreous hemorrhage. Insulin dependent type 1 diabetes patients are at more risk of developing diabetic retinopathy when compared to type 2 diabetes patients. The percentage of diabetic retinopathy differ from 85 percentage of type 1 diabetes patients to 58 percentage of type 2 diabetes patients for more than 15 years after diagnosis <sup>25</sup>.

#### **Diabetic Nephropathy (DN)**

In patients starting renal replacement therapy, diabetic nephropathy (DN), another diabetic complication is the leading cause of kidney disease. It mostly occurs in patients with history of diabetes and renal failure. Diabetic nephropathy is associated with increased cardiovascular mortality. End stage renal disease is more common in patients with type 1 diabetes and type 2 diabetes. It is more common in ethnic minorities than other groups of society <sup>26</sup>. The progression of disease vary from person to person.

Glomerular filtration rate is the important parameter to determine kidney function and it should be measured in all diabetes patients. Diabetic nephropathy refers to the structural and pathological changes in the kidney of the patients with diabetes mellitus, due to effects of diabetes mellitus on the kidney. This can be characterized by proteinuria, hypertension and progressive reduction in kidney function.

## **Diabetic Foot (DF)**

Diabetic foot ulcer or an injury to all layers of skin, that mainly occurs on the soles of the feet. It mainly occurs as a result of peripheral neuropathy or any peripheral arterial disease in diabetes mellitus. For the understanding of the diabetic foot ulcer, all should know about necrosis or gangrene, which is a tissue death due to blockage of blood vessels. Foot ulcer can be followed by bacterial invasion resulting in infection in any part of the body especially in the lower leg.

The risk factors of foot ulcers are loss of sensation caused by peripheral neuropathy, ischemia or a combination of these. 20% of the diabetic patients are admitted to hospital due to complaints of diabetic foot ulcer<sup>27</sup> and it can also lead to death if proper treatment is not given <sup>28</sup>. Once the patient has developed diabetic foot ulcer, then the patient is at higher risk of developing ulcer that may lead to amputation.

#### **Myocardial Infarction (MI)**

The most common form of coronary heart disease and also most important complication of diabetes is myocardial



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infarction (MI). When a coronary artery is occluded, it creates decreased blood flow, causing some of the heart muscle being supplied by that artery to become infracted, in MI<sup>29</sup>. In MI, a part of the heart muscle will be affected, when the blockage occurs in the artery, due to plague buildup on vessel walls (fig.no.1). There are two types of MI are ST-segment elevation MI (STEMI) and Non- STsegment elevation MI (NSTEMI). MI is diagnosed by characterized by changes on the electrocardiography (ECG). One of the main ECG changes is the ST- segment elevation which is called as STEMI and if there is STsegment elevation and presence of cardiac biomarker such as troponin are called as NSTEMI.It has been debated for decades that thrombosis can cause acute myocardial infarction. Atherosclerosis with inflammation is the most important factor for thrombosis. High blood glucose from diabetes can damage blood vessels and nerves that control heart and blood vessels. The longer a person have diabetes, the higher the chance that the patient will develop heart disease like myocardial infarction. People with diabetes tend to develop heart disease at a younger age than people without diabetes. In adults with diabetes, the most common cause for death are heart disease and Stroke. Adults with diabetes are nearly twice as likely to die from heart disease or stroke or myocardial infarction as people without diabetes mellitus <sup>30</sup>.



Figure 1: Myocardial Infarction

## EPIDEMIOLOGY

About 12.2% of death occurs due to ischemic heart disease like myocardial infarction, which is estimated in 2004 in worldwide by WHO. Myocardial infarction is the leading cause of death in high- or middle-income countries <sup>31</sup>. Worldwide, about 15.9 million myocardial infarctions occurred in 2015<sup>32</sup>. Around 3 million people has STEMI and 4 million people have NSTEMI a year<sup>33</sup>. It occurs very common in men than women<sup>34</sup>. According to World health organization, for people more than 60 years of age, coronary heart disease is the most common cause of death and the incidence of myocardial infarction increases in both male and female with age, although this is more marked in men than in women (Fig. No.2)<sup>35,36</sup>. In high income countries, the rate of death due to myocardial infarction has been declined<sup>37</sup>. In variance to that, ischemic heart disease is the common source of death. In developing world, 1.46 million death occurred due to ischemic heart disease in 2004 in India and it is expected to raised during 1985 to  $2015^{38}$ .



**Figure 2:** World Health Organization 2013.Global Health Estimates Summary Tables: Death by Cause, Age and Sex by various regional grouping.

## INCIDENCE

The incidence rate (per 100,000) of STEMI has been decreased considerably (121-77) and the incident rate of NSTEMI has also been decreased slightly (126-132)<sup>39</sup>. There was no difference mortality for both STEMI and NSTEMI on the period of 6 months to 4 years follow up, in a landmark study, whereas, long term prognosis was seen in STEMI patients compared to NSTEMI patients<sup>40</sup>.

The incidence of myocardial infarction in white men and women against black men and women and its comparison was reported in Mozaffarian study. The black men are at the greater risk of developing myocardial infarction especially, in the age group of 75-84 years than white men and women  $^{41}$ .

## PREVALANCE

The prevalence of myocardial infarction was reported as 640,000 in men and 275,000 in women in UK, which represent 915,000 people suffered from myocardial infarction in UK in 2014 according to national survey. In 2013, the prevalence of myocardial infarction was higher in men than women in UK <sup>42</sup>. The age specific myocardial infarction prevalence was about 0.06% of men less than 45 years old age and 2.46% of men greater than 75 years old age (Fig.no.3).



Figure 3: Age-specific prevalence of MI in the UK, 2014. Adapted from Clinical Practice Research Datalink (CPRD),



2014. Evaluations are based on records from a sample of general practices in each of the constituent nations of the UK.

# PATHOPHYSIOLOGY OF MYOCARDIAL INFARCTION AND REPERFUSION INJURY

The process of atherosclerosis forms the plague which is responsible for acute coronary syndrome, which leads to coronary artery thrombosis. These conditions precipitate Myocardial infarction. Tissue factor is a substance which is located inside of the plague. This substance when exposed to bloodstream, activates the clotting cascade, leads to thrombosis. Tissue factor is exposed, when "plaque rupture" occurs. Plaque rupture and plaque erosion (ulceration) can result in coronary thrombosis. STEMI or NSTEMI has a higher incidence of coronary thrombosis. Plaque rupture (most common) or erosion resulting in coronary occlusion is the important mechanism in NSTEMI and STEMI.

The rupture of an atherosclerotic plaque with thrombotic occlusion of an coronary artery and transmural ischemia resulting in acute myocardial infarction. The infarct starts from the subendocardial layers in the middle of the area at risk and expand into the subepicardial layers and to the border zones of area at risk with continuing duration of coronary occlusion.

In human, 30 to 50% of the area at risk is still feasible and therefore salvageable by reperfusion after 4-6 hours from the beginning of anginal symptoms, as evaluated from magnetic resonance imaging (MRI) and biomarker analysis of myocardial salvage <sup>43</sup>. The reperfusion is necessary to salvage ischemic myocardium from nearing infarction, reperfusion also result in additional injury which may be reversible or irreversible <sup>44</sup> and manifest increased infarct size and micro vascular dysfunction.



Schematic diagram of mechanisms in the cardiomyocyte and coronary vascular compartment which interact and contribute to irrerversible ischemia/reperfusion injury Fig(3) explains a schematic diagram of mechanism contributing to myocardial infarction and Reperfusion injury to the cardiomyocyte and coronary vascular compartment. The infracted myocardium is distinguished by swollen mitochondria, rupture in sarcolemma, hemorrhage, micro vascular destruction. These signs indicate necrosis which typically becomes more obvious and it is accelerated during reperfusion <sup>45,46,47</sup>.

However, tissue necrosis is considered to be an unconditional mode of cell death and their quantitative contribution to the infarct size is not clear. The sarcolemmal receptors and release of cytochrome c from damaged mitochondria initiates apoptosis, which is a energy dependent mode of cell death. Opening of the mitochondrial permeability transition pore (MPTP) is important for necrosis and apoptosis. Ischemia or reperfusion injury in the coronary circulation recognized as micro vascular dysfunction, which is increased by capillary permeability and edema and release of platelet, leucocytes and erythrocyte aggregates in the micro circulation from the atherosclerotic lesion and lastly capillary destruction and hemorrhage. Impairment of myocardial blood flow regardless of restoration of epicardial coronary patency was first reported by Krug et al., <sup>48</sup> and Kloner et al., <sup>49</sup>. They characterized the most severe form of myocardial Ischemia or reperfusion injury is no-reflow phenomenon. The delay to reperfusion increases the incidence of no reflow. The no-reflow and intramyocardial hemorrhage are the most important adverse prognostic factors.

# PREVENTIVE MEASURES OF ACUTE MYOCARDIAL INFARCTION

## **PRIMARY PREVENTION**

#### Reducing blood pressure

In patients with acute myocardial infarction and hypertension, reduction of blood pressure is necessary, but not immediately, it should be done gradually, and by that occurrence myocardial infarction can be avoided. Nitrates with labetalol as intravenous infusion, as an initial treatment and sodium nitroprusside, nicardipine are the other alternatives used, mainly in hypertensive emergencies. Oral or intravenous beta blockers are also used because it will decrease the BP within hours and it also have anti-ischemic effect <sup>50</sup>.

## **Correcting Dyslipidemia**

Most of the diabetes mellitus patients will have dyslipidemia and it is associated with increasing risk of myocardial infarction. Treatment of dyslipidemia varies with age and statins are the first line treatment. Diabetic patients under the age of 40 should be treated with high intensity statin, if the atherosclerotic cardiovascular disease is present or a low density lipoprotein cholesterol (LDL-C) greater than 189 mg/dl. Diabetic patient over the age of 40 are recommended to use statin therapy. Around 40% of the patients with 10 years atherosclerotic cardiovascular disease (ASCVD) risk more than 7.5%, are



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treated with high potency statin and other patients with 10 years ASCVD risk less than 7.5%, are treated with moderate potency statins  $^{51}$ .

## **Reducing Obesity**

Improving the level of physical activities and reducing inactive lifestyle are the main objective to reduce obesity. Obesity is the major risk factor for developing diabetes and cardiovascular diseases like myocardial infarction. Several studies have been demonstrated that reducing weight in pre-diabetic patients with control development of diabetes and myocardial infarction. Finnish diabetes prevention studies evaluated the response of behavioral modification of reducing weight, stated that reducing weight will reduce the incidence of diabetes <sup>52,53</sup>.

#### **Smoking Cessation**

Smoking cessation reduces the smokers risk in developing cardiovascular diseases like myocardial infarction. Coronary heart disease risk is eliminated to half within 2 years of smoking cessation. This is rapid improvement in endothelial function and hypercoagulability among smokers who quitted smoking. Pharmacotherapy used for smoking cessation are Nicotine replacement products, Buproprion and varenicline <sup>54</sup>. Among this, Bupropion has many possible interactions with drugs used in cardiology. It is mainly metabolized by cytochrome P450 2B6 and it will interact with drugs which is acting on this isoenzyme, so it will lead to increased effect of Bupropion. Nortryptilline, a tricyclic antidepressant and Clonidine, a antihypertensive agent assumed to have some effect on smoking cessation, but it has no proper evidence <sup>54</sup>.

## Exercise

Sedentary life style is one of the main reason for cardiovascular diseases like myocardial infarction. Regular exercise will reduce the risk of cardiovascular diseases. Exercise can reduce obesity and it will also reduce blood pressure and bad cholesterol in the blood. When an individual changes from being in sedentary lifestyle to moderately active lifestyle, there will be a greatest gain in terms of mortality. In diabetic patients, regular exercise will increase body stability to use insulin, so it will reduce blood glucose level.

## SECONDARY PREVENTION

#### **Reducing Cholesterol**

A low level of LDL-C level is considered good for the health of the heart. A high level of high density lipoprotein (HDL-C) cholesterol is good for healthy heart. Normal triglyceride (TG) level vary with age and sex. A high TG level combined with low HDL-C or high HDL-C is often associated with atherosclerosis, which will deposit fat in the artery walls that leads to increased risk of myocardial infarction. Reducing cholesterol level will prevent reoccurrence of myocardial Infarction. Reducing blood cholesterol is beneficial in minimizing the risk of developing cardiovascular disease like myocardial infarction. Simvastatin is an HMG coA reductase inhibitor, that will reduce LDL-C and also increase HDL-C. It will slow the progression of atherosclerosis and reduce mortality and morbidity in cardiovascular disease patients <sup>55</sup>.

#### **β- Blockers**

Beta- blockers are commonly used in primary therapy and in secondary prevention. In early therapy, in the emergency condition of suspected acute myocardial infarction,  $\beta$ - blockers are used, especially if the patient is having tachycardia or hypertension. Usage of  $\beta$ - blocker in myocardial infarction, will reduce myocardial workload, and also reduce oxygen demand, by decreasing blood pressure and heart rate. It reduces catecholamine levels, decrease ischemia and prevent development of infarction. The incidence of supra ventricular and malignant ventricular arrhythmia will be reduced, by the early usage of beta- blockers in myocardial infarction. It will also reduce chest pain symptoms and sudden cardiac death.

#### Aspirin

Aspirin is a drug therapy which is used for secondary prevention of cardiovascular events and also used in primary prevention <sup>56</sup>. Patients suffers from cardiovascular disease, such as myocardial infarction, are at risk of developing another myocardial infarction <sup>56</sup>. Aspirin is an effective treatment of Acute myocardial infarction. Aspirin therapy reduces mortality in patients with suspected acute myocardial infarction by 23%, which is reported in ISIS-2 <sup>57</sup>. That study, provided evidence on the effect of low dose aspirin. Aspirin is administered immediately after myocardial infarction, in 1000 patient and it prevented 25 death and 10-15 Strokes <sup>58</sup>.

## ACE- Inhibitors

Earlier studies have reported that ACE-inhibitors reduce the size of infarction and improve ventricular remodeling. ACE-inhibitors have a effect on mortality and morbidity in post infarction patients. In the acute phase of myocardial infarction, i.e. within 24 to 36 hours of onset of symptoms, ACE- inhibitors are beneficial <sup>59</sup>.

#### **RISK FACTORS OF MYOCARDIAL INFARCTION**

#### Smoking

It is the most important risk factor of acute myocardial infarction. Smoking results in early STEMI. Smoking increase serum LDL-cholesterol and triglyceride concentration and reduces serum HDL-cholesterol. Smoking appears to increase atherosclerosis, by contributing to vascular inflammation <sup>60</sup>. A recent study found that smoking is also associated with a thickening of the heart and lower's heart pumping ability, both are associated with cardiovascular disease. The more cigarettes people without heart disease smoked, the greater the damage to their heart's structure and function.



#### **Alcohol Consumption**

Most researchers showed that alcohol consumption could increase triglycerides, heart rate and blood pressure <sup>61,62,63</sup> and thus increase the risk of atherosclerosis, atrial fibrillation and anorexia, resulting in damaging cardiovascular system and cardiac muscle cells <sup>64</sup>. Drinking over a long period of time can increase the risk of heart disease. Drinking increase Blood pressure, which is one of the most important risk factors for having a heart attack or acute myocardial infarction. Heavy drinking also weakens the heart muscle.

#### **Diabetes Mellitus**

Diabetes mellitus is the most common risk factor for cardiovascular disease. People with Diabetes have increased morbidity and mortality associated with cardiovascular disease compared to non-diabetic patients<sup>65</sup>. Diabetic patients have increased risk of atherosclerotic vascular disease in the heart. It is also reported that plaque are more possible to rupture in diabetic patients rather than non-diabetic patient <sup>66</sup>. Factors unique to diabetes increase atherosclerotic plaque formation and thrombosis, thereby contributing to myocardial infarction. Bibbins et al.,<sup>67</sup> says that Diabetes mellitus is the biggest individual risk factor of heart disease.

#### Hypertension

The excess strain and damage to coronary arteries serving the heart due to high blood pressure, causes the arteries to narrow from a buildup of fat, cholesterol and other substance called as plaque. This process is called atherosclerosis, which lead to formation of blood clot. When an artery becomes blocked due to blood clot, the blood flow will be interrupted, leading to damage of part of heart muscle called as myocardial infarction. In old age, hypertension is even worse to heart and responsible for atleast 70 percent of heart disease <sup>68</sup>.

## Obesity

Obesity is a risk factor for coronary artery disease among adults and is increasing in prevalence among young adults, as well as adults <sup>69</sup>. Obesity is directly related to incidence of myocardial infarction. Occurrence of infarction is greatly increased by extreme obesity, because it is a recognized risk factor for myocardial infarction.

## Stress

Long term stress, isolation from society, anxiety and depression increases the risk of myocardial infarction and Stroke <sup>70</sup>. Acute stress is also risk factor for Coronary heart disease. Stress due to death of a person may also induce myocardial infarction <sup>71</sup>. Emotional stress leads to rupture of an atherosclerotic plaque, with consequent thrombosis<sup>72</sup>.

# FUTURE RESEARCH IN THE TREATMENT OF DIABETES MELLITUS

Replacing the beta cells that already lost, ensuring their future survival and stopping the autoimmune destruction of beta cells is the main goal in the future research of diabetes mellitus. Currently, whole pancreas or islet cell transplantation are used for the replacement of beta cells. The human pancreas availability is limited, that is the major drawback. Nowadays, stem cell replacement therapy are used for restoration of beta cells. It is also done by new beta cells generation. There are many observational trials that suggest that there is an association between cardiovascular disease and glycemic control. ADVANCE, a large randomised control trial suggests that, there is only modest effect of glycemic control on further cardiovascular disease <sup>73-76</sup>. Much more studies are required for the better understanding of the relationship between cardiovascular disease like myocardial infarction and glycemic control. Further research is needed to determine the best treatment to reduce the risk of cardiovascular disease in patients with diabetes mellitus. Additional research is needed for the better understanding of how risk factors of myocardial infarction such as blood pressure, obesity and dyslipidemia should be monitored and ho it should be managed in diabetes patients. The studies like IMPROVE-IT could help to determine which therapy will be more effective for the management of dyslipidemia in diabetes patients 77. Encapsulation will give protection against rejection without the complications of immunosuppressive therapy. For growing beta cells in culture, many attempts have been made and to introduce these into the body without provoking their immune destruction. These biological approaches offers improved technology for controlling type 1 diabetes mellitus. EMPA-REG OUTCOME 78 and Canagliflozin Cardiovascular Assessment Study (CANVAS) <sup>79</sup> studied the effect of SGLT2 inhibitors and identified significant reduction in the cardiovascular events with empagliflozin and canagliflozin respectively.

## CONCLUSION

In summary, myocardial infarction is the most important complications of diabetes mellitus. Diabetes increase the morbidity and mortality associated with myocardial infarction. Because of the increased morbidity and mortality of myocardial infarction, aggressive glycemic control is the only way to minimize the risk of occurrence of myocardial infarction. Further understanding of the effect of diabetes on myocardial infarction may lead to more specialized treatment for high risk patients.



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