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REVIEWED STUDY ON DIABETES MELLITUS AND CORONARY HEART DISEASE RISK

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ABSTRACT

In this paper will investigate whether or whether there is a connection between type 2 diabetes, dyslipidemia, and the risk of coronary heart disease. Typical dyslipidemic symptoms of diabetes include increased amounts of microscopic, dense low-density lipoprotein cholesterol (LDL-C) particles, decreased levels of high-density lipoprotein cholesterol (HDL-C), and elevated triglyceride levels. These lipid abnormalities, in addition to the underlying insulin resistance and hyperglycemia, play a part in the accelerated atherosclerosis process that is found in diabetes. The link between dyslipidemia, diabetes, and coronary heart disease has been hypothesised to be caused by a number of different routes. Insulin resistance is a defining feature of type 2 diabetes. This trait, in turn, contributes to the development of dyslipidemia by reducing HDL-C levels and impeding the clearance of triglyceride-rich lipoproteins. People who have diabetes also likely to have higher than average quantities of LDL-C particles that are very small and very dense. These particles are more atherogenic. The risk of developing cardiovascular disease is raised significantly when a person also has dyslipidemia in addition to diabetes mellitus. People who suffer from diabetes and dyslipidemia have been found to experience a higher incidence of cardiovascular events when compared to individuals who do not suffer from either condition. In light of these findings, it is abundantly obvious that proper control of lipids is essential for both the treatment of diabetics and the prevention of coronary heart disease.

INTRODUCTION

Atherosclerosis is mostly driven by inflammation. Adipose tissue releases a considerable number of inflammatory and pro-inflammatory cytokines in response to the acute phase reaction that occurs in type 2 DM as a result of obesity and insulin resistance. Diabetic individuals with CAD typically have endothelial dysfunction, as seen by elevated endothelin 1 and depleted nitric oxide. Relative to endothelin 1, vascular endothelial (VE)-cadherin has been found to be a more recent and accurate measure of endothelial function in diabetic individuals with CAD.

Increased platelet activity and blood coagulability contribute to increased thrombus development in type 2 DM. Short-term cardiovascular events are mostly unaffected by pathological changes in fibrinogen and plasminogen activation inhibitors in individuals with type 2 diabetes.

It is important to note that not all diabetes people with risk factors for cardiovascular disease really end up with cardiovascular disease. Recent research, however, has zeroed in on the significance that biomarkers such serum phospholipids play in the development of CVD in diabetes individuals. Recently, Beatriz Garca-Fontana and coworkers discovered that diabetic individuals with CVD have lower blood levels of four phospholipids compared to diabetic patients without CVD.

Recent research has identified a novel biomarker that is considerably higher and positively connected with the degree of CAD stenosis in patients with type 2 diabetes who also suffer from coronary artery disease. Osteonectin Secreted Protein Acidic and Rich in Cysteine (SPARC) is the name given to this novel biomarker. More investigation is needed on how SPARC could lead to the onset of CAD.

A cross-sectional research by Palazhy et al. compared oxidative stress in three groups of patients using statins for coronary artery disease: Group 1, healthy controls; Group 2, patients taking statins for both diabetes and CAD; and Group 3, exclusively diabetic patients. Despite receiving statin treatment, the oxidative stress levels were greater in the CAD and DM group. In light of these findings, the significance of oxidative stress becomes clear.

DIABETES IN CAD PATIENTS

Several studies carried out in the Arabian Gulf region experienced methodological issues as a result of the presence of a large number of employees from other countries. The inclusion of these individuals was reflected in the data, which demonstrated a prevalence that was not dissimilar to that which was observed in the location where they had originally come from. As a direct consequence of this, we were unable to incorporate a significant number of these studies into our analysis.

In light of the fact that coronary heart disease affects around 85 percent of the population and cerebrovascular disease (CVD) affects approximately 15 percent, the World Health Organisation (WHO) decided to conduct a cross-sectional research on 10,000 patients residing in 10 different countries, the majority of which are located in the Middle East. It was discovered that the incidence of specific risk factors was quite high, and diabetes was diagnosed in about one third of the patients (31.5%).

There are not many national data for Lebanon. From the Lebanese Interventional Registry, we were able to get data about the cardiovascular risk factors of patients who had undergone coronary angiography. Diabetes mellitus (29%) cigarette usage (50%) abnormal lipid profiles (29%). high blood pressure (60%) abnormal lipid profiles.

Patients who had acute myocardial infarction and had modifiable risk factors were the subjects of the case-control research that was conducted by INTERHEART. The total number of patients in the research was 15,152, while the number of controls was 14,820. The Middle East contributed more than 1500 patients and 1700 controls to the whole study. According to the statistics, around 15% of persons in the Middle East subgroup suffered from diabetes, 9% of them had hypertension, and 45% of them smoked cigarettes regularly. A prevalence of 70% was found for dyslipidemia, while the prevalence of abdominal obesity was just 25%.

Imaging studies allow for extremely detailed examinations of both the heart and the arteries that supply it with blood. Take, for instance:

a. An echocardiography is a diagnostic procedure that uses sound waves to produce images of the patient's heart. In addition to monitoring heart function and diagnosing issues, it may be able to assess the thickness of the heart muscle as well as its motion.

b. b. Coronary Computed Tomography Angiography (CTA): This procedure creates detailed photographs of the coronary arteries and identifies any areas of constriction or blockages.

c. Magnetic resonance imaging (MRI) of the heart offers a comprehensive view of the structure of the organ as well as its electrical activity and blood supply. It is helpful in locating specific areas of the cardiac muscle that are not receiving the adequate amount of oxygen.

d. In order to observe the circulation of blood through the heart, nuclear imaging, which is also known as myocardial perfusion imaging, involves the introduction of a radioactive tracer. CAD-related regions that have reduced blood flow can be located and identified.

REVIEWS

S. Durrani, S. 2017. A comparison will be made in this study between a novel biomarker called adiponectin and other variables that are already known to increase the risk of cardiovascular disease in people who live in Khyber Pakhtunkhwa and have type 2 diabetes. Substances and Techniques: Researchers at the Bio-Chemistry Department of Khyber Medical College in Peshawar, Pakistan, conducted a cross-sectional survey of patients at three of the city's tertiary care institutions from January through December of 2016. During this time, the researchers analysed the data acquired from the survey. In this study, participants were divided into two distinct groups. Group A consisted of sixty patients who were diagnosed with type 2 diabetes and coronary heart disease. On the other hand, Group B consisted of healthy controls. On a questionnaire, we recorded in great detail the medical histories of all of the participants, including information on their blood pressure and body mass index. Blood was drawn from subjects while they were fasting, and the samples were tested for a number of different biomarkers. These biomarkers included adiponectin, glycosylated haemoglobin, glucose, and lipids (cholesterol, triglycerides, HDL, LDL, and VLDL).

PATHOGENESIS OF TYPE 2 DIABETES MELLITUS

The pathogenesis of type 2 diabetes is still not very well understood, despite the fact that a lot has been learned in recent years. The development of obesity is significantly influenced by a number of environmental factors, the most prominent of which are an unhealthy diet and an insufficient amount of physical activity. However, when looking at type 1 diabetes, the role of genetics becomes far more important. The proportion of concordance between identical twins ranges from 50% to 90%, and the risk of having type 2 diabetes from first-degree relatives ranges from 20% to 40%, whereas the risk ranges from 5% to 7% in the general population. Identical twins have a higher chance of having a similar set of characteristics than fraternal twins. Diabetes mellitus type 2 is genetically unique from diabetes type 1, yet there is scant evidence to support the concept that it has an autoimmune basis. Type 1 diabetes is characterised by a genetic predisposition to developing the disease.

Two metabolic disorders are responsible for the development of type 2 diabetes:

1) Decreased insulin sensitivity in the tissues of the periphery (also known as insulin resistance). and

2) B-cell dysfunction is characterised by inadequate insulin production, which manifests itself in the presence of both hyperglycemia and insulin resistance. Insulin resistance is the root cause of many of the issues, and B-cell malfunction can range from mild to severe depending on the severity of the condition.

INSULIN ACTION

Insulin

Insulin is a hormone that is necessary for healthy development and growth when it is present in enough amounts. Its one and only application is in the direct regulation of sugar levels in the blood. In human beings, the half-life of insulin is somewhere between 5 and 10 minutes. Insulin originates from a precursor protein that already possesses the A, B, and C domains. In order to form mature insulin, the C-domain of proinsulin must first be cleaved. Mature insulin consists of 51 amino acids and the connecting (C)-peptide. The effect of insulin is mediated by the fact that it attaches to the receptor for it on the cell membrane. When insulin attaches to its receptor, signals are sent to a network of intracellular pathways that regulate cellular metabolism, growth, differentiation, and survival. These signals are generated when insulin interacts with its receptor. Insulin is responsible for the stimulation of translation initiation, which in turn increases the number of active ribosomes and therefore increases the rate of protein synthesis.

Target organs

Insulin influences a vast variety of tissues throughout the body. However, the principal targets of insulin are adipose tissue, skeletal muscle, and the liver. In the process of regulating glucose levels, both the liver and skeletal muscle are essential organs. Insulin works by attaching itself to insulin receptors on the surface of the cells that it is trying to influence. Insulin increases the activity of glycogen synthase in multiple tissues, which in turn speeds up the creation of glycogen. This accounts for approximately 70% of the total glucose disposal that occurs after a meal. Insulin's primary effect is on skeletal muscle, specifically, and it does this by forcing the Glut4 glucose

transporter to migrate to the plasma membrane, which then makes it easier for the muscle to take in glucose. The insulin-mediated portion of the overall glucose excretion that is carried out by skeletal muscle accounts for between 70 and 80% of the total. The binding of insulin receptors in hepatocytes, which results in a decrease in hepatic glucose synthesis via gluconeogenesis and glycogenolysis, is responsible for regulating the levels of glucose in the blood. Insulin stimulates both the breakdown of glycogen into glucose and the synthesis of glycogen in the liver. It is essential for insulin to have a high concentration in the portal vein in order for these effects to be transmitted. In contrast to skeletal muscle, hepatocytes, which are cells that express Glut 2, have an absorption pattern that is tolerant rather than stimulatory when it comes to glucose. When insulin binds to its receptor, adipocytes experience an activation of the process known as Glut4 translocation to the plasma membrane. However, only around five percent of glucose uptake is mediated by insulin, and this process takes place in adipocytes. Glucose transport rates are increased by a factor of 20–40 immediately following activation of the Glut 4 translocation pathway. If there is a surplus of glucose, insulin will encourage the conversion of glucose to glycerol 3-phosphate. Glycerol 3-phosphate will then be connected to fatty acids to generate triacylglycerol. Triacylglycerol is the form in which fat is stored in adipocytes. Insulin slows down the breakdown of fat by inhibiting an enzyme called hormone-sensitive lipase. The pancreas of a rat, like the pancreas of a mouse, has cells that express insulin receptors. These types of receptors control the growth of the cell and are maybe involved in the production of insulin that is prompted by glucose. When the insulin receptor is removed from some cells, there is a reduction in the first phase of glucose-stimulated insulin production, which leads to the development of age-dependent glucose intolerance. In addition to its many other mitogenic activities, insulin is responsible for the initiation of DNA synthesis in certain cells, as well as the promotion of cell growth and differentiation. At healthy quantities, insulin can increase the generation and release of nitric oxide (NO) via the phosphoinositide 3-kinase (PI3K) signalling pathway, hence reducing atherosclerosis. Insulin also has an effect on vascular smooth muscle.

Vascular Actions of Insulin

Recent studies have demonstrated that insulin plays an important part in ensuring that healthy blood vessels continue to function properly. When insulin attaches to its receptor, two primary pathways are engaged, which begins the process of activating the vascular system. Phosphatidylinositol 3-kinase (PI3K) is responsible for mediating the metabolic (glucose action) signalling pathway (33), whereas mitogen-activated protein kinase (MAPK) is responsible for mediating the mitogenic, proliferative, and proinflammatory signalling route. One of the most important vascular actions that insulin performs takes place on an endothelium via the PI3K pathway. This activity mimics the generation of the powerful vasodilator nitric oxide (NO), which results in an increase in glucose absorption in skeletal muscles and adipose tissues (33). Endothelin-1 (ET-1) is a potent vasoconstrictor that has been shown to play a significant part in the progression of hypertension via the mitogen-activated protein kinase (MAPK) pathway. Insulin is also responsible for stimulating the production of endothelin-1 (ET-1).

Insulin modulates endothelial function by way of the mediators indicated above, despite the fact that these hemodynamic effects on vascular receptivity, coagulation, and tone could be considered to be in conflict with one another. ET-1 encourages platelet aggregation, increases the expression of adhesion molecules, and stimulates the contraction, proliferation, and migration of VSMC (34, 35). On the other hand, NO decreases the expression

of adhesion molecules in the endothelium, inhibits the adhesion and access of VSMC, and stimulates vasorelaxation, secretion, activation, and aggregation of platelets. Insulin modifies hemodynamics when it works on the vascular endothelium and wall by increasing blood flow and decreasing resistance to it (36). The PI3K-dependent pathway controls insulin's vasodilator effects, while the MAPK promotes insulin's proinflammatory effects. Insulin's effects on the vascular endothelium and wall are what cause insulin to have this effect.

According to research, MAPK inhibition reduces insulin's ability to constrict blood vessels and increases insulin's ability to dilate blood vessels. This results in a decrease in insulin's ability to promote cell proliferation and inflammation. A decrease in insulin-induced capillary recruitment has been linked to a decrease in the amount of glucose that is taken up by muscle when ET-1 is infused. In normal endothelium, the vasodilator PI3K/AKt/nitric oxide route is more active than the vasoconstrictor MAPK/ET-1 pathway; however, if there is an imbalance between these two routes, insulin's effects on the vascular and metabolic systems are disrupted.

Several studies have revealed that insulin protects the heart against reperfusion injury by way of the PI3K/Akt signalling pathway. This route has been termed the "survival pathway" due to the fact that it protects the heart from injury after it has been exposed to an oxygen-poor environment.

2.3.4 Insulin Signalling Pathways

Insulin's mitogenic and etabolic effects are the climax of a chain reaction of signalling events that start with insulin binding to its receptor and progress to a series of protein phosphorylation and dephosphorylation in succession. These processes are initiated by insulin binding to its receptor. To create an insulin receptor, a tetramer is formed from the assembly of four subunits: two a-subunits and two b-subunits. Within the cytosolic area of the B-subunit is where the tyrosine kinase activity is found. When insulin binds to the extracellular domain of the a-subunit, it activates the tyrosine kinase domain of the ß-subunit. This results in the phosphorylation of components in the downstream signal transduction pathway as well as the autophosphorylation of the receptor. The notion that there may be extensive cross-talk between protein intermediates enables one to divide the signalling pathways into two primary functional groups: metabolic and mitogenic. Both of these groups serve different purposes in the cell. The mitogenic activities of insulin (and insulin-like growth factors) are dependent on the pathway that is activated by mitogen-activated protein kinase (MAP-Kinase), which encourages the growth and division of cells (26). Phosphatidylinositol 3-kinase, also known as PI-3K, is an enzyme that plays a vital part in modulating the metabolic effects of insulin.

Insulin resistance

Insulin resistance is the core pathophysiological defect that underlies diabetes type 2 (also known as adult-onset diabetes). The presence of hyperglycemia often comes before the manifestation of insulin resistance. Individuals who are insulin resistant, on the other hand, might not have the same degree of resistance to the effects of insulin (40). There is a correlation between insulin resistance and congestive heart failure. Insulin resistance is present in up to fifty percent of those who have essential hypertension.

Insulin resistance is the condition that occurs when the tissues that insulin normally acts on no longer respond to insulin. Insulin resistance leads to a decrease in glucose absorption by skeletal muscle and decreased regulation of glucose synthesis in the liver, both of which are essential for maintaining glucose homeostasis. Insulin resistance also causes an increase in glucose production in the blood. Insulin resistance has been linked to a number of different genetic predisposing factors. It is the most important risk factor for developing diabetes and may be the earliest indicator of the likelihood of developing cardiovascular disease in the future. Insulin resistance is elevated in people who have Type 2 Diabetes, central obesity, atherosclerotic cardiovascular disease, and the majority of dyslipidaemias. Insulin resistance is also enhanced in people who have dyslipidemias. -cell function, in addition to that of skeletal muscle and liver, may be significantly impacted by the insulin resistance that is generated by hyperlipidemia, as well as by other changes in nutritional and hormone levels. However, not everyone who has insulin resistance develops type 2 diabetes later in life. Insulin resistance can be brought on by a disruption in the chain of metabolic activities that insulin normally sets in motion.

Changes in adipose tissue could be responsible for at least some of the reduction in insulin resistance. The amounts of free fatty acids in the plasma are regulated by adipose tissue, which in turn has an effect on the way glucose is metabolised throughout the body. It is now known that adipose tissue is an endocrine organ. Some of the adipokines that can be released by adipose tissue are adiponectin, leptin, tumour necrosis factor a, resistin, interleukin-6, and insulin-like growth factor I (IGF-I).

Adipose tissue may also affect glucose homeostasis throughout the body via a different mechanism, namely adipokines (44), which influence both insulin sensitivity and appetite. Studies have revealed correlations between adiponectin, insulin sensitivity, cardiovascular disease, and endothelial functions. Lipids have been connected to the development of vascular difficulties associated with diabetes (45), and diabetes has been linked to the development of vascular problems. Within cells that are not adipocytes, the hormone leptin may play a role in the maintenance of normal levels of fatty acids and triglycerides. This is in addition to its involvement in regulating the amount of food that is taken in. This prevents an overabundance of triglycerides while also maintaining fatty acid supply at a level sufficient to support essential cellular functions.

It is possible that the development of leptin resistance in diet-induced obesity may contribute to the lipotoxicity that is gradually detected in a variety of tissues in type 2 diabetes. Many researchers believe that insulin resistance can be traced back to shifts in the percentage of fat that is stored in adipose tissue, muscle, and the liver. Because of these changes, the levels of fatty acid metabolites that are found within the liver as well as the muscle cells increase. Proteins in the insulin receptor signalling pathway, such as insulin receptor substrate (IRS) proteins and phosphoinositide 3-kinase (PI-3K), have serine residues that serine kinases can phosphorylate in order to activate the proteins. This allows the proteins to perform their function. In contrast to tyrosine phosphorylation, serine phosphorylation lowers the activity of these proteins, which may lead to insulin resistance (46). This may also result in a decreased translocation of the glucose transporter that is dependent on insulin. Glut4, which is found in the cells of skeletal muscle, has been linked to reduced insulin signalling protein activity (47). It was shown that C57BL/6J mice who were given a high-fat diet had impaired translocation of Glut2 to the plasma membrane of the cells (48). This finding is quite interesting. Patients diagnosed with type 2 diabetes have been shown to have glycogen synthase activity that is 35–50% lower than that of healthy individuals (49). In these people,

glucose-6-phosphate fails to allosterically activate glycogen synthase as effectively as it would in healthy individuals. People who have type 2 diabetes produce less glycogen as a direct consequence of their condition. It has not been determined to what extent the underlying mechanism is responsible.

Vascular complications in Type 2 Diabetes Mellitus

Diabetes mellitus type 2 is linked to an increase in the risk of developing cardiovascular disease. Vascular disease can be divided into two categories, microvascular disease and macrovascular disease, according to the diameter of the arteries that are affected.

Vascular Complications

- Microvascular
- Macrovascular
- Retinopathy
- Nephropathy
- Neuropathy
- Coronary Artery Disease
- Cerebrovascular Disease
- Peripheral Vascular Disease

Microvascular disease is characterised by a thickening and a weakening of the vascular wall, both of which can result in leakage of proteins, bleeding, and a reduction in blood flow. Damage to the cells in the area around the affected area can lead to several different types of neuropathy, nephropathy, and retinopathy. Microvascular complications are something that will affect the majority of people who have type 1 diabetes at some time in their lives. Twenty percent of persons who have type 2 diabetes also have neuropathy, and up to ten percent of them have overt nephropathy. Retinopathy affects twenty percent of people with type 2 diabetes. Diabetic nephropathy is responsible for around forty percent of all newly diagnosed cases of kidney failure. Peripheral neuropathy and peripheral vascular disease are two conditions that frequently lead to problems in diabetes patients, the most common of which being foot ulcers and amputations. The most common reason for blindness in adults is a condition called diabetic retinopathy, which strikes virtually all diabetics during the first 20 years after their diabetes has been diagnosed. Hyperglycemia that persists for an excessive amount of time is the most common suspect in the development of microvascular illness. Other key contributors include insulin resistance, obesity, advanced age at diagnosis, and hypertension. The risk of developing microvascular issues is reduced when glucose levels in the blood are effectively managed.

Atherosclerosis is a chronic inflammatory disorder that is triggered when the endothelium is damaged in some way. The prolonged inflammation is caused by interactions between altered lipoproteins, macrophages, and components of the arterial wall. People who have type 2 diabetes have a significantly increased likelihood of developing macrovascular diseases. Just as atherosclerosis is made worse by thromboembolic sickness in persons who do not have diabetes, macrovascular disease is made worse by thromboembolic illness. This means that fatty deposits and blood clots build up in the vessels, sticking to the vessel walls and decreasing blood flow. If the clots break away, it is possible that smaller blood veins will get clogged. Atherosclerosis is a significant factor in the progression of macrovascular disease, which encompasses cerebrovascular accident, coronary heart disease, and peripheral arterial disease.

People who have diabetes have a greater risk of passing away as a result of cardiovascular disease than the general population does. The risk of developing coronary artery disease and stroke is increased by a factor of two to four when diabetes is present. In point of fact, cardiovascular disease is the leading cause of death among persons who have diabetes type 2. According to the findings of a recent study, those who have impaired fasting glucose levels, impaired glucose tolerance, or Type 2 Diabetes have an increased chance of passing away from cardiovascular causes.

People who have diabetes have an increased risk of developing peripheral artery disease, as well as an increased risk of having the condition progress to a more severe stage. In persons who already have macrovascular disease, the connection between glycemic management and the development of macrovascular issues is not well understood. It has been hypothesised that hyperglycemia makes the inflammatory processes that are a contributor to atherosclerosis worse by increasing the impact of oxidative stress and dyslipidaemia. This is the case because hyperglycemia raises blood sugar levels. In addition, high blood pressure, which is a typical consequence of diabetes, plays a part in the progression of heart failure. In addition to that, cardiomyopathy associated with diabetes. Nevertheless, regardless of the presence or absence of coronary atherosclerosis, it is a risk factor for heart failure and should not be ignored. The development of cardioneuropathy, oxidative stress, and the glycosylation of proteins in a non-enzymatic manner are all consequences of elevated blood sugar levels.

Type 2 Diabetes Mellitus and Coronary artery Disease (CAD)

Epidemiology of CAD and Type 2 Diabetes Mellitus

First place on the list of things that can kill you is coronary artery disease (also known as CAD). Despite considerable advances in medical research that have produced new diagnostic tools and had a significant influence on reducing human suffering, such as early morbidity, death, and a diminished quality of life, the situation has not improved.

In addition to this, it has far-reaching implications on the costs of health care and the costs of impairment across the board for people of all ages. In recent decades, there has been a consistent and significant growth in the prevalence of diabetes mellitus (DM) around the world, most notably the more frequent type 2 diabetes mellitus, which accounts for roughly 90% of adult diabetic patients. This rise in prevalence has been attributed to a number of factors, including a rise in obesity rates and an increase in the number of people living longer. This tendency

is being driven in part by the fact that as people get older, they tend to put on weight and become less active. This is one of the main drivers of this trend. The disease continues to worsen in developing nations despite advances in both invasive and noninvasive therapies for coronary artery disease (CAD). This is due to factors such as a decline in physical activity and an uptick in the prevalence of obesity caused by the widespread availability of high-calorie, high-saturated-fat foods. In developed nations, the disease has already reached an advanced stage.

These societal and economic developments contribute to the acceleration of the onset of type 2 diabetes and the clustering of established risk factors for cardiovascular disease.

It was estimated that 4.0% of the adult population around the world had diabetes in 1995; it is anticipated that this percentage will climb to 5.4% by the year 2025. As a consequence of this, medical professionals forecast that the number of people living with diabetes in prosperous nations will more than double by the year 2025, reaching millions among those aged 65 and older. People in developing nations who are between the ages of 40 and 65 will make up the vast majority of those who are affected.

Those who have type 2 diabetes lose the normal protection that females have against the mortality caused by coronary heart disease. According to the findings of a 20-year follow-up study of the Nurses' Health Study, which included 121046 diabetic women aged 30-55 years, the age-adjusted relative risks of fatal CAD were 8.7 for women with a history of type 2 diabetes mellitus and no CAD at baseline, 10.6 for women with no history of diabetes at baseline and a previous history of CAD, and 25.8 for women with type 2 diabetes mellitus and CAD at baseline.

During the course of a 13-year follow-up research, men with type 2 diabetes had a risk that was three to four times higher for coronary artery disease events (CAD death or non-fatal MI) as compared to the risk that their non-diabetic counterparts experienced. There was a 9.5-fold increase in risk for diabetic women.

The 7-year mortality rate from coronary artery disease was compared between a sample of persons without diabetes consisting of 1373 individuals and a sample of people with type 2 diabetes consisting of 1059 individuals. Patients who had type 2 diabetes but no previous history of a myocardial infarction had a greater risk of dying from coronary artery disease (CAD) than those who either had diabetes or experienced a MI.

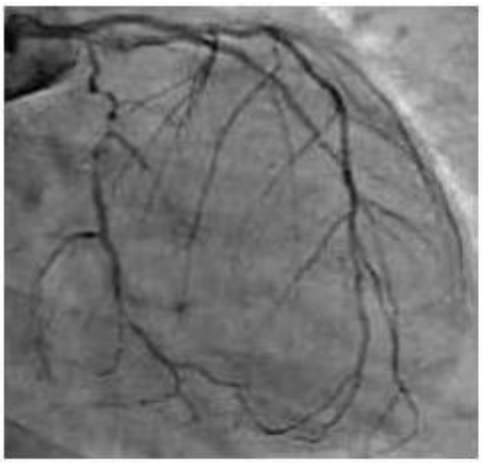
A registry study that was carried out by the Organisation to Assess Strategies for Ischaemic Syndromes (OASIS) uncovered evidence that pointed in the same direction as the previous finding. Accurate diagnosis might be challenging to get while dealing with type 2 diabetes. Mortality rates are considerable following a severe MI, with 44.2% of males with diabetes and 36.9% of females with diabetes going died within a year, with many more passing away before even reaching the hospital. In addition, mortality rates are significant following a mild MI, with 36.9% of females with diabetes passing away within a year.

persons with type 2 diabetes have been demonstrated to have a case of coronary artery disease that is more severe, complicated, and extensive than non-diabetic persons do. According to findings from computed tomography, coronary artery calcification is significantly more prevalent in people who have diabetes than in people who do not have diabetes.

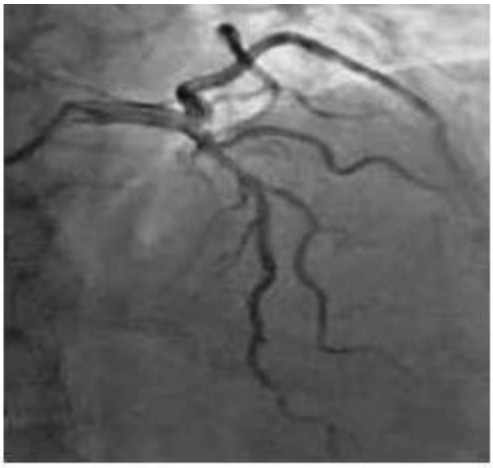
NATURE OF CORONARY ARTERY DISEASE IN TYPE 2 DIABETES MELLITUS

Case-control studies have demonstrated that patients with type 2 diabetes who have coronary angiograms that show their arteries are normal have smaller-diameter arteries compared to people without diabetes who act as controls. This is because people with type 2 diabetes have a higher risk of developing coronary artery disease. In patients with type 2 diabetes who also have coronary artery disease (CAD), there is a higher prevalence of many conventional risk factors for CAD as well as concomitant vascular issues.

In persons who have type 2 diabetes mellitus, coronary artery disease (CAD) is frequently more severe and complicated, and a greater number of coronary arteries are afflicted. Patients suffering from diabetes have much higher calcification of the coronary arteries than people who do not suffer from diabetes. It would suggest that diseases affecting the left main stem are more prevalent than those affecting the right. These features have also been discovered during postmortem exams.



Coronary Arteries of a Diabetic subject



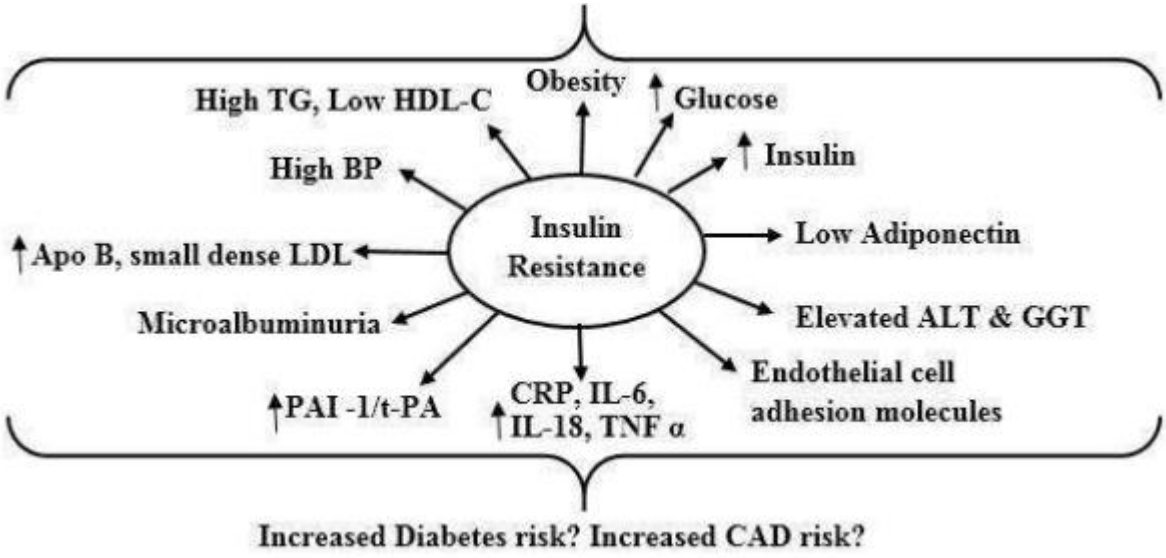
Coronary Arteries of a Non-Diabetic subject

IMPACT OF TYPE 2 DIABETES MELLITUS ON NATURAL HISTORY AND PROGNOSIS OF CORONARY ARTERY DISEASE

People who have type 2 diabetes mellitus have a mortality rate nearly three times higher than the general population. In this demographic, this condition is the major cause of death as well as disability. The Framingham study was the first epidemiological report, and it discovered that people with diabetes had a risk of AMI and angina pectoris that was anywhere from two to four times higher than those without diabetes. Those who are less than 45 years old (78) are at an increased risk for the complications that can result from these symptoms. People who have diabetes enter the category of having a higher risk of cardiovascular disease at an earlier age than those people who do not have diabetes, according to a recent study that was carried out in Canada.

It has become abundantly clear that diabetes mellitus type 2 does not represent a hyperglycemic state. Despite this, these individuals are associated with an increased risk of cardiovascular illness as a component of the spectrum of metabolic diseases. Insulin resistance is present in the great majority of individuals who suffer from

type 2 diabetes (80). When risk factors like dyslipidaemia, which is characterised by low HDL-cholesterol and high triglyceride levels, as well as central obesity, high blood pressure, oxidative stress, haemostatic alterations, low-grade inflammation, and endothelial dysfunction, are addressed, hypotriglyceridemia can be brought under control.



Changes in the majority of these risk variables associated to vascular disease either directly or indirectly are expected to cause an increase in the vascular burden many years before the overt hyperglycemic condition of type 2 diabetes becomes obvious. This rise in vascular burden is expected to occur. That is to say, the risk of developing vascular disease begins to accrue a significant amount of time prior to the diagnosis of diabetes (82). The pancreas is often able to produce increasing quantities of insulin over a period of several years in order to maintain glucose homeostasis. Insulin resistance worsens with age. A person is diagnosed with diabetes when their pancreas 'breaks down,' as it were, and their glucose concentrations climb into the range that is considered diabetic.

Endothelial Dysfunction in Type 2 Diabetes Mellitus: The primary event involved in the development of coronary artery disease

A disruption in normal endothelium function or dysfunction is one of the first steps in the advancement of atherosclerosis. This is one of the first steps in the progression of atherosclerosis. The endothelium, adventitial tissue, and vascular smooth muscle cells are the three components that comprise the fundamental framework of the human vasculature. The endothelium, which is made up of only one layer of endothelial cells, is an essential component in the maintenance of proper blood artery function. When the body is healthy, the endothelium is responsible for maintaining a balance between vascular constriction and vasodilation, prothrombotic and antithrombotic activities, as well as inflammatory and antiinflammatory processes. In each of these processes, the production of nitric oxide (NO) serves as an essential moderator. This chemical is produced when the amino acid L-arginine is converted to the molecule L-citrulline by the enzyme known as endothelial nitric oxide synthase

(eNOS). Vascular tone is maintained through a complex balancing act between the production of NO and that of vasoconstrictors such as endothelin. This helps to keep vascular tone in balance. After nitric oxide (NO) stimulates guanylate cyclase in vascular smooth muscle cells, vasodilation is mediated by cyclic guanosine monophosphate (cGMP), which is also known as guanosine triphosphate (GTP). In addition, nitric oxide prevents platelets from adhering to one another, leukocytes from migrating, and vascular smooth muscle cells from multiplying. When all of the components are functioning as they should, the end result is a vascular phenotype that reduces the risk of atherosclerosis.

Endothelial dysfunction is the term used to describe pathological conditions in which the endothelium is unable to carry out its usual duties. As a result, problems in vasoregulation, leukocyte adhesion and migration, vascular smooth muscle cell proliferation, and platelet aggregation are all the result of impaired endothelial function. As we've seen, each of these factors contributes significantly to the formation of atherosclerotic plaques in the body. In order to improve endothelial dysfunction, it is necessary to reduce the bioavailability of NO. Endothelial dysfunction is characterised by a number of symptoms, one of which is reduced NO-dependent vasodilation.

Impaired arterial stiffness and vascular endothelial dysfunction are well supported by research in individuals with type 2 diabetes that employs a range of techniques at diverse sites, such as the brachial arteries, coronary vessels, and subcutaneous channels. These findings were found in research that was conducted on people who had type 2 diabetes. Insulin resistance is a condition that is characterised by irregularities in lipids, elevations in free fatty acids (FFAs), low-grade inflammation, obesity, and hypertension. All of these factors may contribute to the dysfunction that occurs in diabetes individuals. In addition, excessive blood sugar levels could make it even more difficult for blood vessels to do their job. In conclusion, new evidence reveals that although insulin can restore vasodilator and vasoconstrictor actions on the endothelium, the latter effects may be dampened by features common to diabetes patients. This is the last point, but it is an important one. Researchers have discovered that many risk factor pathways in type 2 diabetes can have a negative impact on endothelial function.

Pathophysiology of Coronary Artery Disease in Type 2 Diabetes Mellitus

Evidence-based treatment concepts of CAD in type 2 diabetic patients require data ranging from fundamental mechanisms of atherothrombosis to outcomes from clinical investigations. Recent years have seen significant progress in our understanding of the pathophysiology of atherosclerosis, leading to the identification of potentially novel approaches and risk factors for atherosclerosis and thrombosis. For instance, inflammation is now considered a major risk factor for the onset of coronary artery disease. However, not all risk elements are easy to appraise, and it might be even more difficult to demonstrate how they affect CAD. For instance, whereas measuring C-reactive protein (CRP) is relatively simple, measuring endothelial dysfunction is not. It is impossible for a risk factor to be considered a 'proven' risk factor for cardiovascular disease if it cannot be assessed.

The endothelium is widely believed to play a crucial role at the outset of atherosclerosis (92). Nitric oxide, which regulates vascular relaxation and structure, is crucial. The endothelium also releases reactive oxygen species, endothelin-1, prostaglandins, and angiotensin II. Nitric oxide generation is inhibited in type 2 diabetes because of the disease's hallmark hyperglycemia, insulin resistance, and high levels of free fatty acids (FFA). Hyperinsulinemia and hyperglycemia, on the other hand, increase endothelin-1 synthesis.

In the early stages of atherosclerosis, the accumulation of low-density lipoprotein (LDL)-cholesterol in the sub endothelial matrix is the most important initiating event. Type 2 diabetics often have high concentrations of oxidised, tiny, dense LDL particles. The oxidative modification of LDL particles is initiated by these changes, making them more likely to contribute to atherosclerosis. In addition, the excessive breakdown of fatty acids is caused by a disruption in insulin metabolism, which reduces insulin's anti-lipolytic impact. Very low-density lipoprotein (VLDL) particles are synthesised at a higher rate due to the translocation of excess fatty acids to the liver. Cholesterol ester transfer protein mediates the exchange of cholesterol from HDL to VLDL, which contributes to the low HDL levels observed in people with type 2 diabetes.

RESULT

The most significant thing that can be learned from this research is that individuals who have a previous history of coronary heart disease or diabetes are at a significantly higher risk than individuals who do not have such a previous history for acquiring various phenotypes of peripheral vascular disease. people diagnosed with diabetes had a lower risk of developing PAD and CAS compared to people diagnosed with CHD. Although this difference has a high level of statistical significance, it is extremely improbable that it will have any real-world impact on the treatment of patients.

Our findings add credibility to the concept that diabetes and coronary heart disease are major contributors to the development of peripheral arterial disease and coronary arteriopathy syndrome (PAD and CAS), respectively. People who have diabetes have an adjusted odds ratio of 2.03, which indicates that they have a nearly two-fold increased risk of PAD in comparison to people who do not have diabetes. The 95% confidence interval for this number is between 1.91 and 3.46. People who have a history of coronary heart disease have a risk of peripheral artery disease (PAD) that is comparable to that of people who have diabetes. This assertion is supported by evidence that comes from studies that take a prospective cohort approach as well as research that takes a cross-sectional approach. Diabetes and a family history of coronary heart disease are two other independent risk factors for CAS that receive significantly less attention. Previous research has looked at the relationship between diabetes and a history of coronary heart disease (CHD), but those studies had low power and omitted adults over the age of 75 from their samples. The participation of senior people in our research gives us the opportunity to investigate age-related patterns of PAD and CAS in relation to diabetes and previous CHD. This is an essential investigation because diabetes and vascular illnesses such as PAD and CAS are significantly connected with age. This is due to the fact that diabetes is more common in people of advanced age.

CONCLUSION

Diabetes has been regarded as a potential contributor to the development of coronary heart disease ever since the Adult Treatment Panel III guidelines were made public. This classification of the cardiovascular risk associated with diabetes has also been confirmed by investigations that were conducted more recently. According to a recent meta-analysis of follow-up data from 1.2 million people who participated in population cohort studies, those who have both diabetes and coronary heart disease have a risk of mortality that is twice as high as those who do not

have either of these conditions. Despite the fact that having diabetes is related with having a higher risk of coronary heart disease (CHD), there is a large amount of diversity in the risk of CHD among the different groups of people who have diabetes. The severity of diabetes (as measured by glycated haemoglobin levels), the length of time that a person has had diabetes, and the amount of insulin that they use are all factors that contribute to an increased risk of cardiovascular disease, and in particular of peripheral arterial disease (PAD). In this particular investigation, the participants' dependency on glucose-lowering medicines or insulin was used to infer the degree to which they were affected by diabetes. Insulin-treated diabetics had an increased risk of developing PAD and CAS compared to those whose diabetes was managed with other methods. In spite of the fact that there were multiple ways to classify diabetes, there was an undeniable connection between PAD and CAS. According to the findings of this study, the degree to which diabetes is connected with peripheral vascular disease may vary from patient to patient. This suggests that the degree of association may depend on the individual patient. It's probable that people with type 1 and type 2 diabetes are both affected by this relationship in the same way. In order to get a better understanding of the connection between diabetes and peripheral vascular disease, additional research should be conducted using clearly defined markers of the severity of diabetes.

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