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Research Article

Leveraging the Biochemical Basis of Heart Failures in Type2 Diabetics, Through a Few Case Studies and Review of Literature

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Abstract

This study delves into the intricate biochemical mechanisms underlying heart failure in individuals with type 2 diabetes, aiming to provide valuable insights through a few compelling case studies. The prevalence of heart failure in type 2 diabetics has been a growing concern, necessitating a thorough exploration of the biochemical pathways that contribute to this complex interplay between metabolic disorders and cardiovascular complications. The limitations of current prediction models for assessing cardiovascular risk in individuals with diabetes present a significant challenge This research employs an epidemiology and etiology approach, combining clinical data and biochemical analyses, to unravel the nuanced connections between diabetes and heart failure. This study underscores the importance of a comprehensive approach to managing heart failure in type 2 diabetics, emphasizing the need for tailored treatment strategies that can address the specific biochemical imbalances identified in individual cases. By leveraging the biochemical insights gleaned from these case studies, clinicians and researchers alike can contribute to the development of more effective and targeted therapeutic interventions, ultimately improving outcomes and quality of life for individuals grappling with the challenging intersection of type 2 diabetes and heart failure.

Keywords: Type 2 Diabetes; CVD; MI; Biochemistry; Epidemiology; Etiology; Drugs; Pathophysiology

Introduction

Numerous studies have contributed to some understanding of diabetes mellitus (DM) in the context of cardiovascular disease (CVD), however additional efforts are required to improve the identification and measurement of the cardiovascular risk in patients with DM [1,2]. In the dynamic landscape of modern healthcare, the intersection of cardiovascular diseases, diabetes, and drug interactions presents a complex and challenging realm for medical professionals. Among the myriad cardiovascular complications, myocardial infarction (MI) and heart failure (HF) stand out as critical concerns, particularly when coupled with the intricate interplay of diabetes and drug interactions. This multifaceted nexus requires a thorough exploration to unravel the pathophysiological and biochemical intricacies that underlie the manifestation of myocardial infarction and heart failure in diabetic patients induced by drug-drug interactions. Despite the implementation of global risk assessment through various biomarkers, the accuracy of risk prediction for type 2 diabetes (T2D) and cardiovascular disease (CVD) remains less than optimal. Consequently, there remains a quest for additional biomarkers to enhance predictive capabilities. In this regards we tried to look deeply at biochemical parameter (very economical) for evaluating the potential clinical utility of biomarkers for combined diseases like cardio-metabolic disease risk prediction.

Diabetes and heart failure (HF) are both global epidemics with tremendous costs on society with increased rates of HF hospitalizations and worsened prognosis when co-existing, making it a significant “deadly duo.” Several case studies are presented, each offering a unique perspective on the biochemical basis of heart failure in type 2 diabetes [3]. Through a meticulous examination of these cases, commonalities and distinctive factors emerge, shedding light on potential biomarkers.

As diabetes continues to reach epidemic proportions globally, its coexistence with cardiovascular disorders raises profound clinical implications [4]. The interweaving of these conditions is exacerbated by the intricate pharmacological landscape, where drug interactions can either ameliorate or exacerbate the risk of cardiovascular events. Myocardial infarction, commonly known as a heart attack, and heart failure, a chronic condition impairing the heart's ability to pump blood effectively, pose formidable challenges when they occur in tandem with diabetes.

This exploration embarks on a journey through few case studies, each a unique narrative encapsulating the complexities of these interconnected health issues. By delving into the specific instances where drug-drug interactions play a pivotal role in precipitating or mitigating cardiovascular events, we aim to enhance our understanding of the underlying mechanisms. These case studies serve as real-world vignettes, offering valuable insights into the intricate web of pathophysiological and biochemical factors influencing the cardiovascular health of diabetic individuals.

Diabetes drugs were divided into 2 categories based on their date of FDA approval: first-generation drugs were approved before 2000, and second-generation drugs were approved after 2000. All drugs were identified in Part D using National Drug Codes. First-generation diabetes drugs include metformin, sulfonylureas, Thiazolidinedione, α-glucosidase inhibitors, meglitinides, and insulin. Second-generation Diabetes drugs include amylin analogs (e.g., pramlintide), glucagon-like peptide-1 (GLP-1) receptor agonists (e.g., exenatide, Liraglutide, albiglutide, dulaglutide), dipeptidyl peptidase 4 (DPP-4) inhibitors (e.g., Saxagliptin, saxagliptin), and sodium-glucose cotransporter 2 (SGLT-2) inhibitors (e.g., Canagliflozin, dapagliflozin, empagliflozin). The mechanism of action of some of these drugs has been revealed in this study with respect to their impact on HF [5].

Our aim was to dissect the pharmacokinetic and pharmacodynamic nuances of such drug interactions, scrutinize the altered biochemical milieu in diabetes, and decipher the molecular and biochemical cascades triggering myocardial infarction and heart failure. Through this exploration, we aspire to contribute to the evolving landscape of personalized medicine, where a nuanced understanding of individual patient profiles, coupled with insights from case studies, can guide clinicians in navigating the labyrinth of cardiovascular complications in diabetic populations [6]. Further we try to unravel the intricacies of pathophysiological and biochemical case studies of myocardial infarction and heart failure in diabetic patients induced by drug-drug interactions. This may not only underscore the pressing need for precision in therapeutic interventions but can also pave the way for a holistic approach to cardiovascular care in an era marked by the convergence of diverse medical challenges.

Methods and Materials

Patient's selection

- **Inclusion criteria:** Only those patients were selected who were confirmed diabetics and were suffering from CVD, with the help of attending health professionals.
- **Exclusion criteria:** Patients suffering from only or other heart diseases and patients with other comorbidities (non-diabetics) were excluded in this study.

Patient's demography

Patients demographics were collected in a prepared questionnaire, after obtaining their consent.

Biochemical parameters

Collection of blood samples for biochemical evaluations: 5ml blood samples from all patients were collected for various analysis and diagnostic tests. All Standard diagnostic protocols were used in this study.

- **HbA1C Test:** This test is a simple blood test performed to check the sugar level over the past 3 months it is commonly used to diagnose diabetes and prediabetes. Methodology involved in this test is immunoturbidimetry.
- **Fasting Blood sugar Test:** This measures the blood sugar after an overnight fast. A fasting blood sugar level of 99 mg/dL or lower is normal, 100 to 125 mg/dL indicates the prediabetes, and 130 mg/dL or higher indicates the diabetes.
- **Random Blood Sugar Test:** This measures the blood sugar at the time being tested. This test can be performed at any time and does not need to fast. A blood sugar level of 200 mg/dL or higher indicates the diabetes.

Lipid profile test

A lipid profile or lipid panel test is a panel of blood test used to find abnormalities in lipids such as cholesterol, triglycerides. The

results of the test identify certain genetic diseases and approximate risk of cardiovascular disease. The lipid profile test usually consists of low density cholesterol levels (LDL), high density cholesterol (HDL), triglycerides and total cholesterol. This test is performed upon fasting for 10-12 hrs.

Liver function test

This test is used to diagnose and monitor liver disease or damage; it measures the level of enzymes which are made by the liver and few proteins in the blood. These include Albumin, alkaline phosphatase (ALP), ALT/ SGPT (alanine transaminase), AST/SGOT (aspartate aminotransferase), and gamma glutamyl transferase (GGT).

Other biochemical parameters measured include: Bilirubin (direct and indirect), a waste product made by the liver. Lactate dehydrogenase (LD) an enzyme released into the blood when cells have been damaged by disease or injury. Prothrombin- a protein involved in blood clotting. This can help distinguish among different types of liver disorders, gauge the extent of known liver damage, and monitor the response to treatment. Some or all of these measurements are also carried out on individuals taking certain medications, to ensure that these medications are not adversely impacting the liver of the patient.

TSH (Thyroid stimulating Hormone)

This test measures the value of thyroid hormone whether too high i.e. hyperthyroidism or low i.e. hypothyroidism. This TSH blood test measures thyroid stimulating hormone (TSH), which stimulates the thyroid to produce two additional hormones, T4 (thyroxine) and T3 (triiodothyronine), both of which play a critical role In controlling the body's metabolism and normal functioning of thyroid gland.

Blood grouping test

This test is mainly performed in order to identify the blood group of a person. A blood type lab test identifies certain inherited substances (antigens) that are present on the surface of red blood cells and classifies them into four common groups: A, B, AB, Or O, and is known as the ABO system. In addition, a second system, the Rh system, determines if the red blood cells are Rh-positive or Rh-negative. It is Rh-positive when it has the Rh factor. It is important to know both the ABO and Rh types in that a mismatch is capable of inducing an Intense immunogenic reaction that can be fatal.

Combination Therapeutic recommendations used in these case studies

Combination therapies for type 2 diabetes mellitus (T2DM) and cardiovascular disease (CVD) comorbidities aim to manage both conditions concurrently. Drugs are recommended for tight glycaemic control, and simultaneously for cardiac disease. Further, drugs are selected based on CVD screening, and adhering to recommended lifestyle modifications upon receiving their T2DM diagnosis. Some of the basic drugs used in this study are listed in the results. We also discussed their importance in this study and how they impact the comorbidity.

Results

Elevated cardiovascular disease (CVD) risk in type 2 diabetes mellitus (T2DM) stems from a intricate interplay of both traditional and non-traditional risk factors. These factors play a crucial role in initiating and advancing atherosclerosis throughout its extended natural progression, encompassing endothelial dysfunction to eventual clinical events.

Case studies

Primarily all patients selected for the case-studies were long term diabetic patients suffering from diabetes for more than 10 years and were on medication. These patients were admitted to

Parameters	P1	P2	P3	P4	P5
Age	47	70	65	63	56
Gender	M	M	M	F	F
Weight	62	70	65	63	62
Occupation	Businessmen	RTC Driver	Electrician	Housewife	Housewife
Habits	Ex-tobacco chewer and chronic alcoholic	Alcoholic	Tobacco chewer	Not available	Not available
Diabetes since last	12yrs	20yrs	15yrs	12yrs	10 years

Table 1: Patients Epidemiological Details and Risk Factors.

Intensive care units (ICU) of the hospital due to heart problems. Upon admission to the Hospital, the following data was collected as shown below.

Among the above five patients, 3 were males and 2 were females with a history of T2DM. We found all men had the habit of smoking and alcohol. And all 5 cases had a diabetic history of 10-20 years and the reason for their admission to the hospital was due to severe chest pain.

The habit of tobacco chewing and smoking is correlated with a decline in metabolic control among individuals with diabetes. This connection is linked to a heightened risk of both macrovascular and microvascular complications, as well as increased mortality in diabetes.

The patients were further tested for the following parameters.

Sugar levels in Blood	Reference range	P1	P2	P3	P4	P5
HbA1C	4.6-6.2%	12.3	10.3	7.0	8.1	6.5
Fasting Blood Sugar	70-110	227	447	159	106	179
Random Blood Sugar	70-160mg/dl	415	433	115	208	183

Table 2: Sugar Test.

Elevated blood glucose levels are a hallmark of diabetes. Persistent hyperglycaemia can lead to damage of blood vessels and the heart muscle over time, contributing to the development and progression of heart failure. HbA1c reflects average blood glucose levels over the past 2-3 months. Higher HbA1c levels indicate poorer glycemic control and are associated with an increased risk of cardiovascular complications, including heart failure. Glycated hemoglobin (HbA1c) stands as the foremost benchmark for evaluating glycemic control and gauging the effectiveness of therapy in individuals diagnosed with type 1 (T1D) and type 2 (T2D) diabetes.

In one study it was reported that hyperglycemia and its effect on CVD outcomes in patients with T2DM showed how controlling blood sugar levels before meals (prandial) versus between meals (fasting) affects the risk of heart problems in people with Type 2 Diabetes after a heart attack.

Cholesterol	Reference range	P1	P2	P3	P4	P5
Total cholesterol	150-200	326	221	135	125	150
Triglycerides	50-150	580	168	80	90	89
HDL- Cholesterol	M-40-55,F- 45-60	50	50	44	35	35
LDL- Cholesterol	<130mg/dl	160	137	75	72	97
VLDL- Cholesterol	20-30	116	34	16	18	35

Table 3: Biochemical Tests - Lipid Profile Test.

People with type 2 diabetes often experience dyslipidaemia, characterized by elevated triglycerides and reduced levels of high-density lipoprotein (HDL) cholesterol. These lipid abnormalities contribute to atherosclerosis, increasing the risk of coronary artery disease and heart failure. In type 2 diabetes mellitus (T2DM), insulin resistance (IR) enhances the release of free fatty acids from adipose tissue. Additionally, three mechanisms contribute to heightened hepatic production of very low-density lipoproteins (VLDL): increased lipogenesis, exacerbated substrate availability, and reduced degradation of apolipoprotein B-100 (ApoB). These alterations lead to a lipid profile characterized by low levels of high-density lipoprotein cholesterol (HDL-C), elevated triglycerides (TGs), increased synthesis of ApoB, and the presence of small dense LDL particles.

Chronic inflammation is common in diabetes and is linked to cardiovascular complications. Inflammation can contribute to endothelial dysfunction, atherosclerosis, and myocardial damage, all

	Reference range	P1	P2	P4	P4	P5
Serum sodium	135-155	142	142.3	138.2	138.9	142.5
Serum potassium	3.5-5.5 mEq/l	3.73	4.38	5.25	3.87	4.12
Serum creatinine	0.7-1.4 mg/dl	0.8 m/dl	1.5	4.3	1.0	1.0

Table 4: Serum Analysis.

of which play a role in heart failure development. Diabetes is a leading cause of chronic kidney disease. Impaired renal function is a significant risk factor for heart failure. Monitoring kidney function is important for assessing cardiovascular risk in individuals with type 2 diabetes.

Elevated levels of hs-CRP have been correlated with insulin resistance (IR), type 2 diabetes mellitus (T2DM), and the onset of cardiovascular disease (CVD). Notably, inflammation, particularly associated with endothelial dysfunction, is acknowledged as a key cardiovascular risk factor, clustering within the insulin resistance syndrome or metabolic syndrome.

LFT Test	Reference range	P1	P2	P3	P4	P5
Total Bilirubin	0.2-1.2md/dl	2.5	0.4	0.7	0.6	0.5
Direct Bilirubin	0-0.2mg/dl	0.8	0.2	0.2	0.2	0.2
Indirect Bilirubin		1.7	0.2	0.5	0.4	0.3
Alkaline Phosphatase (women)	64-306U/L				128	201
Alkaline Phosphatase (Men)	82-306U/L	152	163	177		
AP (children)	180-1200U/L					
SGPT	5-35u/l	86	28	16	28	23
SGOT	8-40u/l	88	38	31	25	65
Total protein	6.0-8.0g/dl		6.9	7.1	6.7	6.9
Albumin	3.8-5.0g/dl	7.5	3.9	3.9	4.0	3.8
Globulin	2.3-3.5g/dl	4.1	3	3.2	2.7	3.1
HIV		Non-reactive	Non -reactive	Non-reactive	Non -reactive	Non -reactive
HBsAg		Negative	Negative	Negative	Negative	Negative
HCV						
Anti HCV		Negative	Negative	Negative	Negative	Negative

Table 5: Liver Function Test.

Elevated levels of homocysteine are associated with an increased risk of cardiovascular disease. People with type 2 diabetes may have higher homocysteine levels, contributing to the development of heart failure. Further, elevated levels of natriuretic peptides are indicative of heart failure. Individuals with diabetes may have an increased risk of heart failure, and measuring these peptides can help in the early detection and management of cardiac dysfunction. Increased levels of alanine aminotransferase (ALT) within the high-normal range is associated with type 2 diabetes independently along with other confounding factors such as obesity.

	P1	P2	P3	P4	P5
Blood Group	O"+"	A"+"	O"+"	AB "+"	A"+"

Table 6: Blood Group of Patients.

Patients' blood grouping was done only to see any commonality between blood grouping and diabetes, As seen in the above table O positive ad A group is common among these patients. Further we also measured BP of these patients and (Table- not included) and realised that Hypertension is a common comorbidity in individuals with type 2 diabetes. Elevated blood pressure can strain the heart

and increase the risk of heart failure. Monitoring and managing blood pressure are crucial for preventing cardiovascular complications.

A Complete Blood Picture (CBP) is essential in CVD patients with T2DM as it provides valuable information about various aspects of their health, including the presence of anemia, infections, inflammation, kidney function, and potential side effects of medications. Regular monitoring allows for timely interventions and improved management of both diabetes and cardiovascular disease. Some medications commonly prescribed for diabetes or cardiovascular conditions may have side effects on blood cell counts. Monitoring CBC helps in identifying and managing such side effects. Serum creatinine can provide insights into kidney function.

Monitoring and managing these biochemical parameters through lifestyle modifications, medication, and regular medical check-ups are essential in preventing and managing the cardiovascular complications associated with type 2 diabetes, including heart failure.

CBP	Reference range	P1	P2	P3	P4	P5
Haemoglobin	13-17g/dl	15.4	13.3	12.6	11.9	11.8
PCV	40-50%	43.5	38.8	36.7	32.0	33.4
RBC	4.5-5.5L/cumm	4.5	4.3	3.26	3.86	4.0
MCV	83-101fl	94.9	90.3	112.7	85.0	83.3
MCH	27-32pg	33.6	30.9	38.7	30.8	29.4
MCHC	31.5-34.5g/dl	35.4	34.3	34.3	36.3	35.3
Total White Cell Counts	4000-11000 cell/ cumm	4700	13000	13209	6900	22400
Differential count						
Neutrophils	40-70%	68	85	80	69	85
Lymphocytes	20-40%	25	12	16	27	12
Eosinophils	1-6%	1	1	02	02	01
Monocytes	2-10%	6	2	02	02	02
Basophils	0-1%	0	0	0	0	0
Platelets	1.5-5.0 lakhs/cumm	1.6	3.24	2.81	2.11	3.67
Absolute neutrophils count	1500-8000/cumm	3196	11815	10560	4761	19040
Absolute lymphocytes	1000-4800/cumm	1175	1668	2112	1863	2688
(Childrens)	3000-9500/cumm					
Peripheral smear		Normocytic/ Normochromic	Normocytic/ Normochromic	Normocytic/ Normochromic	Normocytic/ Normochromic	Normocytic/ Normochromic

Table 7: Complete Blood Picture of Patients.

TSH levels	Reference range	P1	P2	P3	P4	P5
TSH	0.35-5.5	4.45	2.48	4.83	6.51	0.50
Trop1 -Quantitative	<19ng/L	1.6	1253.2	226.5	2.5	8.8

Table 8: Thyroid Test.

Thyroid function tests are generally important in assessing overall health, and abnormalities in thyroid function. This can have implications for both type 2 diabetes mellitus (T2DM) and cardiovascular disease (CVD). Thyroid hormones play a role in regulating metabolism, and imbalances that can affect insulin sensitivity. Both hypo- and hyperthyroidism can impact glucose metabolism.

Drugs	P1	P2	P3	P4	P5
S.no 1.	Clopidogrel	Clavin	Clavin	Clavin	Vildasmart
2.	Aspirin	Metxl	Lanoxin	Glycomet	
3.	NA	NA	NA	NA	NA
Injection	Heparin	Heparin	Heparin	Heparin	
	Insulin	Insulin	Lasix	Insulin	Insulin

Table 9: A few important drugs for Diabetes and CVD control (not exhausive) with local names.

NA- not available.

Various drugs can influence biochemical parameters in individuals with type 2 diabetes, and some medications may impact the risk of heart failure. It's important to note that the effects of medications can vary from person to person, and healthcare professionals carefully consider the individual's overall health and medical history when prescribing medications. Patients with T2DM have an increased risk of cardiovascular events, and antiplatelet medications like Clopidogrel may be prescribed to reduce the risk of clot formation and cardiovascular events in these individuals.

Clavin Tablet is an antibiotic that helps the body fight infections caused by bacteria.

Vildasmart Tablet is used in the treatment of Type 2 diabetes mellitus.

Lanoxin Tablet is prescribed for the management of heart failure, often in conjunction with other medications. It facilitates symptomatic relief by enhancing the efficiency of the heart's blood-pumping function. Additionally, this medication is employed to address abnormal heart rhythm (arrhythmia), aiding in the restoration and maintenance of a regular and steady heartbeat.

Insulin is always effective and is often used when other treatments fail to achieve the desired level of glycemic control. However, it comes with the risk of hypoglycemia and weight gain. It is also observed that Sulfonylureas (e.g., glyburide, glipizide) may cause hypoglycemia, and long-term use may be associated with weight gain. Metformin reduces glucose production by the liver

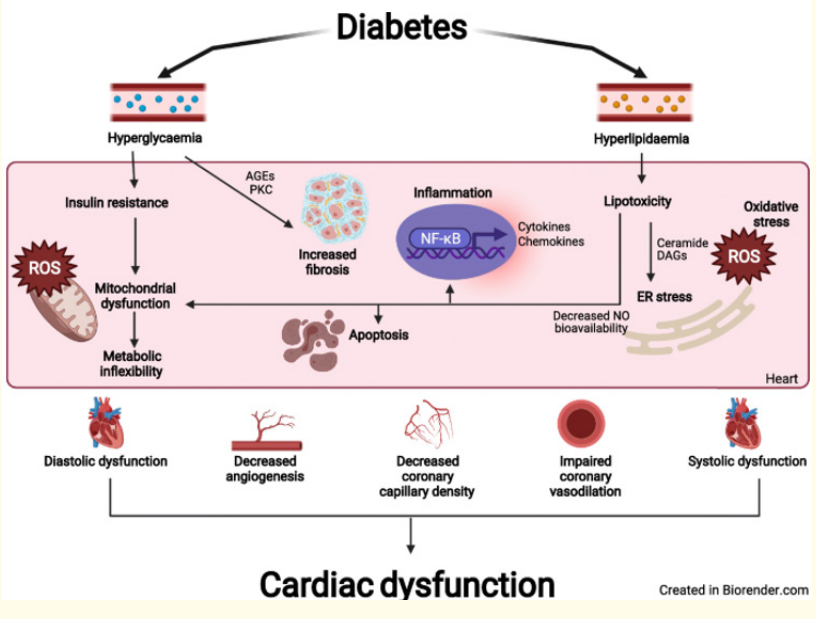

Figure 1: Metabolic, structural and biochemical changes in diabetes and the development of heart failure. Source: Power point slide.

and improves insulin sensitivity. Generally it is well-tolerated, but in rare cases, it may cause lactic acidosis, especially in individuals with impaired kidney function. The findings presented in this study not only enhance our understanding of the intricate relationship between diabetes and heart failure but also pave the way for personalized and targeted interventions

Hyperglycaemia and insulin resistance play significant roles in the onset of heart failure, engaging through various mechanisms that act both independently and synergistically. These include impaired microvascular endothelial function, altered cardiac metabolism (shifting myocardial glucose utilization towards less efficient fatty acid oxidation), heightened myocardial fibrosis, increased oxidative stress, and the local activation of the renin-angiotensin system and sympathetic nervous system. These factors collectively contribute to the development of heart failure.

Discussion

In this study we are trying to leverage if biochemical parameters can be useful to unravel new biomarkers into why T2DM is a risk factor for MI or HF. A Complete Blood Count (CBC), is a common blood test that provides important information about the cellular components of the blood. In the context of cardiovascular disease (CVD) patients who are already suffering from Type 2 Diabetes Mellitus (T2DM), there are several reasons why a CBP is considered essential for example, Platelets are crucial for blood clotting. An abnormal platelet count can be associated with both diabetes and cardiovascular disease. Too many platelets can contribute to blood clot formation, while too few can lead to bleeding issues. CBP includes platelet count, which is valuable in assessing these risks [7]. People with diabetes, particularly those with poorly controlled blood sugar levels, may be at a higher risk of infections. Infections can further stress the cardiovascular system. The white blood cell count (WBC) component of the CBP helps in monitoring for signs of infection. While HbA1c reflects 3-month glycemic control, it overlooks short-term glycemic variability (GV), daily fluctuations in blood glucose, and hypoglycemic events. Though the mechanisms are not fully understood, evidence suggests that daily glucose fluctuations are associated with endothelial dysfunction, inflammation, and oxidative stress, factors contributing to vascular damage and atherosclerosis [8]. Chronic inflammation is a common feature of both diabetes and cardiovascular disease. CBC may include markers such as C-reactive protein (CRP), which can provide information about the level of inflammation in the body and determining the cholesterol levels could indicate the heart disease condition [9].

Following is the list of drugs linked with heart failure in type 2 diabetic patients Thiazolidinedione, Sulphonylureas, Meglitinides, Metformin, Saxagliptin, Alogliptin, Glumetza. Diabetes patients face an elevated risk of heart failure due to the aberrant cardiac processing of glucose and free fatty acid (FFAs) and the impact of diabetes-related disruptions on the cardiovascular system [10]. The metabolic hazard of diabetes in heart failure is exacerbated by the administration of antidiabetic medications [11]. Glucose-lowering agents may contribute to heart failure development through various pathophysiological mechanisms, such as heightened insulin levels, water retention, and reduced glucose availability for the heart and muscles.

There is evidence to suggest that subclinical hypothyroidism (a mild form of underactive thyroid) may be associated with an increased risk of developing T2DM. Also, thyroid dysfunction, especially hypothyroidism, has been associated with various risk factors for cardiovascular disease, such as elevated cholesterol levels, increased blood pressure, and impaired vascular function. Abnormalities in thyroid-stimulating hormone (TSH), free thyroxine (FT4), and free triiodothyronine (FT3) levels can indicate thyroid dysfunction, which may warrant further investigation and management [12,13].

One very important parameter linking biochemical parameters to Heart failure is the fact that that Advanced Glycation End Products (AGEs) are formed when glucose reacts with proteins in the body. They can contribute to vascular damage and stiffness, increasing the risk of heart failure in individuals with diabetes [14,15].

Unravelling the potential adverse effects of glucose-lowering drugs is challenging, as it involves deciphering more than just the negative consequences of excessive glucose reduction in diabetic individuals. While insulin itself does not induce hyperglycaemia, improper dosing or administration may lead to hypoglycaemia. Hypoglycaemia can trigger a stress response that may temporarily increase blood pressure and heart rate. The Vildasmart Tablet combines two anti-diabetic medications: Metformin and Vildagliptin. Metformin, classified as a biguanide, is an anti-diabetic agent that reduces glucose production in the liver, delays glucose absorption

from the intestines, and enhances the body's responsiveness to insulin [16].

Lanoxin tablets prescribed to our patients in case studies were for the treatment of chronic cardiac failure, particularly when systolic dysfunction was the primary issue. The most significant therapeutic advantages were found in patients with ventricular dilatation. Specifically, Lanoxin tablets are recommended when cardiac failure is concurrent with atrial fibrillation [17].

Each drug class has its own advantages and disadvantages in terms of efficacy, safety, weight influence, and cost. Combination therapy often achieves better glycemic control [18]. The modified systemic and cardiac glucose metabolism observed in patients spanning from impaired glucose control to diabetes mellitus plays a pivotal role in the structural and functional anomalies affecting the heart, ultimately leading to cardiac dysfunction. In individuals with diabetes, the onset of heart failure is not solely attributed to underlying coronary artery disease but is also influenced by various pathophysiological and metabolic irregularities stemming from altered glucose metabolism. The compromised cardiac glucose metabolism, coupled with the transition from glucose to free fatty acid (FFA) oxidation in diabetic hearts, significantly impairs cardiac contractility and function. This, in turn, induces left ventricular systolic and diastolic dysfunction, even in the absence of coronary artery disease (CAD) or other structural heart conditions. Combination therapies for managing both the diseases has been a challenge for the physicians [19]. The concurrent use of SGLT-2 inhibitors and MRAs has the potential to diminish cardiovascular events more effectively when compared to the use of either SGLT-2 inhibitors or MRAs in isolation. This combined approach emerges as a promising treatment strategy for patients with both Type 2 Diabetes and CVD.

Several case studies have offered a unique perspective on the biochemical basis of heart failure in type 2 diabetes. Through a meticulous examination of our cases, commonalities and distinctive factors have emerged, shedding light on potential biomarkers, pathways, and therapeutic targets. The findings presented in this study not only enhance our understanding of the intricate relationship between diabetes and heart failure but also pave the way for personalized and targeted interventions. In patients with CVD, platelets are often hyperactive, contributing to the formation of blood clots. Clopidogrel helps reduce the risk of clot formation by inhibiting platelet function. Clopidogrel is an antiplatelet medication that inhibits the activity of platelets, preventing the formation of blood clots [20]. It achieves this by irreversibly binding to the P2Y12 receptor on platelets, inhibiting ADP-induced platelet aggregation.

The impairment of cardiac function in diabetic individuals manifests through diverse mechanisms, including reduced glucose transport and carbohydrate oxidation, elevated FFA utilization, diminished sarcolemmal calcium transport, and alterations in myofibrillar regulatory contractile proteins. Multiple points in cardiac glucose metabolism are compromised in diabetes mellitus patients, including glucose uptake, glycolysis, and intramitochondrial pyruvate oxidation. The decrease in glucose uptake is attributed to the sluggish rate of glucose transport across the sarcolemmal membrane into the myocardium, resulting from a reduction in the myocardial concentration of glucose transporter type 1 (GLUT 1) and glucose transporter type 4 (GLUT 4) [21,22]. Additionally, individuals with diabetes mellitus exhibit higher plasma levels and myocardial uptake of FFAs. The elevated circulating FFAs and their increased oxidation are primarily responsible for inhibiting both glycolysis and glucose oxidation in the heart. T2DM is characterized by insulin resistance and impaired insulin secretion. Hyperglycemia and insulin resistance can contribute to inflammation, oxidative stress, and endothelial dysfunction, which are factors that increase the risk of cardiovascular complications [23]. While it has not been easy to select a particular biomarker but this study has resulted in some understanding of the "Deadly Duo". Regular monitoring of the biochemical parameters allows for timely interventions and improved management of both diabetes and cardiovascular disease. Additional efforts are needed to advance our understanding of the disease state and its influence on cardiovascular function, aiming to improve medical interventions and cardiovascular outcomes in individuals with diabetes.

Conclusion

In order to determine emerging risk parameters to be of genuine utility, they must exhibit a substantial enhancement in predicting the risk of future diabetes to mitigate CVD. A mere comparison between conventional risk factors readily accessible through historical data, basic examination measures, or routine blood tests may not solve the problem. Alternatively, these novel parameters should offer valuable insights into the accelerated progression of

microvascular or macrovascular diseases in individuals with diabetes or non-diabetic hyperglycemia—an aspect that has been inadequately explored until now. Furthermore, even if these epidemiological risk factors demonstrate efficacy in predicting risk, critical considerations such as cost–benefit relationships and the standardization of testing procedures must be thoroughly addressed before their widespread implementation.

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Conflict of Interest

None.

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Ethical Approval

We conducted this study according to the guidelines stipulated in the Declaration of Helsinki. The institutional IEC board of Bhagwan Mahavir Medical Research Centre, approved this study.

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