Bulletin of Environment, Pharmacology and Life Sciences
Bull. Env. Pharmacol. Life Sci., Spl Issue [2] 2022 : 430-436

Online ISSN 2277-1808
Journal's URL:http://www.bepls.com
CODEN: BEPLAD

REVIEW ARTICLE **OPEN ACCESS**

Biochemical Cardiac Marker in Prediction of Hypertension in Diabetes Patients: A Review

Nihaika Singh[1*],Juhi Aggarwal[2], Jyoti Batra[3],Nitin Srivastava[4]
[1-3] Department of Biochemistry, Santosh Medical College and Hospital, Ghaziabad, Uttar Pradesh -201009
[4]Department of Medicine, MIMS, Barabanki, Uttar Pradesh-225001

ABSTRACT
The objective of this narrative review was to update the knowledge on the differential use of circulating cardiac biomarkers in patients with type 2 diabetes mellitus (T2DM) with hypertension. A number of circulating biomarkers have yet to be confirmed as prognosticators of clinical outcomes in pre-diabetic and diabetic individuals. The cardiac biomarkers reported here have been established as predictive and their role in prognosis remains under study. Cardiovascular (CV) risk may be assessed using conventional cardiac biomarkers, such as natriuretic peptides (NPs), LDH, high-sensitivity circulating cardiac troponins, and CK-MB. Various cardiac biomarkers have strengths and weaknesses that determine the price of their use, specificity, sensitivity, predictive value and superiority when compared to one another. Additionally, there have been conflicting reports regarding the predictability of their effects among patients without known cardiovascular disease.
KEYWORDS: *- type 2 diabetes mellitus (T2DM), cardiovascular (CV), natriuretic peptides (NPs), Lactate dehydrogenase (LDH).*

Received 20.08.2022 Revised 11.09.2022 Accepted 19.10.2022

INTRODUCTION

In the south Asia region, high blood pressure (BP) is ranked third as one of the main risk factors [1]. As a result of hypertension, cardiovascular health status and healthcare systems in India are substantially constrained [2, 3]. An analysis of worldwide data for HTN showed that 21,6% of Indian men and 21,9% of Indian women were suffering from hypertension in 2005 [4]. By 2025, India's rate of HTN in women will be 22.9 percent, and in men 23.6 percent, according to projections [4]. According to studies conducted in India, the prevalence of HTN is 25% in urban people and 10% in rural people [5]. In India, the WHO estimates that 32.5% of people had high blood pressure (33.2% men and 31.7% women) [6]. However, only 25.6% of those who were treated for HTN had their blood pressure under control, according to a multinational study addressing HTN awareness, treatment, and adequacy of control [7]. Among the rural and urban populations of north India, HTN prevalence is 14.5% (13.3–15.7) and 28.8% (26.9–30.8), respectively. Heterogeneity was significant in those populations as well [I2 = 99.3% (95% CI: 95–100; P <0.001); I2 = 91.1% (97–99; P< 0.001). HTN prevalence in North India was not significantly different between rural and urban areas (P = 0.07) [8].

Diabetes ranks among the top ten leading causes of death along with cardiovascular disease (CVD), respiratory diseases, and cancer [9]. World Health Organization (WHO) statistics show that non-communicable diseases (NCDs) accounted for 74% of all deaths globally in the year 2019, including 1.6 million deaths from diabetes. [10] By the year 2035, nearly 592 million people are expected to die from diabetes [11]. The National Family Health Survey, four surveys [12] conducted in 15 Indian states and union territories during the 2014–2015 fiscal year, found that the Andaman and Nicobar Islands had the highest prevalence of diabetes (26 and 14.5% among women and men, respectively), while Haryana had the lowest prevalence (8.2%) for men and Bihar (6.1%) for women. There was a higher prevalence in urban than rural areas. Secular Trends in Diabetes in India, a study that analyzed the change in diabetes prevalence between 2006 and 2016 in urban and rural areas of Tamil Nadu, found that the prevalence of diabetes increased from 18.6% in 2006 to 21.9 in 2016, while in smaller towns, it increased from 16.4 to 20.3, and in peri-urban villages, from 9.2 to 13.4%, respectively [13].

There is a rising incidence of diabetes and prediabetes in India, as well as a rising prevalence of diabetes. Comparatively few longitudinal studies have been conducted to assess diabetes incidence and

prediabetes prevalence in India. Diabetes and prediabetes incidence rates in the Chennai Urban Population Study cohort were reported as 20.2 and 13.1 per 1000 person-years, respectively [14]. In the Chennai Urban Rural Epidemiology Study (CURES), the incidence rates for diabetes, prediabetes, and dysglycemia were found to be 22.2, 29.5, and 51.7 per 1000 person-years, respectively. Based on research reported by the National Diabetes Statistics Center, the conversion rate to diabetes was reported to be 19.4% among those with normal glucose tolerance, 58.9% among those with prediabetes, and 78.9 cases per 1000 person-years in patients with prediabetes [15].

Diabetes has a multifactorial etiology. There are numerous non-modifiable risk factors such as genetics, age, ethnicity, and family history that are potentially associated with type 2 diabetes but the prevalence of the disease has likely increased because of modifiable factors. There are many reasons for this including sedentary lifestyles and lack of exercise, an increase in overweight/obesity, unhealthy diets (refined grains, fats, sugars, sweetened beverages, and reduced intake of fruits and vegetables), unhealthy habits (smoking and alcohol abuse), pollution exposure, a stress-related intrauterine environment, short sleep duration, and the built environment. According to the India state-level disease burden report [16], nearly 10% of the total disease burden in India was caused by a cluster of risk factors that included unhealthy diet, being overweight/obese, high blood pressure, blood sugar, and cholesterol, which led to ischemic heart disease, stroke, and diabetes, which accounted for one quarter of the total disease burden in India in 2016 [16].

CO EXISTENCE OF DIABETES AND HYPERTENSION

Cardiovascular diseases are the gateway to DM and HTN, which never abandon any community or population. Approximately 366 million people will have diabetes by 2030, an increase of 171 million from 2000. According to estimates, the number of adults affected by hypertension will increase by 60% by 2025 to 1.56 billion [17]. It is estimated that up to 75% of people with DM also have HTN, and people with only HTN often have insulin resistance as well. HTN and DM are thus interconnected conditions that share many common underlying risk factors (e.g., ethnicity, family history, dyslipidemia, and lifestyle determinants [18]. HTN may precede the onset of diabetes mellitus. In 95% of the cases, the HTN is essential and the other 5% are secondary [19].

PATHOPHYSIOLOGY OF HYPERTENSION IN DIABETES

Several factors are involved in the pathophysiology of hypertension in diabetes, including maladaptive changes of the autonomic nervous system, a maladaptive immune system, and enhanced activity of the renin-angiotensin-aldosterone (RAAS) system. Hypertension is attributed to the following factors, some of which have been targeted for therapeutic intervention [20]

➢ Sedentary Lifestyle

The combination of sedentary behavior and excessive intake of calories can lead to increased adiposity, which has been linked to an increased risk of insulin resistance [21].

➢ Elevated Intravascular Volume

Increased sodium concentration within the bloodstream stimulates water transport along the osmotic gradient, thus increasing intravascular volume. According to the Frank Starling Law, an increased intravascular volume leads to increased venous return to the heart, increasing cardiac output and increasing arterial pressure [22]. Increasing evidence suggests that increased sodium inward transport in endothelial cells contributes to increased arterial stiffness and elevated blood pressure in states of obesity and insulin resistance, such as found in most T2DM patients.

➢ Premature Vascular Aging

Individuals with diabetes can develop symptoms such as vessel remodeling, low grade inflammation, fibrosis, and stiffening as a result of high blood pressure. Diabetic patients, therefore, experience accelerated premature vascular aging due to impaired endothelial mediated relaxation, enhanced vascular smooth muscle contraction, and increased stiffness [23].

➢ Renin Angiotensin Aldosterone System

RAAS is physiologically activated by hypovolemia, resulting from renal hypoperfusion. The release of renin from the juxtaglomerular apparatus leads to an increased production of angiotensin II. The direct effects of angiotensin II involve direct vasoconstriction as well as aldosterone secretion, which lead to sodium and water retention, and restores intravascular volume.

➢ Environmental and Socioeconomic Factors

Dietary components that are traditionally considered healthy and promoted as components of the DASH diet [24] are often not available to the general population for economic or access reasons. Instead, they consume high salt and high calorie foods that lead to obesity and hypertension [25]. Further, lack of access to safe outdoor spaces discourages exercise, and targeted advertising encourages poor health decisions such as smoking.

WAYS OF DETECTION OF HYPERTENSION

- A blood test may be required to determine if you suffer from secondary hypertension as a result of a serious health condition.
- A urine test is required.
- A home blood pressure monitor (HBPM) is available
- Ambulatory Blood Pressure Monitoring (APBM)
- Electrocardiogram (EKG)
- Echocardiogram.
- Ultrasound.
- CT Scan or MRI.

BIOCHEMICAL CARDIAC MARKERS USED IN HYPERTENSION

Biochemical Markers used in hypertensive patients.

- Aspartate aminotransferase.
- Lactate dehydrogenase and its isoenzyme LD1
- Creatine kinase and its isoenzyme MB
- Myoglobin
- Cardiac Troponins.
- C-reactive protein (Inflammation marker)
- Cardiac Natriuretic Peptides

ASPARTATE AMINOTRANSFERASE.(AST)

For the first time, AST was used as a cardiac biomarker in 1954.The AST marker is found in the liver, heart, skeletal muscles, brain and kidneys, but is no longer used for diagnosing AMI because of its lack of specificity for the cardiac tissue [26-27].

AST, also known as aspartate aminotransferase or (serum) glutamic oxaloacetic transaminase (GOT, SGOT), is a Pyridoxal phosphate (PLP)-dependent transaminase enzyme first recognized by Arthur Karmen in 1890. AST catalyzes the reversible transfer of a α-amino group from aspartate to glutamate, making it an important enzyme in amino acid metabolism. Serum AST (alanine transaminase) and ALT (alanine transaminase) levels, as well as their ratio (AST/ALT ratio) are routinely measured clinically to evaluate liver health [28].

A key function of the AST is the metabolism of amino acids, maintenance of a healthy NAD+/NADH ratio in cells, Krebs cycle activity, purine/pyrimidine synthesis, urea and protein synthesis, and gluconeogenesis. There are two genetically distinct iso-enzymes of AST in humans: cytoplasmic AST and mitochondrial AST. Both types of AST are found in the body. AST activity is found in most tissues of the body with the highest levels in the heart, liver, skeletal muscle, kidney, and brain. As a result of tissue damage (plasma membrane disruption or apoptosis), plasma membrane bleb formation, increased tissue expression, and macroenzymes (complexes of AST and plasma proteins) elevated AST activity may indicate these factors. The extent of myocardial necrosis is associated with increased serum AST activity in patients with acute myocardial infarction [29].

AST levels are associated with cardiovascular disease or mortality with positive, inverse or U-shaped association patterns, according to epidemiological research. AST levels that are not elevated in the presence of inflammatory liver disease may indicate an increased cardiovascular risk associated with nonalcoholic fatty liver disease (NAFLD), cardiometabolic risk factors (metabolic syndrome, abdominal obesity, insulin resistance, and diabetes), chronic alcoholism and structural heart disease (myocardial infarction). A positive association between AST and CVD is more common in epidemiological studies in Asian population Low levels of AST may reflect increased cardiovascular risk caused by vitamin B6 deficiency, chronic kidney or liver disease, or inflammation. High and low levels of AST are clinically relevant, and both should be considered [30].

LACTATE DEHYDROGENASE (LDH)

A key enzyme in the anaerobic metabolic pathway is lactate dehydrogenase (LDH). It is an enzyme that catalyzes the reversible conversion of lactate to pyruvate with the reduction of NAD+ to NADH [31]. Lactate Dehydrogenase is an oxidoreductase enzyme that regulates the reversible conversion of pyruvate to lactate using NADH. As a result, it plays a role in the anaerobic metabolism of glucose in the absence or in limited amounts of oxygen.

Pyruvate + NADH + H+ --> Lactate + NAD+

A cell's oxidative phosphorylation process becomes disrupted when it is exposed to anaerobic or hypoxic conditions. In these conditions, LDH is upregulated to accommodate the need for energy production,

which is why cells produce energy by alternate metabolism. As a result of anaerobic conversion of glucose, lactate is produced, but it cannot be further metabolized in any tissue except the liver. The lactate is released into the bloodstream and transported to the liver, where it is converted into pyruvate by LDH through the Cori cycle [32].

Generally, serum levels (normal values may vary widely depending on the technique) increase within 12 to 24 hours after myocardial infarction, reach their peak in 2 to 4 days, and gradually return to normal by the eighth to fourteenth day after the infarction. The correlations are sometimes as high as 100%, but there have been numerous reports of "false" positives and negatives as well. A number of conditions have been associated with elevated levels, including severe congestive failure, pulmonary thrombosis, bacterial pericarditis, digitalis intoxication, cardiac catheterization, cardiac surgery, including valve implants, as well as diseases of the liver, muscles, kidneys, neoplastics, and hematopathology (especially hemolytics).In the overall clinical context, these "false" positives usually occur as isolated instances of the entities noted, and rarely pose any major limitations on the physician [33].

They do, however, emphasize the lack of specificity of serum values and of the recent concept that what is measured as overall LDH activity consists of several molecular entities that are actually distinct - isozymes. This concept of molecular heterogeneity led to the development of methods for detecting the serum component originating in the myocardium Electrophoretic studies have identified five LDH isozymes; the most rapidly migrating fractions are observed in heart LDH (as well as kidney and erythrocyte LDH), and the "slow" fractions appear in liver and skeletal muscle.Therefore, when myocardial infarction occurs, serum LDH activity is principally influenced by the rapid fraction; elevated rapid fraction levels have been seen in accepted cases of infarction with normal total serum levels, and have persisted for a period of up to 10 days after normal serum levels have returned.Two promising new methods have gained greater acceptance due to the consideration that the rapidly migrating "heart" LDH isozyme may be a more sensitive, specific, and long-lasting indicator of myocardial necrosis than total LDH activity [34]

CREATINE KINASE

These enzymes are mainly found in heart muscle cells, which is why this test measures levels of creatine kinase-MB in the blood CK-MB is one of three forms (isoenzymes) of creatine kinase (CK) These include CK-MM (found in skeletal muscles and the heart) CK-MB, which is a form of creatine kinase. Creatine kinase provides energy for the regeneration of ATP [35].

In 1966, the first creatine kinase enzymes were found in various tissues. There are two main CK isoenzymes, BB and MM, which are polypeptide chains of either type B or type M. BB isoenzymes are found in the central nervous system, and MM isoenzymes are found primarily in skeletal muscles [36]. CK-MB is found at 15% concentration in the myocardium and CK-MM at 85% concentration in the skeleton [37-38].

CARDIAC TROPONIN

The troponin complex consists of three protein molecules: troponin T, troponin I, and troponin C. They are found in actin filaments in skeletal and myocardial muscle cells. Troponin T and troponin I come in several forms; one is specific to cardiac muscle, and the other is not expressed in adult skeletal muscle [39]. Myocardium contains 3 units of troponin attached to the actin filaments of the tropomyosin complex, though there is also unbound/free troponin in the cytosol, also called the cytosolic pool. In the event of myocardial damage, the unbound troponin is released first [40].Approximately 6% of the total troponin in the myocardium is unbound. The rest, which is bound to actin, is released slowly with structural damage, leading to a prolonged period of elevated troponin levels in the plasma [41-42]. Troponin elevation > 99th percentile is generally considered the cutoff value for diagnosing AMI. Troponin concentrations rise 4 to 6 hours after onset of symptoms, peak by about 18 to 24 hours, and remain detectable for a period of 72 to 96 hours [43-44]. There is greater specificity for troponin in cardiac muscle compared to CKMB, and current methods for measuring troponin are more sensitive and specific than those used to measure CK-MB. Since CK-MB can be expressed in skeletal muscle, and because CK-MB relative index is ineffective and there are numerous other causes of CK-MB elevation other than AMI, Troponin has been identified as a viable biomarker for detecting myocardial damage [45].

MYOGLOBIN

Due to its relatively low molecular weight, myoglobin may leak from muscle tissue into the blood stream as a result of skeletal or cardiac muscle damage. Myoglobinuria and myoglobinemia have been used to diagnose myopathies and cardiopathies. The myocardium is composed of bundles of striated muscle fibers which produce cardiac-specific contractile proteins (actin and myosin), regulatory proteins (troponins and tropomyosins), and proteins necessary for converting chemical energy into work (muscle

contraction), e.g., myoglobin; and enzymes active in metabolism of lactic acid and creatine kinase.These proteins are released into the circulation in the presence of cardiac tissue damage, and serve as cardiac injury biomarkers [46].

CRP

Increased CRP has been linked to several disease conditions, including coronary heart disease and ischemic stroke. It has also been associated with insulin resistance, hypertension, metabolic syndrome, and peripheral arterial disease. Its role as a sign of coronary heart disease has been extensively studied. At the Rockefeller Institute for Medical Research, in New York, William Tillet and Thomas Francis first discovered CRP in 1930. Inflammation, in its multiple forms, is the most studied process, both as a cause and a predictor of cardiovascular disease. CRP has been the forerunner of the hunt for inflammatory markers, and extensive research has been conducted on it worldwide [47]. CRP is a preeminent marker of inflammation and has been the subject of intense research in numerous studies worldwide. Unlike other markers of inflammation, CRP is stable over long periods, has no daily variations, can be measured inexpensively by available high-sensitivity assays, and has been specifically linked to CVD outcome [48]. The presence of CRP in atherogenesis may be due to the fact that it inhibits nitric oxide synthase and prostacyclin synthase activity, and binds LDL-C and influences its uptake by macrophages, which is a crucial step of atherogenesis. CRP may also alter the expression of adhesion molecules on endothelial cells [49].

CARDIAC NATRIURETIC PEPTIDES

Natriuretic peptides regulate the rate of natriuresis, electrolyte and water retention, vascular permeability and vasodilatation, cardiac contractility and blood pressure; as a consequence, NPs are physiologic antagonists of the renin-angiotensin-aldosterone system as well as the sympatho-adrenal system [50]. Numerous types of NPs are released primarily from the myocardium, the atrium (ANP) and the brain (BNP) NPs, and vessels, bones and the brain (C-type NPs) [51]. Through physiologic effects, NPs bind to NPR-A, NPR-B, and NPR-C. These receptors are extensively expressed on the surface of target cells, where they regulate NP bioavailability independently of circulating neprilysin activity [52]. There is an increase in the metabolism of nonessential proteins, predominantly ANP and BNP, in response to myocardial stretching and fluid overload, while ischemia/hypoxia, inflammation hormones (catecholamines, aldosterone, renin) and growth factors (transforming growth factor beta, vascular endothelial growth factor) have direct and indirect effects on these processes [53]. C-type NPs regulate vascular function, bone ossification, and brain development through their autocrine activity. In addition, they inhibit the lipolytic activity of adipocytes by inhibiting the expression of NPR-A and NPR-C by adipocytes [54].

CONCLUSION

Diabetes and hypertension share common pathways such as SNS, RAAS, oxidative stress, and insulin resistance. These pathways interact and influence each other and may even cause a vicious cycle. Hypertension and diabetes are both end results of the metabolic syndrome. They may, therefore, develop one after the other in the same individual. The biochemical cardiac markers such as CK-MB, LDH have a great role in prediction and assessment of cardiac changes, which may lead to various cardio vascular diseases. Cardiac biomarkers are of great importance in the timely, accurate diagnosis and management of hypertension in diabetic patient as well as the prognosis. Diagnosis in the golden period is of outmost importance to start therapy at the earliest and possibly reverse the cardiac damage. Cardiac biomarkers are also a powerful tool for triaging.

REFERENCES

1. Lim SS, Vos T, Flaxman AD, Danaei G, Shibuya K, Adair-Rohani H. (2012). A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, a systematic analysis for the Global Burden of Disease Stud. Lancet. 380: 2224–2260.
2. Leeder S, Raymond S, Greenberg H, Liu H. (2004). A race against time. The challenge of cardiovascular disease in developing economies. New York: Columbia University.
3. Srinath Reddy K, Shah B, Varghese C, Ramadoss A. (2005). Responding to the threat of chronic diseases in India. Lancet. 366: 1744–1749.
4. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. (2005). Global burden of hypertension: analysis of worldwide data. Lancet. 365: 217–223.
5. Thankappan KR, Sivasankaran S, Sarma PS, Mini G, Khader SA, Padmanabhan P, et al. (2006). Prevalence-correlates-awareness-treatment and control of hypertension in Kumarakom, Kerala: baseline results of a community-based intervention program. Indian Heart J. 58:28–33.
6. Non communicable diseases country profiles (2011). http://www.who.int/nmh/countries/ind_en.pdf

7. Hypertension Study Group Prevalence, awareness, treatment and control of hypertension among the elderly in Bangladesh and India: a multicentre study. Bull World Health Organ. 2001; 79:490–500
8. Devi P, Rao M, Sigamani A, Faruqui A, Jose M, Gupta R. (2013). Prevalence, risk factors and awareness of hypertension in India: a systematic review. *J Hum Hypertens.* 27: 281–287.
9. International Diabetes Federation. (2019). IDF Diabetes Atlas. 9th ed. Brussels, Belgium: International Diabetes Federation.
10. World Health Organization. (2020). The top 10 causes of death. Available from: http://www.who.int/en/news-room/fact-sheets/detail/ the-top-10-causes-of-death.
11. Tao Z, ShiA, Zhao J. (2015). Epidemiological perspectives of diabetes. Cell Biochem Biophys. 73: 181-5.
12. KumarA, Kalra S, Unnikrishnan AG. (2016). Metabolic state of the nation: Results of the national family health survey-4. Indian J Endocrinol Metab. 20: 429-31.
13. Nanditha A, Snehalatha C, Satheesh K, Susairaj P, Simon M, Vijaya L. (2019). Secular Trends in Diabetes in India (STRiDE-I): Change in prevalence in 10 years among urban and rural populations in Tamil Nadu. Diabetes Care ;42: 476-85.
14. Mohan V, Deepa M, Anjana RM, Lanthorn H, Deepa R.(2008). Incidence of diabetes and pre-diabetes in a selected urban south Indian population (CUPS-19). J Assoc Physicians India. ;56: 152-7.
15. Anjana RM, Shanthi Rani CS, Deepa M, Pradeepa R, Sudha V, Divya Nair H. (2015). Incidence of diabetes and prediabetes and predictors of progression among Asian Indians: 10-year follow-up of the Chennai Urban Rural Epidemiology Study (CURES). Diabetes Care. 38: 1441-8.
16. India state level disease burden report. (2020). Available from: https://vikaspedia.in/health/health-directory/india-state-level-disease-burden-report-released.
17. Rodrigo M Lago, Premranjan P Singh and Richard W Nesto, (2007). Diabetes and hypertension, Nature clin. practice endo and metabolism, Editorial. 3(10): 667
18. Amanda N. Long, DOand Samuel Dagogo-Jack, MD, (2011). The Comorbidities of Diabetes and Hypertension: Mechanisms and Approach to Target Organ Protection, J Clin Hypertens (Greenwich). 13(4): 244–251.
19. Klein, Klein, Lee, Cruickshanks and Moss. (1996). The incidence of hypertension in insulin-dependent diabetes. Archives of Internal Medicine. 156(6): 622–627.
20. Oparil S, Zaman MA, Calhoun DA.(2003). Pathogenesis of hypertension. Ann Intern Med. 139(9): 761–776.
21. Sowers JR. (2013). Diabetes mellitus and vascular disease. Hypertension. 61(5): 943–7.
22. Victor RG. (2022). Braunwald's heart disease: A textbook of cardiovascular Medicine. 9th Edition. Philadelphia PA:Elsevier, Sauders.
23. Hill M, Yanag Y, Zhang L, Sun Z. jia G, Sowers J Parrish A, Insulin resistance, cardiovascular stiffening, cardiovascular disease. Metabolism Clinical Experimental. 2021;119: 154766.
24. Appel LJ, Brands MW, Daniels SR, Karanja N, Elmer PJ, Sacks FM., American Heart Association. Dietary approaches to prevent and treat hypertension: a scientific statement from the American Heart Association. Hypertension. 2006 ;47(2): 296–308.
25. Belanger MJ, Hill MA, Angelidi AM, Dalamaga M, Sowers JR, Mantzoros CS. Covid-19 and Disparities in Nutrition and Obesity. N Engl J Med. 2020; 383(11): e69.
26. Dolci A and Panteghini M. The exciting story of cardiac biomarkers: From retrospective detection to gold diagnostic standard for acute myocardial infarction and more. Clin Chim Acta. 2006;369: 179-187.
27. Ladenson JH. A personal history of markers of myocyte injury (myocardial infarction). Clin Chim Acta.2007; 381: 3-8.
28. Ladue, Wroblewski, Karmen. "Serum glutamic oxaloacetic transaminase activity in human acute transmural myocardial infarction". Science. 1954**;** (3117): 497–9.
29. Schumann G, Bonora R, Ceriotti F, Clerc-Renaud P, Ferrero CA, Férard G, Franck PF, Gella FJ, Hoelzel W, Jørgensen PJ, Kanno T, Kessner A, Klauke R, Kristiansen N, Lessinger JM, Linsinger TP, Misaki H, Panteghini M, Pauwels J, Schimmel HG, Vialle A, Weidemann G, Siekmann L. IFCC primary reference procedures for the measurement of catalytic activity concentrations of enzymes at 37 degrees C. Part 3. Reference procedure for the measurement of catalytic concentration of lactate dehydrogenase. Clin Chem Lab Med. 2002;40(6): 643-8.
30. AlexanderE.Berezin, (2020). Circulating cardiac Biomarkers in Diabetes Mellitus: A New Dawn for Risk Stratification-A Narrative Review. 11: 1271-1291.
31. Adeva-Andany M, López-Ojén M, Funcasta-Calderón R, Ameneiros-Rodríguez E, Donapetry-García C, Vila-Altesor M, Rodríguez-Seijas J. (2014). Comprehensive review on lactate metabolism in human health. Mitochondrion. 17:76-100.
32. Passarella S, Schurr A. (2018). l-Lactate Transport and Metabolism in Mitochondria of Hep G2 Cells-The Cori Cycle Revisited. Front Oncol. 8;8: 120.
33. Snodcgrass, Wacken, Eppinger and Vallee. (1959). Metalioenzymes and myocardial infarction: III. Lactic dehydrogenase activity of serunm-a determinate diagnostic measure. New Eng J Med. 261: 1259.
34. Milton W.Hamolsky,(1956). Enzyme In Acute Myocardial Infarction. Circulation. 35(3).19-23
35. van der Veen KJ, Willebrands AF. (1996). Isoenzymes of creatine phosphokinase in tissue extracts and in normal and pathological sera. Clin Chim Acta. ;13(3): 312-6.
36. Dawson DM, Eppenberger HM, Kaplan NO. (1965). Creatine kinase: evidence for a dimeric structure. Biochem Biophys Res Commun. 21(4): 346-53.
37. Lee TH, Goldman L. (1986). Serum enzyme assays in the diagnosis of acute myocardial infarction. Recommendations based on a quantitative analysis. Ann Intern Med. 05(2): 221-33.

38. Tsung JS, Tsung SS. (1986). Creatine kinase isoenzymes in extracts of various human skeletal muscles. Clin Chem. 32(8): 1568-70.
39. Babuin L, Jaffe AS. (2005). Troponin: the biomarker of choice for the detection of cardiac injury. CMAJ. 173(10): 1191-202.
40. Katus HA, Remppis A, Scheffold T, Diederich KW, Kuebler W. (1991). Intracellular compartmentation of cardiac troponin T and its release kinetics in patients with reperfused and nonreperfused myocardial infarction. Am J Cardiol. 67(16):1360-7.
41. Adams JE, Schechtman KB, Landt Y, Ladenson JH, Jaffe AS. (1994). Comparable detection of acute myocardial infarction by creatine kinase MB isoenzyme and cardiac troponin I. Clin Chem. ;40(1): 1291-5.
42. Katus HA, Remppis A, Neumann FJ, Scheffold T, Diederich KW, Vinar G, Noe A, Matern G, Kuebler W. (1991). Diagnostic efficiency of troponin T measurements in acute myocardial infarction. Circulation. ;83(3): 902-12.
43. Remppis A, Scheffold T, Greten J, Haass M, Greten T, Kübler W, Katus HA. (1995). Intracellular compartmentation of troponin T: release kinetics after global ischemia and calcium paradox in the isolated perfused rat heart. J Mol Cell Cardiol. ;27(2):793-803.
44. Ricchiuti V, Voss EM, Ney A, Odland M, Anderson PA, Apple FS. (1998). Cardiac troponin T isoforms expressed in renal disease skeletal muscle will not cause false-positive results by the second generation cardiac troponin T assay by Boehringer Mannheim. Clin Chem. ; 44(9):1919-24.
45. Allaf M, Chapelle JP, el Allaf D, Adam A, Faymonville ME, Laurent P, Heusghem C. (1986). Differentiating muscle damage from myocardial injury by means of the serum creatine kinase (CK) isoenzyme MB mass measurement/total CK activity ratio. Clin Chem.; 32(2): 291-5.
46. Palanisamy Pasupathi, YY Rao, Farook J, Sathiyamoorthy Subramaniyam, Babu Shankar Ponnusha, Athimoolam Ambika. (2011). The combinational effect of cardiac and biochemical markers in diabetic patients with cardiovascular disease. Int J Cur Bio Med Sci. 5-10.
47. Calabro P, Golia E, Yeh ET. (2012). Role of C-reactive protein in acute myocardial infarction and stroke: possible therapeutic approaches. Curr Pharm Biotechnol. 13:4 –16.
48. Devaki RN, Basavana Gowdappa H, Suma MN, Prashanth V, Akila P, Anjali Devi BD. (2011). A study of C-reactive protein and its relationship with CHD and lipid metabolism. Int J Pharm Sci Rev Res. 6: 125–7.
49. Mehta JL, Sukhija R, Romeo F, Sepulveda JL. (2007). Value of CRP in coronary risk determination. Indian Heart J. ;59: 173–7.
50. Potter LR, Abbey-Hosch S, Dickey DM. (2006). Natriuretic peptides, their receptors, and cyclic guanosine monophosphate-dependent signaling functions. Endocr Rev. 27: 47–72.
51. Potter LR, Hunter T. (2001). Guanylyl cyclase-linked natriuretic peptide receptors: structure and regulation. J Biol Chem. 276:6057–60.
52. Kovacova Z, Tharp WG, Liu D, Wei W, Xie H, Collins S. (2016). Adipose tissue natriuretic peptide receptor expression is related to insulin sensitivity in obesity and diabetes. Obesity (Silver Spring).24(4): 820–8.
53. Moro C. (2016). Targeting cardiac natriuretic peptides in the therapy of diabetes and obesity. Expert Opin Ther Targets. ;20(12): 1445–52.
54. Bordicchia M, Ceresiani M, Pavani M, Minardi D, Polito M, Wabitsch M. (2016). Insulin/glucose induces natriuretic peptide clearance receptor in human adipocytes: a metabolic link with the cardiac natriuretic pathway. Am J Physiol Regul Integr Comp Physiol. 311(1): 104–14.

CITATION OF THIS ARTICLE

N Singh, J Aggarwal, J Batra, N Srivastava . Biochemical Cardiac Marker in Prediction of Hypertension in Diabetes Patients: A Review. Bull. Env. Pharmacol. Life Sci., Spl Issue [2]: 2022: 430-436