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A STUDY OF BIOCHEMICAL PARAMETERS IN PATIENTS WITH AND WITHOUT DIABETES MELLITUS DIAGNOSED FOR MYOCARDIAL INFARCTION

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ABSTRACT

Aims: Coronary heart disease (CHD) is currently the leading cause of death worldwide and together with diabetes, poses a serious health threat, particularly in the Indian Asiatic population. **Methods:** A retrospective observational study on biochemical parameters in patients with and without diabetes diagnosed for myocardial infarction was conducted at Madras Medical hospital located in Chennai/Tamilnadu/India. **Results:** The result of this study showed that out of 200 subjects, 160 were males and 40 were females, and amongst them 149 were found to be Diabetic and 51 were found to be Non Diabetic. The outcome of this study revealed that there is a strong association between diabetes mellitus and heart diseases. There is significant increase in the level of Troponin I to be recognised as a single parameter to confirm the diagnosis of Myocardial Infarction. More than 75% of people have responded at minimal elevated value of Troponin I. There was no significant correlation in the level of troponin I amongst diabetic and non-diabetic. There was a statistically significant difference in the HBA1C level amongst diabetic and non-diabetic though there was no such significant in the other parameter (Lipid profile, SGOT, SGPT and LDH). There was a significant increase in urea over the treatment

phase. There was a considerable percentage of samples with deranged renal function with background of diabetes at the onset of MI. **Conclusion:** Diabetes mellitus is considered as a risk equivalent for coronary artery disease; hence routine screening for both coronary artery disease and diabetes in the patients is justified.

KEYWORDS: Diabetes mellitus, HBA1C, Myocardial infarction, Troponin I.

INTRODUCTION

Cardiovascular disease

Cardiovascular disease (CVD) has been defined as "Impairment of heart function due to inadequate flow of blood to the heart compared to its need caused by obstructive changes in the coronary circulation to the heart".[1] Worldwide, there are approximately 17 million deaths annually from CVD, 7.2 million due to ischemic heart disease, 5.5 million due to cerebrovascular disease, and 4.0 million due to hypertensive and other cardiac conditions.[2] In India, the cardiovascular disease epidemic appears to overlap with the epidemic of diabetes. Of all the complications that beset diabetic subjects, the most dangerous and life threatening is cardiovascular disease. Prevalence of coronary artery disease is also increasing at an alarming proportion in India. The present prevalence of this disease among Indians range from 9-14%.[3] There is a lot of evidence to suggest that Asian Indians have an increased risk for coronary artery disease compared to other ethnic groups.[4]

Many risk factors, including family history of heart disease, smoking, obesity, lack of exercise, diabetes, high levels of low density lipoprotein cholesterol (LDL), low levels of high density lipoprotein cholesterol (HDL), and high blood pressure have been documented to increase the risk of heart disease.[5]

Myocardial Infarction: Myocardial infarction (MI) or acute myocardial infarction (AMI), commonly known as a heart attack occurs when blood flow stops to part of the heart causing damage to the heart muscle. MI is the most important consequences of coronary artery disease (CAD). Hence CAD is sometimes called "The Captain of the men of death".[6]

Diabetes Mellitus: Diabetes mellitus (DM) is one of the most common endocrine diseases in all populations and age groups. It is a syndrome of disturbed intermediary metabolism caused by inadequate insulin secretion, or impaired insulin action, or both. Globally, as of 2010, an estimated 285 million people had diabetes, with type 2 making up about 90% of the cases. Its

incidence is increasing rapidly, and by 2030, this number is estimated to almost double.[7] Diabetes mellitus occurs throughout the world, but is more common (specially type 2) in the more developed countries.

The classic symptoms of untreated diabetes are loss of weight, Polyuria (frequent urination), Polydipsia (increased thirst), and Polyphagia (increased hunger).[8] India has more diabetics than any other country in the world. According to the international diabetes foundation, the disease affects more than 50 million adults and kills about 1 million Indians a year.[9]

Cardiovascular Disease and Diabetes

Type-2 diabetes is present in 10-30% of patients presenting with myocardial infarction (MI) and given the expected doubling in the incidence of diabetes over the next 25 years, represent a major public health concern. The clinical features in these patients may include hyperglycemia, hypertension, microalbuminuria, nephropathy, dyslipidaemia.[10]

Early MI prediction provides an opportunity for appropriate intensive management.[11] In addition, MI may be associated with the first presentation of glucose intolerance or overt diabetes, early diagnosis providing an opportunity for appropriate intensive management and risk stratification.[12]

Although recent advances in treatment for acute myocardial infarction have dramatically improved survival in both non diabetic and diabetic patients, diabetes still double the case of fatality rate.[13]

Cardio renal Disease with Associated Diabetic Nephropathy: Diabetes mellitus is the leading cause of renal failure worldwide with prevalence greater than that of glomerulonephritis and hypertensive renal disease. Diabetic nephropathy is a clinical syndrome characterized by persistent albuminuria, elevated blood pressure, a relentless decline in glomerular filtration rate, and a high risk of cardiovascular morbidity and mortality.[14] Diabetic kidney disease affects 20-30% of patients with diabetes and it is also one of the most common causes of end-stage kidney disease, which account for a large proportion of patients beginning dialysis therapy. According to the U.S. Renal Data System (USRDS), 45% of patients with End stage Renal Disease in 2002 had diabetes as the primary cause.[15] In patients with ESRD, clinical and subclinical coronary artery disease is common in both diabetics and non diabetics at the time of initiation of ESRD therapy. Patients with

chronic kidney disease have accelerated atherosclerosis and are at increased risk for cardiovascular events although direct evidence demonstrating a causal relationship is lacking.[16]

Biochemical Markers

A biochemical marker is defined as any hormone, enzyme, antibody, or other substance that is detected in the urine, blood, or other body fluid or tissues that may serve as a sign of disease or other abnormality. The biomarkers are the major diagnostic tool and also may be used to develop patient demographics, which may be useful in developing health policies.[17] The purpose of this study is to evaluate biochemical parameters in patients diagnosed for myocardial infarction with and without diabetes mellitus'.

MATERIAL AND METHODS

Study approach, design, population, and area: A retrospective observational study on biochemical parameters was conducted at Madras Medical Mission, a prime institute of cardiac speciality in Chennai, Tamilnadu (India) including the division of Department of Biochemistry and Institute of Cardiovascular Disease. The study was done on patients who reported with symptoms of chest pain to the critical care unit of the hospital and diagnosed and treated for myocardial infarction with and without diabetes. The study population consisted of 200 subjects who reported to the hospital from December 2015 to June 2016.

Inclusion criteria

- Patients with symptoms suggestive of heart attack who had raised cTnI and diagnosed to have myocardial infarction (Both diabetic and non diabetic) and underwent treatment in the hospital.
- Gender: Males & Females
- Age: 25-80 years

Exclusion criteria

- Patients reported with symptoms suggestive of heart attack who did not have raised troponin I (cTnI).
- Patients with symptoms suggestive of heart attack who had raised cTnI and diagnosed to have myocardial infarction (Both diabetic and non diabetic) but did not undergo treatment in the hospital.

- Patients with increased cTnI following other cardiac procedures (interventional and surgical)
- Age: less than 25 years.

Ethical consideration

The study was approved by the ethics Committee of Madras Medical Mission.

Data collection

All tests included for the study were within the scope of the Department of Biochemistry (Madras Medical Mission). The tests were conducted by validated and approved methodology with Quality assurance in compliance with NABL standards. The study involved the review of data from patient's records. Patient's case sheets have been used to collect data on relevant history of patients.

Sample collection

Venous blood sample (3ml) was collected in EDTA container for HbA1C (whole blood) and subjected to analysis. 5ml of venous blood was collected in plain tubes/ heparin tubes for other biochemical parameters. After allowing it to clot (plain tubes) they were centrifuged at 3000 rpm for 10-12 minutes, Serum or plasma was separated and proceeded for analysis.

Statistical analysis

Statistical analysis was done by using IBM SPSS (version 21) software programme. Mean and standard deviation of all parameters were calculated. Independent't' test was used to analyse clinical and laboratory data. Chi-square test, Wilcoxen signed rank sum test and Man Whitney U test were used wherever required. $P \leq 0.05$ was considered statistically significant and $P \leq 0.01$ was considered highly significant.

RESULTS

In this study Out of 200 respondents there were 160 males and 40 females corresponding to 80% and 20% respectively of the total number of study group.

Table. 1: Personal characteristics of the respondents N=200.

Demographic Variable	Frequency	Percentage (%)
Gender		
Male	160	80.0
Female	40	20.0
Age (Years)		
<30	2	1.0
31-40	9	4.5
41-50	35	17.5
51-60	53	26.5
61-70	78	39
> 70	23	11.5

Age distribution

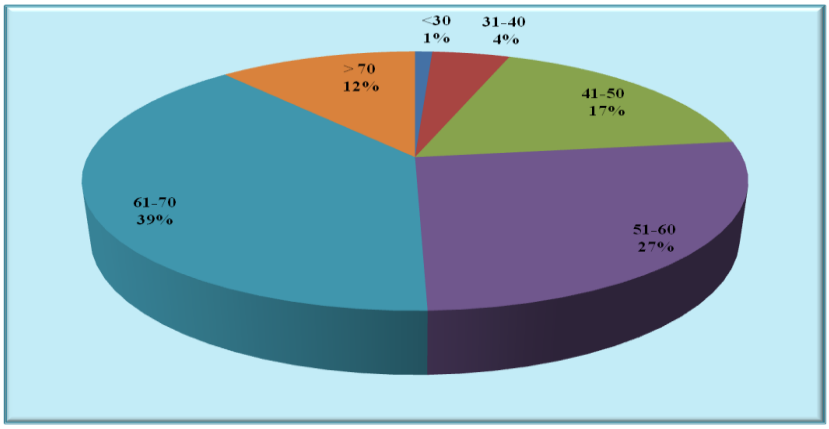

Figure. 1: Age distribution of the respondents (In percentage).

Age: A maximum of 78 patients were in the age group of 60 – 70 (39%), 53 patients were in the age group of 51 – 60(26.5%) and 35 patients were in the age group of 41 – 50(17.5%). It was observed that 23 patients were in the age group of more than 70(11.5%). In total 83% of patients diagnosed with myocardial infarction were in the age group between 40 – 70.

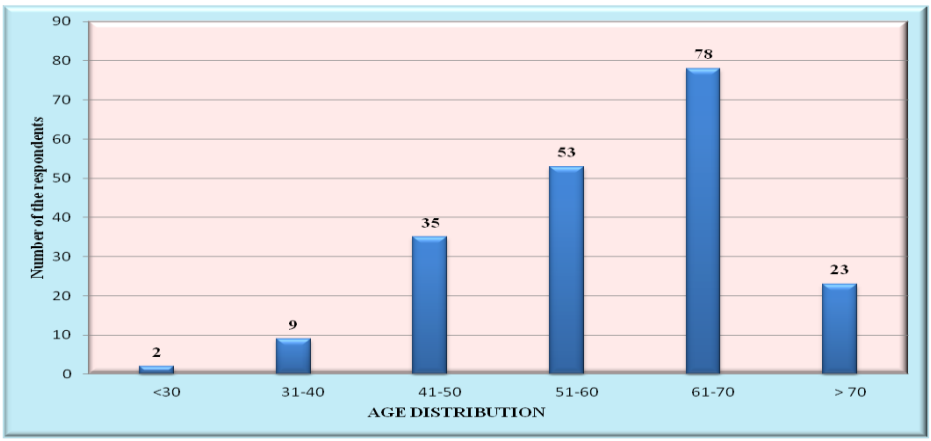

Figure. 2: Age distribution of the respondents (In Frequency).

Table 2: Demographic characteristics of myocardial infarction patients with and without diabetes.

Variable	Diabetic	Non Diabetic
No of case	149 (75%)	51 (25%)
Age (Years)*	59.45±10.07	55.29±12.05
Gender		
Male	118 (79%)	42 (82%)
Female	31 (21%)	9 (18%)

*Mean±S.D

Diabetic status: Out of 200 respondents there were 149 diabetic and 51 non diabetic corresponding to 75% and 25% respectively of the total number of study group.

Gender: Out of 149 respondents with diabetes 118 were males, and 31 were females corresponding to 79% and 21% respectively while out of 51 respondents with non diabetes 42 were males and 9 were females corresponding to 82% and 18% respectively.

Percentage of Diabetic and Non Diabetic

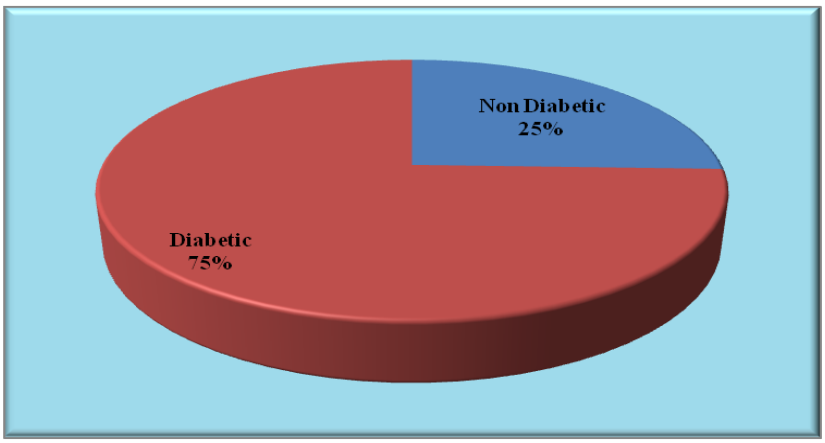

Figure. 3: Distribution of Diabetic and Non-Diabetic patients with proven MI.

Table. 3: Comparison of troponin level in myocardial infarction patients with and without diabetes.

	Median (Quartile)		P Value
	Measurement 1	Measurement 2	
Diabetic	1.73 (0.2-11.2)	11.60 (0.97-59.8)	0.01
Non Diabetic	1.26 (0.14-24.75)	13.30 (1.89-70.0)	0.01

P<0.05; statistically significant.

There was no statistical significance of troponin level when diabetic and non diabetic patients with myocardial infarction were compared.

Table. 4: Age and HbA1C.

Age (years)	Good Control (HBA1C: 6 % – 7%)	Bad Control (HBA1C >8.0%)	Total	P value
<30	1	0	2	**0.050**
31-40	2	3	5	
41-50	5	16	21	
51-60	10	30	40	
61-70	17	41	58	
>70	10	8	18	

There was statistical significance between HbA1c level and age of the patients. The percentage of respondents with bad control was positively associated with age. Age group between 61-70 years showed higher frequency when compared to other age group.

Table. 5: Mean comparison of renal parameters in myocardial infarction patients with and without diabetes.

		Measurement 1	Measurement 2	P Value
Creatinine	Diabetic	1.07.03±0.61	1.06±0.63	0.513
	Non Diabetic	1.05±0.53	0.99±0.48	0.090
Urea	Diabetic	31.54±19.89	34.46±18.67	0.002
	Non Diabetic	26.06±9.03	29.38±12.34	0.088

P<0.05; statistically significant.

The respondents showed no significant difference in Creatinine level among diabetic and non diabetic patients at arrival during diagnosis of MI and across the treatment period. Statistically significant difference in urea was observed amongst diabetic and non diabetic at arrival, during diagnosis of MI (measurement 1 – p=0.002).

Table. 6: Biochemical and Cardiac markers in myocardial infarction patients with and without diabetes.

	Non Diabetic	Diabetic	P Value
HBA1C	5.56±0.31	8.01±1.69	0.00
Cholesterol	163.98±44.38	154.46±56.98	0.31
Triglyceride	139.66±82.38	139.79±76.7	0.99
HDL	35.51±11.68	36.78±12.54	0.82
LDL	100.35±39.07	95.03±45.54	0.48
SGOT	44.0(29-134)	53.0 (29-121)	0.65
SGPT	38.0(24-54)	34.0 (24-52)	0.36
LDH	601.5 (487-817)	556.0 (448-1055)	0.33

P<0.05; statistically significant.

There was highly statistically significant difference in the level of HBA1C when diabetic to non diabetic patients were compared. There was no statistically significant difference in the level of other markers (SGOT, SGPT, and LDH) and lipid profile when compared among diabetic and non diabetic patients. Significant increase above the normal reference range is observed in the biochemical cardiac markers SGOT (53%), SGPT (13%) and LDH (48%).

Table. 7: Characteristics of study population based on medical history.

Medical History	Percentage
Diabetic Mellitus	(47.5 %)
Hypertension	(44%)
Hypertension and Diabetes	(30%)
CAD	(19%)
Hypothyroidism	(2%)
CKD	(1.5%)
Asthma	(2%)
Smoking	(3.5%)
Alcohol	(0.5%)

The respondents showed a high frequency of history of diabetes (47.5%) and history of hypertension (44%) when compared to other risk factors of myocardial infarction.

DISCUSSION

Diabetes mellitus is commonly associated with both micro vascular and macro vascular complications, and specifically type 2 DM contributes to subclinical myocardial injury. Type 2 DM, is also associated with increased arterial stiffness consequence to increased oxidative stress accelerated endothelial cell apoptosis, endothelial dysfunction, and depletion of endothelial progenitor cells all of which may predispose to increased cardiovascular risk.[18]

Early prediction of this risk will be very valuable in the clinical management of the disease. Hence, several studies have focused on the prediction of cardiovascular disease among diabetic patients.[19]

The study included 200 cases diagnosed for myocardial infarction. Within the study, there was a higher incidence of MI in males (80%) compared to females (20%).The increase in incidence in male can be contributed to multiple factors including, life style changes, habit of smoking, genetic pre-dispositions, etc.[20] Regular and moderate physical activity may help to reduce the occurrence and mortality of CHD events especially in young males.[21]

The decrease in incidence of MI in woman can be contributed to the protective effect of oestrogen, the ovarian hormone. It protects against cardiovascular disease by decreased LDL cholesterol and lipoprotein a. It also prevent oxidation of LDL cholesterol and increased HDL cholesterol. However after menopause, the level of oestrogen is reduced and the absolute numbers of women living and dying of CVD and stroke exceed those of men in this age group. Many women at risk for cardiovascular disease are unwilling to take oestrogen compounds as replacement because of sides effects and cancer concerns (i.e.: uterine and breast cancer risks) which may occur following prolonged use of oestrogen.[22]

In the present study, age group between 61-70 years showed higher frequency of 39% of the total case. Cardiovascular heart disease represents the leading cause of death in both men and women older than 65 years.[23] The prevalence and the severity of atherosclerotic coronary artery disease (CAD) increase with age in both men and women. Autopsy studies have shown that, more than 50% of the people older than 60 years have significant CAD, with increasing prevalence of left main and/or triple-vessel CAD with older age.[24]

In our study, Out of 200 respondents, Diabetic group consisted of 75% (149) while Non diabetic group were of 25% (51). The mean average of the age of patients diagnosed with MI irrespective of sex was found to be 59.45±10.07 for diabetic patients and 55.29±12.05 for non diabetic patients. The average age group of non diabetic is observed less than the diabetic patients in the study. It explains the impact of other risk factors other than diabetes like genetic predisposition, obesity, smoking, and high risk life style.

In this study, we observed a significant difference of cTnI level in both diabetic and non diabetic (p= 0.01) based on arriving time of patients to the hospital [The difference in the troponin value on arrival (measurement - 1) and the serial measurement after 6 to 12 hours (measurement- 2)]. In contrast to the study of ShoebQureshi et al[25], which indicated a significant (p=0.014) increase in cTnI among diabetic group when compared with the non diabetic group, the present study did not reflect such difference. As the variation of cTnI level doesn't depend on diabetic status, and depend on patient's reporting time to the hospital after occurrence of MI, we observe significant increase of cTnI level in both diabetic and non diabetic group.

HBA1C values were reviewed for good control (6% – 7%) and bad control (>8.0%) and observed statistically significant (p=0.05) association of increased age with poor control of

diabetes. The percentage of people diagnosed with MI with bad control (98/200) was more than with good control (45/200). This finding is comparable with study done by J.D. Kesqsvadev et al and others.[26] HbA1c is higher in the elderly, suggesting effect of long duration of the disease not balanced with the required awareness and appropriateness of treatment. Age should be taken into consideration when using HbA1c for the diagnosis and management of diabetes and prediabetes.[27]

Within the study we found no significant difference in creatinine among both diabetic and non diabetic patients in all the serial measurements in contrast to Tarigkarar et al[28] and Ramya S et al.[29] Statistically significant difference was seen in urea among diabetic patient over the treatment period in the hospital (p=0.002). Mean urea for diabetic patients on arrival was 31.54± 19.89, and across treatment was 34.46± 18.67 as against urea for non diabetic patient being 26.06± 9.03 and 29.38 ±12.34 respectively. Measurement of urea on arrival and across treatment had statistically significant increase in diabetic patient against non diabetic patient.(p=0.05,0.04) .Impairment of renal function among diabetic group may be due to hyperglycemia induced hemo-concentration effecting the renal filtering physiology eventually leading to systemic accumulation of waste products.[30]

In this study, there was highly significant difference between mean HbA1C level (p=0.00) in diabetic compared to non diabetic group, this is similar to the Study by Nayak lashmi.[31] There was no significant difference in lipid profile, SGOT, SGPT and LDH in diabetic patients compared to non diabetic patients. Best explained as these marker's relative role in the diagnosis and as risk strategies is associated with the event of MI in both the groups, diabetic and non diabetic. Increase in other cardiac biomarkers including SGOT, SGPT, and LDH above the normal range in patients with MI irrespective of diabetic status proves their role as cardiac makers for diagnosis of MI though less specific and have been replaced over time with more specific and sensitive cardiac markers like Troponin I.

Asper the known association of MI with conventional risk factors, like the distribution of history of diabetes, hypertension, and CAD, the present study also shows that history of diabetes mellitus was present in 47.5% of cases; History of hypertension was present in 44% and history of CAD in 19% cases. History of hypothyroidism was present in 2% cases while history of CKD and asthma were present in 1.5% and 2% cases respectively. Among the personal history of smoking, and alcohol intake, only smoking was found to be significantly

higher. This is similar to the study done by Rajni.D Mahajan et al.[32] As evidenced, diabetes (95/200) and hypertension (88/200) are identified as major risk factors for the event of MI.

CONCLUSION

This project study helped us to conclude that, public awareness has to be created amongst diabetic patients for regular check up of well-known risk factors of coronary heart disease and for prevention of cardiac and renal complications induced by diabetes mellitus. Patients can be treated with anti-ischemic therapy as well as insulin and oral hypoglycaemic drugs. Patients have to be encouraged on lifestyle changes to prevent the occurrence of diabetes and Myocardial Infarction.

RECOMMENDATIONS

The patients included in this study attempted to the hospital at early stage of myocardial infarction. This has played a major role in the treatment and prognosis of these patients. Awareness about symptoms suggestive of heart attack has to be emphasized to all people preferably with the background of risk factors as diagnosis and prognosis of myocardial infarction depend on patient's reporting time to the hospital. Also the laboratory role in making available and performing the right cardiac marker test within the least turnaround time.

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