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STUDY OF COMBINATION OF PREGNANCY ASSOCIATED PLASMA PROTEIN-A [PAPP-A] AND TROPNIN T IN EARLY DIAGNOSIS OF ACUTE MYOCARDIAL INFARCTION

Biochemistry

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ABSTRACT

The aim of study was to measure serum level of PAPP-A and troponin T in acute myocardial infarction (AMI) patients and compaire with controls. Serum level of PAPP-A were also correlated with troponin T, risk factors, BMI and time of presentation of patient to cardiac emergency. In this case control study, age and sex matched 100 diagnosed cases of acute myocardial infarction were compared with 100 healthy participants at Jawaharlal Nehru Medical College & Associated Group of Hospitals, Ajmer (Rajasthan). Mean level of PAPP-A and Troponin T in cases (1.21 ± 0.41 µg/ml and 1.35 ± 0.78 µg/L respectivily) were significantly higher ($p < 0.001$) then healthy controls (0.51 ± 0.12 µg/ml and 0.23 ± 0.06 µg/L respectivily). The level of PAPP-A was significantly higher with low troponin T in patients with unstable angina. In this study, PAPP-A level was not associated with age, sex, risk factors and time of presentation of patients.

KEYWORDS

AMI, PAPP-A, Troponin T

INTRODUCTION

Cardiovascular disease is the major cause of death and disability worldwide, with an ongoing increase in Incidence. Acute myocardial infarction (AMI) is a potentially life threatening manifestation of the ischemic heart disease. It is caused by myocardial ischemic necrosis due to sudden occlusion of a coronary artery, usually due to thrombus formation over an atherosclerotic plaque that has got dissected, ulcerated or has undergone hemorrhage. Despite advances in management, it still holds considerable mortality (10-30%), with most of deaths occurring in the first few hours due to ventricular arrhythmias. Diagnosis of AMI is based on classic clinical presentation, Electrocardiogram (ECG) and changing pattern of serum cardiac biomarkers. The complications after acute myocardial infarction are maximum in the first few hours, early detection and diagnosis of MI is vital for institution of therapy to limit myocardial damage and preserve cardiac function. The most widely established and useful biomarker for myocardial injury is cTn. Troponin I (cTnI) and troponin T (cTnT) are expressed only in cardiac muscle, started increasing within a few hours after the onset of symptoms (median, 4 hours; range, 1-10 hours), peak at 12 hours, and stay elevated for 4–7 days for cTnI and 10–14 days for cTnT. The 12-hour wait for the levels to peak remains the Achilles heel of this biomarker. PAPP-A is a pro atherosclerotic metalloproteinase which is highly expressed in unstable plaques and their extracellular matrice. It is not expressed in stable plaques. It was identified in 1972 in blood samples from pregnant women. However, the term “pregnancy-associated plasma protein A” is misleading, because the peptide is not secreted only during pregnancy. Interest in cardiovascular applications first arose in 2001, when it became clear that the peptide is abundantly expressed in eroded and ruptured, but not in stable, atherosclerotic plaques. PAPP-A acts as a metalloproteinase causing rupture of the plaques.

PAPP-A is secreted by activated macrophages during the atherosclerotic process, plays a pivotal role in the pathophysiology of atherosclerotic plaque formation and development. Cosin-Sales et al. confirmed that PAPP-A levels are significantly higher in patients with complex plaques compared to those with smooth plaques. In addition, PAPP-A has been shown to be associated with recurrent cardiovascular events and mortality in patients with certain forms of ACS. PAPP-A is also a useful marker for early detection of ACS and identification of patients at risk for an acute ischemic cardiac event. The purpose of the present study was to evaluate the combination of PAPP-A and Troponin T levels as a tool for early diagnosis of ACS.

MATERIAL AND METHODS

In this case control study, we have studied age and sex matched 100 cases of acute coronary syndrome and 100 normal participants from J.L.N. Medical College and Associated Group of Hospitals, Ajmer, Rajasthan during the period of May 2016 to September 2017. The diagnosis will be made on the basis of history, 12 lead ECG and cardiac biomarkers (cTnT, PAPP-A).

Venous blood samples were collected in a sterile bulb under all aseptic precautions soon after admission of ACS patient. Additional 5ml blood samples were collected in EDTA tube for troponin T measurement. Samples centrifuged in REMI at 3000 rpm for a period of 10 minutes at central laboratory of J.L.N. hospital. Serum were separated after centrifugation and analyzed. Glucose, total cholesterol and TG were measured by means of enzymatic assays, and HDLc concentrations were determined using a direct method. LDL and VLDL were calculated from the friedwald's formula.

PAPP-A was analysed by ELISA method as per the instructions given by the manufacturer DRG international, Germany. Serum Troponin T concentration were measured using a commercial ELISA kit. Serum levels of PAPP-A up to 0.68 µg/ml and Troponin T up to 0.5 µg/L are considered as normal.

Statistical analysis were conducted using SPSS 20.0 software. Appropriate statistical test (chi squire, t test, one way anova, cohen kappa ext.) were applied. Results are depicted in the form of table, graphs and charts. Differences were considered significant when $p < 0.05$.

RESULTS AND OBSERVATION

In this study 100 cases of acute coronary syndrome (80 male and 20 female) were compared with 100 healthy controls (70 male & 30 female).

Table 1: Clinical and metabolic characteristics of healthy controls and ACS patients.

parameter	Healthy controls	ACS patients	P - value
Age (years)	58.4 ± 5.07	58.9 ± 6.2	P=0.514
BMI (kg/m²)	24.7 ± 1.92	25.1 ± 2.02	P=0.231
SBP (mm Hg)	123.4 ± 15.6	140.0 ± 21.6	p<0.001
DBP (mm Hg)	81.60 ± 7.30	86.2 ± 8.2	p<0.001
Glucose (mg/dl)	139.6 ± 58.9	172.7 ± 61.1	<0.001
TC (mg/dl)	163.7 ± 24.2	205.1 ± 30.8	<0.001
TG (mg/dl)	147.5 ± 27.4	168. ± 33.5	<0.001
LDLc (mg/dl)	98.1 ± 14.9	117.0 ± 21.2	<0.001
HDLc (mg/dl)	39.6 ± 5.1	37.4 ± 6.2	<0.001
PAPP-A (µg/ml)	0.51 ±0.12	1.21± 0.41	<0.001
TROPONIN T (µg/L)	0.23 ± 0.06	1.35 ±0.78	<0.001

SBP: Systolic blood pressure, DBP: diastolic blood pressure, TC: total cholesterol, TG: triglycerides, LDLc: LDL cholesterol, PAPP-A : pregnancy associated plasma protein A . *Data are expressed as mean ± SD.

SBP, DBP, glucose was found to be higher in ACS patients than controls (p <0.001). High TC, TG, LDLc and low HDLc (p <0.001) in ACS patients is shown in Table1.

Among 100 cases of ACS, 48 were having STEMI, 32 were having NSTEMI and 20 were having Unstable angina. Serum PAPP-A and Troponin T were measured immediately after admission within different time of presentation.

Table 2 : Time of presentation and cardiac biomarker in STEMI

Time of presentation	Number	PAPP-A (µg/ml)	TROPONIN-T (µg/L)
Within 3 hours	32	1.65 ± 0.32	0.66 ± 0.22
Within 6 hours	12	1.47 ± 0.11	3.05 ± 0.69
Within12 hours	4	1.40 ± 0.02	7.80 ± 0.01
Total	48	1.58 ± 0.28	1.85 ± 2.12

Table 3 : Time of presentation and cardiac biomarker in NSTEMI

Time of presentation	Number	PAPP-A (µg/ml)	TROPONIN-T (µg/L)
Within 3 hours	20	0.96 ± 0.15	0.41 ± 0.08
Within 6 hours	8	1.02 ± 0.09	1.80 ± 0.11
Within12 hours	4	0.90 ± 0.01	4.80 ± 0.01
Total	32	0.97 ± 0.13	1.31 ± 1.47

Table 4 : Time of presentation and cardiac biomarker in Unstable Angina

Time of presentation	Number	PAPP-A (µg/ml)	TROPONIN-T (µg/L)
Within 3 hours	12	0.92 ± 0.16	0.26 ± 0.08
Within 6 hours	4	1.12 ± 0.02	0.17 ± 0.01
Within12 hours	4	0.90 ± 0.02	0.18 ± 0.01
Total	20	0.95 ± 0.15	0.22 ± 0.07

Serum PAPP-A level increases significantly in patients with ACS, higher in STEMI then NSTEMI and USA. In patients with NSTEMI, it was higher then USA. Serum PAPP-A level was not affected by time of presentation of patient. PAPP-A level was increased even in patients who presented early within 3 hours and in patients who had USA, where Troponin T level was low. So Serum PAPP-A helps in early dignosis of patients with ACS.

Serum Troponin T increases with time and higher in STEMI, NSTEMI and lower in USA.

DISCUSSION

Our main finding was that serum PAPP-A level was significantly higher in cases of ACS compare to controls (Bayes-Genis et al. 2001; Heeschen et al.2005)

Mean ± S.D. level of PAPP-A was significantly higher in patients with STEMI than those with NSTEMI and USA (Iversen et al. 2011).

Mean ± S.D. level of PAPP-A was significantly higher with low troponin T in patients with unstable angina. It shows that PAPP-A is released in circulation earlier than troponin T and thereby confirms that PAPP-A is a marker of plaque instability, released into circulation before myocardial necrosis (Lund et al. 2003, Bayes-Genis et al. 2001).In this study PAPP-A level was not associated with age, sex, risk factors and time of presentation of patients.

Serum troponin T level is increases with time of onset of symptoms and become highest level up to 12 hours in current study. It is also concluded that troponin T level were high in patients suffering from STEMI compare to NSTEMI and lowest in USA (<0.5 µg/L).

We also found increased cholesterol, LDL & Triglyceride (p <0.001) with decreased HDL (p <0.001) in ACS patients similar to study of P. Gururajan et al. (2012), G. Wang et al.(2016).

Limitations of Study

First, our sample size was relatively small, and the age range of subjects was relatively limited.

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NIL

CONFLICTS OF INTEREST

We have no competing interests.

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CONCLUSIONS AND FUTURE STUDY

It is thus concluded from our study that cardiac troponins currently are the biomarker of choice for the serologic diagnosis of AMI. Our results confirm the delay of several hours between onset of symptoms and rise of troponin in AMI observed in previous studies.Our study results have shown PAPP-A levels are elevated in cases of both AMI and UA, when compared to asymptomatic controls, thus proving PAPP-A to be a marker in ACS. Moreover, elevation of PAPP-A levels in cases of USA, when myocardial necrosis markers are within the normal range and ECG changes are inconclusive, highlights the utility of PAPP-A in the early diagnosis of ACS.Increase PAPP-A level in patients with USA reflect the instability of atherosclerotic plaques. Our study cannot answer questions such as whether PAPP-A is a primary or secondary component of acute coronary syndromes. Further studies are required to characterize the importance of PAPP-A within unstable coronary plaques and to elucidate the diagnostic and prognostic significance of elevated PAPP-A levels in patients with acute coronary syndromes. Our study was limited in terms of the number of patients examined and single centre study,it is important to confirm the findings with studies of more patients.However, further larger clinical trials would help in enhancing the diagnostic capability of this novel biomarker.To conclude about the influence of risk factors on PAPP-A levels in the circulation, long term studies on a larger population are required.

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