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Clinical Utility of Procalcitonin in The Prediction of Cardiovascular Complications in Patients with Type 2 Diabetes Mellitus

Hanaa Hamdy[1],Wafaa Ghoneim[2], Hatem Abdelmonem[2],Ibrahim Ali[3] ,Marwa Emam[3]

[1] Hormones Department,National Research Center,[2]Biochemistry Departments, Faculty of Science, Helwan University, [3]Biochemistry Department, National Institute of Diabetes and Endocrinology

ABSTRACT

Objective:this study was initiated to assess procalcitoninas prognostic marker forcardiovascular complication in type2 diabetic patients.

Subjects and methods:forty type 2 diabetic patients without cardiovascular disease, forty type 2 diabetic patients with cardiovascular disease and twenty healthy control counterparts were included in the present study. Serum procalcitoninlevels were assayed and correlated with metabolic parameters.ROC curve analysis was also done for this biochemical marker.

Results:the mean level of procalcitonin was 707.17± 99.19ng/l in diabetic subjects versus 881.30± 123.56ng/l for the cardio-diabetic subjects ($P < 0.0001$).Procalcitonin levels were significantly amplified in the cardio-diabetic patients with increasing C-reactive protein (CRP), triglycerides (TG), fasting blood glucose (FBG),and cholesterol (P = 0.004, 0.0005, 0.002 and 0.01 respectively). From ROC curve analysis, it was observed that the area under curve for procalcitoninwas 0.878. This finding indicates the good validity of the above biomarker as aprognostic factor for cardiovascular complication in type 2 diabetic patients.

Conclusion:this study evidences the usefulness of measuring serum levels of procalcitoninin diagnosis of cardiovascular complication in type 2 diabetic patients.

Keywords:procalcitonin, diabetes mellitus, cardiovascular complications,prognosis.

INTRODUCTION

Diabetes mellitus is a chronic disease that affects 415 million people worldwide and 5 million people died from diabetes-related complications[1].Type 2 diabetes mellitus (T2DM) is characterized by hyperglycemia,that results from lack of endogenous insulin or resistance to the action of insulin in muscle, fat and liver in addition to an inadequate response by the pancreatic beta cells[2].

T2DM isconsiderd as a risk factor for cardiovascular disease (CVD). This is due to a complex group of risk factors associated with T2DM including insulin resistance, hyperglycemia, diabetic dyslipidemia, hypertension, hyperinsulinemia, systemic inflammation and adipose tissue-derived factors [3, 4, 5]. Worthmentioning , the changes in the mass and metabolism of adipose tissue may be accompaniedwith insulin resistance and visceral obesity commonly associated with T2DM[6].

Inflammatory mediators play an important role in the pathogenesis of cardiovascular (CV) disease.In particular, acute coronary syndrome (ACS), is an inflammatory disease and the serum levels of inflammatory factors, such as interleukin (IL)-6, IL-18 and C-reactive protein (CRP) are used to identify patients with cardiovascular (CV) disease especially coronary artery disease[7].

CRP and procalcitonin (PCT) are well known acute inflammatory markers that have been used as markersof infection[8].These two indicators are easy to be detected, reliable and inexpensive, and they are used for the diagnosis and follow-up of several diseases[8,9].

PCT is produced during bacterial infections, sepsis and cardiogenic shock, major surgery, burns, multiple trauma, and after cardiac surgery[10,11]. It is a 116-amino acid hormone that is implicated in calcium metabolism, firstly identified as prohormone of calcitonin, and is synthesized by the medullary C-cells of the thyroid gland[12,13,14]. Even thyroidectomized subjects have a PCT response during acute inflammation[15]indicating that there are other probable origins of PCT production.

Some researches have suggested that PCT may be produced by other tissues like liver and inflammatory cells [16,17]. The inflammatory response is a key feature of acute coronary syndrome (ACS) and myocardial infarction (MI). In acute myocardial infarction(MI), signs of inflammation are well identified and enhanced levels of acute phase reactants have been found to be paralleled by a worse short- and long-term prognosis[18]. Signs of a systemic

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inflammatory response, like fever, leucocytosis and increased acute phase reactants, are frequently noticed in patients with acute coronary syndrome (ACS)[19]. PCT has been manifested as a novel cardiac marker in acute myocardial infarction(MI)[20].Circumstantial evidence showed that bacterial endotoxins and tumour necrosis factor-α (TNF-α) both induced PCT *in vitro*[11, 21]. Based on this document, PCT may be an alternative newindicator with prognostic value in ACS. Many research studies have cited higher PCT levels in patients versus healthy controls following severe sepsis, cardiac surgery or trauma[22,23,24].

The focus of our interest was to assess the kinetics of procalitonin production as a novel prognostic marker for cardiovascular complication in type 2 diabetic patients.

SUBJECTS AND METHODS

Forty type 2 diabetic patients with cardiovascular disease (cardio-diabetic group) and forty type 2 diabetic patients without evidence of CVD (diabetic group) were included in the current study and collected from clinic's national institute of diabetes and endocrinology. In addition,twenty apparently healthy subjects with no history of type 2 DM, other endocrine dysfunctions, hyperlipidemia, hypertension, or coronary heart diseases were enrolled in the study and served as controls.Patients in the group without vascular disease were T2DM patients who had no history of vascular disease and those with normal ECG findings at exercise and normal peripheral artery Doppler ultrasonography. Exclusion criteria involved the presence of sustained type 1 DM, acute and chronic infections, malignancy, hepatic or renal disease, diabetic retinopathy and nephropathy, and other endocrine dysfunctions.This study was approved by Ethical Committee of Ethics commission and Scientific Research of the General Authority for hospitals and educational institutes

Blood and urine samples: venous blood was collected from all participants and each blood sample was divided into two portions. The small portion was collected on EDTA coated tube for determination of $HbA1_{C,}$ and the large portion was collected on plain tube for separation of serum. Serum samples were obtained for determination of CRP, TG, FBG, cholesterol and procalcitonin. All biochemical variables were measured on the same day of the blood collection. Remaining serum specimens were stored at -20˚C until analysis of procalcitonin. Urine was collected for determination of microalbumin.

Quantitative determination of glucose was carried out colorimetrically using method of Thomas[25].Quantitative estimation ofserum cholesterol was donecolorimetrically using method of Richmond[26].Serum HDL-cholesterol was assayed colorimetrically using method ofAssmann[27].LDL-cholesterol was quantified in serum using method of Okada *et al*[28]. Triglycerides in serum was measured colorimetrically using method of Jacobs and Van Denmark[29].Glycated hemoglobin was determined usingmethod described by Trivelli *et al*[30].Serum C-reactive protein (CRP) was measured by ELISA using method of Hedlund[31].Quantitative estimation of micro-albumin in urine was done by immunoturbidimetric assay using method of Mogensen and Schmitz [32].Serum procalcitonin was evaluated by solid-phase enzyme-linked immunosorbent assay (ELISA kit) using method described by Arkader *et a*l[33].

Statistical analysis

Data were expressed as mean ± SDand analyzed using MedCalc software, version 11. The Student's t test was used to assess the significance of difference in the levels of procalcitonin between the patient groups (diabetic and cardio-diabetic) and the control group. The correlation analysis between serum procalcitonin level and other measured parameters in the different studied groups was performed by correlation coefficient test. The cut-off value was determined for procalcitonin in the current study according to the best discrimination between diabetic patients and cardio-diabetic patients regarding optimal values of sensitivity and specificity using ROC curves analysis. AUC of the ROC curve was calculated for procalcitonin. $P < 0.05$ was accepted as significant.

RESULTS

Laboratory assessments of the measured parameters in the different submitted groups are presented in Table (1).Cholesterol, CRP, FBG, HbA1c, LDL, TG, micro-albumin, and procalcitonin levels were significantly higher in diabetic patients than in healthysubjects (P=0.022, P<0.0001, P<0.0001, P<0.0001, P=0.042, P=0.007, P=0.016 and P<0.0001 respectively). Likewise,CRP, FBG, HbA1c,

LDL, TG, cholesterol, procalcitonin, and micro-albumin levels were significantly higher in cardio-diabetic patients than inhealthy subjects (P<0.0001, P<0.0001, P<0.0001, P<0.0001, P=0.009, P=0.007, P< 0.0001 and P<0.0001 respectively).In addition, CRP, LDL, procalcitonin and micro-albumin levels were significantly higher in cardio-diabetic patients as compared to diabetic patients (P=0.0003, P<0.0001, P<0.0001, and P<0.0001 respectively).Whereas, HDL level showed significant drop in cardio-diabetic patientsversus diabetic patients and control subjects (P=0.0002, and P<0.0001,respectively).Also,it revealed significant declin in diabetic patients relative to healthy subjects(P=0.038).

The results of correlation between serum procalcitonin concentration and metabolic parameters in the different studied groups were depicted in Table (2). Significant positive correlation between serum procalcitonin concentration and cholesterol, TG, CRP and FBG has been recorded in cardio-diabetic patients (P=0.011, P=0.0005, P=0.004, and P=0.002 respectively).As well, significant positive correlation between serum procalcitonin concentation and LDL, cholesterol, TG, CRP, FBG and HbA1c has been recorded in diabetic patients(P=0.052,P=0.013,P=0.003,P<0.0001,P <0.0001and P=0.009 respectively). However, significant negative correlation has been observed between serum procalcitonin and micro-albumin in diabetic patients(P=0.016).

The receiving operating characteristic (ROC) curve was designed for procalcitonin (Fig:1). The cut-off values for procalcitonin was750 ng/l**,**. Area under curve (AUC) for procalcitonin was 0.878. This result indicates the good validity of the above biochemical marker to discriminate diabetic patients fromcardio-diabetic patients**.**

DISCUSSION

Patients with type 2 diabetes mellitus have a high risk of cardiovascular disease. This risk is associated with many factors such as hypertension, dyslipidaemia and obesity in these patients. However, the onest of cardiovascular disease in type 2 diabetes mellitus patients isnot related to the high prevalence of traditional risk factors only, but other non-traditional risk factors may be implicated. Thus,cardiovascular disease is increased in type 2 diabetes mellitus patients due to a complex combination of various traditional and non-traditional risk factors.This has a pivotal role to play in the evolution of atherosclerosis over its long natural history from endothelial function to clinical events [34]. The objective of this studywas to assess procalcitoninas prognostic markers for cardiovascular complication inpatients with type2 diabetes mellitus.

The results obtained in this study showed that cholesterol, LDL and TG were significantly higher in diabetic patients when compared to control subjects.Whereas, HDL was significantly lower in diabetic patients versus the control subjects. These results are in conformity with those of Tarek and Khalid[35] who stated that all the above parameters are significantly higher,while HDL is significantly lower in type 2 diabetes mellitus group when compared to the control group . These results were explained by Ronald[36] who cited that insulin resistance may contributein the development of dyslipidemia in diabetic patients. As in type 2 diabetes,insulin resistance increases the flow of free fatty acids from adipose tissue and impairs insulin-mediated skeletal muscle uptake of free fatty acids leading to increased fatty acid flow to the liver [37,38]. It has been found an increase infree fatty acid levels in individuals with impaired glucose tolerance suggesting that insulin resistance is associated with elevated free fatty acid levels which occurs before the onset of hyperglycemia [39]. One study have demonstrated a relationship between plasma free fatty acid levels and insulin resistance [40]**.**Free fatty acids in the form of triglycerides are deposited in muscle, liver, heart and pancreas in the presence of insulin resistance. Also, insulin resistance increases the activity of hepatic lipase, which is responsible for hydrolysis of phospholipids into LDL and HDL particles with consequent formation of very small and dense LDL particles and a reduction in HDL particles[41,42]. This hypothesis is appreciated when some drugs that lowered the high level of free fatty acids, (thiazolidinediones), could improve insulin sensitivity in muscle, liver, and adipose tissues [43,44].

FBG and HBA1C levels were significantly higher in diabetic patients compared to healthy subjects.Study ofTarek and Khalid[35] revealed that FBG and HBA1C levels were significantly higher in diabetic patients when compared to

healthy subjects.Also,Makris *et al*.[45] found a significant relation between FBG and HBA1C in diabetic patients. The studies ofPeterson *et al***.**[46]and Miedema.[47] have shown that the increased blood glucose leads to the increased attachment of glucose molecules to the hemoglobin in red blood cells. The longer hyperglycemia occurs in the blood, the more glucose binds to hemoglobin in the red blood cells and the higher in glycated hemoglobin. It is formed in a non-enzymatic glycation pathway of hemoglobin exposure to plasma glucose,then reaction occurs between glucose and the N-end of the beta chain in heamoglobin. In diabetes mellitus, higher amounts of glycated hemoglobin, indicating a poorer control of blood glucose levels with consequent complications such ascardiovascular disease, nephropathy,neuropathy, and retinopathy.

CRP level was significantly higher in diabetic patients when compared to healthy subjects. Study of Belfki *et al*.[48]demonstrated that levels of CRP are significantly higher in patients with Type 2diabtes mellitus than control subjects. Morohoshi *et al*.[49]and Guha *et al*.[50]mentioned that hyperglycemia stimulates the libration of the inflammatory cytokine such as interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) from different cell types and results in the secretion of acute-phase reactants by adipocytes .Grunfeld *et al*.[51] and Hirschfield *et al*.[52]proved that CRP is an acute-phase reactant that is produced primarily in the liver under the activation of adipocyte-derived proinflammatory cytokines.

Serum procalcitonin level was significantly higher in diabetic patientsrelative to healthycontrol subjects. Study of Mehment *et al.*[53] reported that procalcitonin levels were elevated in type 2 diabetic subjects when compared with healthycontrols.In addition, Schiopu *et al*.[54]found that procalcitoninis positively correlated with the presence of hyperglycemia and with systolic blood pressure(SBP). Moreover, hyperglycemia is associated with increased systemic inflammatory activation and thus,it seems that thisinflammation may stimulateprocalcitonin production.

These investigators explained the elevated levels of procalcitonin intype 2 diabetes mellitus by the fact that type 2 diabtes mellitus is related to oxidative stress and advanced glycation end products (AGEs) elevation. Advanced glycation end products interact with its receptor that is called RAGE. Activation of RAGE leads to regulation of the transcription factor nuclear factor-kB and its target genes and also activator protein-1(AP-1). These factors could ultimately lead to upregulation of procalcitonin gene expression[53,54].

There were significantly higher differences in micro-albumin between diabetic patients and control subjects .Study of Chowta *et al* [55]found high prevalence of microalbuminuria (37%) in type-2 diabetes mellitus, and The incidence of micro-albuminuria increases with the increased duration of diabetes mellitus.Mogensen Et al[56]proved a positive correlation between micro-albuminuria and the duration of diabetes mellitus.Long duration of diabetes has significant contribution for the development of micro-albuminuria as prolonged exposure to hyperglycemia could induce advanced glycation end products accumulations.Bucala *et al*[57]and KathrynEt al[58]stated that hyperglycemia may cause tissue damage by several mechanisms, one of which is non-enzymatic glycation of intra- and extracellular proteins. Glucose possesses a reactive aldehyde moiety that reacts non-enzymatically with the amino groups of proteins in the extracellular matrix, forming slowly reversible Amadori products, and advanced glycation end products (AGEs), that can impair degradation of proteins, and induce of cytotoxic pathways.So, serum concentrations of AGEs increased in patients with type 2 diabetes, and this leads to increased level of micro-albumin.

Cholesterol, TG, and LDL were significantly higher in cardio-diabetic group in respect to healthy control group. Meanwhile, HDL was significantly lower in cardio-diabetic patients versus healthy subjects.The study of *Haddad et al.*[59] found that cholesterol, LDL-C and triglycerides are increased, but HDL-C is decreased in diabetic patients with coronary artery disease (CAD) comparing with the control group.These data were explained by Celermejer[60] who mentioned that dyslipidemia is an important mechanism by which atherosclerosis and endothelial dysfunction can occur in diabetic patients. Healthy endothelium regulates activation of platelet, tone of blood vessel, leukocyte adhesion, inflammation and thrombogenesis. Thus,healthy endothelium is anti-atherogenic ,vasodilatory, and anti-inflammatory [60]. Affection of these mechanisms

leads to atherosclerosis. Therefore, both insulin resistance and insulin deficiency lead to dyslipidemia accompanied by increased glycosylation,oxidation, and triglyceride enrichment of lipoproteins.

Also Betsy.[61]has shown that oxidized LDL is pro-atherogenic because when the particles of LDLare oxidized, they showed new properties that are recognized by the immune system as "foreign." Also, oxidized LDL produces several abnormal biological responses, such as promoting the ability of leukocytes to ingest lipids and differentiate into foam cells, attracting leukocytes to the intima of the vessel, and stimulating leukocytes, endothelial cells and smooth muscle cell proliferation [62].All of these lead to the formation of atherosclerotic plaque. Furthermore,in diabetic patients, LDL particles can glycated, in a process similar to the glycation of hemoglobin (HbA1C). Glycation of LDL lengthens its half-life [63]and therefore increases the ability of LDL to induceatherogenesis.

FBG and HBA1C levels were significantly higher in cardio-diabetic patients in comparison with healthy control counterparts.Study of Anping *et al*.[64]stated that levels of HbA1C are gradually increased in unstable angina and acute myocardial infarction subjects versus healthy subjects.Biologically, glycated hemoglobin is an advanced glycosylation end-product, and the increased level of HbA1C leads to the formation of advanced glycosylation end-product, which attaches to the vessel wall and leads to dysfunction of endothelium and oxidative stress progression [65,66]. Also, the binding of advanced glycosylation end-product is associated with overproduction of inflammatory cytokines such as CRP [67]. Increased CRP level has been found to be significantly associated with the instability of plaque [68,69].This explains why that after adjustment of CRP, there is no significant association between HbA1C and the severity of coronary artery disease (CAD). Finally, increased level of advanced glycosylation end-product interferes with the endogenous fibrinolytic system which might result in high risk of coronary artery stenosis [70].

CRP was significantly higher in cardio-diabetic patientsin respect to healthy subjects. Study of Paul [71]proved that the increased level of CRP is related to an eight-fold increase in cardiovascular mortality.Also Liang *et al* [72]stated that the level of CRP is significantly higher in acute myocardial infarction (AMI) and unstable angina(UA) patients thanin stable angina (SA) patients and healthy control. These observations areinterpretted by Amit Kumar *et al* [73] who reported that atherosclerotic process is characterized by a low-grade inflammation, and increased concentration of the inflammatory modulators such as acute phase proteins and cytokines. In addition, CRP is also produced locally the in atherosclerotic lesions by inflamed smooth muscle cells (SMCs) lymphocytes and monocytic cells.

Paffen and DeMaat[74]and Hanefeld *et al*[75] found that CRP plays a pivotal role in many aspects of atherogenesis including, activation of the classical pathway of the complement system and by this action, CRP directly amplifies and facilitates the innate immunity, a process that has already been associated with the initiation and progression of coronary heart disease (CHD)[75.]CRP also increases LDL uptake into macrophages and enhances the ability of macrophages to form foam cells. Moreover, CRP up-regulates the expression of adhesion molecules in endothelial cells (ECs) that can attract monocytes to the site of injury. Therefore, CRP is ahigh sensitive biomarker that can be used as a clinical guide for diagnosis, management and prognosis of coronary heart disease(CHD)[74].

Serum procalcitonin level was significantly higher in cardio-diabetic subjects when compared to healthy controls. Study of Sinning *et al*.[76]cited that patients with acute coronary syndrome have increased concentration of procalcitonin. Likewise,Christoph *et al*.[77] found that procalcitonin level is higher in patients with cardiovascular events and this increment in procalcitonin level is according to the number of affected coronary arteries.As well, Erren *et al*.[78]reported that the increased procalcitonin level is related to the extent of atherosclerosis in coronary artery disease (CAD) patients and peripheral arterial disease. In atherosclerotic patients, ischemia and inflammatory processes lead to procalcitonin production. In addition, increased levels of procalcitonin in the setting of CAD are more as a result of non-specific libration of cytokine in the context of local tissue damage to myocardium due to ischemia and necrosis.This explains theassociation

between procalcitonin and low-grade inflammatory activity within the vascular wall caused by atherosclerosis.Schlitt *et a*l.[79] found that procalcitonin mRNA expression by peripheral blood mononuclear cells is stimulated indirectly *via* pro-inflammatory cytokines (IL-1β, IL-2, IL-6 and TNF-α) which play an important role in the atherosclerotic process. These together explain the increased procalcitonin concentration in diabetic patients with cardiovascular complication. Furthermore, patients with severe damage of myocardium after myocardial infarction had elevated procalcitonin level [80].Remskar *et al*.[81]observed a relation between procalcitonin concentration and severe heart failure and cardiogenic shock after acute myocardial infarction particularly in patients with procalcitonin concentration >0.5 ng/ml.

Micro-albumin level was significantly higher in cardio-diabetic patient sversus healthy subjects.Study of Klaus *et al*.[82]demonstrated that subjects who developed CHD during follow-up had higher urinary albumin excretion than control subjects. Also, Jensen *et al*.[83] found apositive association between urinary albumin excretion rate and acute myocardial infarction .Several hypotheses explain the relation between micro-albuminuria and cardiovascular disease. One of them suggests that a dysfunction of the vascular endothelium causes both micro-albuminuria and cardiovascular disease [84,85]. Endothelial dysfunction can be defined as any change in theendothelial properties that is inappropriate with regard to the preservation of organ function. Therefore, many types of endothelial dysfunctioncould be existed depending on which function is affected (*e.g.* the regulation of hemostasis and fibrinolysis, vasomotor activity, permeability to macromolecules, leukocyte adhesion and vascular smooth muscle cell proliferation). Generalized endothelial dysfunction is now considered as a transducer of atherogenic risk factors and is thought to play an important role in both initiation and progression of atherosclerosis. Therefore, the association of micro-albuminuria with generalized endothelial dysfunctioncould explain why micro-albuminuria strongly predicts cardiovascular disease. Indeed, micro-albuminuria in type 1 and type 2 diabetes is usually accompanied by endothelial dysfunction with regard to the regulation of hemostasis, fibrinolysis, leukocyte adhesion, and NO synthesis and/or availability. This was documented by the estimated plasma levels of endothelial function markers such as von Willebrand factor, tissue-type plasminogen activator, soluble vascular cell adhesion molecule-1 and soluble E-selectin [84].Jager *et al*.[86]and Stehouwer *et al*.[87] have shown that chronic, low-grade inflammation is associated with the occurrence and progression of micro-albuminuria and with risk for atherothrombotic disease. From the above considerations, endothelial dysfunction and chronic low-grade inflammation are important candidates to explain the association between microalbuminuria and cardiovascular disease.

In view of our data, significant positive correlation between serum procalcitonin and cholesterol, TG, CRP, LDL, HbA1C and FBG in diabetic patients has been found. Likewise, significant positive correlation has been detected between procalcitonin and cholesterol, TG, CRP, and FBG in cardio-diabetic patients. Study of Schiopu *et al*.[54]found that procalcitonin is associated with several of the already established cardiovascular risk factors (CRP, hypertension, diabetes and renal function). Also, Christoph *et al*.[77]stated that procalcitonin level isassociated with the CRP and TG concentration in patient with coronary artery disease (CAD).

ROC curve was done to detect the best cut off value of serum procalcitonin in diabetic and cardio-diabetic patients. It has been found that procalcitonin at concentration 750ng/l has 87.5% sensitivity and 72.5% specificity. Christoph *et al*.[77] and Farzad *et al*.[88]revealed that procalcitonin level is high in patients with cardiovascular disease.In addition, the studies of Erren *et al*.[78]and Christoph *et al*.[77]reported that the elevated procalcitonin level isrelated to the extent of atherosclerosis in patients with CAD and peripheral arterial disease. In addition, These findings indicate that procalcitonin is a biomarker of CAD in patients with type 2 diabetes mellitus.

The present findings provide a clear evidence favoring the clinical significance of measuring serum level of procalcitonin as diagnostic candidates for cardiovascular complication in patients with type 2 diabetes mellitus.

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Table 1:Laboratory assessments in the different studied groups.

Parameters	Control subject (C)	Diabetic patients (D)	Cardio –diabetic patients (CD)	P1	P2	P3
Cholesterol (mg/dl)	194.15± 36.70	225.70 ± 54.40	233.02 ± 57.47	0.022	0.007	0.560
CRP (mg/l)	14.53 ± 3.41	34.43 ± 8.60	50.32 ± 12.58	< 0.0001	< 0.0001	0.0003
FBG (mg/dl)	87.40 ± 6.91	256.07± 64.01	272.80± 68.2	< 0.0001	< 0.0001	0.166
HBA1C (%)	5.45 ± 0.51	9.74 ± 1.67	10.16± 2.10	< 0.0001	< 0.0001	0.325
HDL (mg/dl)	40.25 ± 7.67	35.35± 8.8	27.57± 8.83	0.038	< 0.0001	0.0002
LDL (mg/dl)	122.90 ±25.04	146.25± 46.94	202.47± 36.48	0.042	< 0.0001	< 0.0001
TG (mg/dl)	121.60 ±55.44	183.47 ± 45.88	237.70 ± 60.02	0.007	0.009	0.080
Procalcitonin (ng/l)	381.67± 100.2	707.17± 99.19	881.30± 123.56	< 0.0001	< 0.0001	< 0.0001
Micro-alb (mg/ml)	7.48 ± 2.1	11.61± 7.07	37.78±13.97	0.016	< 0.0001	< 0.0001

P1:- Diabetic group compared to control group.
P2:- Cardio-diabetic group compared to control group.
P3:- Cardio-diabetic group compared to diabetic group

Table 2:Correlation between serum procalcitonin concentration and metabolic parameters in the different studied groups

Parameters	Serum Procalcitonin level in control groups		Serum Procalcitonin level in diabetic group		Serum Procalcitonin level in cardio-diabetic groups	
	r	p	r	p	r	p
Cholesterol(mg/dl)	0.231	0.325	0.385	0.013*	0.395	0.011*
TG (mg/dl)	0.688	0.0008**	0.448	0.003**	0.524	0.0005**
HDL (mg/dl)	0.245	0.296	-0.281	0.078	0.207	0.198
LDL (mg/dl)	0.132	0.576	0.308	0.052*	0.185	0.250
CRP(mg/l)	-0.133	0.575	0.760	<0.0001**	0.437	0.004**
FBG(mg/dl)	-0.416	0.068	0.718	<0.0001**	0.470	0.002**
HBA1C (%)	0.337	0.146	0.4036	0.009**	0.211	0.190
Micro-alb (mg/ml)	0.230	0.327	-0.377	0.016*	0.292	0.067

r: Correlation coefficient ,*P<0.05, **P<0.01, not significant (P >0.05)

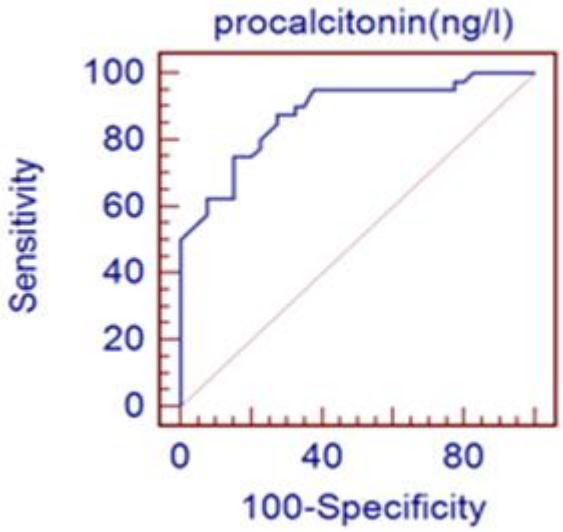

Fig 1:-ROC curve for differentiation between diabetic and cardio-diabetic patients by procalcitonin (P=0.0001)