Homocysteineandhs-CRPlevelsincontrolledanduncontrolledType2diabeticpatients

Dr.HarikaKolli[1],Mrs. SamathaPavuluri[2*],Dr.SivaprabodhV[3]

1.Asst.Professor,Departmentofbiochemistry,NRImedicalcollege,Chinakakani,Gunturdist.AP.

2*. Lecturer, Departmentofbiochemistry, NRImedicalcollege, Chinakakani, Guntur dist. AP.

3. Professor&HOD,Departmentofbiochemistry,NRImedicalcollege,Chinakakani,Gunturdist.AP.

4.*CorrespondingAuthor:

Mrs.SamathaPavuluri,Lerurer,

5.Departmentofbiochemistry,NRImedicalcollege,Chinakakani,Gunturdist.AP.

Abstract

Diabetes Mellitusis themostcommon non –communicable diseasein the world. High CRPlevels may be a marker of oxidative stress on the endothelium in diabetic patients. Diabete smell it usisoneofthemajorriskfactorfortheprogressionofatherosclerosis.Hyperhomocysteinemia is increased in insulin resistant andhyperinsulinemic patients, and alsoin T2DM patients with intact pancreatic β-cell function. To determine hsCRP and Homocysteinelevels in controlled and uncontrolled diabetes and to determine the association of hsCRP andHomocysteine and to find its correlation with lipid profile. The cross sectional study was done on80 diabetic patients, concentrations of hsCRP, Homocysteine, HbA1c, FBG, PPBS, lipid profilewere assayed.Correlation of hs-CRP and homocysteine levels with lipid profile parameterswasobserved among the 2 groups. There was elevation of HbA1C, Homocysteine, FBS, PPBS,Cholesterol, Triglycerides, VLDL, LDL, hS-CRP in diabetes cases. There is significant elevationofHbA1C,Homocysteine,FBS,PPBS,Cholesterol,Triglycerides,VLDL,inuncontrolleddiabetes when compared with controlled diabetes cases. Hs-CRP is elevated in uncontrolleddiabetics when comparedwith controlled diabetes. There is sign if I cant negative correlation between cholesterol, LDL and homocysteine whereas there is significant positive correlation between HbA 1 can dHs-CRP in controlled diabetes In our study we founde levatedhs-CRPand

homocysteine levels in uncontrolled diabetes. Hence it is prudent to estimate hs-CRP and levelsin all diabetic patients to predict the future complications which warrant timely intervention leading tolowered morbidityand mortality.

Keywords:Homocysteine,Inflammation,uncontrolleddiabetes,hs-CRP.

Introduction:

Diabetes Mellitus is the most common non –communicable disease in the world.[1] Based on thecurrent scenario, the International Diabetes Federation Projects that by the year 2030,438 millionindividualswillhavediabetes.[2]Astheyearsprogresstheriskofchroniccomplicationsincrease s. They do not become apparent until the second decade of hyperglycemia. High level oftotalcholesterolandlowdensitylipoproteincholesterolisrelatedtothedevelopmentofatherosclerosis while high HDL is protective for atherosclerosis. Excessive accumulation ofoxidized LDL particles in vascular endothelium in an environment milieu of increased oxidativestress in type 2 DM promotes formation of atherosclerotic plaques. High CRP levels may be amarker of oxidative stress on the endothelium in diabetic patients. Diabetes Mellitus being achronicdisorderresultsfromvariousfactorsinwhichacompleteorpartialdeficiencyorimpairedfunctio nofinsulinoccurs.Amongdiabeticsubjectstheriskforcardiovasculardiseaseis 2-4folds greater in comparison tonormal subjects.[3] Diabetes mellitus is one of themajorrisk factor for the progression of atherosclerosis, which is two to four folds more common ascompared to that of normal population. Elevated concentrations of serum Homocysteine (Hcy) isexpected toenhancetheproduction of oxidation products such as Hcydisulfidesand Hcythiolactone, leading toendothelial cell damage by extra vagantsulfation of collagen which in creases the thrombosis and arteriosclerosis. Hyperhomocysteinemiais increasedin insulinresistant and hyperinsulinemic patients, and also in T2DM patients with intact pancreatic β-cellfunction.[4]

Inflammation predisposes to dyslipidemia characterized by low HDL, total cholesterol, and ApoA-I levels and increased levels of low density lipoprotein (LDL) cholesterol, triglycerides (TGs),and Apo B. Several investigatorsreported that patients with inflammatorydiseases have anadverselipidprofile.[5,6]Numerousstudiesandexperimentalevidenceindicatethatatherosclerosis represents a chronic inflammatory process.[7,8] Resear chershypothesized that in flamma torymarkersuchas high-sensitivity C-reactiveprotein (hs-CRP) mayprovidean

Adjunctive emethodforglobal assessment of cardiovascularriskthat could result from

dyslipidemia.[9,10]

Plasma levels of hs-CRP are independent predictor of peripheral arterial disease and vasculardeath among individuals without known CVD. Diabetes mellitus is considered to be a state of persistent low grade in flammation which contri but estothe pathogenesis of disease.[11]In flammation is a state of local protective response to tissue injury.[12] In addition to localresponse, systemic response called as acute-phaseresponseis depicted by the changesin level so facutephasereactants like C-Reactive Protein (CRP) ,complement system proteins,serumamyloid A, haptoglobin and fibrinogen.[13] Patients with diabetes mellitus aggravate other co-morbidities like hypertension, obesity and dyslipidemia which in turn increase the risk for Cardio Vascular Disease (CVD).[14]C- reactive protein, measured as high sensitivity C reactive protein(hsCRP), an acute phase protein is produced by theliver and their levels increase whenever there is instances of in flammation in the body.[13]

This study aims at finding a reliable correlation between serum Homocysteine levels and insulinlevels which shall indicate the degree of insulin resistance in patients with Type 2 Diabetes Mellitus,and hence predicttheir riskfor atherosclerosisand cardiovascular disease.

Aimsand objectives:

1) TodeterminehsCRPandHomocysteine levelsincontrolledanduncontrolleddiabetes.
2) TodeterminetheassociationofhsCRPandHomocysteineandtofindits correlationwithlipidprofile.

Materialsandmethods:

The cross sectional study was done on 80 diab eticpatients who come foroutpatientd epartmentin NRI medical college and hospital Guntur, Andhra Pradesh, India, in a period of two monthsduring April to May 2022.In all the subjects the concentrations of hsCRP,Homocysteine,HbA1c,FBG,PPBS,lipid profile were assayed.

Fasting blood sample from subjects were collected in plain vacutainer. Informed consent wasobtained. Samples of the patients were analysed on Vitros 5600 fully automated analyser. Hs CRP by immunoturbidometric method,Homo cysteine by immunometri method,fasting blood glucose by GOD-POD method,Total cholesteroland triglycerides were determined

enzymatically with the cholesterol oxidase peroxidase, 4-aminophenazone (CHOD-PAP) and Glycerophosphateoxidase-peroxidase-4aminophena-zone(GPO-PAP) methodsrespectively,HDL-

Cby Non –HDL precipitation method, LDL by calculated method, HbA1Cby HPLC method in D10 analyser.

The data was analyzed using descriptive statistics like Mean and standard deviation. Correlationof hs-CRP and Homocysteine levels with lipid profile parameters was observed among the 2groups.Thepvalue was calculated according to student paired test.

Results:

Table–1: ShowstheBiochemicalparametersindiabetescasesn=80.

S.NO	Parameters	Mean±S.D	Normalvalues
1	FBS(mg/dl)	134±45.5	70-100
2	PPBS(mg/dl)	178± 56	70-140
3	HbA1C	7.7± 1.58	6-6.5
4	Cholesterol(mg/dl)	202±41.2	150-200
5	Triglycerides(mg/dl)	169± 87	<150
6	HDL(mg/dl)	40.7±9.7	30-60
7	LDL(mg/dl)	129±35.8	<100
8	VLDL	33.6± 17.5	5-30
9	HS–CRP(mg/dl)	10.7±32.9	<6
10	Homocysteine(mg/dl)	8.14±4.6	6.0-14.8

TherewaselevationofHbA1C,Homocysteine,FBS,PPBS,Cholesterol,Triglycerides,VLDL,LDL,hS-CRPindiabetes cases.

Table–2: ShowstheBiochemicalparameters incontrolledanduncontrolleddiabetescasesn=40.

S.No	Parameters	ControlledDiabetes	UncontrolledDiabetes	p
		Mean±S.D	Mean±S.D	
1	FBS	115.9± 19.2	159.7± 45.4	<0.01*
2	PPBS	146±22.6	210±60.2	<0.01*
3	HbA1C	6.6± 0.35	8.7± 1.6	<0.01*
4	Cholesterol	189±44.8	208.2±42	0.05*
5	Triglycerides	147±58.3	191.8±105	0.02*
6	HDL	41.9± 8.9	39.5± 10.5	0.27
7	LDL	120±38.7	131±40.8	0.21
8	VLDL	29.5±12	37.5± 20.9	0.03*
9	HS – CRP	7.96± 34.3	13.4± 31.6	0.46
10	Homocysteine	6.59± 3.74	9.6± 4.9	0.00*

There is significant elevation of HbA1C, Homocysteine, FBS, PPBS, Cholesterol, Triglycerides,VLDL,in uncontrolled diabetes when compared with controlled diabetes cases.Hs-CRP is elevatedinun controlled diabetics when compared with controlled diabetes.p<0.05isstatistically significant.

Table 3 showing correlation of hs-CRP and Homocysteine with Lipid Profile and HbA1c inDIABETEScases

Overall data	hs-CRP		Homocysteine	
	r	p	r	p
Cholesterol	0.02	0.84	0.20	0.62
TG	0.03	0.76	0.19	0.76

HDL	-0.04	0.67	0.01	0.97
LDL	0.15	0.15	0.15	0.18
HbA1c	0.29	0.01*	0.37	0.07

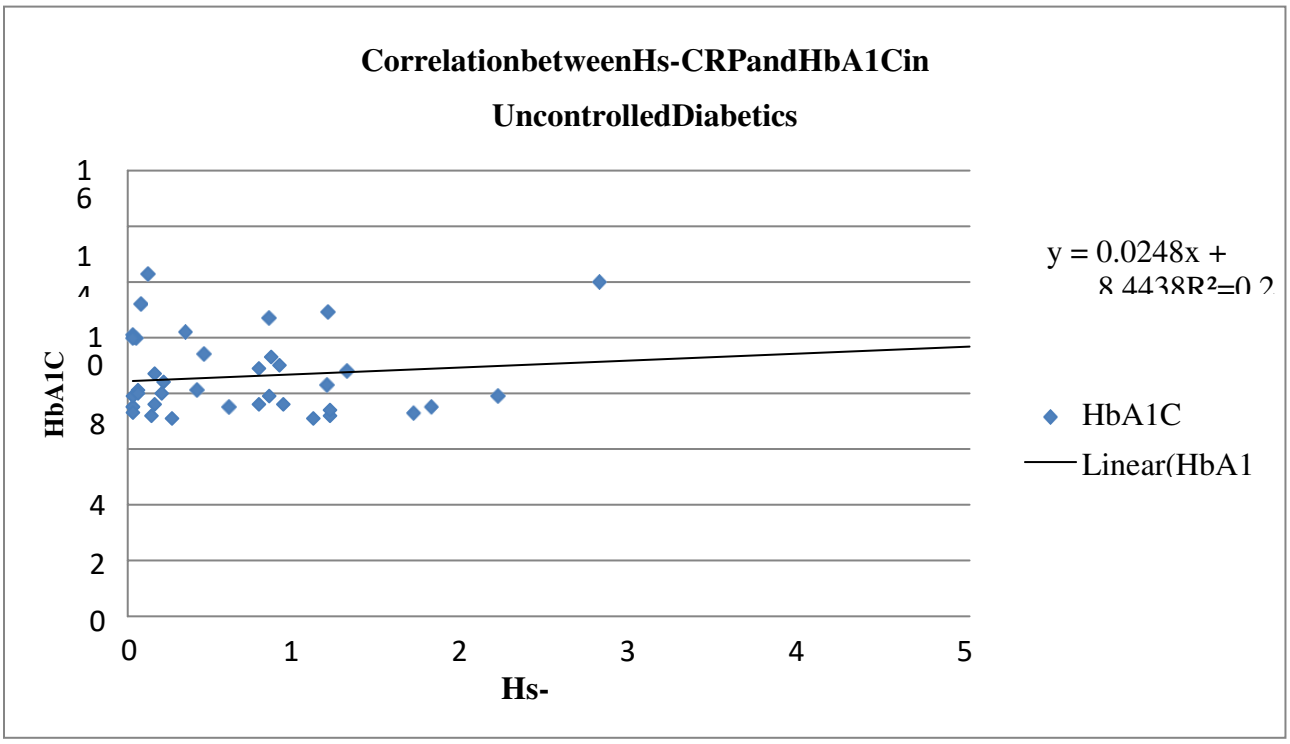
Table4showingcorrelationofhs-CRPandHomocysteinelevelsinUncontrolledandcontrolleddiabetes.

	hs-CRP				**Homocysteine**			
	Uncontrolled Diabetes		**Controlled Diabetes**		**Uncontrolled Diabetes**		**Controlled Diabetes**	
	r	**p**	**r**	**p**	**r**	**p**	**r**	**p**
Cholesterol	0.54	0.01*	-0.26	0.11	0.20	0.20	-0.36	0.02
TG	-0.01	0.97	0.05	0.76	0.20	0.19	-0.06	0.69
HDL	-0.04	0.83	-0.04	0.81	0.05	0.72	0.18	0.83
LDL	0.66	0.01*	-0.23	0.14	0.07	0.64	-0.38	0.01*
HbA1c	0.48	0.01*	0.33	0.03*	0.21	0.18	0.07	0.06

Thereissignificantnegativecorrelationbetweencholesterol,LDLandHomocysteinewhereasthereissignificantpositivecorrelationbetweenHbA1candHs-CRPincontrolled diabetes.

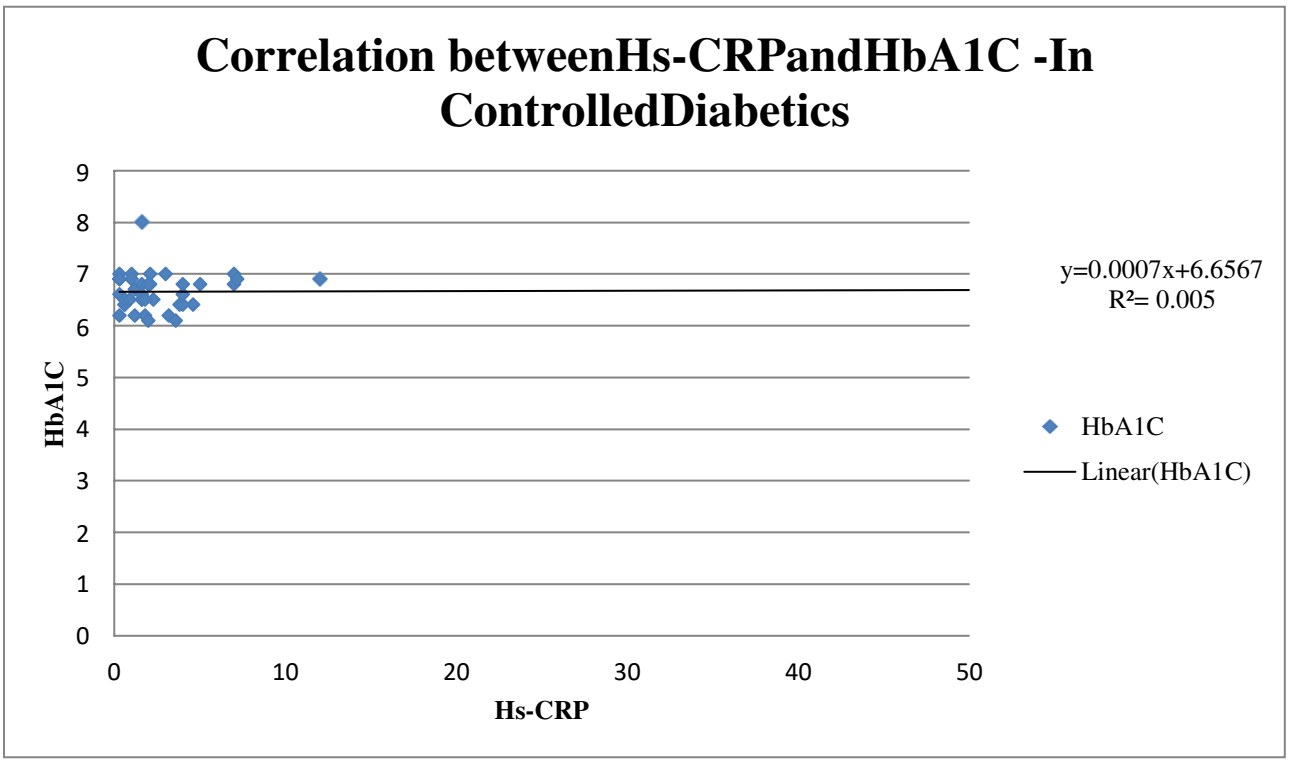
r=correlationcoefficient.

Graph1showingcorrelationbetweenHs-CRPandHbA1Cinuncontrolleddiabetes



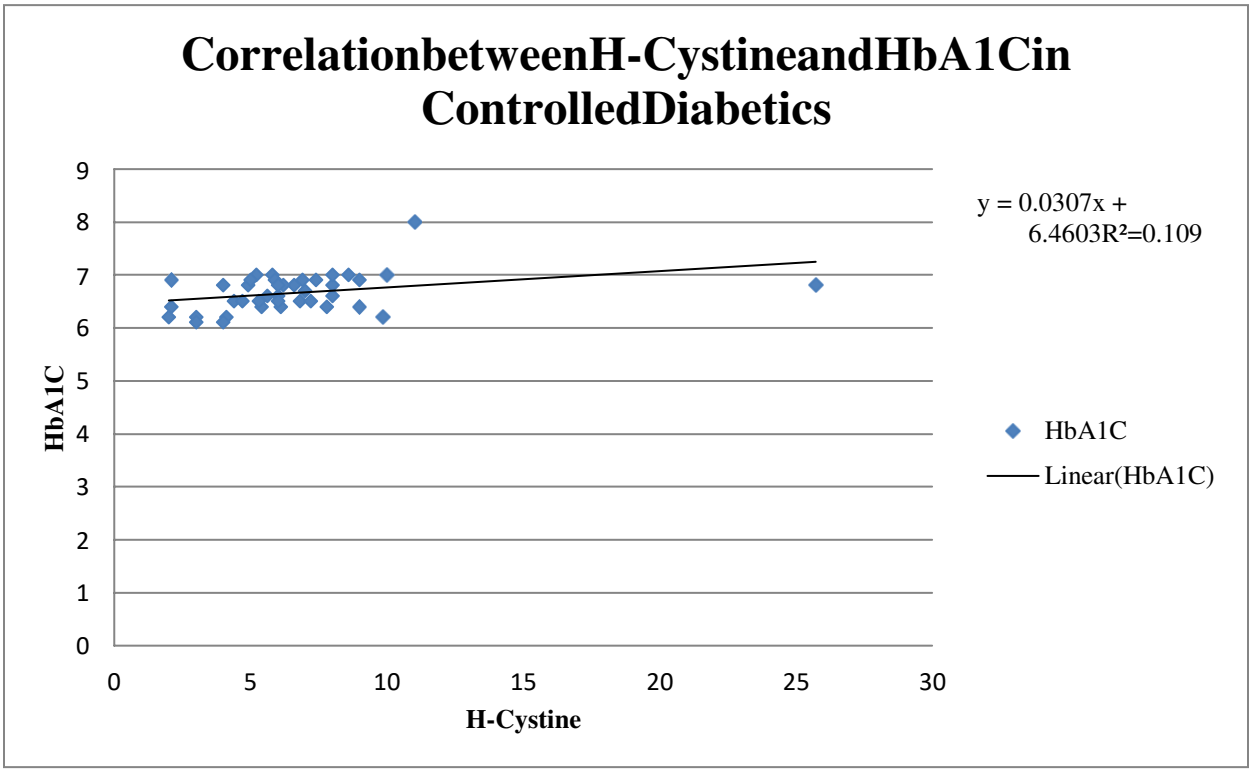
There issignificantpositivecorrelationbetweenhs-CRPandHbA1cinuncontrolleddiabetes.

Graph2showingcorrelationbetweenHs-CRP andHbA1Cincontrolleddiabetes.



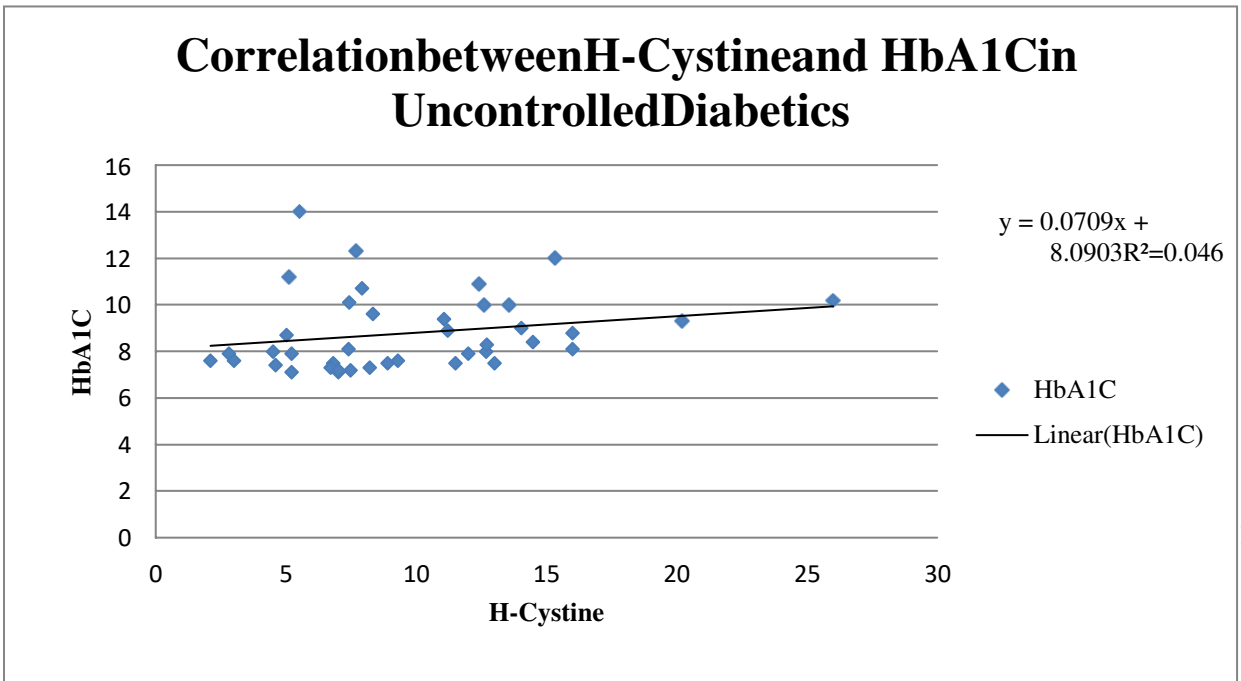
There is significant positive correlation between hs-CRPandHbA1cincontrolled diabetes.

Graph3showing correlation between Homocysteine and HbA1Cin controlled diabetes.



There is positive correlation between Homocysteine and HbA1cin controlled diabetes which is in significant.

Graph4showing correlation between Homocysteine and HbA1Cinun controlled diabetes.



There is positive correlation between Homocysteine and HbA1cinun controlled diabetes which is in significant.

Discussion:

Diabetes Mellitus (DM) consists of a set of metabolic disorders that share a common phenotypeof hyperglycemia. Several different types of diabetes mellitus exist having different etiologicalfactors such as genetic, environmental and life style changes. Depending on the etiology, variousfactors may influence hyperglycemia through various mechanisms which may include either lowinsulin secretion and diminished glucose usage or increased glucose production. The metabolicdysregulation in diabetic individuals leads to secondary pathophysiological changes in multi-organ systems which in turn aggravate the heavy burden on the diabetic individuals and on thehealth care system. The marker included in the present study - serum Homocysteine (Hcy) can beused as predictors for atherogenesis leading to CAD. Hyperglycemiais the condition that the bodyhas high blood sugar level sresultsin the insulinresistan ceandin flammation with in

The body. It can increase the level of in flamm atory markers such as high sensitivityC-reactive protein(hs-CRP) and Homo cysteine in the blood.The high sensitivity C-reactiveprotein(hs-CRP) and Homo cysteine are involved in inflammation with in the body and also areassociated with arteriosclerosis diseases such as coronary arterydisease ,stroke and perip her alvasculardisease(Koenig,2013).[15]

The present study shows elevated fasting blood sugar, postprandial blood sugar, HbA1Clevels in uncontrolled diabetes when compared with controlled diabetes. Many studies haveindicated the association between FBS and PPBS with HbA1c level[16, 17], we also found thatmean FBS and PPBS level was significantly ($p<0.01$) elevated in patients with poor glycemiccontrol (HbA1c>7%) similar to the study done by Khattab *et al.*[18]. Mohammed etal.[19] whichcorrelates with the present study. Type 2 diabetes is associated with a marked increase in thefasting blood sugar (FBS), postprandial blood sugar (PPBS) and glycosylated hemoglobin A1C(HbA1c) level of the blood test.[20, 21] Controlling FBS, PPBS and HbA1c is the strategy for achieving optimalglycemic control and preventing or reducing the risk of diabetic complications.[22,23]

The present study shows elevated lipid profile in uncontrolled diabetes when compared

withcontrolled diabetes. In the study by Gangadhar M et al, Samatha P et al,Lipid profile waselevated in uncontrolled diabetes when compared with controlled diabetes which correlateswith the presentstudy.[24,25] AmerW etal was a similarstudy wherein all thelipidfractions were deranged in uncontrolled type 2 DM patients which is comparable with presentstudy.[26] Diabetes mellitus is a common secondary cause of hyperlipidaemia, particularly, ifglycaemic control is poor which is an important risk factor for atherosclerosis and coronaryheart disease.[27] There is two to four times increased risk of coronary artery disease amongdiabetics compared to non diabetic patients.[28,29] The increased risk of vascular disease indiabetics is in part due to the lipid abnormalities.[30] Many studies have shown altered lipidprofilein diabetes mellitus anddyslipidemia predisposes to cardiovascular complicationsspeciallycoronaryheartdiseaseamongdiabetic patients.[31,32]

The presentstudy shows elevated hs-CRPlevelsin uncontrolled diabetes when comparedwithcontrolleddiabetes.Anubhaet.alshowedthaths-CRPlevelswaselevatedin

uncontrolled diabetes which correlates with the present study.[33]Similar observations havebeen made in previous studies.[34,35] Over the years, accumulating evidence suggests thathsCRP may be associated with an increasing risk of future cardiovascular events in otherwisehealthy individuals.[36] Chaudari et al observed elevated hs-CRP levels in diabetic patientswhich correlate with the present study.[37] The levels of hsCRP correlated with duration ofdiabetes and HbA1c by the study done by Gupta et.al which is in consistent with the presentstudy.[38]Inflammatory marker hsCRP was found to be related to the metabolic profiles andwas found to be a good prognostic marker of cardiovascular complications in type 2 diabetic patients with out clinical the roscleroticmani festations by variousstudies.[39,40]This in dicates the significance of hs CRP in predicting cardiovascular complications in health ypatientswithraised blood glucose levels.

The present study shows increased levels of Homocysteine levels in uncontrolled diabetes whencompared with compared diabetes. Wollesen et al, sourabh etal observed the insignificant levels($p>0.05$) of serum Homocysteine in type 2 diabetic patients which correlates with the presentstudy.[41,42]PlattetalobservedelevatedHomocysteinelevelsindiabeticpatientswhichcorrelates with the present study.[43]A study done by Kurowska et al. reported that the patientswithout previously diagnosed diabetes, the increased Homocysteine level and the intensity

ofchronicandacuteinflammatoryreactionscouldberelatedtolatent,long-termmetabolicdisturbances existing in the great percentage of these patients.[44] The present study clearlyshows elevate hs-CRP and Homocysteine levels in uncontrolled diabetes than controlled diabeteswhich has similar findings with the study done by debnathet.al.[45] kotchapetch et.al study hadfound that elevated HbA1C has elevated Homocysteine and hs-CRP values which correlates with the present study.[46] Recently, ithas been suggested that Homo cysteinemia can beanin dependent predictor of risk associated with DM, especially athero thrombotic events. Elevated plasma Homo cysteinecon centrationiscon side redasanin depend entrisk factor foratherosc lerosis in subjects with normal glucose tolerance. Although type-II diabetes is as sociated with premature eather osclerosis,very few studies have explored the as sociation among hyperhomo cysteinemiaandmicro/macroangiopathy complications with contradictory results .Hyperhomocystein emiahas been demonstratedin type-IIDMin previous studies,[47,48]andmay be a contributory factor in the development of vascular complications.[49] According toWijekoonetal,[50]an increase eintheplasma level of Homocysteinehas beenid entifiedasarisk factor for many diseases, including CVD. In type II diabetes, betaine Homocysteine methyltrans feraseenzyme was observed to play amajorroleinthein creased catabolism of Homocysteinein addition to the trans-sulfurationenzymes .Elevated level so fserum Homocysteine have been associated with state of CHD

The outcome of earlier studies is variable but many of them have shown increased serum H cylevelsin T2D Mpatients .Hyperhomocystein emiaisin fluenced by insul in resistantand hyperinsuline micpatients ,and also in T2D Mpatients with in tactpancreaticβ-cell function. [51]But when these patients lose pancreatic β-cells, they might then show a fall inplasma Homocysteineconcentrations.Non-diabetici.e.normal in dividuals who are having insulin-resistance syndrome also show higher plasma Homocysteine concentrations which provethe association between elevated plasma Homocysteine concentrations and increased plasmainsulincon centrations.[52,53]

Conclusion:

In our study we found elevated hs-CRP and homocysteine levels in uncontrolled diabetes. Wealsofound there was significantpositivecorrelation between HbA1C,lipid parameters

andhsCRP whereas no significant correlation with homocysteine in uncontrolled diabetes. But stillmuch more studies are needed to find out the homocysteine association with HbA1C, lipidparameters in uncontrolled diabetes. Hence it is prudent to evaluate hs-CRP and homocysteinelevelsinalldiabeticpatientstopredictthefuturecomplicationswhichwarranttimelyinter ventionleadingtoloweredmorbidityandmortality.

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