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A STUDY ON GLYCATED HEMOGLOBIN IN RELATION TO SERUM ALKALINE PHOSPHATASE, C REACTIVE PROTEIN AND LIPID PROFILE IN TYPE II DIABETES MELLITUS

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ABSTRACT

Diabetes is a group of metabolic disorders, characterized by hyperglycemia which results from defects in insulin secretion, insulin action, or both. The chronic hyperglycemia in relation to diabetes is linked with long-term damage, dysfunction, and failure of different organs. This has been reported that many patients of diabetes may also exhibit elevated serum alkaline phosphatase level. Both Alkaline Phosphatase (ALP) and C Reactive Protein (CRP) have been time and again shown to be directly and considerably related with each other, with indications that they share common biological pathways. The purpose of this study was to investigate a possible significant correlation between raised ALP levels in type II diabetic and non-diabetic patients. In conclusion, we aimed to investigate for the extent to which ALP measurements could improve the prediction of first-onset Cardio Vascular Disease (CVD) outcomes in Type II Diabetes Mellitus patients. This study is aimed to assess and find the relationship between Glycated Hemoglobin and the Serum Alkaline Phosphatase, C Reactive Protein and Lipid Profile measurements in patients with Type II Diabetes Mellitus. In the present case-control study, a total of 74 subjects (37 diagnosed cases of Type II Diabetes Mellitus and 37 healthy controls) who are aged between 30-65 years were enrolled. The Glycated Hemoglobin (HbA1C), serum Alkaline Phosphatase (ALP), C-Reactive Protein (CRP), and Lipid Profile levels were estimated in all the subjects. For all the data analyzed a P value <0.05 was considered as statistically significant. In this study, the mean age of TIIDM patients (50.86±11.77years) and healthy controls (40.27±11.03years) have been found. HbA1c (mg/dl) have significantly increased in Type II Diabetes Mellitus (TIIDM) patients compared to healthy control subjects ($p<0.0001$). Serum ALP (U/L) levels were considerably raised in TIIDM patients compared to healthy controls ($p<0.0001$). CRP (Units/L) levels were significantly raised in TIIDM patients as compared to healthy controls ($p<0.0001$). Serum Triglyceride (TGL) (mg/dl), Serum Cholesterol (mg/dl) levels were significantly raised in TIIDM patients as compared to healthy controls ($p<0.0001$), Serum High Density Lipoprotein (HDL) (mg/dl) have considerably decreased in T2DM patients as compared to healthy controls ($p<0.0001$). Serum Low Density Lipoprotein (LDL) (mg/dl), Serum Very Low Density Lipoprotein (VLDL) (mg/dl) was considerably raised in TIIDM patients as compared to healthy controls ($p<0.0001$). The present study suggests that serum ALP and CRP concentrations are significantly raised in type II diabetes mellitus. Both are further increased in diabetic patients with complications and poor glycemic control. It is found that there is a significant positive association between serum ALP activity and CRP. Serum ALP level and CRP concentration was independently and positively correlated with TC, TGL, LDL, VLDL, HDL and HbA1c (marker of glycemic control). All these findings suggest a connection between CVD, inflammation and glycemic control in patient with type II diabetes mellitus.

KEYWORDS: HbA1c, ALP, CRP, Inflammation and CVD.

INTRODUCTION

Diabetes Mellitus is a group of metabolic disorders which is characterized by hyperglycemia due to the defects in insulin secretion, action of insulin, or both. The chronic hyperglycemia of diabetes mellitus is linked with long-term damage, disordered function and failure of different organs, especially the eyes, kidneys, nerves, heart, and blood vessels (1).

Various pathogenic processes are concerned in the development of diabetes mellitus. These processes range from autoimmune destruction of β-cells of the pancreas which results in deficiency of insulin to

abnormalities that causes resistance to insulin action. The basis of the disordered metabolism of carbohydrate, fat, and protein in diabetes mellitus is due to the deficient action of insulin on target tissues (2). Deficient action of insulin is the result of inadequate insulin secretion and/or decreased tissue responses to insulin at one or more points in the complex pathways of action of hormone (3). Impairment in secretion of insulin and defects in action of insulin frequently coexist together in the same patient, and it is often unclear which abnormality, if either alone, is the primary cause of the hyperglycemia (4).

Characteristics of marked hyperglycemia are polyuria, polydipsia, weight loss, sometimes with polyphagia, and blurred vision. Chronic hyperglycemia may lead to impairment of growth and susceptibility to certain infections. Acute, life-threatening consequences of uncontrolled diabetes mellitus are hyperglycemia with ketoacidosis or the nonketotic hyperosmolar syndrome (5).

The most common classifications include Insulin Dependent Diabetes Mellitus (IDDM) now called as Type I diabetes mellitus, Non-insulin Dependent Diabetes Mellitus (NIDDM) which is called as Type II diabetes mellitus, and gestational diabetes. The characteristics of Type II diabetes mellitus (TIIDM) include insulin resistance and a relative deficiency of insulin secretion (6). Diabetes mellitus (DM) is an increasing public health problem worldwide which has high levels of morbidity and mortality

Recent research work established that the number of adults with diabetes in the world raised from 108 million in 1980 to 422 million in 2014, due to population increase, aging and the rise in overweight and obesity (7). Worldwide the prevalence of diabetes mellitus has raised in both gender equally, in men from 4.3% in 1980 to 9.0% in 2014 and in women from 5.0% to 7.9% (8). India comes after China being the largest contributor to regional mortality, with one million deaths attributable to diabetes mellitus. India had 69.2 million people in 2015, suffering with diabetes (20-79years) which is expected to increase to 123.5 million by 2040 (9).

Alkaline phosphatase (ALP) is a ubiquitous enzyme found in almost every tissue in the body. ALP has a variety of physiological roles as well as functional applications. ALP is a non-specific enzyme and it catalyzes the hydrolysis of a broad range of phosphate esters (10).

Independent of ALP's roles in clinical diagnostics, alkaline phosphatase is one of the most common enzymes used in chromogenic assays. This is due to a very convenient substrate (p-nitrophenylphosphate) that is essentially colorless, but when ALP hydrolyzes the phosphate ester, the bright yellow p-nitrophenylate is formed (11).

Even though ALP can be found in nearly every tissue in the body, the most clinically relevant forms come from liver, bone, intestine and placenta. The predominant form of ALP in the serum of healthy adults is from liver, the next most predominant form is from bone (12). Therefore the elevation of the liver form of alkaline phosphatase is often due to liver pathologies, and likewise elevation of the bone form often indicates a bone pathology such as Paget's disease (13). However, elevated ALP can be due to non-specific causes and does not always indicate serious disease. Nevertheless alkaline phosphatase is a very useful serum marker, with wide applications from diagnosing hepatoma to predicting mortality in dialysis patients (14).

It has been reported that many diabetic patients may also exhibit elevated serum alkaline phosphatase level. ALP is an inflammatory mediator which is similar to C-reactive protein (CRP) (15). Both ALP and CRP have been time and again shown to be directly and considerably related with each other, with suggestions that they share common biological pathways (16).

CRP acts as inflammatory blood test marker in the body. CRP is produced in the live and its level is measured by testing the blood (17).

CRP is classified as an acute phase reactant, which means that its levels will rise in response to inflammation (18). There are no signs or symptoms that are specific for an elevated C-reactive protein level, because it is not a specific test. Signs or symptoms, if present, would depend on the underlying inflammatory condition that is the cause of the elevated CRP level (19).

CRP is an inflammatory marker which is typically not detected in the blood unless some degree of inflammation is present in the body (20).

The present study aimed to investigate a possible significant correlation between raised ALP levels in type II diabetic and non-diabetic patients. Since the inflammation seems to be a major component of many reactions related with poor glycemic control and further pathogenesis of type II diabetes mellitus and its complications; we found it interesting to study serum ALP activity (marker of CVD) and CRP level (marker of inflammation) in diabetic patients (21). Further, we investigated association between serum ALP and CRP with glycemic control in subjects. We also aimed to

assess whether the ALP-CVD association is confounded or modified by CRP, therefore the interdependence between ALP and CRP levels were put into clinical perspective. Finally, we aimed to investigate for the extent to which ALP measurements could improve the prediction of first-onset CVD outcomes in Type II diabetes mellitus patients.

METHODS

This study was a hospital based cross sectional study conducted at Integral Institute of Medical Sciences and Hospital, Lucknow, U.P., (India) between January, 2018 to June, 2018. A cross sectional study consists of 74 subjects out of them 37 established cases of Type II Diabetes Mellitus patients (Group II), and 37 normal healthy control (Group I) were selected. Subjects were recruited according to simple random sampling method meeting the selection criteria.

Inclusion Criteria:

- Age between 30 to 65 Years.
- Diagnosed Cases of Type II Diabetes Mellitus (n = 37), they were on life style modifications and oral hypoglycemic drugs and without any secondary complication of diabetes mellitus.
- Subject or subject's representative has signed the consent form.

Exclusion Criteria:

- The patients with type 1 diabetes mellitus, high (>120g/dl).
- Patients with alcohol intake.
- With liver enzyme concentrations higher than three times the upper limit.
- On corticosteroids, methotrexate, amiodarone, tamoxifen or other hepatotoxic drugs.
- Any chronic infection like tuberculosis, sarcoidosis etc. anaemia (Hb< 9mg/dl) haemoglobin variants were excluded from this study.

Selection of Controls

- Age Group : 30 to 65 Years.
- Control group (n=37), this group consisted of age and sex matched healthy

subjects. They were taken from general population who came for routine

checkup to IIMSR&H, Lucknow.

Blood Sample Collection

Total 5ml venous blood was collected from the subjects after an overnight or 12 hours of fasting to analyze HbA1c, Serum Alkaline Phosphatase, C Reactive Protein and Lipid Profile.

Samples of the whole blood were collected and processed in the Department of Biochemistry, IIMS&R, IU, Lucknow. Blood sample was collected from clinically diagnosed cases of diabetes and healthy controls under aseptic condition. 1 ml is separated in EDTA vial to measure HbA1c and the rest 4 ml blood sample will be immediately centrifuged at 3000 rpm for 5 min and serum will be separated into 3 test tubes, marked as 1, 2 and 3 to evaluate Serum Alkaline Phosphatase, C Reactive Protein and Lipid Profile.

1. 1ml of blood will be taken for estimation of Glycated Hemoglobin.
2. 1ml of blood will be taken for estimation of serum Alkaline Phosphatase.
3. 1ml of blood will be taken for estimation of serum C Reactive Protein.
4. 2ml of blood will be taken for estimation of serum Lipid Profile.

Glycosylated Hemoglobin was estimated by Nephelometry Method (By Agappe kit), estimation of Alkaline Phosphatase (ALP) was done by DEA (Pnpp Kinetic Method) method, Serum CRP was measured by GenX CRP (C – Reactive Protein) Turbilatex Method, Protocol for estimation of cholesterol and HDL was done using the kit coral clinical system, India and serum total cholesterol was determined by an enzymatic (CHOD-PAP) colorimetric method**,** for estimation of Triglycerides GPO/ PAP method was used.

Calculation for LDL cholesterol (mg/dl):

Total Cholesterol = (Triglycerides/5) - (HDLcholesterol) (Freidwald's equation)

Calculation for VLDL cholesterol (mg/dl):

VLDL Cholesterol = Triglycerides/5 (Freidwald's equation)

STATISTICALANALYSIS

Statistical analysis was applied to all data using SPSS software version 24.0 (Armonk, NY, USA). Mean ± SD (Standard Deviation) of all clinical parameters were calculated in T2DM and healthy controls. P values were calculated by student unpaired t-test. All p values were two sided and differences were considered statistically significant for $p<0.05$; all significant data suggest the strength of case-control association with clinical parameters

RESULTS

In this study, 37 T2DM patients aged between 30-65 years along with 37 aged and gender matched healthy

controls were included. The mean age of T2DM patients (50.86±11.77 years) and healthy controls (40.27±11.03 years) have been found (Table1 & Fig.1). HbA1c have significantly increased in T2DM patients compared to healthy controls ($p<0.0001$) (Table2 & Fig.2). Serum ALP have significantly increased in T2DM patients compared to healthy controls ($p<0.0001$) (Table3 & Fig.3). CRP have significantly increased in T2DM patients compared to healthy controls ($p<0.0001$) (Table4 & Fig. 4). Serum TGL have significantly increased in T2DM patients compared to healthy controls ($p<0.0001$) (Table 5). Serum Cholesterol have significantly increased in T2DM patients compared to healthy controls ($p<0.0001$) (Table5). HDL have significantly decreased in T2DM patients compared to healthy controls ($p<0.0001$) (Table 7). Serum LDL have significantly increased in T2DM patients compared to healthy controls ($p<0.0001$) (Table6). Serum VLDL have significantly increased in T2DM patients compared to healthy controls ($p<0.0001$) (Table 9).

Study Variable	Cases	Controls	p Value
	(N=37)	(N=37)	
Age (years)	50.86±11.77	40.27±11.03	<0.0001

Table 1: Age Wise Distribution of Cases And Controls

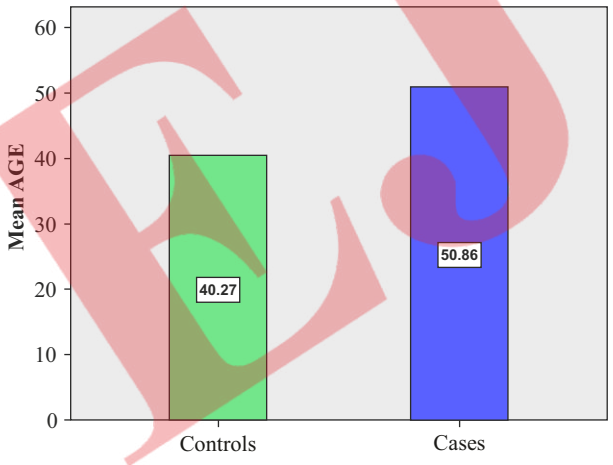

Fig 1: Age Wise Distribution Of Cases And Controls

Study Variable	Cases	Controls	p Value
	(N=37)	(N=37)	
HbA1c%	7.06±1.57	5.11±0.39	<0.0001

Table 2: Comparison Of Hba1c Level Between Cases And Controls

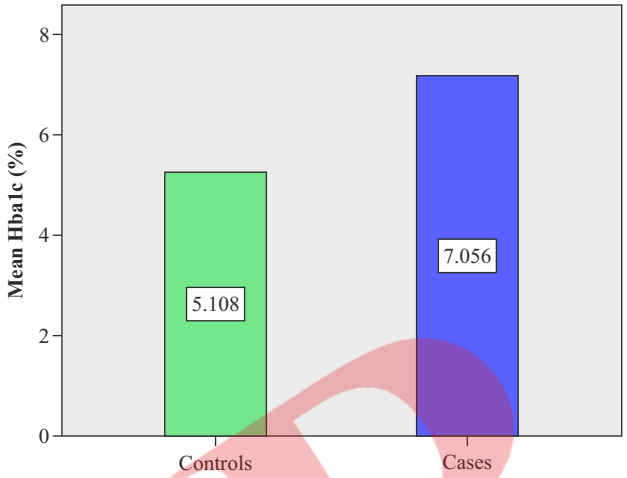

Fig 2: Comparison Of HBA1C Level Between Cases And Controls

Study Variable	Cases	Controls	p Value
	(N=37)	(N=37)	
ALP (U/L)	148.9±27.43	135.6±11.89	<0.0001*

Table 3: Comparison of ALP Level Between Cases and Controls

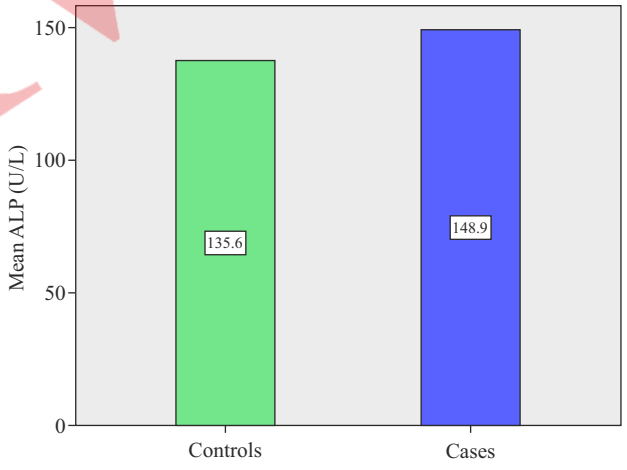

Fig 3: Comparison of ALP Level Between Cases and Controls

Study Variable	Cases	Controls	p Value
	(N=37)	(N=37)	
CRP Units/L	4.69±2.30	1.49±0.51	<0.0001*

Table 4: Comparison of CRP Level Between Cases and Controls

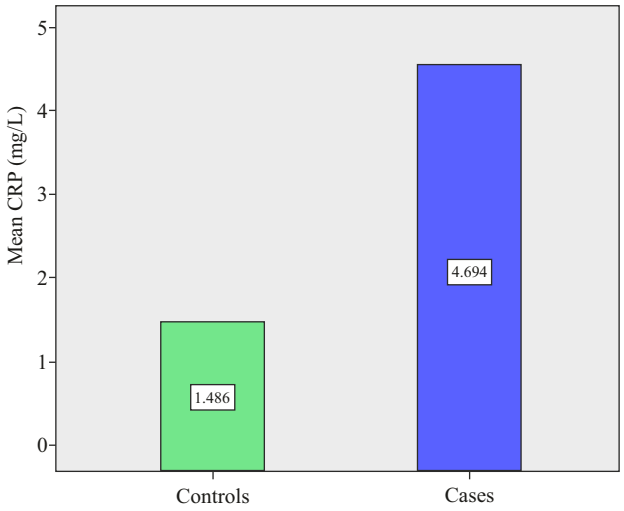

Table 4: Comparison of CRP Level Between Cases and Controls

Study Variable	Cases	Controls	p Value
	(N=37)	(N=37)	
Triglyceride (mg/dl)	148.9±27.43	135.6±11.89	<0.0001*

Table 5: Comparison of TGL Level Between Cases and Controls

Study Variable	Cases	Controls	p Value
	(N=37)	(N=37)	
Cholesterol (mg/dl)	192.58±17.09	152.19±8.08	<0.0001

Table 6: Comparison of Cholesterol Level Between Cases and Controls

Study Variable	Cases	Controls	p Value
	(N=37)	(N=37)	
HDL (mg/dL)	38.78±5.30	51.22±5.79	<0.0001

Table 7: Comparison of HDL Level Between Cases and Controls

Study Variable	Cases	Controls	p Value
	(N=37)	(N=37)	
LDL (mg/dl)	126.92±19.92	77.19±12.12	<0.0001

Table 8: Comparison of LDL Level Between Cases and Controls

Study Variable	Cases	Controls	p Value
	(N=37)	(N=37)	
VLDL (mg/dl)	27.17±2.85	23.70±1.51	<0.0001

Table 9: Comparison of VLDL Level Between Cases and Controls

Patients	Cases (n=37)	Controls (n=37)	*t* or χ^2	*P* value
Age (years)	50.86±11.77	40.27±11.03	3.96	<0.0001
Gender				
Male (n,%)	19 (51.4)	19 (51.4)	0.02	P=0.903
Female (n,%)	18 (48.6)	18 (48.6)		
HbA1c (%)	7.06±1.57	5.11±0.39	7.33	<0.0001
ALP (U/L)	148.9±27.43	135.6±11.89	9.83	<0.0001
CRP (mg/L)	4.69±2.30	1.49±0.51	8.27	<0.0001
HDL (mg/dL)	38.78±5.30	51.22±5.79	9.58	<0.0001
LDL (mg/dL)	126.92±19.92	77.19±12.12	12.93	<0.0001
Total Cholesterol (mg/dL)	192.58±17.09	152.19±8.08	12.97	<0.0001
Triglyceride (mg/dL)	135.50±14.30	118.59±7.98	6.22	<0.0001
VLDL (mg/dL)	27.17±2.85	23.70±1.51	6.46	<0.0001

Table 10: Baseline Clinical Characteristics of Cases (n=155) and Controls (n=185)

Significance < 0.05

Clinical parameters HbA1c, ALP, CRP TC, TGL, HDL, LDL and VLDL, have significant positive correlation in T2DM patients (p<0.01). HbA1c has significant positive correlation with ALP, CRP TC, TGL, HDL, LDL and VLDL.

(p<0.05,p<0.01,p<0.01,p<0.01,respectively)

Correlations									
		HbA1C	ALP	CRP	TG	CHOL	HDL	LDL	VLDL
HbA1C	Pearson Correlation	1	.335*	-.042	.383*	.422**	-.600**	.466**	.384*
	Sig. (2-tailed)		.043	.806	.019	.009	.000	.004	.019
	N	37	37	37	37	37	37	37	37
ALP	Pearson Correlation	.335*	1	.117	.171	.050	-.323	.103	.171
	Sig. (2-tailed)	.043		.491	.311	.770	.051	.544	.313
	N	37-	37	37	37	37	37	37	37
CRP	Pearson Correlation	.042	.117	1	.161	.020	-.097	.020	.161
	Sig. (2-tailed)	.806	.491		.341	.905	.567	.907	.341
	N	37	37	37	37	37	37	37	37
TG	Pearson Correlation	.383*	.171	.161	1	-.012	-.192	-.104	1.000**
	Sig. (2-tailed)	.019	.311	.341		.944	.255	.539	.000
	N	37	37	37	37	37	37	37	37
CHOL	Pearson Correlation	.422**	.050	.020	-.012	1	-.391*	.967**	-.012
	Sig. (2-tailed)	.009	.770	.905	.944		.017	.000	.942
	N	37	37	37	37	37	37	37	37
HDL	Pearson Correlation	-.600**	-.323	-.097	-.192	-.391*	1	-.572**	-.193
	Sig. (2-tailed)	.000	.051	.567	.255	.017		.000	.252
	N	37	37	37	37	37	37	37	37
LDL	Pearson Correlation	.466**	.103	.020	-.104	.967**	-.572**	1	-.104
	Sig. (2-tailed)	.004	.544	.907	.539	.000	.000		.539
	N	37	37	37	37	37	37	37	37
VLDL	Pearson Correlation	.384*	.171	.161	1.000**	-.012	-.193	-.104	1
	Sig. (2-tailed)	.019	.313	.341	.000	.942	.252	.539	
	N	37	37	37	37	37	37	37	37
*. Correlation is significant at the 0.05 level (2-tailed).									
**. Correlation is significant at the 0.01 level (2-tailed).									

Table 11: Correlations of Clinical Parameters in T2DM Cases

HbA1c has significant positive correlation with ALP in T2DM cases ($p<0.05$).

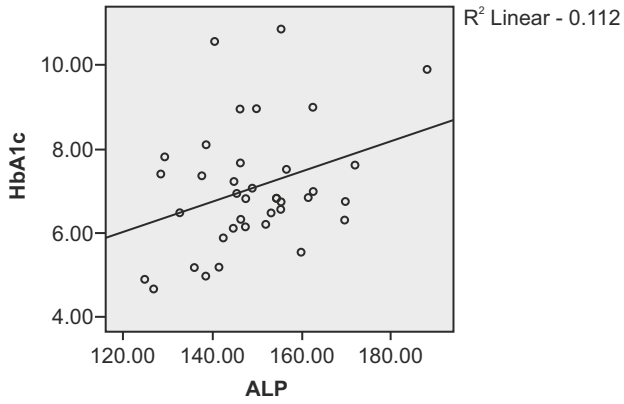

Fig 5: Correlation of ALP and HbA1c in T2DM Cases

HbA1c has significant positive correlation with CRP in T2DM cases ($p<0.05$).

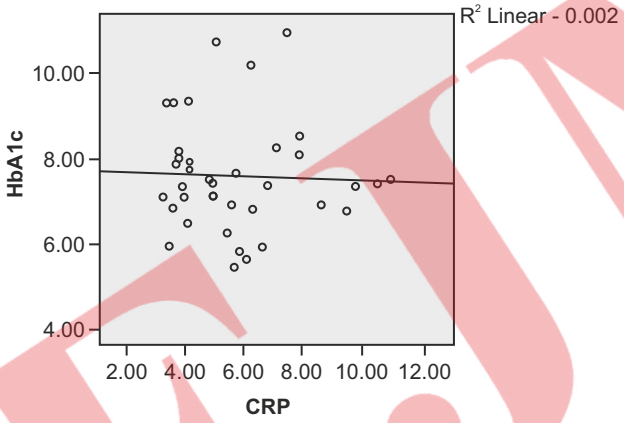

Fig 6: Correlation of CRP and HbA1c in T2DM Cases

CRP has significant positive correlation with ALP in T2DM cases ($p<0.05$).

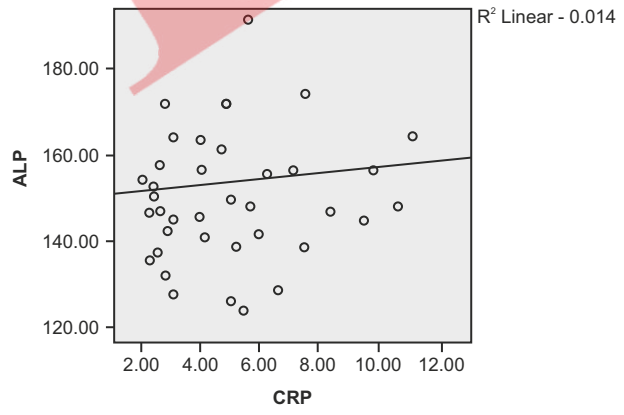

Fig . 7: Correlation of CRP and ALP in T2DM Cases

DISCUSSION

Our study shows statistical significantly elevated concentration of ALP and CRP in serum in patient with type II diabetes mellitus with poor glycemic control in comparison to healthy persons. A crucial positive linear relationship was found between ALP and CRP concentration. Also a significant positive relationship of both ALP and CRP was found with HbA1C, TC, TGL, LDL, VLDL and HDL. These findings suggest an association between Table 10 Values of Serum ALP and CRP concentration between Study Groups I and II.

Activity signified by increased serum ALP concentration, inflammation (raised CRP concentration) and glycemic control in patients with type II diabetes mellitus and related complications. Also at levels of ALP and CRP considered well within the normal limits, there was a substantial and significant increased concentration in patients with type II diabetes mellitus in comparison to healthy controls. This finding suggests that oxidative stress and chronic low grade inflammation plays a role in pathogenesis of type II diabetes mellitus. Numerous possible mechanisms which explain increased serum ALP activity and CRP level in patients with type II diabetes mellitus and its association with glycemic control.

Increase in serum ALP could be the result of raised fat deposition in the liver, known as non-alcoholic fatty liver disease. Fatty liver is considered to be a cause of hepatic insulin resistance and also adds to the development of systemic insulin resistance and hyperinsulinemia (22). Therefore, ALP could be used as a marker of insulin resistance syndrome in the pathogenesis of type II diabetes mellitus. Now there is an increasing evidence to suggest that ALP not only serves as a marker of fatty liver but also of CVD (23). It has been reported in several experimental studies that there is a key role of ALP in maintaining intracellular antioxidant defences through its mediation of extracellular glutathione transport into most cell types. ALP is an ectoenzyme, present at the outer side of the cell membrane and it has the primary function of the maintainance of intracellular concentrations of glutathione (GSH) which is a critical antioxidant defence for the cell (24).

Inflammatory tissue is presently suggested to be a pathologic mechanism underlying type II diabetes mellitus and its complications. Recently, there has been an increased attention on the role of CVD, and it has been reported that the key and common event in the pathogenesis of secondary complications of diabetes is due to inflammation.

Insinuation of inflammation in the pathogenesis of type II diabetes mellitus is recommended by oxygen

free-radical generation and also owing to non-enzymatic protein glycosylation, autoxidation of glucose and impaired glutathione metabolism.

There are a number of studies which support our results. R Sharma et al. presents an increase in levels of CRP and ALP in diabetic subjects and their significant association which might be a result of inflammation in diabetes mellitus (21). Ahmed Khan D, et al studied diabetic patients had significantly raised median of HbA1c, CRP, total cholesterol, nitrate and GGT as compared to controls. HbA1c suggested a positive correlation with CRP, total cholesterol, nitrate and ALP inflammatory markers should be used in addition to HbA1c for assessment of increased cardiac risk in uncontrolled diabetic patients due to accelerated atherosclerosis due to free radical injury (25). Sarinnapakorn V, et al found CRP levels associated with levels of HbA1c. Mean HbA1c levels were crucially increased in patients who had raised CRP levels. Other factors like age, LDL cholesterol, Screenings correlated with CRP level (26). Also Bahceci M, et al compare serum CRP levels in males with type II diabetes mellitus without coronary heart diseases (CHD), non-diabetic CHD patients and type II diabetes mellitus patients with CHD and shows type II diabetes mellitus men without CHD had similar CRP levels with non-diabetic CHD patients, whereas CRP levels of type II diabetes mellitus men with CHD were greater than non-diabetic men with CHD (27).

Due to the presence of a significant positive relationship between CRP and HbA1c, ALP, TC, TGL, LDL, VLDL and HDL, inflammation, insulin resistance and hyperglycemia together leads to the cardiovascular risk in type II diabetes mellitus patients. Additional lines of evidence which supports an association between elevated levels of serum GGT and poor glycemic control and metabolic syndrome are also found. Higher ALP levels are accompanied by higher insulin resistance and greater risk for developing type II diabetes mellitus and poor glycemic control. The significant relationship of serum ALP activity with various diabetes related metabolic disorders, such as poor glycemic control and atherogenic dyslipidemia can be explained by certain underlying biological mechanisms such as insulin resistance, fatty liver and increased oxidative stress (28).

It is likely that the incidence of ALP reactions have a direct role in the pathogenesis of poor glycemic control and atherogenic dyslipidemia, autonomously of the presence of fatty liver, possibly through the initiation of insulin resistance and chronic inflammation, which supports a role of serum ALP in the increased levels of inflammatory markers, like fibrinogen, uric acid, CRP, and F2-isoprostanes, in a dose response method (26).

Several studies describe that serum CRP levels remained a significant predictor of diabetes risk even after adjusting with body mass index (BMI), family history of diabetes mellitus, smoking history and other factors (29).

In addition, to predict the incidence of type 2 diabetes, insulin resistance, and cardiovascular disease independently of obesity, the markers of fatty content of liver , such as serum gamma-glutamyl transferase (GGT) activity and other liver enzymes, have been described in large prospective studies (30). Results from our study also suggest that liver enzymes are strongly linked with the risk of metabolic syndrome and type II diabetes mellitus and that serum ALP is the most significant risk indicator for developing the metabolic syndrome and type II diabetes mellitus. An additional possible physiological mechanism is inflammation may be due to raised liver enzymes, leads to impaired insulin signaling both in the liver and systemically.

ALP showed a significant increase in type II diabetes mellitus patients as compared to control subjects. Comparing diabetics (Group II) and nondiabetics (Group I) have, elevated blood glucose level in diabetic patients and change in medium make the individual susceptible to infection due to depressed immunity. It can be seen that crucial increase of ALP in diabetics (Group II) and non-diabetics (Group I) and CRP during follow-up was not included in this study. Also, several confounding variables were not included in this study, such as serum levels of fasting insulin. Therefore, serum levels of fasting insulin should be included in further studies.

Inspite of these possible limitations, our findings, obtained from a cross sectional study shows that serum ALP activity and CRP level is significantly elevated in patients with type II diabetes mellitus in comparison to healthy control subjects. Both are further raised in diabetic patients with complications and poor glycemic control.

Also there is a significant positive correlation between serum ALP activity and CRP. Both are also independently positively correlated with HbA1c, FBS and PP2BS (short and long term glycemic control). So far, the underlying pathogenesis is not fully understood. It also seems that oxidative stress, insulin resistance and chronic low grade systemic inflammation may be involved. All these findings suggests an association between inflammation, oxidative stress and glycemic control in patient with

type II diabetes mellitus. Further studies are required to investigate the biological mechanisms leading to this relationship.

CONCLUSION

The present study suggests that serum ALP and CRP concentration is significantly raised in type II diabetes mellitus. Both are further increased in diabetic patients with complications and poor glycemic control. There is a significant positive association between serum ALP activity and CRP. Serum ALP level and CRP concentration was independently and positively correlated with TC, TGL, LDL, VLDL, HDL and HbA1c (marker of glycemic control). All these finding suggesting a relationship between inflammation, CVD and glycemic control in patient with type II diabetes mellitus.

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