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ASSOCIATION OF PLAMSA LACTATE TO DIABETIC AND LIVER INDICES

[1]Rajeswari S, [2]Arun Kumar D, [3]Swaminathan S

[1]Junior Technical Officer, [2]Senior Lab Technologist, [3]Senior Consultant and Head,
[1, 2, 3] Department of Biochemistry, Apollo Speciality Hospitals, Ayanambakkam, Chennai – 600 093

Abstract: **Blood lactate serve as a sensitive marker to assess patients in critical conditions, especially during hyper and hypoglycemic attacks and the increase is blood lactate level is always suggestive of lactic acidosis. Numerous studies have been done in the past to evaluate its clinical usefulness mostly in critically ill diabetic patients as well as in evaluating liver cirrhosis and to find its correlation to liver function tests. The aim of this study is to evaluate the correlation of plasma lactate to diabetic, liver and atherogenic triglycerides. The association found out between plasma lactate to FBG, HbA1c, TP, Alb, ALT and triglycerides were found to be highly significant (P<0.0001). The outcomes of this research articles will open more avenues for future research scholars to establish plasma lactate as a routine lab investigation.**

Keywords: **Lactate, ALT, Albumin, HbA1c, Diabetes mellitus.**

1. INTRODUCTION

Lactate is the end product of anerobic carbohydrate metabolism and is being produced by skeletal muscles, brain and erythrocytes. It is metabolised by liver. When the level exceeds 2 mmol/L toxic develops leading to lactic acidosis, a serious health disorder seen mostly is diabetic coma and liver cirrhosis. The measurement of plasma lactate is very useful in critically ill patients. This research article is an attempt to correlate plasma lactic acid with biochemical profiles of diabetes and liver function.

The final diagnosis of death in hypoglycaemic or diabetic coma should always be done as a synopsis of anamnestic response, morphology, biochemical (glucose, lactate, HBA1c, ketone bodies, insulin, and C-peptide) and toxicological findings. The combined values of glucose and lactate in vitreous humour and in cerebrospinal fluid were 3.3 and 4.1 mmol/L, respectively (Karlovsek MZ, 2004). In Type 1 diabetes Mellitus (T1DM) subjects, despite considerable hyperglycemia, blood lactate concentration remained unchanged and there was a significant negative correlation between delta lactate and glucose and a significant positive correlation between delta lactate and delta C- peptide. Hyperglycemia itself and the lack of increase in insulin secretion do not affect blood lactate increase during Oral Glucose Tolerance Test (OGTT); blood concentration of this metabolite depends mainly on an early insulin secretion to enhance tissue glucose uptake and to inhibit gluconeogenesis (Prando R etal., 1988).

In patients treated either with sulphonylurea or biguanide drug alone, the mean plasma lactate and pyruvate levels were not increased significantly. Plasma lactate did not correlate with any clinical or biochemical measurement in any of the treatment groups except for a correlation with serum creatinine in those patients taking metformin alone. The finding of raised plasma lactate levels in diabetic patients treated with metformin suggests that this drug should be prescribed with caution (Waters AK, 1978). Plasma lactate concentration was lowest in the non-obese group with normal glucose tolerance, highest in the obese subjects with Type 2 Diabetes Mellitus (T2DM), and intermediate in obese individuals with normal OGTT. All three groups were significantly different from each other. In addition, plasma lactate concentrations were associated with both fasting plasma glucose and glycated haemoglobin concentrations (HbA1c) (Chen YD, 1993).

Plasma lactate was strongly associated with T2DM in older adults. Plasma lactate deserves greater attention in studies of oxidative capacity and diabetes risk (Crawford SO et., 2010) The postprandial highest increase of the lactate and lactate/pyruvate ratio observed in patients with the highest degree of carnitine imbalance, in regulated diabetes, raises the question of a coincidental mitochondrial dysfunction and such a claim cannot be substantiated for some patients. In contrast, the role of other factors like increased gluconeogenesis, degree of ketosis need to be sought (Evangeliou A etal., 2010). Lactic acidosis is occasionally responsible for metabolic acidosis in diabetics. It may occur in the presence of normal blood levels of the ketone bodies, and such cases are often described as having "non-ketotic diabetic acidosis." Lactic acid may contribute to the metabolic acidosis in patients with true diabetic ketoacidosis, but the plasma lactate concentrations in these patients are not usually very high. In some patients the ketoacidosis is replaced by a lactic acidosis during treatment. This usually occurs in association with a serious underlying disorder with a poor prognosis. A transient increase in plasma lactate concentration was in fact observed in most patients after the beginning of treatment, but the significance of this finding is uncertain (P. J. Watkins, 1969).

The elevation of plasma lactate is associated with a greater carbohydrate oxidation in T2DM patients, but the mechanisms underlying the alteration of substrate utilization need to be clarified. Furthermore, increased lactate levels cannot be explained by alterations of lactate transport in red blood cells, but it could affect monocarboxylate transporter 1 properties (Metz L et al., 2005). CSF lactate levels increase with glycaemic levels in DM owing to enhanced glucose influx into glycolytic pathway of the brain, and also increases in treated hypoglycaemic coma probably due to mitochondrial dysfunction or damage (Yao H, 1989). Plasma Lactate may be increased in vivo in DM as a result of increased glucose flux through the glyoxalase pathway and/or via hepatic ketone metabolism, and it did not correlate with plasma glucose, and in vitro erythrocyte lactate formation did not increase in the presence of hyperglycemia. These data suggest that hepatic ketone metabolism, rather than hyperglycemia, may be a major source of plasma lactate in DM (Christopher MM, 1995). Plasma lactate levels in ambulatory elderly patients with T2DM receiving metformin therapy did not differ from those in a younger age group. Patients with fasting plasma glucose levels > 130 mg/dL had a 2.8-fold risk of developing hyperlactemia, but none of them developed lactate acidosis (Lin YC, 2010).

In poorly controlled T1DM subjects, the primary mechanism by which metformin improves glycemic control is related to the suppression of accelerated basal hepatic glucose production, and this most likely is secondary to an inhibition of hepatic glycogenolysis. Metformin has no effect on the rate of lactate turnover or gluconeogenesis from lactate in either the basal or insulin-stimulated states (Cusi K,1996). Lactate, an indicator of oxidative capacity, predicts incident diabetes independent of many other risk factors and is strongly related to markers of insulin resistance. Future studies should evaluate the temporal relationship between elevated lactate and impaired fasting glucose and insulin resistance (Stephen P. Juraschek,2013) Plasma lactate concentration is one of the most often measured parameters during clinical exercise testing as well as during performance testing of athletes. While an elevated lactate may be indicative of ischemia or hypoxemia, it may also be a "normal" physiological response to exertion. whole plasma lactate values are on average 70% of the corresponding plasma lactate values; thus when analyzing lactate, care should be taken to both validate the lactate measuring instrument with the criterion/reference enzymatic method and interpret the results correctly based on what is being measured (plasma or whole blood). Overall, it is advantageous for clinicians to have a thorough understanding of lactate responses, plasma lactate transport and distribution, and lactate analysis (Matthew L. Goodwin)

2. MATERIALS AND METHODS

50 patients and controls in the age group of 15-73 years consisting of males and female were selected for this study. 50 normal patients attending Master Health Checkup were enrolled as controls and another 50 patients attending the Diabetic Clinic were selected as patients. The main aim of this study is to find out the association between plasma lactate to Fasting Plasma Glucose (FPG), Total protein, Albumin, Triglycerides, ALT and HbA1c.

Diuri CS 1300 B analyser and Dialab reagents were used to measure FBG, Total protein, Albumin, Triglycerides, ALT and Plasma Lactate and Biorad D10 analyser and the kit supplied by that company was used to measure HbA1c. The accuracy of all analytes were validated by the use of Bio-Rad accuracy controls at two levels.

Inclusion Criteria:

Patients who attended Diabetic clinic and routine Master Health Checkup who were investigated for HbA1c and whose HbA1c >8.0% were included as patients and the Master Health Checkup patients whose HbA1c <6.0% were included as control group.

Exclusion Criteria:

All other patients and controls who did not fall in the inclusion criteria were excluded.

For Statistical analysis of data, a software downloaded from the website http:// www.graphpad.com\quickcalcs was used to calculate Student't' distribution (t) and probability (p) between analytes.

Table I: Mean & SD for Control & Patient groups (n=50)

		FBS	HbA1C	LACTATE	TP	ALB	TGL	ALT
	Mean	96.24	6.57	9.41	7.48	4.2	115.94	25.24
Control n=50	**SD**	9.54	7.43	3.02	0.53	0.23	50.77	6.69
	Mean	200.72	9.59	13.04	7.17	4.09	153.71	37.78
Patients n=50	**SD**	78.26	1.44	4.06	0.71	0.39	77.53	37

Table II: Statistical Parameters (t & p) Patients

S No	Pairs compared	t	P
1	Lactate Vs FBS	16.9348	<0.0001
2	Lactate Vs HbA1c	11.8014	<0.0001
3	Lactate Vs TP	10.0706	<0.0001
4	Lactate Vs Albumin	15.516	<0.0001
5	Lactate Vs TGL	12.812	<0.0001
6	Lactate Vs ALT	4.6999	<0.0001

Table III: Statistical Parameters (t & p) Controls

S No	Pairs compared	t	P
1	Lactate Vs FBS	61.3576	<0.0001
2	Lactate Vs HbA1c	2.5039	0.0139
3	Lactate Vs TP	4.4509	<0.0001
4	Lactate Vs Albumin	12.1635	<0.0001
5	Lactate Vs TGL	14.8109	<0.0001
6	Lactate Vs ALT	15.249	<0.0001

3. RESULTS

Table I shows the Mean and SD for the analytes measured in this study for patients and controls. The difference in the mean values of the analytes between the controls and patients shows significant increase in all the analytes.

Table II gives the statistical parameters t and p obtained for patients when plasma lactate was compared with other analytes studied. Very good correlation (P<0.0001) was observed between plasma lactate and each of the other analytes measured to evaluate diabetic, liver and cardiac functions.

Table III gives similar statistical data as was presented in Table I but for controls. For controls also very good association was found between plasma lactate to all analytes (P<0.0001) except HbA1c in which a moderately association at P<0.05 was observed. From Table II & III, it is clear that irrespective normal or abnormal status of DM, liver & cardiac functions, plasma lactate was found to correlate to profile tests linked to Diabetes, liver and cardiac organs.

4. DISCUSSION

Many studies done in the past have established good association between plasma lactate to both FPG and HbA1c and our study has confirmed it (Chen YD ,1993) and warrants further studies to establish the role of plasma lactate is evaluating lactoacidosis and oxidative stress (Evangeliou A et al, 2010). Studies have shown that hepatic ketone metabolism rather than hyperglycaemia may be a source of increased plasma lactate suggesting that plasma lactate level may be linked to liver function and our study has proved this as we got good correlation between plasma lactate to TP, ALB &ALT and increased plasma glucose is directly linked to lactate (Christopher MM etal, 1995) (Lin YC etal, 2010) In some cases, it has been pointed out that elevated plasma lactate may be linked to ischemic status and this previous observation has been proved in this study which shows an association of plasma lactate to circulating triglycerides (P<0.0001).(Matthew L)

5. CONCLUSION

The clinical usefulness of plasma lactate has been studies extensively with contradictory outcome, but most of the studies done in the past have predicted its usefulness in the diagnosis of DM, liver and cardiac functions. The outcome of this study is an extension of previous studies findings and it has established a very strong association between plasma lactate to individual profile package tests for DM, liver and cardiac suggesting its usefulness in the diagnosis of disorders associated with DM, liver and cardiac muscles. By undertaking more research in this field with large number of patients, one can arrive at the recommendation of including lactate as routine test for the laboratory diagnosis of diabetes, liver and cardiac functions.

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Conflict of Interest: None

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