



STUDIES ON SOME POSSIBLE BIOCHEMICAL DIAGNOSTIC INDICES IN *DIABETES MELLITUS*

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ABSTRACT

The clinical utility of specific and non-specific biochemical investigations carried out on fifty-four (54) and fifty-five (55) diabetics and non-diabetics showed that the pancreatic amylase activity was significantly ($p=0.0002$) higher by 45.57 % and 60.25 % for non-diabetic compared among males and females respectively. The lipase activity in diabetics was significantly ($p=0.0001$) depressed when compared to the apparently healthy non-diabetic individuals. Lipase activity also showed a significantly ($p=0.049$) weak inverse relationship ($p=0.247$) with sugar level in diabetics that showed an insignificantly ($p=0.049$) weak direct relationship ($p=0.029$) in non-diabetics. However, the total cholesterol indicated evidence of hyperlipidemia in both diabetics and non-diabetics. An overall 15.78% decrease in non-cholesterol lipids of the diabetics was observed over non- diabetics. Comparatively, 16.72% and 16.12% significant ($p=0.010$) decreases were observed in the females and males respectively. These variations (from 100%) in biochemical parameters and their associated significant relationships between sexes suggest a stimulation of lipase activity as well as balance in proportion or derivative of insulin secretion and action in non-diabetics.

KEY WORDS: Diabetes, hyperglycemia, hyperlipidemia, amylase, lipase, cholesterol.

INTRODUCTION

There is known symmetry between the glucose taken up and converted by muscle into glycogen and its fate upon diversion to adipose tissue. The carbon skeleton of glycogen stored by muscle is eventually released from the tissue mostly as lactate, while when glucose is converted in adipose tissue, its carbon re-enters the circulation mostly as non-esterified fatty acids (NEFA), only to cause further insulin resistance, lipotoxicity of pancreatic B-cells, and type-2-diabetes (Lee *et al.*, 1994). The inflexibility in fuel selection, as well as differences in fuel partitioning has been ascribed as the pathophysiological characteristics that contribute to an altered composition of muscle in obesity and insulin resistance diabetes mellitus (Kelly, 2002). Diabetes mellitus has absolute and relative insulin deficiency with its major manifestations, those of metabolic disease with complex disturbance of carbohydrate, lipid and protein metabolism. Recent advances in B-cell dysfunction caused by hyperlipidemia resulted in perturbed insulin secretory capacity and hyperglycemia. Studies have shown that high carbohydrate diet are more potent inducers of type-2-diabetes mellitus than high fat diets (Chen *et al.*, 1995); an increased rate of hepatic VLDL (Blades and Garg, 1995) secretion and the determination of lipoprotein profile occur in parallel before a rise in plasma esterified fatty acid concentration (Chen *et al.*, 1995; Dreon *et al.*, 1999). Also test-meal induced postprandial hyperglycemia is exacerbated in subjects previously fed with high-refined carbohydrate diets (Chen *et al.*, 1995; Kousari *et al.*, 2000). Similarly, dietary fat is able to modulate insulin action through modifications in the compositions of cell membrane. Cross-country comparisons and migrant studies uniformly

show associations between higher prevalence of diabetes and of fat intake. This observation is greatly confounded by many variables differing in these comparisons that relate to the development of diabetes (Mandarino *et al.*, 1996). As a major health care problem all over the world, there is a growing belief that insulin secretion may be linked to glucose and lipid metabolism. Therefore there is need for simple biochemical investigation for the early detection of diabetes since the most staple foods in Africa and Nigeria in particular, are predominantly carbohydrates and lipid based coupled with sedentary lifestyle in our societies. In view of these, specific and non-specific biochemical investigations were carried out to clarify the clinical utility of these biochemical investigations (sugar level, total cholesterol, non-cholesterol lipid, pancreatic amylase and lipase activities) in diagnosis of insulin action in diabetes and hyperlipidemia.

MATERIALS AND METHODS

The study was randomized sampling with 54 clinically established diabetes mellitus patients according to WHO (WHO, 1999) criteria and 55 non-diabetic controls ranging with mean age of 52 ± 10.06 who attended diabetes clinic in University of Nigeria, medical centre, Nsukka. These were 32 male and 22 female diabetics and 41 male and 14 female non-diabetics.

Fasting blood samples were collected after overnight fast from diabetics and non-diabetics in heparinised bottle to determine their blood glucose and the plasma separated immediately for other analyses. Blood glucose was determined using glucometer (Ames glucometer). Lipase activity was measured using turbidometric method (Verdum *et al.*, 1973) and amyloclastic method for

estimation of pancreatic amylase activity (Baker and Silverton, 1985). Total cholesterol was according to Libermann- Buchard reaction (King and Wootton, 1959) while total lipid was evaluated by oxidising the unsaturated lipid fraction (Siroev and Makarova, 1998). The non-cholesterol lipid was a difference from total lipid and total cholesterol values.

Statistical Analyses

Statistical Analysis was performed using SPSS version 11.00. The t-test was used in comparing differences and correlation analysis for relationships in diabetics and non-

diabetics. All tests were considered significant at a p value of less than 0.05.

RESULT

Plasma pancreatic amylase activity in diabetics and non-diabetics

The actual values obtained for pancreatic amylase activity for diabetics and non-diabetics (PAA) are shown in Figure 1.0. When compared with the diabetics, the non-diabetics pancreatic amylase activity was higher by 45.57% and 60.25% for male and females respectively. The decrease was more significant ($p=0.006$) < ($p=0.011$) in females (PAF) than in males (PAM).

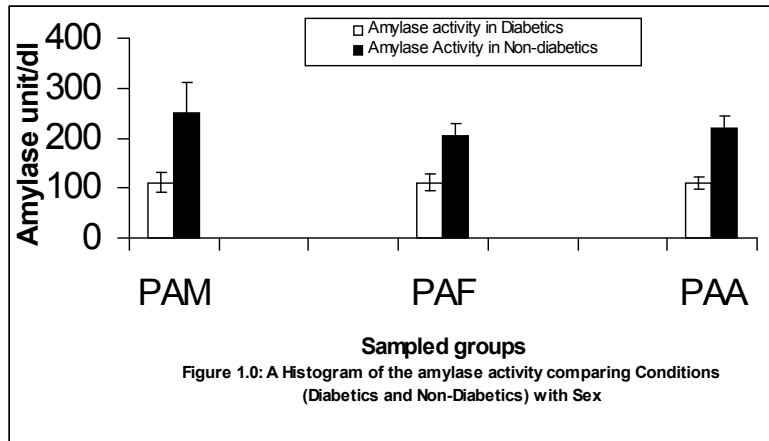


FIGURE 1.0: Pancreatic amylase activity for diabetic and non-diabetics

Lipase activity when compared in diabetics and non-diabetics (PLA) is shown figure 2.0. The activity in diabetics was significantly ($p= 0.0001$) depressed when compared to the apparently healthy non-diabetic

individuals. For non-diabetics, the mean lipase activity is higher by 65.29% for males (PLM) and 76.15% for females (PLF) over the diabetics.

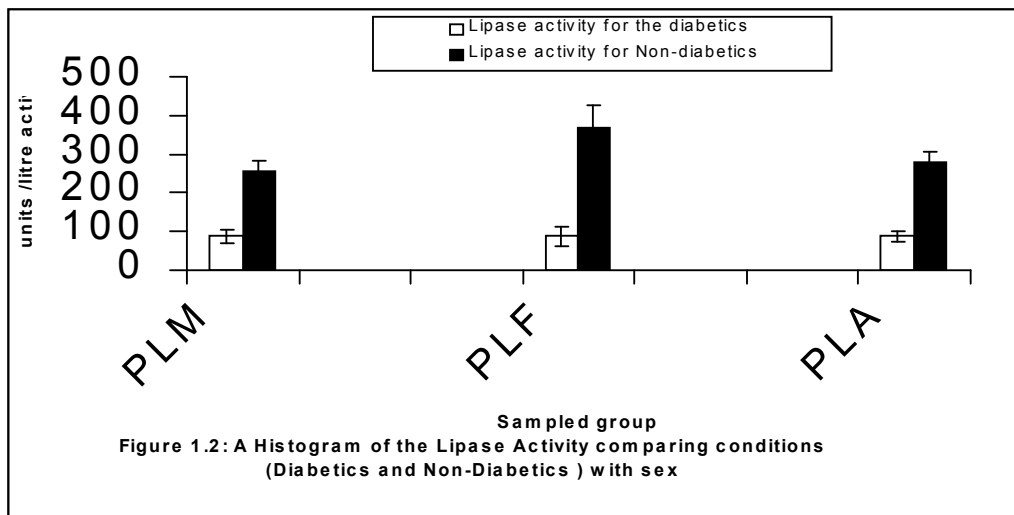


FIGURE 1.2: Lipase activity comparing conditions with sex

Total cholesterol in diabetics and non-diabetics

Total cholesterol above 202mg/dl was considered as hyperlipidemic (Akbar, 2001). Hyperlipidemia was evident in both the diabetics and non-diabetics. In Diabetics 74.0% were considered hyperlipidemic of which 25.73% and 48.15% females (TC27F) were and males

(TC₂₇M) respectively. Comparatively these differences were insignificant. The figure 1.3 shows the difference in the total cholesterol with conditions [Diabetics and non-diabetics (TC₂₇A)] and between sexes. Similar conditions were evident among the non-diabetics.

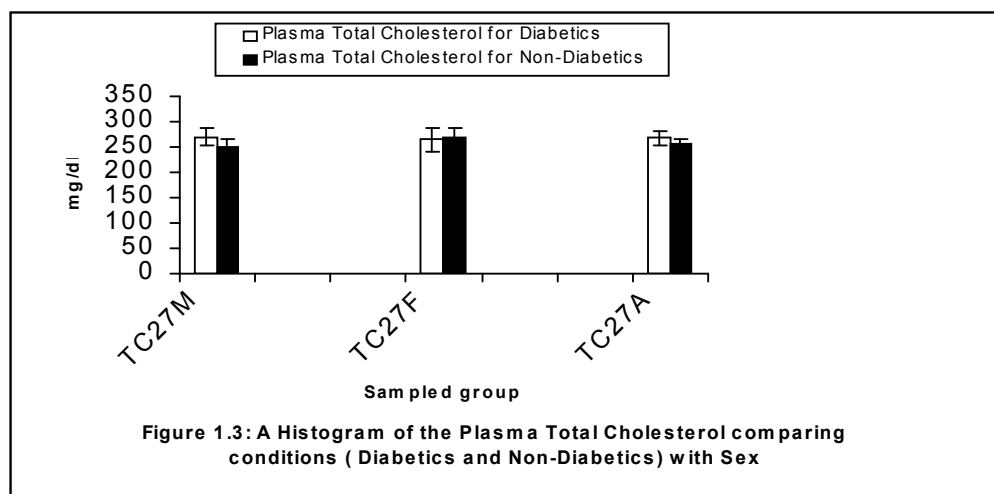


FIGURE 1.3: Plasma total cholesterol comparing with sex

Non –cholesterol lipid in diabetics and non-diabetics

An overall 15.78% decrease in non-cholesterol lipids of the diabetics was observed. Comparatively, 16.72% and

16.12% significant ($p=0.010$) decreases were observed in the females and males respectively. These differences are shown in the figure 1.4.

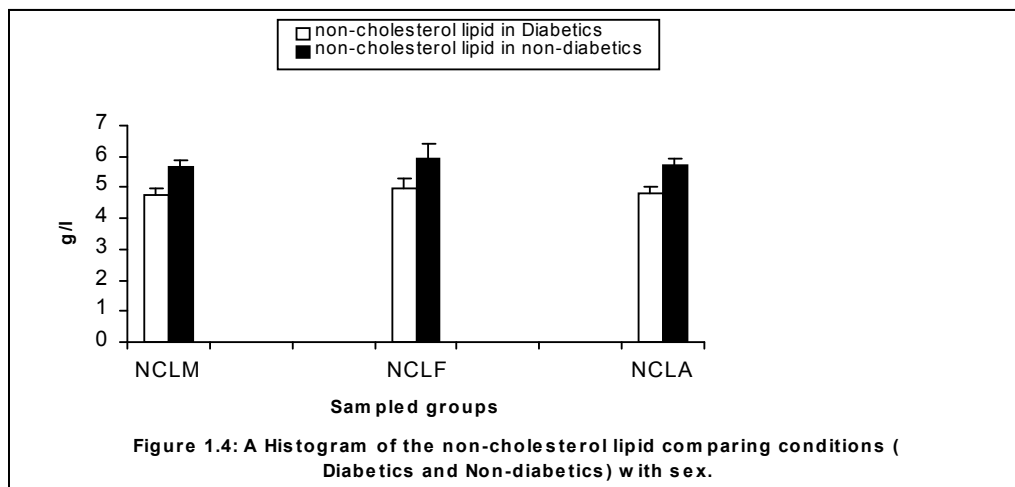


FIGURE 1.4: Compares the conditions of non-cholesterol lipid with sex

DISCUSSION

Pancreatic amylase and lipase activities

A decrease in pancreatic amylase and lipase activities was demonstrated in diabetic relative to non-diabetic individuals. The female diabetics showed 60.25% and 76.17% decreases in amylase and lipase activities while the males had 45.57% and 65.59% decreases respectively. The reason for these decreases was seen in several studies as a demonstration that the degree of lipid infiltrations into various tissues especially muscles and liver correlates highly with insulin resistance. Nonetheless, the rise in serum lipase activity above normal values as seen in diabetics is observed clinically in acute pancreatitis, pancreatic carcinoma and both acute and chronic renal diseases. However, pancreatic amylase activity does not correlate with blood sugar. This is possibly due to unavailable sugar substrate and/or dependence on the degree of saturation with its cofactor in diabetes. Lipase activity also showed a significantly ($p=0.049$) weak inverse relationship ($p=0.247$) with sugar level in diabetics

but showed an insignificantly ($p=0.049$) weak direct relationship ($p=0.029$) in non-diabetics. Nutritional states of individuals have been shown to be depressed under conditions such as restricted caloric intake, high fat diet and when there is deficiency in insulin secretion as in diabetes. Nevertheless, bile is known as an important adjunct to accomplish digestion and absorption of fat as well as the absorption of fat-soluble vitamins. When fat digestion is impaired, other nutrient molecules are poorly digested, since fat covers the food particle and thus preventing enzyme hydrolysis (Hudgin, 1996).

Hyperlipidemia and non-cholesterol lipid

Hyperlipidemia has been considered in patients with total plasma cholesterol above 5.2mM ($> 202.8\text{mg/dl}$) or low-density lipoprotein (LDL) cholesterol above 2.6 mM/litre (Akbar, 2001). In diabetics, 74.07% were considered hyperlipidemic of which 25.73% and 48.15% were females and males respectively. 78.18% was also considered hyperlipidemic in non-diabetics. Hyperlipidemia is evident in both diabetics and non-

diabetics. However, an overall (TC_{27A}) 4.57% increase in total cholesterol and 15.78% decreases in non-cholesterol lipid of the diabetics were found (Figures 1.3 and 1.4). Comparatively, the significant ($p=0.002$) difference in the non-cholesterol lipid of the diabetics and non-diabetics with the observed increase in total cholesterol may be due to quantitative differences in lipoprotein fractions. The increase (4.57%) in total cholesterol in the decreasing (15.78%) non-cholesterol lipid associated with the poor glycaemia control in diabetics. Hyperlipidaemia however, is known to accelerate glomerulosclerosis and chronic renal failure (Philips *et al.*, 1999) while poor glycaemia control of diabetes, hypertension and history of smoking are common and contributing factors to end stage renal diseases (Stevenson and Kayson, 1999). Also elevated serum lipid level is associated with a higher risk of coronary heart disease for patients with diabetes, as they are for non-diabetics (Lehto *et al.*, 1997). Hyperlipidaemia does not only increase the risk of ischemic heart disease (IHD) in diabetic patients, but also, may impair glycaemia control, accelerate the progression of renal insufficiency, and increase mortality (Akbar, 2001).

The nature of the relationships (appendix 2) suggests a probable inflexibility of the enzymes to utilize their nutrient-based molecules in diabetics. In the foregoing, these significant differences with the various percentage variance (difference) in enzyme activities (from 100%), showed a multi-factorial and complex regulations beyond one common determinant (i.e. physiological variable). In the same note, it is worthy to indicate a cluster of physiological functions such as insulin secretion and action, glucose homeostasis, lipid metabolism and sex hormones that take on characteristic values in any one individual and tend to co vary between individual. It is possible that this consensual variance also applies to the same individual over time and/or across different life circumstances e.g. stress, age and intercurrent illness (WHO, 1999). This emphasis that association of metabolic and some haemodynamic variable are already demonstrable in healthy population, accounts for the observed deviations from the sampled mean values. In other words, the extent of the various relationships, though weak, may represent the daily recommended calories into meals, which takes into consideration food preference, psychological, physiological and social status of individual diabetic.

CONCLUSION

The results from this study tend to indicate lipase activity as an index to the overall observed metabolic and physiological disorders or impairments associated with insulin action. The various increases in Hyperlipidaemia with sex show a male-associated metabolic derangement that is pronounced with diabetes. Therefore, it is possible the entire sets of variable (non-cholesterol lipid, total cholesterol, pancreatic amylase and lipase activities and insulin action) are at least in part, under genetic influence as a cluster or network. The various associations of Hyperlipidaemia parameters with lipase activity suggest a stimulation of lipase activity as well as balance in proportion or derivative of insulin secretion and action in non-diabetics.

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