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## **Changes in Plasma Fibrinogen, Viscosity and Electrolyte Levels among Some Nigerian Diabetics Receiving Treatment.**

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### **Abstract:**

In order to assess the impact of the various treatment approaches adopted to manage diabetes mellitus (DM) in Nigeria, one hundred and ninety-five fresh cases of DM were investigated. Fifty-five non-diabetic individuals in apparent good health were included as control subjects. The DM patients were separated into 3 groups depending on the treatment they received. Group 1: diet, 2: insulin, and 3: oral hypoglycemic drugs. Basal plasma fibrinogen concentration (PFC), relative plasma viscosity (RPV), packed cell volume (PCV), hemoglobin (Hb) concentration, plasma sodium and potassium levels were determined in both DM patients and control subjects by standard analytical procedures, and the results were compared with those obtained after about  $6 \pm 1$  (5-7) months of managing the ailment. The data indicate that after about 5-7 months treatment of the disease, PFC for group 1 patients ( $4.00 \pm 3.0 \text{g/L}$ ;  $n=75$ ) and plasma sodium levels ( $130.0 \pm 4.6 \text{mmol/L}$ ;  $n=75$ ;  $134.2 \pm 3.2 \text{mmol/L}$ ;  $n=55$ ; and  $132.1 \pm 4.3 \text{mmol/L}$ ;  $n=65$ ) for groups 1, 2 and 3 DM patients were demonstrated to be significantly different ( $P < 0.05$ ) when compared with control values (PFC =  $3.02 \pm 0.31 \text{g/L}$ ; sodium =  $142.3 \pm 3.2 \text{mmol/L}$ ;  $n=53$ ) using the Student t-test. Results suggest poor control of DM by diet and drug, and this may be due to patients' non-compliance to recommended diets and drug dosage. Since not all cases require insulin administration in the first instance, then ways of enforcing strict compliance should be explored and tested.

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Key Words: Diabetics, fibrinogen, viscosity, insulin, hyperglycaemic.

## **Introduction:**

Diabetes mellitus, a syndrome, characterized by hyperglycaemia, polyuria and excessive thirst could be classified into: insulinopenic diabetes mellitus which is primarily the result of pancreatic beta-cell destruction, resulting in progressive loss of pancreatic islet beta cell, and is characterized by absolute insulin deficiency, abrupt onset of severe symptoms, proneness to ketosis and dependence on exogenous insulin to sustain life. The other is insulinoplethoric diabetes mellitus which is caused by relative lack of insulin due to excess antagonizing hormones or other insulin inhibiting factors and so, these groups of patients are judged clinically not to be in urgent need of insulin to preserve life (WHO, 1992). This latter class constitute about 85% of all cases of diabetes in developed countries (Glattaar, 1988) and the majority of cases in developing countries (Dowse & Zimmet, 1989).

Diabetics normally have polyuria resulting in dehydration and insatiable thirst which dominates the patient's existence, that his daily routine is centered on his need for water, and his sleep is often disturbed either by the need to drink water or urinate. This increased drinking is the response to a normally functioning thirst mechanism to urinary loss of fluid (Deutron, 1967).

Simple water depletion will in the first place be indicated by the presence of clinical conditions known to lead to water deficiency, and by thirst. Laboratory confirmation will be obtained by decreased sodium and chloride levels, associated perhaps with increase in

potassium levels, high globulin protein concentration, raised hematocrit values, in the absence of hematological complications (Gray & Howorth, 1979). The serum pH could be slightly acidic due to the presence of ketone bodies which arise from the oxidation of fatty acids, indicating a change from carbohydrate to fatty acid metabolism for cellular energy provisions in diabetics, and this could distort the acid/base balance of the plasma (Mongomery, et al., 1977).

This paper thus, reports the influence of diabetic treatment on some biochemical parameters, whose changes in plasma levels is a reflection of the degree of dehydration and as such, these changes could be used to evaluate the response of patients to the management strategies adopted to treat the disease.

## **Materials and Methods:**

**Subjects:** One hundred and ninety-five freshly diagnosed cases of diabetes mellitus were selected from the Diabetics' Clinics of University of Benin Teaching Hospital, Ugbowo, and Central (Specialist) Hospital, both in Benin City, Nigeria. The patients were separated into three groups depending on the treatment later adopted to manage each case. Group 1-diet therapy (n=75), group 2-insulin therapy (n=55), and group 3-drug (hypoglycaemic agents) therapy (n=65).

## **Collection and Storage of Blood**

**Specimens:** Fasting whole blood samples were collected from these patients before commencement of the various treatments, and then again, after about 5-7 months of receiving such

therapy. Blood samples were collected into: capillary tubes for packed cell volume (PCV), plain sterile bottles for haemoglobin (Hb), heparinized bottles for sodium (Na), potassium (K), fibrinogen and viscosity analysis. The PCV and Hb determinations were done immediately after sample collection, while the plasma obtained from the whole blood in the heparinised bottles following centrifugation (1,200xg for 5min at room temperature: 25-29°C) were stored frozen and analysed within 48 hours. Fifty-three non-diabetic, fasting, whole blood samples were collected at random from individuals in apparent good health, and these served as control samples.

**Determination of plasma sodium and potassium:** The method used was automated and essentially that described by Williard and John, in Tietz, 1986. 1 to 200 dilution with deionised water was made for each sample and standard before being flamed. The emission flame photometer was then, set up according to its operative manual instructions and the concentration of sodium and potassium were taken for each sample.

**Estimation of packed cell volume (PCV) or haematocrit:** The sealed capillary tube containing the collected venous whole blood was centrifuged at 12,000 x g for 5 minutes and then, placed in the haematocrit reader and read as a fraction of the total blood volume, normally expressed as a percentage (%).

**Determination of Haemoglobin (Hb) level in blood:** The Drabkin & Austin

(1936) method was used. Here, 0.02ml of whole blood was added to 4.0ml of the modified diluent (Drabkin's solution) in a tube. The tube was then stoppered and inverted for several times, after which it was allowed to stand at room temperature for about 10 minutes. The test and standard samples were then read at 540nm against the reagent blank. The concentration of standard and the absorbance values were used to calculate the Hb level.

**Estimation of plasma fibrinogen concentration (PFC):** The clot- weight method of Ingram (1961) was used. 1.0 ml of the prewarmed, 25mmol/L calcium chloride solution was dispensed into the tube, then 1.0ml of plasma was added and the content thoroughly mixed. An applicator stick was inserted and this was allowed to incubate for 30 minutes at room temperature. At the end, a clot was formed round the applicator stick which was carefully wound round until all the fluids were squeezed out, rinsed in distilled water, blotted in filter paper and pulled out from the stick and dried. The weight was then determined and recorded.

**Estimation of the relative plasma viscosity (RPV):** The modified needle and syringe method of Reid and Ugwu (1987) was used. Plasma viscosity was measured using 1.0ml graduated syringe to which a vertical needle was fitted. The composite syringe with its plunger and needle was held vertically in a retort stand. The plasma to be tested was drawn up carefully, excluding air bubbles into the vertical syringe until the end of the plunger passed the 1.0ml mark. The

plunger was then completely withdrawn, and immediately the lower meniscus of the plasma fell to the 1.0ml mark, a stop-watch was started. The time required by 1.0ml of plasma to flow down the syringe was noted. The plasma viscosity is expressed as relative plasma viscosity (RPV) which is the ratio of the flow-time for 1.0ml of plasma to the flow-time for 1.0ml of distilled water at 37°C.

**Statistics:** Student t-test was used to compare two related mean values, and significant difference established at the

5% probability level. The EPI computer software package was used.

### Results:

The results obtained are shown on Table 1. Changes in plasma fibrinogen concentration (PFC) for group 1 (diet therapy) diabetic patients, and plasma sodium levels for all the diabetic groups were demonstrated to be significantly different ( $P < 0.05$ ) when compared with control values, using the Student t-test analysis. The data obtained suggests that group 1 diabetics responded the least to treatment.

Table 1: Changes in some blood parameters following the various treatments of diabetics

Parameter	Fibrinogen (g/L)		Viscosity		PCV (%)		Hb (g/dL)		Sodium (mmol/L)		Potassium (mmol/L)	
	0	5-7	0	5-7	0	5-7	0	5-7	0	5-7	0	5-7
Group 1 (n=75)	4.36±0.38*	4.00±0.30*	1.98±0.08	1.90±0.07	44.2±2.8	44.5±2.3	14.7±1.2	13.5±0.8	128.3±3.1*	130.0±4.6*	5.32±0.41	4.61±0.24
Group 2 (n=55)	4.33±0.41*	3.32±0.27	1.91±0.10	1.61±0.05	42.8±2.9	40.2±2.6	14.3±1.5	12.9±1.1	128.1±2.6*	134.2±3.2*	5.23±0.46	4.41±0.33
Group 3 (n=65)	4.38±0.35*	3.67±0.33	1.96±0.11	1.86±0.08	44.6±3.1	43.9±3.2	15.1±1.8	14.6±1.6	129.2±3.8*	132.1±4.3*	5.31±0.44	4.91±0.38
Group 4 (n=53)	3.05±0.34	3.02±0.31	1.61±0.05	1.58±0.04	39.7±3.1	39.3±2.5	12.7±0.9	12.5±0.8	141.7±3.4	142.3±3.2	4.25±0.24	4.28±0.26
Reference	2.50-3.80	2.50-3.80	1.50-1.75	1.50-1.75	37.0-54.0	37.0-54.0	11.0-18.0	11.0-18.0	136.0-148.0	136.0-148.0	3.80-5.00	3.80-5.00

Values are expressed as mean±SD for 'n' subjects, \* $P < 0.05$ : compared with control value. Rx: Treatment, Group 1: Diet therapy, Group 2: Insulin therapy. Group 3: Drug therapy. Group 4: Control subjects, M: Months, PCV: Packed Cell Volume, Hb: Hemoglobin.

### Discussion:

Diabetic induced polyuria could cause hyponatraemia (Fitzsimons, 1979). In hyponatraemia, the sodium and chloride concentrations in the plasma are usually low, while the plasma globulin proteins and the haematocrit values are high (Gray and Howarth, 1979). Among the one hundred and ninety-five diabetics

investigated across the groups; 40% and 20% of the groups 1 and 3 patients respectively were hyponatraemic (i.e plasma sodium of less than 125mmol/L). Plasma sodium concentration of £135mmol/L (reference range: 136-148mmol/L) observed in some patients especially in group 1 and 3 could be responsible for the relatively raised PCV in 54.7% and 49.2% of the groups 1 and

3 diabetics; and this in turn resulted in the increased plasma fibrinogen concentration to levels that were above 3.80g/L in 42.7% and 21.5% of the diabetics in these groups. 23.6% of the group 2 patients, who were not hyponatraemic, had increased PFC. This suggests that other associated pathological complications could influence the level of plasma proteins. 33.80% of the group 3 patients, who had elevated levels of PFC, also had increased RPV. There is thus, a direct relationship between RPV and PFC and this confirm earlier report (Lawrence, 1950). RPV has been proposed to be a useful index in evaluating protein status, since alterations in the RPV are mainly due to changes in the protein constitution of the plasma (Harkness and Whittington, 1971).

Reid and Ugwu (1987) reported an RPV mean value of  $1.65 \pm 0.09$  and a PFC mean value of  $3.29 \pm 0.85$ g/L for 41 normal subjects, and RPV and PFC values of  $1.81 \pm 0.13$  and  $3.82 \pm 0.95$ g/L respectively, for 50 diabetic patients. In another case reported by Montgomery et al. (1977), a 21 year old female with a four year history of insulinopenic diabetes mellitus had plasma sodium, potassium, PCV and pH values of 134mmol/L, 6.4mmol/L, 49% and 6.8 respectively. They explained that the sodium, potassium and PCV values indicated dehydration, probably caused by the excess polyuria that characterized the life of diabetics, and the pH showed that the plasma was acidotic, possibly due to oxidation of fatty acids in lieu of glucose, to yield energy.

Similarly, our data suggest that Groups

1 and 3 patients were still dehydrated after 5-7 month treatment, and this may be responsible for the increased thirst and the sodium appetite experienced by majority of these diabetics. Clinically, they have poor control of the metabolic disorder. This of course, correlates to the research interview finding of non-compliance to the management strategies. Dietary and drug control therefore, could only be effective if the recommended "traditional diet" and drug dosage are strictly adhered to. However, since sufficient intake of water alone is not the appropriate restoring fluid, it is hereby advised that sodium replacement therapy be used to complement the recommended treatment. Meanwhile, ways of enforcing patients' compliance should be explored and the outcome tested. This may improve the management of diabetic cases in Nigeria. This is important because not all cases of DM require insulin administration in the first instance.

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