

# Sorbitol Dehydrogenase Activity in Diabetes Mellitus and Cataract Patients

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## Abstract

Accumulation of sorbitol in the pathogenesis of cataract in susceptible subjects has long been an issue. Sorbitol dehydrogenase (SDH) activity in 25 diabetes mellitus (DM) patients and 15 patients having cataract was investigated using 10 subjects without diabetes or cataract as the control. Results of fasting plasma glucose assay done on the DM patients showed a mean range of 64 – 144mg/dl in cataract patient, 67 – 293mg/dl in DM patient and 60 – 100mg/dl in the control subjects. Also, SDH activity in the three categories of patients were 0.7 – 5.6 IU/ml, 3.5 – 11.2 IU/ml and 0.7 – 4.2 in cataract, DM and control subjects respectively. A comparative analysis of the sorbitol level in cataract and DM patients showed that DM patients have a higher level of SDH activity than cataract patients while the level of SDH activity in both cataract and control subject were statistically similar. While we concluded from this work that SDH activity or sorbitol accumulation may not necessarily be a predisposing factor in the development of cataract secondary to diabetes mellitus in the group of subjects studied, it is our opinion that the generalized mode of managing cataract patients with the administration of aldose-reductase inhibitors should be reviewed.

**Keywords:** Cataract, Diabetes Mellitus, Sorbitol Dehydrogenase, Aldose-reductase inhibitors

## 1 Introduction

Diabetes mellitus (DM) is a group of metabolic disorders with one common manifestation-hyperglycaemia. It is a chronic disease in which there is evidence of significant hyperglycaemia due to absolute or relative insulin deficiency with signs and symptoms of polyuria, glycosuria and weight loss [Akinkugbe, 1992]. The disease develops because the body does not produce or properly use insulin- a hormone that is

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needed to convert sugars, starches and other foods into energy for daily life leading to accumulation of sugar in the blood circulation (hyperglycaemia). The attendant hyperglycaemia in DM causes damage to the eyes, kidneys, nerves, heart and blood vessels [Vipan Datta *et. al.*, ; 1997]. The cause of diabetes mellitus continue to be a mystery although, both genetics and environmental factors such as obesity and lack of exercise appear to play roles. The etiology and pathophysiology of hyperglycaemia however, are markedly different among patients with diabetes mellitus, dictating different prevention strategies, diagnostic screening methods and treatment. It is these differences in the pathophysiology of the associated hyperglycaemia in diabetes mellitus that lead to the various complications associated with this disease. Hyperglycaemia causes the excessive glucose that cannot be phosphorylated by hexokinase to enter the polyol pathway which is an alternative route of glucose metabolism. In the polyol pathway, aldose-reductase (an enzyme) catalyses the production of sorbitol from excess glucose in this alternative pathway. Sorbitol, a sugar-alcohol produced in the polyol pathway has been implicated in the pathogenesis of diabetes complications.

The increase in aldose reductase activity in hyperglycaemia has been implicated as the underlying metabolic cause of secondary diabetic complications such as cataractogenesis, retinopathy, neuropathy and nephropathy. In diabetes retinopathy, hyperglycaemia increases glucose concentration in the lens and optic humors resulting in blurring of vision, weakness of accommodation and myopia. Opacification of the lens of the eyes may also be due to sorbitol accumulation in metabolic cataract lending credence to its involvement in the pathophysiology of the disease.

Sorbitol dehydrogenase activity was therefore evaluated in some cases of DM and cataract subjects with a view to establishing the role of sorbitol accumulation in comparison with normal nondiabetic and noncataractogenic subjects in this environment.

## **2 Materials and Methods**

### **2.1 Selection of Subjects**

A total of fifty subjects consisting of 29 males and 21 females (ages ranging between 17yrs and 62yrs) were recruited for this study. These were divided into 3 groups.

Group One consisted of 10 subjects who were apparently healthy individuals with no history of diabetes, cataract or any other eye diseases, these were the control subjects.

Group two consisted of 15 subjects clinically diagnosed for diabetes mellitus and were attending the medical out- patient clinic of the University College Hospital, Ibadan.

Group three consisted of 25 subjects clinically diagnosed for cataract and were attending the Ophthalmology out-patient clinic of the University College Hospital, Ibadan. Ethical Clearance was obtained from the Medical ethical Committee of the hospital.

### **2.2 Specimen Collection**

Fasting blood samples were collected by venepuncture without stasis from subjects in the three groups after an overnight fast of 10hours. Blood for glucose estimation was dispensed into flouride oxalate bottles while blood for sorbitol assay was dispensed into plain bottles to obtain their serum.

The blood samples were all spun for 5 minutes and the plasma for glucose estimation and

serum for sorbitol dehydrogenase were separated respectively. The serum samples for sorbitol dehydrogenase were stored frozen until ready for analysis.

Plasma glucose was estimated using the standard Trinders method (1969) while sorbitol concentration was estimated using the method of Ulrich Gerlach (1974).

### 2.3 Statistical Method

Results of these assays were analyzed using ANOVA while significance was observed at  $P < 0.05$

## 3 Main Results

Tables 1 and 2 show the mean $\pm$ 2SD of fasting blood glucose (FBS), sorbitol dehydrogenase (SDH) and SDH/FBS value in control (group 1), diabetic patient (group 2) and cataract (group 3). The mean value of the fasting plasma glucose (FPG) in diabetic patient was significantly ( $P < 0.05$ ) higher (140.07mg/dl) than the mean FPG value of 86.8mg/dl and 81.80mg/dl obtained for the cataract and control groups respectively.

The sorbitol dehydrogenase (SDH) mean value was also significantly ( $p < 0.05$ ) higher in group 2 (6.6IU/ml) than in group 1 (1.82IU/ml) and group 3 (2.13IU/ml).

The mean SDH value was expressed as a ratio of its corresponding FBS value; this was done to determine average clearance rate of the excess glucose relative to the SDH activity. The mean SDH/FBS value was also significantly ( $p < 0.05$ ) higher in group 2 than in group 1 and 3.

However, no significant ( $p > 0.05$ ) mean differences existed between mean values of FBS, SDH and SDH/FBS ratio of Cataract patients when compared with control.

## 4 Tables and Figures

Table 1: Mean and P-values of Blood glucose (FBS), Sorbitol dehydrogenase (SDH) and ratio of SDH/FBS results in Controls, DM and Cataracts subjects

Parameter	Groups	n	Mean $\pm$ 2SD	p-Value
Fasting Blood Glucose (FBS) (mg/dl)	Group 1: Control	10	81.80 $\pm$ 14.27	-
	Group 2: DM	15	140.07 $\pm$ 69.61	0.016
	Group3: Cataract	25	86.80 $\pm$ 16.19	0.400
Sorbitol Dehydrogenase (SDH) (IU/ml)	Group 1: Control	10	1.82 $\pm$ 1.15	-
	Group 2: DM	15	6.60 $\pm$ 2.34	0.000
	Group3: Cataract	25	2.13 $\pm$ 1.45	0.554
SDH/FBS	Group 1: Control	10	0.02 $\pm$ 0.01	-
	Group 2: DM	15	0.05 $\pm$ 0.02	0.000
	Group3: Cataract	25	0.02 $\pm$ 0.02	0.505

Significant level is at  $P \leq 0.05$

## 5 Discussion and Conclusion

Diabetes mellitus is a chronic disease in which there is hyperglycaemia due to absolute or relative insulin deficiency with signs and symptoms of polyuria, glucosuria and weight losses (Akinkugbe, 1992). It is a disease in which the glucose level in the blood is high and there is low utilization of glucose by the peripheral tissues due to low or absence of insulin in the blood.

This has been reported to be the basis of various complications such as neuropathy, retinopathy, nephropathy and cataract (Asmal et al, 1977) that occur later in diabetes mellitus.

Cataract has been described as the opacification of the crystalline lens of the eyes which disturb visual acuity, it could be due to excessive deposition of sorbitol as in diabetic cataract where excess glucose is diverted into the polyol pathway or it could be due to the thickening of the cornea as a consequence of age or infection which is manifested in metabolic cataract (Vipan Datta *et. al.*; 1997)

As stated above, the objective of this work was to investigate the role of sorbitol concentration in the aetiology of cataract especially secondary to DM. Expectedly, results of this work has shown that the DM patients exhibited hyperglycaemia as shown by their mean blood glucose level of  $140.07 \pm 69.61$  while cataract patients had a mean glucose level of  $86.80 \pm 16.19$  in comparison with that of the control  $81.80 \pm 14.27$  ( $p < 0.016$  and  $p > 0.400$  respectively). While an increased sorbitol level was seen in the DM patients as depicted by their mean SDH activity of  $6.60 \pm 2.34$  IU/ml, the mean SDH activity in the cataract patients was  $2.13 \pm 1.45$  IU/ml. this value was statistically non-significant when compared with the control unlike that of the DM patients which was significant. From the foregoing, it could be said that there was no significant accumulation of sorbitol in the group of cataract patients studied. That the DM patients showed a high sorbitol level as depicted by the high SDH activity could be understood from the biochemical fact that excessive glucose level in this group of patients had to be mopped up by the body's natural homeostatic mechanism; hence, diverting the excess glucose into the polyol pathway resulting in the observed excessive SDH activity would be expected under normal homeostatic condition. However, the issue of cataract patients in this group not showing any biochemical evidence of excessive sorbitol level needs further clarification. Perhaps, the bulk of the cataract patients recruited for this project belong to the metabolic type or there could be other underlying pathophysiology for their subtype of cataract. Based on this, the need for a review of the treatment regimen for cataract patients become imminent. This is because the general mode of management of cataract utilizes the administration of aldose-reductase inhibitors. This is aimed at reducing the activity of this enzyme thus preventing the accumulation of sorbitol since the latter is formed by the conversion of excess glucose through this enzyme in the polyol pathway. Findings in this work has thus reaffirmed others ( Kadsor, (1988) De Leeuw, Vertommen and Rillaerts, (1993); Kador *et. al.*, (1998), Kubo *et. al.*, (2001), thus highlighting the need to establish the involvement of sorbitol deposition in the pathophysiology of cataract cases seen in this environment. Hence, proper differential diagnosis of the type of cataract to avoid generalized administration of aldose-reductase inhibitors need to be institutionalized. Again, recourse to routine investigation for DM in all cases of cataract along with the above investigation is imperative by the findings of this work.

The introduction of a factor/ module that expressed the sorbitol level as a function of the coincident plasma glucose concentration i.e SDH/FPG ratio was aimed at essentially correcting the intracellular sorbitol concentration for the influence of variable plasma glucose levels common to Type 1 DM. Since prevention is now more of the rule than exception, a closer look at the SDH/FPG ratio in the three groups of subjects would reveal that any slight increase in this ratio above the figure obtained for the control group, could serve as an indicator of the development of cataract especially in non-diabetic patients with other ophthalmic problems. The picture of the SDH/FPG ratio as shown in the Tables above clearly show the benefit of a concurrent estimation of SDH and calculation of the SDH/FPG ratio in following the course of DM towards avoiding complications like cataract.

In conclusion, methods that can directly monitor aldose-reductase activity and also measure the thickness of the cornea could be sought as ways of unraveling the riddle behind the pathophysiology of cataract, a debilitating disease ravaging our society.

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