

A STUDY ON CORRELATIONS OF FASTING PLASMA GLUCOSE WITH AQUEOUS HUMOR GLUCOSE AND HBA1C IN CATARACT PATIENTS.

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Abstract: Background & objectives: Indian guideline approved the cataract surgery with fasting plasma glucose of <140 mg/dl and random plasma glucose of less than 180mg/dl but no data on the relationship of fasting plasma glucose with aqueous glucose level and HbA1c in cataract patients was available in India. Hence our study will try to explore the relationship of fasting plasma glucose with aqueous glucose level and HbA1c in cataract patients. **Methods:** Thirty-six (Group A) & 40 (Group B) cataract patients with fasting plasma glucose in between 100 – 125mg/dl and 126 – 139mg/dl respectively were evaluated for aqueous glucose level and HbA1c. Forty age & sex matched normoglycemic senile cataract patients were taken as control. **Results and Interpretation:** There were significant positive correlations among fasting plasma glucose, aqueous humor glucose & HbA1c in controls but no significant correlations were found between fasting plasma glucose with aqueous humor glucose & HbA1c in fasting hyperglycemic cataract patients suggesting fasting plasma glucose did not reflect the aqueous humor glucose & HbA1c in those cases. Moreover significantly positive correlations were found between aqueous humor glucose with HbA1c in hyperglycemic cataracts suggesting HbA1c was the better predictor of aqueous humor glucose level in such cases. **Conclusion:** Glycemic control must be ensured by the monitoring the HbA1c along with plasma glucose value in hyperglycemic cataract patients before proceeding for cataract surgery to predict the significant changes in aqueous glucose value that might have adverse outcome on the surgery in the form of infection, delayed wound healing, macular edema etc which needs to be studied further.

Keywords: Aqueous humor glucose concentrations, Cataract, Diabetes, HbA1c.

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Introduction:

Cataract is considered a major cause of visual impairment in diabetic patients as the incidence and progression of cataract is elevated in patients with diabetes mellitus.^{1,2} Biochemical changes have been studied extensively and certain mechanisms related to cataractogenesis have been suggested.³ The enzyme aldose reductase catalyzes the reduction of glucose to sorbitol that creates a hyper osmotic effect leading to the development of diabetic cataract.⁴

Aqueous humor is a clear fluid that provides nutrition to the avascular structures (Lens & cornea). It also removes excretory products from metabolism, transports neurotransmitters, helps in the formation & stabilization of the anterior and posterior chambers of the eye.⁵ Aqueous humor is formed by the mechanisms involving diffusion, ultrafiltration and active secretion.⁶ Reference interval of aqueous humor glucose concentration is

50 ± 2.6 mg/dl.⁷ Aqueous humor glucose concentrations in cataracts are said to be higher in diabetes than non diabetes patients.⁸

HbA1c is the nonenzymatic addition of sugar to amino groups of Hemoglobin (Hb). Blood glucose concentrations exhibit wide diurnal fluctuations due to food ingestion, exercise, and other factors. In contrast, the concentration of HbA1c remains relatively stable with time hence directly proportional to the blood glucose concentration over the preceding 8 to 12 weeks. Thus it directly correlates with glycemic control.⁹ Asmita et al showed correlation of Glycated Hb with fasting & post prandial plasma glucose.¹⁰

U K guideline recommends that preoperative HbA1c of <8.5% should be considered as acceptable for surgery.¹¹ But Indian guideline approved the cataract surgery with fasting plasma glucose of <140 mg/dl and random plasma glucose of less than 180mg/dl.¹² But no data on the relationship of

fasting plasma glucose with aqueous glucose level and HbA1c in cataract patients was available in India. Hence our study will try to explore the relationship of fasting plasma glucose with aqueous glucose level and HbA1c in cataract patients who had first time diagnosed hyperglycemia but with fasting plasma glucose value less than 140mg/dl, random plasma glucose value less than 180mg/dl and without hypoglycemic medication.

Materials & methods:

A total of 156 cataract patients attending the outpatient department of ESIPGIMSR & ESIC Medical College, Joka, West Bengal, were diagnosed to have hyperglycemia for the first time on routine biochemical examination in the eight months long cross-sectional case control non interventional study. Seventy six (76) cataract patients including 45 males and 31 females who had fasting plasma glucose level less than 140mg/dl & random plasma glucose value less than 180mg/dl without medication, undergone cataract extraction under local anesthesia. Group A had 36 patients with fasting plasma glucose in between 100 – 125mg/dl & Group B had 40 patients with fasting plasma glucose in between 126 – 139mg/dl. Aqueous glucose concentration and HbA1c of 40 age & sex matched normoglycemic (fasting < 100 mg/dl, post prandial < 140 mg/dl, HbA1c < 5.6%) senile cataract patients were taken as control. Cataract was diagnosed after doing visual acuity, intraocular pressure measurement and slit lamp examination after dilation of pupil. The age of patients ranged from 52 to 67 years. The institutional ethics committee approved the study and informed consent was obtained from all the study populations, in accordance with the Declaration of Helsinki. A detailed questionnaire on family history, social status, and dietary habits, including other habits such as smoking, alcohol intake, history of systemic diseases, and drug history (steroid, diuretics, hypoglycemic agents), radiation exposure, ocular history (trauma or infection or inflammation) were completed by all the study subjects. Cardiovascular disease, renal disease, liver disease, known hypertensive & diabetes with medication, serum electrolyte disturbance as well as traumatic & inflammatory cataract and retinopathy were

ruled out in the present study based on the biochemical and ocular tests apart from the questionnaire.

Collection of aqueous humor:

All cataract patients were prepared for the surgery by maintaining the required asepsis. Peribulbar block was performed with the injection of 3 cc of lignocaine mixed with hyaluronidase. 0.4 c.c of aqueous humor was collected from the anterior chamber by using a 26 gauge needle and an insulin syringe intra operatively without touching the corneal endothelium & anterior lens capsule & without dislodging the needle. The anterior chamber was reformed with ringers lactate solution through the same needle and the cataract surgery was then continued in its regular way.⁷

Aqueous humor glucose concentration was estimated by glucose oxidase-peroxidase method from the reagent provided by Coral.¹³ 10µl of aqueous humor is treated with 1000µl glucose oxidase-peroxidase reagent to give a pink color solution. Absorbance of the solution is measured by the semi-automated analyzer provided by ERBA diagnostics. Intensity of the color of the solution is directly proportional to the concentration of glucose in aqueous humor.

Five (5) cc of venous blood was collected from anti-cubital vein of forearm by venepuncture in fasting condition. Two (2) cc was poured into fluoride-oxalate vial for fasting plasma glucose estimation¹³ and 3 cc was poured into EDTA vial for HbA1c estimation on the day of cataract extraction (HbA1c test does not require fasting condition). HbA1c were measured using a Bio-Rad D-10 HPLC instrument, whose compliance with the latest Diabetes Control and Complications Trial (DCCT) reference method has been documented by the National Glycohemoglobin Standardization Program (NGSP).¹⁴ Both the intra- and inter assay coefficients of variation were < 2.6% & < 3.0%. Pearson's correlation was applied to find out any significant correlation using the Minitab 16 software.

Results:

There were significantly high fasting plasma glucose, aqueous humor glucose and HbA1c in both groups over control. But there were no significant

changes in the aqueous glucose level and HbA1c in between two groups (Table 1).

There were significant positive correlations among fasting plasma glucose, aqueous humor glucose & HbA1c in controls (Table 2). But no significant correlations were found between fasting plasma glucose with aqueous humor glucose & HbA1c in hyperglycemic cataracts, moreover significantly positive correlations were found between aqueous humor glucose with HbA1c in hyperglycemic cataracts (Table 3) (Table 4).

Table 1

Descriptive Statistics of fasting plasma glucose, Aqueous humor glucose and HbA1c in controls & cases

Variable	Controls	Group A (FPG 100-125mg/dl)	Group B (FPG 126-139mg/dl)
Sample size	40	36	40
Fasting plasma glucose	83.1 ± 8.1	112.4 ± 5.5*	131.2 ± 3.8*
Aqueous humor glucose	49.2 ± 2.7	57.1 ± 3.9*	56.4 ± 3.9*†
HbA1c	5.0 ± 1.1	5.9 ± 1*	5.9 ± 0.9*†

* 'P' value <0.05 in respect to controls

† 'P' value >0.05 in respect to group A

Table 2

Correlations of fasting plasma glucose with aqueous humor glucose & HbA1c in controls

	Fasting plasma glucose	Aqueous humor glucose
Aqueous humor glucose	0.674	
	0.000	
HbA1c	0.602	0.982
	0.000	0.000

Cell Contents: Pearson correlation

P-Value significant at the 0.05 level

Table 3

Correlations of fasting plasma glucose with aqueous humor glucose & HbA1c in group A

	Fasting plasma glucose (100 – 125mg/dl)	Aqueous humor glucose
Aqueous humor glucose	0.218	
	0.059	
HbA1c	0.216	0.968
	0.060	0.000

Cell Contents: Pearson correlation

P-Value significant at the 0.05 level

Table 4

Correlations of fasting plasma glucose with aqueous humor glucose & HbA1c in group B

	Fasting plasma glucose (126 – 139mg/dl)	Aqueous humor glucose
Aqueous humor glucose	0.143	
	0.378	
HbA1c	0.279	0.956
	0.082	0.000

Cell Contents: Pearson correlation

P-Value significant at the 0.05 level

Discussions:

It was well established that HbA1c directly correlates with glycemic control⁹ and it also correlates with fasting & post prandial plasma glucose.¹⁰ UK guideline recommends that preoperative HbA1c of <8.5% should be considered as acceptable for surgery.¹¹ Indian guideline approved the cataract surgery with fasting plasma glucose of <140 mg/dl and random plasma glucose of less than 180mg/dl.¹² But cataract surgery under loco regional anesthesia did not have such guideline in India in relation to the incidence of post operative infection and delayed wound healing.¹⁵ Our study observed significant positive correlations among fasting plasma glucose, aqueous humor glucose & HbA1c in controls (Table 2) that suggested against the routine measurement of HbA1c prior to the cataract surgery in normoglycemic patients as fasting plasma glucose

levels reflected the aqueous humor glucose level in controls.

A significant rise in fasting plasma glucose, aqueous humor glucose and HbA1c were observed in both groups over controls in our study (Table 1). Decreased collagen formation was observed in hyperglycemic rats during wound healing, and collagen formation is normalized by controlling hyperglycemia.^{16,17} The postoperative infection rate was higher in diabetic patients than in nondiabetic patients (10.7% vs 1.8%).¹⁸ A correlation between acute postoperative infection and blood glucose level was also found.¹⁹ Moreover, rapid preoperative correction of HbA1c would aggravate the retinopathy & maculopathy.²⁰

The aqueous glucose level and HbA1c did not change significantly in between two groups (Table 1) moreover no significant correlations were found between fasting plasma glucose with aqueous humor glucose & HbA1c (Table 3) (Table 4) in fasting hyperglycemic cataracts patients suggesting fasting plasma glucose did not reflect the aqueous humor glucose & HbA1c in those cases. These could probably be explained by the fact that fasting hyperglycemia was for short duration due to apprehension of surgery or other metabolic causes leading to the stress induced hyperglycemia which was not enough to raise the aqueous humor glucose due to blood aqueous barrier as aqueous humor was produced by diffusion, ultrafiltration and active secretion from plasma.⁶ Hence HbA1c level needs to be determined prior to the cataract surgery in fasting hyperglycemic patients to predict the aqueous humor glucose as significantly positive correlations were found between aqueous humor glucose with HbA1c in hyperglycemic cataracts (Table 3) (Table 4).

In conclusion we could say that glycemic control must be ensured by the monitoring the HbA1c along with plasma glucose value in hyperglycemic cataract patients before proceeding for cataract surgery to predict the significant changes in aqueous glucose value that might have adverse outcome on the surgery in the form of infection, delayed wound healing, macular edema etc which needs to be studied further.

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