

## 8-Isoprostaglandin F<sub>2a</sub> Levels in Aqueous Humor of Senile and Diabetic Cataract Patients

Amena Rahim<sup>1</sup>, Khadija Iqbal<sup>2</sup>, Tehmina Qamar<sup>3</sup>, Komal Zulfiqar<sup>4</sup>

<sup>1</sup>(Department of Biochemistry, Rawal Institute of Health Sciences, Islamabad, Pakistan)

<sup>2</sup>(Department of Anatomy, Al Nafees Medical College, Isra University, Islamabad, Pakistan)

<sup>3</sup>(Department of Biochemistry, Federal medical and dental college, Islamabad, Pakistan)

<sup>4</sup>(Department of community medicine, Islamic International Medical College, Rawalpindi, Pakistan)

**Abstract:** We investigated the concentrations of 8-isoprostaglandin F<sub>2a</sub>, a marker of oxidative stress in aqueous humor of patient's of senile cataract and compared the results with diabetic cataract to determine whether diabetic cataract is associated with increased oxidative stress. Aqueous humor was aspirated at the beginning of phacoemulsification cataract surgery from 25 eyes of 25 patients with senile cataract and 25 eyes of age matched diabetic cataract patients. 8-Isoprostaglandin F<sub>2a</sub> (8-IPGF) concentration in the aqueous was determined with an immunoassay method. The mean concentration of 8-isoprostaglandin F<sub>2a</sub> in the aqueous from patients with diabetic cataract i.e. 624 ± 95.7 pg/ml (range 400–750 pg/ml), was significantly higher than that measured in the aqueous of age matched senile cataract i.e. 190 ± 41.2 pg/ml ((range 100-290 pg/ml). 8-Isoprostaglandin F<sub>2a</sub> was significantly increased in the aqueous of patients with diabetes, confirming the evidence of a role for free radical induced oxidative damage in the pathophysiology of diabetic cataract. The antioxidative capacity of aqueous humor should next be investigated in these two types of cataracts.

**Key words:** aqueous humor, cataract, diabetic, senile, 8-Isoprostaglandin F<sub>2a</sub>

### I. Introduction

The most common cause of blindness in the world is cataract. Cataract formation is a very complex process and multiple factors are involved in its formation. Potential risk factors include age, sex female, exposure to ultraviolet light, smoking, diabetes, and oxidative stress [1]. There is a disturbed balance between oxidative and antioxidative processes. Lens opacification is either initiated or promoted by the oxidative stress [2]. Diabetes is one of the processes that accelerate damage to the eye. F<sub>2</sub>-isoprostanes are prostaglandin derivatives, and these are formed by free-radical-catalysed peroxidation of arachidonic acid. These compounds are bioactive and may be responsible for the adverse effects of the oxidative stress. 8-Iso-PGF<sub>2α</sub> is a major F<sub>2</sub>-isoprostane, currently it is regarded as one of the most reliable indicators of in vivo lipid peroxidation and oxidative stress [3]. Levels of isoprostanes have a wide daily variation in their secretion in plasma, creatinine and aqueous humor in humans. These compounds are found in increased concentrations in different pathophysiological states [4]. In this study we wanted to evaluate the oxidative effects of F<sub>2</sub>-isoprostanes on both types of cataract.

### II. Material And Methods

Patients were recruited from Layton Rehmatullah Benovolent Trust free Eye hospital (LRBT) Mandra, Punjab. Two groups of patients of cataract were included in the study: senile cataract and diabetic cataract, matched for age and gender. All patients had a complete ophthalmologic examination. Cataract status was determined by ophthalmoscope. Patients with complicated systemic diseases that can cause cataract and patients with ocular diseases were excluded from the study. A total of 50 patients: 25 senile and 25 diabetic cataract patients were included. Fasting blood samples were obtained and hyperglycemic status was determined. Blood was kept at room temperature and then centrifuged at 10,000 rpm for 10 mins and serum was pipetted. Test applied for the detection of glucose was glucose oxidase method. Type 2 diabetic patients with random blood glucose levels ≥ 200 mg/dl with symptoms such as polyuria, polydipsia, polyphagia and fasting blood glucose ≥ 126 mg/dl. Aqueous humor samples were obtained by making a scleral tunnel. A small amount of aqueous humor i.e. 10–40 µl was aspirated by means of a 27 gauge needle on a tuberculin syringe. Immediately after collection, aqueous samples were stored at –70°C until biochemical analysis. The aqueous concentration of 8-IPGF was measured by competitive enzyme linked immunoassay kit (8-Isoprostane EIA Kit -Cayman chemicals, New Orleans, USA).

**III. Result**

Significantly higher 8-isoprostaglandin F<sub>2α</sub> concentrations were observed in the aqueous humor of diabetic patients cataract i.e.624 ± 95.7 pg/ml, then in the case of senile patient’s cataract i.e.190 ± 41.2 pg/ml, Table 1 and 2.

**Table 1: Values of isoprostane in diabetic cataract**

	N	Minimum	Maximum	Mean	Std. Deviation
Isoprostane (pg/ml)	25	400.00	750.00	624.4000	95.78970
FBS Diabetic (mmol/l)	25	8.30	19.90	13.3160	3.10157

**Table 2: Values of isoprostane in senile cataract**

	N	Minimum	Maximum	Mean	Std. Deviation
Isoprostane pg/ml	25	100.00	290.00	190.4000	41.27953
FBS senile (mmol/l)	25	3.80	5.60	4.7440	.64877

**Table 3: mean values of isoprostane in diabetic & senile cataract**

	N	Minimum	Maximum	Mean	Std. Deviation
Isoprost pg/ml(senile)	25	100.00	290.00	190.4000	41.27953
Isoprost pg/ml(diabetic)	25	400.00	750.00	624.4000	95.78970

**IV. Discussion:**

Literature review shows a direct relationship between glucose levels and micro and macrovascular complications of diabetes [5]. The exact molecular mechanisms for these complications are not known so far. The most favored assumption so far by means of which hyperglycemic induced complication can occur is by means of reactive oxygen species [6]. Many ocular diseases are related to damage caused by oxidative stress [7]. Recent data in the literature by Kao et al [8], support an important role of oxidative damage in promoting cataract formation. 8-isoprostane has been widely used as a valid marker of oxidative stress and it is generated by the free radical-mediated peroxidation of arachidonic acid [9]. We observed in our study that the levels of 8-iso-PGF<sub>2α</sub> were higher in the diabetic cataract patients as compared to senile cataract patients. It is in accordance with the study conducted by Koliakos et al [10], in which it was observed that the mean concentration of 8-iso-PGF<sub>2α</sub> in aqueous humor from patients with exfoliation syndrome and cataracts was approximately 5 times higher than that measured in the aqueous humor from control cataract patients. On other hand in one of the study conducted by Siegelaar et al [11], no relationship was found between fluctuating glucose levels and 8-iso-PGF<sub>2α</sub> excretion in well regulated diabetes patients. These prostanoids can exert potent biological activity and can participate as mediators of oxidant injury as seen in the study conducted on the rat kidney[12]. One of the advantages of their quantification is that it is a noninvasive procedure as its levels can easily be assessed in the plasma and urine of patients. The antioxidative capacity of aqueous humor should next be investigated in these two types of cataracts.

**V. Conclusion:**

8-Isoprostaglandin F<sub>2α</sub> was significantly increased in the aqueous of patients with diabetes, confirming the evidence of a role for free radical induced oxidative damage in the pathophysiology of diabetic cataract. Their quantification is a noninvasive procedure as its levels can easily be assessed in the plasma and urine of patients. The antioxidative capacity of aqueous humor should next be investigated in these two types of cataracts.

**References:**

- [1]. Congdon N, West SK, Buhrmann RR, Kouzis A, Munoz B, Mkocha H. Prevalence of the different types of age-related cataract in an African population. *Invest Ophthalmol Vis Sci* 2001;42:2478-2482.
- [2]. Marsili S, Salganik RI, Albright CD, Freel CD, Johnsen S, Peiffer RL, et al. Cataract formation in a strain of rats selected for high oxidative stress. *Exp Eye Res* 2004;79:595-612
- [3]. Basu S: F<sub>2</sub>-isoprostanes in human health and diseases: from molecular mechanisms to clinical implications. *Antioxid Redox Signal* 2008, 10:1405–1434.
- [4]. Basu S, Helmersson J. Factors regulating isoprostane formation in vivo. *Antioxid Redox Signal*. 2005 Jan-Feb;7(1-2):221-35.
- [5]. Liang FQ, Godley BF. Oxidative stress-induced mitochondrial DNA damage in human retinal pigment epithelial cells: a possible mechanism for RPE aging and age-related macular degeneration. *Exp Eye Res* 2003;76:397-403.
- [6]. Stratton IM, Adler AI, Neil HA, Matthews DR, Manley SE, Cull CA, Hadden D, Turner RC, Holman RR. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ*. 2000;321(7258):405–412.
- [7]. Wentholt IM, Kulik W, Michels RP, Hoekstra JB, DeVries JH. Glucose fluctuations and activation of oxidative stress in patients with type 1 diabetes. *Diabetologia*. 2008;51(1):183–190.
- [8]. Siegelaar SE, Barwari T, Kulik W, Hoekstra JB, DeVries JH. No relevant relationship between glucose variability and oxidative stress in well-regulated type 2 diabetes patients. *J Diabetes Sci Technol*. 2011 Jan 1;5(1):86-92.
- [9]. Kao CL, Chou CK, Tsai DC, Hsu WM, Liu JH, Wang CS, et al. Nitric oxide levels in the aqueous humor in cataract patients. *J Cataract Refract Surg* 2002;28: 507-512.
- [10]. Montuschi P, Barnes PJ, Roberts LJ. Isoprostanes: markers and mediators of oxidative stress. *FASEB J* 2004;18:1791-1800
- [11]. Koliakos GG, Konstas AG, Schlotzer-Schrehardt U, Hollo G, Katsimbris IE, Georgiadis N, et al. 8-Isoprostaglandin F<sub>2a</sub> and ascorbic acid concentration in the aqueous humour of patients with exfoliation syndrome. *Br J Ophthalmol* 2003;87:353-356.
- [12]. Morrow JD, Hill KE, Burk RF, Nammour TM, Badr KF, Roberts LJ. A series of prostaglandin F<sub>2</sub>-like compounds are produced in vivo in humans by a non-cyclooxygenase, free radical-catalyzed mechanism. *Proc Natl Acad Sci U S A* 1990;87:9383-9387.