



Types of Human Age-Related Cataract and Its Relationship between Some Serum Routine Biochemical Parameters of Indian Population

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Abstract: *Cataract is one of change in human aging process, generally the lens become clouding and disturb normal vision of every individuals. The routine biochemical analysis shows, there is significant changes in blood parameters between normal and cataract population that were reported by many previous experiments but study related to routine biochemical parameters and its phenomenon were not known among different types of cataract. Hence, a study was planned to understand the relationship among the different types cataract population among Indian ethnics to fill-up the lacuna that could facilitate the prevention of those types by simply identifying them using routine biochemical analysis. About 25 samples in each group were planned. Biochemical data were retrieved from medical records and analyzed by statistical tools, one way ANOVA followed by an ad hoc Turkey's Multiple Comparison Test ($P < 0.05$) to compare variances among the four experimental groups, they are Cortical, Nuclear Sclerotic, and Posterior Subcapsular and Mixed types. Results indicated that there is no characteristics significance among different types of cataract in serum biochemical parameters analyzed. This study suggest that, there is a need to identify some simple markers from blood samples and exploring the fact behind the appearance of these markers which may be useful for diagnostic and prevention systems of health care market.*

Keywords: *Cortical cataract, Nuclear Sclerotic, Posterior Sub capsular, mixed type, Biochemical parameters.*

Introduction

Blindness is thought to reach 75 million by 2020. Of these, unoperated cataract may be expected to account for at least 35 million. Thus, the burden of cataract is increasing remorselessly (Kavitha et al. 2010). A cataract is a clouding of the lens that develop on aging. The lens consists mostly of water and protein. When the protein clumps up, it clouds the lens. If the lens is not clear and cloudy the image we see will be blurred. A cataract is not a tumor, nor is it a "film" or tissue, majority of cataracts are not visible to the naked eye, and pupil may appear White when the lens is completely clouded by a very dense cataract. Cataracts can form after surgery for other eye problems, such as glaucoma (Secondary cataract), it may develop after an eye injury (Traumatic

cataract), some babies are born with cataracts or develop them in childhood, often in both eyes (Congenital cataract) and exposure to some types of radiation causes the development (Radiation cataract). In recent years there many endogenous and exogenous that influence cataract formation are well documented but study related to routine biochemical parameters and its phenomenon were not known among different types of cataract.

Materials and Method

All patients were natives of south India and having the same ethnicity. About 25 samples in each groups were planned. This study was the part of a project which obtained permission from Institutional human ethical committee. Biochemical parameters were analyzed by the in-house

biochemistry laboratory. Experiments neither conducted nor examined directly on human individual for this purpose. Ethically sensitive data were totally omitted, only numerical and clinical data related information were accessed from

record. Table - 1 shows the selected biochemical parameters and their functions, metabolic and physiologic role which could possibly influence the rate of cataract formation. Experimental groups are given in Table - 2.

Table 1: List of Biochemical parameters

Profile	Metabolic role	Physiologic role	Parameters
Diabetic	Carbohydrate and Proteins	Glucose intolerance and Nitrogen balance	Glucose, Urea, Uric acid, Total Prot, Albumin
Lipid	Lipid	CVD and inflammation	TGL, Chol, HDL, LDL, CRP
Liver	Liver function	Toxicity and Tissues degenerative disorders	T Bili, D Bili, SGOT, SGPT, ALP, LDH
Minerals	Micro Nutrients	Deficiency diseases and mineral deposition	Ca, Cu, Fe, Mg, Zn
AGE	Glycosylation	Gene expressions and Oxidative stress	Fructose amine, Hb A1c

Table 2: Experimental groups

Group	Type of cataract	No. of Samples
I	Cortical	25
II	Nuclear Sclerotic	25
III	Posterior Subcapsular	24
IV	Mixed (Combination of any of the two or more)	25

There are three primary types of age-related cataracts: Nuclear Sclerotic, Cortical, and Posterior Subcapsular. When aging progress any one type, or in combination of these three types may develop over time.

Cortical cataract usually develop from the peripheral (outside) edge of the lens due to Changes in the water content of the lens fibers create clefts, or fissures, that look like the spokes of a wheel pointing from the outside edge of the lens in toward the center. These fissures can cause light scattering with blurred vision.

Nuclear Sclerotic is the most common type of age-related cataract. A nuclear sclerotic cataract progresses slowly and may require many years of gradual development. It develops slowly by the hardening and yellowing of the lens over time usually at the central portion of the lens. Sclerosis refers to the hardening of the lens nucleus.

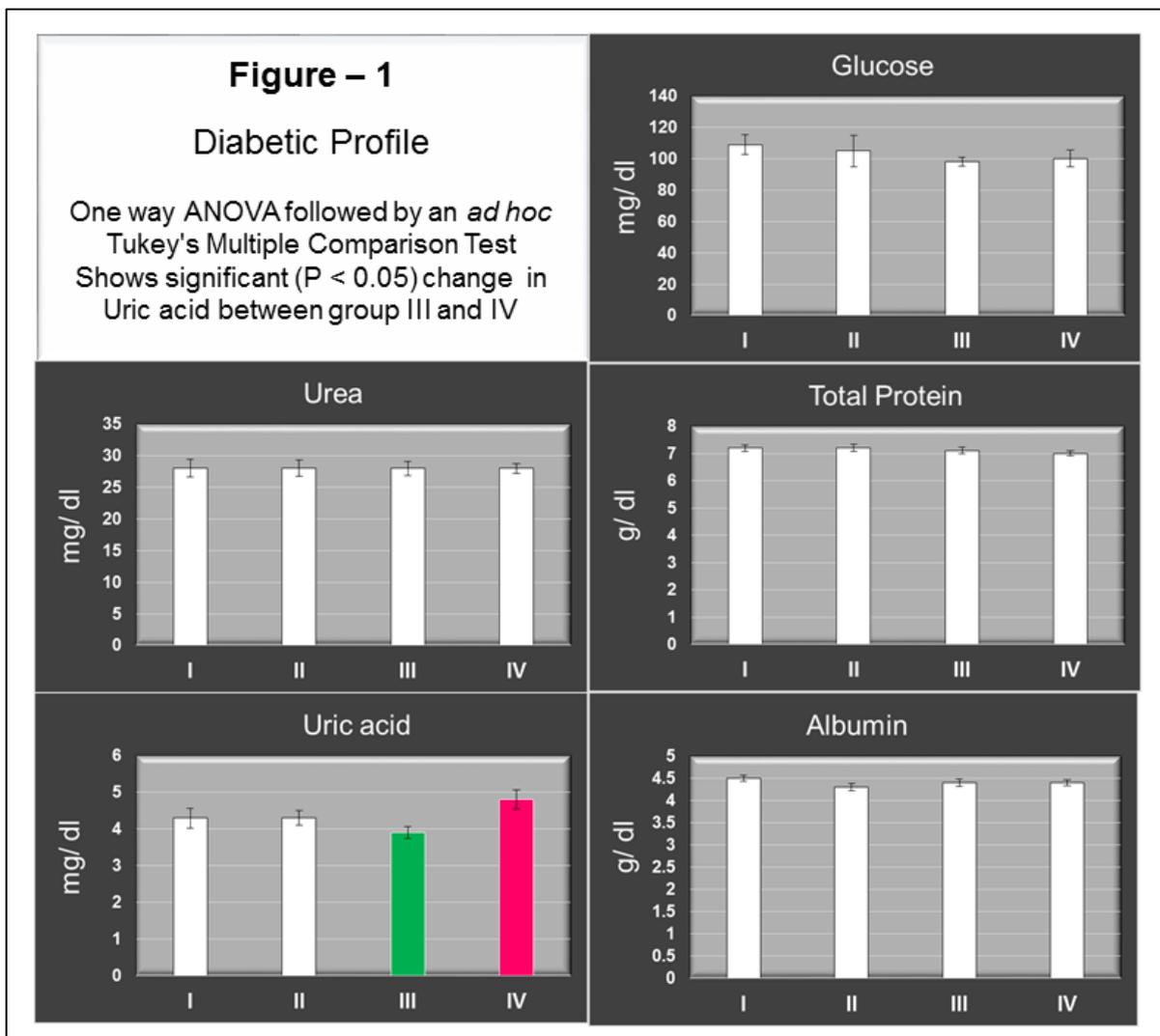
Posterior Subcapsular cataract begins to develop from back surface of the lens (subcapsular) because it forms beneath the lens capsule, which is a small "sac," or membrane. Diabetes, steroids usage,

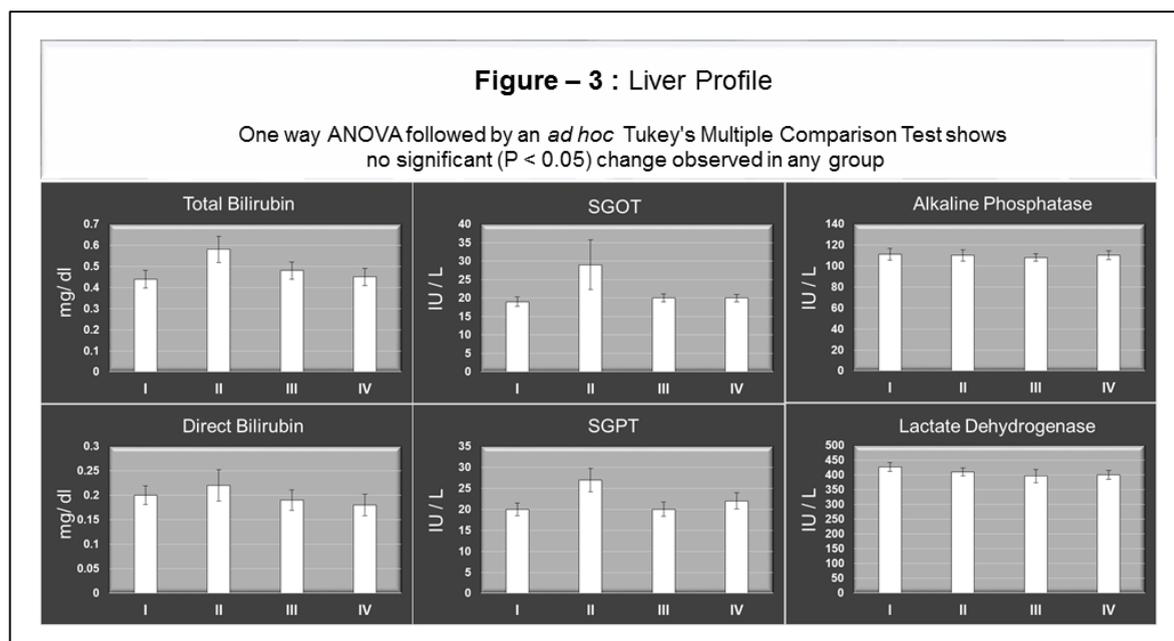
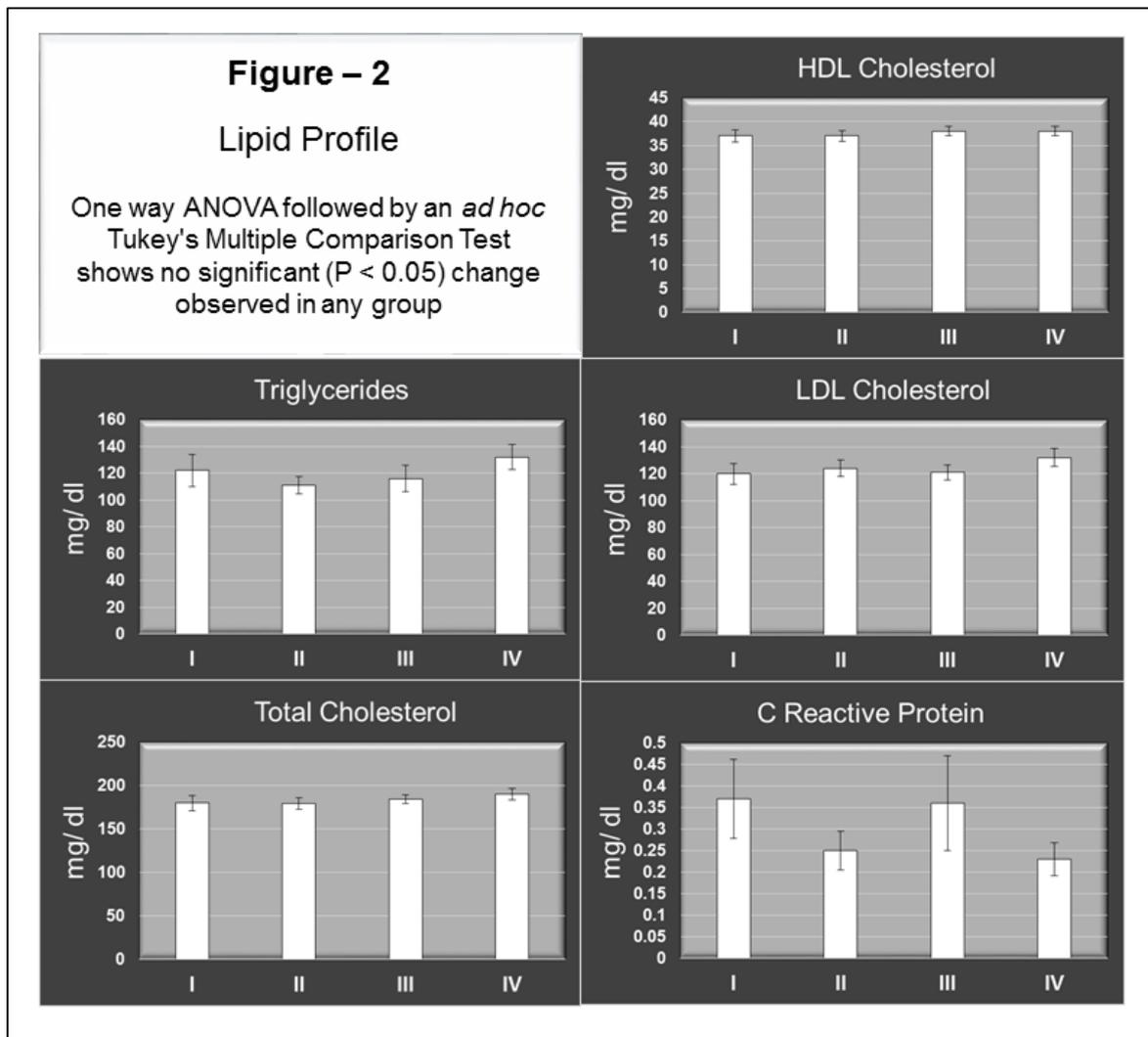
retinitis and extreme nearsightedness may develop this type of cataract. It can be noticeable within months.

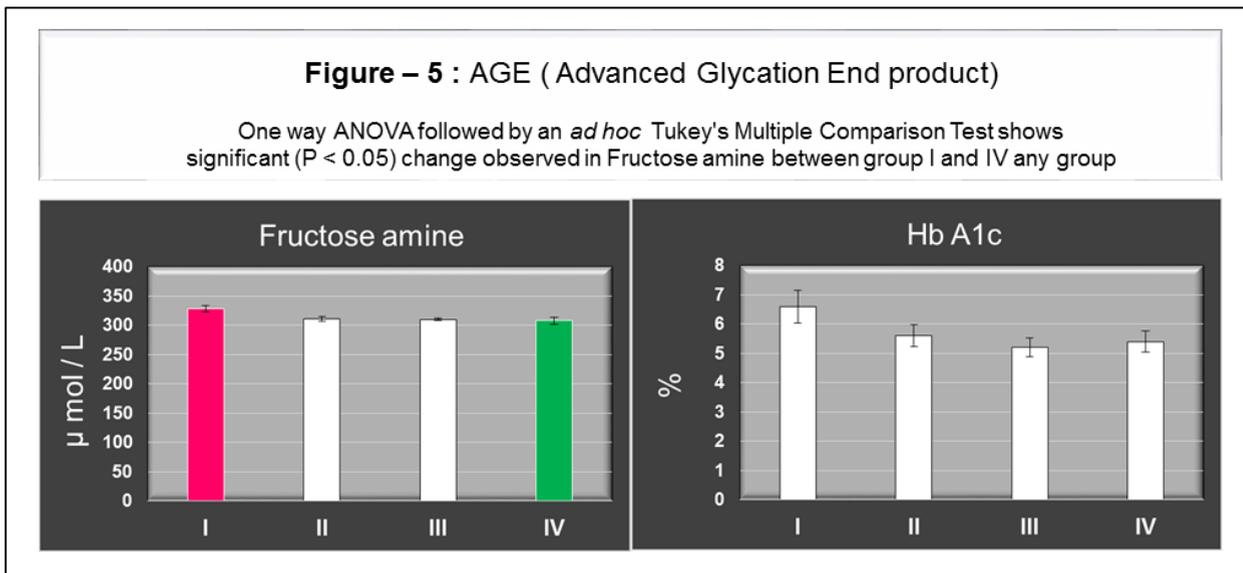
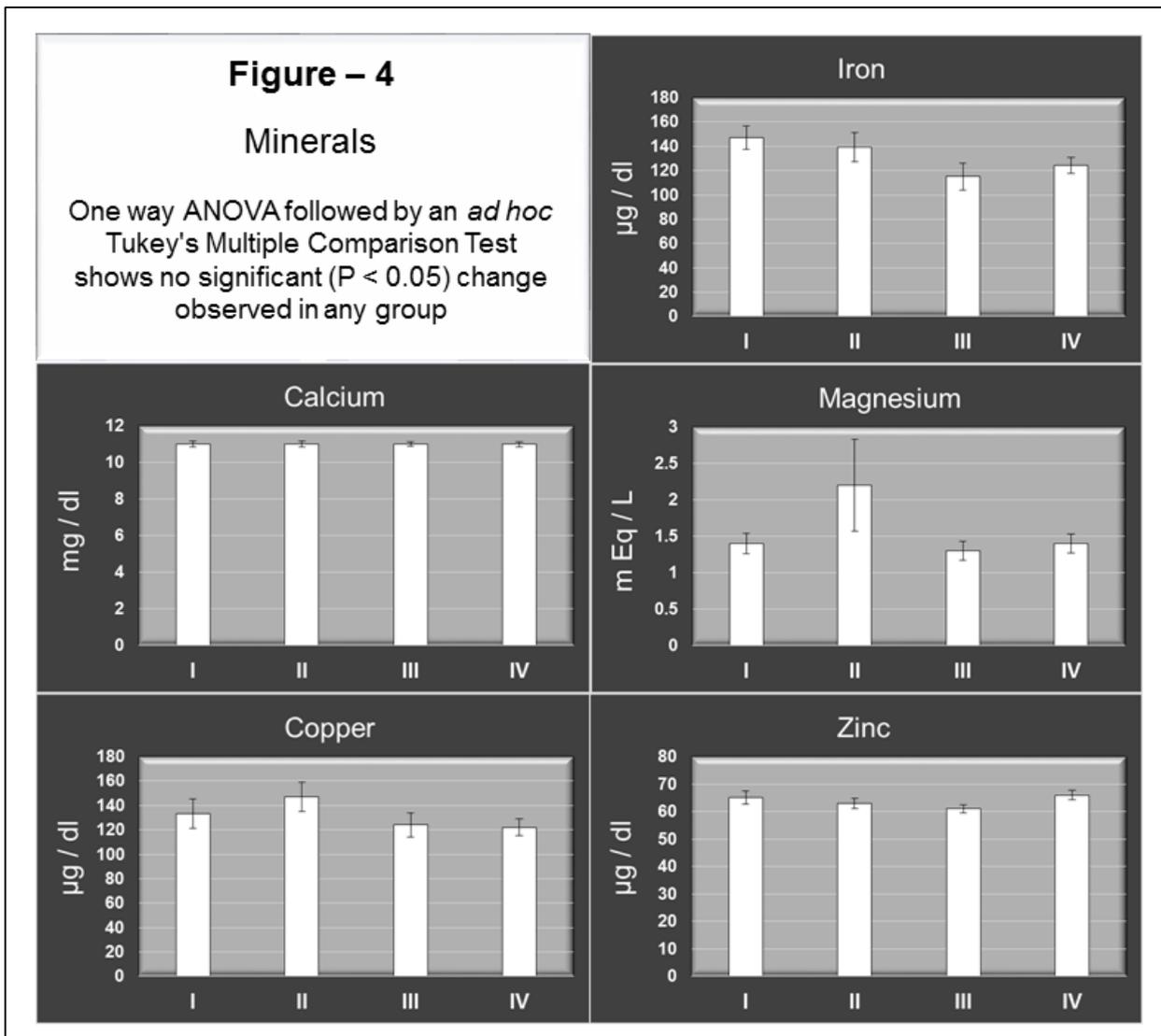
Interpreting results: Retrieved biochemical data from medical records were analyzed using statistical tools, one way ANOVA followed by an *ad hoc* Tukey's Multiple Comparison Test ($P < 0.05$) to compare variances. These tests were performed using GraphPad Prism version 5.00 for Windows, GraphPad Software, San Diego California USA, www.graphpad.com.

Results and Discussion

Results of the entire study is given in the figure 1- 6. Results indicated that there is no characteristics significance among different types of cataract in serum biochemical parameters analysed. This shows that the routine biochemical analysis are note the indicator of different cataract development. The recent reviews shows that there many others issues that play vital role in cataract formation even though their all routine biochemical parameters are normal. Some of such parameters and aspects are discussed under the respective headings below.







General consideration:

Causes of blindness varied substantially by region. Worldwide and in all regions more women than men were blind or had MSVI due to cataract and macular degeneration (Bourne et al. 2013).

Significant baseline risk factors were increasing age, smokeless tobacco use, and no history of cataract surgery. Incident monocular blindness was found in 132 participants, it was significantly more in the rural population than in the urban population (Vijaya et al. 2014).

Genetic factors

Congenital cataracts are one of the leading causes of visual impairment and blindness in children, and genetic factors play an important role in their development. This study aimed to identify the genetic defects associated with autosomal dominant congenital progressive punctate cataracts in a Chinese family and to explore the potential pathogenesis. Study presented genetic and functional evidence linking the new MIP mutation of G215D to autosomal dominant congenital cataracts, which adds to the list of MIP mutations linked to congenital progressive punctate cataracts (Ding et al. 2014).

To identify the genetic defects and investigate the possible mechanism of cataract genesis in a five-generation family with autosomal dominant congenital posterior polar cataracts. This study reported a novel c.59C > G (P20R) missense mutation in CRYAB in a five-generation Chinese family with posterior polar cataract (Xia et al. 2014).

Diseases

Retinal dystrophy and congenital glaucoma were the most common eye diseases. Heredity was the main etiology, and consanguinity was high. To decrease their incidence, awareness of the family members of the risks of consanguineous marriage and appropriate therapy for congenital glaucoma/ataract may significantly improve the child's visual prognosis (Chouchene et al. 2014).

Patients with POAG presenting for anterior segment surgery had a lower AG compared to age-related cataract surgery patients. The etiology of this reduced gap is unclear but the possible contribution of IgG warrants further exploration. The etiology of higher red blood cell counts in POAG cases is unknown and deserves further exploration (Cohen et al. 2014).

Therapeutic consequences

Metabolic changes in the rabbit lens have been studied by means of nuclear magnetic resonance spectroscopy. These changes have been induced by prolonged topical treatment with dexamethasone. Dexamethasone treatment induces a decrease in GSH. The decreasing or the loss of GSH has been suggested as a possible pathogenic mechanism in the cataract formation (Pescosolido et al. 2001).

AGE product and Antioxidants roles

Oxidative mechanisms are thought to have a major role in several biological phenomena, including cataract formation and diabetic complications. Glycation induced losses of antigenicity and inactivation simultaneously. The glycated enzymes had entirely lost their antigenicity compared with non-glycated enzyme. These results further support the idea that inactivation of enzyme and loss of antigenicity are simultaneous (Yan and Harding 1997).

Studies indicate that it is the biophysical response of the lens to osmotic stress that results in an increased intralenticular production of basic-FGF and TGF-beta and the altered cytotoxic signaling that is observed during sugar cataract formation (Zhang et al. 2012). Study indicate that dietary fructose disturbs lens integrity and exogenous CA may safeguard the lens by preventing glycation and oxidative stress (Balasaraswathi et al. 2008).

Protein glycation and formation of advanced glycation end products (AGEs) play an important role in the pathogenesis of diabetic complications like retinopathy. Glycation of proteins interferes with their normal functions by disrupting molecular

conformation, altering enzymatic activity, and interfering with receptor functioning. AGEs form intra- and extracellular cross linking not only with proteins, but with some other endogenous key molecules including lipids and nucleic acids. Recent studies suggest that AGEs interact with plasma membrane localized receptors for AGEs (RAGE) to alter intracellular signaling, gene expression, release of pro-inflammatory molecules and free radicals (Singh et al. 2014).

Oxidative mechanisms during nuclear sclerosis of the lens are poorly understood, in particular metal-catalyzed oxidation. The lysyl oxidation product adipic semialdehyde (allysine, ALL) and its oxidized end-product 2-amino adipic acid (2-AAA) were determined as a function of age. The findings strongly implicate dicarbonyl/metal catalyzed oxidation of lysine to allysine, whereby low GSH combined with ascorbate-derived H₂O₂ likely contributes toward 2-AAA formation, since virtually no 2-AAA formed in the presence of methylglyoxal instead of ascorbate. An important translational conclusion is that chelating agents might help delay nuclear sclerosis (Fan et al. 2009). Oxidative DNA damage may be one of the etiologies of age-related cataract (ARC). DNA damage in lens and peripheral blood lymphocytes increased in ARC. The results imply that local and systemic oxidative DNA damage might play certain roles in ARC pathogenesis (Zhang et al. 2014).

Gene expression and markers

Formyl peptide receptors (FPRs) are G protein-coupled receptors (GPCRs) expressed on a variety of cell types. These receptors play an important role in the regulation of inflammatory reactions and sensing cellular damage. They have also been implicated in the pathogenesis of various diseases, including neurodegenerative diseases, cataract formation, and atherogenesis (Schepetkin et al. 2014).

Alpha-Crystallin is a member of the small heat-shock protein (sHSP) family and consists of two subunits, alphaA and alphaB. Both alphaA- and alphaB-crystallin

act as chaperones and anti-apoptotic proteins. Intraperitoneal injection of the peptides inhibited cataract development in selenite-treated rats, which was accompanied by inhibition of oxidative stress, protein insolubilization, and caspase activity in the lens. These inhibitory effects were more pronounced for acetyl peptides than native peptides (Nahomi et al. 2013).

If the lens reducing environment is compromised, the ascorbylation of lens crystallins can significantly change the short range interactions between different classes of crystallins leading to protein aggregation, light scattering and eventually to senile cataract formation (Linetsky et al. 2008). The chaperone-like activity of alpha-crystallin is considered to play an important role in the maintenance of the transparency of the eye lens. Study indicates the susceptibility of alpha-crystallin to non-enzymatic glycation by various sugars and their derivatives and described the effects of glycation on the structure and chaperone-like activity of alpha-crystallin (Kumar et al. 2007).

Major decreases in protein connexin levels precede the development of cataracts. These mice represent a useful model for elucidation of the progression of lens abnormalities during cataractogenesis especially as caused by a mutant connexin (Berthoud et al. 2014). Activation of calpains (calpain 2 and Lp82) in rodent lenses readily causes proteolysis and cataract formation. In contrast, primate lenses are quite resistant to activation of calpains. The hypothesis is that high levels of human endogenous calpain inhibitor, calpastatin (CS), prevent calpain activation in human lenses. Age-related oxidation might cause loss of CS activity in human lens epithelial cells, allowing activation of long-dormant calpain 2, proteolysis of critical cytoskeletal proteins, and cataract formation (Nakajima et al. 2014). Overexpression Keap1 protein suppresses the Nrf2 protein through ERAD leading to suppression of Nrf2/Keap1 dependent antioxidant protection in the HLECs treated with sodium selenite. As an outcome, the cellular redox status is altered towards lens oxidation and results in cataract formation (Palsamy et al. 2014).

Conclusion

This study suggest that, there is a need to identify some simple markers from blood samples and exploring the fact behind the appearance of these markers which may be useful for diagnostic and prevention systems of health care market.

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