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Relationship between Human Age-Related Cataracts and Some Serum Routine Biochemical Parameters of Indian Population

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Abstract: *Formation of cataract is one of change in human aging process. Although it is common in all individuals the rate of development differ from each other due to many factors like life style, environmental and hereditary causes. All these factors are believed to make cataract through modified serum biochemical parameters and or capable of making impact on serum biochemical parameters. Hence, a study was programmed to measure the level of biochemical parameters for two study groups having clinically negative cataract as normal control group and positive cataract as diseased group. All patients were natives of south India and having the same ethnicity. About 100 samples in each groups were planned. Biochemical data were retrieved from medical records and analyzed by statistical tools, unpaired t test with Welch's correction - Two-tailed - P < 0.05 and F test to compare variances. Results indicated that there is a significant difference in serum biochemical parameters between normal control and diseased groups. The observed elevated parameters in diseased groups were Total protein, Cholesterol, LDL, CRP, SGOT, SGPT, ALP, LDH, Calcium, Copper, Magnesium and Iron in both T test and F test. This study suggest that monitoring these parameters at regular intervals may be helpful to prolong the duration of obvious development of cataract which require medical intervention.*

Keywords: *Cataract, Diabetic, Lipid, Liver, minerals, Biochemical parameters, Indian population.*

Introduction

Cataract is clouding of the eye lens that reduces the amount of incoming light and results in deteriorating vision. 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). The mean age of the global population is rising, and with this growth in the number of elderly, we are faced with greater challenges in meeting the health and nutritional needs of this expanding population group. One of the often seen consequences of the aging process is the development of senile cataract, a disease which affects one of our most precious gifts, that of sight. This so-called 'senile cataract', usually affecting those over 45 years of age, is the major cause of eye disorder and blindness worldwide (West SK and Valmadrid CT. 1995).

Although the causes of senile cataract are poorly understood, much of the biochemical data obtained from human blood or the lens gives rise to the hypothesis that the development of senile cataract is highly complex and depends on numerous factors such as genetic makeup, gender, diabetes, geographical location, exposure to UV light, level of education, occupational status and finally, the role of nutritional factors in the daily diet (Heiba et al 1995; Pierscionek BK and Weale RA. 1996; Leske et al 1997). Particular consideration has been given by many researchers to the underlying role of the nutritional status in the process of cataract formation and the

possibility that biochemical parameters can be used as markers to determine the risk involved for cataractogenesis, considering the fact that it is possible to modify these factors (Mansour and Issa 2003).

Although the development of cataract is common in all individuals the rate of development differ from each other due to many factors like life style, environmental and hereditary causes. All these factors are believed to make cataract through modified serum biochemical parameters and or capable of making impact on serum biochemical parameters. Hence, a study was programmed to measure the level of biochemical parameters for two study groups having clinically negative cataract as normal control group and positive cataract as diseased group.

Materials and method

All patients were natives of south India and having the same ethnicity. About 100 samples in each group 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 number of samples, male, female, types of cataract and groups. Table – 2 shows the selected biochemical parameters and their functions, metabolic and physiologic role which could possibly influence the rate of cataract formation.

Retrieved biochemical data from medical records were analyzed using statistical tools, unpaired t test with Welch's correction - Two-tailed - $P < 0.05$ and F test to compare variances. These tests were performed using GraphPad Prism version 5.00 for Windows, GraphPad Software, San Diego California USA, www.graphpad.com.

Interpreting results: Unpaired t (GraphPad)

The unpaired t test compares the means of two groups. The most useful result is the confidence interval for the difference between the means. If the assumptions of the analysis are true, you can be 95% sure that the 95% confidence interval contains the true difference between the means. The P value is used to ask whether the difference between the mean of two groups is likely to be due to chance. For the unpaired t test, the number of degrees of freedom (df) equals the total sample size minus 2. Welch's t test (a modification of the t test which doesn't assume equal variances) calculates df from a complicated equation.

F test for unequal variance (GraphPad)

The unpaired t test depends on the assumption that the two samples come from populations that have identical standard deviations (and thus identical variances). Prism tests this assumption using an F test. First compute the standard deviations of both groups, and square them both to obtain variances. The F ratio equals the larger variance divided by the smaller variance. So F is always greater than (or possibly equal to) 1.0.

Table1:
Sample distribution

Groups	Diseased								Normal	
Total	99								100	
Sex	Male				Female				Male	Female
	47				52				56	44
Types	CORTICAL	NSC	PSC	Mixed	CORTICAL	NSC	PSC	Mixed	Not applicable	
	11	10	11	15	14	15	13	10		

Table 2:
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

Results and Discussion

Carbohydrates and proteins play vital role in energy and maintenance mechanism of living system. The process of glycosylation resulting from the slow reaction of carbohydrates and proteins is an important step in ageing and degeneration. Table – 3 shows the parameters related to carbohydrates and proteins metabolism which shows the level of total protein was significantly higher in diseased group than the normal control followed by urea.

Table 3: Diabetic Profile

Glucose (mg/dl) Mean ±SEM		Urea (mg/dl) Mean ±SEM		Uric Acid (mg/dl) Mean ±SEM		Total Prot. (g/dl) Mean ±SEM		Albumin (g/dl) Mean ±SEM	
Control	Diseased	Control	Diseased	Control	Diseased	Control	Diseased	Control	Diseased
107 ±2.8	103 ±3.4	24* ±0.53	28* ±0.58	4.5 ±0.11	4.3 ±0.12	6.4*# ±0.036	7.1*# ±0.057	4.5 ±0.031	4.4 ±0.037

*Significant (Unpaired t test with Welch's correction - Two-tailed - $P < 0.05$)
Significant (F test to compare variances)

Soluble protein concentrations in lenses from undernourished patients were significantly lower as compared to those from well-nourished patients suggest that nutritional factors could influence the composition of cataractous lenses (Bhat 1982). Low total protein consumption as a risk factor that may account for as much as 40% of the excess prevalence of Punjab cataract over that in a US population study (Chatterjee et al. 1982).

Post-translational modifications of lens proteins play a crucial role in the formation of cataract during ageing. A study was conducted by Molnar et al. 2005 to analyze protein composition of the cataractous lenses by electrophoretic and high-performance liquid chromatographic (HPLC) methods. Presence of high-molecular weight protein aggregates in cataractous total homogenates, and a decrease of protein concentration in the water-soluble phase of cataractous lenses

The protein composition in aqueous humor was significantly different in Primary open angle glaucoma (POAG) patients versus non-POAG patients. The identified proteins could be a potential biomarker for POAG and may play a role in the mechanisms of elevated intraocular pressure and optic neuropathy in POAG (Duan et al. 2010).

A dependency was found between total protein content and cataract maturity (Kudryavtseva et al. 2012). Aqueous humour protein concentration was significantly higher in retinoblastoma patients than controls patients with secondary glaucoma presented the highest values. Although these results suggest that aqueous humour protein pattern in retinoblastoma is characteristic, several aspects of the study are still under investigation (Hadjistilianou et al. 2012).

Lipids are the important constituents of membranes and many intracellular components. However they have tendency to accumulate at the micro vascular system and block the circulatory supply which lead ischemia followed by inflammation and cell destruction. Table – 4 shows that there is a significantly elevated level of total cholesterol, Lactate Dehydrogenase (LDL) and C Reactive protein (CRP) in diseased group.

Table 4: Lipid Profile

TGL (mg/dl) Mean ±SEM		Chol (mg/dl) Mean ±SEM		HDL (mg/dl) Mean ±SEM		LDL (mg/dl) Mean ±SEM		CRP (mg/dl) Mean ±SEM	
Control	Diseased	Control	Diseased	Control	Diseased	Control	Diseased	Control	Diseased
113 ±5.1	120 ±4.9	174*# ±2.6	183*# ±3.4	39 ±0.63	38 ±0.55	114*# ±2.1	125*# ±3.3	0.15*# ±0.0086	0.30*# ±0.038

*Significant (Unpaired t test with Welch's correction - Two-tailed - P < 0.05)
Significant (F test to compare variances)

When a study was conducted with the aim of evaluating the quantitative change, if any, in the phospholipids and protein contents of lens proteolipids during cataract formation, and to establish whether the phospholipid/protein content of the blood is related to cataractogenesis. An alteration was also noticed in the protein content of proteolipids in the cataractous lenses. Changes were also observed in serum total phospholipids and total protein in cataractous patients. As proteolipids are the main constituents of the membranes of lens fibres, the alterations in its phospholipid and protein moieties may be suggestive of the disintegration of lens membranes, which ultimately leads to cataract formation. Gradual and constant variation in serum parameters may be one of the predisposing factors in cataractogenesis (Siddique et al. 2010).

A dependency was found between total protein content and cataract maturity. LPO intensity sharply increased and remained stably high after appearance of lens opacity. The content of conjugated dienes, crotonic aldehyde, and Schiff bases decreased during cataract development. The content of vitamins B (2), A, and E decreased with increasing brown coloration of lens nucleus. Some markers in the blood of patients with cataract change during progress of lens opacity and intensification of brown coloration of lens nucleus, but these changes are inspecific and reflect general activation of peroxidation processes and antioxidant system (Kudryavtseva, Chuprov, Ivanova, Tsapok, Tsibel', & Bojko 2012).

Assays of immune privilege markers in AqH suggest that PK surgery may result in a sustained loss of integrity of the blood-aqueous barrier. Studies determining additional immune privilege markers have to be conducted in order to find out whether these markers might serve as predictive parameters for immune reactions (Mo et al. 2012).

Hepatotoxicity and diagnostics important enzyme are good indicator of many degenerative diseases. Table – 5 shows that all enzymes subjected for experiment were significantly having higher activity in diseased group than the normal control. The level of bilirubin did not show any significant difference between study groups.

Table 5: Liver Profile

T. Bili (mg/dl) Mean ±SEM		D. Bili (mg/dl) Mean ±SEM		SGOT (IU/L) Mean ±SEM		SGPT (IU/L) Mean ±SEM		ALP (IU/L) Mean ±SEM		LDH (IU/L) Mean ±SEM	
Control	Diseased	Control	Diseased	Control	Diseased	Control	Diseased	Control	Diseased	Control	Diseased
0.53 ±0.020	0.49 ±0.024	0.20 ±0.012	0.20 ±0.012	18*# ±0.53	22*# ±1.8	19*# ±0.76	22*# ±1.1	87*# ±1.8	110*# ±2.3	316*# ±3.2	408*# ±8.4

*Significant (Unpaired t test with Welch's correction - Two-tailed - P < 0.05)
Significant (F test to compare variances)

Concentrations of various plasma constituents which might indicate dysfunctions associated with cataract. A constellation of three bilirubin, alkaline phosphatase, and gamma glutamyl transpeptidase--was significantly higher in the cataract group, suggesting subclinical liver dysfunction as a risk factor (Donnelly et al. 1995).

The causes of age-related cataract are multifactorial and particular

consideration has been given to the role of nutritional factors in cataract formation. Mean levels of total protein, bilirubin, calcium, sodium, alanine aminotransferase and alkaline phosphatase differed significantly between patient and control groups. It is possible that a gradual and constant variation in these parameters may be predisposing factors in cataractogenesis (Mirsamadi and Nourmohammadi 2003).

Minerals are the important elements for the activity of many metalloenzymes and proteins essential for normal cellular activities. Deposition of unutilized minerals may cause irreversible cell packing by precipitating proteins and forming crystalline mineral salts. The current study results are given in table – 6 which shows that there is a significantly elevated level of Calcium, Copper, Iron, Magnesium, and Zinc in diseased group than the normal control.

Table 6: Minerals Profile

Ca (mg/dl) Mean ±SEM		Cu (µg/dl) Mean ±SEM		Fe (µg/dl) Mean ±SEM		Mg (mEq/L) Mean ±SEM		Zn (µg/dl) Mean ±SEM	
Control	Diseased	Control	Diseased	Control	Diseased	Control	Diseased	Control	Diseased
9.0*# 0.093	11.0*# 0.071	108*# 10	132*# 5.2	108*# 2.8	132*# 5.2	2.1*# 0.020	1.6*# 0.17	85* 0.78	64* 0.94

*Significant (Unpaired t test with Welch's correction - Two-tailed - P < 0.05)
Significant (F test to compare variances)

Study was undertaken to isolate and characterize the protease activity of human eye lens sample of mature and hyper mature cataract. Effect of different metal ions such as potassium, lead, silver, zinc and borate was studied. In each case protease activity was increased (Sami et al. 2007). Increased activities of metalloproteinases 2 (MMP-2) in aqueous humour of patients with proliferative diabetic retinopathy (PDR) may be related to the disease process and support the hypothesis that MMP-2 may be of particular importance in diabetic retinal neovascularization (Klysik et al. 2010).

Conclusion

It is concluded that there is a significant difference in serum biochemical parameters between normal control and diseased groups and suggest that monitoring these parameters at regular intervals may be helpful to prolong the duration of obvious development of cataract which require medical intervention.

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