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CORRELATION OF CATARACT WITH BLOOD GLUCOSE, GALACTOSE, CALCIUM AND TOTAL PROTEINS

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ABSTRACT

We studied the blood plasma levels of Glucose, Galactose , Total Proteins and Calcium in 100 cataract patients and 45 controls . The studied analytes are significantly different in different study groups except Galactose. The Total Protein values are significantly lower and Calcium values are significantly higher in cataract cases compared to controls with out cataracts. The Total Protein values are significantly lower and Calcium values significantly higher in non-diabetic cataract cases compared to non-diabetic controls with out cataracts. The Glucose and Galactose values are not significantly different in these two groups. The Total Protein values are significantly lower in diabetic cataract cases compared to diabetic controls with out cataracts. The Glucose, Galactose and Calcium values are not significantly different in these two groups. Except for Glucose values there is no significant difference in studied analytes between diabetic cataract patients and non diabetic cataract patients. At their best cut-off values Total Proteins are best discriminatory markers as assessed by sensitivities, specificities and area under the curve values. No significant correlation is found between any of the analytes in any of the groups studied. Significant differences in Total Proteins and Calcium values suggest a role in cataractogenesis and in regular monitoring of cataract patients with these parameters. Sensitive methods to estimate low Galactose values are required to assess the significance. In diabetics hyperglycemia may not be the only factor that causing the cataract. Total Proteins are best discriminatory markers.

Key words: Cataract, Hyperglycemia, Oxidative stress, Nutritional status.

INTRODUCTION

Cataract is the leading cause of blindness all over the World [1]. In India alone 4 million people turn blind due to cataract every year [2] and visually significant cataract occurred 14 years earlier than in a comparable study in the United States [3]. Any opacity in the lens, whether it is a small localized one or one involving the entire lens, is known as cataract [4]. Cataract is an age related disorder and there is no medical treatment, so approaches have been taken to prevent or delay onset and the progression. While the majority of the cases occur in older age groups, young subjects are not exempt, and in them, the rate of maturation is faster [5]. Various risk factors have been identified in the pathogenesis of cataracts. Apart from ageing, genetic factors, nutrition, UV radiation and smoking have been implicated as significant risk factors in the causation of cataract. Influence of nutritional factors in the formation of cataract is more significant in a developing country like India [2]. Some of the nutrients implicated in the formation of cataract include Total Proteins, Glucose, Galactose and Calcium. The effect of low protein diet on the lens may not be highly cataractogenic, but its effect is additive to other forms of cataract [6]. Cataract formation in low protein diet is accelerated when galactose is included in the diet [2]. Diabetic patients have elevated levels of Glucose in their blood and other body fluids.

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Among its many complications, incidence of cataract formation is significantly higher in the diabetics compared with the normal population [7] .The rate of development of cataract is directly related to degree of hyperglycemia [8] and concentration of Glucose in aqueous humor.

Galactosemia an autosomal recessive condition, when there is deficiency of the enzyme galactose-1-phosphate uridyltransferase involved in the conversion of galactose to Glucose, and the galactose-1-phosphate accumulates in the lens, causing cataract. Cataractogenic action of milk lactose is dependent on the disturbance of galactose metabolism in elderly subjects [9]. Calcium, high or low can cause cataracts. Calcium can induce formation of protein aggregates in lens homogenates and such high molecular weight aggregates may lead to lens opacification [10]. The cure for cataract is surgery; however this surgery is not equally available to all [11]. Although quite effective it has its share of risks and limitations [3]. The occurrence of cataract at a comparatively early age in Indian population, the significant influence of nutritional factors in the formation of cataract, absence of medical therapy and non-equal availability of surgical therapy make more significant and appropriate measures to be taken to prevent cataract. The role of various factors in pathogenesis of cataract should be determined, so that steps can be taken to prevent this highly disabling disease. Therefore this cross sectional case control study is undertaken to know the biochemical role of some of the serum analytes as risk factors in the development of cataract.

MATERIALS AND METHODS

After obtaining permission from the institutional ethical committee, the study was undertaken in the Department of Biochemistry, Osmania general hospital/Osmania medical college, Hyderabad. Blood samples were collected from patients attending Sarojinidevi Eye hospital and Osmania general hospital after obtaining consent. The blood samples were analyzed for Glucose by Glucose oxidase peroxidase method, Galactose by orcinol method, Total Proteins by Biuret method and Calcium by Ortho cresolphthalein complexone method. The blood samples of the age, gender matched controls were also analyzed for the same parameters. Statistical analysis was done using SPSS statistical software.

RESULTS

A total number of 145 subjects were included in the present study. Of the 100 patients with cataracts recruited in the study, 20 were diabetics and 80 were non-diabetics. Of the 45 controls 20 were diabetics and 25 were non-diabetics. They had been grouped into six groups.

The Glucose and Galactose values are expressed in mg/dL of plasma, Calcium in mg/dL and Total Proteins in gm/dL of serum. The data has been statistically analyzed by calculating Mean and Standard Deviation. We analyzed the difference in means between different study groups using ANOVA. Independent samples ‘t’ test is used to assess the significance of difference in the means of values of different parameters in different groups.

We analyzed the difference in means between different study groups using ANOVA and student ‘t’ test and also calculated correlation coefficient (r) to assess correlation between different study parameters. The discriminatory capacity of different study parameters in differentiating different groups of study by calculating Best cut off values using ROC analysis.

Table 1. Distribution of Study Subjects

Sl. No.	Group	Type of Subjects	No. of Subjects
1	Group I	All Cases III &IV	100
2	Group II	All Controls V&VI	45
3	Group III	Non Diabetic cases	80
4	Group IV	Diabetic cases	20
5	Group V	Non Diabetic controls	25
6	Group VI	Diabetic controls	20

Table 2. Mean±SD, F and P values (ANOVA) for all parameters in all groups.

Sl. No	Group	Glucose (mg/dL)	Galactose (mg/dL)	Total Proteins (g/dL)	Calcium (mg/dL)
1	I	116.23±49.58	3.55±2.68	6.73±1.14	10.44±2.25
2	II	131.26±49.16	3.46±1.66	7.68±0.88	9.5±1.09
3	III	101.12±15.81	3.52±2.5	6.66±1.24	10.46±2.26
4	IV	176.65±83.48	3.67±3.37	7.02±0.88	10.35±2.3
5	V	97.8±14.61	3.72±1.84	7.74±0.84	9.29±1.05
6	VI	173.10±44.86	3.14±1.4	7.60±0.93	9.77±1.12
ANOVA					
F		17.534	0.156	9.925	2.937
P		0.000	0.978	0.000	0.013

The blood Glucose, Total Proteins and Calcium values are significantly different in different study groups compared. No statistically significant difference in blood Galactose values is present between different groups studied.

Table 3. Comparison between cases and controls

Sl. No.	Parameter	Groups	Mean±SD	t-value	p-value
1	Glucose	I II	116.23±49.58 131.26±49.16	1.70	0.09
2	Galactose	I II	3.55±2.68 3.46±1.66	0.24	0.81
3	Total Proteins	I II	6.73±1.18 7.68±0.88	5.34	0.00
4	Calcium	I II	10.44±2.25 9.50±1.09	3.37	0.00

The mean blood Glucose and Galactose values are not statistically significantly different in cases compared to controls. The mean serum Total Proteins values are significantly lower in cases compared to controls. The serum Calcium values are significantly higher in cases compared to controls.

Table 4. Comparison between cases and controls without Diabetes

Sl. No.	Parameter	Groups	Mean±SD	t-value	p-value
1	Glucose	III V	101.12±15.81 97.80±14.61	0.97	0.34
2	Galactose	III V	3.52±2.50 3.72±1.84	0.44	0.66
3	Total Proteins	III V	6.66±1.24 7.74± 0.84	4.94	0.00
4	Calcium	III V	10.46±2.26 9.29±1.05	3.58	0.00

The mean blood Glucose and Galactose values are not statistically significantly different in non-diabetic cases compared to non-diabetic controls. The serum Total Proteins values are significantly lower in non-diabetic cases compared to non-diabetic controls. The serum Calcium values are significantly higher in non-diabetic cases compared to non-diabetic controls.

Table 5. Comparison between Cases and Controls with Diabetes

Sl. No	Parameter	Groups	Mean±SD	t-value	p-value
1	Glucose	IV VI	176.65±83.48 173.10±44.86	0.17	0.87
2	Galactose	IV VI	3.67±3.37 3.14±1.40	0.65	0.52
3	Total Proteins	IV VI	7.02±0.88 7.60±0.93	1.10	0.05
4	Calcium	IV VI	10.35±2.30 9.77±1.12	1.01	0.32

The mean blood Glucose, Galactose and serum Calcium values are not statistically significantly different in diabetic cases compared to diabetic controls. The serum Total Proteins values are significantly lower in diabetic cases compared to diabetic controls.

Table 6. Comparison between Cases with Diabetes and Cases without Diabetes

Sl. No.	Parameter	Groups	Mean±SD	t-value	p-value
1	Glucose	III IV	101.12±15.81 176.65±83.48	4.03	0.00
2	Galactose	III IV	3.52±2.50 3.67±3.37	0.19	0.86
3	Total Proteins	III IV	6.66±1.24 7.02±0.88	1.49	0.14
4	Calcium	III IV	10.46±2.26 10.35±2.30	0.21	0.84

The mean blood Galactose and serum Total Proteins and Calcium values are not statistically significantly different in diabetic cases compared to non-diabetic cases. The serum Glucose values are significantly lower in diabetic cases compared to non-diabetic cases.

Table 7. Best Cutoff value, Sensitivity, Specificity and Area Under the Curve for cases and controls

Analyte	Best Cutoff Value	Sensitivity (%)	Specificity (%)	Area Under the Curve
Glucose	109.5 mg%	48	73	0.606
Galactose	2.85 mg%	62	61	0.551
Total Proteins	7.3 gm%	71	65	0.732
Calcium	7.7mg%	97	18	0.312

The Total Proteins exhibited best discriminatory capacity in discriminating cases from controls, among the studied parameters.

Table 8. Best Cutoff value, Sensitivity, Specificity and Area Under the Curve for cases and controls without diabetes

Analyte	Best Cutoff Value	Sensitivity (%)	Specificity (%)	Area Under the Curve
Glucose	88.5 mg%	84	20	0.456
Galactose	3.4 mg%	60	70	0.573
Total Proteins	6.75 gm%	92	50	0.751
Calcium	7.35mg%	100	14	0.282

The Total Proteins exhibited best discriminatory capacity in discriminating non-diabetic cases from non-diabetic controls, among the studied parameters.

Table 9. Best Cutoff value, Sensitivity, Specificity and Area Under the Curve for cases and controls with diabetes

Analyte	Best Cutoff Value	Sensitivity (%)	Specificity (%)	Area Under the Curve
Glucose	163.5 mg%	65	60	0.549
Galactose	2.8 mg%	55	70	0.549
Total Proteins	7.5 gm%	60	80	0.681
Calcium	8.0mg%	100	25	0.355

The Total Proteins exhibited best discriminatory capacity in discriminating diabetic cases from diabetic controls, among the studied parameters.

Table 10. Best Cutoff value, Sensitivity, Specificity and Area Under the Curve for cases with diabetes and cases without diabetes

Analyte	Best Cutoff Value	Sensitivity (%)	Specificity (%)	Area Under the Curve
Glucose	126.5 mg%	70	95	0.815
Galactose	6.65 mg%	15	91	0.467
Total Proteins	6.15 gm%	90	43	0.586
Calcium	12.75mg%	20	90	0.485

The Total Proteins exhibited best discriminatory capacity in discriminating diabetic cases from non-diabetic cases, at best cut-off values, among the studied parameters. No significant correlation is found between any of the analytes studied in any of the groups.(p is not significant).

DISCUSSION

Cataract, opacity of the eye lens, is the most common cause of blindness worldwide [4] and accounts for more than 80% of the cases of blindness in India [2]. Lens protein aggregation and oxidative stress have been suggested as the main mechanisms in the development of cataract [12]. Despite the existence of cataract surgery for several years and despite it being an easily curable affliction, cataract continues to remain a major public health problem. The risk factors for the disease include age, genetics, nutritional inadequacies, diabetes, sunlight and other environmental factors [2]. Except age and genetics, other risk factors are preventable or at least modifiable. In our country there is high prevalence of malnutrition among older population. Various studies have shown that the nutritional status of a person determines his/her predisposition to cataract [3].

Many studies attempted to correlate various blood plasma analytes to the presence and development of human cataract [13]. In the present study we have analyzed the levels of Glucose, Galactose, Total Proteins and Calcium levels and studied their correlation with cataract and studied the capacity of these markers to discriminate cases from controls. In the present study the blood plasma Glucose, Total Proteins and Calcium values are significantly different in different study groups. However, the differences observed in Galactose values between different study groups are not statistically significant.

Diabetes is known to be associated with cataract since long. Direct in-vivo and in-vitro experiments suggest that diabetes is a cause of cataract. Epidemiological studies in the past showed that diabetes causes a more rapid maturation of cataract, but may not trigger its initiation. However recent studies suggest that initiation and maturation of cataract are not totally different processes [2]. Small fluctuations in external Glucose levels can cause increased membrane permeability to Glucose, which in turn activate mechanisms that initiate diabetic cataract.

Elevated Glucose is associated with myopic changes indicative of increased lens volume [14]. Increased Glucose concentration in lens causes it to be converted to sorbitol by enzymes aldose reductase and polyol dehydrogenase. Sorbitol once formed cannot diffuse out of the lens and water also enters into the lens to neutralize hyper osmolarity. This causes changes in refractive index of lens [12]. It was proposed that protein glycosylation due to presence of increased Glucose, which causes changes in the chemical structure and conformation of lens crystalline, exposes the free sulfhydryl groups. This makes disulphide linkages to be formed and causes protein precipitation.

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 [15]. Studies by Naseem H Ansari, shows that the quantity of the disulphide bridges does not correlate with extent of glycosylation of Proteins, which is greater in diabetic cataracts [16]. Hence, it is not conclusive that how protein glycosylation could cause lens protein aggregation and precipitation.

Oxidative stress, due to oxygen free radicals, is known to be involved in cataract generation. Oxygen free

radicals may cause deactivation of sulfhydryl dependent enzyme systems, aggregation of Proteins by forming protein-protein disulphide bridges or change lens colour, forming chromophores. Disruption of membrane may also be caused by oxidative stress [12]. Direct oxidation of Glucose is not involved in increased oxidative stress. Activation of hexosamine and polyol pathway, protein kinase C and AGE formation are the mechanisms implicated in increased oxidative stress in diabetes [17]. Similarly, it is found an association between cataract and high levels of oxidative stress among cases than the control group [18].

Patterson, concluded that, his results ruled out hyperglycemia as the direct mediator in the production of diabetic cataract [19]. Though we found significantly higher Glucose in diabetic cataracts than non-diabetic cataracts, there was no significant difference between Glucose levels of diabetic controls and diabetic cataracts or between non-diabetic controls and non-diabetic cataracts. Hence other mechanisms might also play a role in the pathogenesis of the diabetic cataract.

Some adults who consume large quantities of milk have high lactase activity, due to mutation in the gene coding for lactase, and galactose is absorbed in large quantities [20]. Galactose is acted upon by galactokinase but Fredrick J Simmon, showed that RBC galactokinase activity is low in elderly patients[9]. Such persons suffer repeated Galactose challenge [20]. Galactose is metabolized by aldose reductase to galactitol, which is similar to sorbitol and accumulates in the lens and causes hyperosmolarity. In galactosaemia this is one of the primary mechanisms of cataract. K. Sitharam Bhat and Gopalan stated that increased galactose levels are seen in a significant number of cataract patients [21] and suggest that this could also be one of the risk factors of cataract. It has also been shown that cataractous lens contains more galactose than Glucose [22]. We found higher Galactose levels in diabetic cataract patients than in diabetic controls and in cataract cases compared to controls. However this difference in Galactose is not statistically significant. This may be partly due to the probable insensitivity of the method used at low levels find in this study.

Prevalence of severe Protein Energy Malnutrition is higher in cataract patients [22,3]. Low intake of Proteins is shown to be associated with cataract and higher protein intake is protective against cataract [2]. Poor nutrition causes lens protein solubilization. Alpha crystallins in the lens bind to and protect other Proteins from precipitation [23] and this may also be affected by protein restriction, though not substantially. Hence lower protein intake and low Total protein levels may have an additive impact on cataract pathogenesis. Protein malnutrition leads to a decrease in serum Proteins. We found a significantly lower Total protein levels in cataract patients compared to controls. This is in agreement with earlier reports. Lower Total Proteins are seen in diabetic cataracts compared to diabetic controls, indicating that Proteins may have additive effect in diabetic cataractogenesis.

Alterations in Calcium levels are long known to be associated with cataract [24]. Hypercalcemia of extra cellular fluids leads to cataract formation. The activity and extent of opacification correlate well with the increase in Calcium bound to membranes and insoluble Proteins. Calcium can induce the formation of protein aggregates in lens homogenates [10], and Calcium phosphate precipitation may also lead to cataract formation. Stability of protein gel depends on maintaining a low internal level of Calcium. Lenses with normal sodium and increased Calcium were associated with localized lens opacities [24]. Many studies have shown increased Calcium levels in cataract patients. But lens permeability changes leading to cataract are known to occur with decreased Calcium [24]. Significantly higher Calcium levels in cataract patients compared to controls. Significantly higher Calcium levels are seen in non-diabetic cataract patients compared to controls. Hence Calcium levels may have a primary role in pathogenesis of cataract in non-diabetic cases than in diabetic cases. Correlations between studied parameters were reported in earlier studies. No significant correlation is found between any of the analytes in any of the groups in the present study. In the present study we found that serum Total Proteins are better discriminatory factors between cataract cases and controls

CONCLUSION

The blood plasma Glucose, Total Proteins and Calcium values are significantly different in different study groups. Serum Total Proteins are significantly decreased and serum Calcium levels are significantly increased in cataract patients compared to controls. These alterations are also good discriminatory markers between cataract patients and controls.

Total Proteins is the best discriminatory marker in our study. In diabetics hyperglycaemia may not be the only cause of cataract. Higher Galactose levels in all cataract cases indicates that it may have a role to play in senile cataractogenesis.

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CONFLICT OF INTEREST: NIL

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