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ORIGINAL RESEARCH ARTICLE

Impact of clinico-biochemical variations on the etiopathogenesis of cataract: a case-control study

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ABSTRACT

Purpose: Cataract is a major cause of blindness worldwide with a greater prevalence in developing countries like India. Owing to speculations about the relationship of various biochemical markers and cataract formation this case-control study was designed with the aim to know the impact of serum blood sugar, serum electrolytes and serum calcium on the etiopathogenesis of cataract in Kashmiri population.

Methods: A total of 300 cases diagnosed with cataract and 360 healthy controls were taken for the study. Serum of all the cases and controls was analyzed for blood sugar and calcium using spectrometric techniques. Sodium and potassium were analyzed using Ion-Selective Electrode technology. All the investigations were done on *ABBOTT c4000* fully automatic clinical chemistry analyzer.

Results: Most of the patients in our study were ≥50 years of age having posterior subcapsular cataract. The mean levels of serum fasting blood sugar (mg/dL), serum sodium (mmol/L), serum potassium (mmol/L) and serum calcium (mg/dL) were 99.4 ± 7.7; 140.4 ± 2.5; 4.2 ± 0.5; and 8.9 ± 0.5, respectively, in cases compared to 107.7 ± 12.3; 142.9 ± 5.0; 3.8 ± 0.5; and 8.3 ± 1.7, respectively, in healthy controls. A significantly higher number of cataract cases had elevated serum glucose and sodium levels, low serum potassium and calcium levels compared to healthy controls.

Conclusions: Hyperglycemia, hypernatremia, hypokalemia and hypocalcemia can independently increase the patients' risk to cataracts. Corrections in these biochemical parameters may reduce cataract incidence.

Keywords: Blood pressure, Blood sugar, Calcium, Cataract, Intraocular pressure, Potassium, Sodium

Introduction

The International Agency for the Prevention of Blindness has defined cataract as the clouding or opacification of the normally clear lens of the eye or its capsule that obscures the passage of light through the lens to the retina (1,2). This disease, which can significantly reduce patient's quality of life, is still one of the main ophthalmic public health conditions in developed and developing countries (3). Cataracts are mainly divided into nuclear cataract (NC), cortical cataract (CC), posterior sub capsular (PSC) cataract, acquired cataract and congenital cataract (4). Senile cataract is one of the common types of acquired cataract which occurs as a consequence of the aging process. It is characterized by initial opacity in the lens with subsequent swelling of lens and final shrinkage with complete loss of transparency (5). Cataract is detected by an eye examination that includes a visual activity test, slit lamp exam (SLE) and dilated eye exam (6).

Worldwide, cataract has caused >50% vision loss including 33.4% blind people and 18.4% people with moderate to severe visual impairment. Globally 10.8 million people were blind and 35.1 million people were visually impaired from cataract in 2010 (7). Additionally, data from the World Health Organization (WHO) has estimated that this number will increase to 40 million in 2025 due to the aging populations with greater life expectancies (8). Up to 50 million people in

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the world suffer from senile cataract (9,10), and its prevalence in developing countries is much more than in developed ones (11). In India, the prevalence of blindness due to cataract was reported to be 8% in the age group of >50 years, as per the National blindness survey (12). An estimated 20 lakh new cases of cataract are being added to the burden every year in this country, showing a steep rise ranging from 0.5% above 30 years to 94.5% above 70 years (13). Cataract accounts for 62.6% of all blindness, affecting 9-12 million bilaterally blind persons (14). The WHO/NPCB (National Programme for Control of Blindness) survey has shown that there are over 22 million blind in India and 80.1% of these are blind due to cataract (15).

Cataract is caused by degeneration and opacification of the lens fibers already formed. Any factor that disturbs the critical intra- and extracellular equilibrium of water and electrolytes or deranges the colloid system within the fibers tends to bring about opacification (16). Several studies have been carried out to elucidate risk factors which are responsible for development of cataract. Extensive research has established age, ion imbalance, altered calcium levels, diabetes and UV light exposure as causative risk factors for cataract, while recent studies have identified other potential risk factors like exogenous estrogen, nutrition, dietary fat and genetics which might play a role in the development of cataract (17). Although cataract affects all age groups its incidence increases with advancing age (18). Senile cataract affects equally persons of either gender, usually above the age of 50 years (19). The association between diabetes and cataract formation has been shown in clinical, epidemiological and basic research studies. Due to increasing numbers of type 1 and type 2 diabetics worldwide, the incidence of diabetic cataracts steadily rises (20). Several clinical studies have shown that cataract development occurs more frequently and at an earlier age in diabetic compared to nondiabetic patients (20). Many studies have shown that serum electrolyte (potassium and sodium) concentration directly affects the concentration of electrolytes in aqueous humor and thereby induces cataract formation. Concentration of sodium in lens is less compared to serum concentrations whereas it is vice versa in case of potassium concentrations, and this cationic balance is maintained by the osmotic pressure and thus water balance by the action of enzyme Na^+/K^+ ATPase. Any imbalance in between the electrolytes leads to cataract formation (21). Calcium is of particular concern in cataract. This cation is essential for various lens fiber cell metabolism processes (22). It has been shown that lens calcium content correlates with opacity in cataractous human lenses (23) and subsequent changes in serum calcium concentration might be an important factor in the development of cataract (24).

Demographic and clinico-biochemical biomarkers have been previously linked with the development of cataract from other parts of the world, but so far only few studies have been reported from the Indian subcontinent regarding the interrelationship of cataract (25,26). Keeping in view the ethnicity and relatively conserved genetic pool of Kashmiri population, this case-control study was designed to elucidate the role of demographic and clinico-biochemical parameters in the etiopathogenesis and severity of cataract in Kashmiri population.

Materials and methods

Ethics

This study was performed in line with the principles of the Declaration of Helsinki. Ethical clearance for the study was sought from Institutional Review Board, Government of Medical College Srinagar vide No. 2022T/ETH/GMC. All the patients included in the study were informed about the study and informed consent both in vernacular as well as in English language was taken before eliciting history and sample collection from study subjects. Standard questionnaire or patient proforma was properly recorded and drafted as per socio-demographic and clinico-biochemical parameters. The authors affirm that human research participants provided informed consent for publication of their details.

Study design

This was a case-control study conducted by the Department of Biochemistry in collaboration with the Department of Ophthalmology, Government Medical College Srinagar and associated SMHS hospital Srinagar, J&K, from March 2020 to March 2022.

Study subjects and sample size

The study was conducted in ethnic population of Kashmir; no restrictions were made among patients with respect to gender and dwelling. A total of 300 patients diagnosed with cataract and 360 healthy controls were enrolled for the study. Keeping the power of study as 80% and allocation ratio of 1.2 and effect size of 0.4, the sample size was calculated by G power 23.0.1 version.

Inclusion and exclusion criteria

"Cases" included all those individuals who were >18 years of age and diagnosed with cataract. "Cases" excluded all those individuals with any other eye ailment and symptomatic disease (liver, kidney, heart or other), trauma, infection, inflammation of eye, cancer or any other genetic abnormality. "Controls" included healthy individuals >18 years of age.

Ophthalmic examination

Each patient was subjected to various ophthalmic measurements. Uncorrected visual acuity was measured with Snellen chart. Refraction was done and the best corrected visual acuity was noted. Intraocular pressure (IOP) measurement was done with non-contact tonometer. Corrected IOP was calculated after measuring central corneal thickness by ultrasonic pachymetry. Detailed anterior segment examination using slit lamp was done to rule glaucoma and associated ocular pathology. Detailed fundus examination under full mydriasis obtained by 0.8% tropicamide and 5% phenylephrine was done with direct ophthalmoscopy, 78D and indirect ophthalmoscopy.

Sample collection

A total of 04 mL of venous blood was collected from each cataract patient and healthy control in a coagulation activating red top vial. Blood was collected from each individual after 8-10 hours of fasting. Blood was immediately centrifuged for separation of serum. Serum was properly stored at –20°C till biochemical analysis was done in the Biochemistry diagnostic laboratory, SMHS hospital Srinagar.

Biochemical analysis for electrolytes

Serum electrolyte levels were estimated on *ABBOTT ARCHITECT c4000* fully automated clinical chemistry analyzer using Ion-Selective Electrode. The reference ranges of serum sodium levels were taken between 135 and 145 mmol/L and serum potassium levels as 3.5-4.5 mmol/L.

Biochemical analysis for calcium

Serum calcium levels were estimated spectrophotometrically on *ABBOTT ARCHITECT c4000* fully automated clinical chemistry analyzer using Arsenazo III dye. The reference ranges of serum calcium were taken as: 8.5-10.2 mg/dL.

Biochemical analysis of glucose

Serum glucose levels were measured spectrophotometrically on ABBOTT ARCHITECT c4000 fully automated clinical chemistry analyzer. Glucose is phosphorylated by hexokinase (HK) in the presence of adenosine triphosphate (ATP) and magnesium ions to produce glucose-6-phosphate (G6P) and adenosine diphosphate (ADP). Glucose-6-phosphate dehydrogenase (G6PDH) specifically oxidizes G6P to 6-phosphogluconate with the concurrent reduction of nicotinamide adenine dinucleotide (NAD) and readily to nicotinamide adenine dinucleotide reduced (NADH). One micromole of NADH is produced for each micromole of glucose consumed. The NADH produced absorbs light at 340 nm and can be detected spectrophotometrically as an increased absorbance. The reference ranges of serum glucose were taken as: 99-100 mg/dL (normal) and >100 mg/dL (impaired).

Statistical analysis

The data was analyzed using IBM Statistical Package for the Social Sciences (SPSS) software v. 25.0. Descriptive statistics was performed and data was presented as frequency (N) and percentage (%). Continuous data was presented as mean and standard deviation. Chi-square test was used to compare proportions between groups as deemed proper by the statistical expert. P value <0.05 was considered statistically significant.

Results

Table I contains the socio-demographic and clinicopathological characteristics of cataract cases and healthy controls. Cases and controls were matched with respect to age and gender; 17.5% (63 of 360) of the controls were <50 years of age as compared to 21% (63 of 300) of cases who were <50 years of age. With respect to gender, 47.5% (171 of 360) controls were men as compared to 52.0% (156 of 300) of men having cataract. Accordingly, 90.0% (324 of 360) of the controls were inhabitants of rural areas as compared to 80% (240 of 300) of cases who belonged to rural areas. The cataract patients were evaluated for various clinical parameters. Hypertension was present in 13.0% (39 of 300) of cataract patients. The family history of cataract was present in 4.0% (12 of 300) of cases. The history of any other eye disorder was present in 23.0% (69 of 300) of cataract cases. Further the IOP of all the patients was measured wherein 91.0% (273 of 300) had normal IOP while 9.0% (27 of 300) had higher IOP.

TABLE I - Socio-demographic and clinicopathological characteristics of cases having cataract and controls included in the study

–	Controls N = 360 (%)	Cases N = 300 (%)	χ^2	p value
Age group				
<50 years	63 (17.5)	63 (21.0)	1.2	0.15
≥50 years	297 (82.5)	237 (79.0)		
Gender				
Men	171 (47.5)	156 (52.0)	1.3	0.15
Women	189 (52.5)	144 (48.0)		
Dwelling				
Rural	324 (90.0)	240 (80.0)	13.1	<0.0001
Urban	36 (10.0)	60 (20.0)		
Hypertension				
No	–	261 (87.0)	–	–
Yes		39 (13.0)		
Family history of cataract				
No	–	288 (96.0)	–	–
Yes		12 (4.0)		
H/o any other eye disorder				
No	–	231 (77.0)	–	–
Yes		69 (23.0)		
Eyes affected				
One	–	177 (59.0)	–	–
Both		123 (41.0)		
Type of cataract				
Nuclear		00 (0.0)		
Cortical	–	75 (25.0)	–	–
Posterior subcapsular		225 (75.0)		
Grade				
I and II	–	165 (55.0)	–	–
III and IV		135 (45.0)		
IOP				
Normal	–	273 (91.0)	–	–
High		27 (9.0)		

H/o = history of; IOP = intraocular pressure.

Table II depicts the biochemical parameters of cataract cases and healthy controls; 69.0% (207 of 300) of cases had impaired blood sugar level as compared to 22.5% (81 of 360) of controls having impaired blood sugar, and the association was found to be statistically significant (p<0.0001); 36.3% (109 of 300) of cases had hypernatremia as compared to only 3.0% (11 of 360) of controls with hypernatremia (p<0.0001). Cataract cases had significantly low potassium levels compared to controls (17.5% vs. 6.1%; p<0.0001). In addition, 38.0% (114 of 300) of cases had hypocalcemia as compared to only 12.5% (45 of 360) of controls with hypocalcemia and the difference was statistically significant (p<0.0001).

TABLE II - Biochemical parameters of cataract cases and healthy controls

Parameters	Controls N = 360 (%)	Cases N = 300 (%)	OR (95% CI)	p value
Fasting blood sugar				
Normal	279 (77.5)	93 (31.0)	7.6 (5.4-10.8)	<0.0001
Impaired	81 (22.5)	207 (69.0)		
Sodium levels				
Normal	349 (97.0)	191 (63.7)	18.1 (9.5-34.4)	<0.0001
High	11 (3.0)	109 (36.3)		
Potassium levels				
Normal	338 (93.9)	249 (83.0)	3.1 (1.9-5.3)	<0.0001
Low	22 (6.1)	51 (17.0)		
Calcium levels				
Normal	315 (87.5)	186 (62.0)	4.2 (2.9-6.3)	<0.0001
Low	45 (12.5)	114 (38.0)		

CI = confidence interval; OR = odds ratio.

Table III shows the mean levels of various biochemical parameters in cases and healthy controls. A statistically significant difference was observed between cases and controls with respect to mean fasting blood sugar levels in mg/dL (107.7 ± 12.3 vs. 99.4 ± 7.7); mean sodium levels in mmol/L (142.9 ± 5.0 vs. 140.4 ± 2.5); mean potassium level in mmol/L (3.8 ± 0.5 vs. 4.2 ± 0.5); mean calcium level in mg/dL (8.3 ± 1.7 vs. 8.9 ± 0.5).

TABLE III - Levels (mean ± SD) of various biochemical parameters in cataract cases and healthy controls

Parameters	Controls (mean ± SD)	Cases (mean ± SD)	p value
Fasting blood sugar (mg/dL)	99.4 ± 7.7	107.7 ± 12.3	<0.0001
Sodium levels (mmol/L)	140.4 ± 2.5	142.9 ± 5.0	<0.0001
Potassium levels (mmol/L)	4.2 ± 0.5	3.8 ± 0.5	<0.0001
Calcium levels (mg/dL)	8.9 ± 0.5	8.3 ± 1.7	<0.0001

SD = standard deviation.

Table IV shows the association of fasting blood sugar levels with various socio-demographic, clinico-pathological and biochemical parameters of cataract patients and controls. In each subgroup of age, gender, dwelling, sodium, potassium and calcium levels, a statistically significant difference in serum blood levels was noted between cases and controls (p<0.0001). Among patients with PSC cataract, 72.0% (162 of 225) had impaired blood sugar level as compared to CC wherein only 60% (45 of 75) had impaired blood sugar, and the difference was statistically significant (p = 0.05). No association was found between blood sugar levels and any other parameter of cases and controls.

Table V describes the association of serum sodium levels with various socio-demographic, biochemical and clinicopathological parameters of cataract cases and controls. A statistically significant difference in serum sodium levels was noted between cases and controls in each subgroup of age, gender, dwelling, potassium and calcium levels (p<0.0001). Among cataract patients with grade I and II disease, 41.2% (68 of 165) had high sodium levels while among cataract patients with grade III and IV disease, only 30.4% (41 of 135) had high sodium levels and the difference was statistically significant (p = 0.05). We did not observe any other parameter influencing the sodium levels in cataract patients.

Table VI displays the association of serum potassium levels with various socio-demographic, clinicopathological and biochemical parameters of cataract patients and controls. Among cases, 20% (48 of 240) of rural inhabitants had low potassium levels as compared to 6.5% (21 of 324) of rural control subjects having low potassium levels (p<0.0001). With respect to calcium level, 31.6% (36 of 114) of hypocalcemia cases had hypokalemia as compared to only 2.2% (01 of 45) of hypocalcemia controls having hypokalemia, and the difference was statistically significant (p<0.0001). Among hypertensive cases, 15.4% (18 of 39) had hypokalemia but among normotensive cases only 12.6% (21 of 261) had hypokalemia, and the difference was statistically significant (p<0.0001). Importantly, 33.3% (09 of 27) cases having high IOP were hypokalemic but among cases having normal IOP, only 15.4% (42 of 273) had hypokalemia, and the difference was statistically significant (p<0.0001). No association was found between serum potassium levels and any other parameter of cases and controls.

Table VII depicts the association of serum calcium levels with various socio-demographic, clinicopathological and biochemical parameters of cataract cases and controls. A statistically significant difference in calcium levels was noted between cases and controls in each subgroup of age, gender and dwelling (p<0.0001). We did not observe any other parameter influencing the calcium levels in cataract patients.

Discussion

We evaluated cataract patients with respect to various socio-demographic, clinicopathological and biochemical characteristics. As aging itself is a major risk factor for the development of cataract in both women and men (27), most of the cataract patients were from the age group of ≥50 years. It has been suggested that with aging the alteration

TABLE IV - Association of fasting serum glucose levels with various socio-demographic, biochemical and clinicopathological parameters of cataract cases and controls

Socio-demographic/ clinicopathological/ biochemical parameters	Fasting serum glucose levels in controls			Fasting serum glucose levels in cases			OR (95% CI)	p value
	N = 360 (%)	Normal 279 (77.5)	Impaired 81 (22.5)	N = 300 (%)	Normal 93 (31.0)	Impaired 207 (69.0)	7.6 (5.4-10.8)	<0.0001
Age group								
<50 years	63 (17.5)	57 (90.5)	06 (9.5)	63 (21.0)	17 (27.0)	46 (73.0)	25.7 (9.3-70.4)	<0.0001
≥50 years	297 (82.5)	222 (74.7)	75 (25.3)	237 (79.0)	76 (32.1)	161 (67.9)	6.2 (4.2-9.1)	<0.0001
Gender								
Men	171 (47.5)	141 (82.5)	30 (17.5)	156 (52.0)	48 (30.8)	108 (69.2)	10.5 (6.2-17.7)	<0.0001
Women	189 (52.5)	138 (73.0)	51 (27.0)	144 (48.0)	45 (31.3)	99 (68.8)	5.9 (3.6-9.5)	<0.0001
Dwelling								
Rural	324 (90.0)	255 (78.7)	69 (21.3)	240 (80.0)	75 (31.3)	165 (68.8)	8.1 (5.5-11.9)	<0.0001
Urban	36 (10.0)	24 (66.7)	12 (33.3)	60 (20.0)	18 (30.0)	45 (70.0)	4.6 (1.9-11.3)	<0.001
Sodium levels								
Normal	349 (97.0)	270 (77.4)	79 (22.6)	191 (63.7)	58 (30.4)	133 (69.6)	7.8 (5.2-11.6)	<0.0001
Elevated	11 (3.0)	09 (81.8)	02 (18.2)	109 (36.3)	35 932.1)	74 (67.9)	9.5 (1.9-46.3)	0.002
Potassium levels								
Normal	338 (93.9)	261 (77.2)	77 (22.8)	249 (83.0)	84 (33.7)	165 (66.3)	6.6 (4.6-9.5)	<0.0001
Low	22 (6.1)	18 (81.8)	04 (18.2)	51 (17.0)	09 (17.6)	42 (82.4)	21 (5.7-77.1)	<0.0001
Calcium levels								
Normal	315 (87.5)	246 (78.1)	69 (21.9)	186 (62.0)	60 (32.3)	126 (67.7)	7.4 (4.9-11.2)	<0.0001
Low	45 (12.5)	33 (73.3)	12 (26.7)	114 (38.0)	33 (28.9)	81 (71.1)	6.7 (3.1-14.6)	<0.0001
Hypertension								
No	–	–	–	261 (87.0)	78 (29.9)	183 (70.1)		0.3
Yes				39 (13.0)	15 (38.5)	24 (61.5)	0.6 (0.3-1.3)	
Family history of cataract								
No	–	–	–	288 (96.0)	84 (29.2)	204 (70.8)		0.002
Yes				12 (4.0)	009 (75.0)	03 (25.0)	0.13 (0.03-0.5)	
H/o any other eye disorder								
No	–	–	–	231 (77.0)	72 (31.2)	159 (68.8)		1.000
Yes				69 (23.0)	21 (30.4)	48 (69.6)	1.03 (0.5-1.8)	
Eyes affected								
One	–	–	–	177 (59.0)	57 (32.2)	120 (67.8)		0.6
Both				123 (41.0)	36 (29.3)	87 (70.7)	1.1 (0.6-1.8)	
Type of cataract								
Cortical	–	–	–	75 (25.0)	30 (40.0)	45 (60.0)		0.05
Posterior subcapsular				225 (75.0)	63 (28.0)	162 (72.0)	1.7 (0.9-2.9)	
Grade								
I and II	–	–	–	165 (55.0)	45 (27.3)	120 (72.7)		0.1
III and IV				135 (45.0)	48 (35.6)	87 (64.4)	0.6 (0.4-1.1)	
IOP								
Normal	–	–	–	273 (91.0)	81 (29.7)	192 (70.3)		0.12
High				27 (9.0)	12 (44.4)	15 (55.6)	0.5 (0.2-1.1)	

CI = confidence interval; H/o = history of; IOP = intraocular pressure; OR = odds ratio.

TABLE V - Association of serum sodium levels with various socio-demographic, biochemical and clinicopathological parameters of cataract cases and controls

Socio-demographic/ clinicopathological/ biochemical parameters	Serum sodium levels in controls			Serum sodium levels in cases			OR (95% CI)	p value
	N = 360 (%)	Normal 349 (97.0)	High 11 (3.0)	N = 300 (%)	Normal 191 (63.7)	High 109 (36.3)	18.1 (9.5 -34.4)	<0.0001
Age group								
<50 years	63 (17.5)	63 (100.0)	0 (0.0)	63 (21.0)	25 (39.7)	38 (60.3)	–	<0.0001
≥50 years	297 (82.5)	286 (96.3)	11 (3.7)	237 (79.0)	166 (70.0)	71 (30.0)	11.1 (5.7-21.5)	<0.0001
Gender								
Men	171 (47.5)	162 (94.7)	09 (5.3)	156 (52.0)	99 (63.5)	57 (36.5)	10.3 (4.9-21.8)	<0.0001
Women	189 (52.5)	187 (98.9)	02 (1.1)	144 (48.0)	92 (63.9)	52 (36.1)	52.8 (12.5-221.7)	<0.0001
Dwelling								
Rural	324 (90.0)	314 (96.9)	10 (3.1)	240 (80.0)	150 (62.5)	90 (37.5)	18.8 (9.5-37.2)	<0.0001
Urban	36 (10.0)	35 (97.2)	01 (2.8)	60 (20.0)	41 (68.3)	19 (31.7)	16.2 (2.0-127.3)	<0.0001
Potassium levels								
Normal	338 (93.9)	329 (97.3)	09 (2.7)	249 (83.0)	162 (65.1)	87 (34.9)	19.6 (9.6-39.9)	<0.0001
Low	22 (6.1)	20 (90.9)	02 (9.1)	51 (17.0)	29 (56.9)	22 (43.1)	7.1 (3.8-13.3)	<0.0001
Calcium levels								
Normal	315 (87.5)	304 (96.5)	11 (3.5)	186 (62.0)	121 (61.5)	65 (34.9)	14.8 (7.5-29.0)	<0.0001
Low	45 (12.5)	45 (100.0)	00 (0.0)	114 (38.0)	70 (61.4)	44 (38.6)	–	<0.0001
Hypertension								
No	–	–	–	261 (87.0)	165 (63.2)	96 (36.8)		0.7
Yes				39 (13.0)	26 (66.7)	13 (33.3)	0.9 (0.4-1.7)	
Family history of cataract								
No	–	–	–	288 (96.0)	184 (63.9)	104 (36.1)		0.7
Yes				12 (4.0)	07 (58.3)	05 (41.7)	1.2 (0.3-4.0)	
H/o any other eye disorder								
No	–	–	–	231 (77.0)	153 (66.2)	78 (33.8)		0.11
Yes				69 (23.0)	38 (55.1)	31 (44.9)	1.6 (0.9-2.7)	
Eyes affected								
One	–	–	–	177 (59.0)	119 (67.2)	58 (32.8)		0.14
Both				123 (41.0)	72 (58.5)	51 (41.5)	1.4 (0.9-2.3)	
Type of cataract								
Cortical	–	–	–	75 (25.0)	53 (70.6)	22 (29.3)		0.16
Posterior subcapsular				225 (75.0)	138 (61.3)	87 (38.6)	1.5 (0.8-2.6)	
Grade								
I and II	–	–	–	165 (55.0)	97 (58.8)	68 (41.2)		0.052
III and IV				135 (45.0)	94 (69.6)	41 (30.4)	0.6 (0.3-1.0)	
IOP								
Normal	–	–	–	273 (91.0)	175 (64.1)	98 (35.9)		0.6
High				27 (9.0)	16 (59.3)	11 (40.7)	1.2 (0.5-2.7)	

CI = confidence interval; H/o = history of; IOP = intraocular pressure; OR = odds ratio.

TABLE VI - Association of serum potassium levels with various socio-demographic, biochemical and clinicopathological parameters of cataract cases and controls

Socio-demographic/ clinicopathological/ biochemical parameters	Serum potassium levels in controls			Serum potassium levels in cases			OR (95% CI)	p value
	N = 360 (%)	Normal 338 (93.9)	Low 22 (6.1)	N = 300 (%)	Normal 249 (83.0)	Low 51 (17.0)	3.1 (1.9-5.3)	<0.0001
Age group								
<50 years	63 (17.5)	62 (98.4)	01 (1.6)	63 (21.0)	48 (76.2)	15 (23.8)	19.3 (2.4-151.8)	<0.0001
≥50 years	297 (82.5)	276 (92.9)	21 (7.1)	237 (79.0)	201 (84.8)	36 (15.2)	2.3 (1.3-4.1)	<0.0003
Gender								
Men	171 (47.5)	163 (95.3)	08 (4.7)	156 (52.0)	132 (84.6)	24 (15.4)	3.7 (1.6-8.5)	<0.0001
Women	189 (52.5)	175 (92.6)	14 (7.4)	144 (48.0)	117 (7.4)	27 (18.8)	2.8 (1.4-5.7)	<0.0002
Dwelling								
Rural	324 (90.0)	303 (93.5)	21 (6.5)	240 (80.0)	192 (80.0)	48 (20.0)	3.6 (2.0-6.2)	<0.0001
Urban	36 (10.0)	35 (97.2)	01 (2.8)	60 (20.0)	57 (95.0)	03 (5.0)	1.8 (0.1-18.4)	1.000
Calcium levels								
Normal	315 (87.5)	294 (93.3)	21 (6.7)	186 (62.0)	171 (91.9)	15 (8.1)	1.2 (0.6-2.4)	0.6
Low	45 (12.5)	44 (97.8)	01 (2.2)	114 (38.0)	78 (68.4)	36 (31.6)	20.3 (2.6-153.2)	<0.0001
Hypertension								
No	–	–	–	261 (87.0)	228 (87.4)	21 (12.6)		<0.0001
Yes				39 (13.0)	33 (84.6)	18 (15.4)	5.9 (2.8-12.2)	
Family history of cataract								
No	–	–	–	288 (96.0)	240 (83.3)	48 (16.7)		0.4
Yes				12 (4.0)	09 (75.0)	03 (25.0)	1.6 (0.4-6.3)	
H/o any other eye disorder								
No	–	–	–	231 (77.0)	195 (84.4)	36 (15.6)		0.27
Yes				69 (23.0)	54 (78.3)	15 (21.7)	1.5 (0.7-2.9)	
Eyes affected								
One	–	–	–	177 (59.0)	150 (84.7)	27 (15.3)		0.35
Both				123 (41.0)	99 (80.5)	24 (19.5)	1.3 (0.7-2.4)	
Type of cataract								
Nuclear								
Cortical	–	–	–	75 (25.0)	57 (76.0)	18 (24.0)		0.07
Posterior subcapsular				225 (75.0)	192 (85.3)	33 (14.7)	0.5 (0.2-1.0)	
Grade								
I and II	–	–	–	165 (55.0)	132 (80.0)	33 (20.0)		0.16
III and IV				135 (45.0)	117 (86.7)	18 (13.3)	0.6 (0.3-1.1)	
IOP								
Normal	–	–	–	273 (91.0)	231 (84.6)	42 (15.4)		0.051
High				27 (9.0)	18 (66.7)	09 (33.3)	2.7 (1.1-6.5)	

CI = confidence interval; H/o = history of; IOP = intraocular pressure; OR = odds ratio.

TABLE VII - Association of serum calcium levels with various socio-demographic, clinicopathological and biochemical parameters of cataract patients and controls

Socio-demographic/ clinicopathological/ biochemical parameters	Serum calcium levels in controls			Serum calcium levels in cases			OR (95% CI)	p value
	N = 360 (%)	Normal	Low	N = 300 (%)	Normal	Low		
		315 (87.5)	45 (12.5)		186 (62.0)	114 (38.0)	4.2 (2.9-6.3)	<0.0001
Age group								
<50 years	63 (17.5)	54 (85.7)	09 (14.3)	63 (21.0)	40 (63.5)	23 (36.5)	3.4 (1.4-8.2)	0.007
≥50 years	297 (82.5)	261 (81.7)	36 (12.1)	237 (79.0)	146 (61.6)	91 (38.4)	4.5 (2.9-6.9)	<0.0001
Gender								
Men	171 (47.5)	147 (86.0)	24 (14.0)	156 (52.0)	96 (61.5)	60 (38.5)	3.8 (2.2-6.5)	<0.0001
Women	189 (52.5)	168 (88.9)	21 (11.1)	144 (48.0)	90 (62.5)	54 (37.5)	4.8 (2.7-8.4)	<0.0001
Dwelling								
Rural	324 (90.0)	282 (87.0)	42 (13.0)	240 (80.0)	144 (60.0)	96 (40.0)	4.4 (2.9-6.7)	<0.0001
Urban	36 (10.0)	33 (91.7)	03 (8.3)	60 (20.0)	42 (70.0)	18 (30.0)	4.7 (1.2-17.3)	0.02
Hypertension								
No	–	–	–	261 (87.0)	168 (64.4)	93 (35.6)		0.3
Yes				39 (13.0)	18 (46.2)	21 (53.8)	2.1 (1.0-4.1)	
Family history of cataract								
No	–	–	–	288 (96.0)	180 (62.5)	108 (37.5)		0.3
Yes				12 (4.0)	06 (50.0)	06 (50.0)	1.6 (0.5-5.2)	
H/o any other eye disorder								
No	–	–	–	231 (77.0)	147 (63.6)	84 (36.4)		0.3
Yes				69 (23.0)	39 (56.5)	30 (43.5)	1.3 (0.7-2.3)	
Eyes affected								
One	–	–	–	177 (59.0)	114 (64.4)	63 (35.6)		0.3
Both				123 (41.0)	72 (58.5)	51 (41.5)	1.2 (0.7-2.0)	
Type of cataract								
Nuclear								
Cortical	–	–	–	75 (25.0)	51 (68.0)	24 (32.0)		0.2
Posterior subcapsular				225 (75.0)	135 (60.0)	90 (40.0)	1.4 (0.8-2.4)	
Grade								
I and II	–	–	–	165 (55.0)	99 (60.0)	66 (40.0)		0.4
III and IV				135 (45.0)	87 (64.4)	48 (35.6)	0.8 (0.5-1.3)	
IOP								
Normal	–	–	–	273 (91.0)	171 (62.6)	102 (37.4)		0.5
High				27 (9.0)	15 (55.6)	12 (44.4)	1.3 (0.6-2.9)	

CI = confidence interval; H/o = history of; IOP = intraocular pressure; OR = odds ratio.

in membrane permeability of the lens epithelium coupled with the changes in sodium and potassium ion levels in aqueous humor may accentuate ionic imbalance within the lens and lead to the development of cataract (28). In our study, a slightly higher percentage of men population was affected compared to women. According to different studies, women are more prone to getting most types of cataract than men. This is most likely due to lower estrogen levels after menopause in women (29). In our study, proportion of rural participants diagnosed with cataract was much higher compared to urban participants, which may be due to the differential exposure to contextual factors (30). Furthermore, we speculate that rural areas lack quality healthcare and hygiene, hence putting inhabitants at more risk of developing cataract and its related complications. Our results are in line with the observations from other parts of the country reporting significantly higher incidence of cataract in rural areas (31). We observed only 13.0% of the cataract cases to be hypertensive, but according to Lee et al hypertension could induce conformational changes to proteins in lens capsules,

thereby exacerbating the cataract formation (32). Per previous reports, the risk of cataract increases with long-standing hypertension (33). Furthermore, some studies suggest that antihypertensive medications (such as diuretics and beta-blockers) are related to cataract (34). In our study, only few cataract patients had a family history of cataract. Our findings are consistent with epidemiological studies demonstrating more prevalent occurrence of age-related cataracts in close relatives of cataract patients than in the general population (35). In addition, genetic studies have shown the effect of specific genes in the development of cataractous lenses (35). Only one eye was affected in most of the cataract patients, which supports the previous findings that cataract may be present in one or both eyes but cannot spread from one eye to another (36). Most of the enrolled patients were having PSC cataract, which is the most common morphological form of cataract (37) and commonly studied across the country (38). PSC cataract produces more and faster vision deterioration than other forms of cataract, and patients report earlier for cataract surgery, which may be a potential explanation for its elevated prevalence (39).

Various studies are going on all over the world to clarify the relationship between biochemical elements and cataract formation (40), and most of the studies from different populations have not found a remarkable difference in blood biochemical elements between cataract patients and healthy controls (41-43). To further explore the biochemical intricacies of cataract we evaluated the cases as well as controls for various biochemical markers and deduced the relationship, if any, between the disease development and biochemical markers. As evident from the dataset, most of the cataract patients in our study were having significantly impaired fasting blood sugar levels compared to controls. A previous study has found a significant relationship between hyperglycemia and incidence of cataracts (44). *In vivo* or *in vitro* studies showed evidence that diabetes mellitus is the cause of cataract (45,46). Cataracts have multiple etiologies, one of which is chronic hyperglycemia which has been related to many systemic and ocular complications such as loss of vision. It has been suggested that the polyol via which the enzyme aldose reductase catalyzes the reduction of glucose into sorbitol is a central part of the mechanism of cataract development. The increased intracellular accumulation of sorbitol leads to a hyperosmotic effect, resulting in hydropic lens fibers that degenerate and form cataract (47,48). In our study population, the frequency of cataract patients having hypernatremia was significantly higher compared to controls, which is in line with the study conducted by Mathur and Pai who reported significant hypernatremia in cataract patients compared to the controls (49). Since the lens metabolism is associated with aqueous humor, which itself is produced from blood secretions, serum electrolyte concentration directly affects electrolytes of aqueous humor and in turn lens metabolism (26). Studies have upheld that, in case of increased concentrations of sodium in aqueous humor, it is difficult for the sodium pumps to maintain a low intracellular sodium ion level. In turn, a higher sodium ion concentration of the aqueous humor, coupled with an altered membrane permeability of lens, increases the intracellular sodium ion concentration leading to hydration of the lens, thereby resulting in loss of its transparency and development of cataract (50). In the current study, we observed hypokalemia in significantly higher number of cataract patients compared to controls. Several studies revealed strong association of low serum potassium levels with CCs (51,52). According to Duncan and Bushell, cortical and mature cataracts had very low serum potassium levels (53). The frequency of hypocalcemia in cataract cases was significantly higher compared to controls. Low serum calcium levels in cataract patients were seen in other populations, clearly supporting our results (54). Cataract is the most common ocular symptom of hypocalcemia (55). Seemingly, because of deposition of calcium in soft tissues producing reduced vision/cataract or calcification of basal ganglia, calcium gets depleted in human serum (56).

In the further part of the study we deciphered the effect of various factors on the relationship between biochemical parameters and cataract. Surprisingly none of the factors significantly affected the relationship of serum glucose, serum sodium and serum calcium with cataract. In addition, we have also identified various factors modifying the association between hypokalemia and cataract. The frequency of hypokalemic rural cataract patients was significantly higher compared to rural hypokalemic controls. Difference in mean serum potassium concentrations among Kashmiri cataract cases and healthy controls residing in rural locations might be due to difference in the quality of diet among the two groups (56,57). Interestingly we observed a significantly higher proportion of hypokalemic cataract patients coexistent with hypocalcemia. Although hypokalemia and hypocalcemia exhibit multiple interrelated acid-base and electrolyte abnormalities such as hypophosphatemia, respiratory/metabolic alkalosis, mixed acid-base disorders (58), the coexistence of these in cataract has not yet been reported and debated upon. Further, hypokalemia was significantly associated with hypertension in cataract patients. Even though the association of hypokalemia and hypertension has been previously reported (33,34), the common causes of hypertension with hypokalemia have been well established, which include essential hypertension with diuretic use, primary aldosteronism, Cushing's syndrome, pheochromocytoma, renal vascular disease and malignant hypertension (59). Therefore, patients with coexistent hypertension and hypokalemia need to be evaluated further to establish the reason for the development of cataract.

Conclusion

In conclusion, serum glucose, sodium, potassium and calcium levels were identified as the potentially modifiable parameters deranged in cataract. In future, large-scale studies to enhance the battery of biochemical markers and to establish cause and effect relationship between biochemical markers and cataract need to be done.

Limitation of the study

The sample size of the study is relatively modest.

Disclosures

Conflict of interest: The authors disclose that there are no financial or non-financial interests that are directly or indirectly related to the work submitted for publication.
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