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Serum Calcium-Magnesium Ratio In Patients With Senile Cataract At A Tertiary Care Hospital In Puducherry Population

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ABSTRACT:
Background: Cataract is a leading cause of visual impairment and the senile cataract is the most common type. The role of Serum calcium to magnesium ratio (Ca-Mg ratio) in the pathogenesis of age-related or senile cataract remains unclear.
Objectives: The objective of the present study is to estimate serum calcium, magnesium and their ratio levels in Senile cataract patients compared to normal healthy individual without cataract and to find out association of serum magnesium and calcium-magnesium ratio with risk of senile cataract.
Subjects and methods: This case-control study consists of 90 Age-related cataracts (ARC) as cases and 90 age and gender matched normal healthy individuals without cataract as controls (age group above 45 years). The ARC patients were sub-grouped into nuclear cataract (NC), cortical cataract (CC), posterior sub-capsular cataract (PSC) and mixed cataract according to WHO cataract grading system. Serum calcium was determined by Arsenazo III method and serum magnesium by xylidyl blue method using Hitachi 902 autoanalyser.
Results: The study shows significantly decreased concentration of serum magnesium and increased concentration of calcium-magnesium ratio ($p<0.001$) in ARC when compared to control. Pearson's correlation analysis showed a significant negative correlation of serum magnesium with calcium was observed. Serum calcium-magnesium ratio was statistically

identified as risk factors in ARC patients by using Multivariate logistic regression analysis (odds ratio, 5.177; 95% confidence interval, 0.483–2.805; p=0.006).
Conclusion: Decreased serum magnesium concentration and increased serum calcium-magnesium ratio were significantly associated with a high risk of cataract formation in patients with age-related cataract.
Keywords: Calcium-magnesium ratio, serum magnesium, Age-related cataract, Senile cataract

1. INTRODUCTION

Cataract is defined as opacity of the crystalline lens, and the most common cause of visual impairment and blindness globally [1]. Age-related cataract (ARC) or Senile cataract (SC) is a multifactorial and the most common type of cataract, which develops in elderly people. Several mechanisms have been proposed for the development of cataract in elderly individuals, but the exact mechanism remains unclear.

Growing evidence highlighted the role of electrolyte imbalance in the development of cataracts and particularly concern to Calcium. Alteration in calcium concentration might be an important factor in the development of cataracts[2]. Calcium is an essential cation for various lens-fiber cell-metabolic processes [3] and high calcium level leads to alterations in the molecular structure and increased light scattering of the lens [4] which correlates with opacity in human cataractous lenses [5]. Nonetheless, previous literature reported inconsistent in serum calcium levels were observed in senile cataract patients.

On contrary, Membrane transport mechanism utilizing several magnesium (Mg)-dependent ATPases, play an important role in maintaining lens homeostasis [6]. Alternation in magnesium concentration also might be an important factor in the development and progression senile cataract is still unknown. However, the association between serum magnesium and calcium- magnesium ratio with age-related cataract remains unclear. Hence, the present study, plan to investigate serum calcium, magnesium and their ratio and to find out their association with risk of development of Age-related cataract compared to normal healthy individuals without cataract.

2. MATERIALS AND METHODS

This case-control study was carried out in the Department of Biochemistry in collaboration with Department of Ophthalmology in a tertiary care hospital from March 2018 to April 2019. This present study population consisted of 90 Age-related cataracts (group I) as cases and 90 normal healthy individuals (group II) as controls of both the genders in the age group between 40 to 75 years. The cases were divided into nuclear cataract (NC), cortical cataract (CC), posterior sub-capsular cataract (PSC) and mixed cataract (MC) according to WHO cataract grading system.

The study protocol was approved by the Institutional Human Ethics Committee and informed consent form was obtained from all participants. The study subjects were selected based on inclusion and exclusion criteria from ophthalmology outpatient department. All subjects underwent complete eye examination in the ophthalmology OPD and the cataract was confirmed by using slit-lamp examination. The grading of the cataract is diagnosed using lens opacities classification system III (LOC system III) by ophthalmologist.

Inclusion criteria: Age-related cataracts who had no history of diabetes having nuclear, cortical, posterior subcapsular type of cataract were included in this study. Normal healthy subjects without cataract and having no history of diabetes were recruited from employees of our institute and diagnosed by clinical and biochemical examination by clinician in the Ophthalmology OPD were included in this study.

Exclusion criteria: steroid intake, renal dysfunction, hepatic disease, hypo or hyperthyroidism, diabetes, hypertension, traumatic or toxic cataract, mixed type of cataract, metabolic cataract and other systemic diseases and Drugs known to affect magnesium status such as Aminoglycosides Amphotericin B Cetuximab, Cyclosporine, Digoxin, Diuretics (loop, thiazide, osmotic), multiminerals supplement, alcohol and smoking were excluded from this study.

Sample collection and processing:

3 ml of venous fasting blood sample was drawn from the subjects and collected in clot activator vacutainers. The serum was separated by centrifuging at 3500 rpm for 15-20 minutes. The estimation of serum magnesium by xylidyl blue method and serum calcium by Arsenazo III method using Beckman Coulter Olympus AU400 auto-analyzer. The calcium-magnesium ratio was calculated by diving serum calcium concentration with serum magnesium concentration.

Statistical analysis:

The present study results were expressed as mean ± standard deviation (SD). Data was analysed using JASP 8.4. Data variations between the two groups by using unpaired t test. Data variations between the sub-groups were analyzed using one-way ANOVA followed by a Tukey's HSD post hoc analysis. Pearson's correlation coefficient (r value) was used to assess the association between the variables. Multivariate logistic regression analysis was performed to assess independent relationship between calcium: magnesium ratio and ARC. A p value of less than 0.05 is regarded as statistically significant.

3. RESULTS

Among the 90 ARC patients, 54 were belonged to nuclear cataract, 16 belonged to cortical cataract, 10 belonged to posterior subcapsular cataract and remaining 10 belonged to mixed cataract. There were 48 males and 42 females in the case study group and 39 males and 51 females in control group. The mean age in age-related cataract study group was 59.9 years old and in the non-cataract mean age group was 57.8 years and the difference was statistically insignificant (p value 0.07).

Table 1 shows that the mean serum magnesium concentration (1.4 ± 0.1, $p<0.001$) was significantly decreased whereas mean serum calcium (9.5 ± 0.5, $p<0.001$) and calcium to magnesium ratio (6.8 ± 1.2, $p<0.001$) levels were significantly increased in ARC subjects when compared to normal healthy individuals without cataract as controls (1.9 ± 0.3, 9.10 ± 0.6 and 4.8 ± 0.8).

Table 1: Comparison of serum magnesium, calcium and their ratio levels among groups

Parameters	Group I (cases) N=90	Group II (controls) N=90	p value
Serum magnesium (mg/dl)	1.4 ± 0.1	1.9 ± 0.3	<.001*
Serum calcium (mg/dl)	9.5 ± 0.5	9.10 ± 0.6	<.001*
Serum calcium to magnesium ratio	6.8 ± 1.2	4.8 ± 0.8	<.001*

*p<0.05 significant;

Table 2 shows that the comparison of serum magnesium, calcium and their ratio between sub-groups and controls using one-way ANOVA followed by Tukey's HSD post hoc analysis test.

Table 2: Comparison of serum magnesium, calcium and their ratio levels among sub-groups by using one-way ANOVA

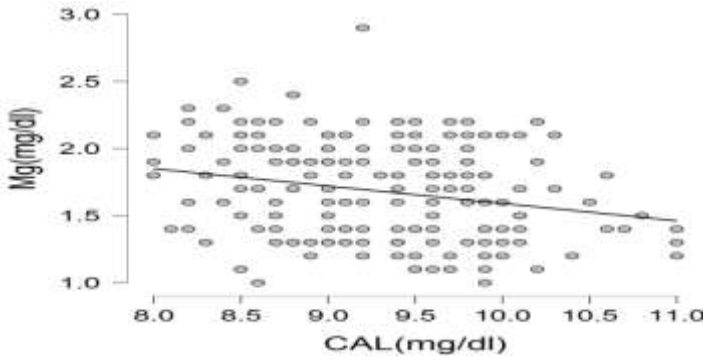
Sub-group	Parameter		
	Magnesium	Calcium	Cal:mg ratio
Group I (Nuclear cataract) n=54	1.36 ± 0.21ab†cd†	9.46 ± 0.60abcd‡	7.09 ± 1.10ab†cd†
Group II (Corticalcataract) n=16	1.36 ± 0.15e†fg†	9.70 ± 0.68 efg‡	7.24 ± 1.03e†fg†
Group III (Posterior subcapular cataract) n= 10	1.84 ± 0.31h¥i	9.20 ± 0.43hi	5.12 ± 0.84h¥i
Group IV (Mixed cataract) n=10	1.50 ± 0.25j†	9.45 ± 0.71j	6.44 ± 1.05j†
Group V (Normal healthy individuals without cataract as control) n=90	1.94 ± 0.26	9.10 ± 0.62	4.79 ± 0.78

a= group I VS group II; b=group I VS group III; c=group I VS group IV; d=group I VS group V; e= group II VS group III; f=group II VS group IV; g=group II VS group V; h=group III VS group IV; i=group III VS group V; j=group IV VS group V;
†post-hoc turkey's HSD test, $p<0.001$;
‡post-hoc turkey's HSD test, $p<0.01$
¥ post-hoc turkey's HSD test, $p<0.05$

The mean serum magnesium levels of sub-groups I, II, III, IV and V were 1.36 ± 0.21, 1.36 ± 0.15, 1.84 ± 0.31, 1.50 ± 0.25 and 1.94 ± 0.26 respectively. The mean serum calcium of sub-group subjects in groups I, II, III, IV and V were 9.46 ± 0.60, 9.70 ± 0.68, 9.20 ± 0.43, 9.45 ± 0.71 and 9.10 ± 0.62, respectively and the mean serum calcium to magnesium ratio were 7.09 ± 1.10, 7.24 ± 1.03, 5.12 ± 0.84, 6.44 ± 1.05 and 4.79 ± 0.78, respectively. The serum magnesium level was significantly decreased whereas serum calcium and their ratio levels were significantly higher in sub-group II as compared with other groups ($p < 0.001$). When the groups were compared in pairs for serum magnesium and serum calcium to magnesium ratio using Tukey's HSD post hoc analysis test, a significant difference were observed between group I VS group III and V($p<0.001$); group II VS III and V ($p<0.001$); group III VS IV ($p<0.05$); group IV VS V ($p<0.001$), whereas serum calcium using Tukey's HSD post hoc analysis test, a significant difference were observed between group I VS group V ($p<0.01$); group II VS group V ($p<0.01$) respectively.

Pearson's correlation coefficient analysis showed a significant negative correlation of serum magnesium with calcium($r = -0.233$, $p=0.002$) was observed as shown in figure1.

Figure 1: Pearson's correlation coefficient between serum calcium (mg/dl) and serum magnesium (mg/dl)



The odd's ratio was calculated to find out the magnitude of association between hypomagnesaemia and risk of Cataract formation. Subjects with hypomagnesaemia has 19.5 times ($p<0.0001$) higher risk of developing cataract when compared with normomagnesaemia subjects as shown in table 3.

Table 3: Odd's ratio for serum magnesium between ARC and control groups:

Parameter	ARC (N=90)	Control (N=90)	Odds ratio	95% confidence interval		p Value
				Lower bound	Upper bound	
Hypomagnesaemia (<1.8 mg/dl)	77	21	19.46	9.06	1.79	<0.0001*
Normomagnesaemia (1.8-2.6 mg/dl)	13	69				

* $p<0.05$ significant

Tables 4 represent the Multivariate logistic regression analysis also revealed that the serum calcium to magnesium ratio (OR= 5.177; 95% CI= 0.483-2.805, P=0.006), was significantly associated with Age-related cataract.

Table 4: Multivariate logistic regression model for odds ratio for Age-related cataract

Risk factors	Odds Ratio	95% Confidence Interval		p value
		Lower bound	Upper bound	
Calcium-magnesium ratio	5.177	0.483	2.805	0.006*
Magnesium	0.503	-4.647	3.272	0.733

* $p<0.05$ significant

4. DISCUSSION

Magnesium ion plays an important role in maintaining lens homeostasis. Hence, in deficiency of magnesium, causes ATPase dysfunctions which lead to the denaturation of lens crystalline protein, the soluble lens protein required for maintaining the transparency of the eye lens. In addition, Magnesium deficiency enhances lenticular oxidative stress by increased production of free radicals and depletion of antioxidant defenses may leads to cataract formation [6].

On contrary, calcium also has been known to play an important role in cataract formation. It is necessary for various lens-fiber cell processes, including differentiation [7]. Calcium homeostasis also play an important role in critical to the clarity of the lens tissue,[8] and abnormal calcium concentration correlates with opacity in human cataractous lenses [5]. Alterations in homeostasis of calcium in lens, which result in increased cytosolic calcium levels, might be an important factor in cataract formation, especially cortical cataract and posterior subcapsular cataract [2]. However, To the best of our knowledge, none of them reported the calcium to magnesium ratio in the pathogenesis of Age-related cataracts, hence the present study investigate the levels of calcium, magnesium and their ratio in serum of Age-related cataract and compared to normal healthy individuals without cataract.

In our study, we found that mean serum calcium and calcium to magnesium ratio levels were significantly elevated whereas serum magnesium level was significantly decreased in Age-related cataract subjects compared normal healthy individuals without cataract. Our results are in accordance with the previous literature reported by Rehab OM Altouhami et al, 2018; Aima Iram Batool et al, 2017; and Chandrasekar R et al, 2014 have reported reduced levels of serum magnesium and increased serum calcium concentrations in ARC cataract patients as compared to healthy controls [9–11]. In addition, there was a significant negative correlation of serum magnesium with calcium. By performing multivariate logistic regression analysis, our study shows that high concentration of calcium to magnesium ratio play potential risk factors of cataractogenesis in Age-related cataract subjects. Our findings revealed that alteration in serum calcium; magnesium and their ratio were indicating an important role in the pathogenesis of Age-related cataract.

5. CONCLUSION:

The present findings indicate that low serum magnesium concentration and high serum calcium to magnesium ratio were significantly associated with a high risk of cataract formation in patients with age-related cataract. Hence serum magnesium and calcium to magnesium ratio may be used as surrogative marker for age-related cataract.

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CONFLICT OF INTEREST: The authors declare that there is no conflict of interests regarding the publication of this manuscript

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